Model Comparison

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1 Case 1: Continuous Outcome and Single Continuous Mediator

1.1 Case 1-1: Continuous Outcome and Single Continuous Mediator Without Interaction

1.1.1 Data simulation

1.1.1.1 Simulation Procedures

1. Simulate the exposure variable A from $Bernoulli(P(A=1))$.
2. Simulate the covariate C from $N(\mu_C, \sigma_C^2)$.
3. Simulate the mediator M from $N((\beta_0 + \beta_1 * A + \beta_2 * C), \sigma_M^2)$.
4. Simulate the outcome Y from $N(\theta_0 + \theta_1 A + \theta_2 M + \theta_4 C, \sigma_Y^2)$.

1.1.1.2 True Parameters

Table 1: True Model Parameters for Data Simulation

Sample Size	θ_0	θ_1	θ_2	θ_4	β_0	β_1	β_2	P(A=1)	μ_C	σ_C	σ_M	σ_Y
10000	-5	0.8	1.8	0.1	-0.25	0.5	0.2	0.4	1	1	0.1	0.2

1.1.1.3 True Models

True model for the mediator:

$$E[M|a,c] = \beta_0 + \beta_1 a + \beta_2 c$$

True model for the outcome:

$$E[Y|a,m^*,c] = \theta_0 + \theta_1 a + \theta_2 m^* + \theta_4 c$$

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

1.1.2.1 Closed-form Parameter Function Estimation and Delta Method Inference

```
causal_mediation(data = df_noint,  outcome = "contY_contM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C",
                 yreg = "linear", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "delta", model = "rb")
```

```
## $effect_estimate
##         cde        pnde        tnde        pnie        tnie          te
##   0.7961788   0.7961788   0.7961788   0.8973026   0.8973026   1.6934814
##          pm      intref      intmed         pie    cde_prop intref_prop
##   0.3604117   0.0000000   0.0000000   0.8973026   0.4701432   0.0000000
## intmed_prop    pie_prop  overall_pm overall_int  overall_pe
##   0.0000000   0.5298568   0.5298568   0.0000000   0.5298568
```

```
##
## $effect_se
##  [1] 0.010783525 0.010783525 0.010783525 0.010633841 0.010633841
##  [6] 0.005535765 0.005656045 0.000000000 0.000000000 0.010633841
## [11] 0.006112265 0.000000000 0.000000000 0.006112265 0.006112265
## [16] 0.000000000 0.006112265
```

1.1.2.2 Direct Imputation Estimation and Bootstrap Inference

```r
causal_mediation(data = df_noint,  outcome = "contY_contM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C",
                 yreg = "linear", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "rb")
```

```
## $effect_estimate
##         cde         pnde         tnde         pnie         tnie           te
##   0.7961788    0.7961788    0.7961788    0.8973026    0.8973026    1.6934814
##          pm       intref       intmed          pie     cde_prop intref_prop
##   0.3604117    0.0000000    0.0000000    0.8973026    0.4701432    0.0000000
## intmed_prop     pie_prop   overall_pm  overall_int   overall_pe
##   0.0000000    0.5298568    0.5298568    0.0000000    0.5298568
##
## $effect_se
##  [1] 1.149598e-02 1.149598e-02 1.149598e-02 1.062575e-02 1.062575e-02
##  [6] 5.607225e-03 5.864467e-03 8.904072e-17 3.221503e-16 1.062575e-02
## [11] 6.343822e-03 5.255547e-17 1.902808e-16 6.343822e-03 6.343822e-03
## [16] 1.828656e-16 6.343822e-03
```

1.1.3 Causal Effects and Standard Errors Estimated By the Weighting-based Approach

```r
causal_mediation(data = df_noint,  outcome = "contY_contM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C",
                 yreg = "linear", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "wb")
```

```
## $effect_estimate
##           cde          pnde          tnde          pnie          tnie
##  7.961797e-01  7.960864e-01  7.961399e-01  8.972652e-01  8.973187e-01
##            te            pm        intref        intmed           pie
##  1.693405e+00  3.604426e-01 -9.334649e-05  5.352502e-05  8.972652e-01
##      cde_prop   intref_prop   intmed_prop      pie_prop    overall_pm
##  4.701650e-01 -5.512354e-05  3.160792e-05  5.298585e-01  5.298902e-01
##   overall_int    overall_pe
## -2.351562e-05  5.298350e-01
##
## $effect_se
##  [1] 1.102477e-02 1.100376e-02 1.100882e-02 1.017299e-02 1.016849e-02
##  [6] 5.802127e-03 5.592096e-03 1.360928e-04 6.772418e-05 1.017299e-02
## [11] 6.047677e-03 8.035024e-05 4.003266e-05 6.039443e-03 6.036515e-03
```

```
## [16] 4.801566e-05 6.047677e-03
```

1.1.4 Causal Effects and Standard Errors Estimated By the Marginal Structural Model

```r
causal_mediation(data = df_noint,  outcome = "contY_contM_noint", exposure = "A",
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C",
                 yreg = "linear", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "msm")
```

```
## $effect_estimate
##         cde        pnde        tnde        pnie        tnie          te
##  0.83510734  0.91921167  0.91921167  0.82087102  0.82087102  1.74008269
##          pm      intref      intmed         pie    cde_prop intref_prop
##  0.30868001  0.08410433  0.00000000  0.82087102  0.47992394  0.04833353
## intmed_prop    pie_prop  overall_pm overall_int  overall_pe
##  0.00000000  0.47174253  0.47174253  0.04833353  0.52007606
##
## $effect_se
##  [1] 6.629523e-02 5.141479e-02 5.141479e-02 3.657940e-02 3.657940e-02
##  [6] 1.991825e-02 2.135303e-02 4.702833e-02 3.033843e-16 3.657940e-02
## [11] 3.537101e-02 2.694193e-02 1.746198e-16 2.481181e-02 2.481181e-02
## [16] 2.694193e-02 3.537101e-02
```

1.1.5 Causal Effects and Standard Errors Estimated By the Inverse Odds-ratio Weighting Approach

```r
causal_mediation(data = df_noint,  outcome = "contY_contM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C",
                 yreg = "linear", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "bootstrap", model = "iorw")
```

```
## $effect_estimate
##       tot       dir       ind
## 1.6934814 1.1778978 0.5155836
##
## $effect_se
## [1] 0.006139942 0.138779474 0.138100915
```

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

```r
causal_mediation(data = df_noint,  outcome = "contY_contM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C",
                 yreg = "linear", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "g-formula")
```

```
## $effect_estimate
##          cde        pnde        tnde        pnie        tnie          te 
##    0.7961788   0.7961788   0.7961788   0.8973026   0.8973026   1.6934814 
##           pm      intref      intmed         pie    cde_prop intref_prop 
##    0.3604117   0.0000000   0.0000000   0.8973026   0.4701432   0.0000000 
## intmed_prop    pie_prop  overall_pm overall_int  overall_pe 
##    0.0000000   0.5298568   0.5298568   0.0000000   0.5298568 
## 
## $effect_se
##  [1] 1.012908e-02 1.012908e-02 1.012908e-02 9.602282e-03 9.602282e-03
##  [6] 5.407039e-03 5.194422e-03 6.280370e-17 3.136711e-16 9.602282e-03
## [11] 5.614750e-03 3.712892e-17 1.852500e-16 5.614750e-03 5.614750e-03
## [16] 1.816816e-16 5.614750e-03
```

1.1.7 Causal Effects and Standard Errors Estimated By the Natural Effect Model

```r
causal_mediation(data = df_noint,  outcome = "contY_contM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C",
                 yreg = "linear", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1, model = "ne")
```

```
##                          Estimate  Std. Error
## natural direct effect   0.7961788 0.010947557
## natural indirect effect 0.8973026 0.010766483
## total effect            1.6934814 0.005534381
```

1.2 Case 1-2: Continuous Outcome and Single Continuous Mediator With Exposure-mediator Interaction

1.2.1 Data simulation

1.2.1.1 Simulation Procedures

1. Simulate the exposure variable A from $Bernoulli(P(A=1))$.
2. Simulate the covariate C from $N(\mu_C, \sigma_C^2)$.
3. Simulate the mediator M from $N((\beta_0 + \beta_1 * A + \beta_2 * C), \sigma_M^2)$.
4. Simulate the outcome Y from $N(\theta_0 + \theta_1 A + \theta_2 M + \theta_3 AM + \theta_4 C, \sigma_Y^2)$.

1.2.1.2 True Parameters

Table 2: True Model Parameters for Data Simulation

Sample Size	θ_0	θ_1	θ_2	θ_3	θ_4	β_0	β_1	β_2	P(A=1)	μ_C	σ_C	σ_M	σ_Y
10000	-5	0.8	1.8	0.2	0.1	-0.25	0.5	0.2	0.4	1	1	0.1	0.2

1.2.1.3 True Models

True model for the mediator:

$$E[M|a,c] = \beta_0 + \beta_1 a + \beta_2 c$$

True model for the outcome:

$$E[Y|a, m^*, c] = \theta_0 + \theta_1 a + \theta_2 m^* + \theta_3 a m^* + \theta_4 c$$

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

1.2.2.1 Closed-form Parameter Function Estimation and Delta Method Inference

```r
causal_mediation(data = df_int,  outcome = "contY_contM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C", EMint = TRUE,
                 yreg = "linear", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "delta", model = "rb")
```

```
## $effect_estimate
##          cde         pnde         tnde         pnie         tnie
##  0.796419787  0.785133639  0.894126874  0.894855413  1.003848648
##           te           pm      intref       intmed          pie
##  1.788982287  0.389978026 -0.011286148  0.108993235  0.894855413
##     cde_prop  intref_prop  intmed_prop     pie_prop   overall_pm
##  0.445180365 -0.006308698  0.060924715  0.500203618  0.561128333
##  overall_int   overall_pe
##  0.054616017  0.554819635
##
## $effect_se
##  [1] 0.011479199 0.011871633 0.011272522 0.011148156 0.011894633
##  [6] 0.005671775 0.006233316 0.000981710 0.009084909 0.011148156
## [11] 0.006211659 0.000546770 0.005075677 0.006062618 0.006452578
## [16] 0.004550481 0.006211659
```

1.2.2.2 Direct Imputation Estimation and Bootstrap Inference

```r
causal_mediation(data = df_int,  outcome = "contY_contM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C", EMint = TRUE,
                 yreg = "linear", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "rb")
```

```
## $effect_estimate
##          cde         pnde         tnde         pnie         tnie
##  0.796419787  0.785133639  0.894126874  0.894855413  1.003848648
##           te           pm      intref       intmed          pie
##  1.788982287  0.389978026 -0.011286148  0.108993235  0.894855413
##     cde_prop  intref_prop  intmed_prop     pie_prop   overall_pm
##  0.445180365 -0.006308698  0.060924715  0.500203618  0.561128333
##  overall_int   overall_pe
##  0.054616017  0.554819635
##
## $effect_se
##  [1] 0.010864026 0.011201588 0.010448003 0.011486679 0.012010581
##  [6] 0.006356973 0.006022102 0.001018087 0.008170581 0.011486679
## [11] 0.006029364 0.000568466 0.004583396 0.005879429 0.006224515
## [16] 0.004119371 0.006029364
```

1.2.3 Causal Effects and Standard Errors Estimated By the Weighting-based Approach

```
causal_mediation(data = df_int,  outcome = "contY_contM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C", EMint = TRUE,
                 yreg = "linear", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "wb")
```

```
## $effect_estimate
##          cde         pnde         tnde         pnie         tnie
##  0.796420696  0.785881764  0.894893173  0.894888259  1.003899669
##           te           pm      intref       intmed          pie
##  1.789781433  0.389763565 -0.010538932  0.109011409  0.894888259
##     cde_prop  intref_prop  intmed_prop     pie_prop   overall_pm
##  0.444982098 -0.005888391  0.060907666  0.499998627  0.560906293
##  overall_int   overall_pe
##  0.055019275  0.555017902
##
## $effect_se
##  [1] 0.0119079449 0.0125395579 0.0106003707 0.0110529664 0.0127430475
##  [6] 0.0057053863 0.0066478397 0.0013484262 0.0089801510 0.0110529664
## [11] 0.0065424767 0.0007558812 0.0050261934 0.0058360475 0.0068787401
## [16] 0.0045406134 0.0065424767
```

1.2.4 Causal Effects and Standard Errors Estimated By the Marginal Structural Model

```
causal_mediation(data = df_int,  outcome = "contY_contM_int", exposure = "A",
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C", EMint = TRUE,
                 yreg = "linear", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "msm")
```

```
## $effect_estimate
##         cde        pnde        tnde        pnie        tnie          te
## 0.888058066 0.898067972 0.936561492 0.891144560 0.929638080 1.827706052
##          pm      intref      intmed         pie    cde_prop intref_prop
## 0.341054714 0.010009905 0.038493520 0.891144560 0.485886702 0.005476759
## intmed_prop    pie_prop  overall_pm overall_int  overall_pe
## 0.021061111 0.487575428 0.508636539 0.026537870 0.514113298
##
## $effect_se
##  [1] 0.10449101 0.07419466 0.03618497 0.03276860 0.06385352 0.02027986
##  [7] 0.03520982 0.03411597 0.06034632 0.03276860 0.05434627 0.01885853
## [13] 0.03338491 0.01809109 0.03784373 0.04808199 0.05434627
```

1.2.5 Causal Effects and Standard Errors Estimated By the Inverse Odds-ratio Weighting Approach

```r
causal_mediation(data = df_int,  outcome = "contY_contM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C", EMint = TRUE,
                 yreg = "linear", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "bootstrap", model = "iorw")
```

```
## $effect_estimate
##       tot       dir       ind
## 1.7891357 1.2526793 0.5364564
##
## $effect_se
## [1] 0.006115981 0.063486952 0.063473454
```

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

```r
causal_mediation(data = df_int,  outcome = "contY_contM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C", EMint = TRUE,
                 yreg = "linear", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "g-formula")
```

```
## $effect_estimate
##          cde         pnde         tnde         pnie         tnie
##  0.796419787  0.785133639  0.894126874  0.894855413  1.003848648
##           te           pm       intref       intmed          pie
##  1.788982287  0.389978026 -0.011286148  0.108993235  0.894855413
##     cde_prop  intref_prop  intmed_prop     pie_prop   overall_pm
##  0.445180365 -0.006308698  0.060924715  0.500203618  0.561128333
##  overall_int   overall_pe
##  0.054616017  0.554819635
##
## $effect_se
##  [1] 0.0120410110 0.0125395910 0.0113860453 0.0112593141 0.0123426383
##  [6] 0.0057612942 0.0065483377 0.0011693238 0.0099059129 0.0112593141
## [11] 0.0064889751 0.0006545836 0.0055481192 0.0061202264 0.0067793064
## [16] 0.0049668356 0.0064889751
```

1.2.7 Causal Effects and Standard Errors Estimated By the Natural Effect Model

```r
causal_mediation(data = df_int,  outcome = "contY_contM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C", EMint = TRUE,
                 yreg = "linear", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1, model = "ne")
```

```
##                        Estimate  Std. Error
## pure direct effect    0.7848034 0.012124815
## total direct effect   0.8946224 0.011321762
## pure indirect effect  0.8945270 0.011190083
## total indirect effect 1.0043460 0.012150380
```

```
## total effect          1.7891494 0.005717872
```

2 Case 2: Continuous Outcome and Single Binary Mediator

2.1 Case 2-1: Continuous Outcome and Single Binary Mediator Without Interaction

2.1.1 Data simulation

2.1.1.1 Simulation Procedures

1. Simulate the exposure variable A from $Bernoulli(P(A = 1))$.
2. Simulate the covariate C from $N(\mu_C, \sigma_C^2)$.
3. Simulate the mediator M from $Bernoulli(expit(\beta_0 + \beta_1 * A + \beta_2 * C))$.
4. Simulate the outcome Y from $N(\theta_0 + \theta_1 A + \theta_2 M + \theta_4 C, \sigma_Y^2)$.

2.1.1.2 True Parameters

Table 3: True Model Parameters for Data Simulation

Sample Size	θ_0	θ_1	θ_2	θ_4	β_0	β_1	β_2	P(A=1)	μ_C	σ_C	σ_Y
10000	-5	0.8	1.8	0.1	-0.25	0.5	0.2	0.4	1	1	0.2

2.1.1.3 True Models

True model for the mediator:

$$logitE[M|a, c] = \beta_0 + \beta_1 a + \beta_2 c$$

True model for the outcome:

$$E[Y|a, m^*, c] = \theta_0 + \theta_1 a + \theta_2 m^* + \theta_4 c$$

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
causal_mediation(data = df_noint,  outcome = "contY_binM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C",
                 yreg = "linear", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "delta", model = "rb")
```

```
## $effect_estimate
##         cde        pnde        tnde        pnie        tnie          te
##   0.8005256   0.8005256   0.8005256   0.2170743   0.2170743   1.0175999
##          pm      intref      intmed         pie    cde_prop intref_prop
##   0.1193946   0.0000000   0.0000000   0.2170743   0.7866801   0.0000000
## intmed_prop    pie_prop  overall_pm overall_int  overall_pe
##   0.0000000   0.2133199   0.2133199   0.0000000   0.2133199
##
## $effect_se
##  [1] 0.004126084 0.004126084 0.004126084 0.018238026 0.018238026
```

```
##  [6] 0.018686175 0.008851872 0.000000000 0.000000000 0.018238026
## [11] 0.014128588 0.000000000 0.000000000 0.014128588 0.014128588
## [16] 0.000000000 0.014128588
```

2.1.2.2 Direct Imputation Estimation and Bootstrap Inference

```
causal_mediation(data = df_noint,  outcome = "contY_binM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C",
                 yreg = "linear", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "rb")
```

```
## $effect_estimate
##           cde          pnde          tnde          pnie          tnie
##  8.005256e-01  8.005256e-01  8.005256e-01  2.143728e-01  2.143728e-01
##            te            pm        intref        intmed           pie
##  1.014898e+00  1.180842e-01  4.440892e-16 -4.440892e-16  2.143728e-01
##      cde_prop   intref_prop   intmed_prop      pie_prop    overall_pm
##  7.887741e-01  4.375701e-16 -4.375701e-16  2.112259e-01  2.112259e-01
##   overall_int    overall_pe
##  0.000000e+00  2.112259e-01
##
## $effect_se
##  [1] 3.951978e-03 3.951978e-03 3.951978e-03 1.872448e-02 1.872448e-02
##  [6] 1.923107e-02 9.100539e-03 2.959097e-16 2.959097e-16 1.872448e-02
## [11] 1.455510e-02 2.910332e-16 2.910332e-16 1.455510e-02 1.455510e-02
## [16] 0.000000e+00 1.455510e-02
```

2.1.3 Causal Effects and Standard Errors Estimated By the Weighting-based Approach

```
causal_mediation(data = df_noint,  outcome = "contY_binM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C",
                 yreg = "linear", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "wb")
```

```
## $effect_estimate
##           cde          pnde          tnde          pnie          tnie
##  8.005265e-01  8.005396e-01  8.005312e-01  2.140183e-01  2.140099e-01
##            te            pm        intref        intmed           pie
##  1.014549e+00  1.179060e-01  1.308296e-05 -8.374244e-06  2.140183e-01
##      cde_prop   intref_prop   intmed_prop      pie_prop    overall_pm
##  7.890463e-01  1.289534e-05 -8.254150e-06  2.109491e-01  2.109408e-01
##   overall_int    overall_pe
##  4.641188e-06  2.109537e-01
##
## $effect_se
##  [1] 3.973629e-03 3.970952e-03 3.975297e-03 1.822485e-02 1.822684e-02
##  [6] 1.847219e-02 8.910944e-03 9.836171e-05 3.726131e-05 1.822485e-02
## [11] 1.427904e-02 9.667693e-05 3.664210e-05 1.427864e-02 1.428039e-02
## [16] 7.223980e-05 1.427904e-02
```

2.1.4 Causal Effects and Standard Errors Estimated By the Marginal Structural Model

```
causal_mediation(data = df_noint,  outcome = "contY_binM_noint", exposure = "A",
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C",
                 yreg = "linear", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "msm")
```

```
## $effect_estimate
##           cde          pnde          tnde          pnie          tnie
##  8.031238e-01  8.014650e-01  8.014650e-01  2.145661e-01  2.145661e-01
##            te            pm        intref        intmed           pie
##  1.016031e+00  1.180559e-01 -1.658845e-03 -4.440892e-16  2.145661e-01
##      cde_prop   intref_prop   intmed_prop      pie_prop    overall_pm
##  7.904520e-01 -1.632671e-03 -4.370823e-16  2.111807e-01  2.111807e-01
##   overall_int    overall_pe
## -1.632671e-03  2.095480e-01
##
## $effect_se
##  [1] 4.579522e-03 4.104312e-03 4.104312e-03 1.744114e-02 1.744114e-02
##  [6] 1.763895e-02 8.530800e-03 1.933117e-03 3.066335e-16 1.744114e-02
## [11] 1.373206e-02 1.903138e-03 3.013652e-16 1.366308e-02 1.366308e-02
## [16] 1.903138e-03 1.373206e-02
```

2.1.5 Causal Effects and Standard Errors Estimated By the Inverse Odds-ratio Weighting Approach

```
causal_mediation(data = df_noint,  outcome = "contY_binM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C",
                 yreg = "linear", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "bootstrap", model = "iorw")
```

```
## $effect_estimate
##       tot       dir       ind
## 1.0148634 0.8006350 0.2142283
##
## $effect_se
## [1] 0.01948072 0.00420279 0.01873007
```

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

```
causal_mediation(data = df_noint,  outcome = "contY_binM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C",
                 yreg = "linear", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "g-formula")
```

```
## $effect_estimate
```

```
##           cde          pnde          tnde          pnie          tnie
##  8.005256e-01  8.005256e-01  8.005256e-01  2.143728e-01  2.143728e-01
##            te            pm       intref       intmed           pie
##  1.014898e+00  1.180842e-01  4.440892e-16 -4.440892e-16  2.143728e-01
##      cde_prop   intref_prop   intmed_prop      pie_prop    overall_pm
##  7.887741e-01  4.375701e-16 -4.375701e-16  2.112259e-01  2.112259e-01
##   overall_int    overall_pe
##  0.000000e+00  2.112259e-01
##
## $effect_se
##  [1] 4.096380e-03 4.096380e-03 4.096380e-03 1.809296e-02 1.809296e-02
##  [6] 1.856797e-02 8.789993e-03 3.064395e-16 3.064395e-16 1.809296e-02
## [11] 1.404503e-02 3.014794e-16 3.014794e-16 1.404503e-02 1.404503e-02
## [16] 0.000000e+00 1.404503e-02
```

2.1.7 Causal Effects and Standard Errors Estimated By the Natural Effect Model

```r
causal_mediation(data = df_noint,  outcome = "contY_binM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C",
                 yreg = "linear", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1, model = "ne")
```

```
##                          Estimate  Std. Error
## natural direct effect   0.8005256 0.004130276
## natural indirect effect 0.2143378 0.018028517
## total effect            1.0148634 0.018470124
```

2.2 Case 2-2: Continuous Outcome and Single Binary Mediator With Exposure-mediator Interaction

2.2.1 Data simulation

2.2.1.1 Simulation Procedures

1. Simulate the exposure variable A from $Bernoulli(P(A = 1))$.
2. Simulate the covariate C from $N(\mu_C, \sigma_C^2)$.
3. Simulate the mediator M from $Bernoulli(expit(\beta_0 + \beta_1 * A + \beta_2 * C))$.
4. Simulate the outcome Y from $N(\theta_0 + \theta_1 A + \theta_2 M + \theta_3 AM + \theta_4 C, \sigma_Y^2)$.

2.2.1.2 True Parameters

Table 4: True Model Parameters for Data Simulation

Sample Size	θ_0	θ_1	θ_2	θ_3	θ_4	β_0	β_1	β_2	P(A=1)	μ_C	σ_C	σ_Y
10000	-5	0.8	1.8	0.2	0.1	-0.25	0.5	0.2	0.4	1	1	0.2

2.2.1.3 True Models

True model for the mediator:

$$logitE[M|a, c] = \beta_0 + \beta_1 a + \beta_2 c$$

True model for the outcome:

$$E[Y|a, m^*, c] = \theta_0 + \theta_1 a + \theta_2 m^* + \theta_3 a m^* + \theta_4 c$$

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

```
causal_mediation(data = df_int,  outcome = "contY_binM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C", EMint = TRUE,
                 yreg = "linear", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "delta", model = "rb")
```

```
## $effect_estimate
##         cde        pnde        tnde        pnie        tnie          te
##  0.80054974  0.89963786  0.92388755  0.21651004  0.24075973  1.14039759
##          pm      intref      intmed         pie    cde_prop intref_prop
##  0.11801742  0.09908813  0.02424969  0.21651004  0.70199178  0.08688911
## intmed_prop    pie_prop  overall_pm overall_int  overall_pe
##  0.02126424  0.18985488  0.21111911  0.10815334  0.29800822
##
## $effect_se
##  [1] 0.006183060 0.004323977 0.004383195 0.018194564 0.020235573
##  [6] 0.019824260 0.008862702 0.004253267 0.002264716 0.018194564
## [11] 0.012674460 0.004269739 0.001670185 0.012749355 0.014180743
## [16] 0.004570958 0.012674460
```

2.2.2.2 Direct Imputation Estimation and Bootstrap Inference

```
causal_mediation(data = df_int,  outcome = "contY_binM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C", EMint = TRUE,
                 yreg = "linear", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "rb")
```

```
## $effect_estimate
##         cde        pnde        tnde        pnie        tnie          te
##  0.80054974  0.89965955  0.92360746  0.21381562  0.23776353  1.13742308
##          pm      intref      intmed         pie    cde_prop intref_prop
##  0.11671766  0.09910982  0.02394790  0.21381562  0.70382758  0.08713540
## intmed_prop    pie_prop  overall_pm overall_int  overall_pe
##  0.02105453  0.18798249  0.20903702  0.10818993  0.29617242
##
## $effect_se
##  [1] 0.006207134 0.004043918 0.004324806 0.018716039 0.020776682
##  [6] 0.020765469 0.009071306 0.004346364 0.002285625 0.018716039
## [11] 0.012852496 0.004468104 0.001681892 0.013129253 0.014568990
## [16] 0.004707135 0.012852496
```

2.2.3 Causal Effects and Standard Errors Estimated By the Weighting-based Approach

```r
causal_mediation(data = df_int,  outcome = "contY_binM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C", EMint = TRUE,
                 yreg = "linear", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "wb")
```

```
## $effect_estimate
##          cde         pnde         tnde         pnie         tnie           te
##   0.80055067   0.89986069   0.92378270   0.21342212   0.23734413   1.13720482
##           pm      intref       intmed          pie     cde_prop intref_prop
##   0.11651276   0.09931003   0.02392201   0.21342212   0.70396348   0.08732818
## intmed_prop     pie_prop   overall_pm overall_int   overall_pe
##   0.02103580   0.18767254   0.20870834   0.10836398   0.29603652
##
## $effect_se
##  [1] 0.006383020 0.004158960 0.004253557 0.018078129 0.020048074
##  [6] 0.019834608 0.008786966 0.004374914 0.002209051 0.018078129
## [11] 0.012394910 0.004482715 0.001636542 0.012734815 0.014118028
## [16] 0.004727470 0.012394910
```

2.2.4 Causal Effects and Standard Errors Estimated By the Marginal Structural Model

```r
causal_mediation(data = df_int,  outcome = "contY_binM_int", exposure = "A",
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C", EMint = TRUE,
                 yreg = "linear", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "msm")
```

```
## $effect_estimate
##          cde         pnde         tnde         pnie         tnie           te
##   0.80499559   0.89998205   0.92397494   0.21397089   0.23796379   1.13794583
##           pm      intref       intmed          pie     cde_prop intref_prop
##   0.11676752   0.09498646   0.02399290   0.21397089   0.70741117   0.08347186
## intmed_prop     pie_prop   overall_pm overall_int   overall_pe
##   0.02108439   0.18803258   0.20911697   0.10455626   0.29258883
##
## $effect_se
##  [1] 0.006638549 0.004585371 0.004620530 0.016984252 0.018995300
##  [6] 0.018518704 0.008357751 0.004651238 0.002185710 0.016984252
## [11] 0.012467474 0.004442454 0.001619824 0.011974678 0.013409128
## [16] 0.004692535 0.012467474
```

2.2.5 Causal Effects and Standard Errors Estimated By the Inverse Odds-ratio Weighting Approach

```r
causal_mediation(data = df_int,  outcome = "contY_binM_int", exposure = 'A',
                 exposure.type = "binary",
```

```r
                 mediator = 'M_bin', covariates.pre = "C", EMint = TRUE,
                 yreg = "linear", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "bootstrap", model = "iorw")
```

```
## $effect_estimate
##       tot       dir       ind
## 1.1374352 0.9239973 0.2134379
##
## $effect_se
## [1] 0.019251232 0.004171046 0.017796892
```

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

```r
causal_mediation(data = df_int,  outcome = "contY_binM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C", EMint = TRUE,
                 yreg = "linear", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "g-formula")
```

```
## $effect_estimate
##         cde        pnde        tnde        pnie        tnie          te
##  0.80054974  0.89965955  0.92360746  0.21381562  0.23776353  1.13742308
##          pm      intref      intmed         pie    cde_prop intref_prop
##  0.11671766  0.09910982  0.02394790  0.21381562  0.70382758  0.08713540
## intmed_prop    pie_prop  overall_pm overall_int  overall_pe
##  0.02105453  0.18798249  0.20903702  0.10818993  0.29617242
##
## $effect_se
##  [1] 0.006774164 0.004614651 0.004701219 0.017807541 0.019750609
##  [6] 0.019645643 0.008663439 0.004592285 0.002191081 0.017807541
## [11] 0.012435892 0.004607834 0.001628468 0.012541703 0.013903624
## [16] 0.004959863 0.012435892
```

2.2.7 Causal Effects and Standard Errors Estimated By the Natural Effect Model

```r
causal_mediation(data = df_int,  outcome = "contY_binM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C", EMint = TRUE,
                 yreg = "linear", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1, model = "ne")
```

```
##                        Estimate  Std. Error
## pure direct effect    0.8997210 0.004330995
## total direct effect   0.9235096 0.004377377
## pure indirect effect  0.2138316 0.017986418
## total indirect effect 0.2376202 0.019997595
## total effect          1.1373412 0.019606885
```

3 Case 3: Continuous Outcome and Single Categorical Mediator

3.1 Case 3-1: Continuous Outcome and Single Categorical Mediator Without Interaction

3.1.1 Data simulation

3.1.1.1 Simulation Procedures

1. Simulate the exposure variable A from $Bernoulli(P(A = 1))$.
2. Simulate the covariate C from $N(\mu_C, \sigma_C^2)$.
3. Simulate the mediator M from $Multinom(\frac{1}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}, \frac{expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}, \frac{expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)})$.
4. Simulate the outcome Y from $N(\theta_0 + \theta_1 A + \theta_{21} I\{M == 1\} + \theta_{22} I\{M == 2\} + \theta_4 C, \sigma_Y^2)$.

3.1.1.2 True Parameters

Table 5: True Model Parameters for Data Simulation

Sample Size	θ_0	θ_1	θ_{21}	θ_{22}	θ_4	β_{01}	β_{11}
10000	-5	0.8	1.8	1.2	0.1	-0.25	0.5
β_{21}	β_{02}	β_{12}	β_{22}	P(A=1)	μ_C	σ_C	σ_Y
0.2	-0.3	0.4	0.3	0.4	1	1	0.2

3.1.1.3 True Models

True model for the mediator:

$$ln\frac{P(M == 1)}{P(M == 0)} = \beta_{01} + \beta_{11} a + \beta_{21} c$$

$$ln\frac{P(M == 2)}{P(M == 0)} = \beta_{02} + \beta_{12} a + \beta_{22} c$$

True model for the outcome:

$$E[Y|a, m^*, c] = \theta_0 + \theta_1 a + \theta_{21} I\{m^* == 1\} + \theta_{22} I\{m^* == 2\} + \theta_4 c$$

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

3.1.2.1 Closed-form Parameter Function Estimation and Delta Method Inference

```
causal_mediation(data = df_noint,  outcome = "contY_catM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C",
                 yreg = "linear", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "delta", model = "rb")
```

```
## $effect_estimate
##         cde      pnde      tnde      pnie      tnie          te
##   0.7976843 0.7976843 0.7976843 0.1792641 0.1792641   0.9769484
##          pm    intref    intmed       pie  cde_prop intref_prop
##   0.1010148 0.0000000 0.0000000 0.1792641 0.8165061   0.0000000
```

```
## intmed_prop    pie_prop  overall_pm overall_int  overall_pe
##   0.0000000   0.1834939   0.1834939   0.0000000   0.1834939
##
## $effect_se
##  [1] 0.004091448 0.004091448 0.004091448 0.014792487 0.014792487
##  [6] 0.015332073 0.007509835 0.000000000 0.000000000 0.014792487
## [11] 0.012390080 0.000000000 0.000000000 0.012390080 0.012390080
## [16] 0.000000000 0.012390080
```

3.1.2.2 Direct Imputation Estimation and Bootstrap Inference

```r
causal_mediation(data = df_noint,  outcome = "contY_catM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C",
                 yreg = "linear", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "rb")
```

```
## $effect_estimate
##         cde        pnde        tnde        pnie        tnie          te
##   0.7976843   0.7976843   0.7976843   0.1778174   0.1778174   0.9755017
##          pm      intref      intmed         pie    cde_prop intref_prop
##   0.1002813   0.0000000   0.0000000   0.1778174   0.8177170   0.0000000
## intmed_prop    pie_prop  overall_pm overall_int  overall_pe
##   0.0000000   0.1822830   0.1822830   0.0000000   0.1822830
##
## $effect_se
##  [1] 3.921988e-03 3.921988e-03 3.921988e-03 1.513582e-02 1.513582e-02
##  [6] 1.526988e-02 7.724408e-03 7.007539e-17 4.452036e-17 1.513582e-02
## [11] 1.274389e-02 7.334681e-17 4.636495e-17 1.274389e-02 1.274389e-02
## [16] 7.330907e-17 1.274389e-02
```

3.1.3 Causal Effects and Standard Errors Estimated By the Weighting-based Approach

```r
causal_mediation(data = df_noint,  outcome = "contY_catM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C",
                 yreg = "linear", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "wb")
```

```
## $effect_estimate
##           cde          pnde          tnde          pnie          tnie
##  7.976853e-01  7.976838e-01  7.976830e-01  1.771532e-01  1.771524e-01
##            te            pm        intref        intmed           pie
##  9.748361e-01  9.994380e-02 -1.502090e-06 -7.997872e-07  1.771532e-01
##      cde_prop   intref_prop   intmed_prop      pie_prop    overall_pm
##  8.182763e-01 -1.540864e-06 -8.204325e-07  1.817261e-01  1.817253e-01
##   overall_int    overall_pe
## -2.361296e-06  1.817237e-01
##
## $effect_se
##  [1] 4.189489e-03 4.186268e-03 4.186343e-03 1.388042e-02 1.388120e-02
```

```
## [6] 1.449507e-02 7.070671e-03 9.712850e-05 3.361530e-05 1.388042e-02
## [11] 1.171671e-02 9.913324e-05 3.443841e-05 1.171264e-02 1.171367e-02
## [16] 7.859071e-05 1.171671e-02
```

3.1.4 Causal Effects and Standard Errors Estimated By the Marginal Structural Model

```r
causal_mediation(data = df_noint,  outcome = "contY_catM_noint", exposure = "A",
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C",
                 yreg = "linear", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "msm")
```

```
## $effect_estimate
##          cde         pnde         tnde         pnie         tnie
##  0.799002018  0.797557066  0.797557066  0.178020441  0.178020441
##           te           pm       intref       intmed          pie
##  0.975577507  0.100398720 -0.001444953  0.000000000  0.178020441
##     cde_prop  intref_prop  intmed_prop     pie_prop   overall_pm
##  0.819004141 -0.001481125  0.000000000  0.182476984  0.182476984
##  overall_int   overall_pe
## -0.001481125  0.180995859
##
## $effect_se
##  [1] 4.281719e-03 3.920382e-03 3.920382e-03 1.406343e-02 1.406343e-02
##  [6] 1.456372e-02 7.175902e-03 2.228057e-03 6.280370e-17 1.406343e-02
## [11] 1.209169e-02 2.295369e-03 6.508352e-17 1.188382e-02 1.188382e-02
## [16] 2.295369e-03 1.209169e-02
```

3.1.5 Causal Effects and Standard Errors Estimated By the Inverse Odds-ratio Weighting Approach

```r
causal_mediation(data = df_noint,  outcome = "contY_catM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C",
                 yreg = "linear", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "bootstrap", model = "iorw")
```

```
## $effect_estimate
##       tot       dir       ind
## 0.9754239 0.7978610 0.1775629
##
## $effect_se
## [1] 0.015395927 0.004431199 0.014862123
```

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

```r
causal_mediation(data = df_noint,  outcome = "contY_catM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C",
```

```r
                 yreg = "linear", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "g-formula")
```

```
## $effect_estimate
##          cde         pnde         tnde         pnie         tnie           te 
##    0.7976843    0.7976843    0.7976843    0.1778174    0.1778174    0.9755017 
##           pm       intref       intmed          pie     cde_prop  intref_prop 
##    0.1002813    0.0000000    0.0000000    0.1778174    0.8177170    0.0000000 
## intmed_prop     pie_prop   overall_pm overall_int   overall_pe 
##    0.0000000    0.1822830    0.1822830    0.0000000    0.1822830 
## 
## $effect_se
##  [1] 4.251101e-03 4.251101e-03 4.251101e-03 1.349170e-02 1.349170e-02
##  [6] 1.411714e-02 6.873497e-03 4.429720e-17 7.007539e-17 1.349170e-02
## [11] 1.137620e-02 4.579182e-17 7.233345e-17 1.137620e-02 1.137620e-02
## [16] 5.618264e-17 1.137620e-02
```

3.1.7 Causal Effects and Standard Errors Estimated By the Natural Effect Model

```r
causal_mediation(data = df_noint,  outcome = "contY_catM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C",
                 yreg = "linear", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1, model = "ne")
```

```
##                           Estimate  Std. Error
## natural direct effect   0.7976843 0.004090788
## natural indirect effect 0.1777395 0.014699961
## total effect            0.9754239 0.015240055
```

3.2 Case 3-2: Continuous Outcome and Single Categorical Mediator With Exposure-mediator Interaction

3.2.1 Data simulation

3.2.1.1 Simulation Procedures

1. Simulate the exposure variable A from $Bernoulli(P(A=1))$.
2. Simulate the covariate C from $N(\mu_C, \sigma_C^2)$.
3. Simulate the mediator M from $Multinom(\frac{1}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}, \frac{expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}, \frac{expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)})$.
4. Simulate the outcome Y from $N(\theta_0 + \theta_1 A + \theta_{21} I\{M == 1\} + \theta_{22} I\{M == 2\} + \theta_{31} A * I\{M == 1\} + \theta_{32} A * I\{M == 2\} + \theta_4 C, \sigma_Y^2)$.

3.2.1.2 True Parameters

Table 6: True Model Parameters for Data Simulation

Sample Size	θ_0	θ_1	θ_{21}	θ_{22}	θ_{31}	θ_{32}	θ_4	β_{01}
10000	-5	0.8	1.8	1.2	0.2	0.40.1	-0.25	
β_{11}	β_{21}	β_{02}	β_{12}	β_{22}	P(A=1)	μ_C	σ_C	σ_Y
0.5	0.2	-0.3	0.4	0.3	0.4	1	1	0.2

3.2.1.3 True Models

True model for the mediator:

$$ln\frac{P(M==1)}{P(M==0)} = \beta_{01} + \beta_{11}a + \beta_{21}c$$

$$ln\frac{P(M==2)}{P(M==0)} = \beta_{02} + \beta_{12}a + \beta_{22}c$$

True model for the outcome:

$$E[Y|a,m^*,c] = \theta_0 + \theta_1 a + \theta_{21}I\{m^* == 1\} + \theta_{22}I\{m^* == 2\} + \theta_{31}a * I\{m^* == 1\} + \theta_{32}a * I\{m^* == 2\} + \theta_4 c$$

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

3.2.2.1 Closed-form Parameter Function Estimation and Delta Method Inference

```
causal_mediation(data = df_int,  outcome = "contY_catM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C", EMint = TRUE,
                 yreg = "linear", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "delta", model = "rb")
```

```
## $effect_estimate
##         cde        pnde        tnde        pnie        tnie          te
##  0.81281714  1.00203129  1.03108682  0.17969475  0.20875027  1.21078156
##          pm      intref      intmed         pie    cde_prop intref_prop
##  0.09433706  0.18921416  0.02905552  0.17969475  0.67131608  0.15627440
## intmed_prop    pie_prop  overall_pm overall_int  overall_pe
##  0.02399733  0.14841219  0.17240952  0.18027172  0.32868392
##
## $effect_se
##  [1] 0.007672036 0.004675061 0.004788722 0.014833316 0.016994995
##  [6] 0.016503572 0.007062459 0.006199352 0.003350492 0.014833316
## [11] 0.010423469 0.005807203 0.002573054 0.010327292 0.011794613
## [16] 0.006067453 0.010423469
```

3.2.2.2 Direct Imputation Estimation and Bootstrap Inference

```
causal_mediation(data = df_int,  outcome = "contY_catM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C", EMint = TRUE,
                 yreg = "linear", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "rb")
```

```
## $effect_estimate
##         cde        pnde        tnde        pnie        tnie          te
##  0.81281714  1.00189217  1.03058650  0.17824474  0.20693907  1.20883124
```

```
##           pm      intref      intmed         pie    cde_prop intref_prop
##   0.09360695  0.18907503  0.02869433  0.17824474  0.67239918  0.15641144
## intmed_prop    pie_prop  overall_pm overall_int  overall_pe
##   0.02373725  0.14745213  0.17118938  0.18014869  0.32760082
##
## $effect_se
##  [1] 0.007765425 0.004557932 0.004429363 0.014455554 0.016511380
##  [6] 0.015313229 0.006946761 0.006465971 0.003259824 0.014455554
## [11] 0.010624988 0.005905250 0.002525575 0.010230363 0.011641616
## [16] 0.006052237 0.010624988
```

3.2.3 Causal Effects and Standard Errors Estimated By the Weighting-based Approach

```r
causal_mediation(data = df_int,  outcome = "contY_catM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C", EMint = TRUE,
                 yreg = "linear", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "wb")
```

```
## $effect_estimate
##          cde        pnde        tnde        pnie        tnie          te
##   0.81281804  1.00231980  1.03093145  0.17759888  0.20621052  1.20853032
##           pm      intref      intmed         pie    cde_prop intref_prop
##   0.09327205  0.18950176  0.02861165  0.17759888  0.67256735  0.15680348
## intmed_prop    pie_prop  overall_pm overall_int  overall_pe
##   0.02367474  0.14695442  0.17062917  0.18047822  0.32743265
##
## $effect_se
##  [1] 0.006992162 0.004722307 0.004873427 0.016313481 0.018212880
##  [6] 0.018118706 0.007525162 0.005655696 0.002949431 0.016313481
## [11] 0.010201312 0.005698660 0.002224007 0.011356133 0.012571418
## [16] 0.005528178 0.010201312
```

3.2.4 Causal Effects and Standard Errors Estimated By the Marginal Structural Model

```r
causal_mediation(data = df_int,  outcome = "contY_catM_int", exposure = "A",
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C", EMint = TRUE,
                 yreg = "linear", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "msm")
```

```
## $effect_estimate
##          cde        pnde        tnde        pnie        tnie          te
##   0.81872387  1.00228550  1.03091732  0.17845820  0.20709002  1.20937552
##           pm      intref      intmed         pie    cde_prop intref_prop
##   0.09363551  0.18356163  0.02863182  0.17845820  0.67698069  0.15178216
## intmed_prop    pie_prop  overall_pm overall_int  overall_pe
##   0.02367488  0.14756227  0.17123715  0.17545704  0.32301931
##
## $effect_se
```

```
##  [1] 0.008967581 0.004766631 0.005316135 0.013626152 0.015791481
##  [6] 0.015855608 0.006542289 0.007981239 0.003427597 0.013626152
## [11] 0.010650144 0.007044170 0.002645229 0.009476827 0.010952189
## [16] 0.007528295 0.010650144
```

3.2.5 Causal Effects and Standard Errors Estimated By the Inverse Odds-ratio Weighting Approach

```
causal_mediation(data = df_int,  outcome = "contY_catM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C", EMint = TRUE,
                 yreg = "linear", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "bootstrap", model = "iorw")
```

```
## $effect_estimate
##      tot      dir      ind
## 1.208825 1.031022 0.177803
##
## $effect_se
## [1] 0.015858619 0.004864557 0.014022247
```

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

```
causal_mediation(data = df_int,  outcome = "contY_catM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C", EMint = TRUE,
                 yreg = "linear", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "g-formula")
```

```
## $effect_estimate
##         cde        pnde        tnde        pnie        tnie          te
##  0.81281714  1.00189217  1.03058650  0.17824474  0.20693907  1.20883124
##          pm     intref      intmed         pie    cde_prop intref_prop
##  0.09360695  0.18907503  0.02869433  0.17824474  0.67239918  0.15641144
## intmed_prop    pie_prop  overall_pm overall_int  overall_pe
##  0.02373725  0.14745213  0.17118938  0.18014869  0.32760082
##
## $effect_se
##  [1] 0.007575854 0.004993177 0.005096075 0.014408854 0.016799912
##  [6] 0.016076454 0.007050891 0.006326239 0.003419341 0.014408854
## [11] 0.010598488 0.005810312 0.002634925 0.010159925 0.011841103
## [16] 0.006225667 0.010598488
```

3.2.7 Causal Effects and Standard Errors Estimated By the Natural Effect Model

```
causal_mediation(data = df_int,  outcome = "contY_catM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C", EMint = TRUE,
```

```
                yreg = "linear", mreg = "multinomial", mval = list(0),
                a_star = 0, a = 1, model = "ne")
```

```
##                         Estimate  Std. Error
## pure direct effect    1.0019836 0.004680053
## total direct effect   1.0304177 0.004783086
## pure indirect effect  0.1782477 0.014751595
## total indirect effect 0.2066818 0.016852435
## total effect          1.2086654 0.016396198
```

4 Case 4: Continuous Outcome and Multiple Mediators

4.1 Case 4-1: Continuous Outcome and Multiple Mediators Without Interaction

4.1.1 Data simulation

4.1.1.1 Simulation Procedures

1. Simulate the exposure variable A from $Bernoulli(P(A = 1))$.
2. Simulate the covariate C from $N(\mu_C, \sigma_C^2)$.
3. Simulate the first mediator M1 from $Multinom(\frac{1}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)},$
$\frac{expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}, \frac{expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}),$
the second mediator M2 from $Bernoulli(expit(\beta_{03} + \beta_{13} * A + \beta_{23} * C))$.
4. Simulate the outcome Y from $N(\theta_0 + \theta_1 A + \theta_{21} I\{M1 == 1\} + \theta_{22} I\{M1 == 2\} + \theta_{23} M2 + \theta_4 C, \sigma_Y^2)$.

4.1.1.2 True Parameters

Table 7: True Model Parameters for Data Simulation

Sample Size	θ_0	θ_1	θ_{21}	θ_{22}	θ_{23}	θ_4	β_{01}	β_{11}	β_{21}
10000	-5	0.8	1.8	1.2	1.5	0.1	-0.25	0.5	0.2
β_{02}	β_{12}	β_{22}	β_{03}	β_{13}	β_{23}	P(A=1)	μ_C	σ_C	σ_Y
-0.3	0.4	0.3	-0.25	0.5	0.2	0.4	1	1	0.2

4.1.1.3 True Models

True model for the first mediator:

$$ln\frac{P(M1 == 1)}{P(M1 == 0)} = \beta_{01} + \beta_{11}a + \beta_{21}c$$

$$ln\frac{P(M1 == 2)}{P(M1 == 0)} = \beta_{02} + \beta_{12}a + \beta_{22}c$$

True model for the second mediator:

$$logitE[M2|a, c] = \beta_{03} + \beta_{13}a + \beta_{23}c$$

True model for the outcome:

$$E[Y|a, m^*, c] = \theta_0 + \theta_1 a + \theta_{21} I\{m1^* == 1\} + \theta_{22} I\{m1^* == 2\} + \theta_{23} m2^* + \theta_4 c$$

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

```
causal_mediation(data = df_multipleM_noint,  outcome = "contY_catMbinM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C",
                 yreg = "linear", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "rb")
```

```
## $effect_estimate
##         cde        pnde        tnde        pnie        tnie          te
##   0.8020494   0.8020494   0.8020494   0.3554609   0.3554609   1.1575102
##          pm      intref      intmed         pie    cde_prop intref_prop
##   0.1813983   0.0000000   0.0000000   0.3554609   0.6929091   0.0000000
## intmed_prop    pie_prop  overall_pm overall_int  overall_pe
##   0.0000000   0.3070909   0.3070909   0.0000000   0.3070909
##
## $effect_se
##  [1] 0.004074097 0.004074097 0.004074097 0.021480204 0.021480204
##  [6] 0.021485298 0.009096656 0.000000000 0.000000000 0.021480204
## [11] 0.013064037 0.000000000 0.000000000 0.013064037 0.013064037
## [16] 0.000000000 0.013064037
```

4.1.3 Causal Effects and Standard Errors Estimated By the Weighting-based Approach

```
causal_mediation(data = df_multipleM_noint,  outcome = "contY_catMbinM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C",
                 yreg = "linear", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "wb")
```

```
## $effect_estimate
##           cde          pnde          tnde          pnie          tnie
##  8.020503e-01  8.020137e-01  8.020353e-01  3.544549e-01  3.544765e-01
##            te            pm        intref        intmed           pie
##  1.156490e+00  1.809935e-01 -3.658239e-05  2.162165e-05  3.544549e-01
##      cde_prop   intref_prop   intmed_prop      pie_prop    overall_pm
##  6.935210e-01 -3.163225e-05  1.869592e-05  3.064919e-01  3.065106e-01
##   overall_int    overall_pe
## -1.293633e-05  3.064790e-01
##
## $effect_se
##  [1] 4.196379e-03 4.199624e-03 4.194554e-03 2.110120e-02 2.110402e-02
##  [6] 2.182024e-02 8.806899e-03 9.664528e-05 3.927785e-05 2.110120e-02
## [11] 1.262813e-02 8.351442e-05 3.398180e-05 1.263395e-02 1.263650e-02
## [16] 6.671342e-05 1.262813e-02
```

4.1.4 Causal Effects and Standard Errors Estimated By the Marginal Structural Model

```r
causal_mediation(data = df_multipleM_noint,  outcome = "contY_catMbinM_noint", exposure = "A",
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C",
                 yreg = "linear", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "msm")
```

```
## $effect_estimate
##           cde          pnde          tnde          pnie          tnie
##  0.8031875484  0.8021162795  0.8021162795  0.3560158771  0.3560158771
##            te            pm       intref        intmed           pie
##  1.1581321566  0.1816177330 -0.0010712690  0.0000000000  0.3560158771
##      cde_prop   intref_prop   intmed_prop      pie_prop    overall_pm
##  0.6935197714 -0.0009249972  0.0000000000  0.3074052258  0.3074052258
##   overall_int    overall_pe
## -0.0009249972  0.3064802286
##
## $effect_se
##  [1] 4.383464e-03 3.987337e-03 3.987337e-03 1.880388e-02 1.880388e-02
##  [6] 1.969563e-02 7.811724e-03 1.922834e-03 4.452036e-17 1.880388e-02
## [11] 1.133617e-02 1.663047e-03 3.886375e-17 1.120583e-02 1.120583e-02
## [16] 1.663047e-03 1.133617e-02
```

4.1.5 Causal Effects and Standard Errors Estimated By the Inverse Odds-ratio Weighting Approach

```r
causal_mediation(data = df_multipleM_noint,  outcome = "contY_catMbinM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C",
                 yreg = "linear", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "bootstrap", model = "iorw")
```

```
## $effect_estimate
##       tot       dir       ind
## 1.1574035 0.8035720 0.3538315
##
## $effect_se
## [1] 0.022355027 0.004725015 0.022498286
```

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

```r
causal_mediation(data = df_multipleM_noint,  outcome = "contY_catMbinM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C",
                 yreg = "linear", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "g-formula")
```

```
## $effect_estimate
##         cde        pnde        tnde        pnie        tnie          te
##   0.8020494   0.8020494   0.8020494   0.3554609   0.3554609   1.1575102
```

```
##          pm      intref      intmed         pie    cde_prop intref_prop
##   0.1813983   0.0000000   0.0000000   0.3554609   0.6929091   0.0000000
## intmed_prop    pie_prop  overall_pm overall_int  overall_pe
##   0.0000000   0.3070909   0.3070909   0.0000000   0.3070909
##
## $effect_se
##  [1] 4.069127e-03 4.069127e-03 4.069127e-03 2.138677e-02 2.138677e-02
##  [6] 2.240253e-02 8.875203e-03 1.134833e-16 9.945095e-17 2.138677e-02
## [11] 1.275122e-02 9.837162e-17 8.506782e-17 1.275122e-02 1.275122e-02
## [16] 9.788024e-17 1.275122e-02
```

4.1.7 Causal Effects and Standard Errors Estimated By the Natural Effect Model

```
causal_mediation(data = df_multipleM_noint,  outcome = "contY_catMbinM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C",
                 yreg = "linear", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1, model = "ne")
```

```
##                         Estimate  Std. Error
## natural direct effect   0.8020494 0.004140881
## natural indirect effect 0.3553542 0.020909324
## total effect            1.1574035 0.021274908
```

4.2 Case 4-2: Continuous Outcome and Multiple Mediators With Exposure-mediator Interaction

4.2.1 Data simulation

4.2.1.1 Simulation Procedures

1. Simulate the exposure variable A from $Bernoulli(P(A = 1))$.
2. Simulate the covariate C from $N(\mu_C, \sigma_C^2)$.
3. Simulate the first mediator M1 from $Multinom(\frac{1}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)},$

$\frac{expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}, \frac{expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}),$

the second mediator M2 from $Bernoulli(expit(\beta_{03} + \beta_{13} * A + \beta_{23} * C))$.

4. Simulate the outcome Y from $N(\theta_0 + \theta_1 A + \theta_{21} I\{M1 == 1\} + \theta_{22} I\{M1 == 2\} + \theta_{23} M2 + \theta_{31} AM2 + \theta_4 C, \sigma_Y^2)$.

4.2.1.2 True Parameters

Table 8: True Model Parameters for Data Simulation

Sample Size	θ_0	θ_1	θ_{21}	θ_{22}	θ_{23}	θ_{31}	θ_4	β_{01}	β_{11}	β_{21}
10000	-5	0.8	1.8	1.2	1.5	0.2	0.1	-0.25	0.5	0.2
β_{02}	β_{12}	β_{22}	β_{03}	β_{13}	β_{23}	P(A=1)	μ_C	σ_C	σ_Y	
-0.3	0.4	0.3	-0.25	0.5	0.2	0.4	1	1	0.2	

4.2.1.3 True Models

True model for the first mediator:

$$ln\frac{P(M1 == 1)}{P(M1 == 0)} = \beta_{01} + \beta_{11}a + \beta_{21}c$$

$$ln\frac{P(M1 == 2)}{P(M1 == 0)} = \beta_{02} + \beta_{12}a + \beta_{22}c$$

True model for the second mediator:

$$logitE[M2|a, c] = \beta_{03} + \beta_{13}a + \beta_{23}c$$

True model for the outcome:

$$E[Y|a, m^*, c] = \theta_0 + \theta_1 a + \theta_{21}I\{m1^* == 1\} + \theta_{22}I\{m1^* == 2\} + \theta_{23}m2^* + \theta_{31}am2^* + \theta_4 c$$

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

```
causal_mediation(data = df_multipleM_EMint, outcome = "contY_catMbinM_EMint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C",
                 EMint = TRUE, EMint.terms = c("A*M_bin"),
                 yreg = "linear", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "rb")
```

```
## $effect_estimate
##         cde        pnde        tnde        pnie        tnie          te
##  0.79655942  0.90110291  0.92636376  0.35488627  0.38014712  1.28125003
##          pm     intref      intmed         pie    cde_prop intref_prop
##  0.17419140  0.10454349  0.02526084  0.35488627  0.62170490  0.08159492
## intmed_prop    pie_prop  overall_pm overall_int  overall_pe
##  0.01971578  0.27698440  0.29670018  0.10131070  0.37829510
##
## $effect_se
##  [1] 0.005706144 0.004257738 0.004264971 0.021194722 0.022834262
##  [6] 0.022312812 0.008807629 0.003977578 0.002365586 0.021194722
## [11] 0.011811833 0.003400520 0.001627919 0.011840031 0.012778996
## [16] 0.003940727 0.011811833
```

4.2.3 Causal Effects and Standard Errors Estimated By the Weighting-based Approach

```
causal_mediation(data = df_multipleM_EMint,  outcome = "contY_catMbinM_EMint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C",
                 EMint = TRUE, EMint.terms = c("A*M_bin"),
                 yreg = "linear", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "wb")
```

```
## $effect_estimate
##          cde         pnde         tnde         pnie         tnie           te 
##   0.79656036   0.90131204   0.92654688   0.35388666   0.37912150   1.28043355 
##           pm       intref       intmed          pie     cde_prop  intref_prop 
##   0.17376980   0.10475169   0.02523484   0.35388666   0.62210207   0.08180955 
## intmed_prop     pie_prop   overall_pm  overall_int   overall_pe 
##   0.01970804   0.27638034   0.29608839   0.10151759   0.37789793 
## 
## $effect_se
##  [1] 0.006036625 0.004421839 0.004247361 0.020972409 0.022589594
##  [6] 0.021922920 0.008739696 0.004123456 0.002395688 0.020972409
## [11] 0.011227801 0.003742142 0.001665735 0.011748257 0.012686310
## [16] 0.003969430 0.011227801
```

4.2.4 Causal Effects and Standard Errors Estimated By the Marginal Structural Model

```r
causal_mediation(data = df_multipleM_EMint,  outcome = "contY_catMbinM_EMint", exposure = "A",
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C",
                 EMint = TRUE, EMint.terms = c("A*M_bin"),
                 yreg = "linear", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "msm")
```

```
## $effect_estimate
##          cde         pnde         tnde         pnie         tnie           te 
##   0.80046091   0.90094862   0.92612822   0.35515194   0.38033154   1.28128017 
##           pm       intref       intmed          pie     cde_prop  intref_prop 
##   0.17428582   0.10048771   0.02517960   0.35515194   0.62473527   0.07842759 
## intmed_prop     pie_prop   overall_pm  overall_int   overall_pe 
##   0.01965191   0.27718523   0.29683714   0.09807950   0.37526473 
## 
## $effect_se
##  [1] 0.007046478 0.004335526 0.004216081 0.020488723 0.021775460
##  [6] 0.021063838 0.008457359 0.005102371 0.002046553 0.020488723
## [11] 0.011643998 0.004261498 0.001421009 0.011597976 0.012291923
## [16] 0.004705939 0.011643998
```

4.2.5 Causal Effects and Standard Errors Estimated By the Inverse Odds-ratio Weighting Approach

```r
causal_mediation(data = df_multipleM_EMint,  outcome = "contY_catMbinM_EMint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C",
                 EMint = TRUE, EMint.terms = c("A*M_bin"),
                 yreg = "linear", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "bootstrap", model = "iorw")
```

```
## $effect_estimate
##       tot       dir       ind 
## 1.2811930 0.9288706 0.3523224
```

```
##
## $effect_se
## [1] 0.023518505 0.005424143 0.022104803
```

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

```r
causal_mediation(data = df_multipleM_EMint,  outcome = "contY_catMbinM_EMint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C",
                 EMint = TRUE, EMint.terms = c("A*M_bin"),
                 yreg = "linear", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "g-formula")
```

```
## $effect_estimate
##         cde        pnde        tnde        pnie        tnie          te
##  0.79655942  0.90110291  0.92636376  0.35488627  0.38014712  1.28125003
##          pm      intref      intmed         pie    cde_prop intref_prop
##  0.17419140  0.10454349  0.02526084  0.35488627  0.62170490  0.08159492
## intmed_prop    pie_prop  overall_pm overall_int  overall_pe
##  0.01971578  0.27698440  0.29670018  0.10131070  0.37829510
##
## $effect_se
##  [1] 0.006365412 0.004224833 0.004240470 0.019067108 0.020606620
##  [6] 0.020143295 0.007977176 0.004262198 0.002256582 0.019067108
## [11] 0.010660594 0.003712335 0.001571738 0.010690683 0.011585133
## [16] 0.004127028 0.010660594
```

4.2.7 Causal Effects and Standard Errors Estimated By the Natural Effect Model

```r
causal_mediation(data = df_multipleM_EMint,  outcome = "contY_catMbinM_EMint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C",
                 EMint = TRUE, EMint.terms = c("A*M_bin"),
                 yreg = "linear", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1, model = "ne")
```

```
##                        Estimate  Std. Error
## pure direct effect    0.9013755 0.004330497
## total direct effect   0.9259488 0.004431440
## pure indirect effect  0.3550411 0.020883776
## total indirect effect 0.3796144 0.022430534
## total effect          1.2809899 0.022161749
```

4.3 Case 4-3: Continuous Outcome and Multiple Mediators With Mediator-mediator Interaction

4.3.1 Data simulation

4.3.1.1 Simulation Procedures

1. Simulate the exposure variable A from $Bernoulli(P(A = 1))$.

2. Simulate the covariate C from $N(\mu_C, \sigma_C^2)$.
3. Simulate the first mediator M1 from $Multinom(\frac{1}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)},$
$\frac{expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}, \frac{expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}),$
the second mediator M2 from $Bernoulli(expit(\beta_{03} + \beta_{13} * A + \beta_{23} * C))$.
4. Simulate the outcome Y from $N(\theta_0 + \theta_1 A + \theta_{21} I\{M1 == 1\} + \theta_{22} I\{M1 == 2\} + \theta_{23} M2 + \theta_{31} I\{M1 == 1\} M2 + \theta_{32} I\{M1 == 2\} M2 + \theta_4 C, \sigma_Y^2)$.

4.3.1.2 True Parameters

Table 9: True Model Parameters for Data Simulation

Sample Size	θ_0	θ_1	θ_{21}	θ_{22}	θ_{23}	θ_{31}	θ_{32}	θ_4	β_{01}	β_{11}
10000	-5	0.8	1.8	1.2	1.5	0.2	0.4	0.1	-0.25	0.5
β_{21}	β_{02}	β_{12}	β_{22}	β_{03}	β_{13}	β_{23}	P(A=1)	μ_C	σ_C	σ_Y
0.2	-0.3	0.4	0.3	-0.25	0.5	0.2	0.4	1	1	0.2

4.3.1.3 True Models

True model for the first mediator:

$$ln\frac{P(M1 == 1)}{P(M1 == 0)} = \beta_{01} + \beta_{11}a + \beta_{21}c$$

$$ln\frac{P(M1 == 2)}{P(M1 == 0)} = \beta_{02} + \beta_{12}a + \beta_{22}c$$

True model for the second mediator:

$$logitE[M2|a, c] = \beta_{03} + \beta_{13}a + \beta_{23}c$$

True model for the outcome:

$$E[Y|a, m^*, c] = \theta_0 + \theta_1 a + \theta_{21} I\{m1^* == 1\} + \theta_{22} I\{m1^* == 2\} + \theta_{23} m2^* +$$
$$\theta_{31} I\{m1^* == 1\} m2^* + \theta_{32} I\{m1^* == 2\} m2^* + \theta_4 c$$

4.3.2 Causal Effects and Standard Errors Estimated By the Weighting-based Approach

```
causal_mediation(data = df_multipleM_MMint,  outcome = "contY_catMbinM_MMint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C", MMint = TRUE,
                 yreg = "linear", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "wb")
```

```
## $effect_estimate
##           cde          pnde          tnde          pnie          tnie
##  8.035476e-01  8.035222e-01  8.035364e-01  3.940097e-01  3.940238e-01
##            te            pm       intref        intmed           pie
##  1.197546e+00  1.969067e-01 -2.543393e-05  1.415013e-05  3.940097e-01
##      cde_prop   intref_prop   intmed_prop      pie_prop    overall_pm
##  6.709952e-01 -2.123838e-05  1.181594e-05  3.290142e-01  3.290260e-01
```

```
##   overall_int    overall_pe
## -9.422438e-06  3.290048e-01
##
## $effect_se
##  [1] 4.214533e-03 4.214823e-03 4.214016e-03 2.363392e-02 2.362881e-02
##  [6] 2.344377e-02 9.623900e-03 8.656684e-05 3.963993e-05 2.363392e-02
## [11] 1.344813e-02 7.259563e-05 3.321081e-05 1.344419e-02 1.343976e-02
## [16] 5.525860e-05 1.344813e-02
```

4.3.3 Causal Effects and Standard Errors Estimated By the Inverse Odds-ratio Weighting Approach

```r
causal_mediation(data = df_multipleM_MMint,  outcome = "contY_catMbinM_MMint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C", MMint = TRUE,
                 yreg = "linear", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "bootstrap", model = "iorw")
```

```
## $effect_estimate
##      tot      dir      ind
## 1.198474 0.804899 0.393575
##
## $effect_se
## [1] 0.024341330 0.005627961 0.023907805
```

4.3.4 Causal Effects and Standard Errors Estimated By the Natural Effect Model

```r
causal_mediation(data = df_multipleM_MMint,  outcome = "contY_catMbinM_MMint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C", MMint = TRUE,
                 yreg = "linear", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1, model = "ne")
```

```
##                         Estimate  Std. Error
## natural direct effect   0.8035467 0.004083479
## natural indirect effect 0.3949273 0.023289102
## total effect            1.1984740 0.023642809
```

4.4 Case 4-4: Continuous Outcome and Multiple Mediators With Exposure-mediator-mediator Interaction

4.4.1 Data simulation

4.4.1.1 Simulation Procedures

1. Simulate the exposure variable A from $Bernoulli(P(A=1))$.
2. Simulate the covariate C from $N(\mu_C, \sigma_C^2)$.
3. Simulate the first mediator M1 from $Multinom(\frac{1}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)},$

$\frac{expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}, \frac{expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)})$, the second mediator M2 from $Bernoulli(expit(\beta_{03} + \beta_{13} * A + \beta_{23} * C))$.

4. Simulate the outcome Y from $N(\theta_0+\theta_1 A+\theta_{21} I\{M1 == 1\}+\theta_{22} I\{M1 == 2\}+\theta_{23} M2+\theta_{31} AI\{M1 == 1\}M2 + \theta_{32} AI\{M1 == 2\}M2 + \theta_4 C, \sigma_Y^2)$.

4.4.1.2 True Parameters

Table 10: True Model Parameters for Data Simulation

Sample Size	θ_0	θ_1	θ_{21}	θ_{22}	θ_{23}	θ_{31}	θ_{32}	θ_4	β_{01}	β_{11}
10000	-5	0.8	1.8	1.2	1.5	0.2	0.4	0.1	-0.25	0.5
β_{21}	β_{02}	β_{12}	β_{22}	β_{03}	β_{13}	β_{23}	P(A=1)	μ_C	σ_C	σ_Y
0.2	-0.3	0.4	0.3	-0.25	0.5	0.2	0.4	1	1	0.2

4.4.1.3 True Models

True model for the first mediator:

$$ln\frac{P(M1 == 1)}{P(M1 == 0)} = \beta_{01} + \beta_{11}a + \beta_{21}c$$

$$ln\frac{P(M1 == 2)}{P(M1 == 0)} = \beta_{02} + \beta_{12}a + \beta_{22}c$$

True model for the second mediator:

$$logitE[M2|a, c] = \beta_{03} + \beta_{13}a + \beta_{23}c$$

True model for the outcome:

$$E[Y|a, m^*, c] = \theta_0 + \theta_1 a + \theta_{21} I\{m1^* == 1\} + \theta_{22} I\{m1^* == 2\} + \theta_{23} m2^* + \theta_{31} aI\{m1^* == 1\}m2^* + \theta_{32} aI\{m1^* == 2\}m2^* + \theta_4 c$$

4.4.2 Causal Effects and Standard Errors Estimated By the Weighting-based Approach

```
causal_mediation(data = df_multipleM_EMMint,  outcome = "contY_catMbinM_EMMint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C", EMMint = TRUE,
                 yreg = "linear", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "wb")
```

```
## $effect_estimate
##          cde        pnde        tnde        pnie        tnie          te
##   0.80233240  0.90008964  0.94109447  0.35382755  0.39483238  1.29492203
##           pm      intref      intmed         pie    cde_prop intref_prop
##   0.17987712  0.09775724  0.04100483  0.35382755  0.61959901  0.07549276
## intmed_prop    pie_prop  overall_pm overall_int  overall_pe
##   0.03166587  0.27324236  0.30490823  0.10715863  0.38040099
##
## $effect_se
##  [1] 0.010501379 0.004135947 0.004529360 0.020633924 0.022841617
##  [6] 0.022181141 0.008743005 0.009867502 0.003484372 0.020633924
## [11] 0.013923465 0.007652716 0.002380986 0.011425131 0.012584957
## [16] 0.008301172 0.013923465
```

4.4.3 Causal Effects and Standard Errors Estimated By the Inverse Odds-ratio Weighting Approach

```
causal_mediation(data = df_multipleM_EMMint,  outcome = "contY_catMbinM_EMMint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat','M_bin'), covariates.pre = "C", EMMint = TRUE,
                 yreg = "linear", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "bootstrap", model = "iorw")
```

```
## $effect_estimate
##       tot       dir       ind
## 1.2955119 0.9433042 0.3522077
##
## $effect_se
## [1] 0.021813036 0.006193548 0.019356894
```

4.4.4 Causal Effects and Standard Errors Estimated By the Natural Effect Model

```
causal_mediation(data = df_multipleM_EMMint,  outcome = "contY_catMbinM_EMMint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat','M_bin'), covariates.pre = "C", EMMint = TRUE,
                 yreg = "linear", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = NULL, inf.method = NULL, model = "ne")
```

```
##                          Estimate  Std. Error
## natural direct effect   0.9160813 0.004410808
## natural indirect effect 0.3711166 0.021828683
## total effect            1.2871979 0.022271699
```

5 Case 5: Binary Outcome and Single Continuous Mediator

5.1 Case 5-1: Binary Outcome and Single Continuous Mediator Without Interaction

5.1.1 Data simulation

5.1.1.1 Simulation Procedures

1. Simulate the exposure variable A from $Bernoulli(P(A = 1))$.
2. Simulate the covariate C from $N(\mu_C, \sigma_C^2)$.
3. Simulate the mediator M from $N((\beta_0 + \beta_1 * A + \beta_2 * C), \sigma_M^2)$.
4. Simulate the outcome Y from $Bernoulli(expit(\theta_0 + \theta_1 A + \theta_2 M + \theta_4 C))$.

5.1.1.2 True Parameters

Table 11: True Model Parameters for Data Simulation

Sample Size	θ_0	θ_1	θ_2	θ_4	β_0	β_1	β_2	P(A=1)	μ_C	σ_C	σ_M
10000	-5	0.8	1.8	0.1	-0.25	0.5	0.2	0.4	1	1	0.1

5.1.1.3 True Models

True model for the mediator:

$$E[M|a,c] = \beta_0 + \beta_1 a + \beta_2 c$$

True model for the outcome:

$$logitE[Y|a,m^*,c] = \theta_0 + \theta_1 a + \theta_2 m^* + \theta_4 c$$

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

5.1.2.1 Closed-form Parameter Function Estimation and Delta Method Inference

```
causal_mediation(data = df_noint,  outcome = "binY_contM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C",
                 yreg = "logistic", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "delta", model = "rb")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##       2.5395552       2.5395552       2.5395552       2.2072037
##         tnie_rr           te_rr              pm         cde_err
##       2.2072037       5.6053156       0.6657004       1.6498115
##      intref_err      intmed_err         pie_err          te_err
##      -0.1102563       1.8585567       1.2072037       4.6053156
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##       0.3582407      -0.0239411       0.4035677       0.2621327
##      overall_pm     overall_int      overall_pe
##       0.6657004       0.3796266       0.6417593
##
## $effect_se
##  [1] 1.05361506 1.05361506 1.05361506 0.82182666 0.82182666 1.02103719
##  [7] 0.20706348 1.08996133 0.04109014 0.57171394 0.82182666 1.02103719
## [13] 0.21247764 0.00558709 0.04157512 0.18780334 0.20706348 0.04380281
## [19] 0.21247764
```

5.1.2.2 Direct Imputation Estimation and Bootstrap Inference

```
causal_mediation(data = df_noint,  outcome = "binY_contM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C",
                 yreg = "logistic", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "rb")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##     2.514116381     2.511177168     2.478532465     2.187810691
##         tnie_rr           te_rr              pm         cde_err
##     2.159369675     5.422559825     0.658302606     1.540318273
##      intref_err      intmed_err         pie_err          te_err
##    -0.029141105     1.723571966     1.187810691     4.422559825
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
```

```
##     0.348286588    -0.006589194     0.389722702     0.268579904
##      overall_pm     overall_int      overall_pe
##     0.658302606     0.383133508     0.651713412
##
## $effect_se
##  [1] 1.307996127 1.307691248 1.305520212 1.028718646 1.035639530
##  [6] 1.132961645 0.239609835 1.302580745 0.047851420 0.886298625
## [11] 1.028718646 1.132961645 0.237339384 0.009669264 0.154562349
## [16] 0.247923768 0.239609835 0.150822151 0.237339384
```

5.1.3 Causal Effects and Standard Errors Estimated By the Weighting-based Approach

```
causal_mediation(data = df_noint,  outcome = "binY_contM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C",
                 yreg = "logistic", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "wb")
```

```
## $effect_estimate
##           cde_rr         pnde_rr         tnde_rr         pnie_rr
##     2.5140992553    2.5123543656    2.4758077947    2.1948553299
##          tnie_rr           te_rr              pm         cde_err
##     2.1629273355    5.4340399340    0.6589217986    1.5162883577
##       intref_err      intmed_err         pie_err          te_err
##    -0.0039339920    1.7268302385    1.1948553299    4.4340399340
##     cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##     0.3419654266   -0.0008872252    0.3894485084    0.2694732902
##       overall_pm     overall_int      overall_pe
##     0.6589217986    0.3885612832    0.6580345734
##
## $effect_se
##  [1] 1.183128171 1.180376065 1.182152317 0.883662468 0.871662419
##  [6] 1.066600405 0.229462588 1.178698484 0.041498901 0.728077563
## [11] 0.883662468 1.066600405 0.228349459 0.008186915 0.109954345
## [16] 0.201861110 0.229462588 0.111089859 0.228349459
```

5.1.4 Causal Effects and Standard Errors Estimated By the Marginal Structural Model

```
causal_mediation(data = df_noint,  outcome = "binY_contM_noint", exposure = "A",
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C",
                 yreg = "logistic", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "msm")
```

```
## $effect_estimate
##           cde_rr         pnde_rr         tnde_rr         pnie_rr
##       2.81833790      2.72345307      2.67933186      2.84457356
##          tnie_rr           te_rr              pm         cde_err
##       2.79849014      7.62155657      0.73972086      1.91491742
##       intref_err      intmed_err         pie_err          te_err
```

```
##     -0.19146434      3.05352993      1.84457356      6.62155657
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##      0.28919445     -0.02891531      0.46114987      0.27857099
##      overall_pm     overall_int      overall_pe
##      0.73972086      0.43223456      0.71080555
##
## $effect_se
##  [1] 2.1535531 2.5287192 2.5434730 1.3930477 1.3843586 2.9479066 0.3157022
##  [8] 2.3303925 1.5104054 2.3322858 1.3930477 2.9479066 0.2257273 0.1776786
## [15] 0.2185163 0.2656666 0.3157022 0.1609247 0.2257273
```

5.1.5 Causal Effects and Standard Errors Estimated By the Inverse Odds-ratio Weighting Approach

```
causal_mediation(data = df_noint,  outcome = "binY_contM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C",
                 yreg = "logistic", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "bootstrap", model = "iorw")
```

```
## $effect_estimate
##        ORtot        ORdir        ORind
##   5.61260796 219.75188368   0.02554066
##
## $effect_se
## [1] 1.158816e+00 1.851039e+03 3.598557e-02
```

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

```
causal_mediation(data = df_noint,  outcome = "binY_contM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C",
                 yreg = "logistic", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "g-formula")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##     2.514116381     2.511177168     2.478532465     2.187810691
##         tnie_rr           te_rr              pm         cde_err
##     2.159369675     5.422559825     0.658302606     1.540318273
##      intref_err      intmed_err         pie_err          te_err
##    -0.029141105     1.723571966     1.187810691     4.422559825
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##     0.348286588    -0.006589194     0.389722702     0.268579904
##      overall_pm     overall_int      overall_pe
##     0.658302606     0.383133508     0.651713412
##
## $effect_se
##  [1] 1.34390263 1.34477417 1.34610240 1.22443917 1.24216452 1.06582491
##  [7] 0.25407042 1.34247218 0.04606677 1.01417275 1.22443917 1.06582491
```

```
## [13] 0.25322045 0.01029082 0.20018859 0.30492799 0.25407042 0.19436679
## [19] 0.25322045
```

5.1.7 Causal Effects and Standard Errors Estimated By the Natural Effect Model

```r
causal_mediation(data = df_noint,  outcome = "binY_contM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C",
                 yreg = "logistic", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1, model = "ne")
```

```
##                          Estimate Std. Error
## natural direct effect    2.538200  1.0920976
## natural indirect effect 2.210969  0.8669965
## total effect             5.611881  1.0218206
```

5.2 Case 5-2: Binary Outcome and Single Continuous Mediator With Exposure-mediator Interaction

5.2.1 Data simulation

5.2.1.1 Simulation Procedures

1. Simulate the exposure variable A from $Bernoulli(P(A = 1))$.
2. Simulate the covariate C from $N(\mu_C, \sigma_C^2)$.
3. Simulate the mediator M from $N((\beta_0 + \beta_1 * A + \beta_2 * C), \sigma_M^2)$.
4. Simulate the outcome Y from $Bernoulli(expit(\theta_0 + \theta_1 A + \theta_2 M + \theta_3 AM + \theta_4 C))$.

5.2.1.2 True Parameters

Table 12: True Model Parameters for Data Simulation

Sample Size	θ_0	θ_1	θ_2	θ_3	θ_4	β_0	β_1	β_2	P(A=1)	μ_C	σ_C	σ_M
10000	-5	0.8	1.8	0.2	0.1	-0.25	0.5	0.2	0.4	1	1	0.1

5.2.1.3 True Models

True model for the mediator:

$$E[M|a, c] = \beta_0 + \beta_1 a + \beta_2 c$$

True model for the outcome:

$$logitE[Y|a, m^*, c] = \theta_0 + \theta_1 a + \theta_2 m^* + \theta_3 am^* + \theta_4 c$$

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

5.2.2.1 Closed-form Parameter Function Estimation and Delta Method Inference

```r
causal_mediation(data = df_int,  outcome = "binY_contM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C", EMint = TRUE,
                 yreg = "logistic", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "delta", model = "rb")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##      1.63714781      1.59544985      2.47673901      2.40570529
##         tnie_rr           te_rr              pm         cde_err
##      3.73456060      5.95830413      0.87990857      0.68687138
##      intref_err      intmed_err         pie_err          te_err
##     -0.09142153      2.95714900      1.40570529      4.95830413
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##      0.13852950     -0.01843806      0.59640331      0.28350526
##      overall_pm     overall_int      overall_pe
##      0.87990857      0.57796525      0.86147050
##
## $effect_se
##  [1] 0.65099945 0.63794955 1.13309178 1.11154896 1.29199359 1.06927992
##  [7] 0.11773986 0.69239340 0.06017165 1.00814769 1.11154896 1.06927992
## [13] 0.12733631 0.01109865 0.17821927 0.21904042 0.11773986 0.17232212
## [19] 0.12733631
```

5.2.2.2 Direct Imputation Estimation and Bootstrap Inference

```r
causal_mediation(data = df_int,  outcome = "binY_contM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C", EMint = TRUE,
                 yreg = "logistic", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "rb")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##     1.629434000     1.680084828     2.528003426     2.378052943
##         tnie_rr           te_rr              pm         cde_err
##     3.578227650     6.011725986     0.864301275     0.644766123
##      intref_err      intmed_err         pie_err          te_err
##     0.035318706     2.953588215     1.378052943     5.011725986
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##     0.128651511     0.007047214     0.589335535     0.274965740
##      overall_pm     overall_int      overall_pe
##     0.864301275     0.596382749     0.871348489
##
## $effect_se
##  [1] 0.64189379 0.64767466 1.55405537 1.40193569 1.26893926 1.03253218
##  [7] 0.11625740 0.63921819 0.06114925 1.39456879 1.40193569 1.03253218
## [13] 0.11504127 0.01155285 0.22703043 0.26013305 0.11625740 0.23230008
## [19] 0.11504127
```

5.2.3 Causal Effects and Standard Errors Estimated By the Weighting-based Approach

```
causal_mediation(data = df_int,  outcome = "binY_contM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C", EMint = TRUE,
                 yreg = "logistic", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "wb")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##      1.62943187      1.71463583      2.57625648      2.38790742
##         tnie_rr           te_rr              pm         cde_err
##      3.58785337      6.15186196      0.86128591      0.63318412
##      intref_err      intmed_err         pie_err          te_err
##      0.08145171      3.04931871      1.38790742      5.15186196
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##      0.12290394      0.01581015      0.59188673      0.26939919
##      overall_pm     overall_int      overall_pe
##      0.86128591      0.60769688      0.87709606
##
## $effect_se
##  [1] 0.75259386 0.75708302 1.66266185 1.15606105 1.25034728 1.15522898
##  [7] 0.13501146 0.74545767 0.06592387 1.23072133 1.15606105 1.15522898
## [13] 0.13484693 0.01178908 0.18301369 0.22061403 0.13501146 0.19101015
## [19] 0.13484693
```

5.2.4 Causal Effects and Standard Errors Estimated By the Marginal Structural Model

```
causal_mediation(data = df_int,  outcome = "binY_contM_int", exposure = "A",
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C", EMint = TRUE,
                 yreg = "logistic", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "msm")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##     1.505676652     1.546070641     3.240175250     1.617188366
##         tnie_rr           te_rr              pm         cde_err
##     3.389220118     5.239973719     0.871208956     0.521432228
##      intref_err      intmed_err         pie_err          te_err
##     0.024638413     3.076714712     0.617188366     4.239973719
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##     0.122980061     0.005810983     0.725644760     0.145564196
##      overall_pm     overall_int      overall_pe
##     0.871208956     0.731455743     0.877019939
##
## $effect_se
##  [1] 1.23481308 1.61727202 2.54677609 0.73787917 1.76206006 1.48984538
##  [7] 0.26706678 1.22664113 0.54102585 1.27581971 0.73787917 1.48984538
## [13] 0.20919970 0.09083737 0.25280570 0.18068049 0.26706678 0.22344031
## [19] 0.20919970
```

5.2.5 Causal Effects and Standard Errors Estimated By the Inverse Odds-ratio Weighting Approach

```
causal_mediation(data = df_int,  outcome = "binY_contM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C", EMint = TRUE,
                 yreg = "logistic", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "bootstrap", model = "iorw")
```

```
## $effect_estimate
##        ORtot        ORdir        ORind
##   6.42445095 162.84438486   0.03945147
##
## $effect_se
## [1] 1.138056e+00 1.180499e+03 6.770017e-02
```

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

```
causal_mediation(data = df_int,  outcome = "binY_contM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C", EMint = TRUE,
                 yreg = "logistic", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "g-formula")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##     1.629434000     1.680084828     2.528003426     2.378052943
##         tnie_rr           te_rr              pm         cde_err
##     3.578227650     6.011725986     0.864301275     0.644766123
##      intref_err      intmed_err         pie_err          te_err
##     0.035318706     2.953588215     1.378052943     5.011725986
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##     0.128651511     0.007047214     0.589335535     0.274965740
##      overall_pm     overall_int      overall_pe
##     0.864301275     0.596382749     0.871348489
##
## $effect_se
##  [1] 0.64629637 0.62254352 1.34475500 1.27658565 1.14878925 0.96156917
##  [7] 0.11262879 0.61576866 0.05601186 1.19142301 1.27658565 0.96156917
## [13] 0.11164399 0.01034255 0.21499423 0.23120909 0.11262879 0.22121761
## [19] 0.11164399
```

5.2.7 Causal Effects and Standard Errors Estimated By the Natural Effect Model

```
causal_mediation(data = df_int,  outcome = "binY_contM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cont', covariates.pre = "C", EMint = TRUE,
                 yreg = "logistic", mreg = "linear", mval = list(0),
                 a_star = 0, a = 1, model = "ne")
```

```
##                      Estimate Std. Error
## pure direct effect    1.714311  0.6564823
## total direct effect   2.665699  1.3358989
## pure indirect effect  2.405895  1.1167317
## total indirect effect 3.741090  1.2331054
## total effect          6.413391  1.0924309
```

6 Case 6: Binary Outcome and Single Binary Mediator

6.1 Case 6-1: Binary Outcome and Single Binary Mediator Without Interaction

6.1.1 Data simulation

6.1.1.1 Simulation Procedures

1. Simulate the exposure variable A from $Bernoulli(P(A = 1))$.
2. Simulate the covariate C from $N(\mu_C, \sigma_C^2)$.
3. Simulate the mediator M from $Bernoulli(expit(\beta_0 + \beta_1 * A + \beta_2 * C))$.
4. Simulate the outcome Y from $Bernoulli(expit(\theta_0 + \theta_1 A + \theta_2 M + \theta_4 C))$.

6.1.1.2 True Parameters

Table 13: True Model Parameters for Data Simulation

Sample Size	θ_0	θ_1	θ_2	θ_4	β_0	β_1	β_2	P(A=1)	μ_C	σ_C
10000	-5	0.8	1.8	0.1	-0.25	0.5	0.2	0.4	1	1

6.1.1.3 True Models

True model for the mediator:

$$logitE[M|a, c] = \beta_0 + \beta_1 a + \beta_2 c$$

True model for the outcome:

$$logitE[Y|a, m^*, c] = \theta_0 + \theta_1 a + \theta_2 m^* + \theta_4 c$$

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

6.1.2.1 Closed-form Parameter Function Estimation and Delta Method Inference

```r
causal_mediation(data = df_noint,  outcome = "binY_binM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C",
                 yreg = "logistic", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "delta", model = "rb")
```

```
## $effect_estimate
##          cde_rr        pnde_rr        tnde_rr        pnie_rr
##      2.57872683     2.57872683     2.57872683     1.17765284
##         tnie_rr          te_rr             pm        cde_err
##      1.17765284     3.03684497     0.22491557     0.43270036
```

```
##      intref_err      intmed_err         pie_err          te_err
##      1.14602647      0.28046530      0.17765284      2.03684497
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##      0.21243657      0.56264786      0.13769595      0.08721962
##      overall_pm     overall_int      overall_pe
##      0.22491557      0.70034381      0.78756343
##
## $effect_se
##  [1] 0.27096941 0.27096941 0.27096941 0.01844438 0.01844438 0.32125562
##  [7] 0.02178275 0.09728016 0.20187928 0.05552746 0.01844438 0.32125562
## [13] 0.03163846 0.02666304 0.01121131 0.01554300 0.02178275 0.02922078
## [19] 0.03163846
```

6.1.2.2 Direct Imputation Estimation and Bootstrap Inference

```r
causal_mediation(data = df_noint,  outcome = "binY_binM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C",
                 yreg = "logistic", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "rb")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##       2.5498373       2.5033270       2.4864879       1.2386515
##         tnie_rr           te_rr              pm         cde_err
##       1.2303195       3.0798920       0.2772091       0.6127715
##      intref_err      intmed_err         pie_err          te_err
##       0.8905555       0.3379135       0.2386515       2.0798920
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##       0.2946170       0.4281739       0.1624669       0.1147423
##      overall_pm     overall_int      overall_pe
##       0.2772091       0.5906407       0.7053830
##
## $effect_se
##  [1] 0.27891882 0.26858395 0.26511080 0.03150115 0.03061282 0.32929748
##  [7] 0.03169674 0.12518409 0.16071401 0.07170816 0.03150115 0.32929748
## [13] 0.03180035 0.01901039 0.01562826 0.02244723 0.03169674 0.02473330
## [19] 0.03180035
```

6.1.3 Causal Effects and Standard Errors Estimated By the Weighting-based Approach

```r
causal_mediation(data = df_noint,  outcome = "binY_binM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C",
                 yreg = "logistic", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "wb")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##      2.54994740      2.43065264      2.42201496      1.16780413
##         tnie_rr           te_rr              pm         cde_err
```

```
##      1.16365416      2.82843907      0.21755520      0.43115267
##      intref_err      intmed_err         pie_err          te_err
##      0.99949997      0.22998230      0.16780413      1.82843907
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##      0.23580369      0.54664111      0.12578067      0.09177453
##      overall_pm     overall_int      overall_pe
##      0.21755520      0.67242179      0.76419631
##
## $effect_se
##  [1] 0.28562282 0.26170483 0.25846927 0.01768546 0.01730497 0.30641321
##  [7] 0.02182383 0.10175041 0.18786330 0.04824306 0.01768546 0.30641321
## [13] 0.03398023 0.02937369 0.01086047 0.01632508 0.02182383 0.03186973
## [19] 0.03398023
```

6.1.4 Causal Effects and Standard Errors Estimated By the Marginal Structural Model

```
causal_mediation(data = df_noint,  outcome = "binY_binM_noint", exposure = "A",
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C",
                 yreg = "logistic", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "msm")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##       2.5331669       2.4896463       2.4731550       1.2406671
##         tnie_rr           te_rr              pm         cde_err
##       1.2324490       3.0683620       0.2797942       0.6034949
##      intref_err      intmed_err         pie_err          te_err
##       0.8861514       0.3380486       0.2406671       2.0683620
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##       0.2917743       0.4284315       0.1634378       0.1163564
##      overall_pm     overall_int      overall_pe
##       0.2797942       0.5918693       0.7082257
##
## $effect_se
##  [1] 0.26659617 0.25876125 0.25543501 0.03028917 0.02946891 0.31789144
##  [7] 0.03046398 0.12035619 0.15791439 0.06924776 0.03028917 0.31789144
## [13] 0.03289298 0.02005113 0.01487544 0.02155071 0.03046398 0.02593814
## [19] 0.03289298
```

6.1.5 Causal Effects and Standard Errors Estimated By the Inverse Odds-ratio Weighting Approach

```
causal_mediation(data = df_noint,  outcome = "binY_binM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C",
                 yreg = "logistic", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "bootstrap", model = "iorw")
```

```
## $effect_estimate
```

```
##    ORtot    ORdir    ORind
## 2.973025 2.534125 1.173196
##
## $effect_se
## [1] 0.31245951 0.27132034 0.02296525
```

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

```r
causal_mediation(data = df_noint,  outcome = "binY_binM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C",
                 yreg = "logistic", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "g-formula")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##       2.5498373       2.5033270       2.4864879       1.2386515
##         tnie_rr           te_rr              pm         cde_err
##       1.2303195       3.0798920       0.2772091       0.6127715
##      intref_err      intmed_err         pie_err          te_err
##       0.8905555       0.3379135       0.2386515       2.0798920
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##       0.2946170       0.4281739       0.1624669       0.1147423
##      overall_pm     overall_int      overall_pe
##       0.2772091       0.5906407       0.7053830
##
## $effect_se
##  [1] 0.26710552 0.25728415 0.25380837 0.03122239 0.03035590 0.32074550
##  [7] 0.02952921 0.12395316 0.15289802 0.07252188 0.03122239 0.32074550
## [13] 0.03268182 0.01750075 0.01546088 0.01997610 0.02952921 0.02477930
## [19] 0.03268182
```

6.1.7 Causal Effects and Standard Errors Estimated By the Natural Effect Model

```r
causal_mediation(data = df_noint,  outcome = "binY_binM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C",
                 yreg = "logistic", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1, model = "ne")
```

```
##                         Estimate Std. Error
## natural direct effect   2.528419 0.25986871
## natural indirect effect 1.175055 0.01891764
## total effect            2.971031 0.30788444
```

6.2 Case 6-2: Binary Outcome and Single Binary Mediator With Exposure-mediator Interaction

6.2.1 Data simulation

6.2.1.1 Simulation Procedures

1. Simulate the exposure variable A from $Bernoulli(P(A = 1))$.
2. Simulate the covariate C from $N(\mu_C, \sigma_C^2)$.
3. Simulate the mediator M from $Bernoulli(expit(\beta_0 + \beta_1 * A + \beta_2 * C))$.
4. Simulate the outcome Y from $Bernoulli(expit(\theta_0 + \theta_1 A + \theta_2 M + \theta_3 AM + \theta_4 C))$.

6.2.1.2 True Parameters

Table 14: True Model Parameters for Data Simulation

Sample Size	θ_0	θ_1	θ_2	θ_3	θ_4	β_0	β_1	β_2	P(A=1)	μ_C	σ_C
10000	-5	0.8	1.8	0.2	0.1	-0.25	0.5	0.2	0.4	1	1

6.2.1.3 True Models

True model for the mediator:

$$logitE[M|a, c] = \beta_0 + \beta_1 a + \beta_2 c$$

True model for the outcome:

$$logitE[Y|a, m^*, c] = \theta_0 + \theta_1 a + \theta_2 m^* + \theta_3 am^* + \theta_4 c$$

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

6.2.2.1 Closed-form Parameter Function Estimation and Delta Method Inference

```
causal_mediation(data = df_int,  outcome = "binY_binM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C", EMint = TRUE,
                 yreg = "logistic", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "delta", model = "rb")
```

```
## $effect_estimate
##         cde_rr         pnde_rr         tnde_rr         pnie_rr
##     3.03282614      2.91451949      2.90808046      1.18047904
##        tnie_rr           te_rr              pm         cde_err
##     1.17787101      3.43292802      0.21308010      0.53368505
##     intref_err      intmed_err         pie_err          te_err
##     1.38083444      0.33792950      0.18047904      2.43292802
##   cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##     0.21935916      0.56756075      0.13889827      0.07418182
##     overall_pm     overall_int      overall_pe
##     0.21308010      0.70645902      0.78064084
##
## $effect_se
##  [1] 0.90009403 0.30835800 0.30966344 0.02140945 0.01973579 0.36574552
##  [7] 0.02107187 0.17340742 0.26191765 0.07101808 0.02140945 0.36574552
```

```
## [13] 0.06352098 0.05503015 0.01642131 0.01358248 0.02107187 0.06677473
## [19] 0.06352098
```

6.2.2.2 Direct Imputation Estimation and Bootstrap Inference

```r
causal_mediation(data = df_int,  outcome = "binY_binM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C", EMint = TRUE,
                 yreg = "logistic", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "rb")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##      2.99440131      2.87028501      2.83382392      1.24761522
##         tnie_rr           te_rr              pm         cde_err
##      1.23176682      3.53552185      0.26236683      0.77929260
##      intref_err      intmed_err         pie_err          te_err
##      1.09099240      0.41762162      0.24761522      2.53552185
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##      0.30734998      0.43028318      0.16470835      0.09765848
##      overall_pm     overall_int      overall_pe
##      0.26236683      0.59499153      0.69265002
##
## $effect_se
##  [1] 1.02315251 0.45354190 0.36245579 0.04618248 0.03799897 0.52459676
##  [7] 0.04278138 0.30322195 0.19952773 0.09187698 0.04618248 0.52459676
## [13] 0.07439137 0.03994440 0.03426251 0.01688610 0.04278138 0.06978266
## [19] 0.07439137
```

6.2.3 Causal Effects and Standard Errors Estimated By the Weighting-based Approach

```r
causal_mediation(data = df_int,  outcome = "binY_binM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C", EMint = TRUE,
                 yreg = "logistic", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "wb")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##      2.99436882      2.72499422      2.71358038      1.17211450
##         tnie_rr           te_rr              pm         cde_err
##      1.16720501      3.18062691      0.20894573      0.53517062
##      intref_err      intmed_err         pie_err          te_err
##      1.18982360      0.28351819      0.17211450      2.18062691
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##      0.24542054      0.54563373      0.13001682      0.07892891
##      overall_pm     overall_int      overall_pe
##      0.20894573      0.67565056      0.75457946
##
## $effect_se
##  [1] 0.95047179 0.27119789 0.27576840 0.02116713 0.01928932 0.32134718
```

```
##  [7] 0.02161529 0.17231419 0.24089219 0.06399194 0.02116713 0.32134718
## [13] 0.07135700 0.06288939 0.01726283 0.01493215 0.02161529 0.07590857
## [19] 0.07135700
```

6.2.4 Causal Effects and Standard Errors Estimated By the Marginal Structural Model

```r
causal_mediation(data = df_int,  outcome = "binY_binM_int", exposure = "A",
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C", EMint = TRUE,
                 yreg = "logistic", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "msm")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##      3.05941418      2.91235987      2.87263951      1.24938113
##         tnie_rr           te_rr              pm         cde_err
##      1.23234139      3.58902159      0.26135809      0.79836107
##      intref_err      intmed_err         pie_err          te_err
##      1.11399879      0.42728060      0.24938113      2.58902159
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##      0.30836401      0.43027791      0.16503555      0.09632254
##      overall_pm     overall_int      overall_pe
##      0.26135809      0.59531346      0.69163599
##
## $effect_se
##  [1] 0.99016540 0.49310281 0.40883984 0.04480346 0.03875418 0.57042461
##  [7] 0.04239835 0.31085660 0.21895353 0.09516255 0.04480346 0.57042461
## [13] 0.06606992 0.03296174 0.03016616 0.01886154 0.04239835 0.05774069
## [19] 0.06606992
```

6.2.5 Causal Effects and Standard Errors Estimated By the Inverse Odds-ratio Weighting Approach

```r
causal_mediation(data = df_int,  outcome = "binY_binM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C", EMint = TRUE,
                 yreg = "logistic", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "bootstrap", model = "iorw")
```

```
## $effect_estimate
##    ORtot    ORdir    ORind
## 3.365776 2.854107 1.179275
##
## $effect_se
## [1] 0.33698063 0.28273100 0.01995789
```

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

```
causal_mediation(data = df_int,  outcome = "binY_binM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C", EMint = TRUE,
                 yreg = "logistic", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "g-formula")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##      2.99440131      2.87028501      2.83382392      1.24761522
##         tnie_rr           te_rr              pm         cde_err
##      1.23176682      3.53552185      0.26236683      0.77929260
##      intref_err      intmed_err         pie_err          te_err
##      1.09099240      0.41762162      0.24761522      2.53552185
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##      0.30734998      0.43028318      0.16470835      0.09765848
##      overall_pm     overall_int      overall_pe
##      0.26236683      0.59499153      0.69265002
##
## $effect_se
##  [1] 1.19359141 0.52409049 0.41372140 0.04994012 0.03325902 0.61412138
##  [7] 0.03791073 0.32118226 0.23557018 0.09018616 0.04994012 0.61412138
## [13] 0.06310564 0.03487151 0.02947054 0.01720664 0.03791073 0.05932809
## [19] 0.06310564
```

6.2.7 Causal Effects and Standard Errors Estimated By the Natural Effect Model

```
causal_mediation(data = df_int,  outcome = "binY_binM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_bin', covariates.pre = "C", EMint = TRUE,
                 yreg = "logistic", mreg = "logistic", mval = list(0),
                 a_star = 0, a = 1, model = "ne")
```

```
##                         Estimate Std. Error
## pure direct effect      2.844045 0.29399325
## total direct effect     2.850195 0.29608624
## pure indirect effect    1.178971 0.02170860
## total indirect effect   1.181520 0.02098033
## total effect            3.360296 0.34951472
```

7 Case 7: Continuous Outcome and Single Categorical Mediator

7.1 Case 7-1: Continuous Outcome and Single Categorical Mediator Without Interaction

7.1.1 Data simulation

7.1.1.1 Simulation Procedures

1. Simulate the exposure variable A from $Bernoulli(P(A = 1))$.
2. Simulate the covariate C from $N(\mu_C, \sigma_C^2)$.
3. Simulate the mediator M from $Multinom(\frac{1}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)},$

$\frac{expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}, \frac{expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)})$.

4. Simulate the outcome Y from $Bernoulli(expit(\theta_0 + \theta_1 A + \theta_{21} I\{M == 1\} + \theta_{22} I\{M == 2\} + \theta_4 C))$.

7.1.1.2 True Parameters

Table 15: True Model Parameters for Data Simulation

Sample Size	θ_0	θ_1	θ_{21}	θ_{22}	θ_4	β_{01}	β_{11}
10000	-5	0.8	1.8	1.2	0.1	-0.25	0.5
β_{21}	β_{02}	β_{12}	β_{22}	P(A=1)	μ_C	σ_C	
0.2	-0.3	0.4	0.3	0.4	1	1	

7.1.1.3 True Models

True model for the mediator:

$$ln\frac{P(M == 1)}{P(M == 0)} = \beta_{01} + \beta_{11}a + \beta_{21}c$$
$$ln\frac{P(M == 2)}{P(M == 0)} = \beta_{02} + \beta_{12}a + \beta_{22}c$$

True model for the outcome:

$$logitE[Y|a, m^*, c] = \theta_0 + \theta_1 a + \theta_{21} I\{m^* == 1\} + \theta_{22} I\{m^* == 2\} + \theta_4 c$$

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

7.1.2.1 Closed-form Parameter Function Estimation and Delta Method Inference

```
causal_mediation(data = df_noint,  outcome = "binY_catM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C",
                 yreg = "logistic", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "delta", model = "rb")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##      2.77002121      2.77002121      2.77002121      1.13325025
##         tnie_rr           te_rr              pm         cde_err
##      1.13325025      3.13912723      0.17254982      0.62088029
##      intref_err      intmed_err         pie_err          te_err
##      1.14914092      0.23585577      0.13325025      2.13912723
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##      0.29024935      0.53720083      0.11025794      0.06229188
##      overall_pm     overall_int      overall_pe
##      0.17254982      0.64745877      0.70975065
##
## $effect_se
##  [1] 0.30556870 0.30556870 0.30556870 0.01678709 0.01678709 0.34749558
```

```
##  [7] 0.02039285 0.14823777 0.21414202 0.04941026 0.01678709 0.34749558
## [13] 0.04868064 0.03931671 0.01150613 0.01221603 0.02039285 0.04453187
## [19] 0.04868064
```

7.1.2.2 Direct Imputation Estimation and Bootstrap Inference

```
causal_mediation(data = df_noint,  outcome = "binY_catM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C",
                 yreg = "logistic", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "rb")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##      2.73098443      2.68026517      2.66697363      1.16351322
##         tnie_rr           te_rr              pm         cde_err
##      1.15774331      3.10305906      0.20103757      0.75629519
##      intref_err      intmed_err         pie_err          te_err
##      0.92396998      0.25928068      0.16351322      2.10305906
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##      0.35961671      0.43934571      0.12328740      0.07775018
##      overall_pm     overall_int      overall_pe
##      0.20103757      0.56263311      0.64038329
##
## $effect_se
##  [1] 0.30398066 0.29374621 0.29124787 0.02578455 0.02506765 0.33634208
##  [7] 0.02857819 0.16661040 0.17168427 0.05669468 0.02578455 0.33634208
## [13] 0.04841496 0.03158155 0.01512821 0.01696268 0.02857819 0.04007383
## [19] 0.04841496
```

7.1.3 Causal Effects and Standard Errors Estimated By the Weighting-based Approach

```
causal_mediation(data = df_noint,  outcome = "binY_catM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C",
                 yreg = "logistic", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "wb")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##      2.73102116      2.62691648      2.62065532      1.12284964
##         tnie_rr           te_rr              pm         cde_err
##      1.12017337      2.94260189      0.16250649      0.61763587
##      intref_err      intmed_err         pie_err          te_err
##      1.00928061      0.19283576      0.12284964      1.94260189
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##      0.31794259      0.51955093      0.09926674      0.06323974
##      overall_pm     overall_int      overall_pe
##      0.16250649      0.61881767      0.68205741
##
## $effect_se
```

```
##  [1] 0.30283578 0.28502828 0.28374316 0.01632007 0.01590767 0.31268493
##  [7] 0.02121278 0.16868080 0.17332029 0.03827391 0.01632007 0.31268493
## [13] 0.05356293 0.04275507 0.01095797 0.01298022 0.02121278 0.04760741
## [19] 0.05356293
```

7.1.4 Causal Effects and Standard Errors Estimated By the Marginal Structural Model

```r
causal_mediation(data = df_noint,  outcome = "binY_catM_noint", exposure = "A",
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C",
                 yreg = "logistic", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "msm")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##      2.69856480      2.65281302      2.63987087      1.15975393
##         tnie_rr           te_rr              pm         cde_err
##      1.15409590      3.06160063      0.19828652      0.75547653
##      intref_err      intmed_err         pie_err          te_err
##      0.89733649      0.24903367      0.15975393      2.06160063
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##      0.36645145      0.43526204      0.12079627      0.07749024
##      overall_pm     overall_int      overall_pe
##      0.19828652      0.55605831      0.63354855
##
## $effect_se
##  [1] 0.29790692 0.28679823 0.28408939 0.02890831 0.02801775 0.33371414
##  [7] 0.03086717 0.17610843 0.17603215 0.06265709 0.02890831 0.33371414
## [13] 0.05895318 0.03494989 0.01745604 0.01661585 0.03086717 0.04848911
## [19] 0.05895318
```

7.1.5 Causal Effects and Standard Errors Estimated By the Inverse Odds-ratio Weighting Approach

```r
causal_mediation(data = df_noint,  outcome = "binY_catM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C",
                 yreg = "logistic", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "bootstrap", model = "iorw")
```

```
## $effect_estimate
##    ORtot    ORdir    ORind
## 3.084421 2.728979 1.130247
##
## $effect_se
## [1] 0.34940325 0.31136024 0.02046502
```

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

```
causal_mediation(data = df_noint,  outcome = "binY_catM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C",
                 yreg = "logistic", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "g-formula")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##      2.73098443      2.68026517      2.66697363      1.16351322
##         tnie_rr           te_rr              pm         cde_err
##      1.15774331      3.10305906      0.20103757      0.75629519
##      intref_err      intmed_err         pie_err          te_err
##      0.92396998      0.25928068      0.16351322      2.10305906
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##      0.35961671      0.43934571      0.12328740      0.07775018
##      overall_pm     overall_int      overall_pe
##      0.20103757      0.56263311      0.64038329
##
## $effect_se
##  [1] 0.31530848 0.30366399 0.30088746 0.02877880 0.02789137 0.35419808
##  [7] 0.03061156 0.16555515 0.19161385 0.06563340 0.02877880 0.35419808
## [13] 0.05349899 0.03110164 0.01728808 0.01685501 0.03061156 0.04433173
## [19] 0.05349899
```

7.1.7 Causal Effects and Standard Errors Estimated By the Natural Effect Model

```
causal_mediation(data = df_noint,  outcome = "binY_catM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C",
                 yreg = "logistic", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1, model = "ne")
```

```
##                         Estimate Std. Error
## natural direct effect   2.731587 0.29718655
## natural indirect effect 1.128310 0.01713899
## total effect            3.082078 0.33624646
```

7.2 Case 7-2: Binary Outcome and Single Categorical Mediator With Exposure-mediator Interaction

7.2.1 Data simulation

7.2.1.1 Simulation Procedures

1. Simulate the exposure variable A from $Bernoulli(P(A = 1))$.
2. Simulate the covariate C from $N(\mu_C, \sigma_C^2)$.
3. Simulate the mediator M from $Multinom(\frac{1}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)},$

$\frac{expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}, \frac{expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)})$.

4. Simulate the outcome Y from $Bernoulli(expit(\theta_0 + \theta_1 A + \theta_{21} I\{M == 1\} + \theta_{22} I\{M == 2\} + \theta_{31} A * I\{M == 1\} + \theta_{32} A * I\{M == 2\} + \theta_4 C))$.

7.2.1.2 True Parameters

Table 16: True Model Parameters for Data Simulation

Sample Size	θ_0	θ_1	θ_{21}	θ_{22}	θ_{31}	θ_{32}	θ_4	β_{01}
10000	-5	0.8	1.8	1.2	0.2	0.40.1	-0.25	
β_{11}	β_{21}	β_{02}	β_{12}	β_{22}	P(A=1)	μ_C	σ_C	
0.5	0.2	-0.3	0.4	0.3	0.4	1	1	

7.2.1.3 True Models

True model for the mediator:

$$ln\frac{P(M == 1)}{P(M == 0)} = \beta_{01} + \beta_{11}a + \beta_{21}c$$

$$ln\frac{P(M == 2)}{P(M == 0)} = \beta_{02} + \beta_{12}a + \beta_{22}c$$

True model for the outcome:

$$logitE[Y|a, m^*, c] = \theta_0 + \theta_1 a + \theta_{21} I\{m^* == 1\} + \theta_{22} I\{m^* == 2\} + \theta_{31} a * I\{m^* == 1\} + \theta_{32} a * I\{m^* == 2\} + \theta_4 c$$

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

7.2.2.1 Closed-form Parameter Function Estimation and Delta Method Inference

```r
causal_mediation(data = df_int,  outcome = "binY_catM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C", EMint = TRUE,
                 yreg = "logistic", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "delta", model = "rb")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##      1.59647063      2.43397490      2.45962912      1.14349120
##         tnie_rr           te_rr              pm         cde_err
##      1.15554366      2.81256426      0.20886948      0.15308015
##      intref_err      intmed_err         pie_err          te_err
##      1.28089475      0.23509816      0.14349120      1.81256426
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##      0.08445502      0.70667550      0.12970473      0.07916475
##      overall_pm     overall_int      overall_pe
##      0.20886948      0.83638023      0.91554498
##
## $effect_se
##  [1] 0.63669164 0.24838182 0.25268741 0.01800353 0.01670653 0.28851095
##  [7] 0.02162105 0.14316151 0.24192098 0.05027946 0.01800353 0.28851095
## [13] 0.07647096 0.06874111 0.01589277 0.01551416 0.02162105 0.07948744
## [19] 0.07647096
```

7.2.2.2 Direct Imputation Estimation and Bootstrap Inference

```
causal_mediation(data = df_int,  outcome = "binY_catM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C", EMint = TRUE,
                 yreg = "logistic", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "rb")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##       1.5897305       2.1151091       2.2019490       1.2069904
##         tnie_rr           te_rr              pm         cde_err
##       1.2565457       2.6577313       0.3273282       0.2018384
##      intref_err      intmed_err         pie_err          te_err
##       0.9132707       0.3356318       0.2069904       1.6577313
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##       0.1217558       0.5509160       0.2024645       0.1248637
##      overall_pm     overall_int      overall_pe
##       0.3273282       0.7533805       0.8782442
##
## $effect_se
##  [1] 0.90186095 0.39162327 0.31775122 0.04541205 0.05088883 0.44561389
##  [7] 0.08089806 0.21980005 0.21114024 0.07304674 0.04541205 0.44561389
## [13] 0.11715559 0.05441715 0.06016673 0.03172901 0.08089806 0.10506839
## [19] 0.11715559
```

7.2.3 Causal Effects and Standard Errors Estimated By the Weighting-based Approach

```
causal_mediation(data = df_int,  outcome = "binY_catM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C", EMint = TRUE,
                 yreg = "logistic", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "wb")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##      1.58973637      2.30667589      2.32856753      1.13580600
##         tnie_rr           te_rr              pm         cde_err
##      1.14658543      2.64480098      0.20557204      0.15536293
##      intref_err      intmed_err         pie_err          te_err
##      1.15131296      0.20231908      0.13580600      1.64480098
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##      0.09445698      0.69997099      0.12300521      0.08256683
##      overall_pm     overall_int      overall_pe
##      0.20557204      0.82297619      0.90554302
##
## $effect_se
##  [1] 0.68050895 0.21920470 0.21961964 0.01965902 0.01727302 0.24784363
##  [7] 0.02477102 0.14063178 0.21410899 0.04028034 0.01965902 0.24784363
## [13] 0.08375397 0.07543657 0.01617277 0.01736296 0.02477102 0.08654354
## [19] 0.08375397
```

7.2.4 Causal Effects and Standard Errors Estimated By the Marginal Structural Model

```r
causal_mediation(data = df_int,  outcome = "binY_catM_int", exposure = "A",
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C", EMint = TRUE,
                 yreg = "logistic", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "msm")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##       1.6479917       2.1426869       2.2238826       1.2100535
##         tnie_rr           te_rr              pm         cde_err
##       1.2559077       2.6910170       0.3242606       0.2173277
##      intref_err      intmed_err         pie_err          te_err
##       0.9253592       0.3382766       0.2100535       1.6910170
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##       0.1285190       0.5472205       0.2000433       0.1242173
##      overall_pm     overall_int      overall_pe
##       0.3242606       0.7472638       0.8714810
##
## $effect_se
##  [1] 0.71151290 0.33699505 0.28669182 0.04348237 0.04963822 0.37716739
##  [7] 0.06686551 0.19191858 0.18743095 0.07169870 0.04348237 0.37716739
## [13] 0.09247285 0.04692832 0.04744976 0.03103749 0.06686551 0.08384028
## [19] 0.09247285
```

7.2.5 Causal Effects and Standard Errors Estimated By the Inverse Odds-ratio Weighting Approach

```r
causal_mediation(data = df_int,  outcome = "binY_catM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C", EMint = TRUE,
                 yreg = "logistic", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "bootstrap", model = "iorw")
```

```
## $effect_estimate
##    ORtot    ORdir    ORind
## 2.775554 2.428996 1.142676
##
## $effect_se
## [1] 0.31340057 0.27342346 0.01945173
```

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

```r
causal_mediation(data = df_int,  outcome = "binY_catM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C", EMint = TRUE,
                 yreg = "logistic", mreg = "multinomial", mval = list(0),
```

```r
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "g-formula")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr 
##       1.5897305       2.1151091       2.2019490       1.2069904 
##         tnie_rr           te_rr              pm         cde_err 
##       1.2565457       2.6577313       0.3273282       0.2018384 
##      intref_err      intmed_err         pie_err          te_err 
##       0.9132707       0.3356318       0.2069904       1.6577313 
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop 
##       0.1217558       0.5509160       0.2024645       0.1248637 
##      overall_pm     overall_int      overall_pe 
##       0.3273282       0.7533805       0.8782442 
## 
## $effect_se
##  [1] 0.91043425 0.38638400 0.31326162 0.04063547 0.05119279 0.42470966
##  [7] 0.07581815 0.22904520 0.19272279 0.06787011 0.04063547 0.42470966
## [13] 0.11574833 0.05509644 0.05687963 0.02887703 0.07581815 0.10356532
## [19] 0.11574833
```

7.2.7 Causal Effects and Standard Errors Estimated By the Natural Effect Model

```r
causal_mediation(data = df_int,  outcome = "binY_catM_int", exposure = 'A',
                 exposure.type = "binary",
                 mediator = 'M_cat', covariates.pre = "C", EMint = TRUE,
                 yreg = "logistic", mreg = "multinomial", mval = list(0),
                 a_star = 0, a = 1, model = "ne")
```

```
##                       Estimate Std. Error
## pure direct effect    2.393442 0.24039589
## total direct effect   2.429797 0.24548117
## pure indirect effect  1.141232 0.01833799
## total indirect effect 1.158567 0.01762646
## total effect          2.772964 0.28007690
```

8 Case 8: Binary Outcome and Multiple Mediators

8.1 Case 8-1: Binary Outcome and Multiple Mediators Without Interaction

8.1.1 Data simulation

8.1.1.1 Simulation Procedures

1. Simulate the exposure variable A from $Bernoulli(P(A = 1))$.
2. Simulate the covariate C from $N(\mu_C, \sigma_C^2)$.
3. Simulate the first mediator M1 from $Multinom(\frac{1}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)},$

$\frac{expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}, \frac{expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}),$

the second mediator M2 from $Bernoulli(expit(\beta_{03} + \beta_{13} * A + \beta_{23} * C))$.

4. Simulate the outcome Y from $Bernoulli(expit(\theta_0 + \theta_1 A + \theta_{21} I\{M1 == 1\} + \theta_{22} I\{M1 == 2\} + \theta_{23} M2 + \theta_4 C))$.

8.1.1.2 True Parameters

Table 17: True Model Parameters for Data Simulation

Sample Size	θ_0	θ_1	θ_{21}	θ_{22}	θ_{23}	θ_4	β_{01}	β_{11}	β_{21}
10000	-5	0.8	1.8	1.2	1.5	0.1	-0.25	0.5	0.2
β_{02}	β_{12}	β_{22}	β_{03}	β_{13}	β_{23}	P(A=1)	μ_C	σ_C	
-0.3	0.4	0.3	-0.25	0.5	0.2	0.4	1	1	

8.1.1.3 True Models

True model for the first mediator:

$$ln\frac{P(M1 == 1)}{P(M1 == 0)} = \beta_{01} + \beta_{11} a + \beta_{21} c$$

$$ln\frac{P(M1 == 2)}{P(M1 == 0)} = \beta_{02} + \beta_{12} a + \beta_{22} c$$

True model for the second mediator:

$$logitE[M2|a, c] = \beta_{03} + \beta_{13} a + \beta_{23} c$$

True model for the outcome:

$$logitE[Y|a, m^*, c] = \theta_0 + \theta_1 a + \theta_{21} I\{m1^* == 1\} + \theta_{22} I\{m1^* == 2\} + \theta_{23} m2^* + \theta_4 c$$

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

```r
causal_mediation(data = df_multipleM_noint,  outcome = "binY_catMbinM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C",
                 yreg = "logistic", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "rb")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##       2.2111885       2.1208079       2.0805816       1.4201105
##         tnie_rr           te_rr              pm         cde_err
##       1.3931747       2.9546559       0.4265958       0.2017968
##      intref_err      intmed_err         pie_err          te_err
##       0.9190111       0.4137375       0.4201105       1.9546559
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##       0.1032390       0.4701652       0.2116677       0.2149281
##      overall_pm     overall_int      overall_pe
##       0.4265958       0.6818328       0.8967610
##
## $effect_se
##  [1] 0.16597322 0.15142415 0.14491151 0.03588842 0.03371237 0.22423244
##  [7] 0.02597268 0.03331904 0.12551017 0.06881776 0.03588842 0.22423244
## [13] 0.01205246 0.01964427 0.01242956 0.02436632 0.02597268 0.02133526
## [19] 0.01205246
```

8.1.3 Causal Effects and Standard Errors Estimated By the Weighting-based Approach

```
causal_mediation(data = df_multipleM_noint,  outcome = "binY_catMbinM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C",
                 yreg = "logistic", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "wb")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##      2.21118609      1.96144362      1.93361301      1.29973817
##         tnie_rr           te_rr              pm         cde_err
##      1.28129639      2.51319063      0.36462492      0.12857078
##      intref_err      intmed_err         pie_err          te_err
##      0.83287284      0.25200884      0.29973817      1.51319063
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##      0.08496668      0.55040840      0.16654137      0.19808355
##      overall_pm     overall_int      overall_pe
##      0.36462492      0.71694977      0.91503332
##
## $effect_se
##  [1] 0.157397986 0.119130227 0.115177921 0.024665085 0.022623000
##  [6] 0.160697532 0.022950250 0.023193918 0.103406513 0.038426515
## [11] 0.024665085 0.160697532 0.011285817 0.020288784 0.009570977
## [16] 0.021071907 0.022950250 0.019813833 0.011285817
```

8.1.4 Causal Effects and Standard Errors Estimated By the Marginal Structural Model

```
causal_mediation(data = df_multipleM_noint,  outcome = "binY_catMbinM_noint", exposure = "A",
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C",
                 yreg = "logistic", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "msm")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##       2.2122656       2.1282966       2.0878774       1.4236766
##         tnie_rr           te_rr              pm         cde_err
##       1.3966390       2.9724621       0.4279755       0.2023030
##      intref_err      intmed_err         pie_err          te_err
##       0.9259936       0.4204889       0.4236766       1.9724621
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##       0.1025637       0.4694608       0.2131797       0.2147958
##      overall_pm     overall_int      overall_pe
##       0.4279755       0.6826405       0.8974363
##
## $effect_se
##  [1] 0.15357682 0.14052437 0.13441062 0.04037102 0.03831442 0.20652265
##  [7] 0.02915018 0.03242736 0.11527833 0.06547111 0.04037102 0.20652265
## [13] 0.01263087 0.02100617 0.01271550 0.02516566 0.02915018 0.02008093
## [19] 0.01263087
```

8.1.5 Causal Effects and Standard Errors Estimated By the Inverse Odds-ratio Weighting Approach

```
causal_mediation(data = df_multipleM_noint,  outcome = "binY_catMbinM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat','M_bin'), covariates.pre = "C",
                 yreg = "logistic", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "bootstrap", model = "iorw")
```

```
## $effect_estimate
##    ORtot    ORdir    ORind
## 2.799041 2.107599 1.328071
##
## $effect_se
## [1] 0.20869614 0.15461043 0.02758497
```

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

```
causal_mediation(data = df_multipleM_noint,  outcome = "binY_catMbinM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat','M_bin'), covariates.pre = "C",
                 yreg = "logistic", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "g-formula")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##       2.2111885       2.1208079       2.0805816       1.4201105
##         tnie_rr           te_rr              pm         cde_err
##       1.3931747       2.9546559       0.4265958       0.2017968
##      intref_err      intmed_err         pie_err          te_err
##       0.9190111       0.4137375       0.4201105       1.9546559
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##       0.1032390       0.4701652       0.2116677       0.2149281
##      overall_pm     overall_int      overall_pe
##       0.4265958       0.6818328       0.8967610
##
## $effect_se
##  [1] 0.15979659 0.14507063 0.13880482 0.03875484 0.03642927 0.21197903
##  [7] 0.02785685 0.03147738 0.12151550 0.06553631 0.03875484 0.21197903
## [13] 0.01230650 0.02128625 0.01223800 0.02488902 0.02785685 0.02153366
## [19] 0.01230650
```

8.1.7 Causal Effects and Standard Errors Estimated By the Natural Effect Model

```
causal_mediation(data = df_multipleM_noint,  outcome = "binY_catMbinM_noint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat','M_bin'), covariates.pre = "C",
                 yreg = "logistic", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1, model = "ne")
```

```
##                         Estimate Std. Error
## natural direct effect   2.101974 0.14204225
## natural indirect effect 1.331644 0.02705724
## total effect            2.799080 0.19478614
```

8.2 Case 8-2: Binary Outcome and Multiple Mediators With Exposure-mediator Interaction

8.2.1 Data simulation

8.2.1.1 Simulation Procedures

1. Simulate the exposure variable A from $Bernoulli(P(A = 1))$.
2. Simulate the covariate C from $N(\mu_C, \sigma_C^2)$.
3. Simulate the first mediator M1 from $Multinom(\frac{1}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)},$

$\frac{expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}, \frac{expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}),$

the second mediator M2 from $Bernoulli(expit(\beta_{03} + \beta_{13} * A + \beta_{23} * C))$.

4. Simulate the outcome Y from $Bernoulli(expit(\theta_0 + \theta_1 A + \theta_{21} I\{M1 == 1\} + \theta_{22} I\{M1 == 2\} + \theta_{23} M2 + \theta_{31} AM2 + \theta_4 C))$.

8.2.1.2 True Parameters

Table 18: True Model Parameters for Data Simulation

Sample Size	θ_0	θ_1	θ_{21}	θ_{22}	θ_{23}	θ_{31}	θ_4	β_{01}	β_{11}
10000	-5	0.8	1.8	1.2	1.5	0.2	0.1	-0.25	0.5
β_{21}	β_{02}	β_{12}	β_{22}	β_{03}	β_{13}	β_{23}	P(A=1)	μ_C	σ_C
0.2	-0.3	0.4	0.3	-0.25	0.5	0.2	0.4	1	1

8.2.1.3 True Models

True model for the first mediator:

$$ln\frac{P(M1 == 1)}{P(M1 == 0)} = \beta_{01} + \beta_{11} a + \beta_{21} c$$

$$ln\frac{P(M1 == 2)}{P(M1 == 0)} = \beta_{02} + \beta_{12} a + \beta_{22} c$$

True model for the second mediator:

$$logitE[M2|a, c] = \beta_{03} + \beta_{13} a + \beta_{23} c$$

True model for the outcome:

$$logitE[Y|a, m^*, c] = \theta_0 + \theta_1 a + \theta_{21} I\{m1^* == 1\} + \theta_{22} I\{m1^* == 2\} + \theta_{23} m2^* + \theta_{31} am2^* + \theta_4 c$$

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

```r
causal_mediation(data = df_multipleM_EMint, outcome = "binY_catMbinM_EMint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C",
                 EMint = TRUE, EMint.terms = c("A*M_bin"),
                 yreg = "logistic", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "rb")
```

```
## $effect_estimate
##           cde_rr          pnde_rr          tnde_rr          pnie_rr
##       2.20302492       2.37887173       2.38655905       1.39028315
##          tnie_rr            te_rr               pm          cde_err
##       1.39477585       3.31799284       0.40514409       0.22991983
##       intref_err       intmed_err          pie_err           te_err
##       1.14895190       0.54883796       0.39028315       2.31799284
##     cde_err_prop  intref_err_prop  intmed_err_prop     pie_err_prop
##       0.09918919       0.49566672       0.23677293       0.16837116
##       overall_pm      overall_int       overall_pe
##       0.40514409       0.73243965       0.90081081
##
## $effect_se
##  [1] 0.35029368 0.19239157 0.16535920 0.03609092 0.03561915 0.25243663
##  [7] 0.02997726 0.06205630 0.14258313 0.06909048 0.03609092 0.25243663
## [13] 0.02013058 0.01770741 0.01826191 0.01858673 0.02997726 0.01943407
## [19] 0.02013058
```

8.2.3 Causal Effects and Standard Errors Estimated By the Weighting-based Approach

```r
causal_mediation(data = df_multipleM_EMint,  outcome = "binY_catMbinM_EMint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C",
                 EMint = TRUE, EMint.terms = c("A*M_bin"),
                 yreg = "logistic", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "wb")
```

```
## $effect_estimate
##           cde_rr          pnde_rr          tnde_rr          pnie_rr
##       2.20301631       2.29096748       2.27691173       1.29127127
##          tnie_rr            te_rr               pm          cde_err
##       1.28334894       2.94011070       0.33459081       0.15297047
##       intref_err       intmed_err          pie_err           te_err
##       1.13799701       0.35787195       0.29127127       1.94011070
##     cde_err_prop  intref_err_prop  intmed_err_prop     pie_err_prop
##       0.07884626       0.58656293       0.18445955       0.15013126
##       overall_pm      overall_int       overall_pe
##       0.33459081       0.77102248       0.92115374
##
## $effect_se
##  [1] 0.33384763 0.14024399 0.13899130 0.02177224 0.02029510 0.18167678
##  [7] 0.02004253 0.03531403 0.12169804 0.04840385 0.02177224 0.18167678
## [13] 0.01574233 0.01805770 0.01265131 0.01674757 0.02004253 0.02188120
## [19] 0.01574233
```

8.2.4 Causal Effects and Standard Errors Estimated By the Marginal Structural Model

```
causal_mediation(data = df_multipleM_EMint,  outcome = "binY_catMbinM_EMint", exposure = "A",
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C",
                 EMint = TRUE, EMint.terms = c("A*M_bin"),
                 yreg = "logistic", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "msm")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##       2.1887158       2.3471475       2.3530841       1.3850917
##         tnie_rr           te_rr              pm         cde_err
##       1.3885950       3.2592372       0.4037158       0.2336704
##      intref_err      intmed_err         pie_err          te_err
##       1.1134771       0.5269980       0.3850917       2.2592372
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##       0.1034289       0.4928553       0.2332637       0.1704521
##      overall_pm     overall_int      overall_pe
##       0.4037158       0.7261190       0.8965711
##
## $effect_se
##  [1] 0.34911900 0.19185645 0.16498959 0.03735607 0.03725024 0.25924113
##  [7] 0.02995189 0.06091371 0.14216027 0.07262515 0.03735607 0.25924113
## [13] 0.01976588 0.01751174 0.01881735 0.01814629 0.02995189 0.01856703
## [19] 0.01976588
```

8.2.5 Causal Effects and Standard Errors Estimated By the Inverse Odds-ratio Weighting Approach

```
causal_mediation(data = df_multipleM_EMint,  outcome = "binY_catMbinM_EMint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C",
                 EMint = TRUE, EMint.terms = c("A*M_bin"),
                 yreg = "logistic", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "bootstrap", model = "iorw")
```

```
## $effect_estimate
##    ORtot    ORdir    ORind
## 3.377977 2.575845 1.311405
##
## $effect_se
## [1] 0.24840319 0.18326403 0.02811678
```

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

```
causal_mediation(data = df_multipleM_EMint,  outcome = "binY_catMbinM_EMint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C",
```

```r
                 EMint = TRUE, EMint.terms = c("A*M_bin"),
                 yreg = "logistic", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "g-formula")
```

```
## $effect_estimate
##         cde_rr         pnde_rr         tnde_rr         pnie_rr
##     2.20302492      2.37887173      2.38655905      1.39028315
##        tnie_rr           te_rr              pm         cde_err
##     1.39477585      3.31799284      0.40514409      0.22991983
##     intref_err      intmed_err         pie_err          te_err
##     1.14895190      0.54883796      0.39028315      2.31799284
##   cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##     0.09918919      0.49566672      0.23677293      0.16837116
##     overall_pm     overall_int      overall_pe
##     0.40514409      0.73243965      0.90081081
##
## $effect_se
##  [1] 0.35089956 0.20627331 0.18018958 0.03724027 0.03782281 0.28224681
##  [7] 0.03050771 0.06044110 0.15638803 0.08047518 0.03724027 0.28224681
## [13] 0.01889822 0.01839064 0.01871984 0.01903658 0.03050771 0.01841282
## [19] 0.01889822
```

8.2.7 Causal Effects and Standard Errors Estimated By the Natural Effect Model

```r
causal_mediation(data = df_multipleM_EMint,  outcome = "binY_catMbinM_EMint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C",
                 EMint = TRUE, EMint.terms = c("A*M_bin"),
                 yreg = "logistic", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = NULL, inf.method = NULL, model = "ne")
```

```
##                       Estimate Std. Error
## pure direct effect    2.498818 0.16295708
## total direct effect   2.559651 0.16858515
## pure indirect effect  1.316317 0.02760150
## total indirect effect 1.348362 0.02906912
## total effect          3.369312 0.22659165
```

8.3 Case 8-3: Binary Outcome and Multiple Mediators With Mediator-mediator Interaction

8.3.1 Data simulation

8.3.1.1 Simulation Procedures

1. Simulate the exposure variable A from $Bernoulli(P(A = 1))$.
2. Simulate the covariate C from $N(\mu_C, \sigma_C^2)$.
3. Simulate the first mediator M1 from $Multinom(\frac{1}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)},$

$\frac{expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}, \frac{expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}),$
the second mediator M2 from $Bernoulli(expit(\beta_{03} + \beta_{13} * A + \beta_{23} * C))$.

4. Simulate the outcome Y from $Bernoulli(expit(\theta_0 + \theta_1 A + \theta_{21} I\{M1 == 1\} + \theta_{22} I\{M1 == 2\} + \theta_{23} M2 + \theta_{31} I\{M1 == 1\} M2 + \theta_{32} I\{M1 == 2\} M2 + \theta_4 C))$.

8.3.1.2 True Parameters

Table 19: True Model Parameters for Data Simulation

Sample Size	θ_0	θ_1	θ_{21}	θ_{22}	θ_{23}	θ_{31}	θ_{32}	θ_4	β_{01}	β_{11}
10000	-5	0.8	1.8	1.2	1.5	0.2	0.4	0.1	-0.25	0.5
β_{21}	β_{02}	β_{12}	β_{22}	β_{03}	β_{13}	β_{23}	P(A=1)	μ_C	σ_C	
0.2	-0.3	0.4	0.3	-0.25	0.5	0.2	0.4	1	1	

8.3.1.3 True Models

True model for the first mediator:

$$ln\frac{P(M1 == 1)}{P(M1 == 0)} = \beta_{01} + \beta_{11}a + \beta_{21}c$$

$$ln\frac{P(M1 == 2)}{P(M1 == 0)} = \beta_{02} + \beta_{12}a + \beta_{22}c$$

True model for the second mediator:

$$logitE[M2|a, c] = \beta_{03} + \beta_{13}a + \beta_{23}c$$

True model for the outcome:

$$logitE[Y|a, m^*, c] = \theta_0 + \theta_1 a + \theta_{21} I\{m1^* == 1\} + \theta_{22} I\{m1^* == 2\} + \theta_{23} m2^* +$$

$$\theta_{31} I\{m1^* == 1\} m2^* + \theta_{32} I\{m1^* == 2\} m2^* + \theta_4 c$$

8.3.2 Causal Effects and Standard Errors Estimated By the Weighting-based Approach

```
causal_mediation(data = df_multipleM_MMint,  outcome = "binY_catMbinM_MMint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C", MMint = TRUE,
                 yreg = "logistic", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "wb")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##      2.22082618      1.90804702      1.87741240      1.31524628
##         tnie_rr           te_rr              pm         cde_err
##      1.29412937      2.46925969      0.38196969      0.12037987
##      intref_err      intmed_err         pie_err          te_err
##      0.78766715      0.24596638      0.31524628      1.46925969
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##      0.08193233      0.53609798      0.16740838      0.21456131
##      overall_pm     overall_int      overall_pe
```

```
##      0.38196969      0.70350636      0.91806767
##
## $effect_se
##  [1] 0.131964893 0.092051519 0.088936737 0.026370711 0.024405130
##  [6] 0.122421044 0.024701686 0.034385689 0.082926819 0.030633609
## [11] 0.026370711 0.122421044 0.021737045 0.026865597 0.009016309
## [16] 0.021360127 0.024701686 0.025678748 0.021737045
```

8.3.3 Causal Effects and Standard Errors Estimated By the Inverse Odds-ratio Weighting Approach

```r
causal_mediation(data = df_multipleM_MMint,  outcome = "binY_catMbinM_MMint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat','M_bin"), covariates.pre = "C", MMint = TRUE,
                 yreg = "logistic", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "bootstrap", model = "iorw",)
```

```
## $effect_estimate
##    ORtot    ORdir    ORind
## 2.812577 2.091674 1.344654
##
## $effect_se
## [1] 0.18157852 0.12748179 0.02760453
```

8.3.4 Causal Effects and Standard Errors Estimated By the Natural Effect Model

```r
causal_mediation(data = df_multipleM_MMint,  outcome = "binY_catMbinM_MMint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat','M_bin"), covariates.pre = "C", MMint = TRUE,
                 yreg = "logistic", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = NULL, inf.method = NULL, model = "ne")
```

```
##                         Estimate Std. Error
## natural direct effect   2.071908  0.1270287
## natural indirect effect 1.357942  0.0285880
## total effect            2.813531  0.1802364
```

8.4 Case 8-4: Binary Outcome and Multiple Mediators With Exposure-mediator-mediator Interaction

8.4.1 Data simulation

8.4.1.1 Simulation Procedures

1. Simulate the exposure variable A from $Bernoulli(P(A = 1))$.
2. Simulate the covariate C from $N(\mu_C, \sigma_C^2)$.
3. Simulate the first mediator M1 from $Multinom(\frac{1}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)},$

$\frac{expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}, \frac{expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}{1+expit(\beta_{01}+\beta_{11}*A+\beta_{21}*C)+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)})$, the second mediator M2 from $Bernoulli(expit(\beta_{03} + \beta_{13} * A + \beta_{23} * C))$.

4. Simulate the outcome Y from $Bernoulli(expit(\theta_0 + \theta_1 A + \theta_{21} I\{M1 == 1\} + \theta_{22} I\{M1 == 2\} + \theta_{23} M2 + \theta_{31} AI\{M1 == 1\}M2 + \theta_{32} AI\{M1 == 2\}M2 + \theta_4 C))$.

8.4.1.2 True Parameters

Table 20: True Model Parameters for Data Simulation

Sample Size	θ_0	θ_1	θ_{21}	θ_{22}	θ_{23}	θ_{31}	θ_{32}	θ_4	β_{01}	β_{11}
10000	-5	0.8	1.8	1.2	1.5	0.2	0.4	0.1	-0.25	0.5
β_{21}	β_{02}	β_{12}	β_{22}	β_{03}	β_{13}	β_{23}	P(A=1)	μ_C	σ_C	
0.2	-0.3	0.4	0.3	-0.25	0.5	0.2	0.4	1	1	

8.4.1.3 True Models

True model for the first mediator:

$$ln\frac{P(M1 == 1)}{P(M1 == 0)} = \beta_{01} + \beta_{11} a + \beta_{21} c$$

$$ln\frac{P(M1 == 2)}{P(M1 == 0)} = \beta_{02} + \beta_{12} a + \beta_{22} c$$

True model for the second mediator:

$$logitE[M2|a, c] = \beta_{03} + \beta_{13} a + \beta_{23} c$$

True model for the outcome:

$$logitE[Y|a, m^*, c] = \theta_0 + \theta_1 a + \theta_{21} I\{m1^* == 1\} + \theta_{22} I\{m1^* == 2\} + \theta_{23} m2^* +$$

$$\theta_{31} aI\{m1^* == 1\}m2^* + \theta_{32} aI\{m1^* == 2\}m2^* + \theta_4 c$$

8.4.2 Causal Effects and Standard Errors Estimated By the Weighting-based Approach

```
causal_mediation(data = df_multipleM_EMMint,  outcome = "binY_catMbinM_EMMint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C", EMMint = TRUE,
                 yreg = "logistic", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "wb")
```

```
## $effect_estimate
##          cde_rr          pnde_rr          tnde_rr          pnie_rr
##       3.8188572        2.3161583        2.3333954        1.2881263
##         tnie_rr            te_rr               pm          cde_err
##       1.2977127        3.0057081        0.3437937        0.2575928
##      intref_err       intmed_err          pie_err           te_err
##       1.0585655        0.4014234        0.2881263        2.0057081
##    cde_err_prop  intref_err_prop  intmed_err_prop     pie_err_prop
##       0.1284299        0.5277764        0.2001405        0.1436532
##      overall_pm      overall_int       overall_pe
```

```
##       0.3437937       0.7279170       0.8715701
##
## $effect_se
##  [1] 4.06949575 0.13251451 0.12968734 0.02799888 0.02635202 0.18181071
##  [7] 0.02238361 0.13501427 0.15579147 0.05762851 0.02799888 0.18181071
## [13] 0.06622647 0.06199650 0.01786711 0.01484854 0.02238361 0.06745274
## [19] 0.06622647
```

8.4.3 Causal Effects and Standard Errors Estimated By the Inverse Odds-ratio Weighting Approach

```
causal_mediation(data = df_multipleM_EMMint,  outcome = "binY_catMbinM_EMMint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C", EMMint = TRUE,
                 yreg = "logistic", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "paramfunc", inf.method = "bootstrap", model = "iorw")
```

```
## $effect_estimate
##    ORtot    ORdir    ORind
## 3.470928 2.646711 1.311412
##
## $effect_se
## [1] 0.2244232 0.1704989 0.0279728
```

8.4.4 Causal Effects and Standard Errors Estimated By the Natural Effect Model

```
causal_mediation(data = df_multipleM_EMMint,  outcome = "binY_catMbinM_EMMint", exposure = 'A',
                 exposure.type = "binary",
                 mediator = c('M_cat',"M_bin"), covariates.pre = "C", EMMint = TRUE,
                 yreg = "logistic", mreg = c("multinomial", "logistic"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = NULL, inf.method = NULL, model = "ne")
```

```
##                         Estimate Std. Error
## natural direct effect   2.570512 0.16663572
## natural indirect effect 1.345977 0.02812698
## total effect            3.459851 0.23376038
```

9 Case 9: Post-exposure Confounding

9.1 Data simulation

9.1.1 Simulation Procedures

1. Simulate the exposure variable A from $Bernoulli(P(A = 1))$.
2. Simulate the covariate C from $N(\mu_C, \sigma_C^2)$.
3. Simulate the first post-exposure confounder L1 from $Bernoulli(expit(\beta_{01} + \beta_{11} * A + \beta_{21} * C))$ the second post-exposure confounder L2 from $Multinom(\frac{1}{1+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)+expit(\beta_{03}+\beta_{13}*A+\beta_{23}*C)},$

$\frac{expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)}{1+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)+expit(\beta_{03}+\beta_{13}*A+\beta_{23}*C)}, \frac{expit(\beta_{03}+\beta_{13}*A+\beta_{23}*C)}{1+expit(\beta_{02}+\beta_{12}*A+\beta_{22}*C)+expit(\beta_{03}+\beta_{13}*A+\beta_{23}*C)})$.

4. Simulate the first mediator M1 from $Multinom$

$(\frac{1}{1+expit(\beta_{04}+\beta_{14}*A+\beta_{24}*C+\beta_{34}*L1+\beta_{44}*I\{L2==1\}+\beta_{54}*I\{L2==2\})+expit(\beta_{05}+\beta_{15}*A+\beta_{25}*C+\beta_{35}*L1+\beta_{45}*I\{L2==1\}+\beta_{55}*I\{L2==2\})},$

$\frac{expit(\beta_{04}+\beta_{14}*A+\beta_{24}*C+\beta_{34}*L1+\beta_{44}*I\{L2==1\}+\beta_{54}*I\{L2==2\})}{1+expit(\beta_{04}+\beta_{14}*A+\beta_{24}*C+\beta_{34}*L1+\beta_{44}*I\{L2==1\}+\beta_{54}*I\{L2==2\})+expit(\beta_{05}+\beta_{15}*A+\beta_{25}*C+\beta_{35}*L1+\beta_{45}*I\{L2==1\}+\beta_{55}*I\{L2==2\})},$

$\frac{expit(\beta_{05}+\beta_{15}*A+\beta_{25}*C+\beta_{35}*L1+\beta_{45}*I\{L2==1\}+\beta_{55}*I\{L2==2\})}{1+expit(\beta_{04}+\beta_{14}*A+\beta_{24}*C+\beta_{34}*L1+\beta_{44}*I\{L2==1\}+\beta_{54}*I\{L2==2\})+expit(\beta_{05}+\beta_{15}*A+\beta_{25}*C+\beta_{35}*L1+\beta_{45}*I\{L2==1\}+\beta_{55}*I\{L2==2\})}),$

the second mediator M2 from $Bernoulli(expit(\beta_{06}+\beta_{16}*A+\beta_{26}*C+\beta_{36}*L1+\beta_{46}*I\{L2==1\}+\beta_{56}*I\{L2==2\}))$.

5. Simulate the outcome Y from $Bernoulli(expit(\theta_0+\theta_1 A+\theta_{21}I\{M1==1\}+\theta_{22}I\{M1==2\}+\theta_{23}M2+\theta_{31}AI\{M1==1\}M2+\theta_{32}AI\{M1==2\}M2+\theta_4 C+\theta_5*L1+\theta_6*I\{L2==1\}+\theta_7*I\{L2==2\}))$.

9.1.2 True Parameters

Table 21: True Model Parameters for Data Simulation

Sample Size	θ_0	θ_1	θ_{21}	θ_{22}	θ_{23}	θ_{31}	θ_4	θ_5	θ_6	θ_7
10000	-5	0.8	1.8	1.2	1.5	0.2	0.1	0.3	0.4	0.2
β_{01}	β_{11}	β_{21}	β_{02}	β_{12}	β_{22}	β_{03}	β_{13}	β_{23}	β_{04}	β_{14}
-0.25	0.5	0.2	-0.25	0.5	0.2	-0.3	0.4	0.3	-0.25	0.5
β_{24}	β_{34}	β_{44}	β_{54}	β_{05}	β_{15}	β_{25}	β_{35}	β_{45}	β_{55}	β_{06}
0.2	0.1	0.3	0.25	-0.3	0.4	0.3	0.5	0.1	0.2	-0.25
β_{16}	β_{26}	β_{36}	β_{46}	β_{56}	P(A=1)	μ_C	σ_C			
0.5	0.2	0.1	0.3	0.25	0.4	1	1			

9.1.3 True Models

True model for the first post-exposure confounder:

$$logitE[L1|a,c]=\beta_{01}+\beta_{11}a+\beta_{21}c$$

True model for the second post-exposure confounder:

$$ln\frac{P(L2==1)}{P(L2==0)}=\beta_{02}+\beta_{12}a+\beta_{22}c$$

$$ln\frac{P(L2==2)}{P(L2==0)}=\beta_{03}+\beta_{13}a+\beta_{23}c$$

True model for the first mediator:

$$ln\frac{P(M1==1)}{P(M1==0)}=\beta_{04}+\beta_{14}a+\beta_{24}c+\beta_{34}l1+\beta_{44}I\{l2==1\}+\beta_{54}I\{l2==2\}$$

$$ln\frac{P(M1==2)}{P(M1==0)}=\beta_{05}+\beta_{15}a+\beta_{25}c+\beta_{35}l1+\beta_{45}I\{l2==1\}+\beta_{55}I\{l2==2\}$$

True model for the second mediator:

$$logitE[M2|a,c]=\beta_{06}+\beta_{16}a+\beta_{26}c+\beta_{36}l1+\beta_{46}I\{l2==1\}+\beta_{56}I\{l2==2\}$$

True model for the outcome:

$$logitE[Y|a,m^*,c]=\theta_0+\theta_1 a+\theta_{21}I\{m1^*==1\}+\theta_{22}I\{m1^*==2\}+\theta_{23}m2^*+$$
$$\theta_{31}aI\{m1^*==1\}m2^*+\theta_{32}aI\{m1^*==2\}m2^*+\theta_4 c+\theta_5 l1+\theta_6 I\{l2==1\}+\theta_7 I\{l2==2\}$$

9.2 Causal Effects and Standard Errors Estimated By the Marginal Structural Model

```
causal_mediation(data = df_multipleM_EMint_postcovar,  outcome = "binY_catMbinM_EMint",
                 exposure = "A", exposure.type = "binary",
                 mediator = c('M_bin',"M_cat"), covariates.pre = "C",
                 covariates.post = c("L_bin", "L_cat"),
                 covariates.post.type = c("binary", "categorical"),
                 EMint = TRUE, EMint.terms = c("A*M_bin"),
                 yreg = "logistic", mreg = c("logistic", "multinomial"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "msm")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##      2.46338266      2.45528952      2.40917959      1.37109226
##         tnie_rr           te_rr              pm         cde_err
##      1.34534338      3.30320750      0.36814659      0.22621683
##      intref_err      intmed_err         pie_err          te_err
##      1.22907269      0.47682571      0.37109226      2.30320750
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##      0.09821817      0.53363524      0.20702682      0.16111977
##      overall_pm     overall_int      overall_pe
##      0.36814659      0.74066206      0.90178183
##
## $effect_se
##  [1] 0.33225511 0.16750262 0.14144165 0.03511658 0.03257644 0.21149028
##  [7] 0.02766809 0.04818373 0.12933357 0.05554721 0.03511658 0.21149028
## [13] 0.01603487 0.01744097 0.01652502 0.01659198 0.02766809 0.01583710
## [19] 0.01603487
```

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

```
causal_mediation(data = df_multipleM_EMint_postcovar,  outcome = "binY_catMbinM_EMint",
                 exposure = "A", exposure.type = "binary",
                 mediator = c('M_bin',"M_cat"), covariates.pre = "C",
                 covariates.post = c("L_bin", "L_cat"),
                 covariates.post.type = c("binary", "categorical"),
                 EMint = TRUE, EMint.terms = c("A*M_bin"),
                 yreg = "logistic", mreg = c("logistic", "multinomial"), mval = list(0,0),
                 a_star = 0, a = 1,
                 est.method = "imputation", inf.method = "bootstrap", model = "g-formula")
```

```
## $effect_estimate
##          cde_rr         pnde_rr         tnde_rr         pnie_rr
##      2.38262499      2.47505272      2.44944816      1.36985716
##         tnie_rr           te_rr              pm         cde_err
##      1.35568590      3.35539409      0.37375544      0.21320345
##      intref_err      intmed_err         pie_err          te_err
##      1.26184927      0.51048421      0.36985716      2.35539409
##    cde_err_prop intref_err_prop intmed_err_prop    pie_err_prop
##      0.09051711      0.53572745      0.21672985      0.15702559
```

```
##      overall_pm     overall_int      overall_pe
##      0.37375544      0.75245730      0.90948289
##
## $effect_se
##  [1] 0.30038168 0.16109323 0.13822478 0.03428671 0.03291325 0.21341630
##  [7] 0.02611870 0.04497080 0.12727641 0.06285078 0.03428671 0.21341630
## [13] 0.01514655 0.01669488 0.01692773 0.01473228 0.02611870 0.01522334
## [19] 0.01514655
```