Preoperative Atelectasis

Part 5: Statistical Modelling of Atelectasis

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Setup

Packages used

```
if (!require("pacman", quietly = TRUE)) {
  install.packages("pacman")
}


pacman::p_load(
  tidyverse, # Used for basic data handling and visualization.
  RColorBrewer, #Color palettes for data visualization.
  table1, #Used to add lables to variables.
  dagitty, #Used in conjunction with https://www.dagitty.net/ to create
          #directed acyclic graph to inform statistical modelling.
  lavaan, #Used to create correlation matrix to assess conditional independencies.
  broom, #Used to exponentiate coefficients of regression models.
  sandwich, #Used to calculate robust standard errors for prevalence ratios.
  EValue, #Used to calculate E-values as sensitivity analysis.
  flextable, #Used to export tables.
  rms, #Used to model ordinal outcome (atelectasis percent) and
      #test proportional odds assumptions.
  VGAM, #Used to model partial proportional odds model.
  gt, #Used to present a summary of the results of regression models.
  report #Used to cite packages used in this session.
)
```

Session and package dependencies

```
R version 4.3.3 (2024-02-29 ucrt)
Platform: x86_64-w64-mingw32/x64 (64-bit)
Running under: Windows 11 x64 (build 22631)

Matrix products: default


locale:
[1] LC_COLLATE=Spanish_Mexico.utf8  LC_CTYPE=Spanish_Mexico.utf8
[3] LC_MONETARY=Spanish_Mexico.utf8 LC_NUMERIC=C
[5] LC_TIME=Spanish_Mexico.utf8
```

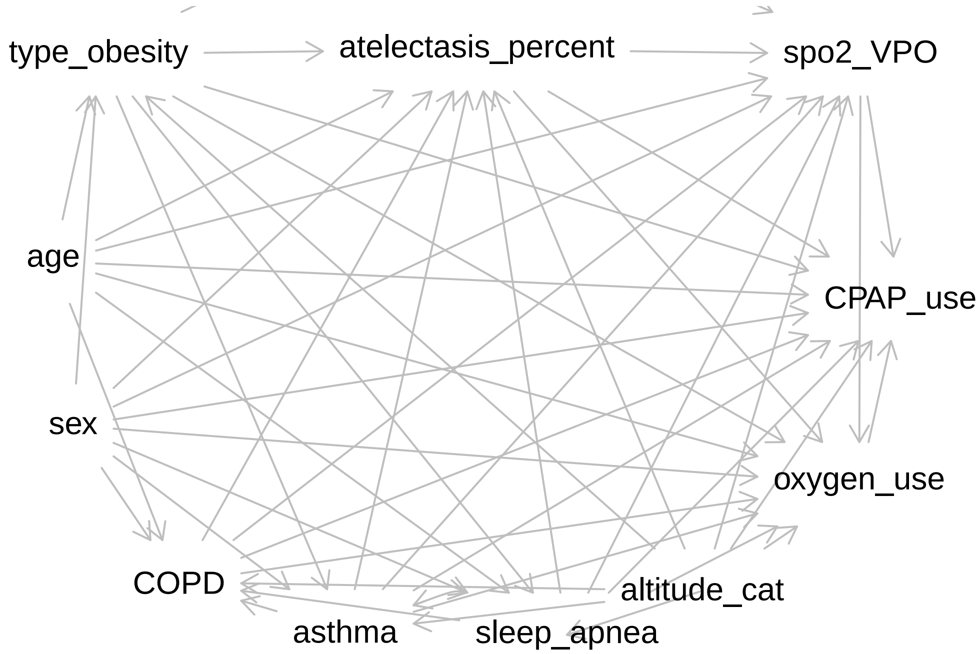
```
time zone: Europe/Berlin
tzcode source: internal

attached base packages:
[1] splines   stats4    stats     graphics  grDevices datasets  utils
[8] methods   base

other attached packages:
 [1] report_0.5.8       gt_0.10.1          VGAM_1.1-10        rms_6.8-0
 [5] Hmisc_5.1-2        flextable_0.9.5    EValue_4.1.3       sandwich_3.1-0
 [9] broom_1.0.5        lavaan_0.6-17      dagitty_0.3-4      table1_1.4.3
[13] RColorBrewer_1.1-3 lubridate_1.9.3    forcats_1.0.0      stringr_1.5.1
[17] dplyr_1.1.4        purrr_1.0.2        readr_2.1.5        tidyr_1.3.1
[21] tibble_3.2.1       ggplot2_3.5.0      tidyverse_2.0.0    pacman_0.5.1
```

DAG

DAG generated in the DAGitty website and sourced from the accompanying script ***DAG_atelectasis.R***



Testing of conditional independencies in DAG:

This procedure was performed as suggested in this article.

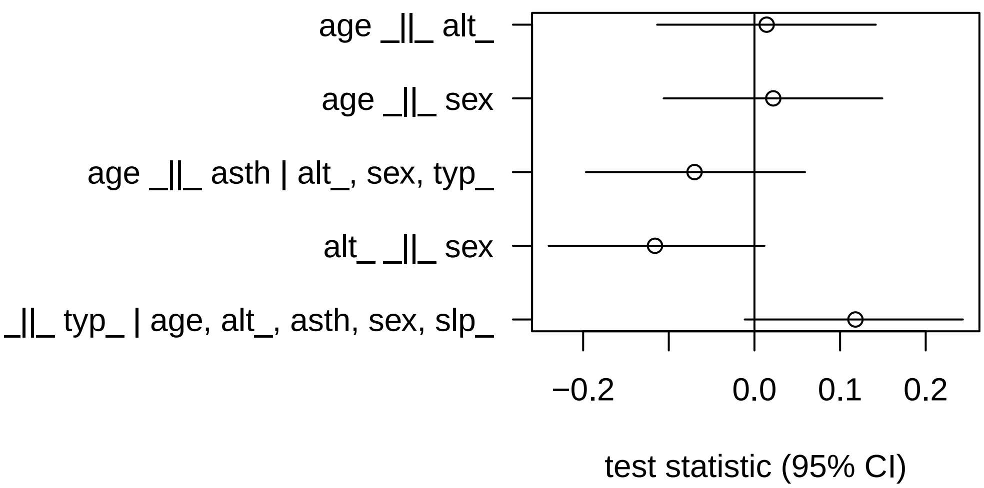
Implied conditional independencies:

```
COPD _||_ typ_ | age, alt_, asth, sex, slp_
age _||_ alt_
age _||_ asth | alt_, sex, typ_
age _||_ sex
alt_ _||_ sex
```

```
                                             estimate    p.value        2.5%
COPD _||_ typ_ | age, alt_, asth, sex, slp_  0.11792926 0.07361203 -0.01132074
age _||_ alt_                                0.01428788 0.82734350 -0.11362118
age _||_ asth | alt_, sex, typ_             -0.06994873 0.28798143 -0.19672176
age _||_ sex                                 0.02198502 0.73714174 -0.10601399
```

```
alt_ _||_ sex                              -0.11611884 0.07499274 -0.24031115
                                                97.5%
COPD _||_ typ_ | age, alt_, asth, sex, slp_ 0.24336140
age _||_ alt_                               0.14173361
age _||_ asth | alt_, sex, typ_             0.05910413
age _||_ sex                                0.14927141
alt_ _||_ sex                               0.01175596
```

Local tests results plot:



Conditional independence assumption OK as all confidence intervals cointain 0.

The minimal set of adjustment for models is ***age***, ***sex***, and **altitude_cat***.

Prevalence Ratio

This paper and accompanying code were used to calculate prevalence ratios.

A modified Poisson regression model with robust errors will be applied to obtain prevalence ratios.

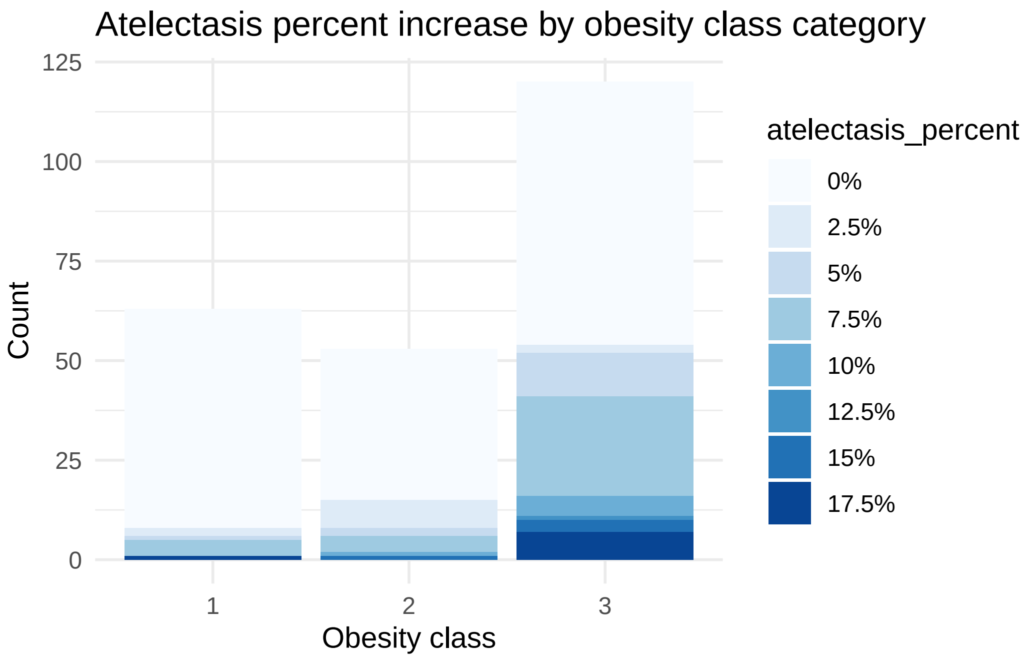
Prevalence ratios were calculated with the accompanying sourced script ***Prevalence_Ratio.R***

Table 2

Category	PR	SE	95%CI	aPR	aSE	a95%CI	Evalue	Evalue_lower
Class 2 Obesity	2.23	0.40	1.03-4.84	2.17	0.39	1-4.7	3.76	1.00
Class 3 Obesity	3.54	0.35	1.8-6.97	3.47	0.35	1.77-6.83	6.40	2.94

Ordinal Logistic Regression Model

This modelling strategy was performed according to:
- Harrel, Frank. March, 2022. "Assessing the Proportional Odds Assumption and its Impact". Statistical Thinking. March 9, 2022.



Check proportional odds assumption for main variable of interest:

	Model Likelihood Ratio Test	Discrimination Indexes	Rank Discrim. Indexes
Obs 236	LR ^{2} 25.40	R^2 0.113	0.313
Distinct Y 8	d.f. 2	$R^2_{2,236}$ 0.094	
$Y_{0.5}$ 1	Pr(> ^{2}) <0.0001	$R^2_{2,163.1}$ 0.134	
max | log $L/$ | 3×10^{-7}	Score ^{2} 23.88	|Pr(Y median)-½| 0.169	
	Pr(> ^{2}) <0.0001		

		S.E.	Wald Z	Pr(>|Z|)
y 2.5%	-1.9303	0.3774	-5.11	<0.0001
y 5%	-2.1743	0.3829	-5.68	<0.0001

		S.E.	Wald Z	Pr(>|Z|)
y 7.5%	-2.5247	0.3915	-6.45	<0.0001
y 10%	-3.7623	0.4385	-8.58	<0.0001
y 12.5%	-4.1806	0.4665	-8.96	<0.0001
y 15%	-4.2669	0.4735	-9.01	<0.0001
y 17.5%	-4.6969	0.5162	-9.10	<0.0001
type_obesity=2	0.8866	0.4802	1.85	0.0648
type_obesity=3	1.8038	0.4186	4.31	<0.0001

Odds ratio for type obesity in an univariable model:

Effects Response: `atelectasis_percent`	Low	High	Δ	Effect	S.E.	Lower 0.95	Upper 0.95
type_obesity --- 2:1	1	2		0.8866	0.4802	-0.05454	1.828
Odds Ratio	1	2		2.4270		0.94690	6.220
type_obesity --- 3:1	1	3		1.8040	0.4186	0.98340	2.624
Odds Ratio	1	3		6.0730		2.67400	13.790

Proportional odds assumption:

Wald Statistics for `atelectasis_percent`	^{2}	d.f.	P
type_obesity	21.55	2	<0.0001
TOTAL	21.55	2	<0.0001

This shows that the proportional odds assumption is not met since p<0.05 in the ANOVA test.

There are a couple of alternatives for modelling. One would be to fit a full multinomial model, although this would be expected to be unoptimal due to loss of statistical power, less parsimonious, and difficult interpretation compared to ordinal. A second approach would be to fir a partial proportional odds model allowing nominal effects for obesity class categories.

However, it is known that violations of the proportional odds assumption may not be as serious in some cases, as explained in the reference provided before. Thus, I will test how these 2 alternative modelling strategies would compare against a proportional odds model.

As a note, it is known that having few observations per category does not affect the results of ordinal regression, and that some categories may need to be combined to assess proportional odds assumption. REF

Thus, I will create atelectasis percent categories by collapsing non-integer atelectasis percentage categories (i.e., 2.5%, 7.5%) against the immediate lower category, resulting in 5% jumps (0-5%, 5-10%, 10-15%, and 15%) which meet the assumption of being equi-distant categories for ordinal regression:

```
 0%  5% 10% 15%
170  47   7  12
```

Are subgroups better represented now?

```
       1  2  3
  0%  57 45 68
  5%   5  6 36
  10%  0  1  6
  15%  1  1 10
```

Some improvement.

Will now test the impact of not meeting the proportional odds assumption in a model adjusted for covariates:

Comparison of proportional odds (PO), partial proportional odds (PPO), and multinomial model:

	PO	PPO	Multinomial
Deviance	391.4100	388.4564	374.3167
d.f.	8	12	18
AIC	407.4100	412.4564	410.3167
p	5	9	15
LR chi^2	72.00508	74.95868	89.09845
LR - p	67.00508	65.95868	74.09845
LR chi^2 test for PO		2.953603	17.093367
d.f.		4	10
Pr(>chi^2)		0.56561956	0.07232336
MCS R2	0.2629550	0.2721218	0.3144513

<table>
<tr><td>MCS R2 adj</td><td>0.2471730</td><td>0.2438276</td><td>0.2694638</td></tr>
<tr><td>McFadden R2</td><td>0.1553792</td><td>0.1617528</td><td>0.1922649</td></tr>
<tr><td>McFadden R2 adj</td><td>0.1338003</td><td>0.1229107</td><td>0.1275281</td></tr>
<tr><td>Mean |difference| from PO</td><td></td><td>0.01328685</td><td>0.03505332</td></tr>
</table>

Lowest AIC is for the proportional odds (PO) model. Likewise, the McFadden adjusted R2 is the highest for the PO model. Thus, I will present the PO model despite proportional odds assumption not met as this is not causing serious problems and seems to be the best model according to the results shown and discussed.

Univariate models for covariates:

<table>
<tr><th></th><th>Model Likelihood
Ratio Test</th><th>Discrimination
Indexes</th><th>Rank Discrim.
Indexes</th></tr>
<tr><td>Obs 236
Distinct Y 8
$Y_{0.5}$ 1
max | log
$L/$ | 2×10^{-5}</td><td>LR ^{2} 58.42
d.f. 1
Pr(> ^{2}) <0.0001
Score ^{2} 70.39

Pr(> ^{2}) <0.0001</td><td>R^2 0.244
$R^2{}_{1,236}$ 0.216
$R^2{}_{1,163.1}$ 0.297
|Pr(Y
median)-½| 0.275</td><td>0.539</td></tr>
</table>

<table>
<tr><th></th><th></th><th>S.E.</th><th>Wald Z</th><th>Pr(>|Z|)</th></tr>
<tr><td>y 2.5%</td><td>-1.1960</td><td>0.1679</td><td>-7.12</td><td><0.0001</td></tr>
<tr><td>y 5%</td><td>-1.4963</td><td>0.1824</td><td>-8.20</td><td><0.0001</td></tr>
<tr><td>y 7.5%</td><td>-1.9260</td><td>0.2063</td><td>-9.34</td><td><0.0001</td></tr>
<tr><td>y 10%</td><td>-3.4122</td><td>0.3139</td><td>-10.87</td><td><0.0001</td></tr>
<tr><td>y 12.5%</td><td>-3.8627</td><td>0.3554</td><td>-10.87</td><td><0.0001</td></tr>
<tr><td>y 15%</td><td>-3.9514</td><td>0.3648</td><td>-10.83</td><td><0.0001</td></tr>
<tr><td>y 17.5%</td><td>-4.3894</td><td>0.4197</td><td>-10.46</td><td><0.0001</td></tr>
<tr><td>sleep_apnea=Yes</td><td>2.7008</td><td>0.3665</td><td>7.37</td><td><0.0001</td></tr>
</table>

Effects Response: `atelectasis_percent`	Low	High	Δ	Effect	S.E.	Lower 0.95	Upper 0.95
sleep_apnea --- Yes:No	1	2		2.701	0.3665	1.982	3.419
Odds Ratio	1	2		14.890		7.260	30.540

	Model Likelihood Ratio Test	Discrimination Indexes	Rank Discrim. Indexes
Obs 236	LR ^{2} 3.06	R^2 0.014	0.104
Distinct Y 8	d.f. 1	$R^2{}_{1,236}$ 0.009	
$Y_{0.5}$ 1	Pr(> ^{2}) 0.0802	$R^2{}_{1,163.1}$ 0.013	
max $\vert$ log	Score ^{2} 2.69	$\vert$Pr(Y	
$L/$ $\vert$ 0.0001		median)-½$\vert$ 0.175	
	Pr(> ^{2}) 0.1007		

		S.E.	Wald Z	Pr(>$\vert Z\vert$)
y 2.5%	-0.6588	0.1430	-4.61	<0.0001
y 5%	-0.8826	0.1487	-5.94	<0.0001
y 7.5%	-1.2022	0.1602	-7.50	<0.0001
y 10%	-2.3759	0.2411	-9.85	<0.0001
y 12.5%	-2.7833	0.2868	-9.70	<0.0001
y 15%	-2.8681	0.2977	-9.63	<0.0001
y 17.5%	-3.2923	0.3608	-9.12	<0.0001
asthma=Yes	-1.0153	0.6414	-1.58	0.1135

Effects Response: `atelectasis_percent`	Low	High	Δ	Effect	S.E.	Lower 0.95	Upper 0.95
asthma --- Yes:No	1	2		-1.0150	0.6414	-2.2720	0.2419
Odds Ratio	1	2		0.3623		0.1031	1.2740

	Model Likelihood Ratio Test	Discrimination Indexes	Rank Discrim. Indexes
Obs 236	LR ^{2} 2.08	R^2 0.010	0.096
Distinct Y 8	d.f. 1	$R^2{}_{1,236}$ 0.005	
$Y_{0.5}$ 1	Pr(> ^{2}) 0.1490	$R^2{}_{1,163.1}$ 0.007	
max $\vert$ log	Score ^{2} 2.24	$\vert$Pr(Y	
$L/$ $\vert$ 3×10^{-7}		median)-½$\vert$ 0.173	
	Pr(> ^{2}) 0.1347		

		S.E.	Wald Z	Pr(>|Z|)
y 2.5%	-0.7883	0.1470	-5.36	<0.0001
y 5%	-1.0111	0.1533	-6.60	<0.0001
y 7.5%	-1.3318	0.1655	-8.05	<0.0001
y 10%	-2.5139	0.2471	-10.17	<0.0001
y 12.5%	-2.9216	0.2921	-10.00	<0.0001
y 15%	-3.0059	0.3028	-9.93	<0.0001
y 17.5%	-3.4289	0.3651	-9.39	<0.0001
sex=Man	0.6380	0.4315	1.48	0.1392

Effects
Response: `atelectasis_percent`

	Low	High	Δ	Effect	S.E.	Lower 0.95	Upper 0.95
sex --- Man:Woman	1	2		0.638	0.4315	-0.2076	1.484
Odds Ratio	1	2		1.893		0.8125	4.409

	Model Likelihood Ratio Test	Discrimination Indexes	Rank Discrim. Indexes
Obs 236 Distinct Y 8 $Y_{0.5}$ 1 max | log $L/$ | 0.003	LR ^{2} 0.63 d.f. 1 Pr(> ^{2}) 0.4273 Score ^{2} 0.63 Pr(> ^{2}) 0.4274	R^2 0.003 $R^2{}_{1,236}$ 0.000 $R^2{}_{1,163.1}$ 0.000 |Pr(Y median)-½| 0.173	0.049

		S.E.	Wald Z	Pr(>|Z|)
y 2.5%	-0.2840	0.5705	-0.50	0.6186
y 5%	-0.5054	0.5715	-0.88	0.3765
y 7.5%	-0.8240	0.5733	-1.44	0.1506
y 10%	-1.9975	0.5986	-3.34	0.0008
y 12.5%	-2.4040	0.6188	-3.89	0.0001
y 15%	-2.4885	0.6239	-3.99	<0.0001
y 17.5%	-2.9121	0.6559	-4.44	<0.0001
age	-0.0110	0.0138	-0.79	0.4278

Effects Response: `atelectasis_percent`	Low	High	Δ	Effect	S.E.	Lower 0.95	Upper 0.95
age	32.75	48.25	15.5	-0.1702	0.2146	-0.5908	0.2504
Odds Ratio	32.75	48.25	15.5	0.8435		0.5539	1.2850

	Model Likelihood Ratio Test	Discrimination Indexes	Rank Discrim. Indexes
Obs 236	LR ^{2} 0.06	R^2 0.000	0.016
Distinct Y 8	d.f. 1	$R^2_{1,236}$ 0.000	
$Y_{0.5}$ 1	Pr(> ^{2}) 0.8060	$R^2_{1,163.1}$ 0.000	
max $\vert$ log $L/\ \vert$ 3×10^{-6}	Score ^{2} 0.06	$\vert$Pr(Y median)-½$\vert$ 0.174	
	Pr(> ^{2}) 0.8050		

		S.E.	Wald Z	Pr(>$\vert Z \vert$)
y 2.5%	-0.7383	0.1491	-4.95	<0.0001
y 5%	-0.9595	0.1551	-6.19	<0.0001
y 7.5%	-1.2772	0.1667	-7.66	<0.0001
y 10%	-2.4491	0.2458	-9.96	<0.0001
y 12.5%	-2.8556	0.2906	-9.83	<0.0001
y 15%	-2.9401	0.3014	-9.76	<0.0001
y 17.5%	-3.3631	0.3638	-9.24	<0.0001
altitude_cat=Moderate	0.0964	0.3906	0.25	0.8051

Effects Response: `atelectasis_percent`	Low	High	Δ	Effect	S.E.	Lower 0.95	Upper 0.95
altitude_cat --- Moderate:Low	1	2		0.09641	0.3906	-0.6692	0.862
Odds Ratio	1	2		1.10100		0.5121	2.368

Multivariable model

	Model Likelihood Ratio Test	Discrimination Indexes	Rank Discrim. Indexes
Obs 236	LR ^{2} 26.65	R^2 0.119	0.305
Distinct Y 8	d.f. 5	$R^2{}_{5,236}$ 0.088	
$Y_{0.5}$ 1	Pr(> ^{2}) <0.0001	$R^2{}_{5,163.1}$ 0.124	
max $\lvert$ log $L/$ $\lvert$ 2×10^{-5}	Score ^{2} 25.19	$\lvert$Pr(Y median)-½$\lvert$ 0.178	
	Pr(> ^{2}) 0.0001		

		S.E.	Wald Z	Pr(>$\lvert Z\rvert$)
y 2.5%	-1.8809	0.7179	-2.62	0.0088
y 5%	-2.1262	0.7208	-2.95	0.0032
y 7.5%	-2.4794	0.7253	-3.42	0.0006
y 10%	-3.7245	0.7531	-4.95	<0.0001
y 12.5%	-4.1421	0.7706	-5.38	<0.0001
y 15%	-4.2282	0.7748	-5.46	<0.0001
y 17.5%	-4.6582	0.8011	-5.82	<0.0001
type_obesity=2	0.8564	0.4815	1.78	0.0753
type_obesity=3	1.7695	0.4222	4.19	<0.0001
sex=Man	0.4720	0.4463	1.06	0.2902
age	-0.0024	0.0145	-0.16	0.8701
altitude_cat=Moderate	0.1856	0.4034	0.46	0.6455

Effects Response: `atelectasis_percent`	Low	High	Δ	Effect	S.E.	Lower 0.95	Upper 0.95
age	32.75	48.25	15.5	-0.03685	0.2253	-0.4785	0.4048
Odds Ratio	32.75	48.25	15.5	0.96380		0.6197	1.4990
type_obesity --- 2:1	1.00	2.00		0.85640	0.4815	-0.0874	1.8000
Odds Ratio	1.00	2.00		2.35500		0.9163	6.0510
type_obesity --- 3:1	1.00	3.00		1.76900	0.4222	0.9420	2.5970
Odds Ratio	1.00	3.00		5.86800		2.5650	13.4200
sex --- Man:Woman	1.00	2.00		0.47200	0.4463	-0.4027	1.3470
Odds Ratio	1.00	2.00		1.60300		0.6685	3.8440
altitude_cat --- Moderate:Low	1.00	2.00		0.18560	0.4034	-0.6051	0.9762
Odds Ratio	1.00	2.00		1.20400		0.5460	2.6540

Package References

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