Logistic Regression Fitting and Multiple Imputation: Frequently Asked Questions after the Quiz 1 Honors Opportunity

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```
library(rms); library(broom); library(NHANES)
library(tidyverse)
```

1 A Sample Data Set

We'll pull a set of NHANES data from the 2011-12 administration.

```
nh <- NHANES %>%
    filter(SurveyYr == "2011_12",
           Age >= 21, Age <= 64,
           Work %in% c("Working", "NotWorking"),
           !is.na(Diabetes)) %>%
    droplevels() %>%
    select(ID, SurveyYr, Age, HomeOwn, Education, BMI, Pulse, Work, Diabetes, SleepTrouble)

summary(nh)
```

```
       ID           SurveyYr         Age          HomeOwn
 Min.   :62172   2011_12:2757   Min.   :21.00   Own  :1675
 1st Qu.:64582                  1st Qu.:31.00   Rent :1012
 Median :67014                  Median :43.00   Other:  58
 Mean   :67055                  Mean   :42.43   NA's :  12
 3rd Qu.:69537                  3rd Qu.:53.00
 Max.   :71915                  Max.   :64.00

          Education        BMI            Pulse                Work
 8th Grade     :127   Min.   :16.70   Min.   : 40.00   NotWorking: 725
 9 - 11th Grade:304   1st Qu.:24.10   1st Qu.: 64.00   Working   :2032
 High School   :505   Median :27.80   Median : 72.00
 Some College  :887   Mean   :28.76   Mean   : 73.03
 College Grad  :934   3rd Qu.:32.00   3rd Qu.: 80.00
                      Max.   :80.60   Max.   :128.00
                      NA's   :20      NA's   :95
 Diabetes    SleepTrouble
 No :2550    No :2033
 Yes: 207    Yes: 724
```

2 m1 = A Simple Logistic Regression Model with lrm

In Model `m1`, let's predict the log odds of `Diabetes` being "Yes" across the 2,757 subjects in these data, on the basis of `Age`, alone.

```
d <- datadist(nh)
options(datadist = "d")

m1 <- lrm((Diabetes == "Yes") ~ Age,
          data = nh, x = TRUE, y = TRUE)

m1
```

```
Logistic Regression Model

 lrm(formula = (Diabetes == "Yes") ~ Age, data = nh, x = TRUE,
     y = TRUE)

                       Model Likelihood     Discrimination    Rank Discrim.
                          Ratio Test           Indexes           Indexes
 Obs           2757    LR chi2      121.40    R2       0.104    C       0.723
  FALSE        2550    d.f.              1    g        1.016    Dxy     0.445
  TRUE          207    Pr(> chi2) <0.0001    gr       2.762    gamma   0.455
 max |deriv| 1e-09                            gp       0.062    tau-a   0.062
                                              Brier    0.066

           Coef    S.E.   Wald Z Pr(>|Z|)
 Intercept -5.7914 0.3625 -15.98 <0.0001
 Age        0.0700 0.0070  10.01 <0.0001
```

2.1 What is the effect of Age in model m1?

By default, `summary` within `lrm` shows the impact of moving from the 25th percentile of a quantitative predictor (like Age) to the 75th percentile.

```
summary(m1)
```

```
             Effects              Response : (Diabetes == "Yes")

 Factor      Low High Diff. Effect S.E.    Lower 0.95 Upper 0.95
 Age         31  53   22    1.5411 0.15391 1.2394     1.8427
  Odds Ratio 31  53   22    4.6697      NA 3.4537     6.3139
```

OK. That's the default. We can plot that, and so forth. The estimated odds ratio is 4.67 with 95% confidence interval (3.45, 6.31). This describes the impact of moving from Age 31 to Age 53, which represent the 25th and 75th percentiles of Age, respectively.

2.1.1 What if we wanted a different confidence level?

```
summary(m1, conf.int = .90)
```

```
             Effects              Response : (Diabetes == "Yes")

 Factor      Low High Diff. Effect S.E.    Lower 0.9 Upper 0.9
 Age         31  53   22    1.5411 0.15391 1.2879    1.7942
  Odds Ratio 31  53   22    4.6697      NA 3.6253    6.0149
```

2.1.2 What if we wanted to show the effect of a one-year change in Age?

Suppose that instead of knowing the impact of moving from Age 31 to 53, we want to know the impact of moving from Age 31 to 32?

```
summary(m1, Age = c(31,32))
```

```
             Effects              Response : (Diabetes == "Yes")

 Factor      Low High Diff. Effect  S.E.      Lower 0.95 Upper 0.95
 Age         31  32   1     0.07005 0.0069959 0.056338   0.083761
  Odds Ratio 31  32   1     1.07260        NA 1.058000   1.087400
```

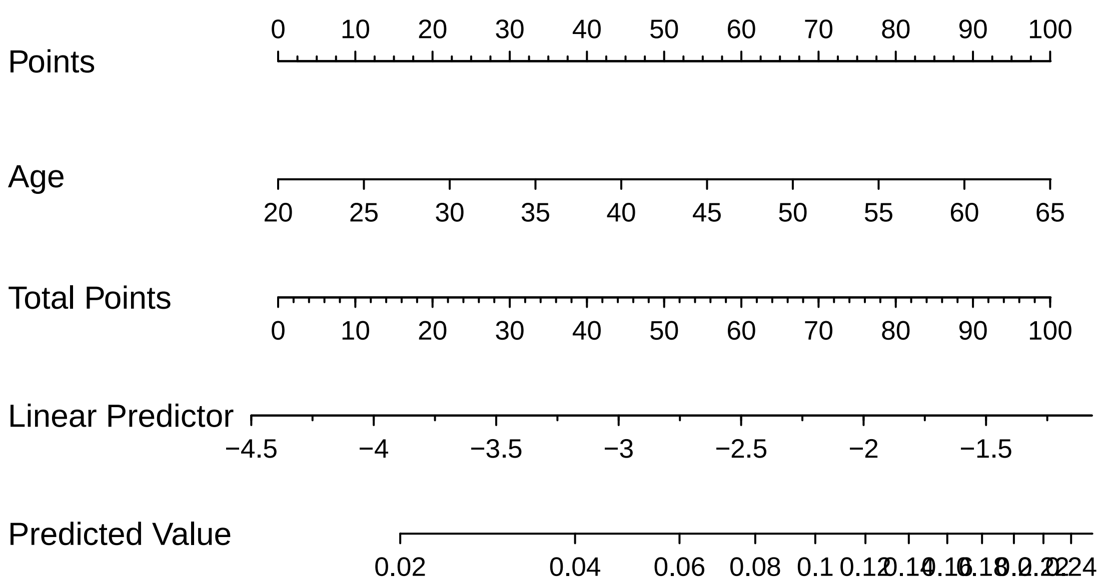
How about moving from 51 to 52? Any difference?

```
summary(m1, Age = c(51,52))
```

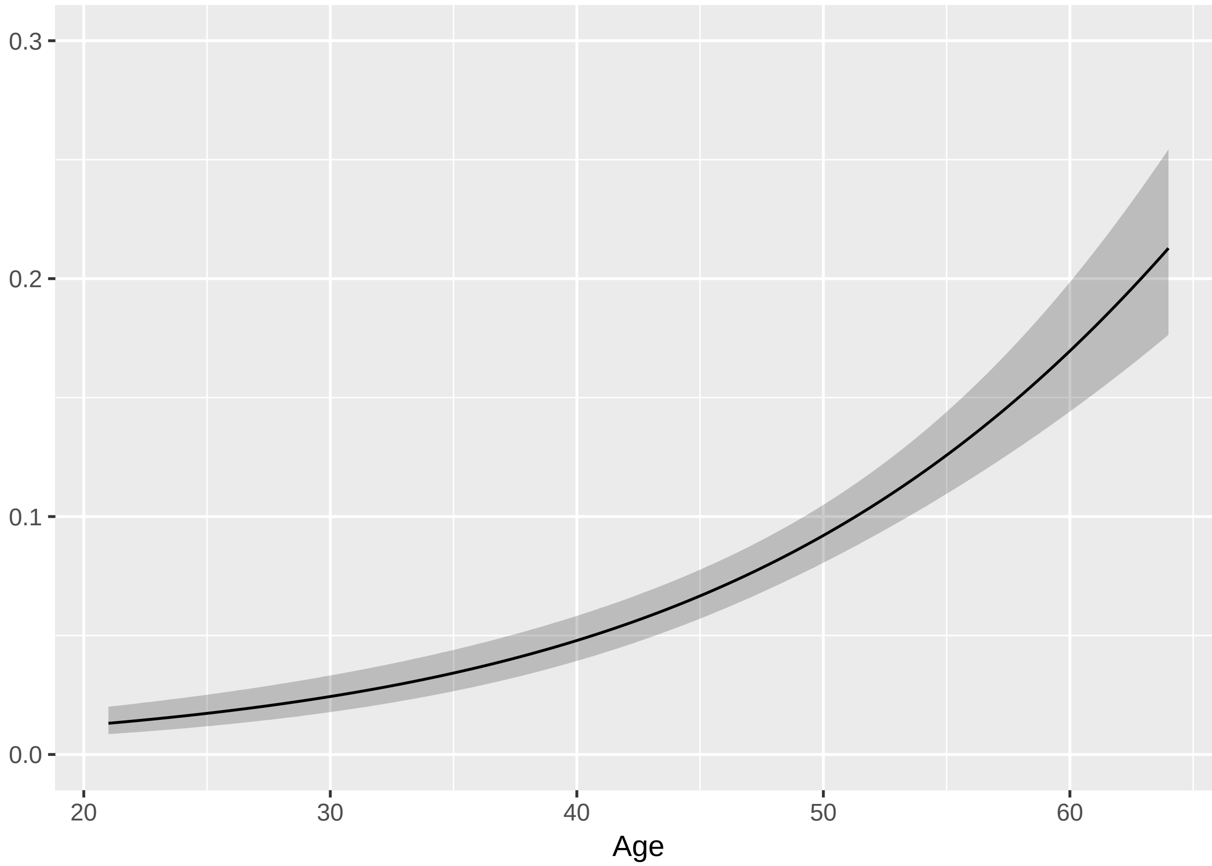
```
             Effects              Response : (Diabetes == "Yes")

 Factor      Low High Diff. Effect  S.E.      Lower 0.95 Upper 0.95
 Age         51  52   1     0.07005 0.0069959 0.056338   0.083761
  Odds Ratio 51  52   1     1.07260        NA 1.058000   1.087400
```

Here, the effect of moving from 31 to 32 is the same as moving from 51 to 52, or, indeed, moving by one year from any starting Age, because the model includes only the main effect of Age, and is linear in Age. We can see that easily in, for example, a nomogram, or a prediction plot (`ggplot(Predict())`)...

```
plot(nomogram(m1, fun = plogis))
```



```r
ggplot(Predict(m1, fun = plogis))
```



2.2 Predicting Alice's probability of diabetes

Suppose Alice is 35 years old. What is her predicted probability of diabetes, according to model `m1`?

```r
predict(m1, newdata = data.frame(Age = 35),
        type = "fitted")
```

```
         1
0.03423479
```

2.3 Comparison to what we get from `glm`

```r
g1 <- glm((Diabetes == "Yes") ~ Age,
          data = nh, family = binomial())
```

```r
exp(coef(g1)); exp(confint(g1))
```

```
(Intercept)         Age
0.003053669 1.072561288
```

```
Waiting for profiling to be done...
```

```
                  2.5 %     97.5 %
(Intercept) 0.001464804 0.00607422
Age         1.058261055 1.08771521
```

Or use broom!

```
tidy(g1, exponentiate = TRUE, conf.int = TRUE)
```

```
# A tibble: 2 x 7
  term        estimate std.error statistic  p.value conf.low conf.high
  <chr>          <dbl>     <dbl>     <dbl>    <dbl>    <dbl>     <dbl>
1 (Intercept)  0.00305   0.362       -16.0 1.82e-57  0.00146   0.00607
2 Age          1.07      0.00700      10.0 1.34e-23  1.06      1.09
```

and this is, indeed, the same answer we would get from our rms fit: m1 comparing any one-year change in Age for this model.

```
summary(m1, Age = c(41,42))
```

```
             Effects              Response : (Diabetes == "Yes")

 Factor      Low High Diff. Effect  S.E.      Lower 0.95 Upper 0.95
 Age         41  42   1     0.07005 0.0069959 0.056338   0.083761
  Odds Ratio 41  42   1     1.07260        NA 1.058000   1.087400
```

2.3.1 Does the prediction for Alice match up, too?

The prediction for Alice we get from g1 matches the one we saw in m1, as well, once we deal with the fact that the appropriate type of prediction to get a probability uses `type = "fitted"` for a fit from rms and `type = "response"` for a glm fit from base R.

```
predict(g1, newdata = data.frame(Age = 35),
        type = "response")
```

```
         1
0.03423479
```

3 What if there was a non-linear Age effect, as in Model m2?

Let's add a restricted cubic spline with three knots in Age to incorporate a non-linear effect.

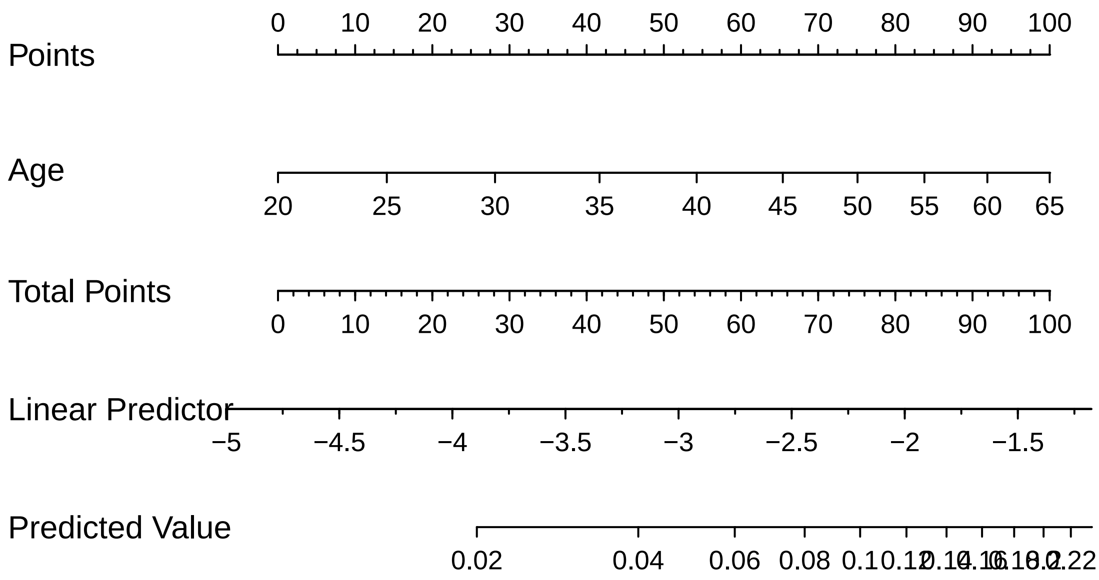
```
d <- datadist(nh)
options(datadist = "d")

m2 <- lrm((Diabetes == "Yes") ~ rcs(Age, 3),
          data = nh, x = TRUE, y = TRUE)

m2
```

```
Logistic Regression Model

 lrm(formula = (Diabetes == "Yes") ~ rcs(Age, 3), data = nh, x = TRUE,
     y = TRUE)

                       Model Likelihood     Discrimination    Rank Discrim.
                          Ratio Test           Indexes           Indexes
 Obs          2757    LR chi2     122.76    R2       0.105    C       0.723
  FALSE       2550    d.f.             2    g        1.104    Dxy     0.445
  TRUE         207    Pr(> chi2) <0.0001    gr       3.016    gamma   0.455
 max |deriv| 1e-05                          gp       0.062    tau-a   0.062
                                            Brier    0.066
```

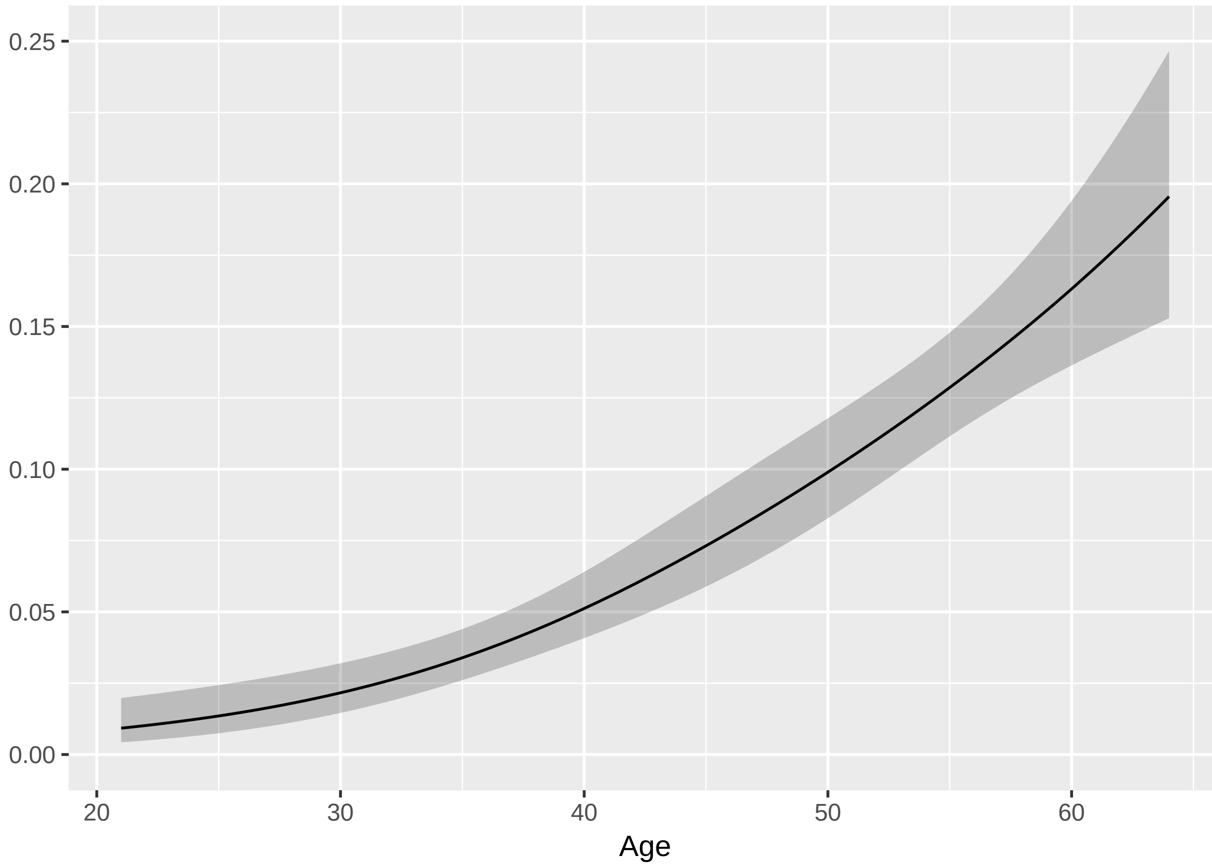
```
           Coef    S.E.   Wald Z Pr(>|Z|)
Intercept -6.6954 0.8922 -7.50  <0.0001
Age        0.0962 0.0243  3.96  <0.0001
Age'      -0.0267 0.0233 -1.15  0.2520
```

3.1 Impact of the Non-Linear Term here in Age?

```
plot(nomogram(m2, fun = plogis))
```




```
ggplot(Predict(m2, fun = plogis))
```



3.2 Now what is the effect of Age in `m2`?

3.2.1 `m2`: Default `summary` - move from Age 31 to 53

As we move from the 25th percentile (Age 31) to the 75th percentile (Age 53), we have…

```
summary(m2)
```

```
             Effects              Response : (Diabetes == "Yes")

 Factor      Low High Diff. Effect S.E.   Lower 0.95 Upper 0.95
 Age         31  53   22    1.6888 0.2105 1.2762     2.1014
  Odds Ratio 31  53   22    5.4130     NA 3.5831     8.1775
```

3.2.2 `m2`: Effect of moving from Age 31 to 32?

As we move by just one year, from Age 31 to 32, we have…

```
summary(m2, Age = c(31, 32))
```

```
             Effects              Response : (Diabetes == "Yes")

 Factor      Low High Diff. Effect  S.E.     Lower 0.95 Upper 0.95
 Age         31  32   1     0.09346 0.022001 0.050338   0.13658
  Odds Ratio 31  32   1     1.09800       NA 1.051600   1.14630
```

3.2.3 m2: Effect of moving from Age 51 to 52 now isn't the same as 31 to 32?

But now this won't be the same as what we see when we move from Age 51 to 52, because of the non-linear effect (thanks to the restricted cubic spline in Age we included in this model.)

```
summary(m2, Age = c(51, 52))
```

```
             Effects              Response : (Diabetes == "Yes")

 Factor      Low High Diff. Effect   S.E.     Lower 0.95 Upper 0.95
 Age         51  52   1     0.060103 0.011106 0.038336   0.081869
  Odds Ratio 51  52   1     1.061900       NA 1.039100   1.085300
```

3.3 Predicting Alice's probability of diabetes

Suppose Alice is 35 years old. What is her predicted probability of diabetes, according to model m2?

```
predict(m2, newdata = data.frame(Age = 35),
        type = "fitted")
```

```
         1
0.03391639
```

4 Fitting m3 to make things more complex

4.1 m3 includes a spline in Age, and an interaction with obesity...

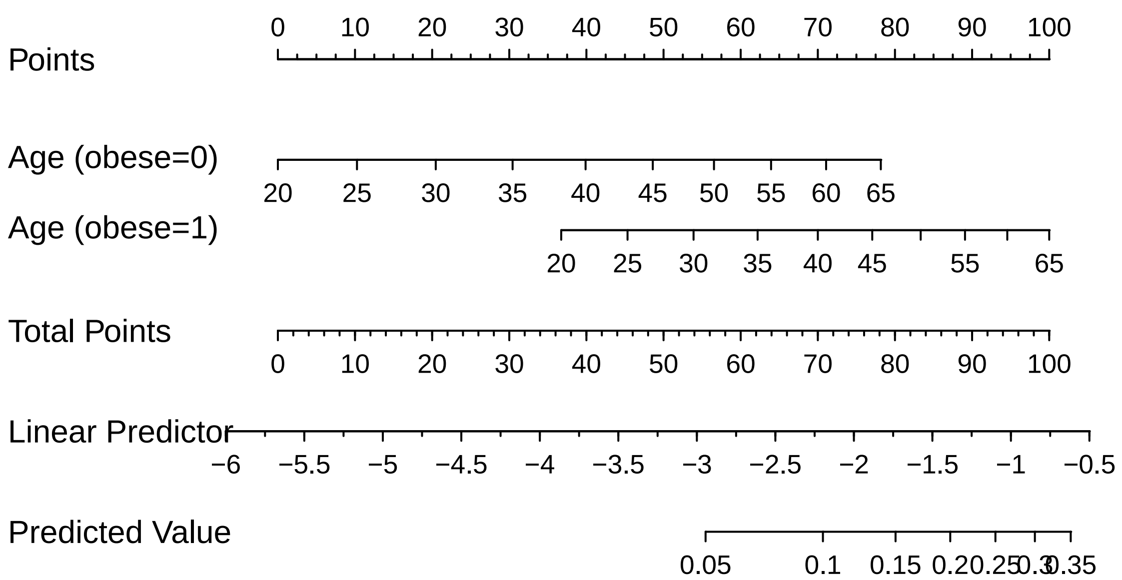
```
nh1 <- nh %>%
    mutate(obese = ifelse(BMI >= 30, 1, 0),
           diabetes = ifelse(Diabetes == "Yes", 1, 0))

d <- datadist(nh1)
options(datadist = "d")

m3 <- lrm(diabetes ~ rcs(Age, 3) + obese +
              Age %ia% obese,
          data = nh1, x = TRUE, y = TRUE)

m3
```

```
Frequencies of Missing Values Due to Each Variable
diabetes      Age    obese
       0        0       20

Logistic Regression Model

 lrm(formula = diabetes ~ rcs(Age, 3) + obese + Age %ia% obese,
     data = nh1, x = TRUE, y = TRUE)


                       Model Likelihood     Discrimination    Rank Discrim.
                          Ratio Test           Indexes           Indexes
 Obs            2737    LR chi2      197.37    R2       0.169    C       0.780
  0             2532    d.f.              4    g        1.440    Dxy     0.559
  1              205    Pr(> chi2) <0.0001    gr       4.221    gamma   0.565
 max |deriv| 1e-08                             gp       0.077    tau-a   0.078
```

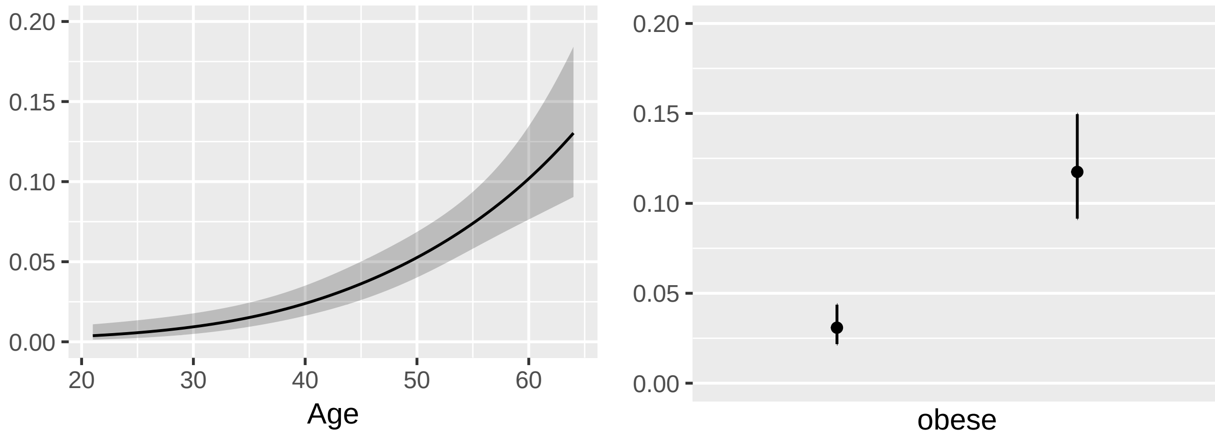
```
                                        Brier      0.064

              Coef    S.E.   Wald Z Pr(>|Z|)
Intercept    -7.6832 1.0973 -7.00  <0.0001
Age           0.1007 0.0277  3.64  0.0003
Age'         -0.0201 0.0239 -0.84  0.3997
obese         2.1296 0.8212  2.59  0.0095
Age * obese  -0.0163 0.0157 -1.03  0.3010
```

4.2 Nomogram and Prediction Plot for Model m3

```r
plot(nomogram(m3, fun = plogis))
```




```r
ggplot(Predict(m3, fun = plogis))
```



4.3 What is the effect of Age, in model `m3`?

It depends.

4.3.1 Age 31 to Age 53 in a non-obese subject

```
summary(m3)
```

```
             Effects              Response : diabetes

 Factor      Low High Diff. Effect S.E.    Lower 0.95 Upper 0.95
 Age         31  53   22    1.8930 0.31848 1.2688      2.5172
  Odds Ratio 31  53   22    6.6390      NA 3.5564     12.3930
 obese        0   1    1    1.4303 0.20384 1.0308      1.8298
  Odds Ratio  0   1    1    4.1799      NA 2.8032      6.2327

Adjusted to: Age=43 obese=0
```

Note the Adjusted to `obese` = 0, which means that this odds ratio for Age is assuming that `obese` = 0.

4.3.2 Age 31 to Age 53 in an obese subject

```
summary(m3, obese = 1)
```

```
             Effects              Response : diabetes
```

```
 Factor       Low High Diff. Effect S.E.    Lower 0.95 Upper 0.95
 Age          31  53   22    1.5352 0.23942 1.0659     2.0044
  Odds Ratio  31  53   22    4.6422      NA 2.9035     7.4219
 obese         0   1    1    1.4303 0.20384 1.0308     1.8298
  Odds Ratio   0   1    1    4.1799      NA 2.8032     6.2327

Adjusted to: Age=43 obese=1
```

Now we see a different odds ratio for the effect of moving from Age 31 to 53, when the subject is in fact obese.

4.4 What about a one-year change in Age?

4.4.1 Age 31 to Age 32 in a non-obese subject

```r
summary(m3, Age = c(31,32))
```

```
             Effects              Response : diabetes

 Factor       Low High Diff. Effect   S.E.     Lower 0.95 Upper 0.95
 Age          31  32   1     0.098661 0.025515 0.048653   0.14867
  Odds Ratio  31  32   1     1.103700       NA 1.049900   1.16030
 obese         0   1   1     1.430300 0.203840 1.030800   1.82980
  Odds Ratio   0   1   1     4.179900       NA 2.803200   6.23270

Adjusted to: Age=43 obese=0
```

Note that the effect shown here (odds ratio = 1.08) is the effect of moving from Age 31 to Age 32, in model `m3`, assuming the subject is not obese (obese = 0), as indicated.

4.4.2 Effect of moving from age 31 to 32 for an obese subject?

```r
summary(m3, Age = c(31,32), obese = 1)
```

```
             Effects              Response : diabetes

 Factor       Low High Diff. Effect   S.E.     Lower 0.95 Upper 0.95
 Age          31  32   1     0.082398 0.022581 0.03814    0.12666
  Odds Ratio  31  32   1     1.085900       NA 1.03890    1.13500
 obese         0   1   1     1.430300 0.203840 1.03080    1.82980
  Odds Ratio   0   1   1     4.179900       NA 2.80320    6.23270

Adjusted to: Age=43 obese=1
```

The change we see is due to the fact that an interaction between `Age` and `obese` was included in the model `m3`.

4.4.3 Effect of moving from age 51 to 52 for a non-obese subject?

```r
summary(m3, Age = c(51,52))
```

```
             Effects              Response : diabetes

 Factor       Low High Diff. Effect   S.E.     Lower 0.95 Upper 0.95
 Age          51  52   1     0.073453 0.014715 0.044611   0.10229
  Odds Ratio  51  52   1     1.076200       NA 1.045600   1.10770
 obese         0   1   1     1.430300 0.203840 1.030800   1.82980
```

```
  Odds Ratio  0    1    1      4.179900       NA 2.803200   6.23270

Adjusted to: Age=43 obese=0
```

Note that this odds ratio is different than the one we saw for moving from Age 31 to 32, because of the non-linear (spline) terms in Age included in `m3`.

4.4.4 Effect of moving from age 51 to 52 for an obese subject?

```r
summary(m3, Age = c(51,52), obese = 1)
```

```
             Effects              Response : diabetes

 Factor      Low High Diff. Effect  S.E.     Lower 0.95 Upper 0.95
 Age         51   52    1     0.05719 0.013239 0.031241   0.083139
  Odds Ratio 51   52    1     1.05890       NA 1.031700   1.086700
 obese        0    1    1     1.43030 0.203840 1.030800   1.829800
  Odds Ratio  0    1    1     4.17990       NA 2.803200   6.232700

Adjusted to: Age=43 obese=1
```

Again, we see the impact of the interaction term.

4.5 Predicting Alice's probability of diabetes

Suppose Alice is 35 years old. To make a prediction for her using model `m3`, we'd have to specify whether or not she is obese, or at least compare those two predicted probabilities. So what do we get?

```r
predict(m3,
        newdata = data.frame(names = c("Alice A", "Alice B"),
                             Age = c(35,35), obese = c(0,1)),
        type = "fitted")
```

```
         1          2 
0.01516586 0.06830481 
```

So if Alice is obese, her predicted probability of diabetes is much larger than if she is not. That makes sense, given the nomogram, and prediction plot we've seen.

5 Multiple Imputation with a Logistic Regression Model

5.1 Adding Pulse to Model `m3`

Now consider a model for `diabetes` that includes the Pulse rate, and leads to more substantial missingness, as a result.

```r
m4 <- lrm(diabetes ~ rcs(Age, 3) + obese + Pulse +
              Age %ia% obese,
          data = nh1, x = TRUE, y = TRUE)

m4
```

```
Frequencies of Missing Values Due to Each Variable
diabetes      Age    obese    Pulse 
       0        0       20       95 


Logistic Regression Model
```

```
lrm(formula = diabetes ~ rcs(Age, 3) + obese + Pulse + Age %ia%
    obese, data = nh1, x = TRUE, y = TRUE)

                      Model Likelihood    Discrimination    Rank Discrim.
                         Ratio Test          Indexes           Indexes
Obs           2646    LR chi2     213.49    R2       0.186    C       0.794
 0            2445    d.f.             5    g        1.480    Dxy     0.589
 1             201    Pr(> chi2) <0.0001    gr       4.393    gamma   0.589
max |deriv| 4e-08                           gp       0.081    tau-a   0.083
                                            Brier    0.064

            Coef    S.E.   Wald Z Pr(>|Z|)
Intercept   -9.8454 1.2448 -7.91  <0.0001
Age          0.1072 0.0283  3.80  0.0001
Age'        -0.0268 0.0245 -1.10  0.2730
obese        1.8427 0.8305  2.22  0.0265
Pulse        0.0266 0.0063  4.19  <0.0001
Age * obese -0.0109 0.0159 -0.68  0.4934
```

Suppose we want to use multiple imputation to deal with this missingness.

5.2 nh_imp = The Imputation Model

We'll run an imputation model with 10 imputations, using 0 or 3 knots to represent non-linear terms. I usually take either this or the default (no knots) approach in practical work.

```
set.seed(432)
d <- datadist(nh1)
options(datadist = "d")

nh_imp <- aregImpute(~ diabetes + Age + obese + Pulse,
                     nk = c(0, 3),
                     tlinear = TRUE, data = nh1,
                     n.impute = 10, pr = FALSE)
```

5.3 m5 = The Fitted Model after Multiple Imputation for diabetes

Let's fit the outcome model now, after multiple imputation.

```
d <- datadist(nh1)
options(datadist = "d")

m5 <- fit.mult.impute(diabetes ~ rcs(Age, 3) + obese +
                          Pulse + Age %ia% obese,
                      fitter = lrm, xtrans = nh_imp,
                      data = nh1, x = TRUE, y = TRUE)
```

```
Variance Inflation Factors Due to Imputation:

  Intercept         Age        Age'       obese       Pulse Age * obese
       1.01        1.00        1.00        1.01        1.01        1.01
```

```
Rate of Missing Information:

  Intercept         Age        Age'       obese       Pulse Age * obese
       0.01        0.00        0.00        0.01        0.01        0.01

d.f. for t-distribution for Tests of Single Coefficients:

  Intercept         Age        Age'       obese       Pulse Age * obese
  347364.42   970946.68 14713067.97    79467.24    64967.11    64078.96

The following fit components were averaged over the 10 model fits:

  stats linear.predictors
```

```r
m5
```

```
Logistic Regression Model

 fit.mult.impute(formula = diabetes ~ rcs(Age, 3) + obese + Pulse +
     Age %ia% obese, fitter = lrm, xtrans = nh_imp, data = nh1,
     x = TRUE, y = TRUE)

                       Model Likelihood     Discrimination    Rank Discrim.
                          Ratio Test           Indexes           Indexes
 Obs          2757    LR chi2     217.63    R2       0.184    C       0.793
  0           2550    d.f.             5    g        1.492    Dxy     0.586
  1            207    Pr(> chi2) <0.0001    gr       4.446    gamma   0.587
 max |deriv| 7e-08                          gp       0.080    tau-a   0.081
                                            Brier    0.063

             Coef     S.E.   Wald Z Pr(>|Z|)
 Intercept   -10.0165 1.2339 -8.12  <0.0001
 Age           0.1101 0.0281  3.92  <0.0001
 Age'         -0.0276 0.0242 -1.14  0.2535
 obese         1.9383 0.8248  2.35  0.0188
 Pulse         0.0273 0.0062  4.38  <0.0001
 Age * obese  -0.0136 0.0158 -0.86  0.3898
```

```r
summary(m5)
```

```
             Effects              Response : diabetes

 Factor      Low High Diff. Effect  S.E.     Lower 0.95 Upper 0.95
 Age         31  53   22    1.97810 0.320790 1.34940     2.60680
  Odds Ratio 31  53   22    7.22910       NA 3.85500    13.55600
 obese        0   1    1    1.35360 0.204650 0.95254     1.75470
  Odds Ratio  0   1    1    3.87150       NA 2.59230     5.78200
 Pulse       64  80   16    0.43608 0.099573 0.24092     0.63124
  Odds Ratio 64  80   16    1.54660       NA 1.27240     1.87990

Adjusted to: Age=43 obese=0
```

Note that the only predictors included in the `Adjusted to:` section are those included as part of interactions.

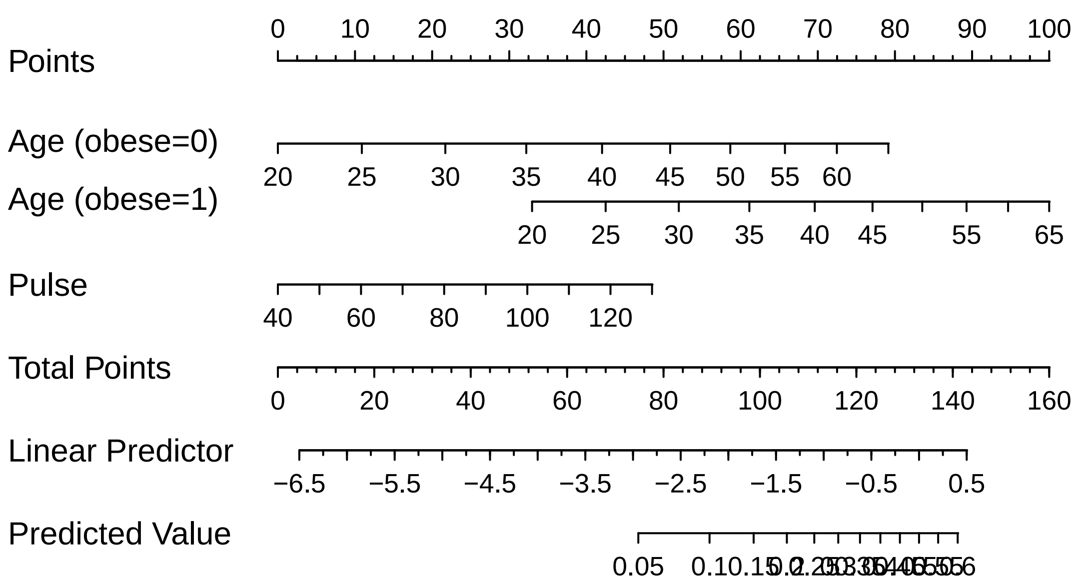
If we want to see the results of adjusting the Age from 31 to 32 among non-obese subjects, or adjusting Pulse by just one beat per minute, we can do that…

```r
summary(m5, Age = c(31,32), obese = 0, Pulse = c(64,65))
```

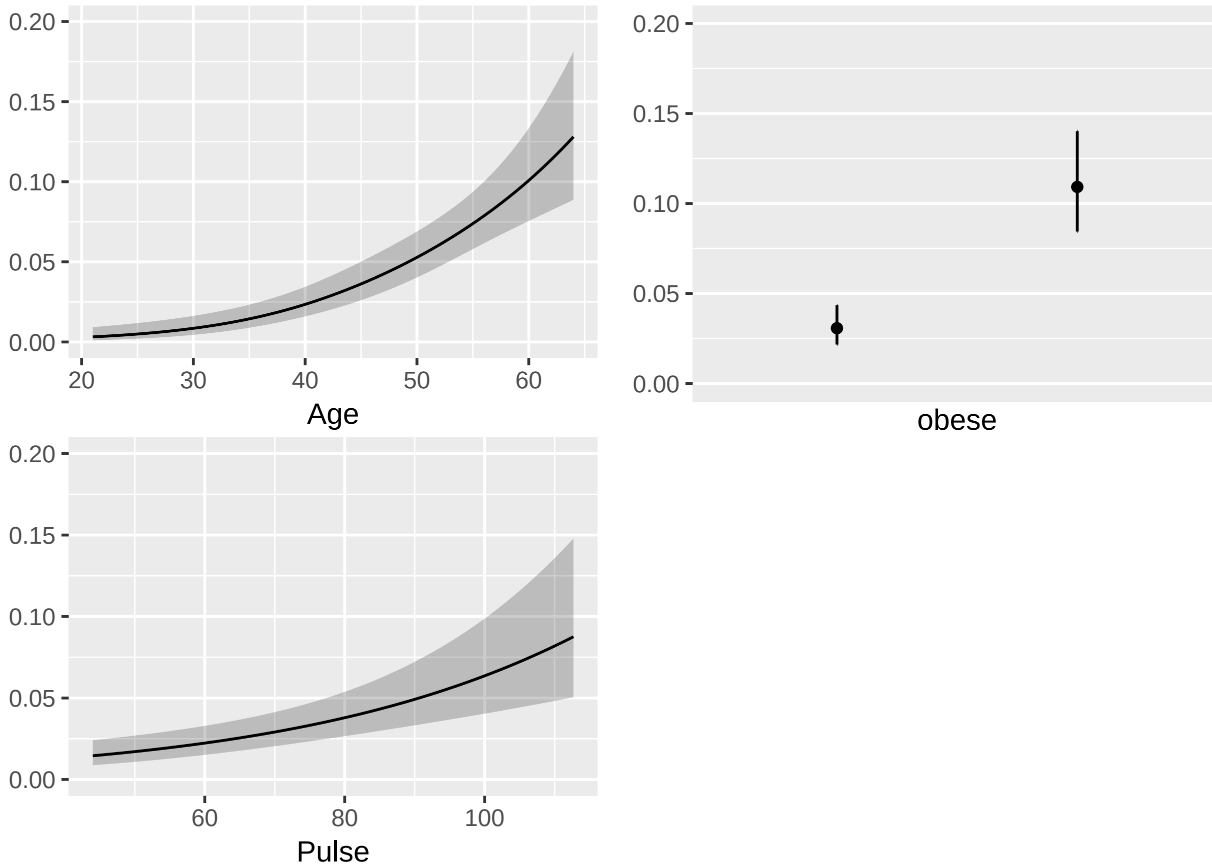
```
             Effects              Response : diabetes 

 Factor       Low High Diff. Effect   S.E.      Lower 0.95 Upper 0.95
 Age          31  32   1     0.107200 0.0258460 0.056547   0.157860  
  Odds Ratio  31  32   1     1.113200        NA 1.058200   1.171000  
 obese         0   1   1     1.353600 0.2046500 0.952540   1.754700  
  Odds Ratio   0   1   1     3.871500        NA 2.592300   5.782000  
 Pulse        64  65   1     0.027255 0.0062233 0.015057   0.039452  
  Odds Ratio  64  65   1     1.027600        NA 1.015200   1.040200  

Adjusted to: Age=43 obese=0  
```

5.4 Prediction Plot and Nomogram for Model m5

```r
plot(nomogram(m5, fun = plogis))
```




```r
ggplot(Predict(m5, fun = plogis))
```



It's hard to read the details of that nomogram. We better be sure we can make predictions using code directly…

5.5 Predicting Alice's probability of diabetes

Suppose Alice is 35 years old and has a Pulse of 100 beats per minute. To make a prediction for her using model `m5`, we'd again have to specify whether or not she is obese, or at least compare those two predicted probabilities. So what do we get?

```
predict(m5,
        newdata = data.frame(names = c("Alice A", "Alice B"),
                             Age = c(35,35), obese = c(0,1),
                             Pulse = c(100, 100)),
        type = "fitted")
```

```
         1          2 
0.03043615 0.11932894 
```

I hope this is helpful.