### 4.1 Joint C.I.'s for $\beta_{0} \boldsymbol{\&} \beta_{1}$

Conservative: For confidence 1- $\alpha$ for Joint Interval...
use ( $1-\alpha / 2$ ) C.I. for each one
e.g. if want $95 \%$ CI's for each, use $97.5 \%$ CI's for each (true coverage $>=1-\alpha$ )

More realistic (not mentioned in text): use Confidence Eclipse
From covar( $\mathrm{b}_{0}, \mathrm{~b}_{1}$ ), given by software, can calculate:


### 4.2 Simultaneous Interval Estimates of $\mathrm{E}\left(\mathrm{Y} \mid \underline{\underline{X_{1}}}\right), \mathrm{E}\left(\mathrm{Y} \mid \underline{\underline{X}}_{2}\right), \ldots$ ( means)

1. Use confidence band for line .. with $\mathrm{W}=$ rather than $\mathrm{t}_{\mathrm{n}-2} \quad\left[\mathrm{~W}^{2}=2 \mathrm{~F}_{(1-\alpha ; 2, n-2)}\right]$,
i.e. $\hat{Y}+/-\mathbf{W} \times \operatorname{SE}(\hat{Y})$ rather than $\hat{Y}+/-\mathbf{t} \times \operatorname{SE}(\hat{Y})$
"W" -- named after Working-Hotelling -- uses one "universal" W, designed for a correct CI for true regression line from $X=-\infty$ to $X=+\infty$, no matter how many/few X values one is actually interested in.

Remember $\mathbf{t}=\sqrt{\mathrm{F}_{(1-\alpha ; \underline{\mathbf{1}}, \mathrm{n}-2)}}$, whereas $\mathbf{W}=\sqrt{2} \sqrt{\mathrm{~F}_{(1-\alpha ; \underline{\mathbf{2}}, \mathrm{n}-2)}}$,
2. Use Bonferroni procedure i.e. use g CI's, each with confidence level $1-\alpha / \mathrm{g}$

See comments on section 4.23 , pages 157-158.

### 4.3 Simultaneous Prediction Intervals for 'New" Observations

[ estimates of $Y\left|\underline{\underline{X}}_{\boldsymbol{h} 1}, \quad Y\right| \underline{\underline{X_{h}}}, \quad, \quad Y \mid \underline{\underline{X}}_{\boldsymbol{h} 3} \ldots \quad$ (individual $Y^{\prime}$ )]
use $\hat{\mathrm{Y}}+/-$ multiple $\times \operatorname{SE}(\hat{\mathrm{Y}}): \quad$ multiple based on F (Scheffé) or t (Bonferroni)
[both incorporate \# of X's in question]
4.4 Regression through Origin: $\mathrm{Y} \mid \mathrm{X}=\beta_{1} \mathrm{X}+\varepsilon ; \mathrm{E}(\mathrm{Y} \mid \mathrm{X})=\beta_{1} \mathrm{X}$;
$\mathrm{Y} \mid \mathrm{X} \sim ? ?\left(\beta_{1} \mathrm{X}, \sigma^{2}\right)$ for Least Squares (LS) Estimation
$\mathrm{Y} \mid \mathrm{X} \sim \operatorname{Gaussian}\left(\beta_{1} \mathrm{X}, \sigma^{2}\right)$ (or Central Limit Theorem) for t-based inferences
LS estimates $\{$ or ML under Gaussian $\varepsilon$ 's \}

$$
\begin{aligned}
\mathrm{b}_{1}=\hat{\beta}_{1} & =\frac{\sum \mathrm{xy}}{\sum \mathrm{x}^{2}} \\
& =\frac{\Sigma \frac{\mathrm{y}}{\mathrm{x}} \mathrm{x}^{2}}{\sum \mathrm{x}^{2}}=\frac{\sum \text { slope } \times \mathrm{x}^{2}}{\sum \mathrm{x}^{2}} \\
& =\frac{\sum \text { slope } \times \text { weight }}{\sum \text { weight }} \text { with slope }=\frac{\mathrm{y}}{\mathrm{x}}, \text { weight }=\mathrm{x}^{2} .
\end{aligned}
$$

$$
\operatorname{Var}\left(\hat{\operatorname{lop}}_{\mathrm{i}}\right)=\operatorname{Var}\left(\frac{\mathrm{y}_{\mathrm{i}}}{\mathrm{x}_{\mathrm{i}}}\right)=\frac{\operatorname{Var}\left[\mathrm{y}_{\mathrm{i}}\right]}{\mathrm{x}_{\mathrm{i}}^{2}}=\frac{\sigma^{2}}{\mathrm{x}_{\mathrm{i}}^{2}} .
$$

$b_{1}$ is a weighted average of individual slope estimates, with weights that are inversely proportional to their variances, i.e.,

$$
\text { weight }_{\mathrm{i}} \propto \frac{\mathrm{x}_{\mathrm{i}}^{2}}{\sigma^{2}} \propto \mathrm{x}_{\mathrm{i}}{ }^{2}
$$

$\operatorname{Var}\left(\mathrm{b}_{1}\right)=\frac{\sigma^{2}}{\sum \mathrm{x}_{\mathrm{i}}{ }^{2}}=\frac{\sigma^{2}}{\mathrm{n} \times \operatorname{average}\left[\mathrm{x}^{2}\right]}$ so $\operatorname{SE}\left(\mathrm{b}_{1}\right)=\frac{\text { RMSE }}{\sqrt{\mathrm{n}} \times \sqrt{\text { average }\left[\mathrm{x}^{2}\right]}}$

## Cautions

Formula for $b_{1}$ is different from one for $\mathrm{E}(\mathrm{Y} \mid \mathrm{X})=\beta_{0}+\beta_{1} \mathrm{X}$ model (force $\beta_{0}$ to 0 before estimating $\beta_{1}$ )
$\hat{\sigma}^{2}=$ MSE $=\frac{\Sigma \mathrm{e}^{2}}{\mathrm{n}-\underline{\mathbf{1}}}$
(note: $\mathrm{n}-1$ free e's)
( $\underline{1}$ constraint: $\Sigma \mathrm{x} . \mathrm{e}=0$. )
careful regarding $\mathbf{r}^{\mathbf{2}}$
(see pp 163...)

I
To $\beta_{0}=0$ or NOT TO $\beta_{0}=0$ ??
Do not force line through intercept unless very clear physical model to justify it ...
usually, one does not loose much by allowing a non-zero incercept when in fact it is zero.
A more serious issue is whether here (and also in the non-zero intercept model) the assumption of the constant variance $\sigma^{2}$ in the $\mathrm{Y} \mid \mathrm{X} \sim ?$ ?( function of $\mathrm{X}, \sigma^{2}$ ) model is appropriate.

For example, if in the zero-intercept model, the variance is proportional to $X$, then the slope estimator $\mathrm{b}_{1}=\Sigma \mathrm{y} / \Sigma \mathrm{x}=\Sigma \mathrm{x}(\mathrm{y} / \mathrm{x}) / \Sigma \mathrm{x}$ (i.e., weight of x for individual slope estimate $\mathrm{y} / \mathrm{x}$ ) is more efficient than the (also unbiased) estimator derived from the constant variance model above.

### 4.5 Measurement Errors and their effects

## a) Measurement Errors in Y

They get absorbed into residuals

$$
\begin{array}{cl}
\mathrm{Y}=\beta_{0}+\beta_{1} \mathrm{X}+\varepsilon+\varepsilon_{\mathrm{m}} & \\
\varepsilon & \text { biologic/real/unexplained } \\
\varepsilon_{\mathrm{m}} & \text { measurement error } \\
\operatorname{var}(\mathrm{Y} \mid \mathrm{X})=\sigma_{\varepsilon}^{2}+\sigma_{\varepsilon_{\mathrm{m}}}^{2} &
\end{array}
$$

Can average several (k) measurements on same individual to reduce effect of measurement error

$$
\operatorname{var}(\mathrm{Y} \mid \mathrm{X})=\sigma_{\varepsilon}^{2}+\frac{\sigma_{\varepsilon_{\mathrm{m}}^{2}}^{2}}{\mathrm{k}} .
$$

## b) Measurement Errors in $\mathbf{X}$

X real/"true" X
X* observed/recorded value

## 2 situations ( difference is quite subtle!!)

- 'Classical" Error Model

$$
X^{*}=X+\delta
$$

$(\mathrm{X}, \mathrm{Y}[\mathrm{X}])$ chosen but $\left(\mathrm{X}^{*}, \mathrm{Y}[\mathrm{X}]\right)$ recorded; $\mathrm{E}[\delta]=0 ; \delta$ uncorrelated with X so that $\operatorname{var}\left(\mathrm{X}^{*}\right)=\operatorname{var}(\mathrm{X})+\operatorname{Var}(\delta) \#$

- 'Berkson" Error Model

$$
\mathrm{X}^{*}=\mathrm{X}+\delta
$$

$\left(\mathrm{X}^{*}, \mathrm{Y}\left[\mathrm{X}^{*}\right]\right)$ targetted but $\left(\mathrm{X}^{*}, \mathrm{Y}[\mathrm{X}]\right)$ recorded; $\mathrm{E}[\delta]=0 ; \delta$ uncorrelated with $\mathrm{X}^{*}$ (but necessarily correlated with X :- if told $\delta$, would know X ) \# Interpreting $\operatorname{Var}(\mathrm{X})$ as observed var; $\operatorname{Var}(\delta)$ in sampling variance (repeatable) sense.

### 4.5 Measurement Errors ... <br> b) Measurement Errors in X ...

## -'Classical" Error Model

True regression model : $\mathrm{Y}=\beta_{0}+\beta_{1} \mathrm{X}+\varepsilon$

BUT the " X " values we record are not correct . i.e. although X generated Y , we record it as $\mathrm{X}^{*}=\mathrm{X}+\delta$

X: true value ; $\mathrm{E}[\delta]=0 ; \delta$ uncorrelated with X

If use naive LS estimator $b_{1}$ to estimate $\beta_{1}$ from the $X^{*}$ 's ...
then $\mathrm{b}_{1}$ biased towards null (zero) ("ATTENUATION")
$\mathbf{E}\left[b_{1}\right]=\beta_{1} \frac{\operatorname{var}(\mathbf{X})}{\operatorname{var}\left(\mathbf{X}^{*}\right)}=\frac{\operatorname{var}(\mathbf{X})}{\operatorname{var}(\mathbf{X})+\operatorname{var}(\delta)}<\beta_{1}$ if $\operatorname{var}(\delta)>0$.

$$
\frac{\operatorname{var}(\mathbf{X})}{\operatorname{var}\left(\mathbf{X}^{*}\right)}=\frac{\operatorname{var}(\mathbf{X})}{\operatorname{var}(\mathbf{X})+\operatorname{var}(\delta)}=\frac{\text { variation in "true" } X \text { values }}{\text { variation in observed values }} \leq 1
$$

alias: 'Intra-Class Correlation Coefficient" or "Reliability Coefficient" is the "ATTENUATION" factor

If pilot studies or literature can furnish an estimate of ICC... one can DE-ATTENUATE:
"bias-corrected" estimator of $\beta_{1}: \quad b_{1[L S]} \times \frac{1}{\text { ICC }}$

## EXAMPLE OF "FLAT" SLOPE ("classical" measurement error model) Ages of 40 students in 1986 class 513-607 (Inferential Statistics)

```
DATA ages; keep age86 age86___ age99;
    INPUT Age86 @@;
    age99 = Age86+13;
    b = int(ranuni(7534567)+0.5) ; /* b ~ Bernoulli( 0,1), prob 0.5 each */
    sign = 2 * b - 1; /* sign ~ Bernoulli(-1,1) prob 0.5 each */
    d = sign * 5 ; /* d ~ Bernoulli(-5,5) prob 0.5 each */
    age86___ = Age86 + d;
```

    LINES;
    | 22 | 22 | 22 | 22 | 23 |  | 25 | 26 | 26 | 26 | 27 | 27 | 27 | 27 |  | 28 | 28 | 28 |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 29 | 29 |  | 30 | 30 | 30 | 30 | 30 | 31 | 31 | 31 | 31 | 32 | 32 |  | 33 | 33 |  |
| 35 |  | 36 | 37 | 38 | 38 | 39 | 42 |  |  | 34 |  |  |  |  |  |  |  |



These 40 students 13 years later ... in 1999


How much, and at what rate, did they age in these 13 years?

| $-\operatorname{AGEg9}$ | $=$ | AGE86 |
| :--- | :--- | :--- |
| Response Distribution: | Normal |  |
| Link Function: | Identity |  |


| Model Equation |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- |
| AGE99 $=13$ | + | 1.0 | AGE86 |  |



What if these 40 students had given their ages as true age +/- 5 years (with the + or - determined at random, without regard to true age)?

Age86___ Age86 +/- 5

| Age86 | Age99 | Age86 |
| :---: | :---: | :---: |
| 30.0 | 43.0 | 28.5 |
| 4.9 | 4.9 | 6.5 |
| 24.4 | 24.4 | 41.9 |
| 22 | 35 | 17 |
| 42 | 55 | 47 |

change__ = Age99-Age86 ;
Mean
Std Dev
Variance
Minimum
Maximum
= Age99 - Age86__;
30.0
4.9
24.4

22
42

47

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$$
\text { AGE99 }=28.39+0.51 \text { AGE86__ }
$$



| $\boldsymbol{\| r \| c \|}$ Analysis of Variance |  |  |  |  |  |
| :--- | :---: | :---: | :---: | :---: | :---: |
| Source | DF | Sum of Squares | Mean Square | F Stat | Prob > F |
| Model | 1.00 | 430.76 | 430.76 | 31.35 | 0.0001 |
| Error | 38.00 | 522.21 | 13.74 |  |  |
| C Total | 39.00 | 952.98 |  |  |  |


| -1 | Model Equation |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- |
| CHANGE__ $\quad=$ | 28.39 | - | 0.49 | AGE86___ |  |


4.5 Measurement Errors ... b) Measurement Errors in X ...
-'Berkson" Error Model
True regression model : $\mathrm{Y}=\beta_{0}+\beta_{1} \mathrm{X}+\varepsilon$
BUT the " $X$ " values we record are not correct . i.e.
we targetted (and recorded) $\mathrm{X}^{*}$ (e.g. thermometer set to $\mathrm{X}^{*}=22 \mathrm{C}$ ) but actual X is different from targetted/recorded $\mathrm{X}^{*}$
i.e. true value $\mathrm{X}=\mathrm{X}^{*}+\delta ; \mathrm{E}[\delta]=0 ; \delta$ uncorrelated with $\mathrm{X}^{*}$

If use naive $L S$ estimator $b_{1}$ to estimate $\beta_{1}$ from the $X$ 's ... then $b_{1}$ unbiased

## The 'Classical" vs. 'Berkson" difference ...

Assume

- No Biologic Variation (i.e. all $\varepsilon$ 's = 0)

$$
\text { i.e. } \mathbf{Y}=\beta_{0}+\beta_{0} \mathbf{X}+\mathbf{0}
$$

- 2-point regression $\left(\mathrm{x}^{*}{ }_{1}, \mathrm{y}_{1}\right)$ and $\left(\mathrm{x}_{2}, \mathrm{y}_{2}\right)$


BERKSON



Without loss of generality, assume $\beta_{0}=0$ and $\sigma^{2}(\varepsilon)=0$

| "Classical" Error Model | "Berkson" Error Model |
| :---: | :---: |
| $\begin{gathered} \frac{\mathbf{y}_{2}-\mathbf{y}_{1}}{\mathbf{x}_{2}-\mathbf{x}_{1} *_{1}} \\ \beta\left\{\mathbf{x}_{2}-\mathbf{x}_{1}\right\} \\ {\left[\mathbf{x}_{2}+\delta_{2}\right]-\left[\mathbf{x}_{1}+\delta_{1}\right]} \\ \frac{\beta\left\{\mathbf{x}_{2}-\mathbf{x}_{1}\right\}}{\left[\mathbf{x}_{2}-\mathbf{x}_{1}\right]+\left[\delta_{2}-\delta_{1}\right]} \\ \frac{\beta}{1+\frac{\delta_{2}-\delta_{1}}{\mathbf{x}_{2}-\mathbf{x}_{1}}} \end{gathered}$ | $\begin{gathered} \frac{\mathbf{y}_{2}-\mathbf{y}_{1}}{\mathbf{x}_{2}-\mathbf{x}_{1}^{*}} \\ \frac{\beta\left\{\mathbf{x}_{2}+\delta_{2}\right\}-\beta\left\{\mathbf{x}_{1} *_{1}+\delta_{1}\right\}}{\mathbf{x}_{2}-\mathbf{x}_{1}^{*}} \\ \frac{\beta\left\{\mathbf{x}_{2} *_{2}-\mathbf{x}_{1}^{*}\right\}+\beta\left\{\delta_{2}-\delta_{1}\right\}}{\mathbf{x}_{2}-\mathbf{x}_{1}^{*}} \\ \beta\left(1+\frac{\delta_{2}-\delta_{1}}{\mathbf{x}_{2}-\mathbf{x}_{1}^{*}}\right) \end{gathered}$ |
| random component $\delta_{2}-\delta_{1}^{1}$ <br> is in denominator | random component $\delta_{2}-\delta_{1}^{1}$ <br> is in numerator |

Replacing subjects' ages ( $\mathbf{X}$ ) with $\mathrm{X}^{*}=$ average age for subjects in an age category, generates Berkson type measurement errors.
4.6 Inverse Predictions (Use of regression for "calibration": see comments p 169) Example:
Estimation of Gestational Age from Ultrasound Measurements of Fetal Head Size


$n(X, Y)$ pairs with known X 's
$==>\left(b_{0}, b_{1}\right.$, MSE, $\left.X_{b a r}\right) \quad Y_{h}==>\hat{X}_{h}=\frac{Y_{h}-b_{0}}{b_{1}}$

Exact $\operatorname{Var}\left(\hat{X}_{h}\right)$ ???

$$
\hat{X}_{h}=\frac{Y_{h}-R V_{0}}{R V_{1}}
$$

(Approx) est. of $\operatorname{Var}\left(\hat{X}_{h}\right): \frac{\operatorname{MSE}}{b_{1}{ }^{2}}\left[1+\frac{1}{n}+\frac{\left(\hat{X}_{h}-X_{b a r}\right)^{2}}{\Sigma\left(X-X_{b a r}\right)^{2}}\right]$
4.7 Choice of X levels

Well explained in book, pp 169-170
Would simply emphasize a different way of viewing the terms

$$
\begin{aligned}
& \frac{\sigma^{2}}{\Sigma\left(\mathrm{X}-\mathrm{X}_{\mathrm{bar}}\right)^{2}}, \\
& \frac{1}{\mathrm{n}}+\frac{\left(\mathrm{X}_{\mathrm{h}}-\mathrm{X}_{\mathrm{bar}}\right)^{2}}{\Sigma\left(\mathrm{X}-\mathrm{X}_{\mathrm{bar}}\right)^{2}}, \text { etc }
\end{aligned}
$$

namely

$$
\begin{aligned}
& \frac{\sigma^{2}}{\mathrm{n} \operatorname{Var}(X)} \\
& \frac{1}{\mathrm{n}}+\frac{\left(X_{\mathrm{h}}-X_{\mathrm{bar}}\right)^{2}}{\mathrm{n} \operatorname{Var}(X)}, \text { etc }
\end{aligned}
$$

This way, for example, $\quad \mathbf{S D}\left(\mathrm{b}_{\mathbf{1}}\right)=\frac{\sigma}{\sqrt{\mathrm{n}} \operatorname{SD}(\mathrm{X})}$

Here, don't fuss about $\operatorname{Var}(\mathbf{X})$ being defined with divisor of $\mathbf{n}$ vs. $\mathbf{n - 1}$. If we have the choice of which $X$ 's to study, we are using our defintion of variance, namely

$$
" \operatorname{Var}^{\prime}(\mathbf{X})=\frac{1}{\mathbf{n}} \Sigma\left(\mathrm{X}-\mathrm{X}_{\mathrm{bar}}\right)^{2}
$$

as a measure of the spread of the chosen $X$ 's.

