Regression Model Checking

February 14, 2017
Biostatistics 208

Model checking for linear regression:

- Linearity
- Normality
- Constant variance
- Influential points
- Covariate overlap

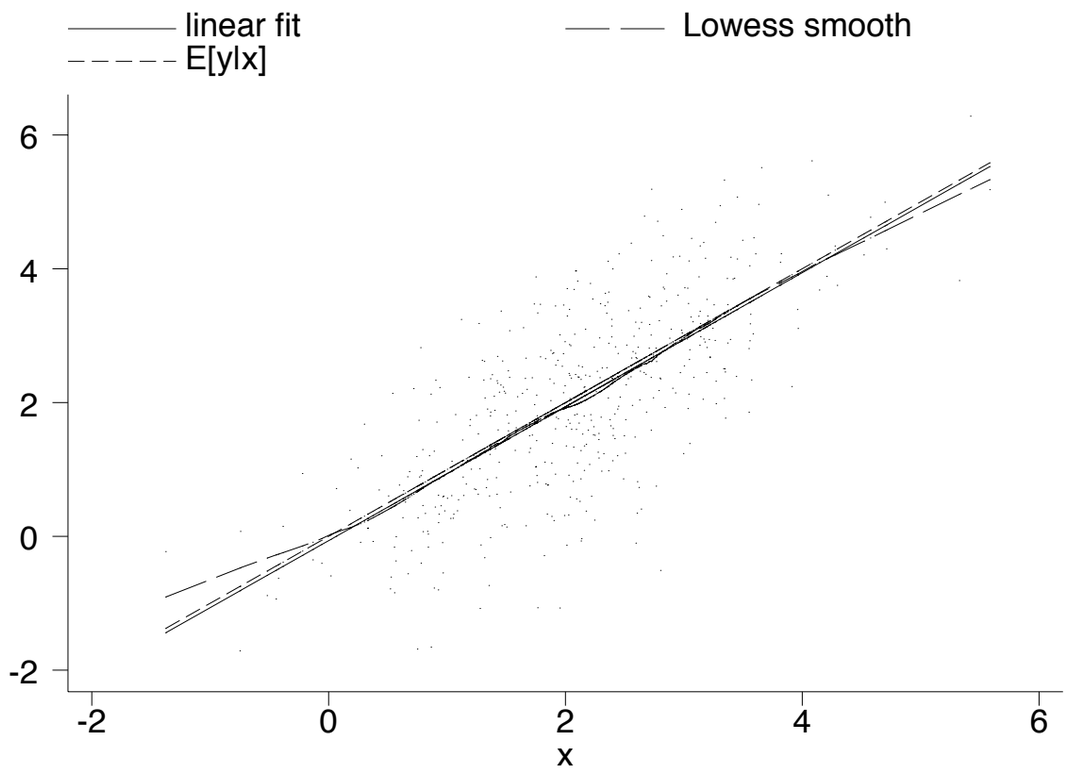
Model checking: linearity

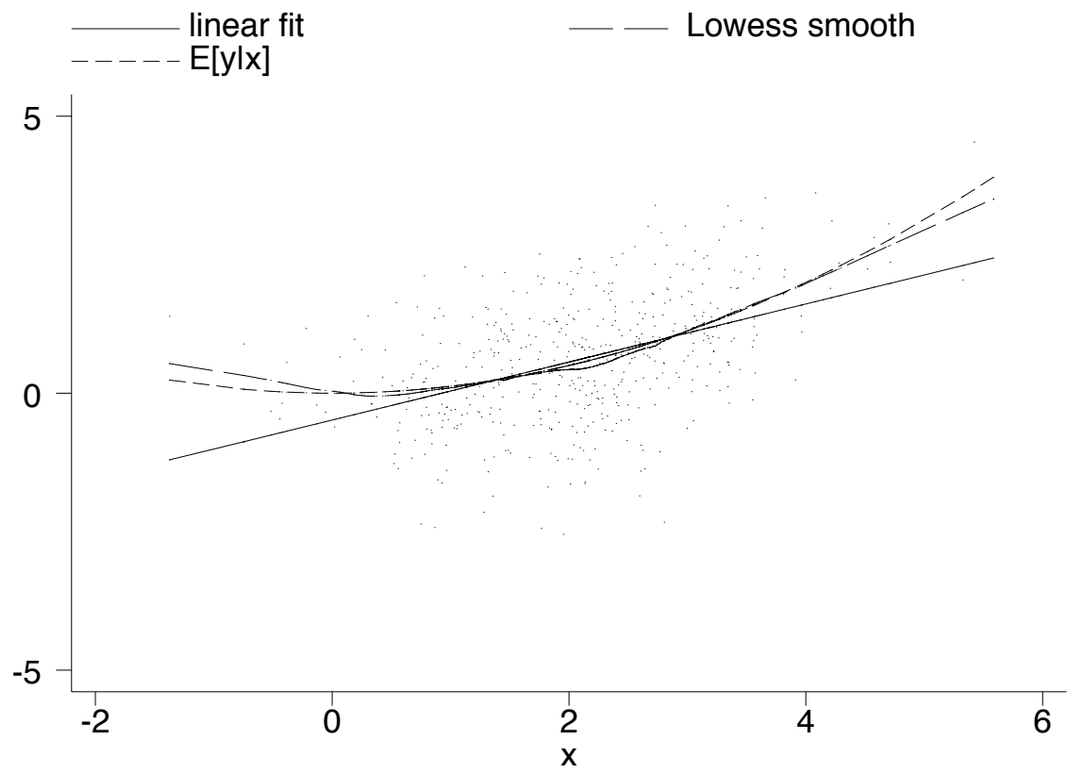
- Regression line assumed linear in continuous predictors
  - i.e., slope is constant
  - equivalently, has no curvature
- If model is correct
  - residuals have mean zero at every value of predictor
  - key to diagnostic tools for departures from linearity

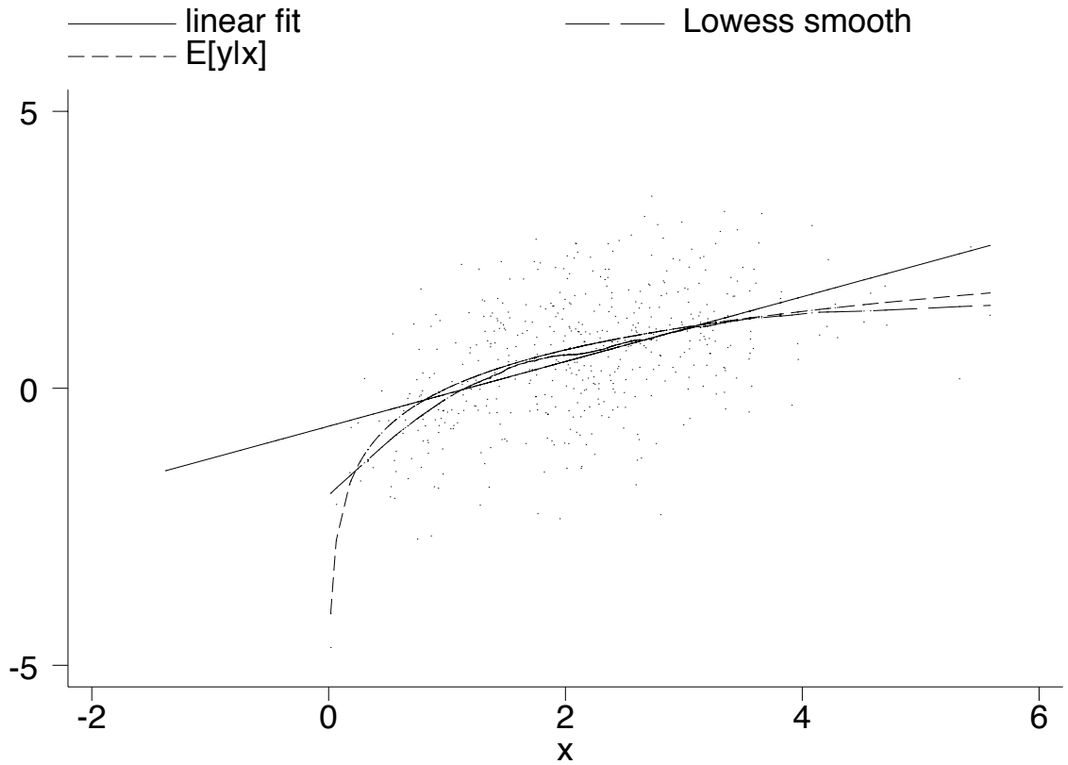
Model checking: linearity

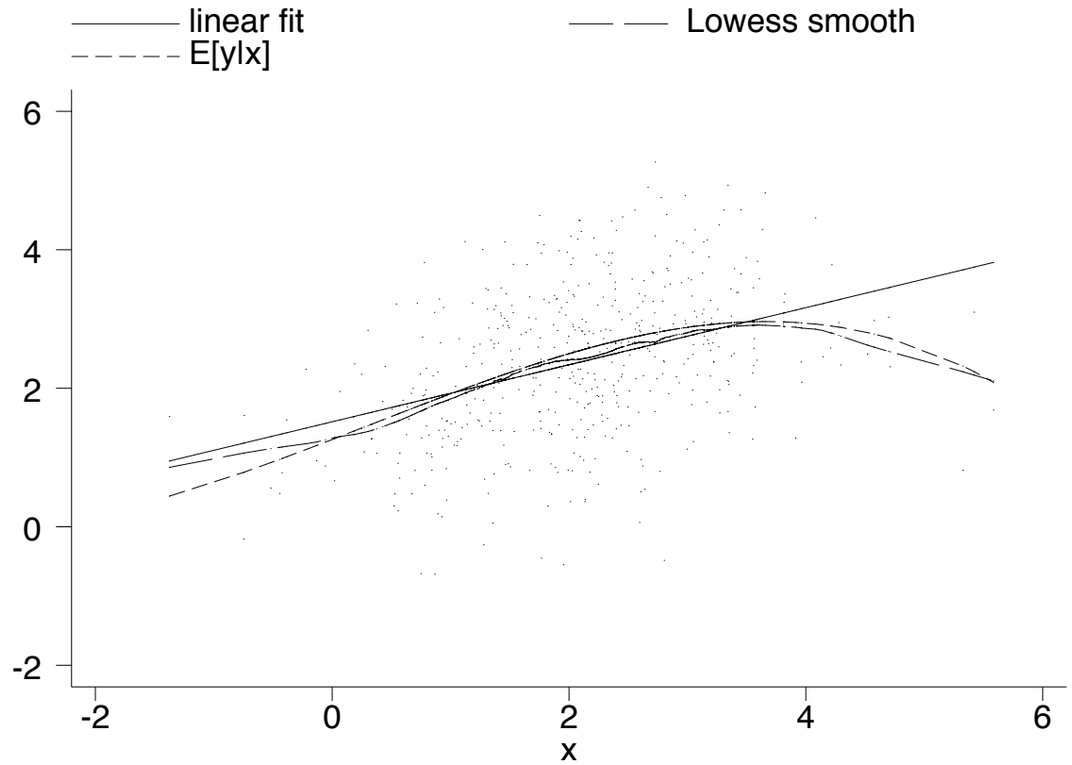
- If assumption badly violated, result can be
  - biased coefficient estimates, residual confounding
  - reduced precision and power, missed real effects
  - misleading, over-simplified conclusions

Three departures from linearity









Diagnostics for nonlinearity: RVP and CPR plots

- To account for effects of other predictors, diagnostics use residuals rather than outcome
- Basic approach: check for non-linear patterns in plots of residuals versus each continuous predictor (RVP) plots
- Better alternative: *component plus residual* (CPR) plots
  - component due to predictor added back into residual
  - results in *partial residual* for that variable
  - e.g. for a model with 2 predictors x_1 & x_2, partial resid. for x_1 :

$$\underbrace{y - (\beta_0 + \beta_1 x_1 + \beta_2 x_2)}_{\text{residual}} + \underbrace{\beta_1 x_1}_{\text{linear component}} = \underbrace{y - (\beta_0 + \beta_2 x_2)}_{\text{partial residual}}$$

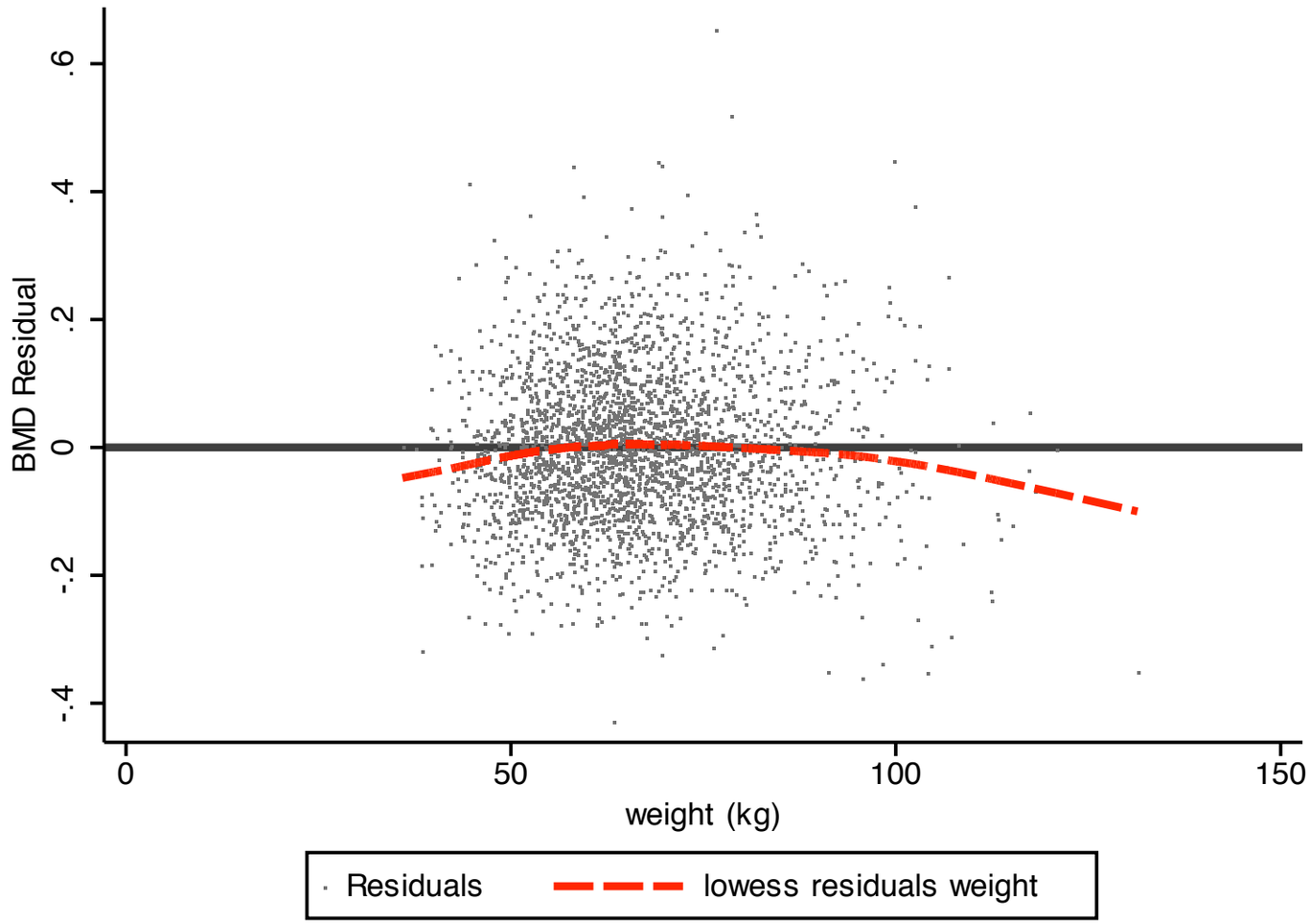
Diagnostics for nonlinearity: RVP and CPR plots

- CPR plots better for diagnosing non-linearity:
  - show trend, RVP plots do not
  - slightly easier to add LOWESS smooth
- Note: use RVP for quadratic, other polynomial models – e.g.,

$$\mathrm{E}\left[y|x\right] = \beta_0 + \beta_1 x + \beta_2 x^2 + \beta_3 x^3$$

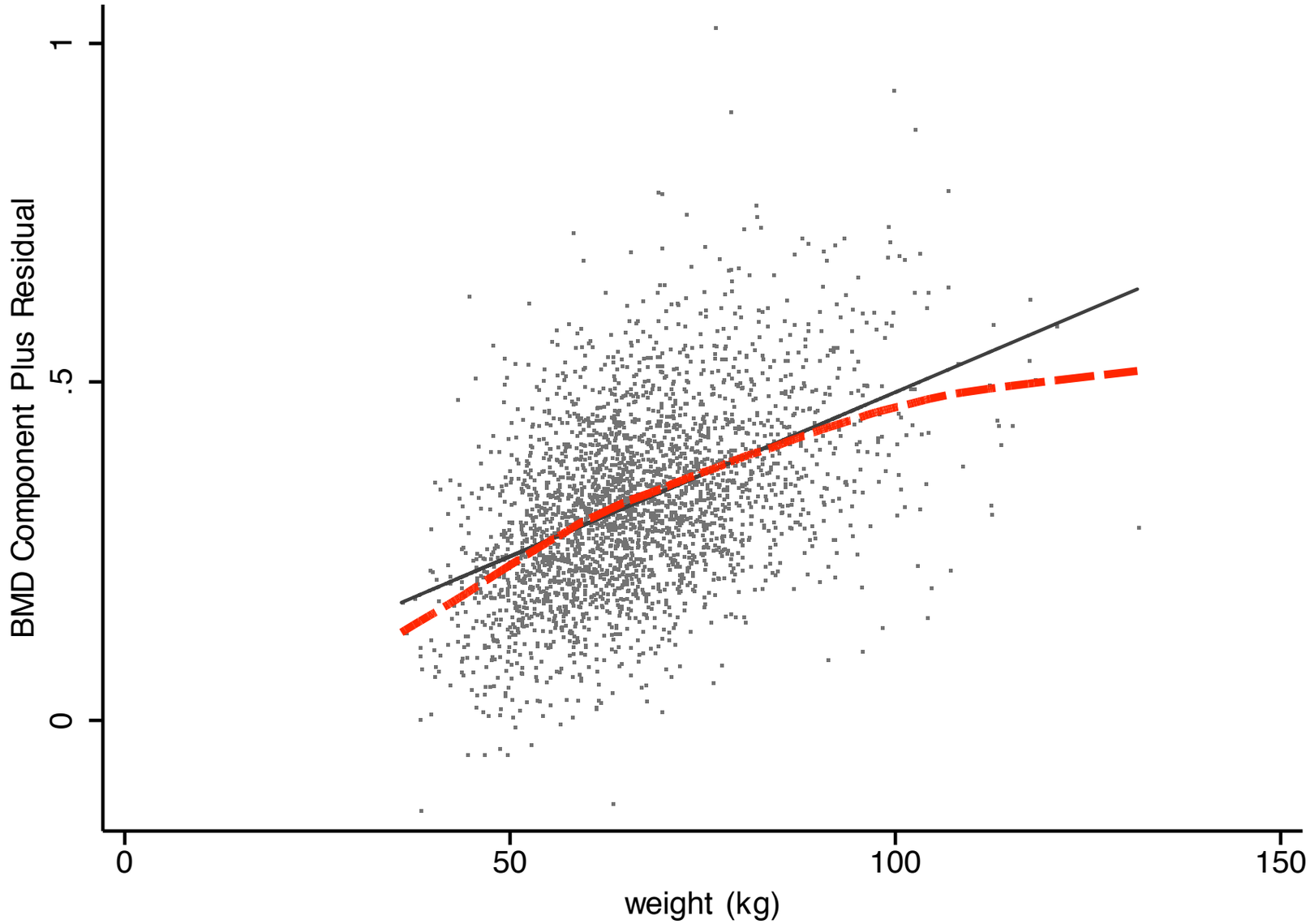
- In both CPR and RVP: mismatch of linear regression line, LOWESS smooth indicates lack of linearity

RVP plot for weight and BMD (SOF data)



Residuals from linear model for dependence of mean BMD on age & weight

CPR plot for weight and BMD



Partial residual for weight = overall residual + estimated linear component from weight

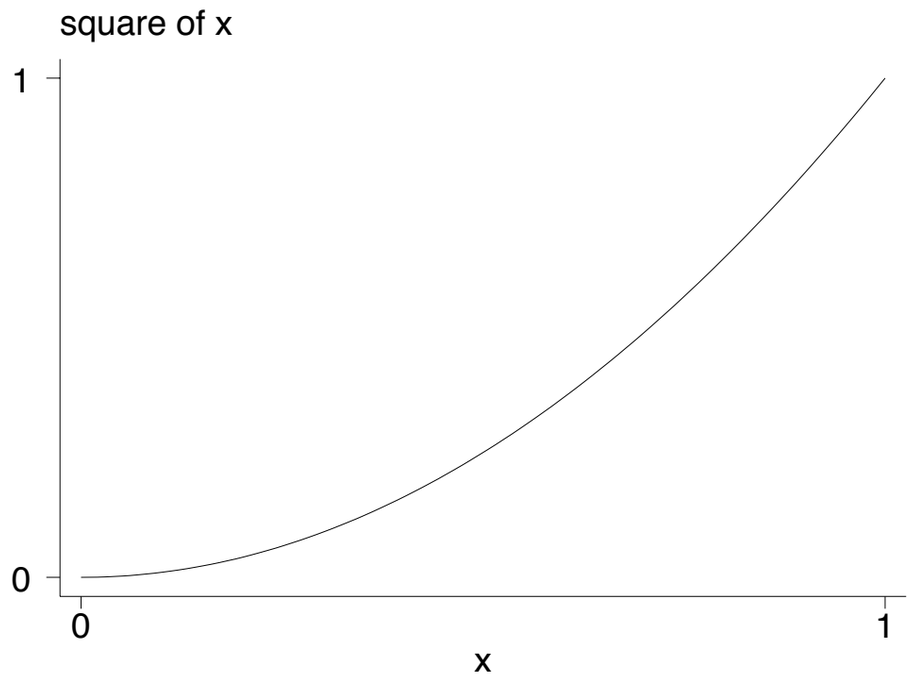
Stata code for RVP and CPR plots

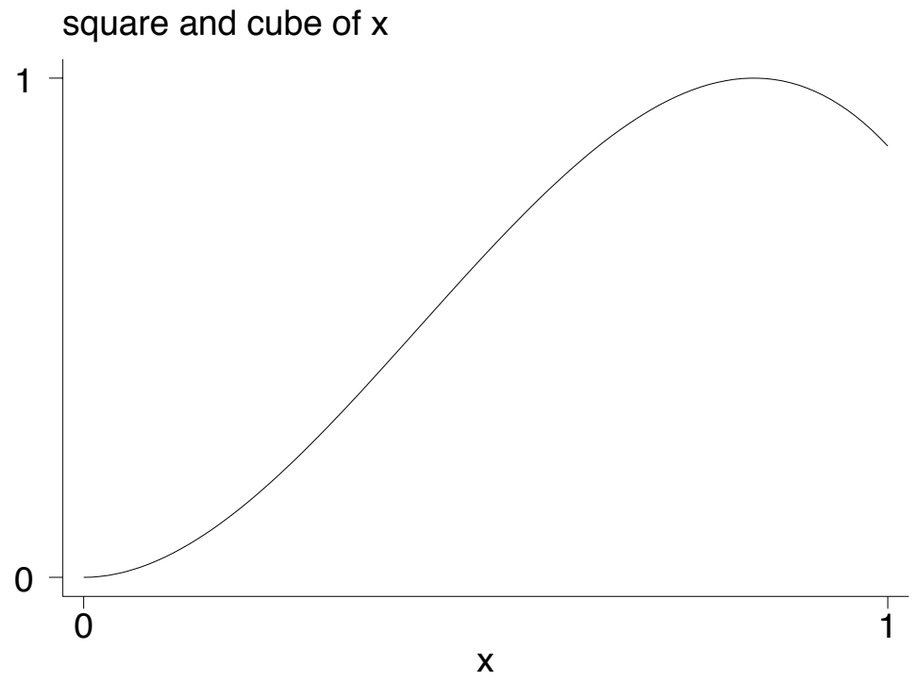
```
regress bmd age weight
predict residuals, resid

rvpplot weight, ///
    lw(thick) msize(tiny) yline(0, lw(thick)) ///
    addplot(lowess residuals weight, lw(thick) lcol(red) clpat(longdash)) ///
    plotregion(style(none)) scheme(s1mono) ytitle("BMD Residual") ///
    xtitle("weight (kg)") xlabel(0(50)150)

cprplot weight, ///
    rlopts(clpat(solid) lw(thick)) ///
    lsopts(bw(.5) clpat(longdash) lw(thick) lcol(red)) ///
    plotregion(style(none)) scheme(s1mono) msize(tiny) ///
    ytitle("BMD Component Plus Residual") xtitle("weight (kg)") ///
    xlabel(0(50)150)
```

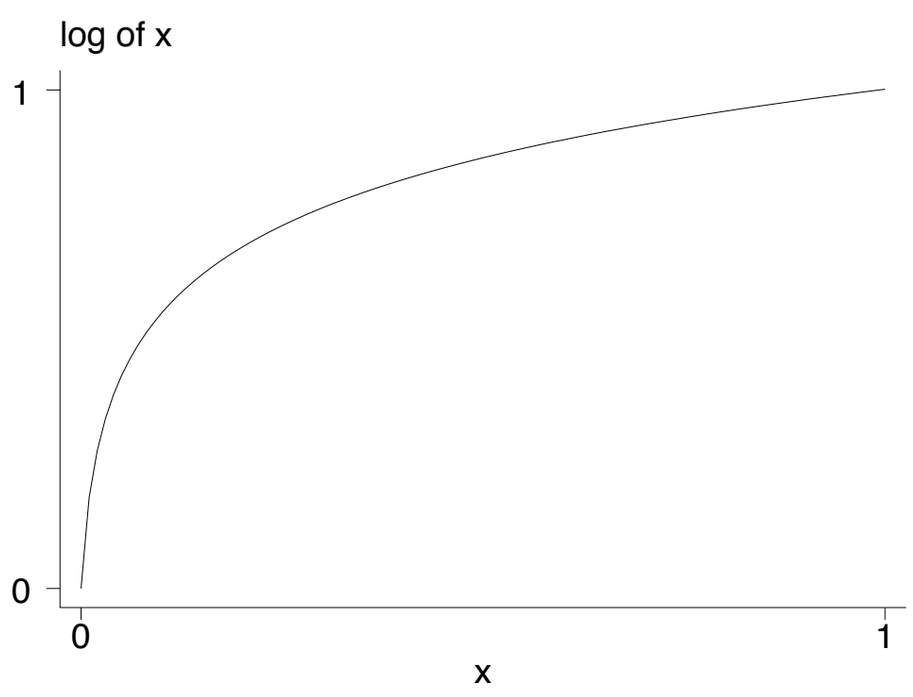
Solution: transform continuous predictors

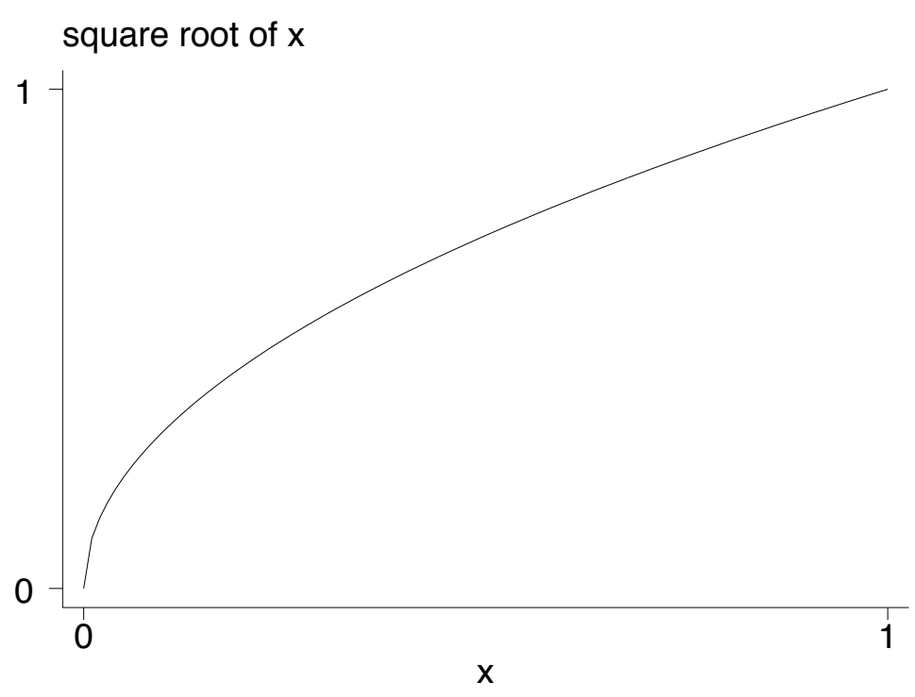
- Smooth predictor transformations to fix non-linearity:
  - $\log(x)$ – provided $\mathrm{E}[y \mid x]$ is "monotone"
  - square root, cube root, other fractional powers of x
  - x^2, x^3 (lower order terms usually included in the model)

Predictor transformations

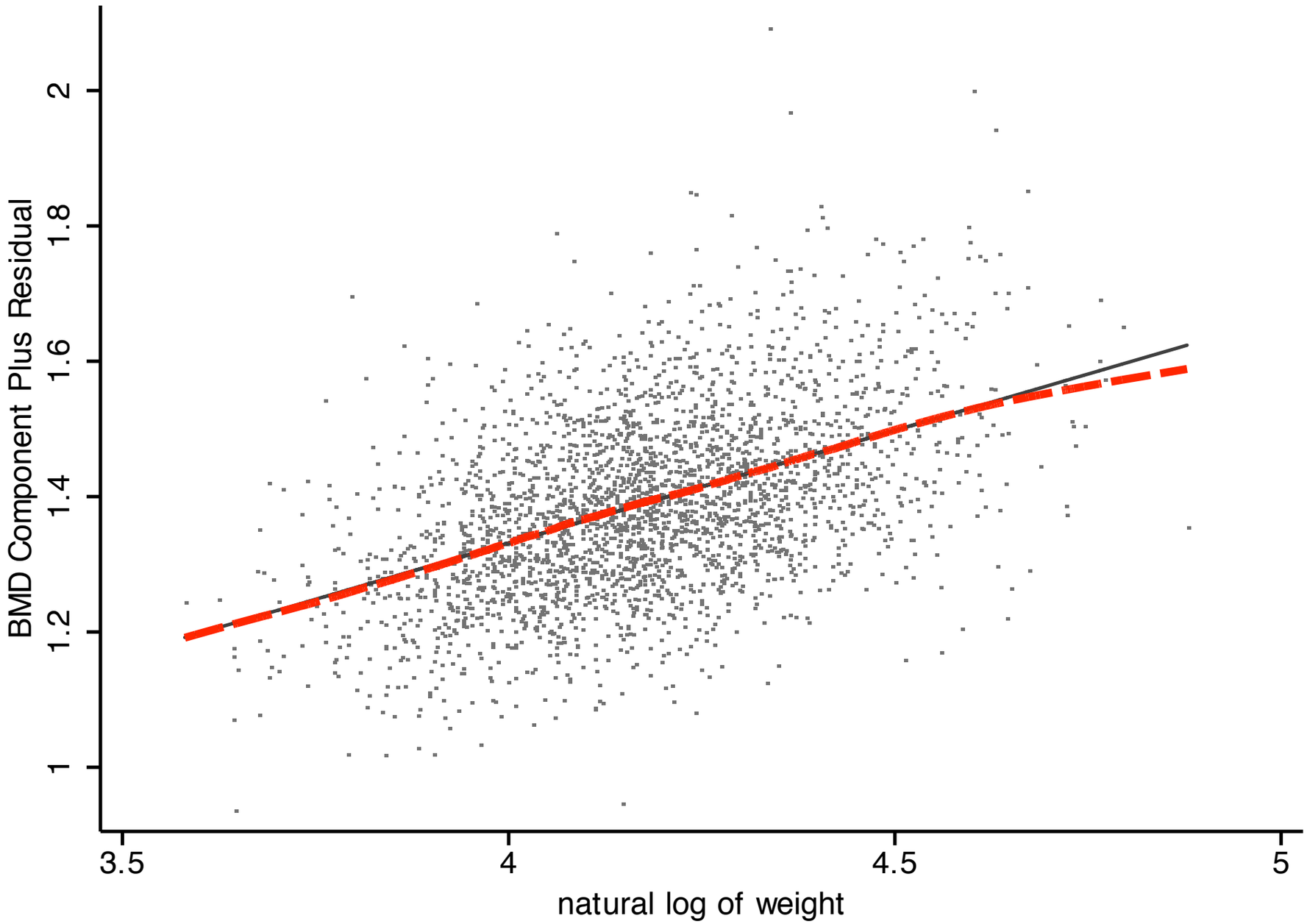








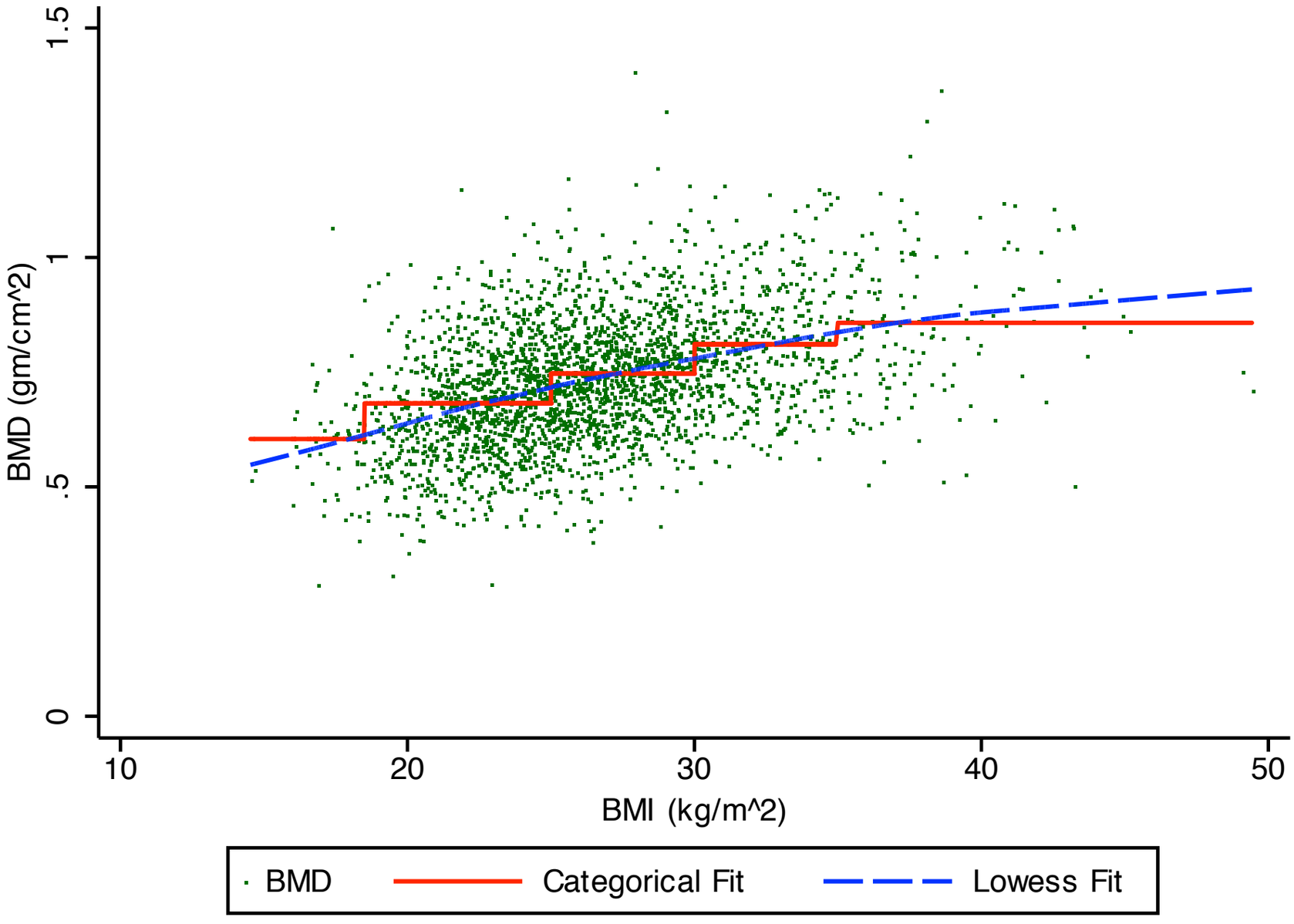
CPR plot for log-weight and BMD (SOF data)



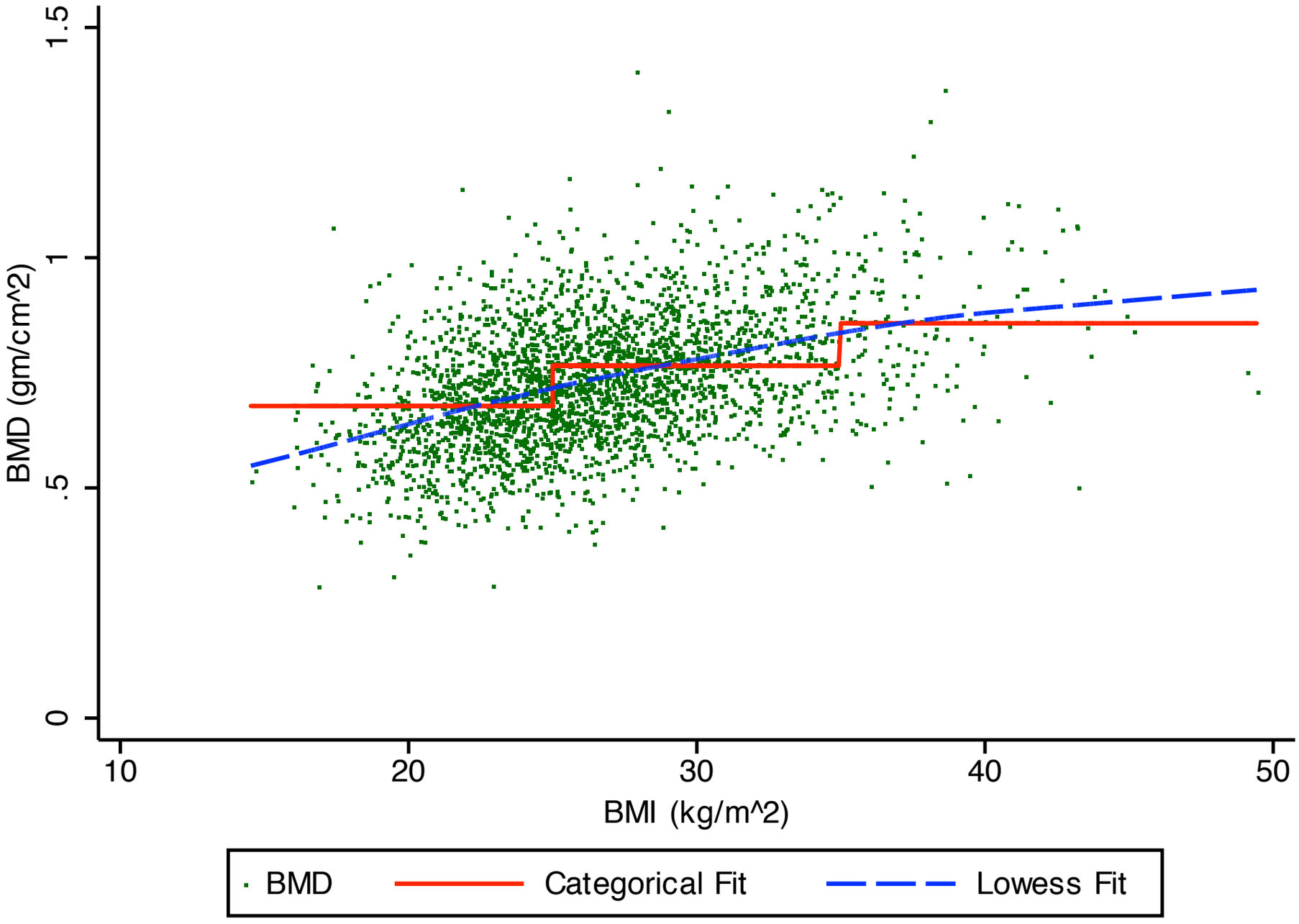
Alternatives: categorize the predictor

- Split at quantiles or clinically familiar cut-points
- Models mean as a "step function"
- Flexible, familiar, clinically interpretable, but
  - unrealistic if the regression line changes smoothly, sensitive to choice of cut-points, inefficient compared to smooth transformations
- Numbers of categories must balance fit against noisiness

Too coarsely categorizing the predictor



A better trade-off



Stata code for categorical transformations

```
recode bmi min/25=2 25/35=3 35/max=4, gen(bmicat)
regress bmd i.bmicat
predict fitted, xb
twoway ///
    (scatter bmd bmi, msize(vtiny)) ///
    (line fitted bmi, sort lpattern(solid) lcolor(red) lwidth(medthick)) ///
    (lowess bmd bmi, lpattern(longdash) lcolor(blue) lwidth(medthick)), ///
    plotregion(style(none)) scheme(s1color) ///
    ytitle("BMD (gm/cm{superscript:2})")  ///
    xtitle("BMI (kg/m{superscript:2})") ///
    legend(label(2 "Categorical Fit") label(3 "Lowess Fit") rows(1))
recode bmi min/18.5=1 18.5/25=2 25/30=3 30/35=4 35/max=5, gen(bmicat2)
regress bmd i.bmicat2
predict fitted2, xb
twoway ///
    (scatter bmd bmi, msize(vtiny)) ///
    (line fitted2 bmi, sort lpattern(solid) lcolor(red) lwidth(medthick)) ///
    (lowess bmd bmi, lpattern(longdash) lcolor(blue) lwidth(medthick)), ///
    plotregion(style(none)) scheme(s1color) ///
    ytitle("BMD (gm/cm{superscript:2})") ///
    xtitle("BMI (kg/m{superscript:2})") ///
    legend(label(2 "Categorical Fit") label(3 "Lowess Fit") rows(1))
```

Alternatives: linear, restricted cubic splines

- *Linear splines*: piecewise linear with changes in slope at "knots"
  - coefficients interpretable as slope between knots
- *Restricted cubic splines*: smooth curve, cubic between knots
  - tails better behaved than polynomials - *restricted* to linearity before first and after last knot
  - easy tests for overall effects and non-linearity, but coefficients uninterpretable; presentation requires plotting
- Also: fractional polynomials (`fracpoly` command)

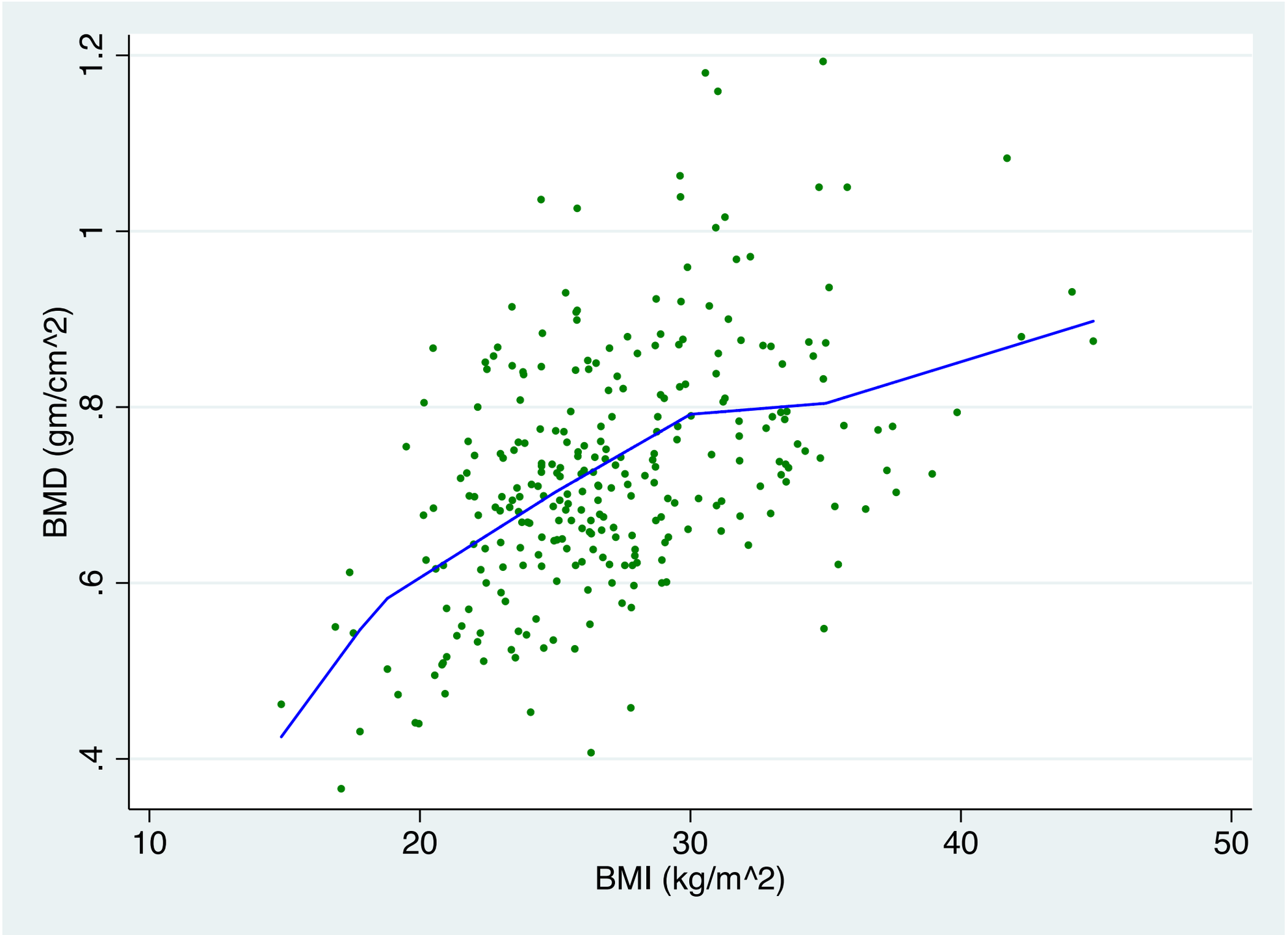
Ref. on cubic splines and fractional polynomials: http://www.stata-journal.com/sjpdf.html?articlenum=st0120

Linear spline model for BMI effect on BMD in SOF

```
. mkspline bmi1 18.5 bmi2 25 bmi3 30 bmi4 35 bmi5 = bmi

. regress bmd bmi1-bmi5

      Source |       SS       df       MS              Number of obs =     278
-------------+------------------------------           F(  5,   272) =   18.91
       Model |  1.34269169     5  .268538337            Prob > F      =  0.0000
    Residual |  3.86165215   272  .014197251            R-squared     =  0.2580
-------------+------------------------------           Adj R-squared =  0.2444
       Total |  5.20434383   277  .018788245            Root MSE      =  .11915

------------------------------------------------------------------------------
         bmd |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        bmi1 |   .0418738   .0300524     1.39   0.165     -.017291    .1010387
        bmi2 |   .0194547   .0060541     3.21   0.001     .0075358    .0313736
        bmi3 |    .017719   .0054267     3.27   0.001     .0070354    .0284027
        bmi4 |   .0024954   .0070065     0.36   0.722    -.0112986    .0162893
        bmi5 |   .0094409    .007597     1.24   0.215    -.0055154    .0243972
       _cons |  -.1979034   .5417402    -0.37   0.715     -1.26444    .8686334
------------------------------------------------------------------------------
```

Interpretation of the overall F statistic for this model?

Linear spline fit



Testing for non-linearity using linear splines

```
. testparm bmi*, equal

(1) -bmi1+bmi2=0
(2) -bmi1+bmi3=0
(3) -bmi1+bmi4=0
(4) -bmi1+bmi5=0

       F(4, 272)= 2.24
            Prob > F = 0.0654
```

F statistic evaluates equality of slopes between knots.

Restricted cubic spline model for BMI effect on BMD in SOF

```
. mkspline bmisp = bmi, cubic
.* selects default knots and creates new predictors bmisp1 - bmisp4
. regress bmd bmisp*

      Source |       SS           df       MS      Number of obs   =       278
-------------+----------------------------------   F(4, 273)       =     25.21
       Model |  1.40393728         4  .350984321   Prob > F        =    0.0000
    Residual |  3.80040655       273  .013920903   R-squared       =    0.2698
-------------+----------------------------------   Adj R-squared   =    0.2591
       Total |  5.20434383       277  .018788245   Root MSE        =    .11799

------------------------------------------------------------------------------
         bmd |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      bmisp1 |   .0367141   .0078805     4.66   0.000     .0211999    .0522283
      bmisp2 |  -.1583327   .0606301    -2.61   0.010    -.2776947   -.0389707
      bmisp3 |   .6911728   .2756232     2.51   0.013     .1485558     1.23379
      bmisp4 |  -.8292426   .3414449    -2.43   0.016    -1.501442   -.1570429
       _cons |  -.1408691   .1695457    -0.83   0.407    -.4746523    .1929141
------------------------------------------------------------------------------
```

spline terms

Note: first term in a restricted cubic spline fit represents the linear component (i.e. `bmisp1` in example)

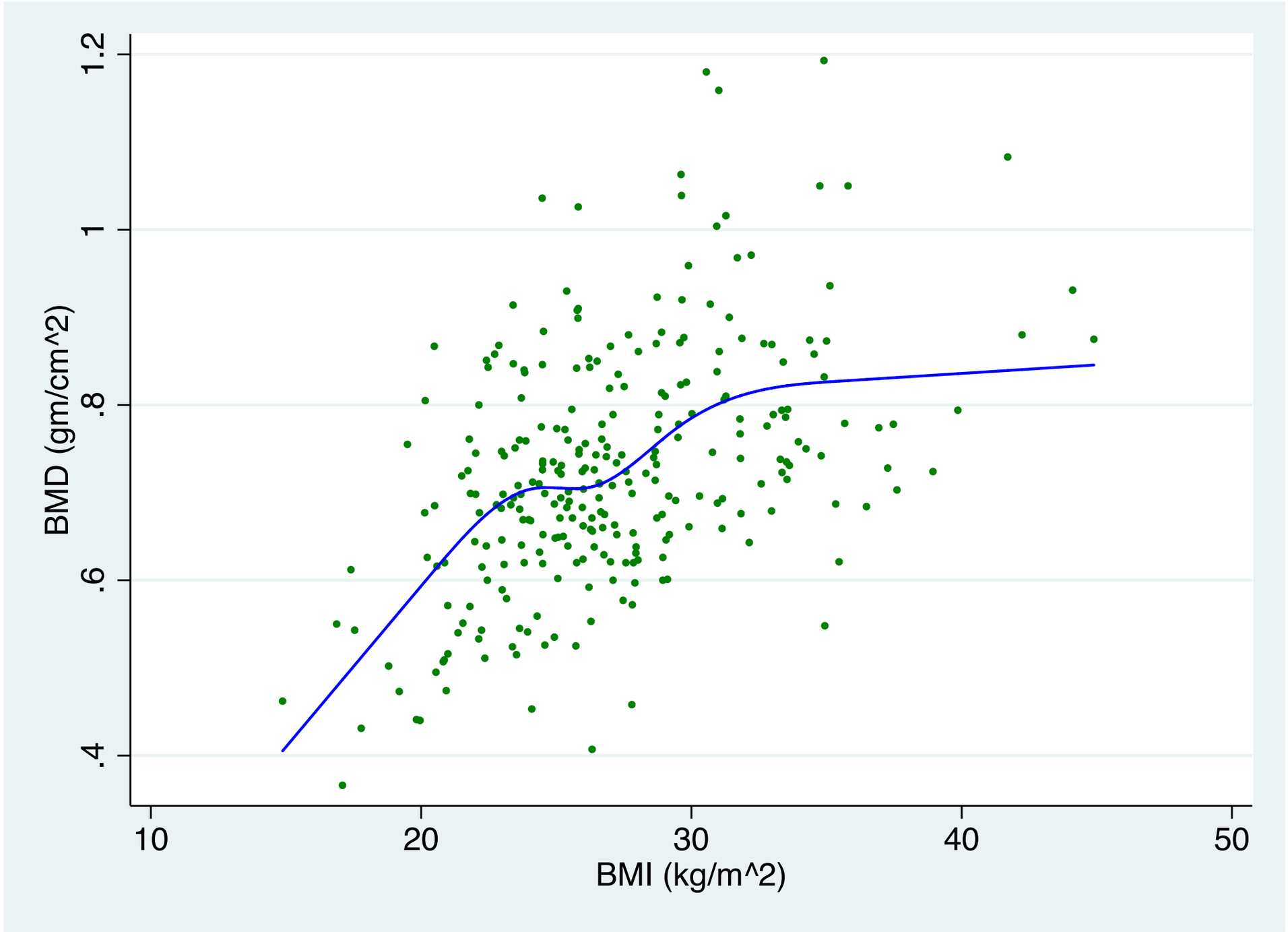
- Test for any BMI effect on BMD

```
. testparm bmisp*

 ( 1)  bmisp1 = 0
 ( 2)  bmisp2 = 0
 ( 3)  bmisp3 = 0
 ( 4)  bmisp4 = 0

       F(  4,   273) =   25.21
            Prob > F =    0.0000
```

- Test for departure from linearity

```
. testparm bmisp2 bmisp3 bmisp4

( 1)  bmisp2 = 0
( 2)  bmisp3 = 0
( 3)  bmisp4 = 0

      F(  3,   273) =    4.51
           Prob > F =    0.0042
```

Cubic spline fit



Checking linearity: summary

- Diagnostics:
  - linear models: curved LOWESS smooth in CPR or RVP plot
  - more generally (i.e., linear, logistic, Cox models): fit restricted cubic spline, test for departure from linearity using `testparm` for all but first spline component

- Solutions: transform predictor, use linear or cubic splines
  - linear splines: piecewise linear; useful when linearity of particular segments is of interest
  - cubic splines: smooth, nonlinear functions

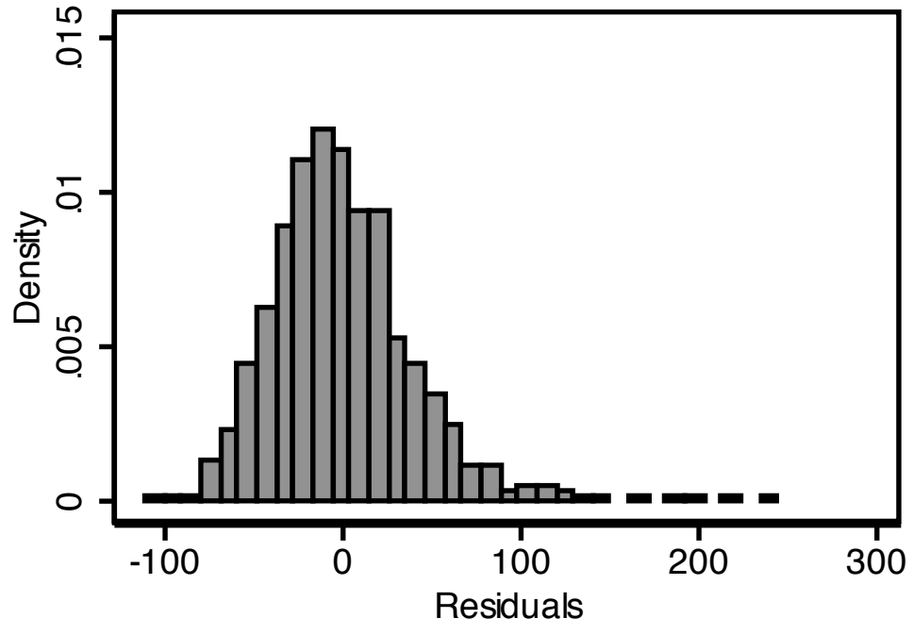
Checking the model: normality

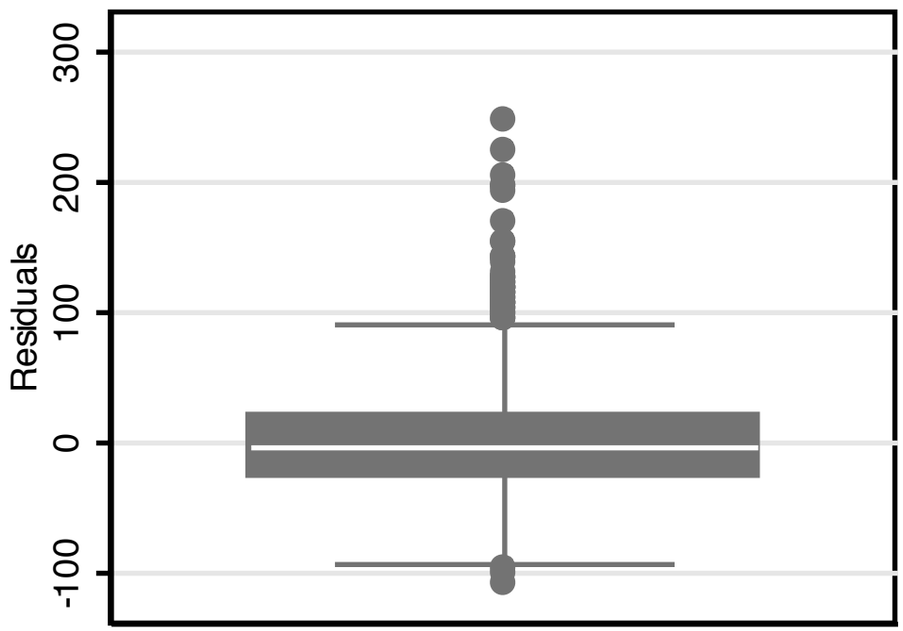
- Validity of *t*- and *F*-tests, CIs depend on assumption of normality of residuals (ε)
- Fairly robust to violations, especially short-tailed errors in larger samples
- However, long-tailed distributions of ε can degrade power, precision
- Diagnostics: Q-Q and other plots of residuals

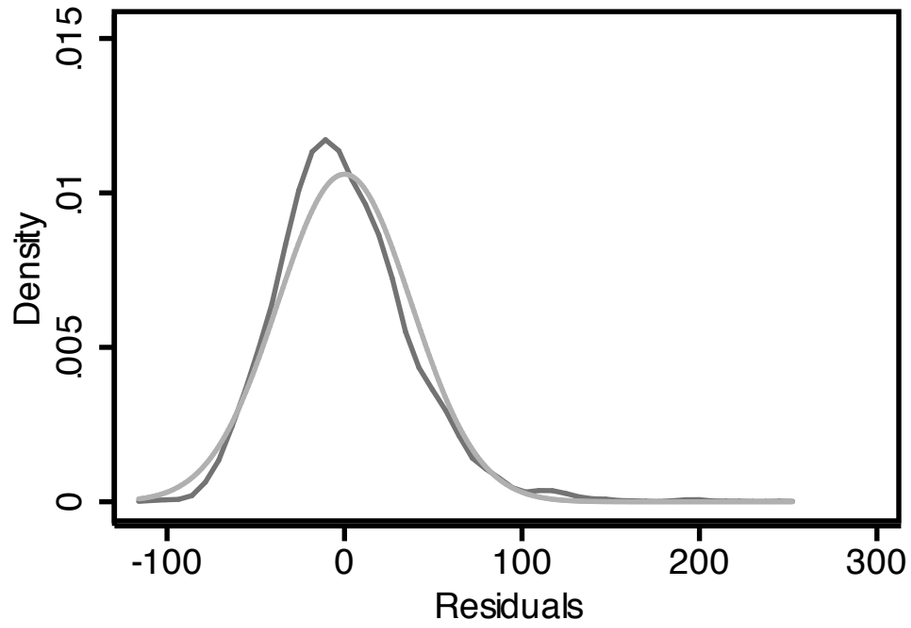
Example: model for mean LDL in HERS

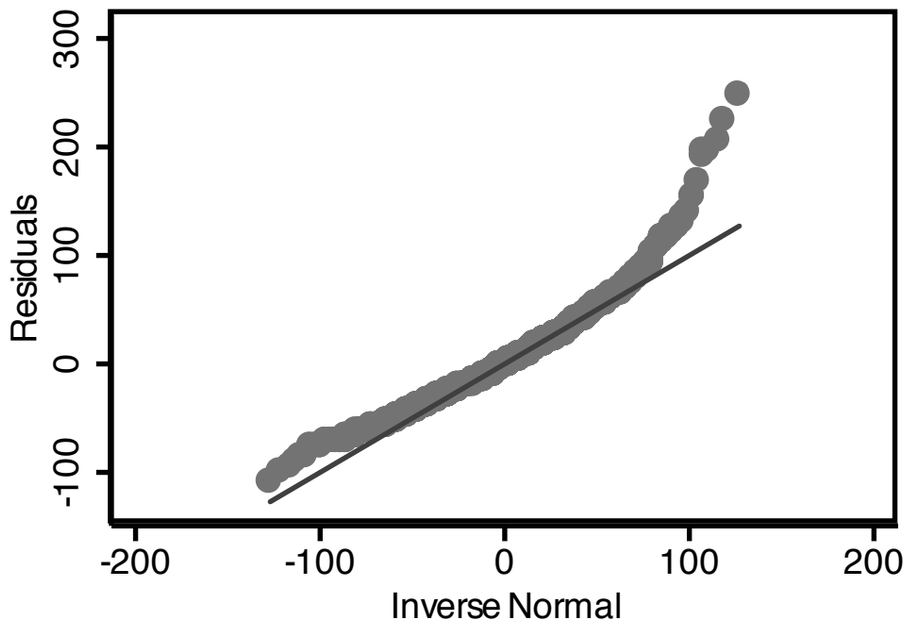
```
. regress LDL BMI age nonwhite smoking drinkany

      Source |       SS       df       MS              Number of obs =    2745
-------------+------------------------------           F(  5,  2739) =    5.97
       Model |  42279.1877     5  8455.83753            Prob > F      =  0.0000
    Residual |   3881903.3  2739  1417.27028            R-squared     =  0.0108
-------------+------------------------------           Adj R-squared =  0.0090
       Total |  3924182.49  2744  1430.09566            Root MSE      =  37.647

------------------------------------------------------------------------------
         LDL |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         BMI |   .3591038   .1341047     2.68   0.007     .0961472    .6220605
         age |  -.1897166   .1130776    -1.68   0.094    -.4114427    .0320095
    nonwhite |   5.219436   2.323673     2.25   0.025     .6631079    9.775764
     smoking |   4.750738   2.210391     2.15   0.032     .4165362     9.08494
    drinkany |  -2.722354   1.498854    -1.82   0.069    -5.661352    .2166445
       _cons |   147.3153   9.256449    15.91   0.000       129.165    165.4656
------------------------------------------------------------------------------
* save residuals in new variable
. predict resid, residuals
```

Diagnosing departures from normality







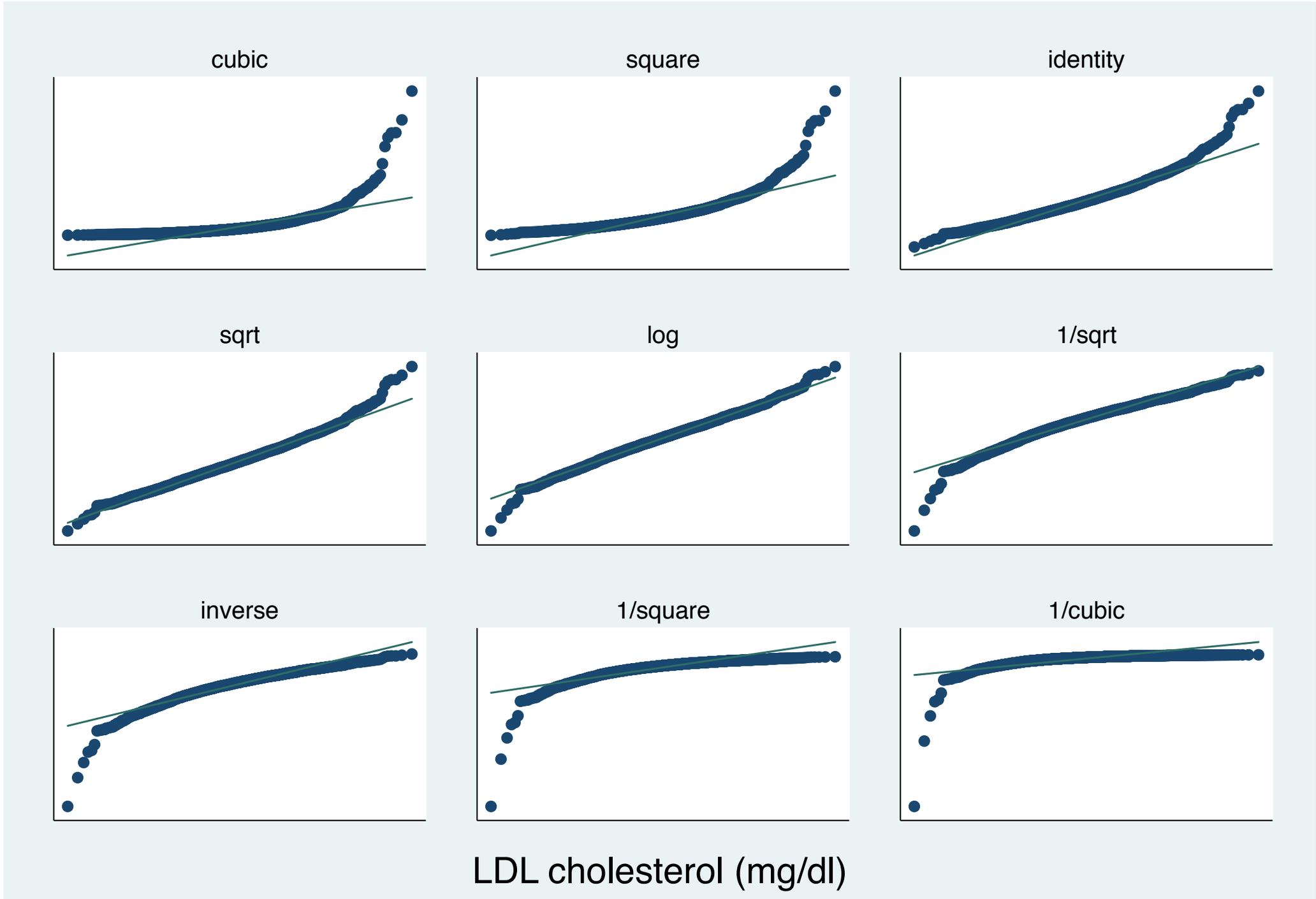


Some apparent evidence for skewness

Solution: transform the outcome

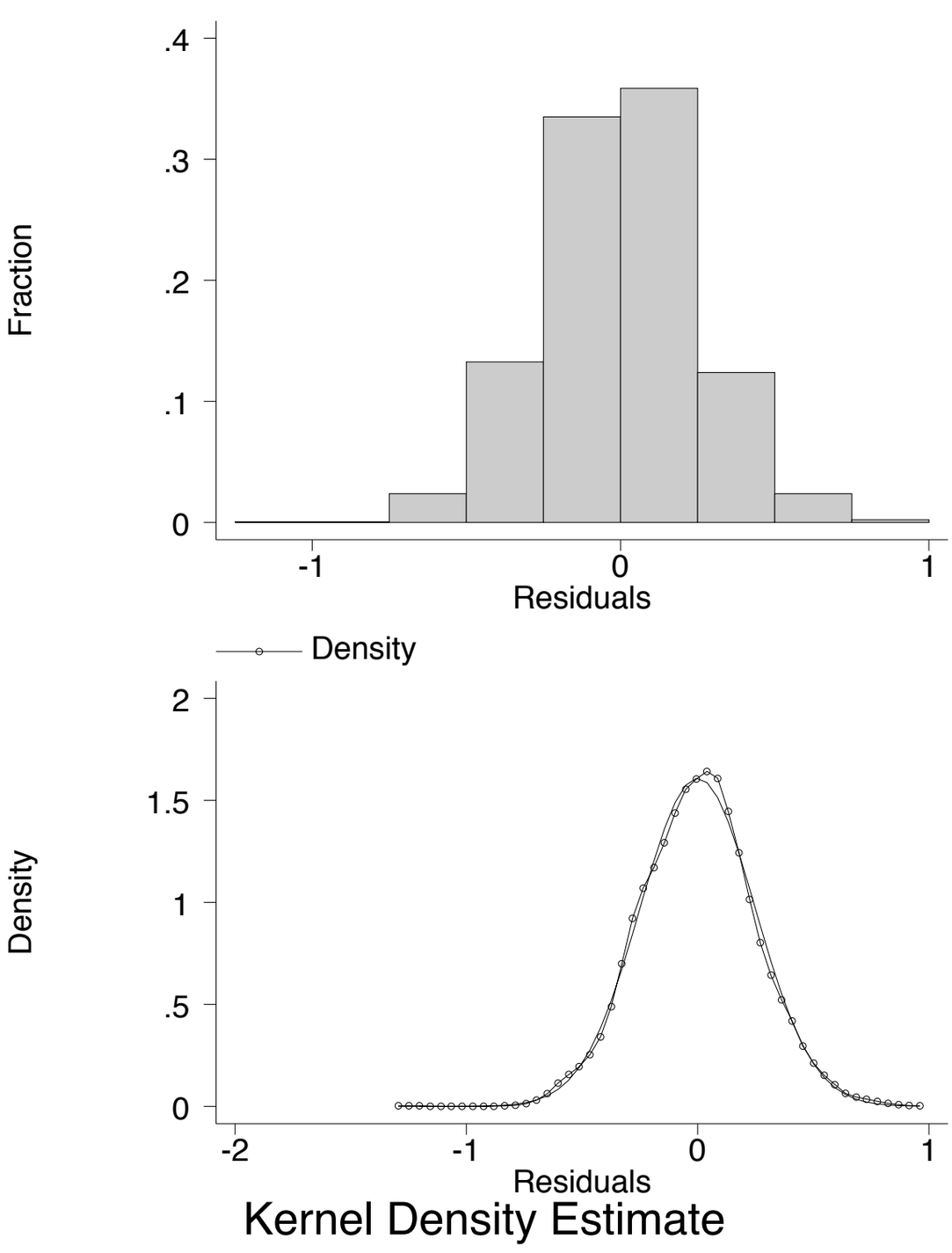
- Residuals skewed (usually to the right):
  - log, square root, other power transformations may help
  - may need to add constant for logs to make all values positive
- Search for best transformation using `qladder` command in Stata
- Residuals symmetrically long-tailed
  - rank transformation, trimming, Winsorization

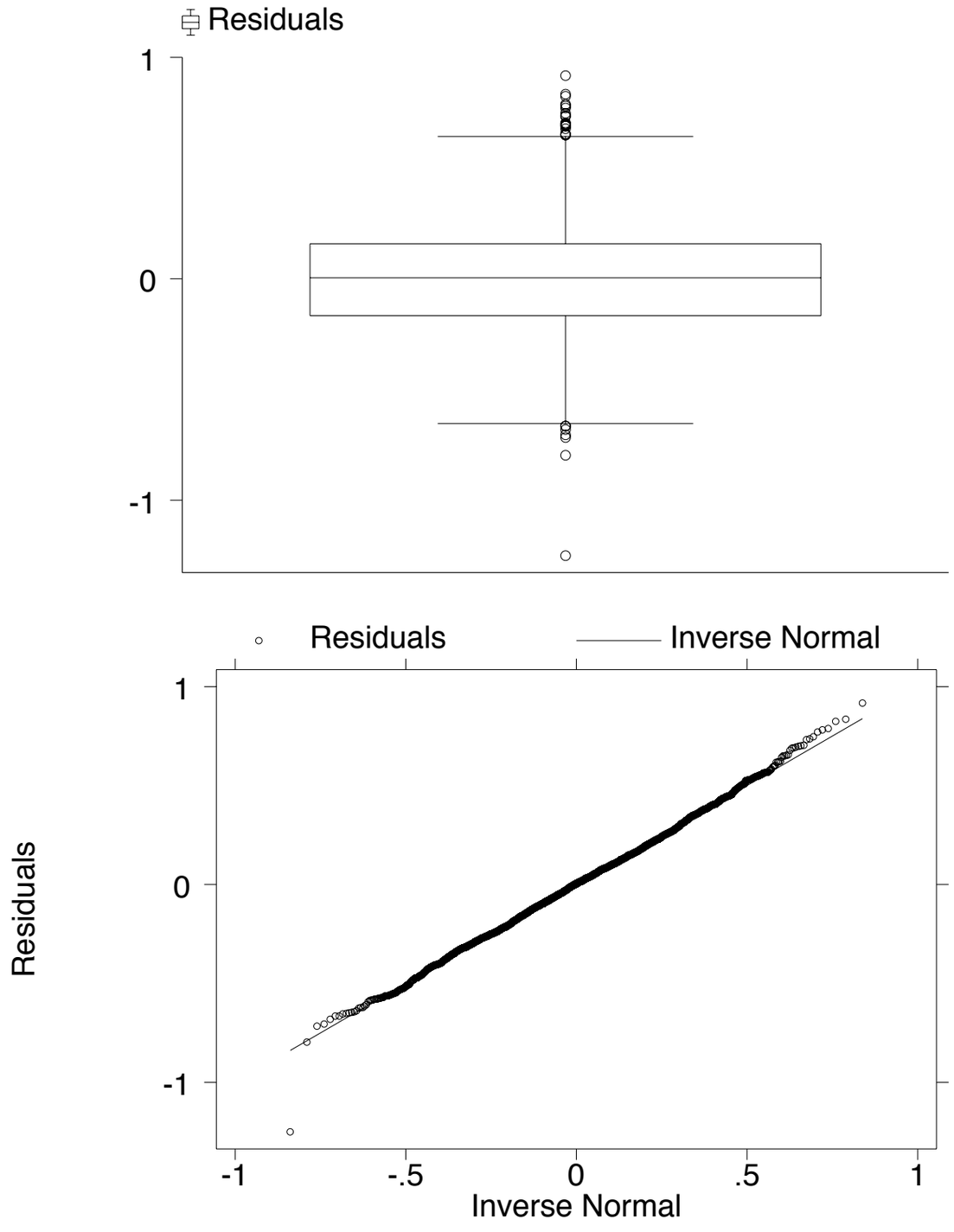
Q ladder plots for LDL



Stata command: `qladder LDL, ylabel(none) xlabel(none)`

Residuals of log-transformed LDL





Another solution: bootstrap CIs

- Resample n observations *with replacement* from data, re-fit model, store estimates, repeat $100, 500, 1{,}000$ times or more
- Distribution of bootstrap estimates models sampling distribution of actual estimate
- Quick, partial solution:
  1. replace model-based SE by SD of bootstrap estimates
  2. construct CIs assuming Normality (i.e. estimate +/- 1.96*SE)

A better solution: percentile bootstrap CIs

- 95% CI: 2.5^{th} to 97.5^{th} percentile of bootstrap estimates
- Bias-correction shifts CI slightly to right or left
- Slower but avoids making Normality assumption
- Requires using many (preferably 1000) bootstrap samples
  - extreme percentiles are noisy!
  - default is 50

Stata code for normal based bootstrap CIs

```
. regress LDL BMI age nonwhite smoking drinkany, vce(bootstrap)
(running regress on estimation sample)

Bootstrap replications (50)
----+--- 1 ---+--- 2 ---+--- 3 ---+--- 4 ---+--- 5
..................................................    50

Linear regression                               Number of obs     =      2745
                                                Replications      =        50
                                                Wald chi2(5)      =     28.49
                                                Prob > chi2       =    0.0000
                                                R-squared         =    0.0108
                                                Adj R-squared     =    0.0090
                                                Root MSE          =   37.6467
------------------------------------------------------------------------------
             |   Observed   Bootstrap                         Normal-based
         LDL |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         BMI |   .3591038   .1462864     2.45   0.014     .0723878    .6458199
         age |  -.1897166   .1020424    -1.86   0.063    -.3897161    .0102829
    nonwhite |   5.219436   2.638803     1.98   0.048      .047478    10.39139
     smoking |   4.750738   2.186506     2.17   0.030      .465265    9.036211
    drinkany |  -2.722354   1.540028    -1.77   0.077    -5.740754    .2960465
       _cons |   147.3153   8.558059    17.21   0.000     130.5418    164.0888
------------------------------------------------------------------------------
```

Stata code for bias-corrected percentile CIs

```
. quietly regress LDL BMI age nonwhite smoking drinkany, vce(bootstrap, reps(1000))
. estat bootstrap

Linear regression                               Number of obs      =      2745
                                                Replications       =      1000

------------------------------------------------------------------------------
             |    Observed                 Bootstrap
         LDL |       Coef.       Bias    Std. Err.  [95% Conf. Interval]
-------------+----------------------------------------------------------------
         BMI |   .35910384   .0041909   .13067908    .1089804   .6241642  (BC)
         age |   -.1897166  -.0004125   .11328262   -.3846027   .0482868  (BC)
    nonwhite |   5.2194359   .0693828   2.5754791    .0820059   10.25661  (BC)
     smoking |    4.750738   .0231322   2.2627561    .4212856   9.389248  (BC)
    drinkany |  -2.7223535    .041779   1.5069455   -5.879202  -.0033287  (BC)
       _cons |   147.31529  -.1740116   9.0724581    129.3511   164.1917  (BC)
------------------------------------------------------------------------------
(BC)   bias-corrected confidence interval
```

Note: "`estat bootstrap, all`" provides normal, percentile & BC intervals

Solution: Generalized Linear Models (GLMs)

- GLMs are available for a variety of outcome distributions and are characterized by a *link function* for the relationship between mean and predictors
- Example: logistic model for binary outcomes uses the log odds to link mean (proportion) and predictor:

$$\log \frac{\mathrm{E}\left[y|x_1, x_2, \ldots\right]}{1 - \mathrm{E}\left[y|x_1, x_2, \ldots\right]} = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \cdots$$

- Other generalized linear models (GLMs) for various (e.g. count and continuous) outcomes, generally model $\log \mathrm{E}[\, y \mid x \,]$ as linear (Biostat 209)

outcome type	*distribution*	*variance-mean relationship*	*std. link*
continuous	normal	constant	identity
continuous	gamma	proportional ($\sigma^2 \propto \mu$)	inverse
binary	binomial	$\sigma^2 = n\,\mu(1 - \mu)$	log odds
count	Poisson	equal ($\sigma^2 = \mu$)	log
count	neg. binomial	$\sigma^2 = \mu + \mu^2/k$	log

Another solution: ordinal models

- Example: distribution of Agatston scores for coronary artery calcium (CAC) mostly zeroes with long right tail
- Log-transformation (after adding 1) does not help: still mostly zeroes with long right tail
- Could dichotomize outcome as CAC > 0 or CAC > 10
  - use logistic model - but potentially wasteful

Ordinal models (continued)

- Alternatively, categorize CAC as 0, 1-9, 10-99, 100-399, ≥ 400, use regression model for ordinal outcomes
- proportional odds (`ologit` - to be discussed with logistic regression)
- Proportional odds assumption relaxed using `gologit2`

Solution: two-part and zero-inflated models

- *Two-part models*:
  1. logistic model for CAC>0
  2. linear model for log-transformed CAC scores >0
- Testing of overall predictor effects uses *seemingly unrelated regressions* approach, `suest` command
- *Zero-inflated models* allow for more zeroes than expected under Poisson or negative binomial distribution (and can be applied to non-count outcomes); `zip` and `zinb` commands

Checking normality: summary

- Diagnostics: curvature in QQ-plot of residuals
- Solutions: transform outcome, use bootstrap percentile CIs, or GLMs including ordinal, two-part, zero-inflated models

Checking the model: constant variance

- If constant variance assumption is violated
  - coefficient estimates unbiased but inefficient
  - tests for between-group differences may be invalid
  - unlike Normality problems, larger samples don't help

Diagnostics: constant variance

- Plot residuals against fitted values, predictors
  - check for horizontal funnel shapes
- Compare sample size, variance of residuals across subgroups:
  - watch out if both differ by factors of more than 2

Solution: transform outcome

outcome	*transformation*
variance ∝ mean	square root
SD ∝ mean	log
proportions	arcsin
correlations	$\log[(1 + \rho)/(1 - \rho)]$

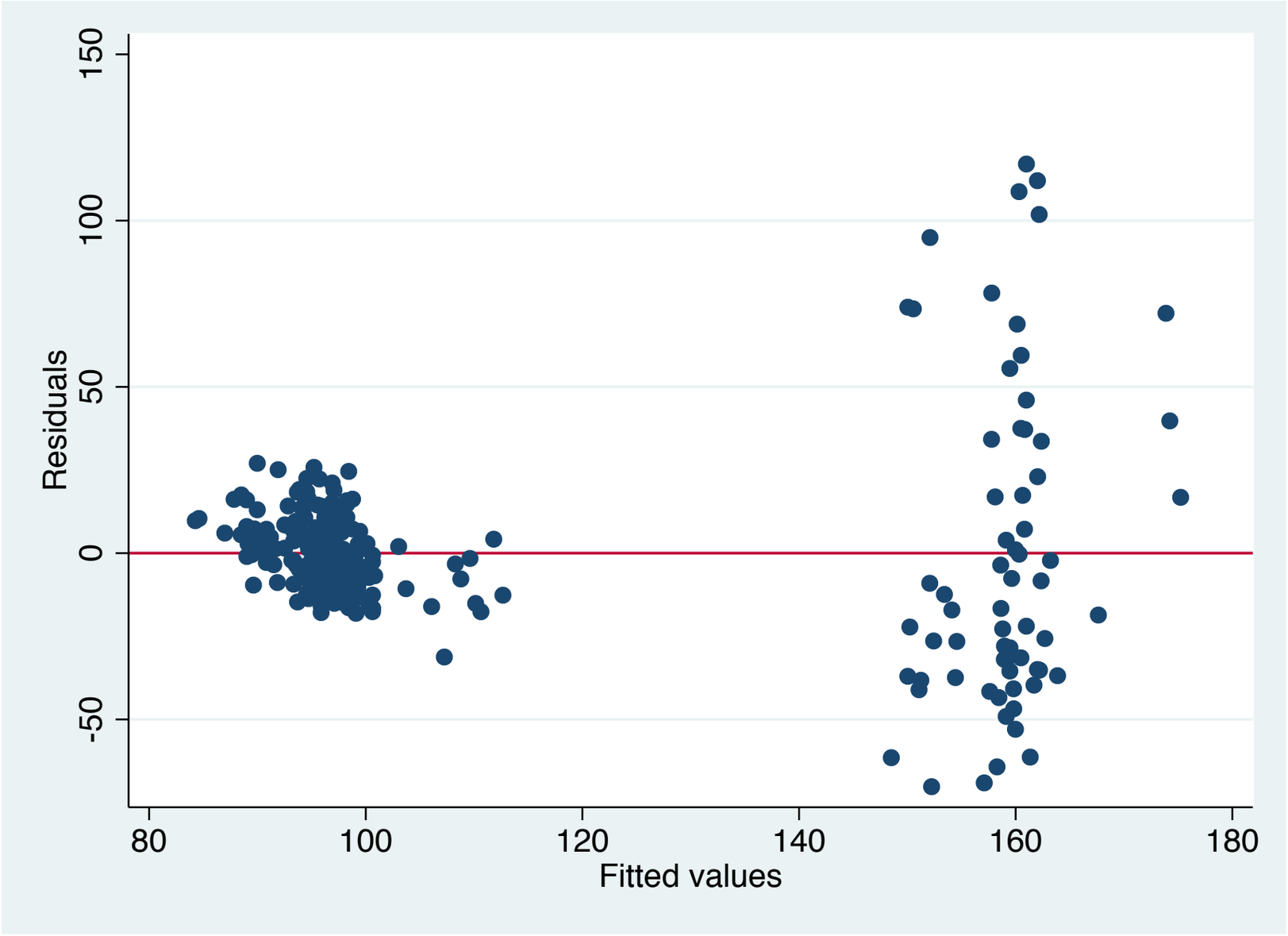
∝ = "proportional to"

ρ = correlation coefficient

Example: model for mean glucose HERS

```
*
. use hersdata, clear
* take a 10% sample to make visualization easier (for illustration)
. sample 10
(2487 observations deleted)
* untransformed outcome - fit model & plot residuals
. quietly regress glucose i.diabetes i.physact age i.raceth i.smoking i.drinkany
. predict resid1, residuals
. rvfplot, yline(0)
. graph export ./figures/rvp1.pdf, replace
```

RVF plot - untransformed outcome



Comparing residual variance by subgroup (un-transormed outcome)

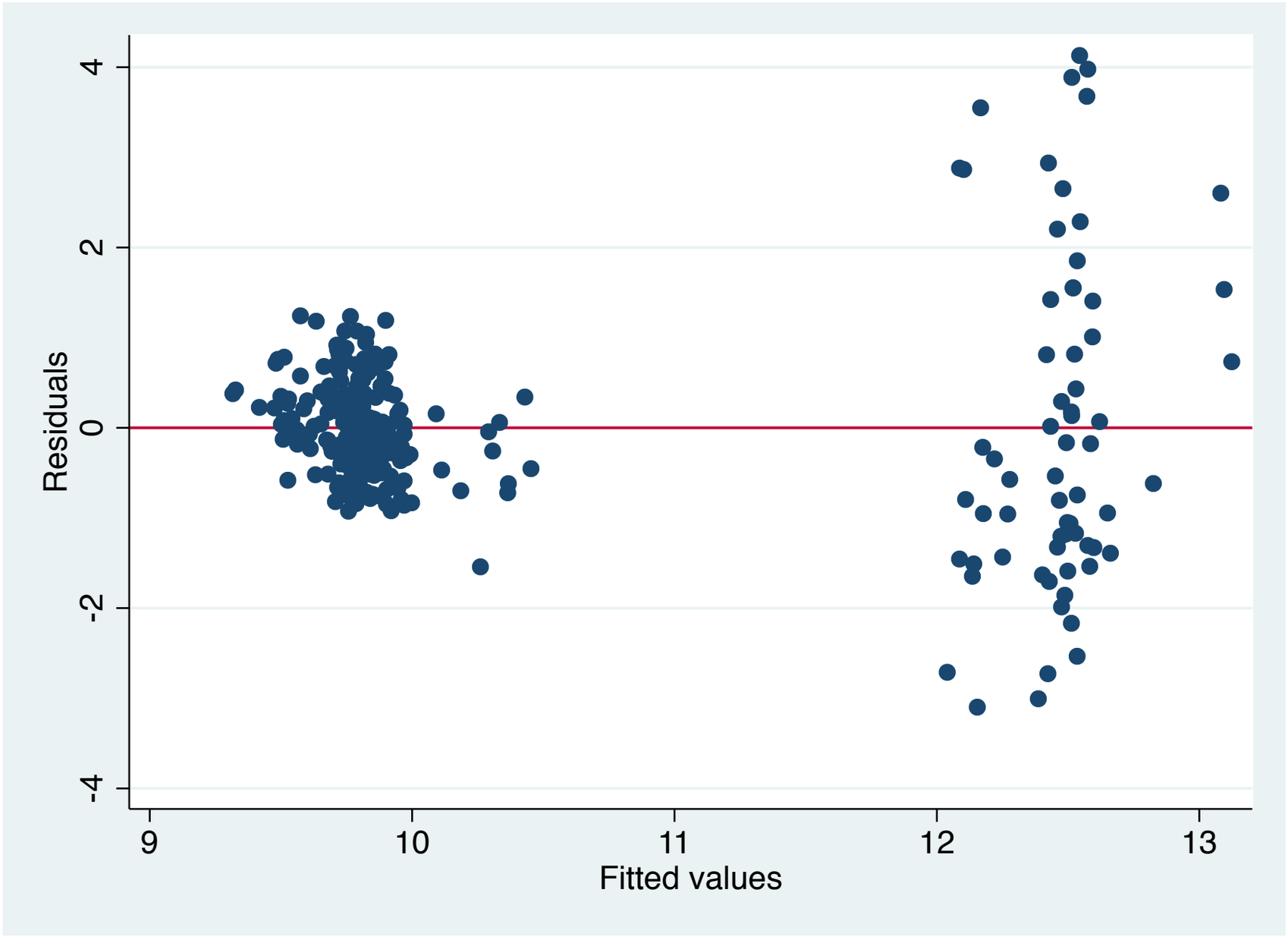
```
. tabstat resid1, by(physact) stat(n var) nototal

Summary for variables: resid1
     by categories of: physact (comparative physical activity)

         physact |         N  variance
-----------------+--------------------
much less active |        26  1057.983
somewhat less ac |        46   792.155
 about as active |        87  731.2216
somewhat more ac |        85  554.0864
much more active |        32  107.7953
-----------------------------------------
```

```
. tabstat resid1, by(diabetes) stat(n var) nototal

Summary for variables: resid1
     by categories of: diabetes (diabetes)

diabetes |         N  variance
---------+--------------------
      no |       196  30.45264
     yes |        80  53.23272
-----------------------------
```

Example: model for mean glucose HERS - square root transformed

```
* square root transformed outcome - fit model & plot residuals
. gen sqrt_glucose = sqrt(glucose)
. quietly regress sqrt_glucose diabetes i.physact age i.raceth smoking drinkany
. rvfplot, yline(0)
. graph export ./figures/rvp2.pdf, replace
```

RVF plot - square root transformed outcome



Solution: use robust SEs

```
. regress glucose diabetes i.physact age i.raceth smoking drinkany, vce(robust)
. . .
```

glucose	Coef.	Robust Std. Err.	t	P>|t|	[95% Conf.	Interval]
diabetes	55.32816	5.704065	9.70	0.000	44.09711	66.55922
physact						
somewhat less active	.5986391	7.670311	0.08	0.938	-14.50387	15.70115
about as active	6.51184	7.519767	0.87	0.387	-8.294252	21.31793
somewhat more active	2.873804	7.282648	0.39	0.693	-11.46541	17.21302
much more active	.4625191	6.907942	0.07	0.947	-13.13892	14.06396
age	-.3130465	.2466262	-1.27	0.205	-.7986428	.1725497
raceth						
African American	9.907849	7.805314	1.27	0.205	-5.460473	25.27617
Other	22.48085	15.08384	1.49	0.137	-7.218569	52.18027
smoking	-4.696382	4.223875	-1.11	0.267	-13.01301	3.620243
drinkany	6.649252	3.427625	1.94	0.053	-.0995925	13.3981
_cons	112.8064	16.89753	6.68	0.000	79.53592	146.0769

... or use more conservative robust SEs

```
. regress glucose diabetes i.physact age i.raceth smoking drinkany, vce(hc3)
. . .
------------------------------------------------------------------------------
             |             Robust HC3
     glucose |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
    diabetes |   55.32816   5.838609     9.48   0.000      43.8322    66.82413
             |
     physact |
somewhat less active |   .5986391   8.082405     0.07   0.941    -15.31526    16.51254
     about as active |    6.51184   7.877636     0.83   0.409    -8.998881    22.02256
somewhat more active |   2.873804   7.619965     0.38   0.706    -12.12957    17.87718
    much more active |   .4625191   7.247594     0.06   0.949    -13.80768    14.73271
             |
         age |  -.3130465   .2557038    -1.22   0.222    -.8165162    .1904231
             |
      raceth |
African American |   9.907849   8.189902     1.21   0.227     -6.21771    26.03341
       Other |   22.48085   16.98321     1.32   0.187    -10.95835    55.92005
             |
     smoking |  -4.696382   4.444625    -1.06   0.292    -13.44765    4.054891
    drinkany |   6.649252   3.505505     1.90   0.059    -.2529339    13.55144
       _cons |   112.8064   17.51732     6.44   0.000     78.31558    147.2972
------------------------------------------------------------------------------
```

- *Note*: `hc3` option provides more conservative robust SE's that may perform better for models with pronounced non-constant variance and/or smaller samples sizes (compare SEs and CIs with previous slide)

Solution: Generalized linear models (GLM)

Choose a GLM with the appropriate variance to mean relationship:

outcome type	*distribution*	*variance-mean relationship*	*std. link*
continuous	normal	constant	identity
continuous	gamma	proportional ($\sigma^2 \propto \mu$)	inverse
binary	binomial	$\sigma^2 = n\,\mu(1-\mu)$	log odds
count	Poisson	equal ($\sigma^2 = \mu$)	log
count	neg. binomial	$\sigma^2 = \mu + \mu^2/k$	log

Note: GLMs will be covered in Biostat 209 (also, see table 8.8 in text)

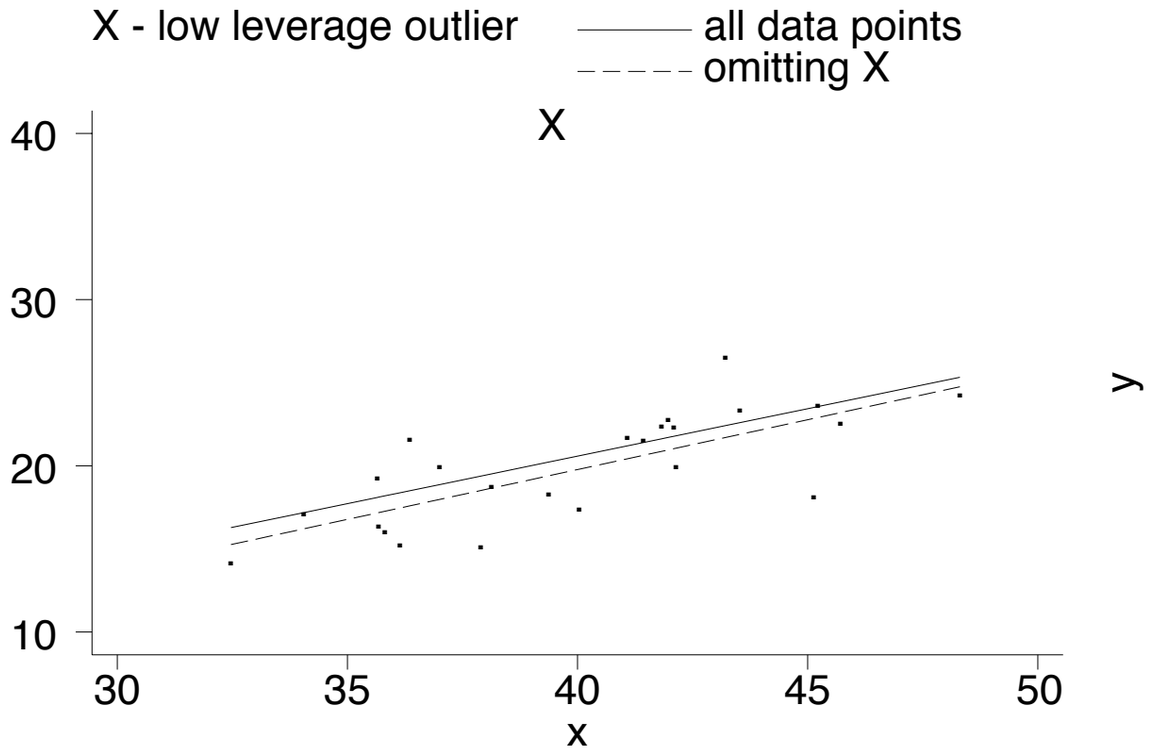
Checking constant variance: summary

- Diagnostics: funnel shapes in RVP plot, variable n, SD across subgroups
- Solutions: transform outcome, use robust SEs or GLMs

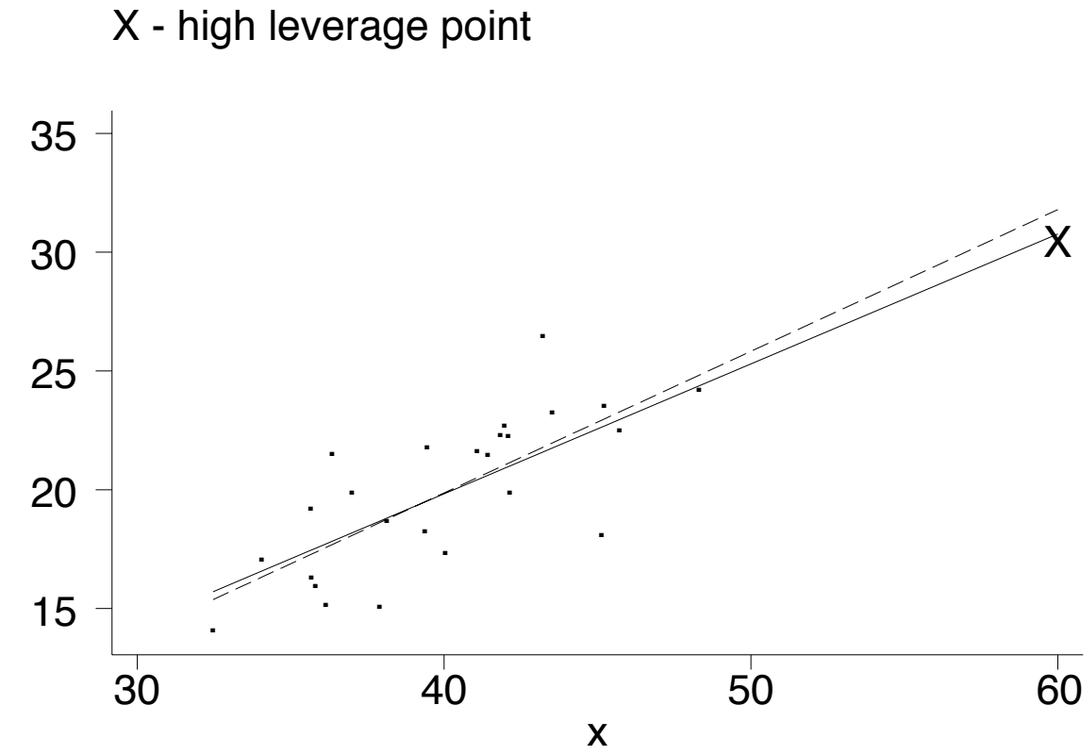
Checking the model: high leverage and influential points

- *High-leverage*:
  - ≥ 1 extreme predictor, or anomalous combination
  - potential to influence coefficient estimates unduly
- *Influential*:
  - high-leverage plus big impact on coefficients
- Inferences that are highly dependent on a few influential observations are potentially misleading

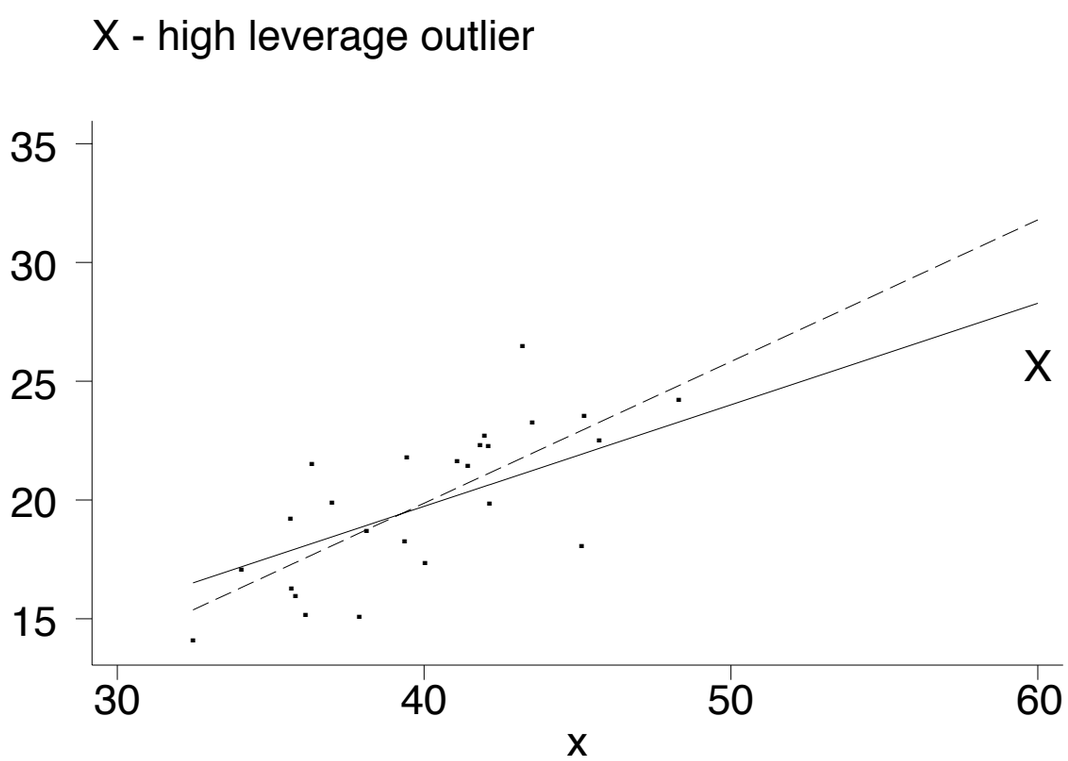
Examples: Simple outlier, high leverage, high influence



leverage = 0.04 dfbeta = -0.25



leverage = 0.52 dfbeta = -.61

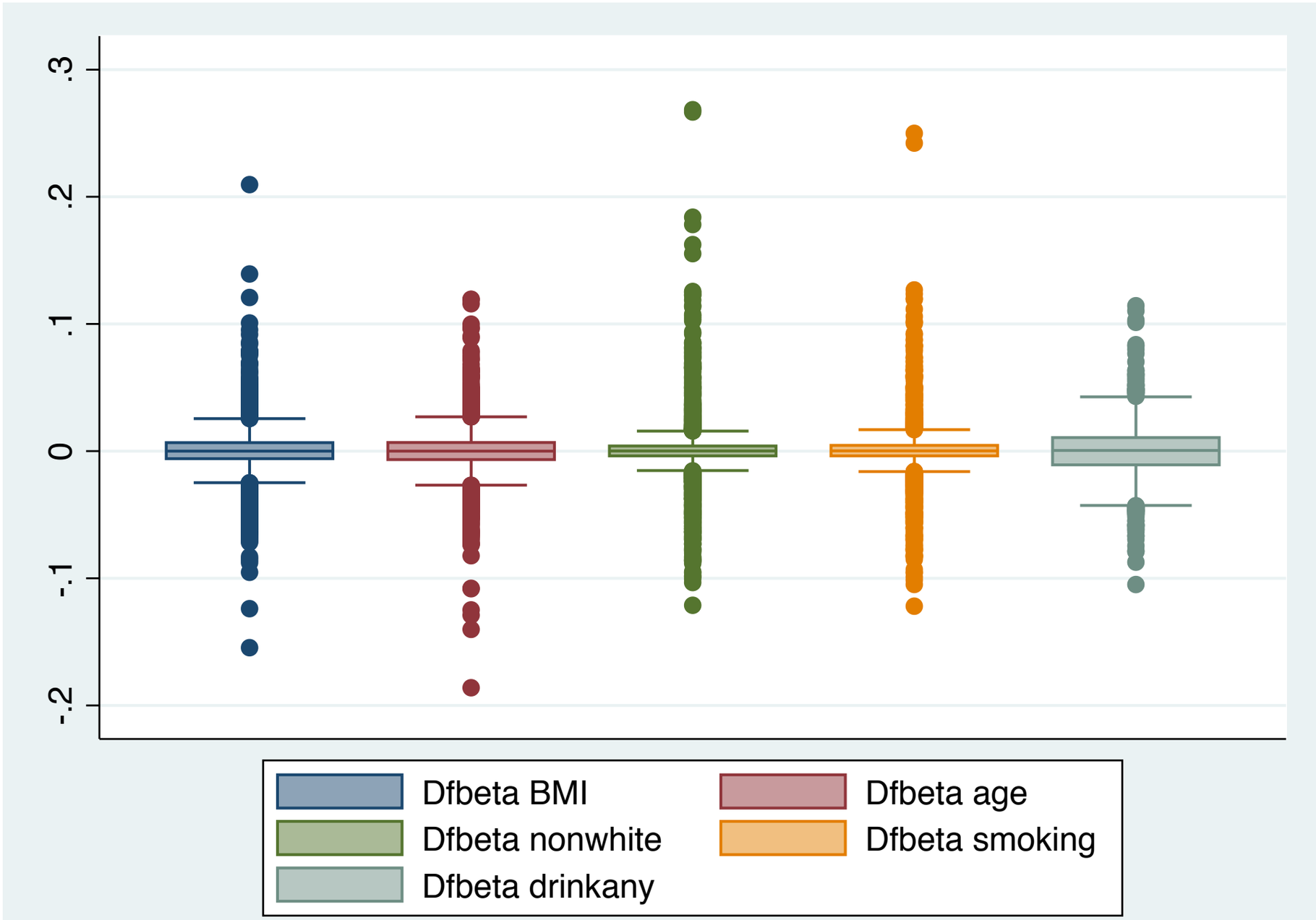


leverage = 0.52 dfbeta = -2.09

Diagnostics: boxplots of `dfbeta` statistics

- `dfbeta` statistics measure changes in each β_j when each data point is omitted
- Defined for each observation and predictor in model
- Check for outliers in boxplots of `dfbetas`

Boxplots of `dfbetas` for BMI - LDL model (slide 27)



Solution:

- Identify up to 10 observations with biggest `dfbeta` values

```
* Stata statements to list observations with large dfbeta (yields four observations)
* Statement for first predictor (BMI) below (repeat for other predictors)
. list id BMI age nonwhite smoking drinkany _dfbeta_1 if abs(_dfbeta_1) > 0.2 &
~missing(_dfbeta_1)
     +-------------------------------------------------------------------+
     |   id     BMI   age   nonwhite   smoking   drinkany   _dfbet~1 |
     |-------------------------------------------------------------------|
  70. |   70   28.74    63        yes        no         no   .2666293 |
1768. | 1768   28.22    61        yes       yes         no   .2684654 |
1020. | 1020   26.22    58         no       yes        yes   .2422048 |
1768. | 1768   28.22    61        yes       yes         no   .2498547 |
     +-------------------------------------------------------------------+
```

- Check for data errors or other anomaly
- Re-fit model without influential points, reassess conclusions, report sensitivities
- Consider deleting influential points if they represent a different population

Sensitivity of LDL model to 4 influential points with dfbeta>0.2 in absolute value

predictor	*all observations*		*omitting 4 points*	
	β	p	β	p
BMI	0.36	0.0007	0.34	0.010
Age	-1.89	0.090	-1.86	0.090
Nonwhite	5.22	0.025	4.19	0.066
Smoking	4.75	0.032	3.78	0.072
Alcohol use	-2.72	0.069	-2.64	0.072

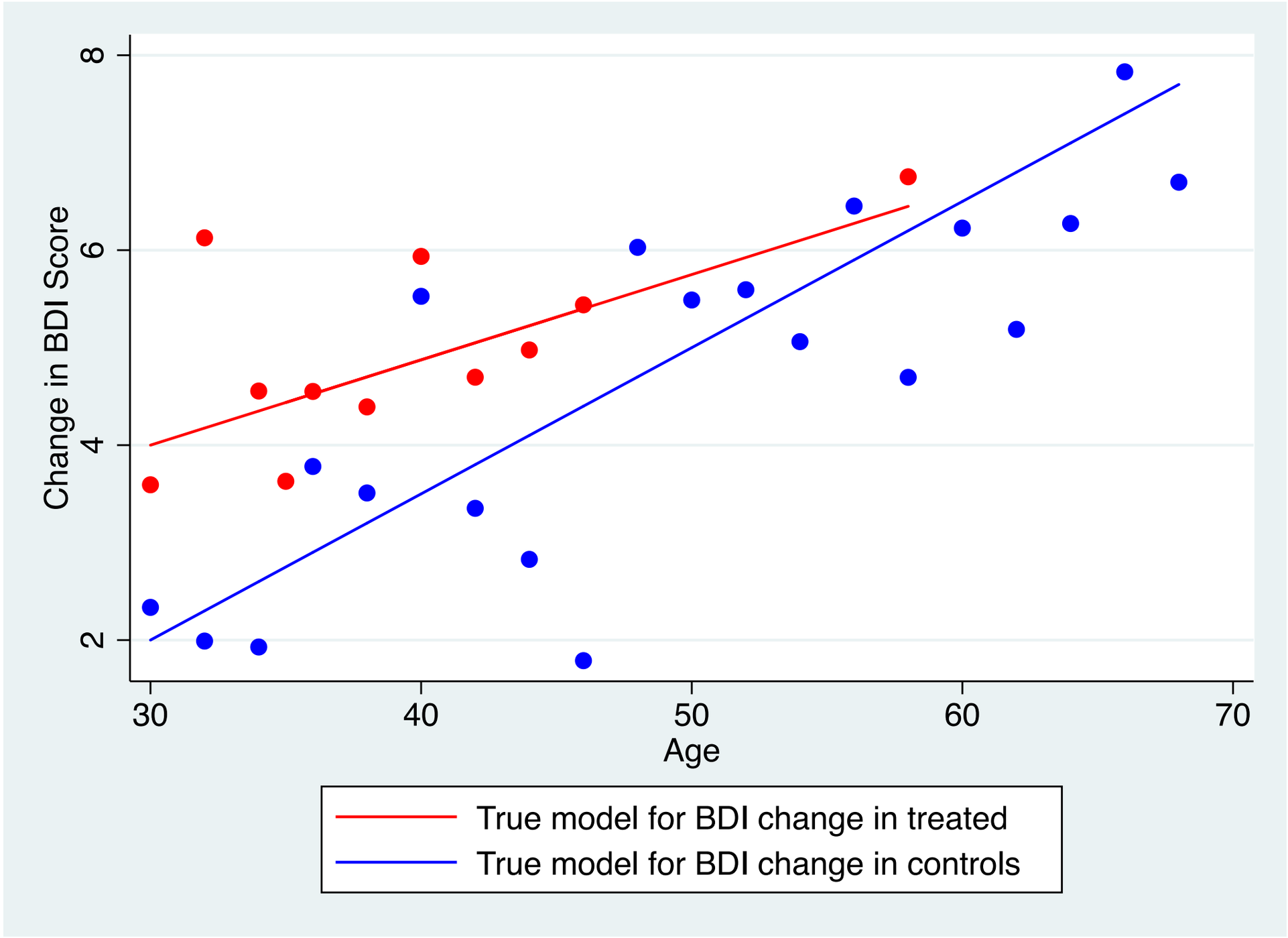
Checking influential points: summary

- Diagnostics: boxplots of `dfbetas`
- Solutions: fix errors, conduct sensitivity analyses omitting influential points

Checking the model: predictor/covariate overlap

- Observational analysis of binary exposure problematic if exposed, unexposed differ substantially with respect to other predictors
- Lack of overlap makes true model hard to find, especially in small datasets
  - conclusions about effect of exposure may be based on *extrapolation*
- Comparing each covariate in exposed and unexposed may not be enough, because covariates are correlated:
  - some *combinations* of predictors may be unrepresented in one group

Example: Lack of age overlap in model for effect of treatment on Beck Depression Inventory score



No power to detect interaction

```
. regress del_bdi i.treatment##c.age
```

```
      Source |       SS       df       MS              Number of obs =      31
-------------+------------------------------           F(  3,    27) =   15.42
       Model |  46.3692007     3  15.4564002            Prob > F      =  0.0000
    Residual |  27.0583639    27  1.00216163           R-squared     =  0.6315
-------------+------------------------------           Adj R-squared =  0.5906
       Total |  73.4275647    30  2.44758549           Root MSE      =  1.0011
```

del_bdi	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
1.treatment	3.217112	1.88746	1.70	0.100	-.6556366	7.08986
age	.1247361	.0194101	6.43	0.000	.0849098	.1645623
treatment#c.age						
1	-.0429515	.0445653	-0.96	0.344	-.1343918	.0484889
_cons	-1.483581	.9770828	-1.52	0.141	-3.488389	.5212275

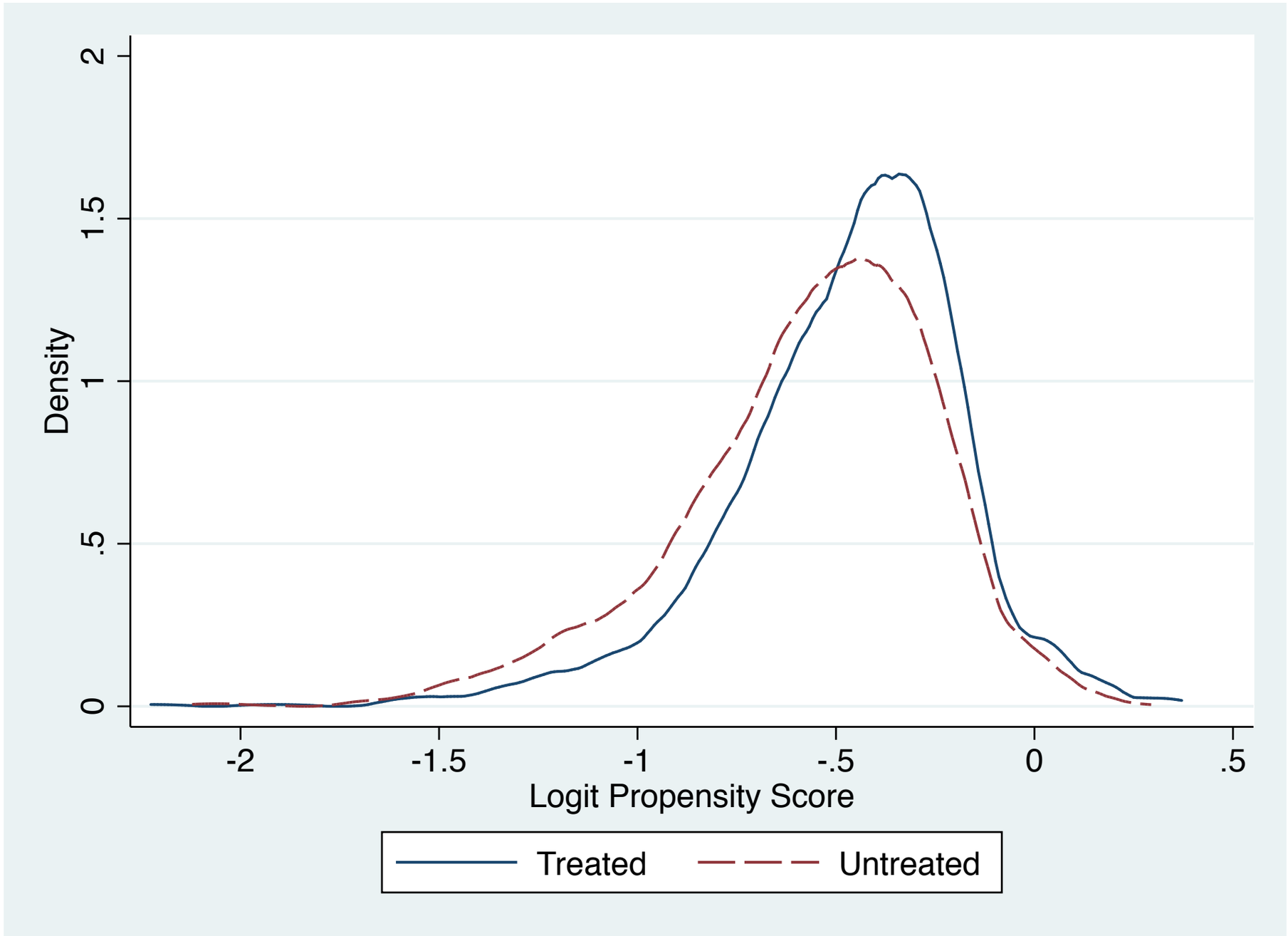
Diagnosing lack of overlap

- Compare mean, quartiles, range of covariates in exposed and unexposed
- Use *propensity scores*
  - fit logistic model for primary predictor
    - include an MSAS for the exposure-outcome relationship
    - capture non-linearities and interactions
  - get fitted values (on linear predictor or probability scale)
  - plot the results by primary predictor and check overlap

Propensity score model for statin use

```
. * logistic model for statin use
. quietly logistic statins agesp* i.raceth i.educ_cat i.smoking##i.lessactive diabetes
. * calculate logit propensity score
. predict logit_ps, xb
. * density plots of logit scores in statin users and non-users
. twoway (kdensity logit_ps if statins==1, area(1) lpattern(solid)) ///
>         (kdensity logit_ps if statins==0, area(1) lpattern(longdash)), ///
>         ytitle("Density") xtitle("Logit Propensity Score") ///
>         legend(order(1 "Treated" 2 "Untreated")) ///
>         saving(pscores, replace)
```

Overlap diagnostics for statin use in HERS

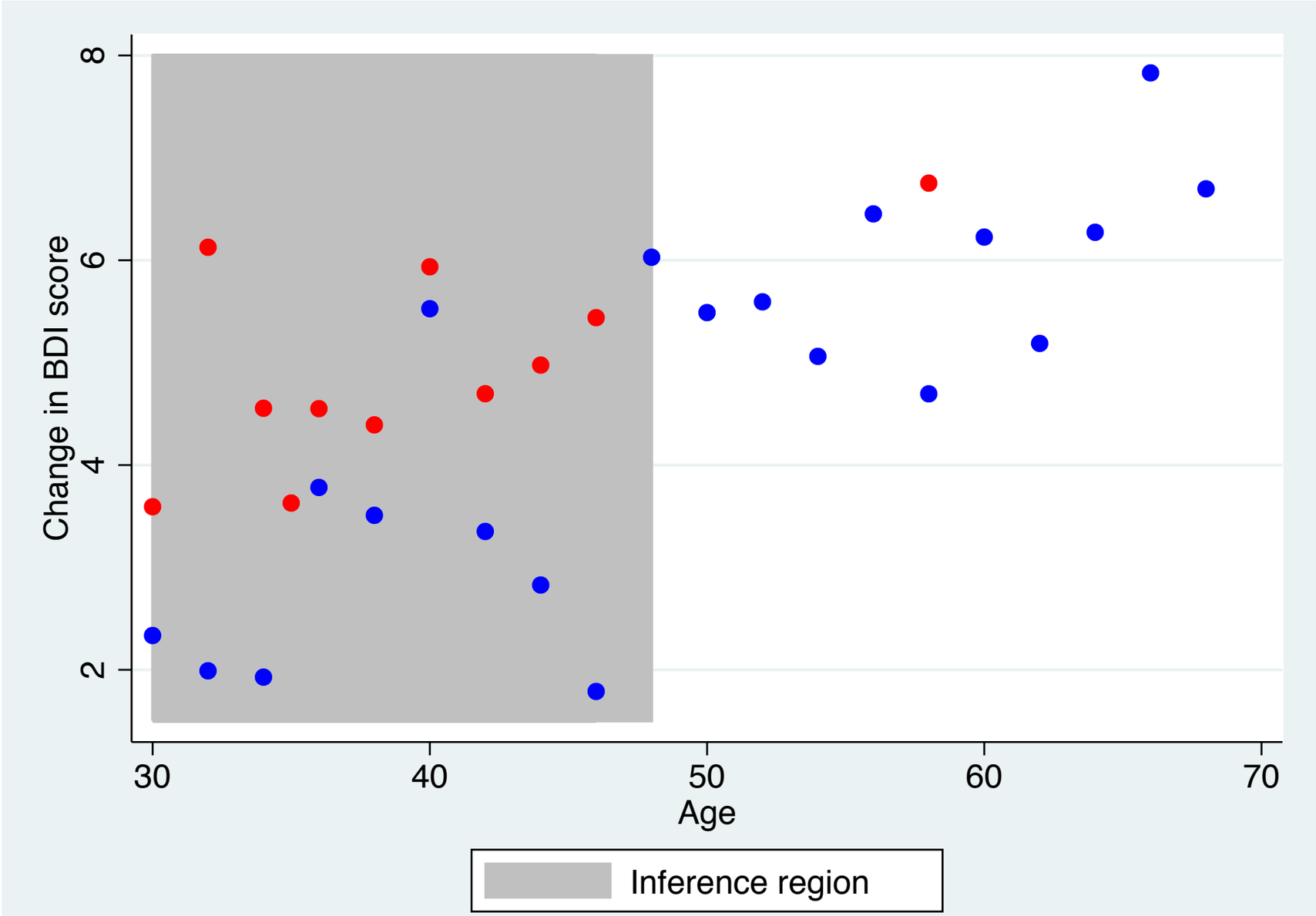


Overlap is generally quite good (thanks to treatment randomization)

Solution: lack of overlap

- Restrict inference to region of good overlap
- Match on prognostic covariates or propensity scores (covered in Biostat 215)

Restricting inference to region of overlap (BDI example)



Compare conclusions based on observations with sufficient overlap to results from full sample

Model checking: to transform or not

- Transformations can help meet assumptions
  - but make results harder to interpret
- If violations mild, results robust, reasonable not to transform
- If conclusions change substantially after transformation
  - model that meets assumptions better is more reliable

Model checking: summary

- Non-linearity:
  - Diagnostics: curved Lowess smooth in CPR or RVP plot
  - Solutions: transform predictor, including splines
- Non-normality:
  - Diagnostics: curvature in QQ-plot
  - Solutions: transform outcome, use bootstrap CIs, GLM or ordinal model

Model checking: summary

- Non-constant variance:
  - Diagnostics: funnel shapes in RVP plot, SDs differ across unequal size subgroups
  - Solutions: transform outcome, use GLM, robust SEs
- Influential points:
  - Diagnostics: boxplots of `dfbeta` statistics
  - Solutions: identify up to 10 influential points, correct data errors, omit influential points if justifiable, present sensitivity analysis

Final note: independence assumption

The assumption of *independent outcomes* applies to all the regression models covered in this course.

- Dependence can arise in a variety of contexts:
  - longitudinal studies of recurrent outcomes (e.g. episodic diseases)
  - multiple "clustered" outcome measures at a single occasion (e.g. characteristics of teeth, disease occurrence within family members)

Regression methods that account for dependent outcomes will be covered in Biostat. 209.