Preoperative Atelectasis

Part 6: Statistical Modelling of SpO2

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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.
```

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] grid stats graphics grDevices utils datasets methods

[8] base

other attached packages:

[1] gratia_0.8.1	${\tt gtsummary_1.7.2}$	gt_0.10.0	mgcv_1.9-0
[5] nlme_3.1-163	<pre>gridExtra_2.3</pre>	table1_1.4.3	RColorBrewer_1.1-3
[9] lubridate_1.9.3	forcats_1.0.0	stringr_1.5.0	dplyr_1.1.3
[13] purrr_1.0.2	readr_2.1.4	tidyr_1.3.0	tibble_3.2.1
[17] ggplot2_3.4.4	tidyverse_2.0.0	pacman_0.5.1	

Model SpO2

The SpO2 variable does not have a normal distribution. Furthermore, the distance between 1% increases in SpO2 cannot be considered equidistant increases since values are determined from the S-shaped curve of hemoglobin saturation. This is the reason why the distribution of SpO2 is negatively skewed, with upper values reaching the saturation point of the hemoglobin curve.

Therefore, modelling SpO2 as a linear term could be potentially misleading. Nonetheless, a model assuming a gaussian distribution for SpO2 may potentially be easier to understand and communicate.

Thus, I first created model SpO2 assuming a gaussian distribution and then applied a fractional regression model which is more appropriate for the distribution of this variable. The rationale for this was that if conclusions were not different with both models, presenting a model assuming a gaussian distribution would have been easier to understand and communicate. However, since conclusions were indeed different, I will present the results for the more appropriate fractional regression model.

Fractional regression model

Convert SpO2 to fractional values between 0 and 1 to model.

```
data <- data %>% mutate(spo2_fraction = spo2_VPO/100)
```

Empty model

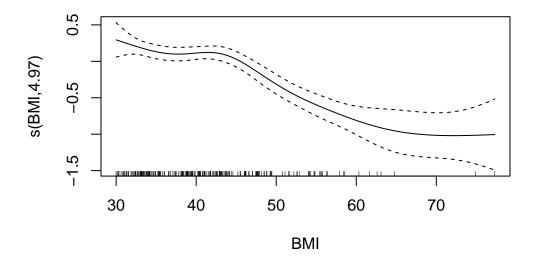
```
R-sq.(adj) = 0 Deviance explained = -3.04e-13\% GCV = 0.015586 Scale est. = 0.015728 n = 236
```

Smooth BMI

Model with a smooth BMI term as the only explanatory variable.

Since we are now using a different family function (quasibinomial with logit link) and we are no longer assuming a Gaussian distribution, it is important to determine the k value that offers the best representation of the change in the outcome variable with this function. I checked this by varying the value of k in the following code and $k=8^*$ offered the best visual representation with the largest increase in deviance explained and optimal k.value. This can be replicated by varying the value of k in the code:

```
Family: quasibinomial
Link function: logit
Formula:
spo2_fraction ~ s(BMI, k = 8)
Parametric coefficients:
           Estimate Std. Error t value Pr(>|t|)
(Intercept) 2.98458
                       0.03212
                                 92.92
                                         <2e-16 ***
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Approximate significance of smooth terms:
        edf Ref.df
                       F p-value
s(BMI) 4.968 5.829 21.79 <2e-16 ***
Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
R-sq.(adj) = 0.386 Deviance explained = 34.1%
GCV = 0.010718 Scale est. = 0.010826 n = 236
```



OSA only

Fit a model that only contains OSA:

```
Family: quasibinomial Link function: logit
```

Formula:

spo2_fraction ~ sleep_apnea

Parametric coefficients:

```
Estimate Std. Error t value Pr(>|t|)
(Intercept) 3.00191 0.03833 78.326 < 2e-16 ***
sleep_apneaYes -0.59672 0.10971 -5.439 1.34e-07 ***
---
```

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

R-sq.(adj) = 0.115 Deviance explained = 10.3% GCV = 0.014099 Scale est. = 0.014441 n = 236

Atelectasis percent

Fit a model that only contains at lectasis percent:

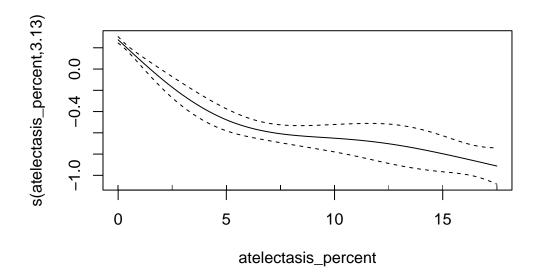
```
Family: quasibinomial
Link function: logit
Formula:
spo2_fraction ~ atelectasis_percent_factor
Parametric coefficients:
                                Estimate Std. Error t value Pr(>|t|)
(Intercept)
                                 3.31028
                                            0.03416 96.903 < 2e-16 ***
                                            0.10713 -5.064 8.45e-07 ***
atelectasis_percent_factor2.5%
                               -0.54251
atelectasis_percent_factor5%
                                -0.79798
                                            0.08751 -9.118 < 2e-16 ***
atelectasis_percent_factor7.5%
                                -0.87205
                                            0.06127 -14.233 < 2e-16 ***
atelectasis_percent_factor10%
                                            0.11831 -8.424 4.10e-15 ***
                                -0.99665
                                            0.29467
atelectasis_percent_factor12.5% -0.86794
                                                     -2.945 0.00356 **
atelectasis_percent_factor15%
                                -0.99665
                                            0.14287 -6.976 3.26e-11 ***
atelectasis_percent_factor17.5% -1.21954
                                            0.09601 -12.703 < 2e-16 ***
               0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Signif. codes:
R-sq.(adj) = 0.676
                      Deviance explained = 62.6%
```

Atelectasis percent smooth term

Fit a model that contains at lectasis percent under a smooth term.

GCV = 0.006189 Scale est. = 0.0063048 n = 236

Note that this is a different function than models created in Part 4 since a gaussian function is no longer used. Thus, I determined the optimal k value which is k=5. This is comparable to having at electasis percentage as categorical as will be shown later. However, the smooth term will allow to have a visual representation of the partial effect of at electasis percent on SpO2. Thus, I will keep the smooth term to model the effect of at electasis.



```
Family: quasibinomial
Link function: logit
Formula:
spo2_fraction ~ s(atelectasis_percent, k = 5)
Parametric coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept) 3.02654
                        0.02526
                                  119.8
                                          <2e-16 ***
               0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Signif. codes:
Approximate significance of smooth terms:
                         edf Ref.df
                                        F p-value
s(atelectasis_percent) 3.131 3.592 105.3 <2e-16 ***
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
R-sq.(adj) = 0.676
                     Deviance explained = 62.3%
GCV = 0.0060413 Scale est. = 0.0062171 n = 236
```

s(BMI) + s(atelectasis percentage)

Fit model sBMI plus atelectasis percentage:

```
Family: quasibinomial
Link function: logit
Formula:
spo2_fraction ~ s(BMI, k = 8) + s(atelectasis_percent, k = 5)
Parametric coefficients:
           Estimate Std. Error t value Pr(>|t|)
(Intercept) 3.02704 0.02516 120.3 <2e-16 ***
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Approximate significance of smooth terms:
                        edf Ref.df
                                       F p-value
s(BMI)
                      3.461 4.248 1.12
                                         0.314
s(atelectasis_percent) 3.059 3.524 54.23 <2e-16 ***
Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' 1
R-sq.(adj) = 0.688 Deviance explained = 63.3%
GCV = 0.0060456 Scale est. = 0.0061669 n = 236
OSA + BMI
Model sleep apnea plus sBMI:
Family: quasibinomial
Link function: logit
Formula:
spo2_fraction ~ s(BMI, k = 8) + sleep_apnea
Parametric coefficients:
              Estimate Std. Error t value Pr(>|t|)
(Intercept)
               3.02564
                          0.03246 93.208 < 2e-16 ***
sleep_apneaYes -0.45017
                          0.09492 -4.743 3.71e-06 ***
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
Approximate significance of smooth terms:
        edf Ref.df
                     F p-value
s(BMI) 5.055 5.91 19.95 <2e-16 ***
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
R-sq.(adj) = 0.43 Deviance explained = 39.8%
GCV = 0.0098803 Scale est. = 0.0099659 n = 236
sBMI + OSA + atelectasis percent
Model sBMI + sleep apnea + atelectasis percent:
Family: quasibinomial
Link function: logit
Formula:
spo2_fraction ~ s(BMI, k = 8) + sleep_apnea + s(atelectasis_percent,
   k = 5)
Parametric coefficients:
              Estimate Std. Error t value Pr(>|t|)
               (Intercept)
sleep_apneaYes -0.09196
                         0.07673 - 1.199
                                           0.232
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Approximate significance of smooth terms:
                       edf Ref.df
                                  F p-value
                     1.083 1.160 1.794 0.192
s(BMI)
s(atelectasis_percent) 3.091 3.554 49.259 <2e-16 ***
Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
R-sq.(adj) = 0.681
                    Deviance explained = 62.8%
GCV = 0.0060627 Scale est. = 0.0062147 n = 236
```

Adjusted model BMI

Fit model for BMI adjusted for confounders:

```
Family: quasibinomial
Link function: logit
Formula:
spo2_fraction ~ s(BMI, k = 8) + sex + age + sleep_apnea + hb +
   altitude cat
Parametric coefficients:
                           Estimate Std. Error t value Pr(>|t|)
                                     0.428386 8.236 1.50e-14 ***
(Intercept)
                           3.528269
                          -0.117513 0.112300 -1.046
                                                       0.296
sexWoman
                          -0.001045 0.003139 -0.333
                                                       0.740
age
                           sleep_apneaYes
                                     0.026525 -0.909 0.364
                           -0.024104
altitude_catModerate altitude -0.028400 0.088623 -0.320 0.749
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Approximate significance of smooth terms:
        edf Ref.df
                     F p-value
s(BMI) 5.032 5.886 19.54 <2e-16 ***
Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
```

Adjusted model Atelectasis Percent

(Intercept)

sexWoman

Fit model for atelectasis percent adjusted for confounders:

R-sq.(adj) = 0.424 Deviance explained = 40.5% GCV = 0.010074 Scale est. = 0.0099703 n = 234

2.9670765 0.3292438

-0.0317677 0.0875122 -0.363

9.012 <2e-16 ***

0.717

```
-0.0003715 0.0024969 -0.149
                                                           0.882
age
                                                           0.246
sleep_apneaYes
                            -0.0973732 0.0836521 -1.164
                             0.0079574 0.0203634
                                                  0.391
                                                           0.696
altitude_catModerate altitude -0.0525988 0.0688772 -0.764
                                                           0.446
Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
Approximate significance of smooth terms:
                       edf Ref.df
                                     F p-value
s(atelectasis_percent) 3.099 3.563 89.51 <2e-16 ***
Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
R-sq.(adj) = 0.678 Deviance explained = 63.2%
GCV = 0.0061173 Scale est. = 0.0061931 n = 234
```

Fully adjusted model

Fit fully adjusted model including both BMI and atelectasis percentage:

```
Family: quasibinomial Link function: logit
```

Formula:

```
spo2\_fraction \sim s(BMI, k = 8) + s(atelectasis\_percent, k = 5) + sex + age + sleep\_apnea + hb + altitude\_cat
```

Parametric coefficients:

```
Estimate Std. Error t value Pr(>|t|)
(Intercept)
                             3.0862682 0.3351823
                                                  9.208 <2e-16 ***
sexWoman
                            -0.0680870 0.0900036 -0.756
                                                           0.450
age
                            -0.0008286 0.0025147 -0.329
                                                           0.742
sleep_apneaYes
                            -0.1097329 0.0844916 -1.299
                                                           0.195
                             0.0032139 0.0205653 0.156
                                                           0.876
altitude_catModerate altitude -0.0350273 0.0699253 -0.501
                                                           0.617
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Approximate significance of smooth terms:

```
edf Ref.df F p-value
s(BMI) 3.244 4.015 1.063 0.366
s(atelectasis_percent) 2.998 3.469 45.713 <2e-16 ***
```

```
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
R-sq.(adj) = 0.687 Deviance explained = 64.2\% GCV = 0.0061332 Scale est. = 0.0061365 n = 234
```

Build a dataframe to compare models:

Sort by deviance

```
Model aR2 dev
1
         Fully_adjusted 68.7 64.2
2
              sBMI_atel 68.8 63.3
3
   adjusted_atelectasis 67.8 63.2
4
          sBMI_atel_OSA 68.1 62.8
5
              atel_only 67.6 62.6
6
            atel_smooth 67.6 62.3
7
           adjusted_BMI 42.4 40.5
8
               sBMI_OSA 43.0 39.8
9
                   sBMI 38.6 34.1
10
               OSA_only 11.5 10.3
11
                  empty 0.0 0.0
```

Sort by R2

```
Model aR2 dev
1
              sBMI_atel 68.8 63.3
2
         Fully_adjusted 68.7 64.2
3
          sBMI_atel_OSA 68.1 62.8
4
  adjusted_atelectasis 67.8 63.2
5
              atel_only 67.6 62.6
6
            atel_smooth 67.6 62.3
7
               sBMI_OSA 43.0 39.8
8
           adjusted_BMI 42.4 40.5
9
                   sBMI 38.6 34.1
10
               OSA_only 11.5 10.3
11
                  empty 0.0 0.0
```

Table S2 Create table for models:

Group	${\bf Characteristic}$	\mathbf{OR}	95% CI	p-value
BMI only	s(BMI)			< 0.001
OSA only	Obstructive sleep			
	apnea			
	No			
	Yes	0.55	$0.44, \\ 0.68$	< 0.001
Atelectasis percent only	s(atelectasis_perce	ent)	0.00	< 0.001
BMI + OSA	Obstructive sleep	J110)		₹0.001
	apnea			
	No	_		
	Yes	0.64	$0.53, \\ 0.77$	< 0.001
	s(BMI)			< 0.001
BMI + Atelectasis percent	s(BMI)			0.3
	s(atelectasis_perce	ent)		< 0.001
BMI + OSA + Atelectasis percent	Obstructive sleep			
	apnea			
	No	_		
	Yes	0.91	$0.78, \\ 1.06$	0.2
	s(BMI)			0.2
	s(atelectasis_perce		< 0.001	
BMI + OSA + age + sex + hb + altitude	Sex	,		
annude	Man		_	
	Woman	0.89	0.71,	0.3
	Wollian	0.00	1.11	0.0
	Age	1.00	0.99,	0.7
	1160	1.00	1.01	0.1
	Obstructive sleep			
	apnea			
	No	_		
	Yes	0.62	$0.51, \\ 0.76$	< 0.001
	Hemoglobin	0.98	0.93,	0.4
	$altitude_cat$		1.03	

Group	Characteristic	\mathbf{OR}	95% CI	p-value
	Low altitude		_	
	Moderate altitude	0.97	0.82, 1.16	0.7
	s(BMI)			< 0.001
Atelectasus percent + OSA + age + sex + hb + altitude	Sex			
	Man		_	
	Woman	0.97	$0.82, \\ 1.15$	0.7
	Age	1.00	1.0, 1.00	0.9
	Obstructive sleep apnea			
	No	_		
	Yes	0.91	$0.77, \\ 1.07$	0.2
	Hemoglobin	1.01	$0.97, \\ 1.05$	0.7
	altitude_cat			
	Low altitude	_	_	
	Moderate altitude	0.95	0.83, 1.09	0.4
Fully adjusted model	s(atelectasis_percer Sex	nt)		< 0.001
Tuny adjusted moder	Man			
	Woman	0.93	0.78, 1.11	0.5
	Age	1.00	0.99, 1.00	0.7
	Obstructive sleep			
	apnea			
	No	—	—	
	Yes	0.90	$0.76, \\ 1.06$	0.2
	Hemoglobin	1.00	0.96, 1.04	0.9
	altitude_cat Low altitude		_	
	Moderate altitude	0.97	0.84, 1.11	0.6
	s(BMI)			0.4
	, ,			•

Save Table S2

Figure SpO2:

Figure 3a: sBMI

Now, take the inverse logit function to assess partial effect on mean SpO2.

Partial effect on mean SpO2:

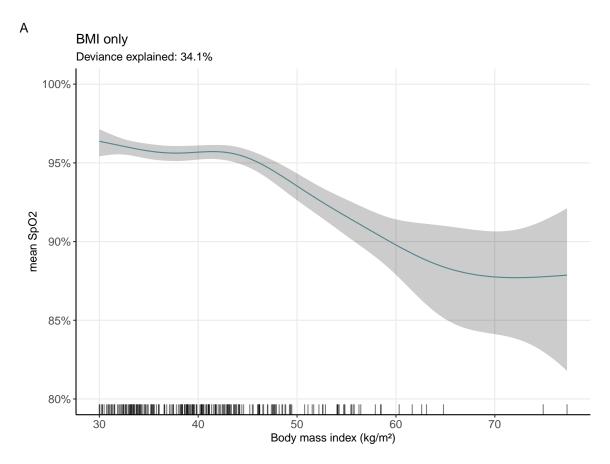


Figure 3b: sBMI_adjusted

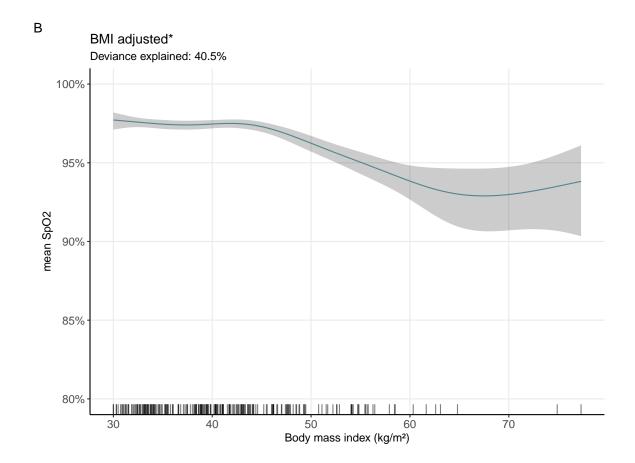


Figure 3c: Fully adjusted BMI

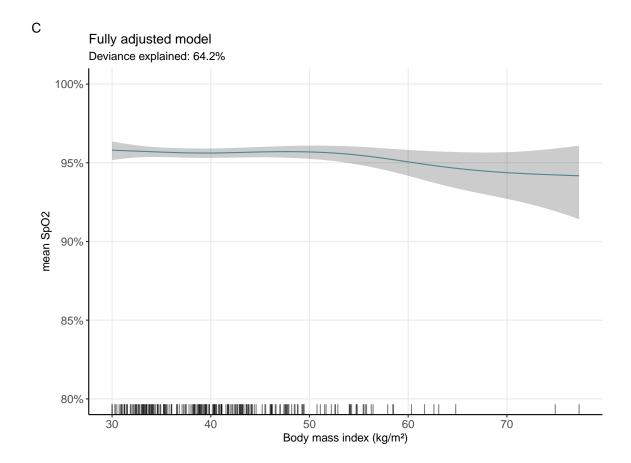


Figure 3d: sAtelectasis percent

Check residuals:

Draw a personalized plot:

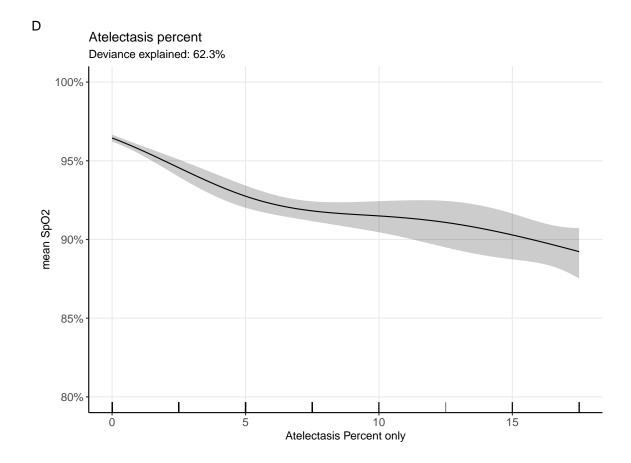


Figure 3e: Atelectasis percent adjusted

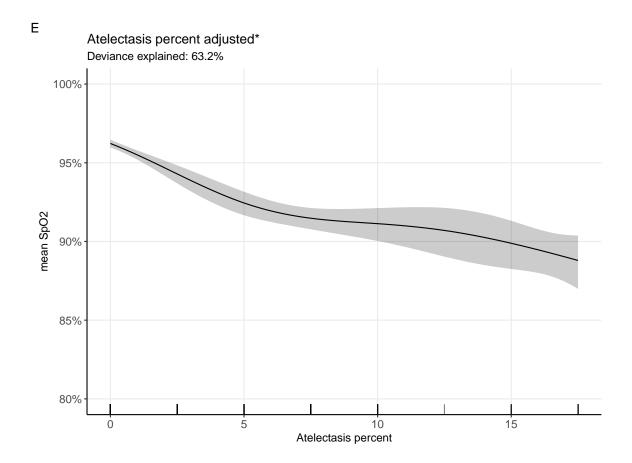


Figure 3f: Fully adjusted Atelectasis Percent

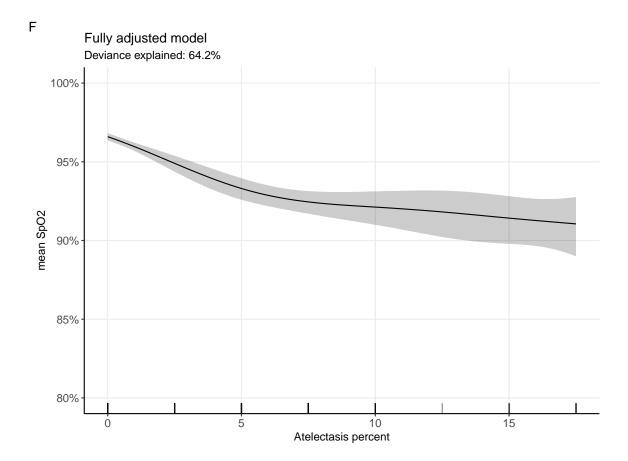


Figure 3

