Preoperative Atelectasis

Part 5: Statistical Modelling of Atelectasis

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2023-12-01

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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.
  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.
)
```

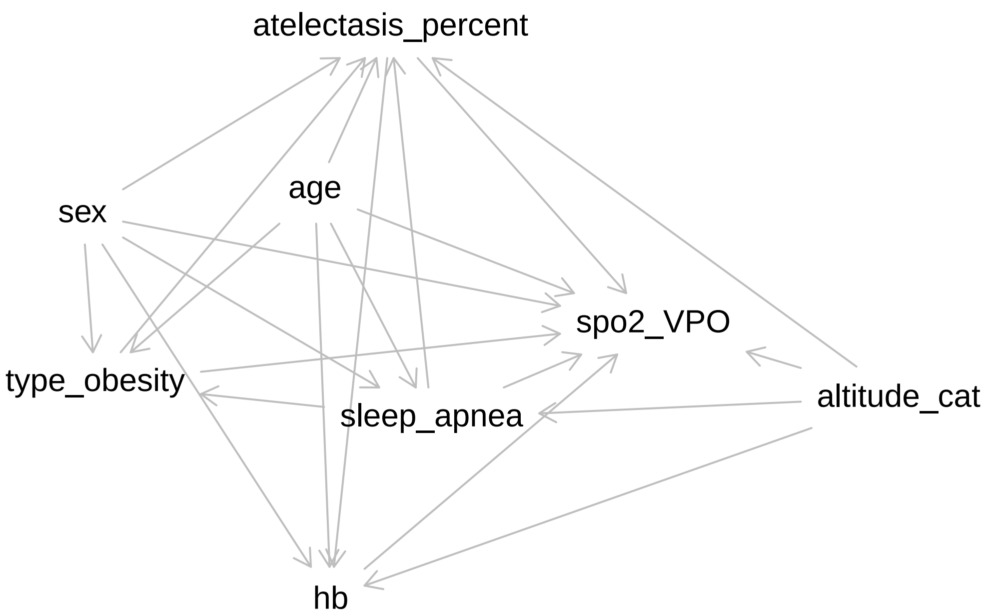
Session and package dependencies

```
R version 4.3.2 (2023-10-31 ucrt)
Platform: x86_64-w64-mingw32/x64 (64-bit)
Running under: Windows 11 x64 (build 22621)

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_0.5.7       gt_0.10.0          VGAM_1.1-9         rms_6.7-1
 [5] Hmisc_5.1-1        flextable_0.9.4    sandwich_3.0-2     broom_1.0.5
 [9] lavaan_0.6-16      dagitty_0.3-1      table1_1.4.3       RColorBrewer_1.1-3
[13] lubridate_1.9.3    forcats_1.0.0      stringr_1.5.1      dplyr_1.1.4
[17] purrr_1.0.2        readr_2.1.4        tidyr_1.3.0        tibble_3.2.1
```

```
[21] ggplot2_3.4.4      tidyverse_2.0.0    pacman_0.5.1
```

DAG

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



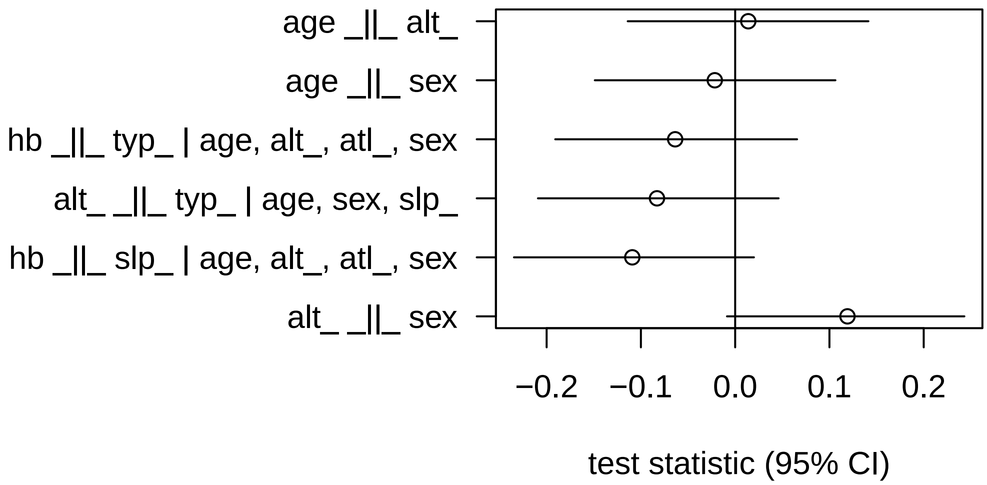
Testing of conditional independencies in DAG:

This procedure was performed as suggested in this article.

Implied conditional independencies:

```
age _||_ alt_
age _||_ sex
alt_ _||_ sex
alt_ _||_ typ_ | age, sex, slp_
hb _||_ slp_ | age, alt_, atl_, sex
hb _||_ typ_ | age, alt_, atl_, sex
```

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 ***sleep_apnea***.

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.

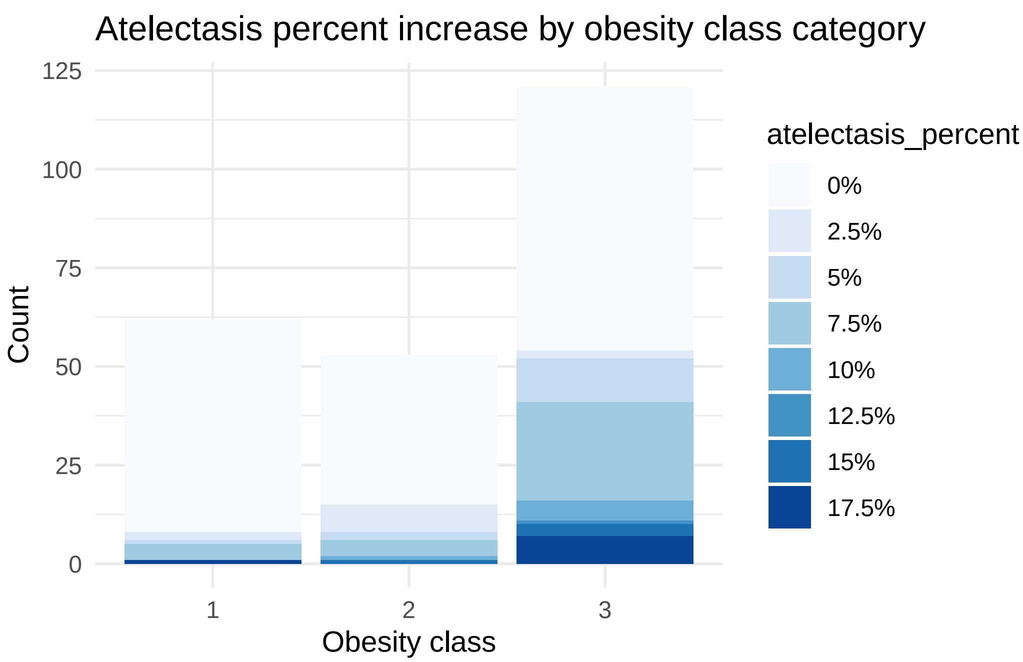
Prevalence ratios were calculated with the accompanying sourced script ***Prevalence_Ratio.R***

Table 2

Category	PR	SE	95%CI	aPR	aSE	a95%CI
Class 2 Obesity	2.19	0.40	1.01-4.76	1.97	0.37	0.95-4.09
Class 3 Obesity	3.46	0.35	1.76-6.8	3.15	0.33	1.66-5.97

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} 24.41	R^2 0.109	0.308
Distinct Y 8	d.f. 2	$R^2_{2,236}$ 0.091	
$Y_{0.5}$ 1	Pr(> ^{2}) <0.0001	$R^2_{2,163.1}$ 0.128	
max $|$ log $L/$ $|$ 3×10^{-7}	Score ^{2} 22.96	$|$Pr(Y median)-½$|$ 0.170	
	Pr(> ^{2}) <0.0001		

		S.E.	Wald Z	Pr(>$|Z|$)
y 2.5%	-1.9123	0.3778	-5.06	<0.0001
y 5%	-2.1553	0.3832	-5.62	<0.0001

		S.E.	Wald Z	$\Pr(>\lvert Z\rvert)$
y 7.5%	-2.5045	0.3918	-6.39	<0.0001
y 10%	-3.7397	0.4386	-8.53	<0.0001
y 12.5%	-4.1576	0.4666	-8.91	<0.0001
y 15%	-4.2438	0.4736	-8.96	<0.0001
y 17.5%	-4.6737	0.5162	-9.05	<0.0001
type_obesity=2	0.8682	0.4805	1.81	0.0708
type_obesity=3	1.7702	0.4187	4.23	<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		0.8682	0.4805	-0.07355	1.810
Odds Ratio	1	2		2.3830		0.92910	6.110
type_obesity --- 3:1	1	3		1.7700	0.4187	0.94970	2.591
Odds Ratio	1	3		5.8720		2.58500	13.340

Proportional odds assumption:

Wald Statistics for `atelectasis_percent`

	^{2}	d.f.	P
type_obesity	20.79	2	<0.0001
TOTAL	20.79	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%  56 45 69
  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	416.6654	412.1552	401.0035
d.f.	8	12	18
AIC	432.6654	436.1552	437.0035
p	5	9	15
LR chi^2	46.74975	51.25994	62.41161
LR - p	41.74975	42.25994	47.41161
LR chi^2 test for PO		4.510197	15.661861
d.f.		4	10
Pr(>chi^2)		0.3413401	0.1097298
MCS R2	0.1797057	0.1952335	0.2323765

MCS R2 adj	0.1621412	0.1639506	0.1820030
McFadden R2	0.1008809	0.1106134	0.1346775
McFadden R2 adj	0.07930200	0.07177138	0.06994077
Mean $\lvert\text{difference}\rvert$ from PO		0.01698003	0.03155911

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:

	Model Likelihood Ratio Test	Discrimination Indexes	Rank Discrim. Indexes
Obs 236	LR ^{2} 26.05	R^2 0.116	0.377
Distinct Y 8	d.f. 1	$R^2{}_{1,236}$ 0.101	
$Y_{0.5}$ 1	Pr(> ^{2}) <0.0001	$R^2{}_{1,163.1}$ 0.142	
max $\lvert$ log $L/$ $\lvert$ 8×10^{-7}	Score ^{2} 32.43	$\lvert$Pr(Y median)-½$\lvert$ 0.224	
	Pr(> ^{2}) <0.0001		

		S.E.	Wald Z	Pr(>$\lvert Z\rvert$)
y 2.5%	-0.9434	0.1518	-6.21	<0.0001
y 5%	-1.1940	0.1611	-7.41	<0.0001
y 7.5%	-1.5483	0.1768	-8.76	<0.0001
y 10%	-2.8408	0.2697	-10.53	<0.0001
y 12.5%	-3.2688	0.3145	-10.39	<0.0001
y 15%	-3.3563	0.3250	-10.33	<0.0001
y 17.5%	-3.7933	0.3856	-9.84	<0.0001
sleep_apnea=Yes	2.1919	0.4287	5.11	<0.0001

Effects
Response:
`atelectasis_percent`

	Low	High	Δ	Effect	S.E.	Lower 0.95	Upper 0.95
sleep_apnea --- Yes:No	1	2		2.192	0.4287	1.352	3.032
Odds Ratio	1	2		8.952		3.864	20.740

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

		S.E.	Wald Z	$\Pr(>\lvert Z\rvert)$
y 2.5%	-0.1503	0.4093	-0.37	0.7134
y 5%	-0.3731	0.4100	-0.91	0.3628
y 7.5%	-0.6938	0.4119	-1.68	0.0921
y 10%	-1.8759	0.4418	-4.25	<0.0001
y 12.5%	-2.2836	0.4676	-4.88	<0.0001
y 15%	-2.3679	0.4745	-4.99	<0.0001
y 17.5%	-2.7909	0.5164	-5.40	<0.0001
sex=Woman	-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	2	1		0.638	0.4315	-0.2076	1.484
Odds Ratio	2	1		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 $\lvert$ log L/ $\lvert$ 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 $\lvert$Pr(Y median)-½$\lvert$ 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

Multivariable model

	Model Likelihood Ratio Test	Discrimination Indexes	Rank Discrim. Indexes
Obs 236	LR ^{2} 47.02	R^2 0.201	0.421
Distinct Y 8	d.f. 5	$R^2{}_{5,236}$ 0.163	
$Y_{0.5}$ 1	Pr(> ^{2}) <0.0001	$R^2{}_{5,163.1}$ 0.227	
max | log L/ | 6×10^{-5}	Score ^{2} 50.97	|Pr(Y median)-½| 0.220	
	Pr(> ^{2}) <0.0001		

		S.E.	Wald Z	Pr(>|Z|)
y 2.5%	-2.1985	0.9201	-2.39	0.0169
y 5%	-2.4694	0.9232	-2.67	0.0075
y 7.5%	-2.8511	0.9268	-3.08	0.0021
y 10%	-4.1901	0.9497	-4.41	<0.0001
y 12.5%	-4.6295	0.9666	-4.79	<0.0001
y 15%	-4.7201	0.9709	-4.86	<0.0001
y 17.5%	-5.1689	0.9948	-5.20	<0.0001
type_obesity=2	0.8102	0.4921	1.65	0.0996

		S.E.	Wald Z	Pr($>|Z|$)
type_obesity=3	1.6660	0.4282	3.89	<0.0001
sleep_apnea=Yes	2.1999	0.4783	4.60	<0.0001
sex=Woman	0.3976	0.5132	0.77	0.4385
age	-0.0054	0.0149	-0.36	0.7160

Effects
Response:
`atelectasis_percent`

	Low	High	Δ	Effect	S.E.	Lower 0.95	Upper 0.95
age	32.75	48.25	15.5	-0.08401	0.2309	-0.5366	0.3686
Odds Ratio	32.75	48.25	15.5	0.91940		0.5847	1.4460
type_obesity --- 2:1	1.00	2.00		0.81020	0.4921	-0.1542	1.7750
Odds Ratio	1.00	2.00		2.24800		0.8571	5.8980
type_obesity --- 3:1	1.00	3.00		1.66600	0.4282	0.8268	2.5050
Odds Ratio	1.00	3.00		5.29100		2.2860	12.2500
sleep_apnea --- Yes:No	1.00	2.00		2.20000	0.4783	1.2630	3.1370
Odds Ratio	1.00	2.00		9.02400		3.5340	23.0400
sex --- Man:Woman	2.00	1.00		-0.39760	0.5132	-1.4030	0.6082
Odds Ratio	2.00	1.00		0.67200		0.2458	1.8370

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