(Pre-requisite)

(AST405) Lifetime data analysis

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Lecture Outline

1. 0. Parametric Regression Models
   - 0.1 Linear Regression Model
   - 0.2 Logistic Regression Model

Section 1

0. Parametric Regression Models

Subsection 1

0.1 Linear Regression Model

Independent two-sample t-test

- Population A
  - Response $Y_1 \sim \mathcal{N}(\mu_1, \sigma^2)$
  - Random sample $\{y_{11}, y_{12}, \dots, y_{1n_1}\}$
- Population B
  - Response $Y_2 \sim \mathcal{N}(\mu_2, \sigma^2)$
  - Random sample $\{y_{21}, y_{22}, \dots, y_{2n_2}\}$

Objective

$$H_0 : \mu_1 = \mu_2$$

Independent two-sample t-test

- **Test statistic**

$$t = \frac{\bar{y}_1 - \bar{y}_2}{se(\bar{y}_1 - \bar{y}_2)} = \frac{\bar{y}_1 - \bar{y}_2}{s_p\sqrt{(1/n_1) + (1/n_2)}} \sim t_{n_1+n_2-2}$$

  - $s_p^2 = \frac{(n_1-1)s_1^2+(n_2-1)s_2^2}{n_1+n_2-2}$
  - $\bar{y}_i = (1/n_i)\sum_{j=1}^{n_i} y_{ij}$
- $(1-\alpha)100\%$ **confidence interval for** $(\mu_1 - \mu_2)$

$$(\bar{y}_1 - \bar{y}_2) \pm t_{n_1+n_2-2,1-\alpha/2}\ se(\bar{y}_1 - \bar{y}_2)$$

Melanoma mortality data

- Incidence of melanoma can be related to the amount of sunshine, equivalently to the latitude of the area
- Data were collected on malignant melanoma of the skin of white males during the period 1950–69 for each state of the US
- Data on mortality rate (per 10 million), 1965 population (in a million), latitude, longitude, and the whether the state borders on the ocean are recorded

Melanoma mortality data

Download `mordat` data

```
glimpse(mordat)
```

```
Rows: 49
Columns: 6
$ state     <chr> "Alabama", "Arizona", "Arkansas", "California", "C
$ mortality <dbl> 219, 160, 170, 182, 149, 159, 200, 177, 197, 214,
$ latitude  <dbl> 33.0, 34.5, 35.0, 37.5, 39.0, 41.8, 39.0, 39.0, 28
$ longitude <dbl> 87.0, 112.0, 92.5, 119.5, 105.5, 72.8, 75.5, 77.0
$ pop       <dbl> 3.46, 1.61, 1.96, 18.60, 1.97, 2.83, 0.50, 0.76, 5
$ ocean     <fct> 1, 0, 0, 1, 0, 1, 1, 0, 1, 1, 0, 0, 0, 0, 0, 0, 1
```

Melanoma mortality data

- For a state, does "contiguous to the ocean" (Yes or No) significantly affect melanoma mortality rate?

$$\text{contiguous to ocean} = \begin{cases} \text{Yes} & \rightarrow \quad \text{ocean}{=}1 \\ \text{No} & \rightarrow \quad \text{ocean}{=}0 \end{cases}$$

Melanoma mortality data

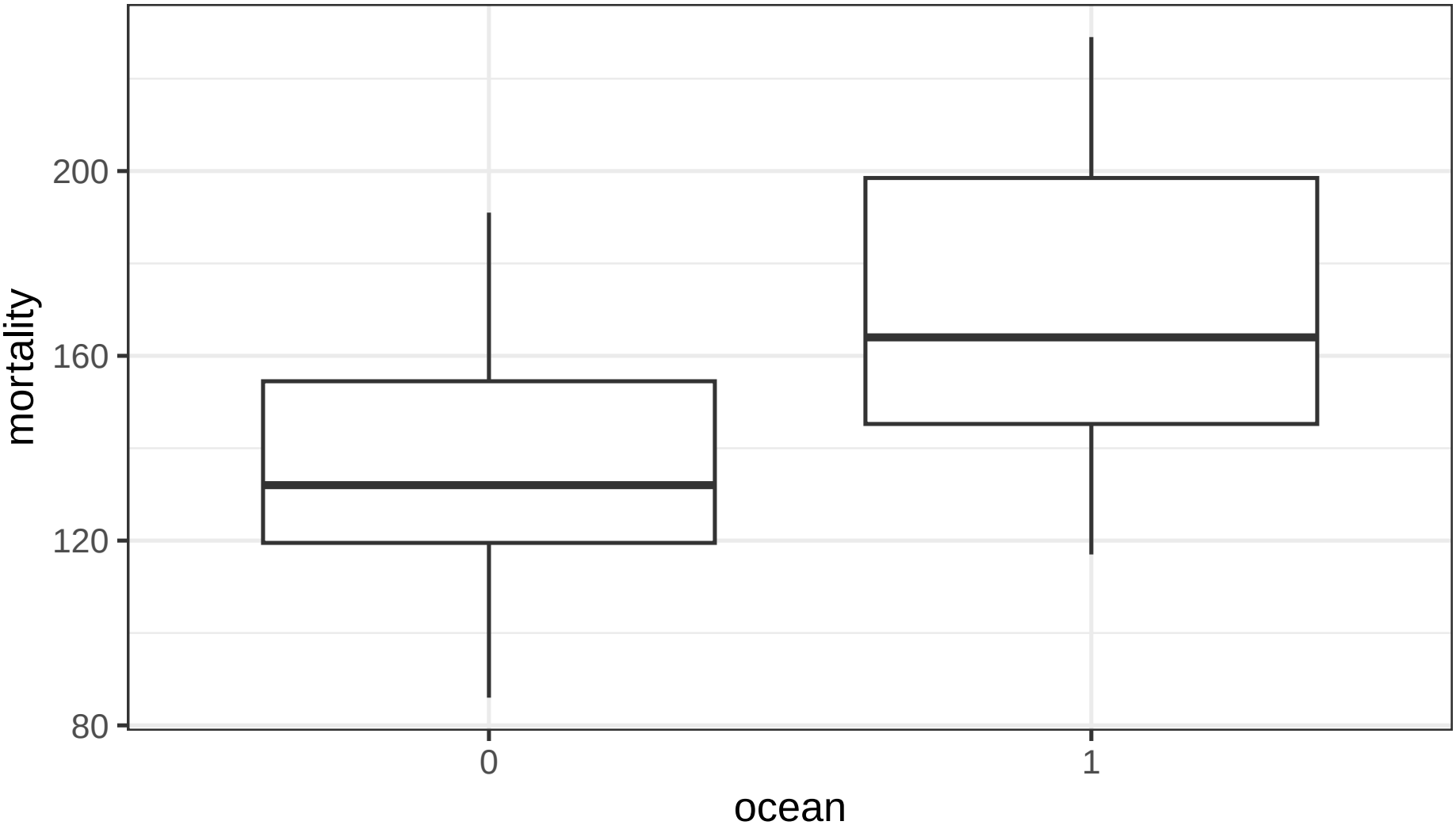


Figure 1: Distribution of mortality rate by contiguous to ocean

Independent two-sample t-test

```
test1 <- t.test(mortality ~ ocean, var.equal = T,
                data = mordat)
broom::tidy(test1) |>
  select(1:8) |> kable(digits = 3)
```

estimate	estimate1	estimate2	statistic	p.value	parameter	conf.low	conf.high
-31.487	138.741	170.227	-3.684	0.001	47	-48.68	-14.293

- **"Contiguity to the ocean" has a significant effect on average mortality rate** $(p < .001)$

Simple linear regression model

- Objective is to compare average mortality rate (Y) between two group of states (ocean=0 or ocean=1)

$$E(Y \,|\, \text{ocean} = 0) = \mu_0 \tag{1}$$

$$E(Y \,|\, \text{ocean} = 1) = \mu_1 \tag{2}$$

- Expressing Equation 1 and Equation 2 in one equation

$$E(Y \,|\, x_1) = \mu_0 + (\mu_1 - \mu_0)x_1 \tag{3}$$

where

$$x_1 = \begin{cases} 1 & \text{if ocean=1} \\ 0 & \text{if ocean=0} \end{cases}$$

Simple linear regression model

- Consider a model for mortality (Y) on ocean (x_1)

$$E(Y \mid x_1) = \mu_0 + (\mu_1 - \mu_0)x_1$$
$$= \beta_0 + \beta_1 x_1$$

where

$$\beta_0 = \mu_0 \quad \text{and} \quad \beta_1 = (\mu_1 - \mu_0)$$

- Comparison between two groups of states

$$H_0 : \beta_1 = 0 \quad \Rightarrow \quad H_0 : \mu_1 = \mu_2$$

Simple linear regression model

- Another way of defining simple linear model, let $Y(x)$ be response corresponding to a subject with predictor x and assume

$$(Y \mid x) = Y(x) \sim \mathcal{N}(\mu(x), \sigma^2) \tag{4}$$

- Parametric regression model

$$\mu(x) = E(Y \mid x) = \beta_0 + \beta_1 x \tag{5}$$

$$V(Y \mid x) = \sigma^2 \tag{6}$$

Simple linear regression model

- Data

$$\{(y_i, x_i),\ i = 1, \ldots, n\}$$

- Assume y's are independent and

$$Y_i \sim \mathcal{N}(\mu(x_i),\ \sigma^2)$$

- Simple linear regression model

$$\mu(x) = E(Y \mid x) = \beta_0 + \beta_1 x \tag{7}$$

$$V(Y \mid x) = \sigma^2 \tag{8}$$

- Both maximum likelihood and ordinary least square methods can be used to estimate the parameters of linear regression models

Estimation of parameters

- Log-likelihood function

$$\ell(\beta_0, \beta_1) = \log \prod_{i=1}^{n} (1/\sigma)\, \phi\Big(\frac{y_i - \mu(x_i)}{\sigma}\Big) \tag{9}$$

$$= -n \log \sigma + \sum_{i=1}^{n} \log \phi\Big(\frac{y_i - \beta_0 - \beta_1 x_i}{\sigma}\Big) \tag{10}$$

- MLEs

$$(\hat{\beta}_0, \hat{\beta}_1)' = \arg\ \max_{\Theta} \ell(\beta_0, \beta_1) \tag{11}$$

Estimation of parameters

- Estimating the effect of "contiguous to ocean" (x_1) on mortality rate (Y) using simple linear regression model

$$E(Y \mid x_1) = \beta_0 + \beta_1 x_1$$

Estimation of parameters

- Fitting a linear model for mortality with "contiguous to ocean" as the only predictor

```
mod_oc <- lm(mortality ~ ocean, data = mordat)
tbl_regression(mod_oc, intercept = T)
```

Characteristic	**Beta**	**95% CI**[1]	**p-value**
(Intercept)	139	127, 150	<0.001
ocean			
0	—	—	
1	31	14, 49	<0.001

[1]CI = Confidence Interval

- **"Contiguity to the ocean" has a significant effect on average mortality rate** $(p < .001)$

Estimation of parameters

- Fitted model

$$E(Y \mid x_1) = 138.741 + 31.487x_1 = \begin{cases} 138.741 & \text{if } x_1 = 0 \\ 170.227 & \text{if } x_1 = 1 \end{cases}$$

- Inland states (ocean=0) are expected to have about 31 fewer melanoma deaths (per 10 million population) compared to other states

t-test and simple linear regression model

- For binary predictors, inference based on independent two-sample t-test and simple linear regression mode are similar
- The method of simple linear regression model for binary predictor can also be used for continuous predictor

Simple linear regression model with a continuous predictor

- Model I: a model for mortality (Y) on latitude (x_2)

$$E(Y \mid x_2) = \beta_0 + \beta_2 x_2 \tag{12}$$

$$V(Y \mid x_2) = \sigma^2 \tag{13}$$

Simple linear regression model with a continuous predictor

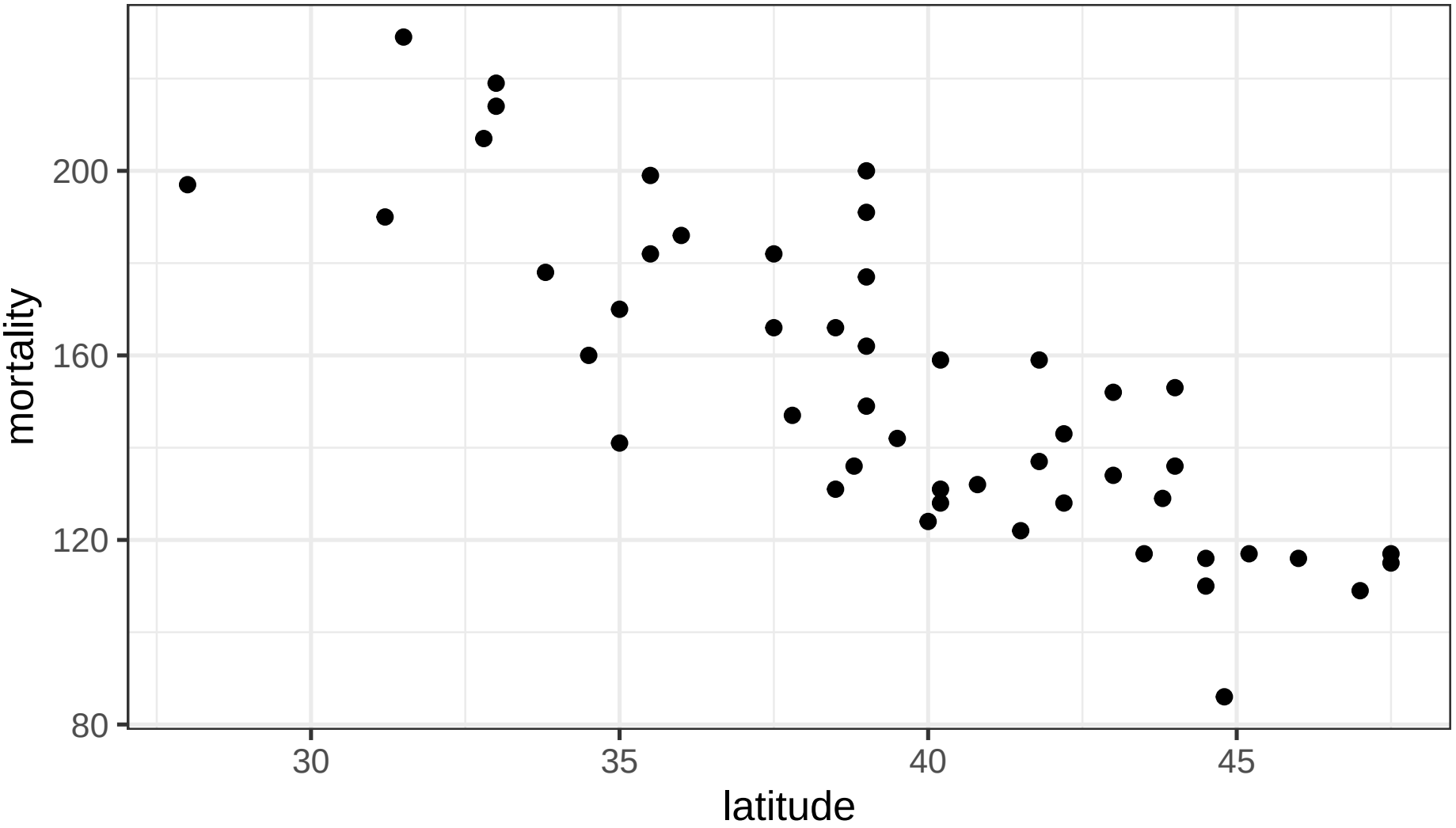


Figure 2: Scatter plot of *mortality* vs *latitude*

Simple linear regression model with a continuous predictor

```
mod_l1 <- lm(mortality ~ latitude, data = mordat)
tbl_regression(mod_l1, intercept = T)
```

Characteristic	**Beta**	**95% CI**[1]	**p-value**
(Intercept)	389	341, 437	<0.001
latitude	-6.0	-7.2, -4.8	<0.001

[1]CI = Confidence Interval

- Latitude has a significant effect on the melanoma mortality rate
- For one-degree increase in latitude (i.e., moving toward the north), melanoma mortality rate decrease by 6 deaths per 10 million population

Simple linear regression model with a continuous predictor

ANOVA table for Model I

```
tidy(aov(mod_l1)) |> kable(digits = 3)
```

term	df	sumsq	meansq	statistic	p.value
latitude	1	36464.20	36464.200	99.797	0
Residuals	47	17173.06	365.384	NA	NA

Simple linear regression model with a continuous predictor

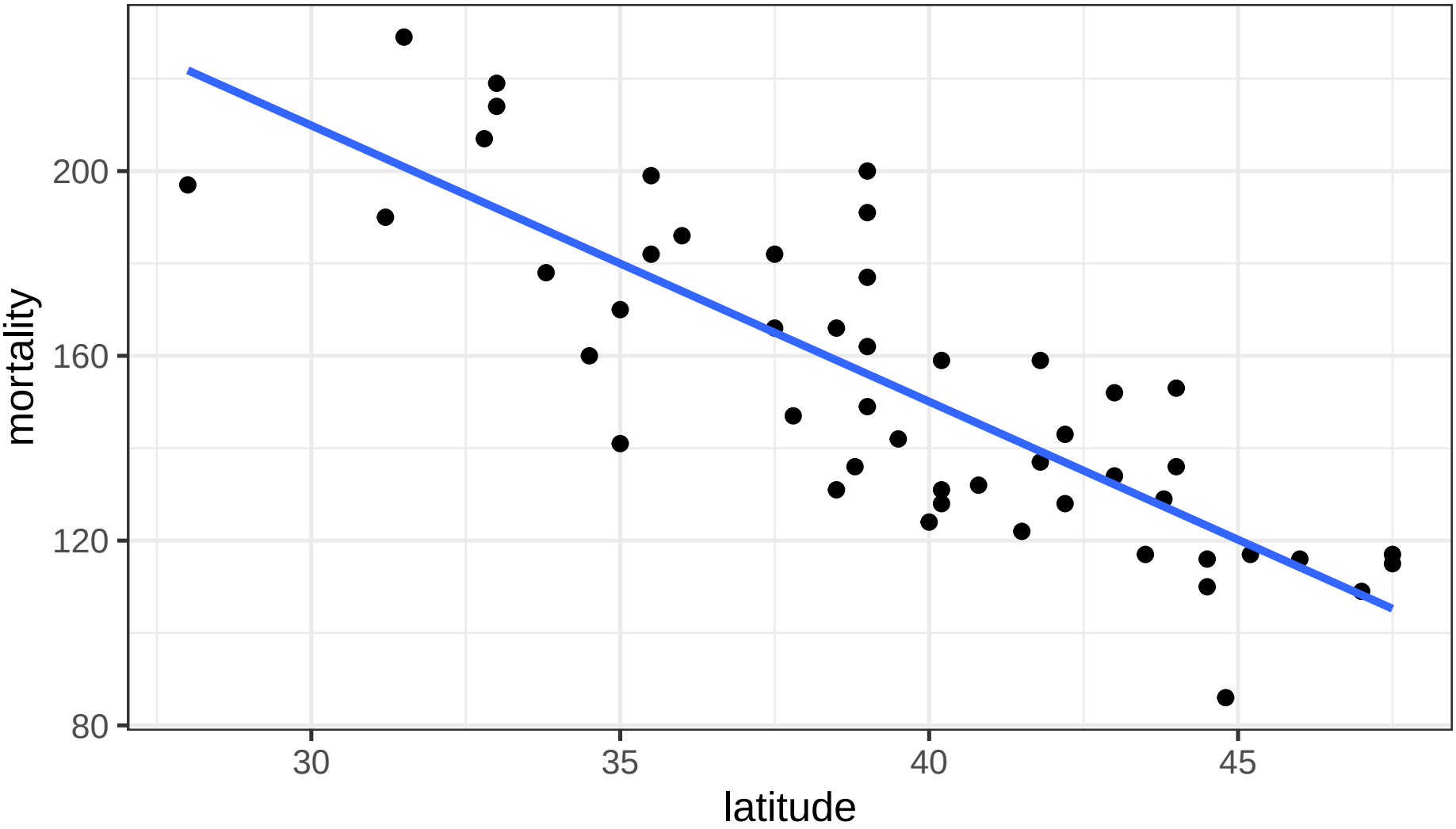


Figure 3: Fit of Model I

Another fit of the model "Mortality on latitude"

- Model I: A model for mortality on latitude (x_2)

$$E(Y \mid x_2) = \beta_0 + \beta_2 x_2 \tag{14}$$

- Model II: A model for mortality on latitude (x)

$$E(Y \mid x) = \beta_0 + \beta_x x \tag{15}$$

Another fit of the model "Mortality on latitude"

```
mod_l2 <- lm(mortality ~ latitudef,
             data = mordat %>%
                 mutate(latitudef = factor(latitude)))
tbl_regression(mod_l2, intercept = T)
```

Characteristic	**Beta**	**95% CI**[1]	**p-value**
(Intercept)	197	163, 231	<0.001
latitudef			
28	—	—	
31.2	-7.0	-55, 41	0.8
31.5	32	-16, 80	0.2
32.8	10	-38, 58	0.7
33	20	-22, 61	0.3
33.8	-19	-67, 29	0.4
34.5	-37	-85, 11	0.12
35	-42	-83, -0.35	0.048
35.5	-6.5	-48, 35	0.7
36	-11	-50, 27	0.6

Another fit of the model "Mortality on latitude"

ANOVA table for Model II

```
tidy(aov(mod_l2)) |> kable(digits = 4)
```

term	df	sumsq	meansq	statistic	p.value
latitudef	31	49326.799	1591.1871	6.2755	1e-04
Residuals	17	4310.467	253.5569	NA	NA

Another fit of the model "Mortality on latitude"

Comparison between Model I and Model II (LRT)

```
tidy(anova(mod_l1, mod_l2)) |> kable(digits = 3)
```

term	df.residual	rss	df	sumsq	statistic	p.value
mortality ~ latitude	47	17173.065	NA	NA	NA	NA
mortality ~ latitudef	17	4310.467	30	12862.6	1.691	0.128

Another fit of the model "Mortality on latitude"

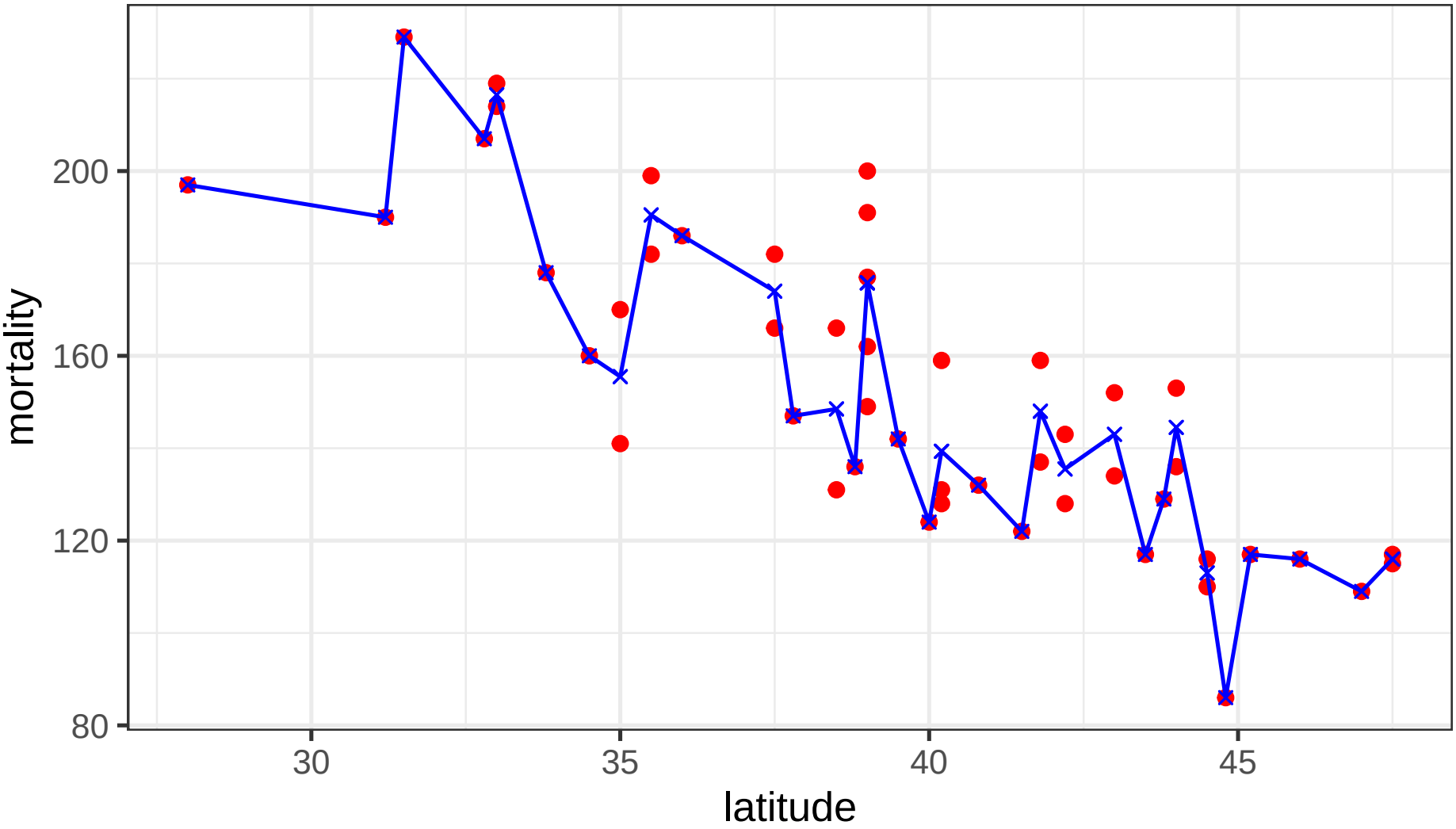


Figure 4: Fit of Model II

Another fit of the model "Mortality on latitude"

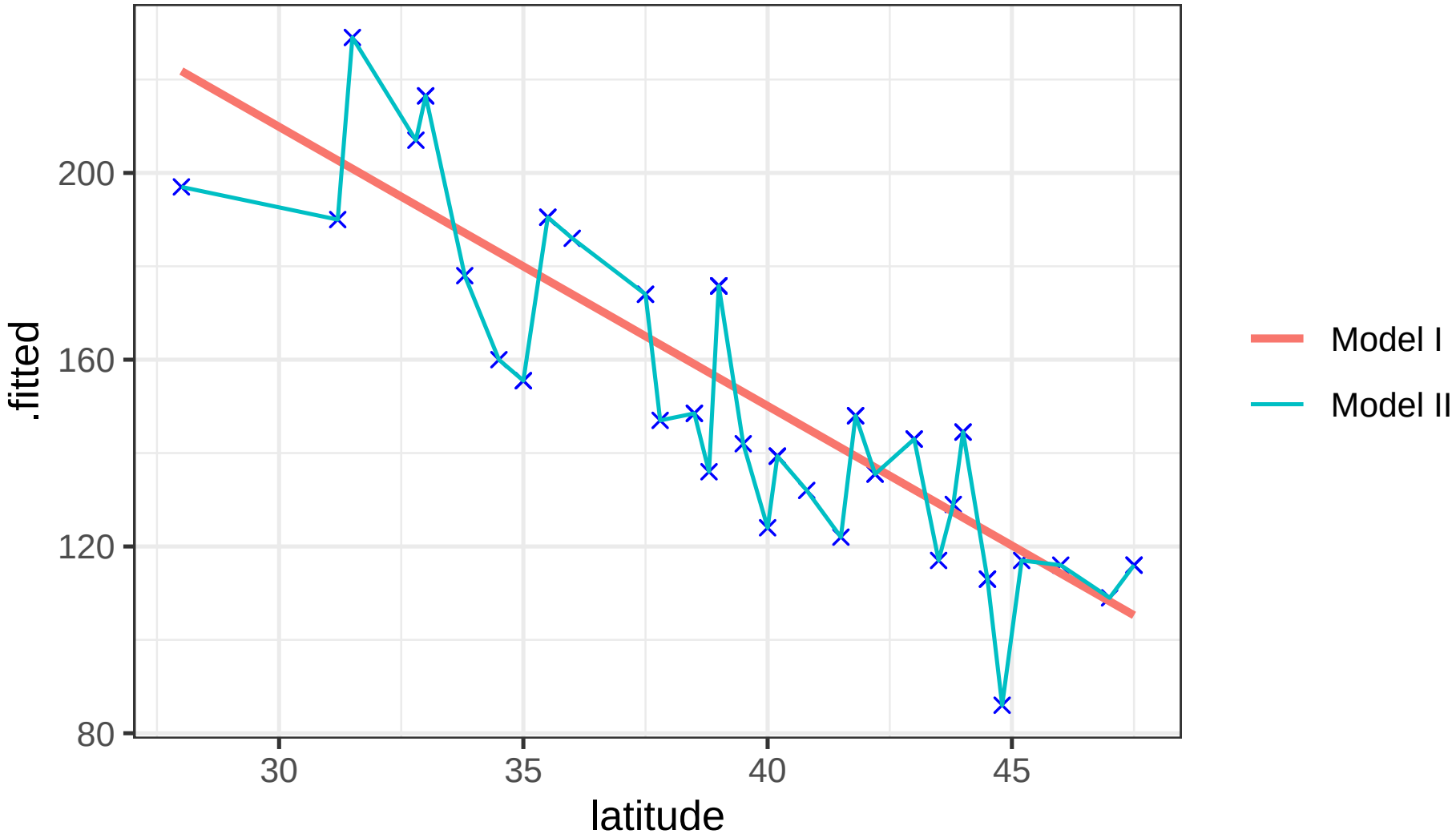


Figure 5: Comparison between the fits of Models I and II

Another fit of the model "Mortality on latitude"

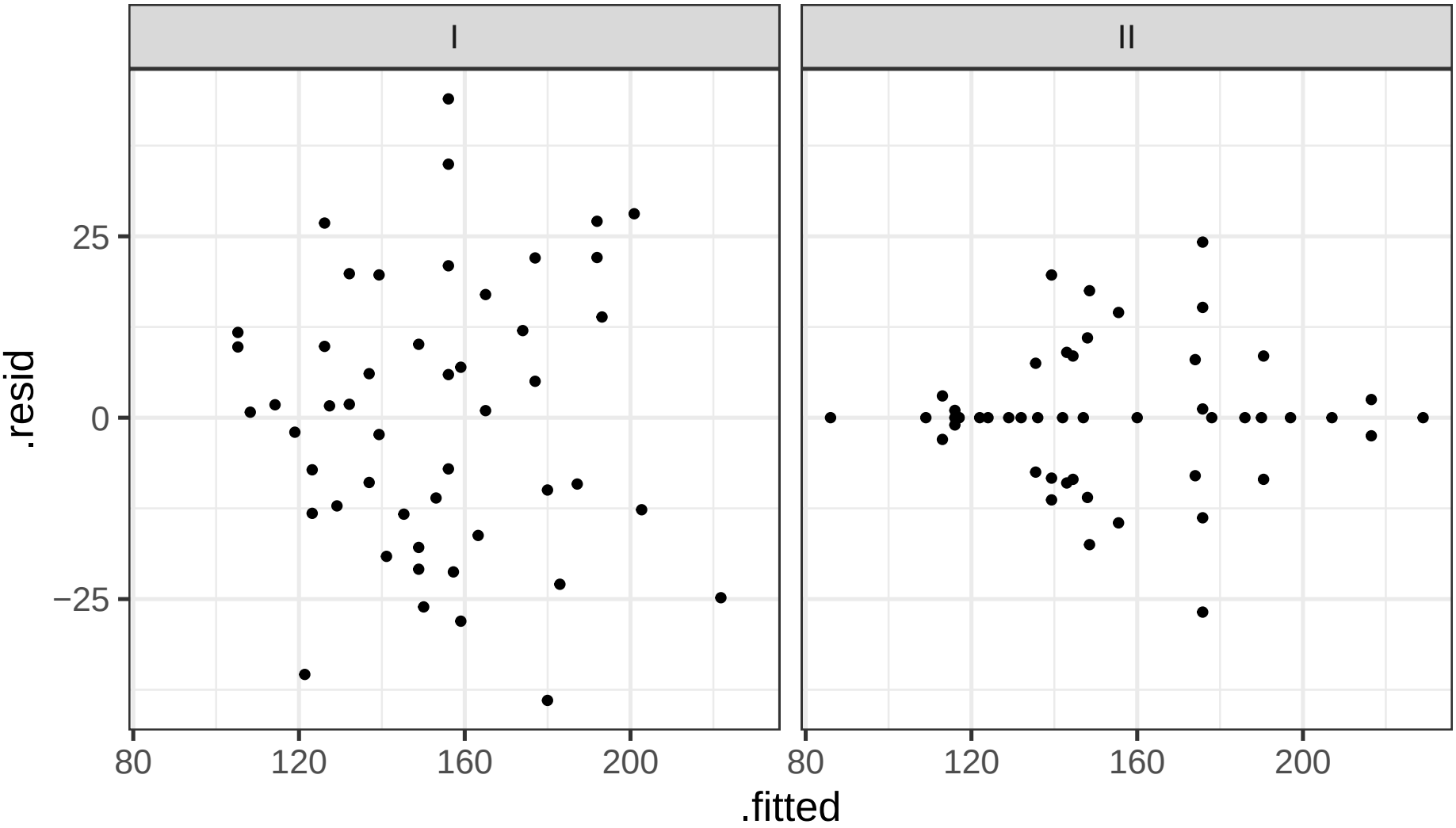


Figure 6: Residuals of Models I and II

Another fit of the model "Mortality on latitude"

Which model (I or II) do you prefer for analyzing the data?

Another fit of the model "Mortality on latitude"

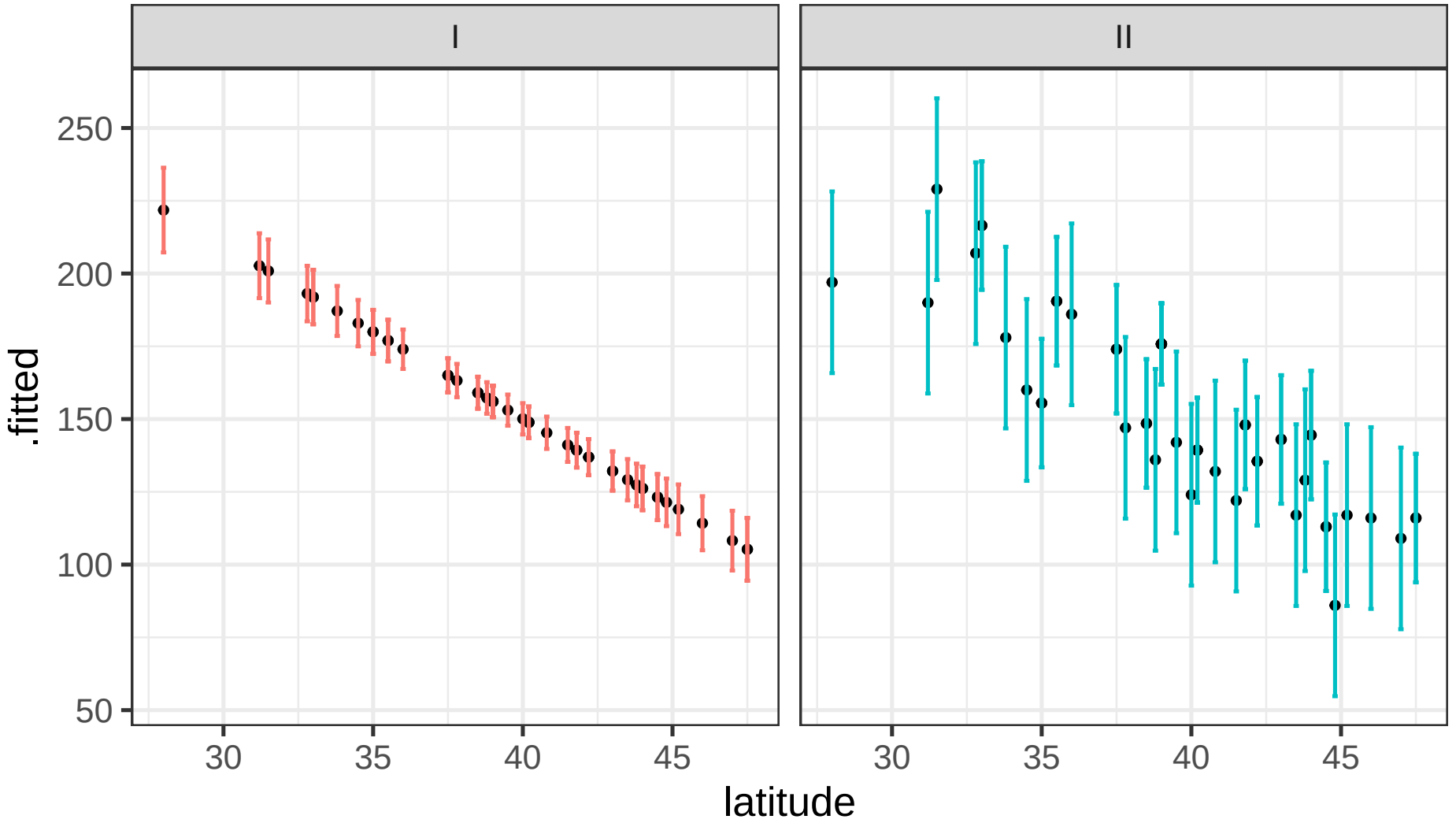


Figure 7: Estimate and corresponding confidence intervals obtained using Models I and II

Multiple linear regression model

- A model for mortality rate (Y) on ocean (x_1) and latitude (x_2)

$$E(Y \mid x_1, x_2) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 \tag{16}$$

$$V(Y \mid x_1, x_2) = \sigma^2 \tag{17}$$

Multiple linear regression model

```
mod_2 <- lm(mortality ~ ocean + latitude,
            data = mordat)
tbl_regression(mod_2, intercept = T)
```

Characteristic	**Beta**	**95% CI**[1]	**p-value**
(Intercept)	361	317, 404	<0.001
ocean			
0	—	—	
1	20	11, 30	<0.001
latitude	-5.5	-6.5, -4.4	<0.001

[1]CI = Confidence Interval

- Both contiguity to ocean and latitude have significant effects on the mortality rate

Multiple linear regression model

- On average, inland states have about 20 fewer melanoma deaths compared to other states provided latitude is fixed
- For one-degree increase of latitude, the average mortality rate decrease by 5 deaths per 10 million population provided contiguity to the ocean is fixed

Multiple linear regression model

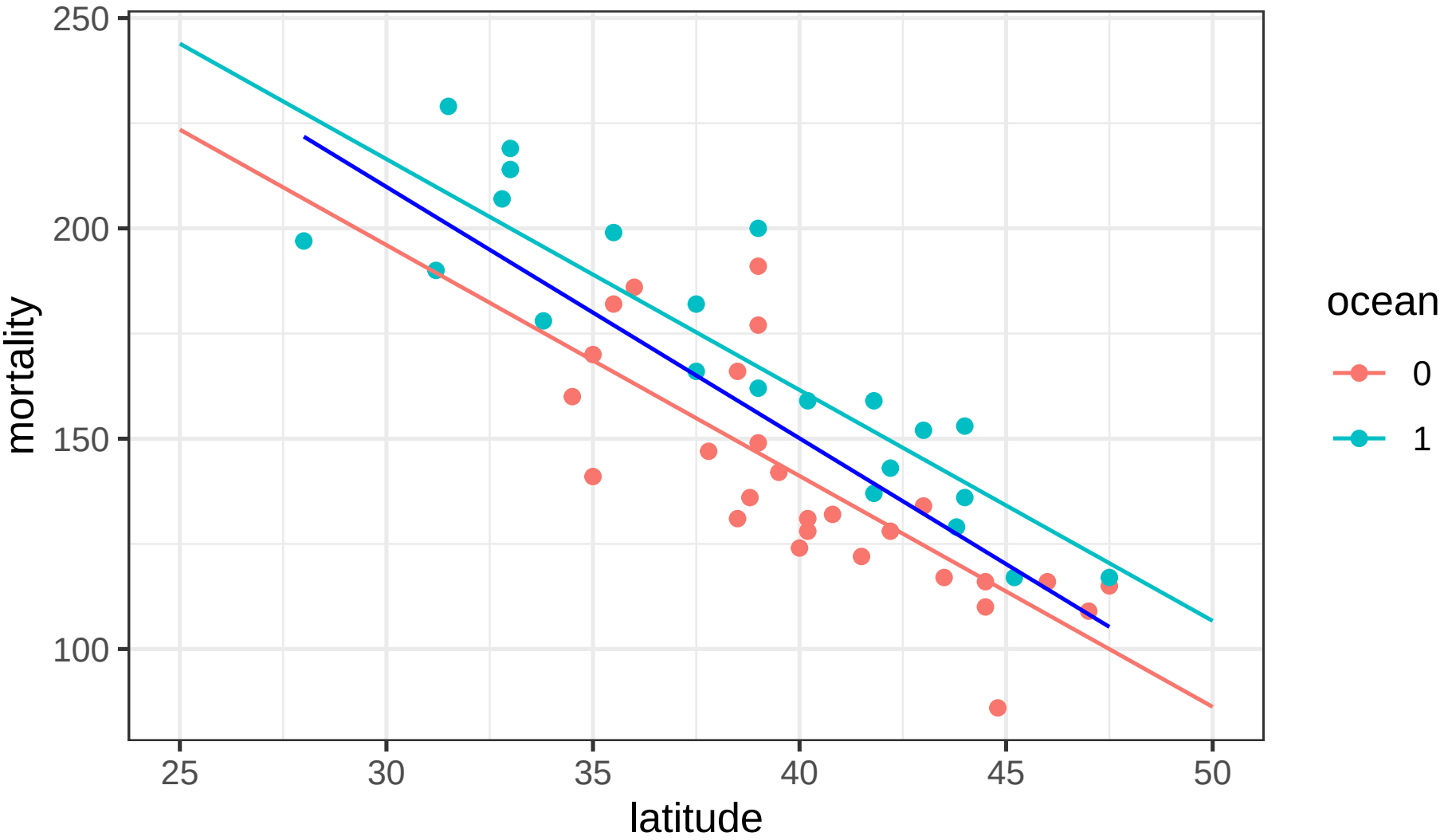


Figure 8: Comparison of the fits of the simple (blue line) and multiple linear regression models for mortality

Subsection 2

0.2 Logistic Regression Model

Contingency table

- Data obtained from different types of study designs (e.g., prospective, retrospective, and cross-sectional) can be expressed in such contingency table to examine the exposure-disease relationship

	Disease		
Exposure	Yes	No	Total
Yes	a	b	n_1
No	c	d	n_2
Total	m_1	m_2	n

Prospective study design

- Let Y_1 and Y_2 be the number of exposed and non-exposed diseased subjects, which follow two independent binomial distributions

$$Y_1 \sim B(n_1, p_1) \text{ and } Y_2 \sim B(n_2, p_2)$$

  - $p_1 = Pr(D = 1 \,|\, E = 1)$
  - $p_2 = Pr(D = 1 \,|\, E = 0)$

- Estimate of model parameters

$$\hat{p}_1 = (a/n_1) \ and \ \hat{p}_2 = (c/n_2)$$

Prospective study design

- Risk difference

$$RD = p_1 - p_2$$

$$\widehat{RD} = \hat{p}_1 - \hat{p}_2$$

$$se(\widehat{RD}) = \left[(\hat{p}_1\hat{q}_1/n_1) + (\hat{p}_2\hat{q}_2/n_2)\right]^{1/2}$$

Prospective study design

- Risk ratio

$$RR = (p_1/p_2)$$

$$\widehat{RR} = (\hat{p}_1/\hat{p}_2)$$

$$se(\log \widehat{RR}) = \left[\frac{\hat{q}_1}{n_1\,\hat{p}_1} + \frac{\hat{q}_2}{n_2\,\hat{p}_2}\right]^{1/2}$$

Prospective study design

- Odds $\Leftrightarrow$ probability

$$o(x) = \frac{p(x)}{1-p(x)} \;\Rightarrow\; p(x) = \frac{o(x)}{1+o(x)}$$

- Odds ratio

$$OR = \frac{p_1/q_1}{p_2/q_2}$$

$$\widehat{OR} = \frac{\hat{p}_1/\hat{q}_1}{\hat{p}_2/\hat{q}_2} = \frac{ad}{bc}$$

$$se(\log \widehat{OR}) = \left[\frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}\right]^{1/2}$$

Case-control study design

- Let Y_1 and Y_2 be the number of exposed subjects in case and control groups, respectively, following two independent binomial distributions

$$Y_1 \sim B(m_1, p_1) \text{ and } Y_2 \sim B(m_2, p_2)$$

  - $p_1 = Pr(E = 1 \,|\, D = 1)$
  - $p_2 = Pr(E = 1 \,|\, D = 0)$
- Estimate of parameters

$$\hat{p}_1 = (a/m_1) \text{ and } \hat{p}_2 = (b/m_2)$$

Case-control study design

- Odds ratio

$$OR = \frac{p_1/q_1}{p_2/q_2}$$

$$\widehat{OR} = \frac{\hat{p}_1/\hat{q}_1}{\hat{p}_2/\hat{q}_2} = \frac{ad}{bc}$$

  - Disease-odds-ratio = Exposure-odds-ratio
  - For case-control study, the RR can be approximated by OR if the disease is rare

Cross-sectional study

- Data of dichotomous disease-exposure study can be considered as an outcome of n tosses of a four-faced dye with the faces

$$\{ED\}, \{E\bar{D}\}, \{\bar{E}D\}, \{\bar{E}\bar{D}\}$$

  - Estimators of odds ratio

$$\widehat{OR} = \frac{ad}{bc}$$

  - Multinomial distribution is associated with the outcome of a cross-sectional study

Western Collaborative Group Study (WCGS)

- A large epidemiological study designed to investigate the association between the `Type-A` behavior pattern and coronary heart disease (CHD)
- `Type-A` behavior is composed of competitiveness, excessive drive, and an enhanced sense of time urgency
- Download `wcgs` data

Western Collaborative Group Study (WCGS)

```
head(wcgs) |> select(1:10) |> kable()
```

age	arcus	behpat	bmi	chd69	chol	dbp	dibpat	height	id
50	1	A1	31.32101	0	249	90	Type A	67	2343
51	0	A1	25.32858	0	194	74	Type A	73	3656
59	1	A1	28.69388	0	258	94	Type A	70	3526
51	1	A1	22.14871	0	173	80	Type A	69	22057
44	0	A1	22.31303	0	214	80	Type A	71	12927
47	0	A1	27.11768	0	206	76	Type A	64	16029

- Outcome: `chd69`
- Exposure: `dibpat`

Western Collaborative Group Study (WCGS)

	CHD				
dibpat	1	0	total	$\hat{p}$	$\hat{o}$
Type A	177	1411	1588	0.111	0.125
Type B	78	1486	1564	0.050	0.053

- $\widehat{RD} = 0.111 - 0.05 = 0.061$
- Subjects with `Type-A` behavior have about 6.1 % higher risk of developing CHD compared with others

Western Collaborative Group Study (WCGS)

	CHD				
dibpat	1	0	total	$\hat{p}$	$\hat{o}$
Type A	177	1411	1588	0.111	0.125
Type B	78	1486	1564	0.050	0.053

- $\widehat{RR} = (0.111/0.05) = 2.22$
- The risk of developing CHD for `Type-A` subjects is about 2.2 times the risk for `Type-B` subjects
- In other words, the risk of developing CHD is about 122% higher for `Type-A` subjects compared to `Type-B` subjects

Western Collaborative Group Study (WCGS)

	CHD				
dibpat	1	0	total	$\hat{p}$	$\hat{o}$
Type A	177	1411	1588	0.111	0.125
Type B	78	1486	1564	0.050	0.053

- $\widehat{OR} = (0.125/0.053) = 2.358$
- The odds of developing CHD for `Type-A` subjects is about 2.4 times that the risk for `Type-B` subjects
- In other words, the odds of developing CHD is about 136% higher for `Type-A` subjects compared to `Type-B` subjects

Western Collaborative Group Study (WCGS)

$$\widehat{RD} \pm se(\widehat{RD}) = 0.061 \pm 0.01$$

$$\log \widehat{RR} \pm se(\log \widehat{RR}) = 0.798 \pm 0.131$$

$$\log \widehat{OR} \pm se(\log \widehat{OR}) = 0.858 \pm 0.141$$

- Obtain confidence intervals for RD, RR, and OR

Regression model for binary response

- Let $Y(x)$ be binary response obtained from a subject with predictor value x and assume

$$Y(x) \sim B(1, p(x))$$

where

$$p(x) = Pr(Y(x) = 1) = Pr(Y = 1 \,|\, x) = E(Y \,|\, x)$$

Regression models for $p(x)$

- Assume $Y(x) \sim B(1, p(x))$

$$p(x) = \beta_0 + \beta_1 x \qquad \text{(Model I)}$$

  - $-\infty < p(x) < \infty$
  - Linear probability model

Regression models for $p(x)$

- Assume $Y(x) \sim B(1, p(x))$

$$\log p(x) = \beta_0 + \beta_1 x \;\Rightarrow\; p(x) = \exp(\beta_0 + \beta_1 x) \qquad \text{(Model II)}$$

  - $0 < p(x) < \infty$
  - Log-binomial model

Regression models for $p(x)$

- Assume $Y(x) \sim B(1, p(x))$

$$\text{logit}\, p(x) = \log \frac{p(x)}{1 - p(x)} = \beta_0 + \beta_1 x$$

$$p(x) = \frac{\exp(\beta_0 + \beta_1 x)}{1 + \exp(\beta_0 + \beta_1 x)} \qquad \text{(Model III)}$$

  - $0 < p(x) < 1$
  - Logistic regression model (related to the distribution function of logistic distribution)

Regression models for $p(x)$

- Assume $Y(x) \sim B(1, p(x))$

$$\Phi^{-1}(p(x)) = \beta_0 + \beta_1 x$$

$$p(x) = \Phi(\beta_0 + \beta_1 x) \qquad \text{(Model IV)}$$

  - $0 < p(x) < 1$
  - Probit regression model

Regression models for $p(x)$

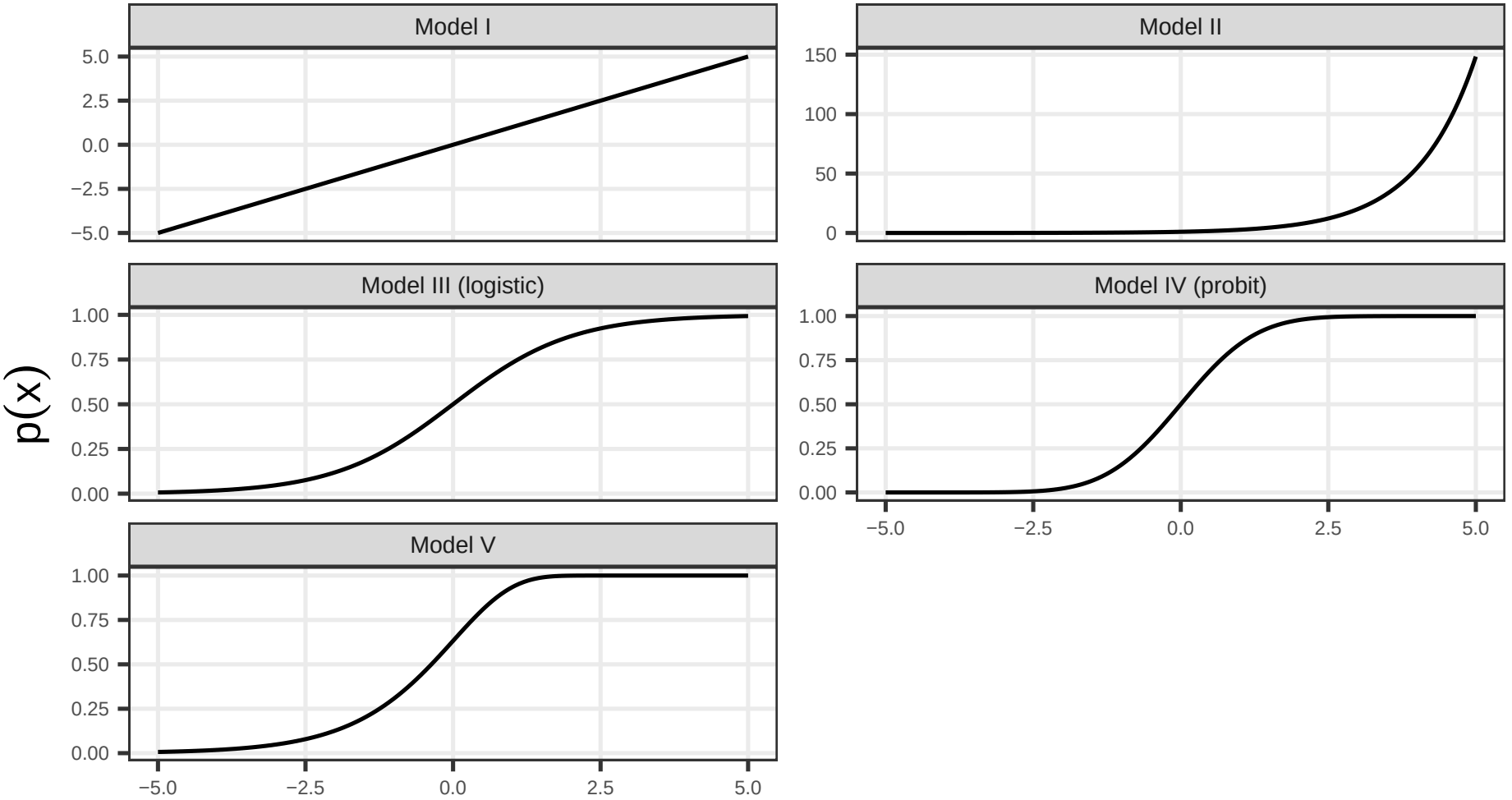
- Assume $Y(x) \sim B(1, p(x))$

$$\log[-\log(1-p(x))] = \beta_0 + \beta_1 x$$

$$p(x) = 1 - \exp\left[-e^{\beta_0+\beta_1 x}\right] \qquad \text{(Model V)}$$

  - $0 < p(x) < 1$
  - Regression model with complementary log-log link (related to the distribution function of extreme-value distribution)

Regression models for $p(x)$



$$\eta_x = \beta_0 + \beta_1 x$$

Model I: $p(x) = \beta_0 + \beta_1 x$

- Probability of developing CHD among subjects with `Type-A` $(x = 1)$ and `Type-B` behavior $(x = 0)$

$$p(1) = P(Y = 1 \,|\, x = 1) = \beta_0 + \beta_1$$
$$p(0) = P(Y = 1 \,|\, x = 0) = \beta_0$$

  - Effect of behavior type on CHD

$$RD = p(1) - p(0) = \beta_1$$

Model I: $p(x) = \beta_0 + \beta_1 x$

Data

$$\{(y_i, x_i),\ i = 1, \ldots, n\}$$

y's are independent and assume

$$Y_i \sim B(1,\ p(x_i))$$

- Linear probability model

$$p(x_i) = \beta_0 + \beta_1 x_i$$

Model I: $p(x) = \beta_0 + \beta_1 x$

Log-likelihood function

$$\ell(\beta_0, \beta_1) = \log \prod_{i=1}^{n} y_i^{p(x_i)} (1 - y_i)^{1-p(x_i)}$$

$$= \sum_{i=1}^{n} \left\{ (\beta_0 + \beta_1 x_i) \log y_i + (1 - \beta_0 - \beta_1 x_i) \log(1 - y_i) \right\}$$

- MLEs

$$(\hat{\beta}_0, \hat{\beta}_1)' = \arg \max_{\Theta} \ell(\beta_0, \beta_1) \tag{18}$$

glm() funciton

R function glm() is used to fit a generalized linear model

```
glm(formula, data, family)
```

- family specifies the distribution of response and link function, which can be either a string or a function, and commonly used family and link function in glm()
  - binomial("logit") → binomial distribution and logit link function
  - binomial("log") → binomial distribution and log link function
  - gaussian("identity") → Gaussian distribution and identity link function
  - poisson("log") → Poisson distribution and log link function

Model I: $p(x) = \beta_0 + \beta_1 x$

```
bmod_1 <- glm(chd69 ~ dibpat, family = binomial("identity"),
              data = wcgs)
tbl_regression(bmod_1, intercept = T)
```

Characteristic	**Beta**	**95% CI**[1]	**p-value**
(Intercept)	0.05	0.04, 0.06	<0.001
dibpat			
Type B	—	—	
Type A	0.06	0.04, 0.08	<0.001

[1]CI = Confidence Interval

- Since response `chd69` is a binary variable and regression function is assumed to be identically linked with the parameter of the response distribution, a `binomial("identity")` is used as `family`
- Effect of behavior type on CHD

$$\widehat{RD} = \hat{\beta}_1 = 0.062$$

Model II: $\log p(x) = \beta_0 + \beta_1 x$

- Probability of developing CHD among subjects with `Type-A` $(x = 1)$ and `Type-B` $(x = 0)$ behavior

$$p(1) = P(Y = 1 \,|\, x = 1) = \exp(\beta_0 + \beta_1) \tag{19}$$

$$p(0) = P(Y = 1 \,|\, x = 0) = \exp(\beta_0) \tag{20}$$

- Effect of `Type-A` behavior

$$RR = \frac{p(1)}{p(0)} = \exp(\beta_1) \quad \Rightarrow \quad \log RR = \beta_1$$

Model II: $\log p(x) = \beta_0 + \beta_1 x$

Log-likelihood function

$$\ell(\beta_0, \beta_1) = \log \prod_{i=1}^{n} y_i^{p(x_i)} (1 - y_i)^{1-p(x_i)}$$

$$= \sum_{i=1}^{n} \Big\{ \exp(\beta_0 + \beta_1 x_i) \log y_i + \big[1 - \exp(\beta_0 + \beta_1 x_i)\big] \log(1 - y_i) \Big\}$$

- MLEs

$$(\hat{\beta}_0, \hat{\beta}_1)' = \arg \max_{\Theta} \ell(\beta_0, \beta_1) \tag{21}$$

Model II: $\log p(x) = \beta_0 + \beta_1 x$

```
bmod_2 <- glm(chd69 ~ dibpat, family = binomial("log"),
              data = wcgs)
tbl_regression(bmod_2, intercept = T)
```

Characteristic	**log(RR)**[1]	**95% CI**[1]	**p-value**
(Intercept)	-3.0	-3.2, -2.8	<0.001
dibpat			
Type B	—	—	
Type A	0.80	0.55, 1.1	<0.001

[1]RR = Relative Risk, CI = Confidence Interval

- Since response `chd69` is a binary variable and regression function is assumed to be linked with the log-transformed parameter of the response distribution, a `binomial("log")` is used as `family`
- Effect of behavior type on CHD

$$\log \widehat{RR} = \hat{\beta}_1 = 0.804 \quad \Rightarrow \quad \widehat{RR} = \exp(\hat{\beta}_1) = 2.235$$

Model III: logit $p(x) = \beta_0 + \beta_1 x$

- Probability of developing CHD among subjects with `Type-A` $(x = 1)$ and `Type-B` $(x = 0)$ behavior

$$p(1) = P(Y = 1 \,|\, x = 1) = \frac{\exp(\beta_0 + \beta_1)}{1 + \exp(\beta_0 + \beta_1)} \tag{22}$$

$$p(0) = P(Y = 1 \,|\, x = 0) = \frac{\exp(\beta_0)}{1 + \exp(\beta_0)} \tag{23}$$

Model III: logit $p(x) = \beta_0 + \beta_1 x$

- Effect of behavior type

$$OR = \frac{p(1)/[1-p(1)]}{p(0)/[1-p(0)]} = \frac{\exp(\beta_0 + \beta_1)}{\exp(\beta_0)} = \exp(\beta_1)$$

$$\Rightarrow \quad \log OR = \beta_1$$

Model III: logit $p(x) = \beta_0 + \beta_1 x$

Log-likelihood function

$$\ell(\beta_0, \beta_1) = \log \prod_{i=1}^{n} y_i^{p(x_i)} (1 - y_i)^{1-p(x_i)}$$

$$= \sum_{i=1}^{n} \left\{ \frac{\exp(\beta_0 + \beta_1 x_i)}{1 + \exp(\beta_0 + \beta_1 x_i)} \log y_i + \frac{\log(1 - y_i)}{1 + \exp(\beta_0 + \beta_1 x_i)} \right\}$$

- MLEs

$$(\hat{\beta}_0, \hat{\beta}_1)' = \arg \max_{\Theta} \ell(\beta_0, \beta_1) \tag{24}$$

Model III: logit $p(x) = \beta_0 + \beta_1 x$

```
bmod_3 <- glm(chd69 ~ dibpat, family = binomial("logit"),
              data = wcgs)
tbl_regression(bmod_3, intercept = T)
```

Characteristic	log(OR)[1]	95% CI[1]	p-value
(Intercept)	-2.9	-3.2, -2.7	<0.001
dibpat			
Type B	—	—	
Type A	0.87	0.60, 1.2	<0.001

[1]OR = Odds Ratio, CI = Confidence Interval

- Since response `chd69` is a binary variable and the regression function is assumed to be linked with a logit-transformed parameter of the response distribution, a `binomial("logit")` is used as `family`
- Effect of behavior type on CHD

$$\log \widehat{OR} = \hat{\beta}_1 = 0.871 \quad \Rightarrow \quad \widehat{OR} = \exp(\hat{\beta}_1) = 2.39$$

Binary response and continuous predictor

- Effect of age (x_2) on CHD (Model I)

$$p(x) = \beta_0 + \beta_1 x_2$$

```
mod_1a <- glm(chd69 ~ age, family = binomial("identity"),
              data = wcgs)
tbl_regression(mod_1a, intercept = T)
```

Characteristic	**Beta**	**95% CI**[1]	**p-value**
(Intercept)	-0.17	-0.25, -0.10	<0.001
age	0.01	0.00, 0.01	<0.001

[1]CI = Confidence Interval

- Age has a significant effect on CHD, and for an increase of 10 years, risk of developing CHD increase by 0.055

Binary response and continuous predictor

- What is the risk of developing CHD for a subject of age 45?

```
predict.glm(mod_1a, newdata = list(age = 45),
            type = "response")
```

```
          1
0.07393095
```

Binary response and continuous predictor

- Predicting linear predictor for a subject of age 45

```
predict.glm(mod_1a, newdata = list(age = 45),
            type = "link")
```

```
          1
0.07393095
```

Binary response and continuous predictor

- Effect of age (x_2) on CHD (Model II)

$$\log p(x) = \beta_0 + \beta_1 x_2$$

```
mod_2a <- glm(chd69 ~ age, family = binomial("log"),
              data = wcgs)
tbl_regression(mod_2a, intercept = T)
```

Characteristic	**log(RR)**[1]	**95% CI**[1]	**p-value**
(Intercept)	-5.7	-6.7, -4.8	<0.001
age	0.07	0.05, 0.09	<0.001

[1]RR = Relative Risk, CI = Confidence Interval

- Age has a significant effect on CHD, and the risk of developing CHD for a subject John is 1.07 $(= e^{0.068})$ times that of a subject who is one year younger than John
- For one year increase of age, the risk of developing CHD is increased by 7%

Binary response and continuous predictor

What is the risk of developing CHD for a subject of age 45?

```
predict.glm(mod_2a, newdata = list(age = 45),
            type = "response")
```

```
          1
0.06891375
```

Predicting linear predictor for a subject of age 45

```
predict.glm(mod_2a, newdata = list(age = 45),
            type = "link")
```

```
       1
-2.6749
```

Binary response and continuous predictor

Effect of age (x_2) on CHD (Model III)

$$\text{logit}\, p(x) = \beta_0 + \beta_1 x_2$$

```
mod_3a <- glm(chd69 ~ age, family = binomial("logit"),
              data = wcgs)
tbl_regression(mod_3a, intercept = T)
```

Characteristic	**log(OR)**[1]	**95% CI**[1]	**p-value**
(Intercept)	-6.0	-7.1, -4.9	<0.001
age	0.07	0.05, 0.10	<0.001

[1]OR = Odds Ratio, CI = Confidence Interval

- Age has a significant effect on CHD, and the odds of developing CHD for a subject John is 1.078 $(= e^{0.075})$ times that of a subject who is one year younger than John
- For one year increase of age, the odds of developing CHD is increased by 7.8%

Binary response and continuous predictor

- What is the risk of developing CHD for a subject of age 45?

```
predict.glm(mod_3a, newdata = list(age = 45),
            type = "response")
```

```
         1
0.06913919
```

- Predicting linear predictor for a subject of age 45

```
predict.glm(mod_3a, newdata = list(age = 45),
            type = "link")
```

```
         1
-2.599988
```

Binary response and continuous predictor

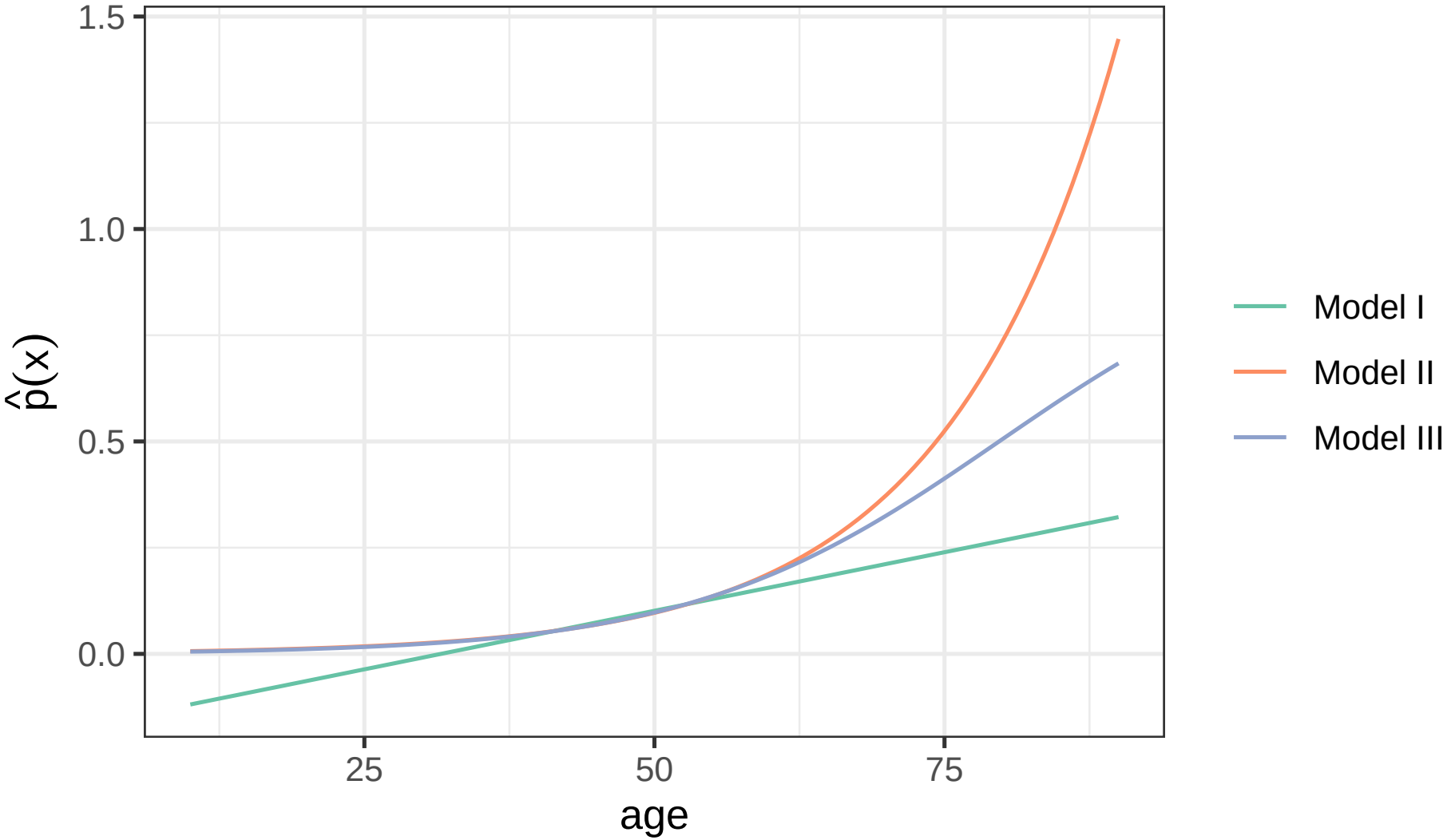


Figure 9: Comparisons among the fits of the regression models I, II, and III with age as the predictor

Multiple logistic regression models

- Model for binary response CHD (Y) with predictors behavior type (x_1) and (x_2)

$$p(x) = \beta_0 + \beta_1 x_1 + \beta_2 x_2$$

```
mod_1b <- glm(chd69 ~ dibpat + age, family = binomial("identity"),
              data = wcgs)
tbl_regression(mod_1b, intercept = T)
```

Characteristic	**Beta**	**95% CI**[1]	**p-value**
(Intercept)	-0.15	-0.22, -0.08	<0.001
dibpat			
Type B	—	—	
Type A	0.05	0.03, 0.07	<0.001
age	0.00	0.00, 0.01	<0.001

[1]CI = Confidence Interval

- The effect of behavior type on CHD is constant over age, and the effect of age is constant over two levels of behavior types

Multiple logistic regression models

- Estimated risks for the subjects John (age 40, `Type-A`), Allan (age 40, `Type-A`), Tom (age 50, `Type-B`), and Steve (age 40, `Type-B`)

```
# A tibble: 4 x 3
  subject   age dibpat
* <chr>   <dbl> <chr>
1 John       40 Type A
2 Allan      40 Type B
3 Tom        50 Type A
4 Steve      50 Type B
```

Multiple logistic regression models

```
predict.glm(mod_1b, newdata = ndat1b,
            type = "response")
```

```
      John       Allan         Tom       Steve
0.07782783 0.02795346 0.12257767 0.07270330
```

- **Estimate of the effect of behavior type in terms of RD, RR, and OR from the pairs John-Allan and Tom-Steve**

Multiple logistic regression models

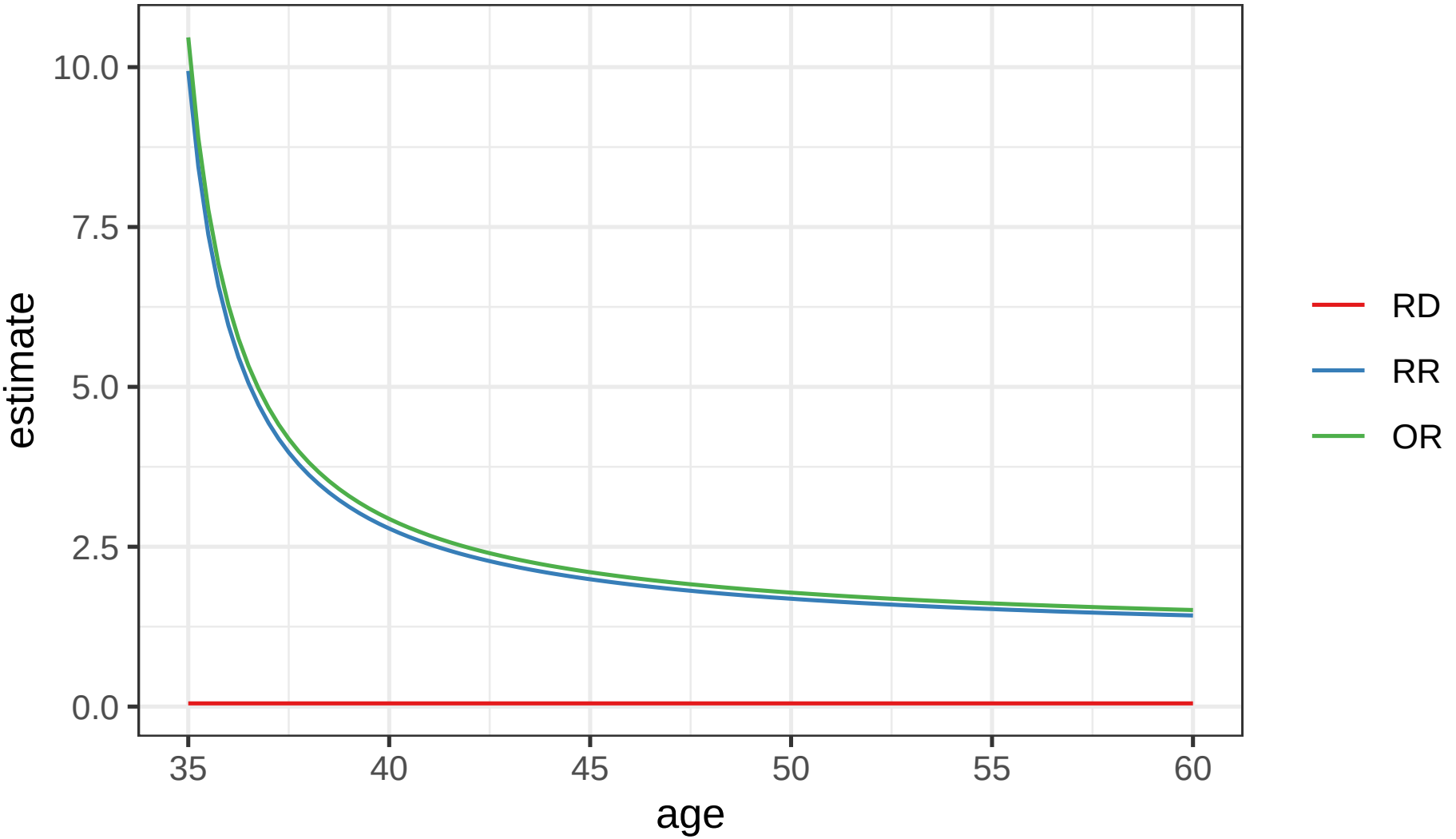


Figure 10: Estimate of RD, OR, and RR for assessing the effects of behavior type on CHD at different values of age using linear probability model

Multiple logistic regression models

- Model for binary response CHD (Y) with predictors behavior type (x_1) and (x_2)

$$\log p(x) = \beta_0 + \beta_1 x_1 + \beta_2 x_2$$

```
mod_2b <- glm(chd69 ~ dibpat + age, family = binomial("log"),
              data = wcgs)
tbl_regression(mod_2b, intercept = T)
```

Characteristic	**log(RR)**[1]	**95% CI**[1]	**p-value**
(Intercept)	-5.9	-6.8, -4.9	<0.001
dibpat			
Type B	—	—	
Type A	0.74	0.48, 1.0	<0.001
age	0.06	0.04, 0.08	<0.001

[1]RR = Relative Risk, CI = Confidence Interval

- The Effect of behavior type on CHD is constant over age, and the effect of age is constant over two levels of behavior types

Multiple logistic regression models

```
ndat1b
```

```
# A tibble: 4 x 3
  subject   age dibpat
* <chr>   <dbl> <chr>
1 John       40 Type A
2 Allan      40 Type B
3 Tom        50 Type A
4 Steve      50 Type B
```

```
predict.glm(mod_2b, newdata = ndat1b,
            type = "response")
```

```
      John       Allan         Tom       Steve
0.06893735 0.03298930 0.12762092 0.06107175
```

- **Estimate of the effect of behavior type in terms of RD, RR, and OR from the pairs John-Allan and Tom-Steve**

Multiple logistic regression models

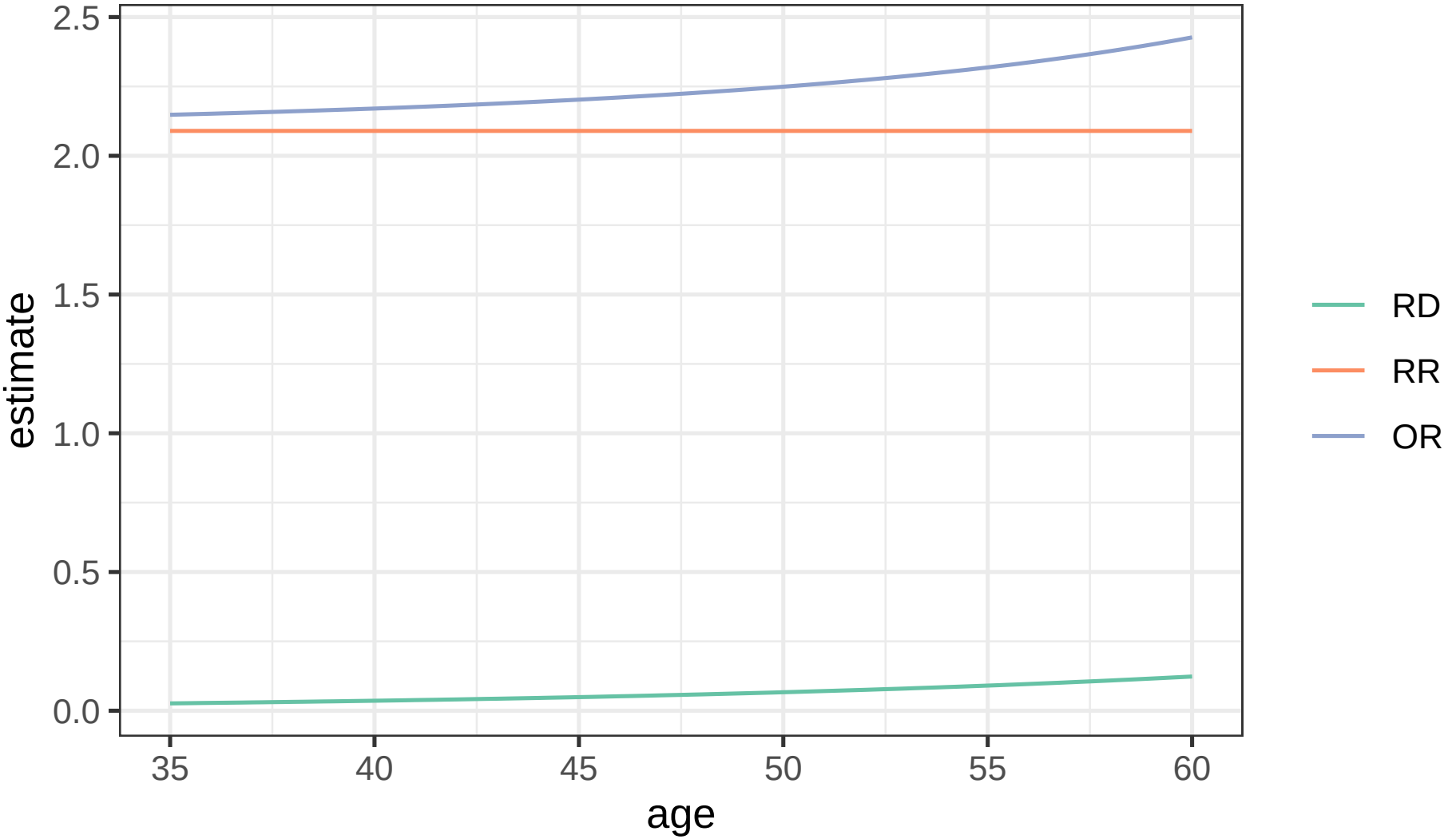


Figure 11: Estimate of RD, OR, and RR for assessing the effects of behavior type on CHD at different values of age using log-binomial model

Multiple logistic regression models

- Model for binary response CHD (Y) with predictors behavior type (x_1) and (x_2)

$$\text{logit}\, p(x) = \beta_0 + \beta_1 x_1 + \beta_2 x_2$$

```
mod_3b <- glm(chd69 ~ dibpat + age, family = binomial("logit"),
              data = wcgs)
tbl_regression(mod_3b, intercept = T)
```

Characteristic	**log(OR)**[1]	**95% CI**[1]	**p-value**
(Intercept)	-6.2	-7.3, -5.1	<0.001
dibpat			
Type B	—	—	
Type A	0.81	0.53, 1.1	<0.001
age	0.07	0.05, 0.09	<0.001

[1]OR = Odds Ratio, CI = Confidence Interval

- The effect of behavior type on CHD is constant over age, and the effect of age is constant over two levels of behavior types

Multiple logistic regression models

```
ndat1b
```

```
# A tibble: 4 x 3
  subject   age dibpat
* <chr>   <dbl> <chr>
1 John       40 Type A
2 Allan      40 Type B
3 Tom        50 Type A
4 Steve      50 Type B
```

```
predict.glm(mod_3b, newdata = ndat1b,
            type = "response")
```

```
      John       Allan         Tom       Steve
0.06885560 0.03198807 0.12857668 0.06185677
```

- **Estimate of the effect of behavior type in terms of RD, RR, and OR from the pairs John-Allan and Tom-Steve**

Multiple logistic regression models

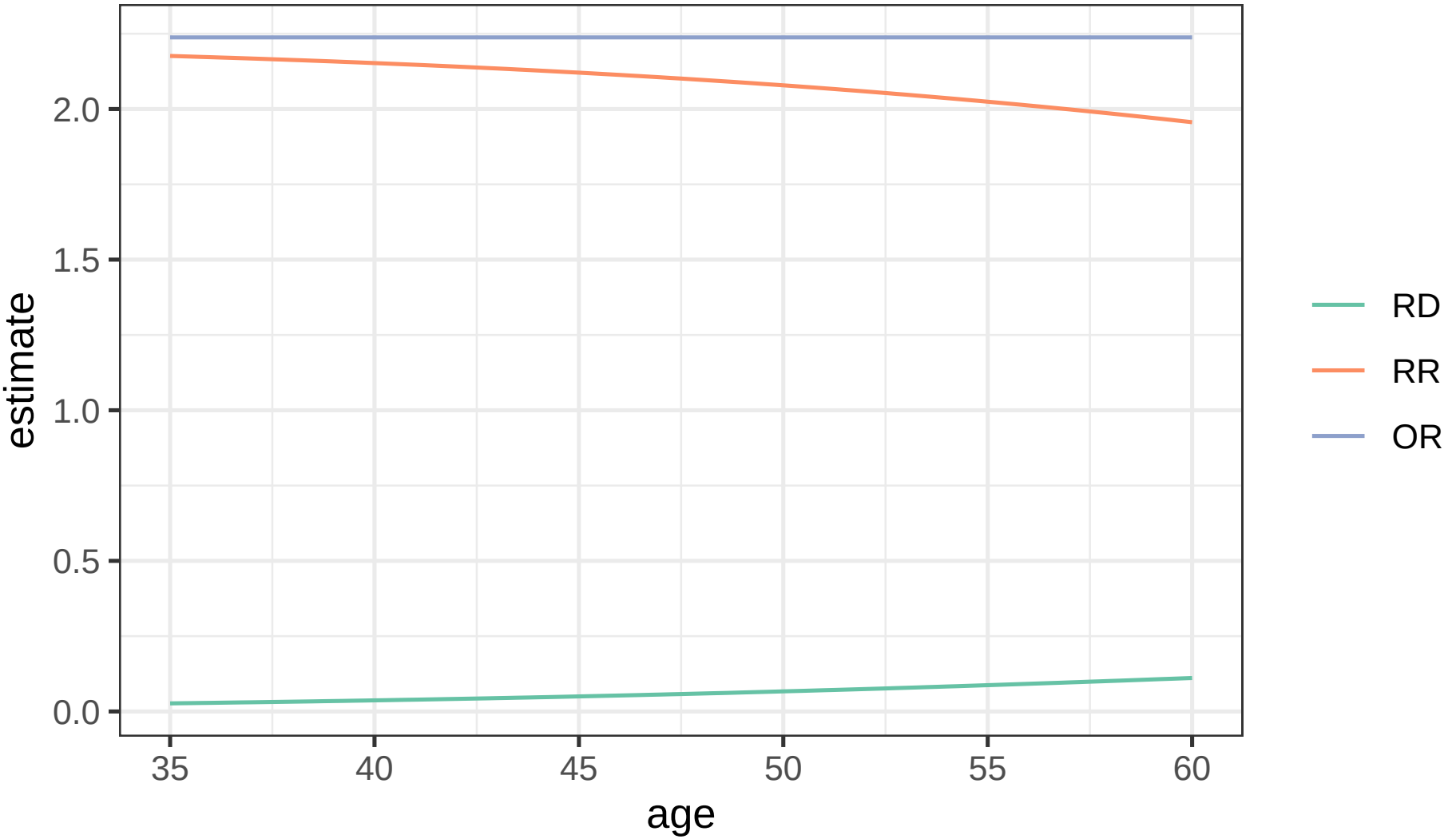


Figure 12: Estimate of RD, OR, and RR for assessing the effects of behavior type on CHD at different values of age using logistic regression model

Interaction

- Consider a model for binary response CHD with three predictors "behavior type" (x_1), "age" (x_2), and "arcus senilis" (x_3)
  - age (x_2) is a continuous predictor
  - behavior type (x_1) and arcus senilis (x_2) are binary predictor

$$x_1 = \begin{cases} 1 & \text{'Type-A'} \\ 0 & \text{'Type-B'} \end{cases}$$

$$x_3 = \begin{cases} 1 & \text{arcus senilis} = \text{Yes} \\ 0 & \text{arcus senilis} = \text{No} \end{cases}$$

Interaction

- Logistic regression model without the interaction term

$$\text{logit}\, p(x) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 \tag{25}$$

  - $\widehat{OR} = \exp(\beta_2) \rightarrow$ Effect of behavior type on the odds of CHD after adjusting for age and arcus senilis

Interaction

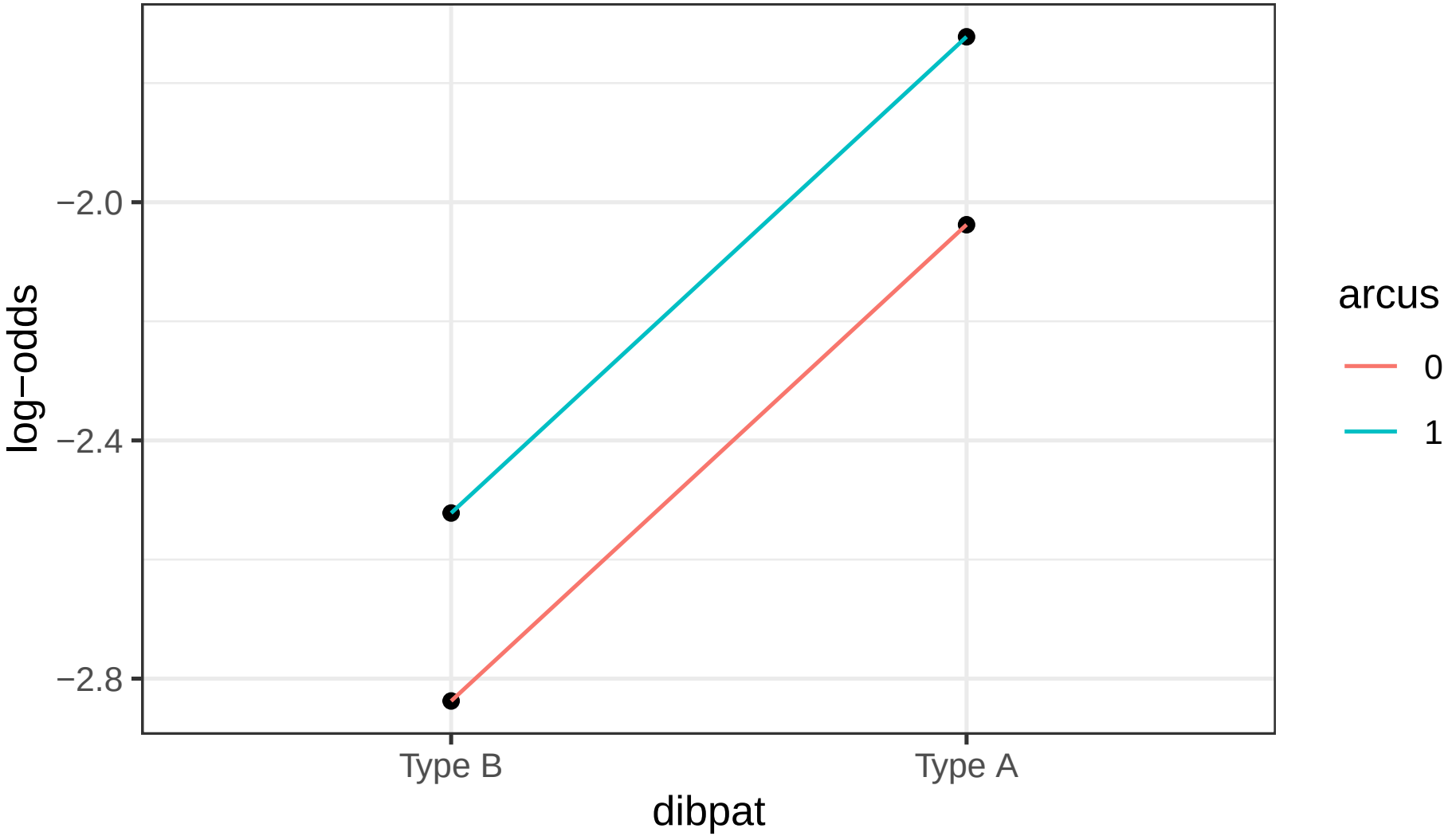
```
mod_3c <- glm(chd69 ~  dibpat + age + arcus,
              data = wcgs, family = binomial("logit"))
tbl_regression(mod_3c, intercept = T)
```

Characteristic	log(OR)[1]	95% CI[1]	p-value
(Intercept)	-6.0	-7.1, -5.0	<0.001
dibpat			
Type B	—	—	
Type A	0.80	0.52, 1.1	<0.001
age	0.06	0.04, 0.09	<0.001
arcus			
0	—	—	
1	0.32	0.04, 0.59	0.023

[1]OR = Odds Ratio, CI = Confidence Interval

- $\widehat{OR} = 2.225 = \exp(0.8)$
- Odds of developing CHD for a subject with `Type-A` behavior is 2.2 times than that of a subject with `Type-B` behavior provided age and arcus senilis is constant

Interaction



Interaction

- Logistic regression model with an interaction term between "behavior type" and "arcus senilis"

$$\text{logit}\, p(x) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \theta x_1 x_3 \tag{26}$$

$$= \begin{cases} (\beta_0 + \beta_3) + (\beta_1 + \theta) x_1 + \beta_2 x_2 & \text{for } x_3 = 1 \\ \beta_0 + \beta_1 x_1 + \beta_2 x_2 & \text{for } x_3 = 0 \end{cases}$$

  - If $\theta \neq 0 \rightarrow$ Association between behavior type and CHD is different in different groups of arcus senilis

$$OR = \begin{cases} \exp(\beta_1 + \theta) & \text{for } x_3 = 1 \\ \exp(\beta_1) & \text{for } x_3 = 0 \end{cases}$$

Interaction

```
mod_3d <- glm(chd69 ~  dibpat + age + arcus + arcus:dibpat,
              data = wcgs, family = binomial("logit"))
tbl_regression(mod_3d, intercept = T)
```

Characteristic	log(OR)[1]	95% CI[1]	p-value
(Intercept)	-6.2	-7.3, -5.1	<0.001
dibpat			
Type B	—	—	
Type A	0.99	0.63, 1.4	<0.001
age	0.06	0.04, 0.09	<0.001
arcus			
0	—	—	
1	0.64	0.17, 1.1	0.007
dibpat * arcus			
Type A * 1	-0.48	-1.0, 0.09	0.10

[1]OR = Odds Ratio, CI = Confidence Interval

- The interaction of arcus senilis and behavior type is significant, so the effect of behavior type on CHD is different between subjects with and without arcus senilis

Interaction

- Association between behavior type and CHD among subjects with and without arcus senilis

$$\widehat{OR} = \begin{cases} 1.664 & \text{for } x_3 = 1 \\ 2.693 & \text{for } x_3 = 0 \end{cases}$$

Interaction