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Overlapping confidence intervals are not a statistical test

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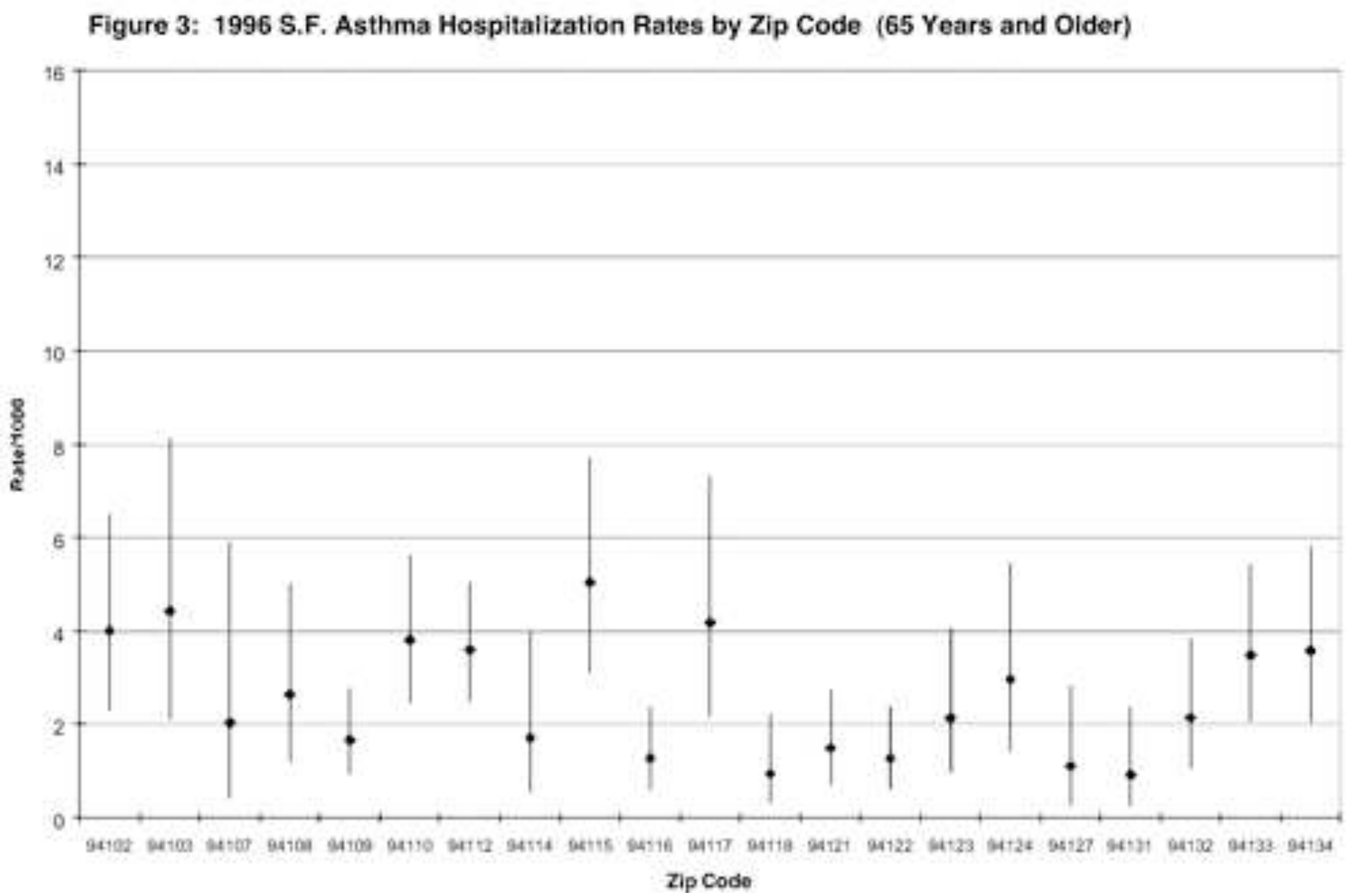
Some examples…



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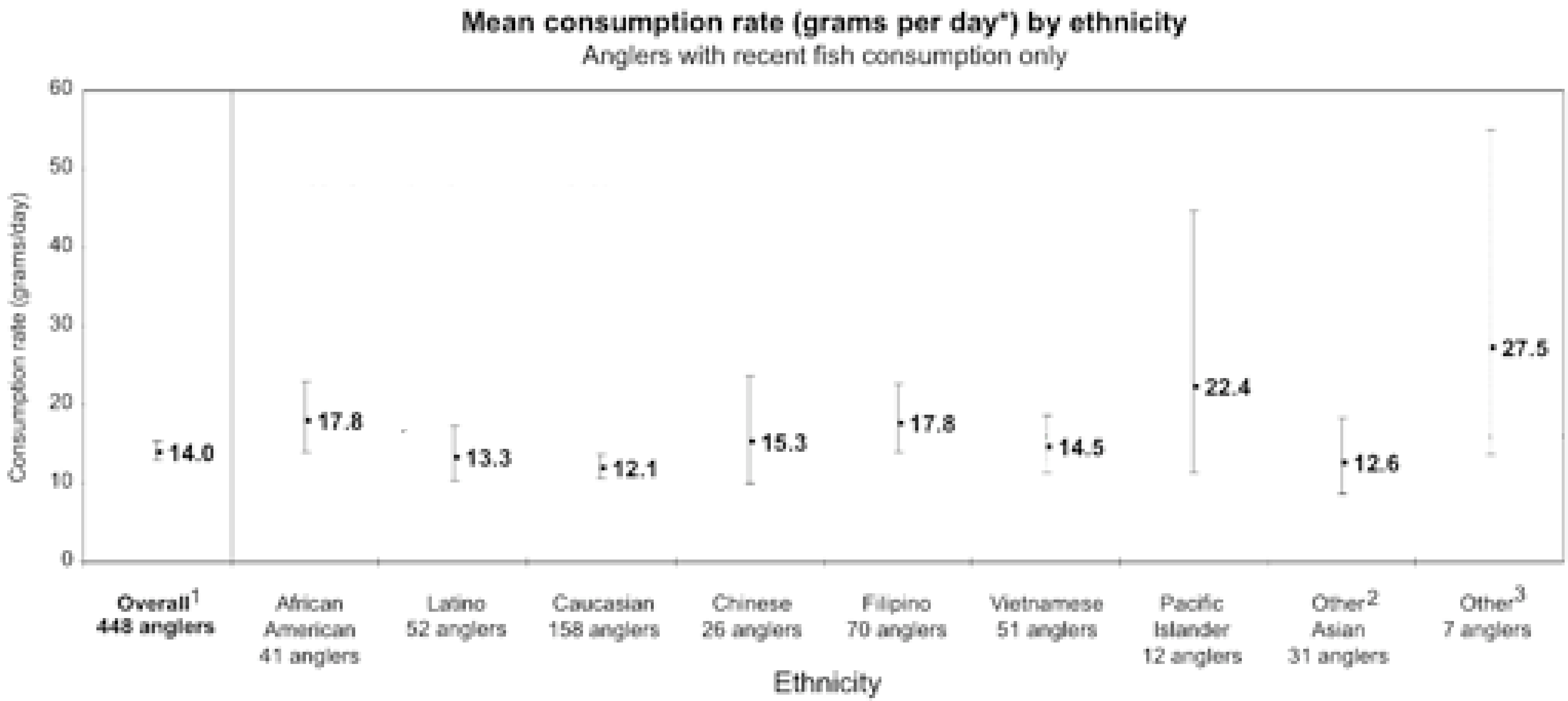
EHIB study of fish consumption…



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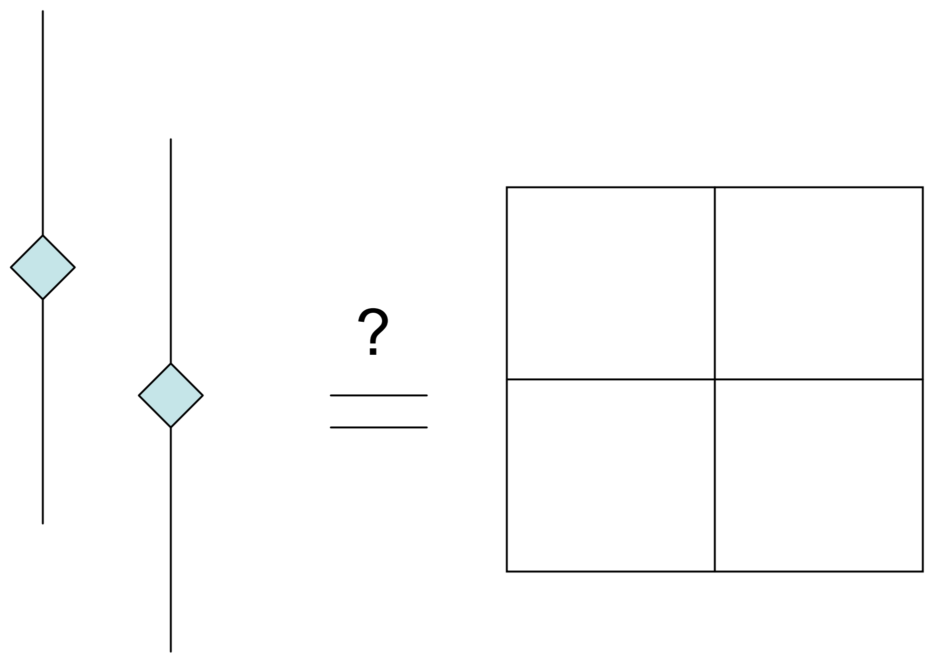
Are the results of the overlap test consistent with the equivalent traditional test?



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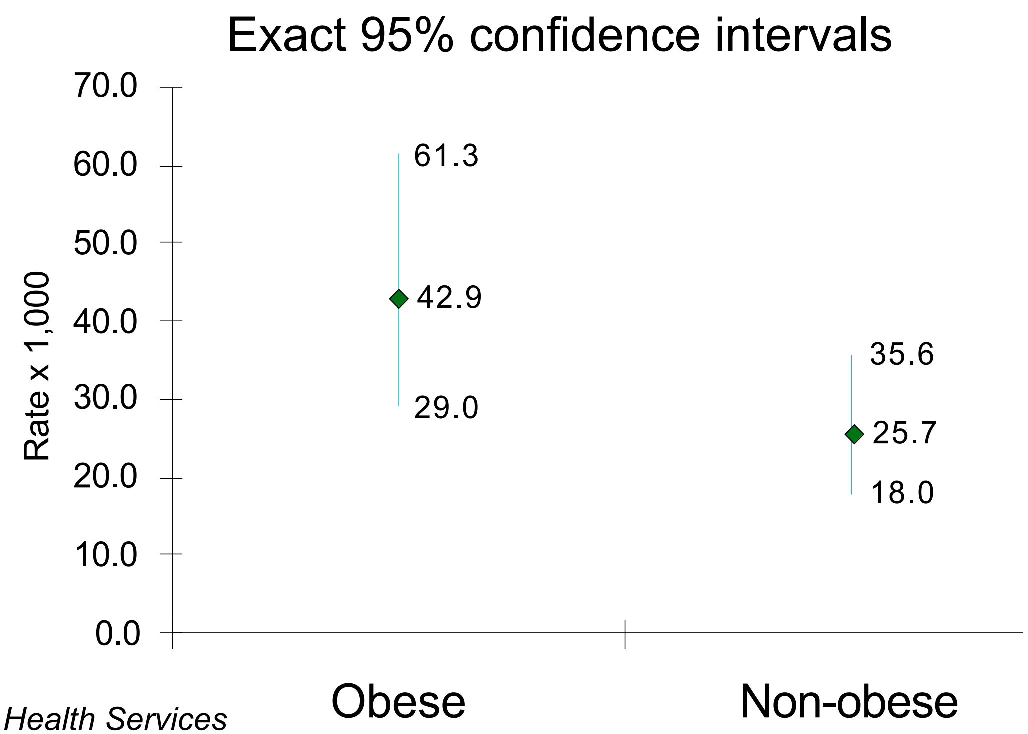
Example 1: Mortality rates among elderly

from Kleinbaum, Kupper, and Morgenstern, 1982, p.287.

	Obese	Non-obese
Deaths	30	36
Person-years	699	1399

$\chi^2 = 4.38$
P value = 0.036

RR=1.67
95% CL: 1.03-2.71



(CI Overlap)

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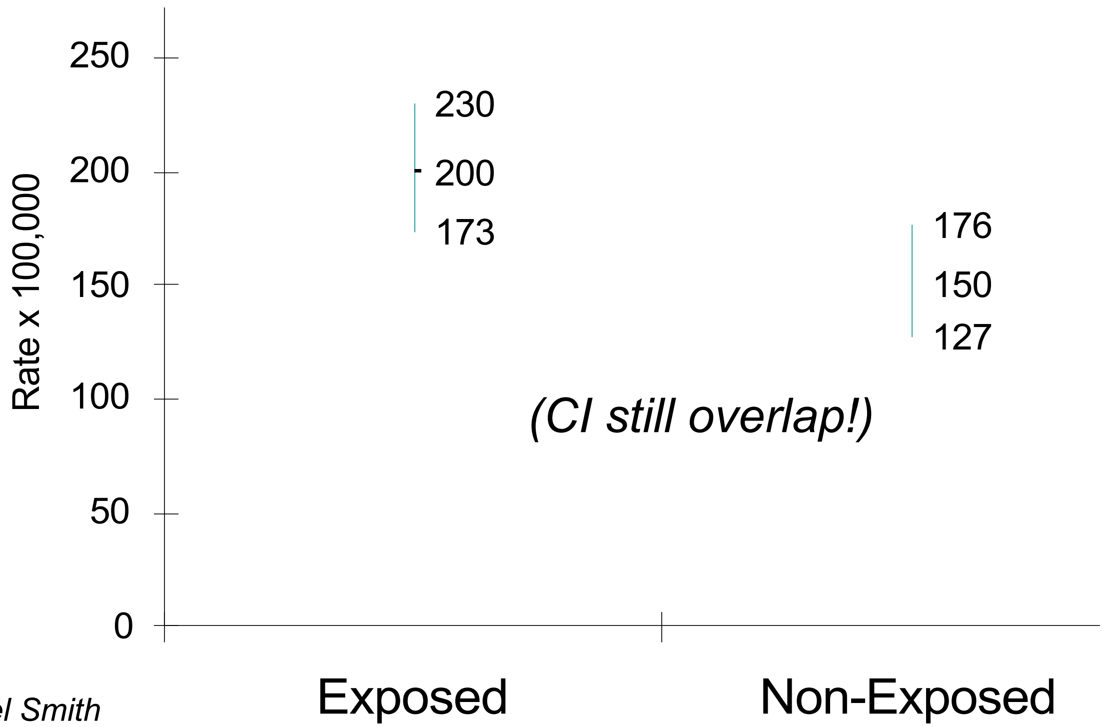
Example 2: Big Numbers

	Exposed	Non-Exposed
Cases	200	150
Person-years	100,000	100,000

$\chi^2 = 7.14$
P value = 0.0075

RR=1.33
95% CL: 1.08-1.65



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The problem is…

- Confidence intervals are too wide
- Confidence intervals are calculated only using the data in each rate
- Confidence interval around *one* rate is not a comparative measure between *two* rates

ANOVA has the concept of Least Significant Difference (LSD), based on the confidence interval for the difference of two means

$$+Z * SE_{\overline{Y}_1-\overline{Y}_2}$$

$$\overline{Y}1 - \overline{Y}2$$

$$-Z * SE_{\overline{Y}_1-\overline{Y}_2}$$

$$\overline{Y}2$$

$$\frac{Z * SE_{\overline{Y}_1-\overline{Y}_2}}{2}$$

$$\frac{Z * SE_{\overline{Y}_1-\overline{Y}_2}}{2}$$

$$\overline{Y}1$$

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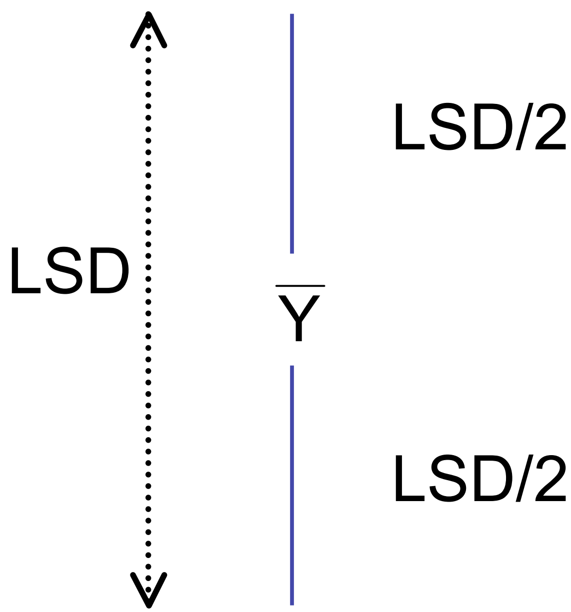
LSD = Least significant difference



Where LSD = Z*(SE of the difference
between two means)

These are *not* confidence intervals,

But “error bars” that show the distance between two significantly different values

Uses a *pooled standard error*,
so can compare means across all groups

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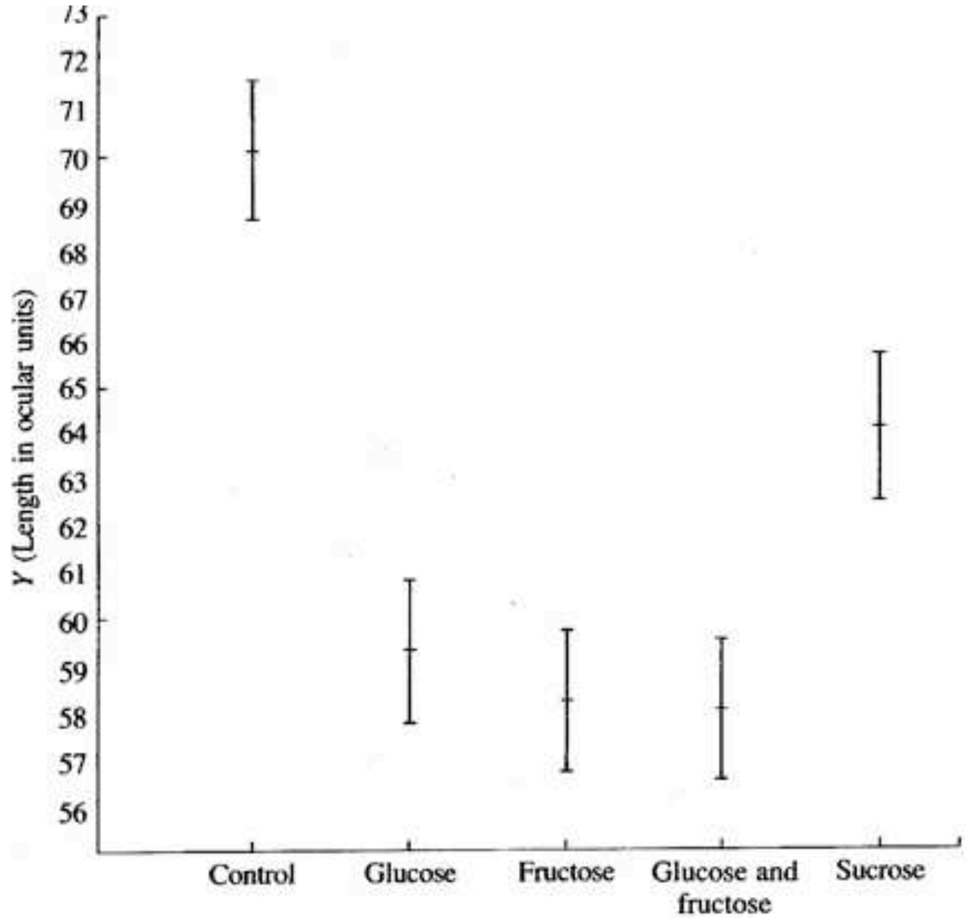
Example from Sokal and Rohlf (1995)



95% comparison intervals by the T-method for the means of the pea section data. Means whose intervals do not overlap are significantly different.

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How to do this for epidemiologic measures?
First, consider Poisson rates…

$$\text{Poisson rate}: \quad \frac{\text{cases}}{\text{person-years}} = \frac{a}{N}$$

$$\text{Variance of } \sqrt{a} = \tfrac{1}{4}$$

$$\text{Variance of } \textit{difference } \sqrt{a}_1 - \sqrt{a}_2 = \tfrac{1}{4} + \tfrac{1}{4} = \tfrac{1}{2}$$

$$SE = \sqrt{Var} = \sqrt{\tfrac{1}{2}}$$

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An LSD-style interval for Poisson rate can be constructed

$$\text{LSD} = Z\sqrt{\tfrac{1}{2}}$$

$$\text{Each arm of "LSD Interval"} = \frac{Z\sqrt{\tfrac{1}{2}}}{2}$$

$$\text{For } Z = 1.96, \text{arm} = 0.693$$

$$\mathit{95\%\ LSD\ limits} = \frac{\left(\sqrt{a} \pm 0.693\right)^2}{N}$$

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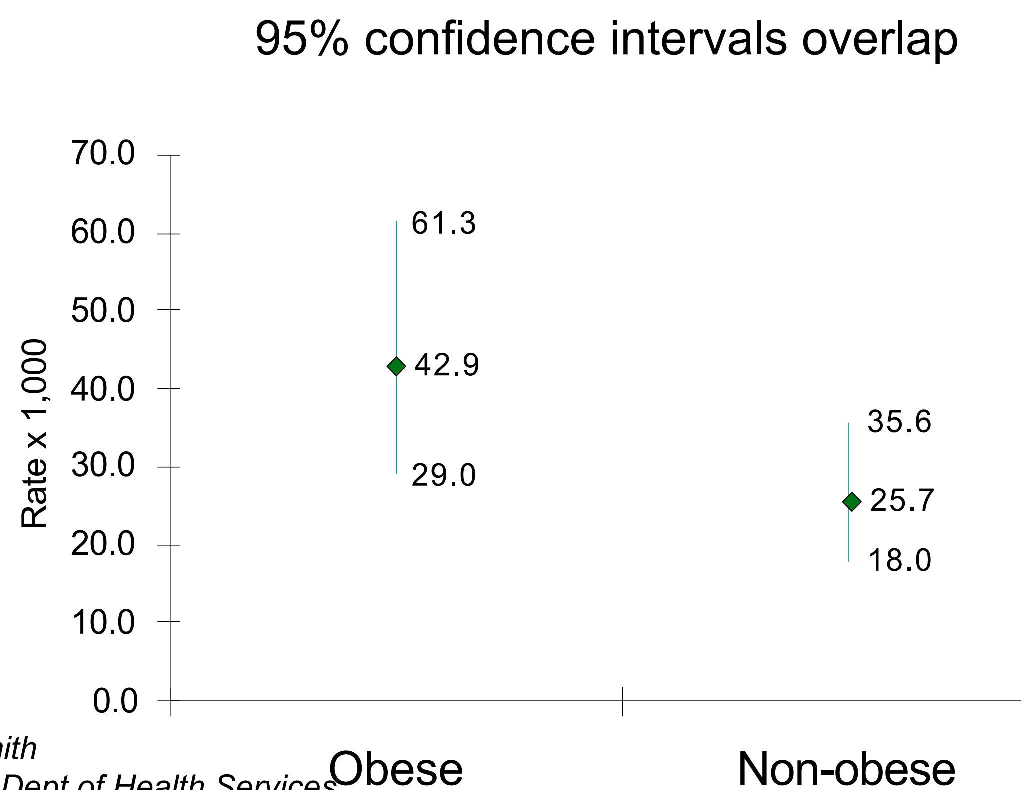
Example 1 again

	Obese	Non-obese
Deaths	30	36
Person-years	699	1399

χ^2 = 4.38
P value = 0.036

RR=1.67
95% CL: 1.03-2.71



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Example 1 again

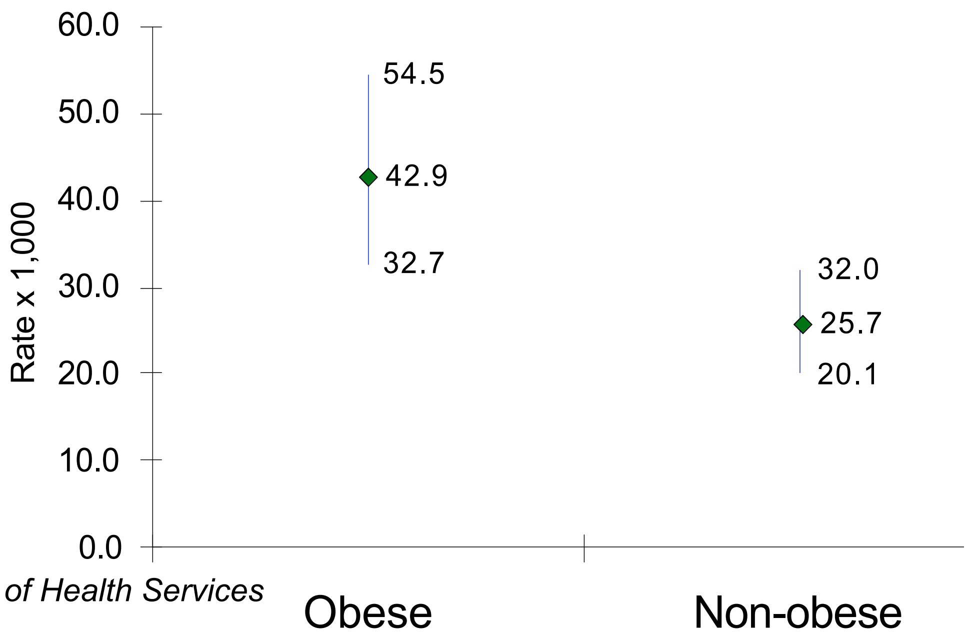
	Obese	Non-obese
Deaths	30	36
Person-years	699	1399

χ^2 = 4.38
P value = 0.036

RR=1.67
95% CL: 1.03-2.71

$$\textit{95\% LSD limits}: \frac{\left(\sqrt{30} \pm 0.693\right)^2}{699} = 32.7/1{,}000 \ - \ 54.5/1{,}000$$

$$\frac{\left(\sqrt{36} \pm 0.693\right)^2}{1399} = 20.1/1{,}000 \ - \ 32.0/1{,}000$$



95% LSD-type intervals don't overlap
(Consistent with χ^2 test)

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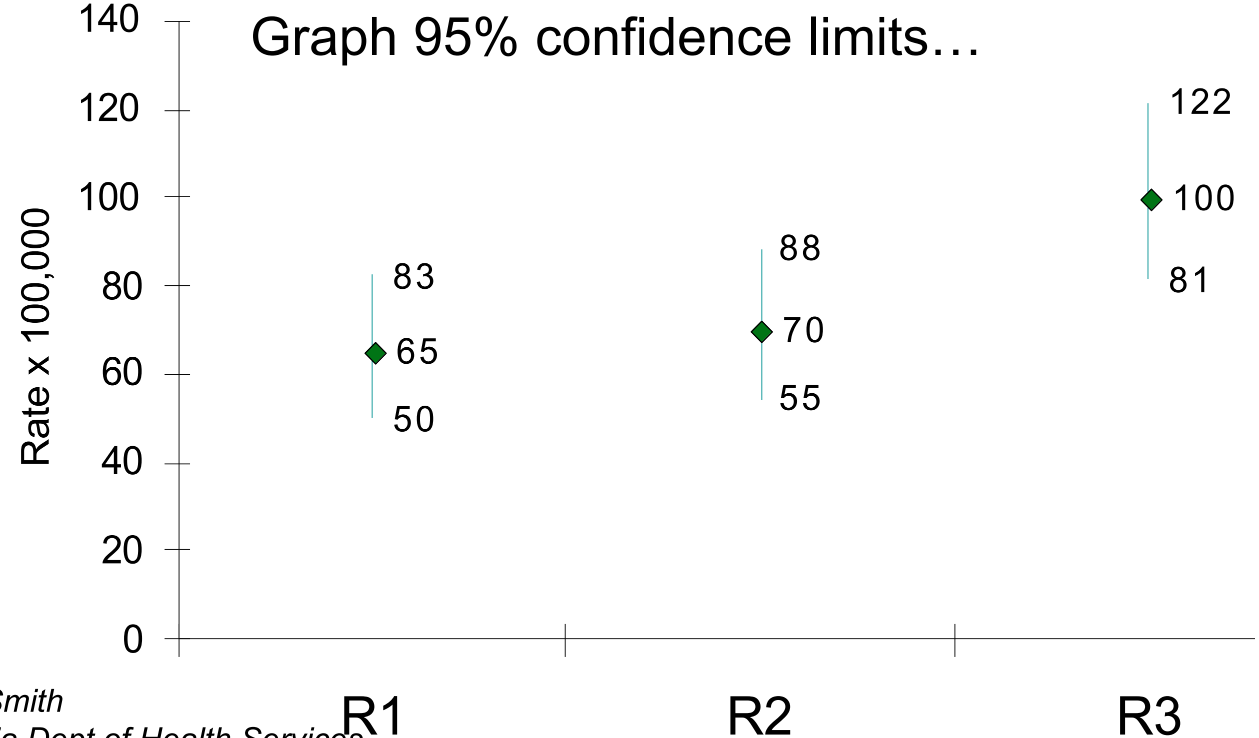
Three or more rates…

R_1	R_2	R_3
65/100,000	70/100,000	100/100,000

$P = 0.67$ (R_1 vs R_2) $P = 0.02$ (R_2 vs R_3)

$P = 0.006$ (R_1 vs R_3)

Graph 95% confidence limits…



All three confidence limits overlap!

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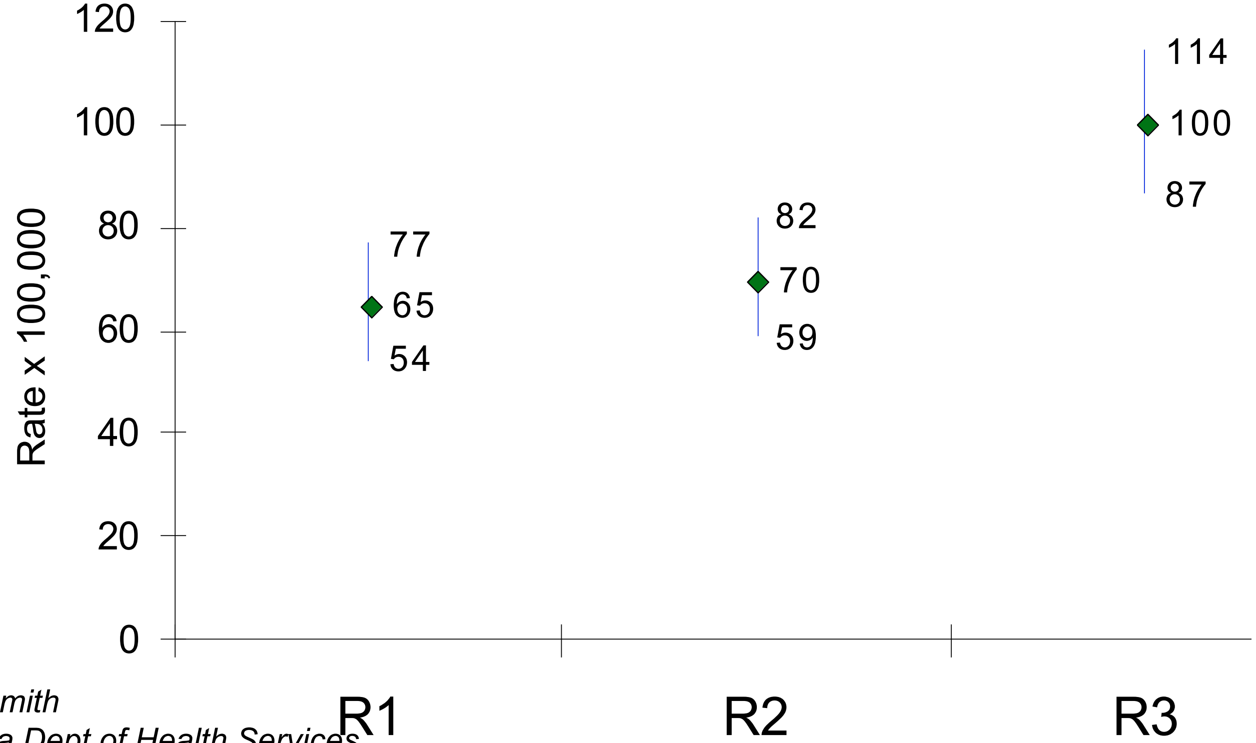
Three or more rates with LSD-style intervals

R_1	R_2	R_3
65/100,000	70/100,000	100/100,000

P = 0.67 (R_1 vs R_2) P = 0.02 (R_2 vs R_3)

P = 0.006 (R_1 vs R_3)



Now, overlaps agree with tests

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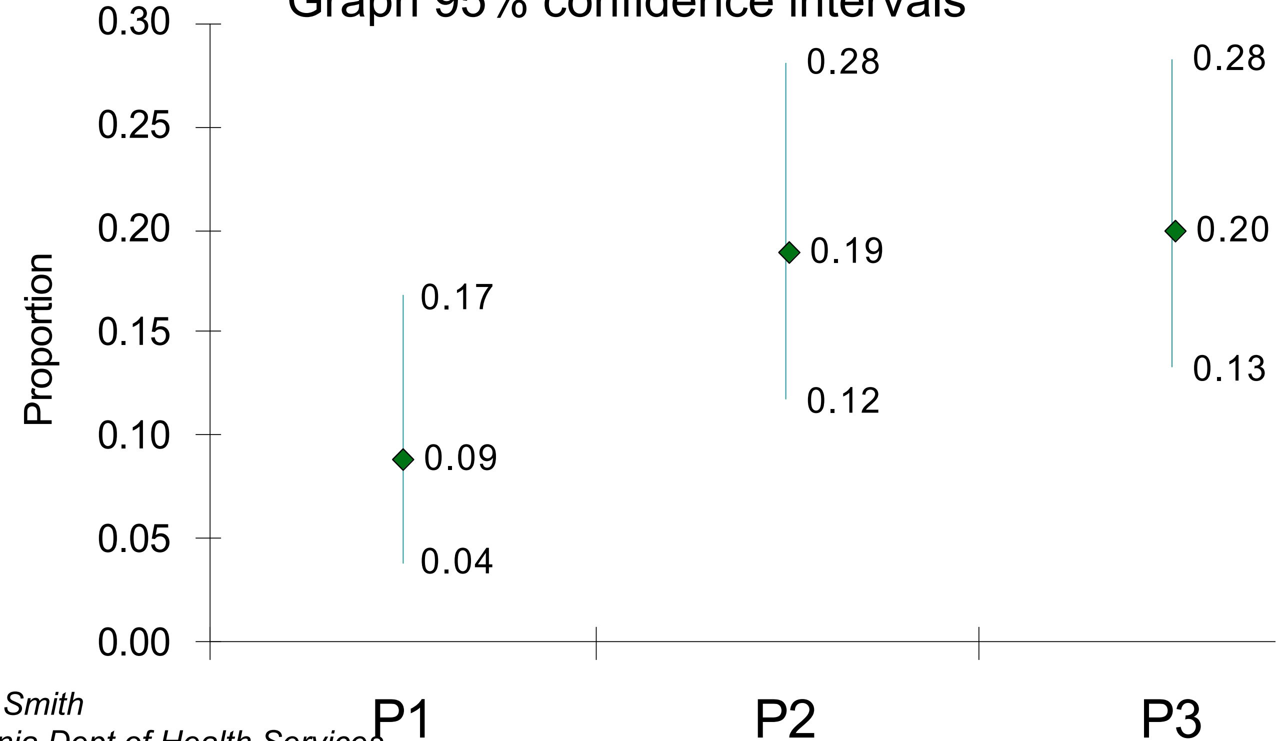
Try to adapt this to binomial case: Three or more proportions…

P_1	P_2	P_3
8/90	19/100	24/120

P = 0.047 *P* = 0.85

P = 0.027

Graph 95% confidence intervals



All three confidence intervals overlap!

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Three or more proportions with LSD-style intervals

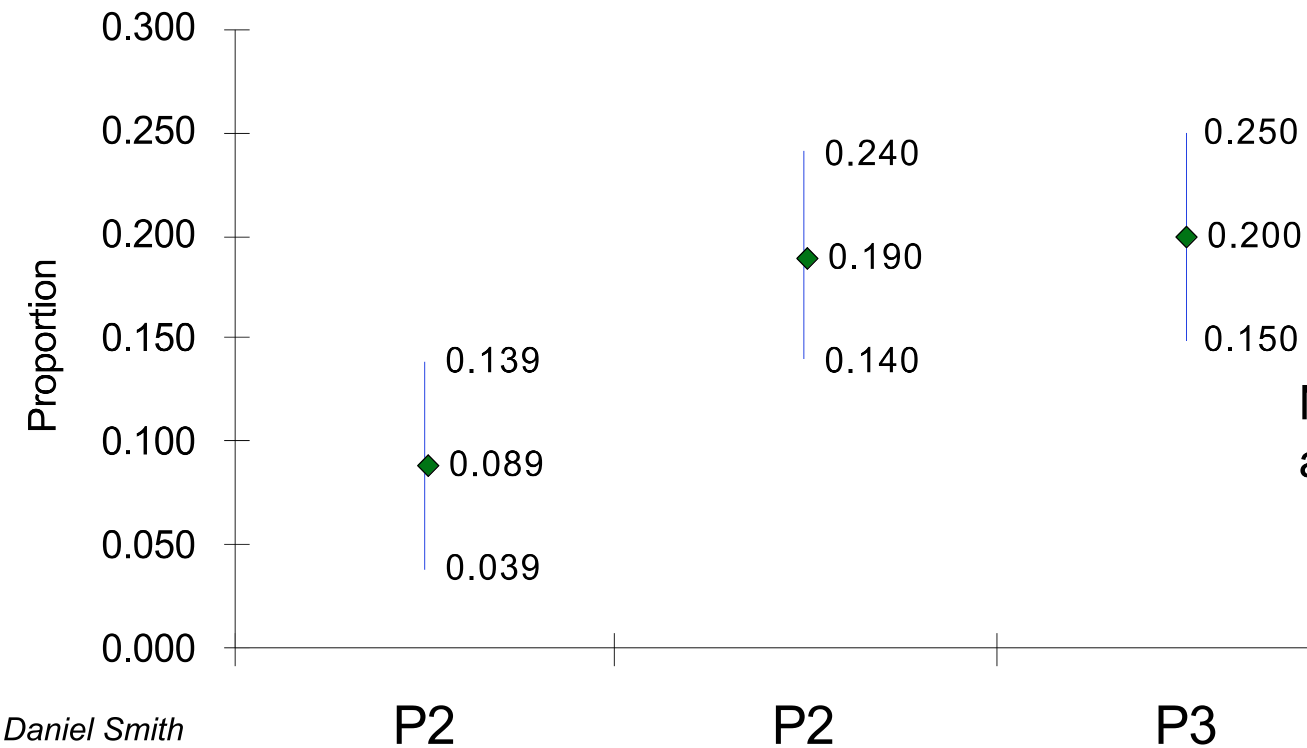
P_1 8/90 P_2 19/100 P_3 24/120

P = 0.047   *P* = 0.85

P = 0.027

Construct LSD-type intervals based on standard error of a test of two proportions:

$$\text{LSD Interval}: \; P \pm \frac{Z\sqrt{\frac{2\bar{p}\bar{q}}{\bar{n}}}}{2}$$



Now, overlaps agree with tests

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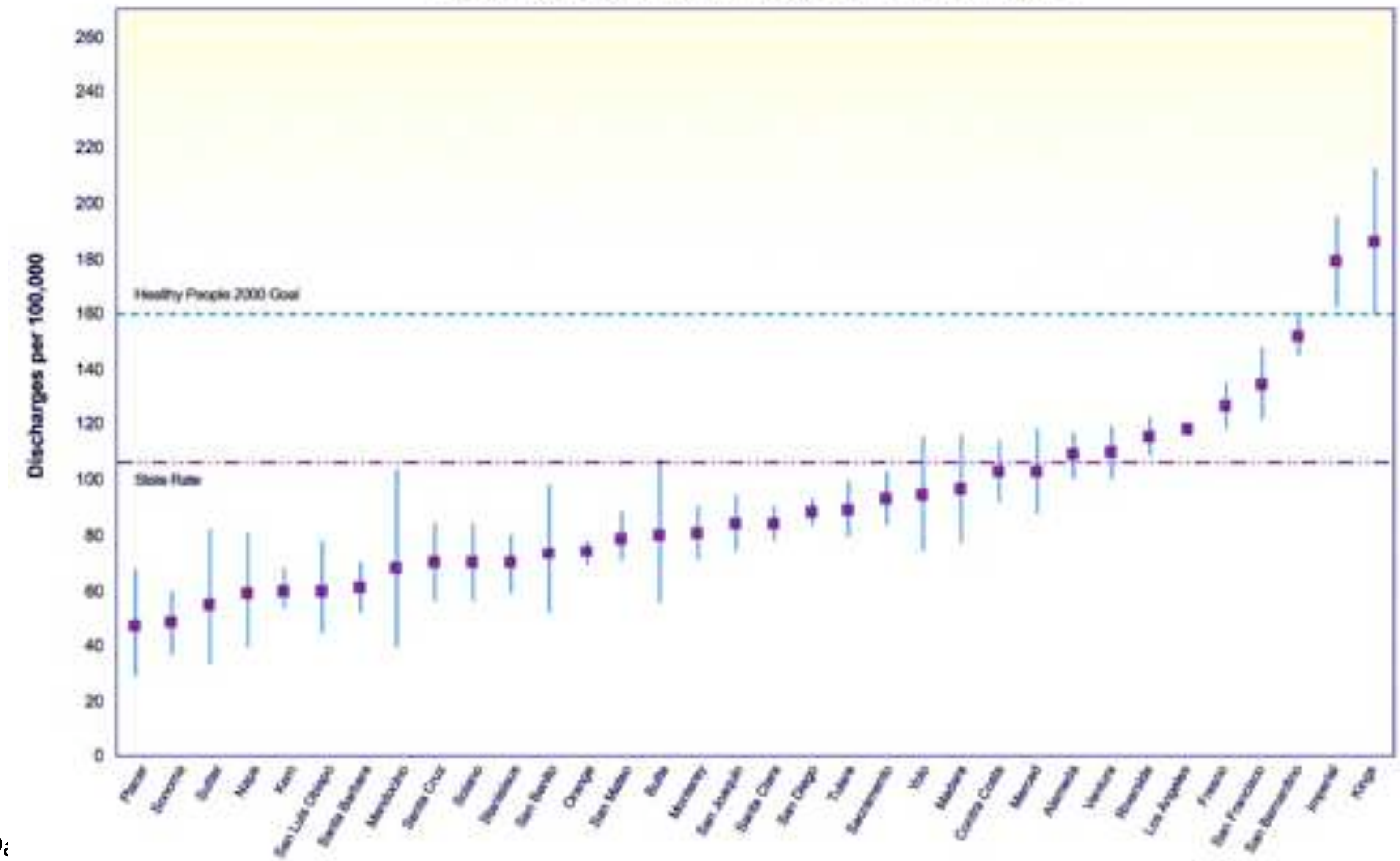
This *is* OK…
Comparing rates to a hypothetical value

Figure 4: Age-Adjusted* Asthma Hospital Discharge Rates for Hispanics by County, 1995-1997, with 95% Confidence Intervals.



*Age-adjusted to the 1990 California population. Counties with less than 20 cases not shown.

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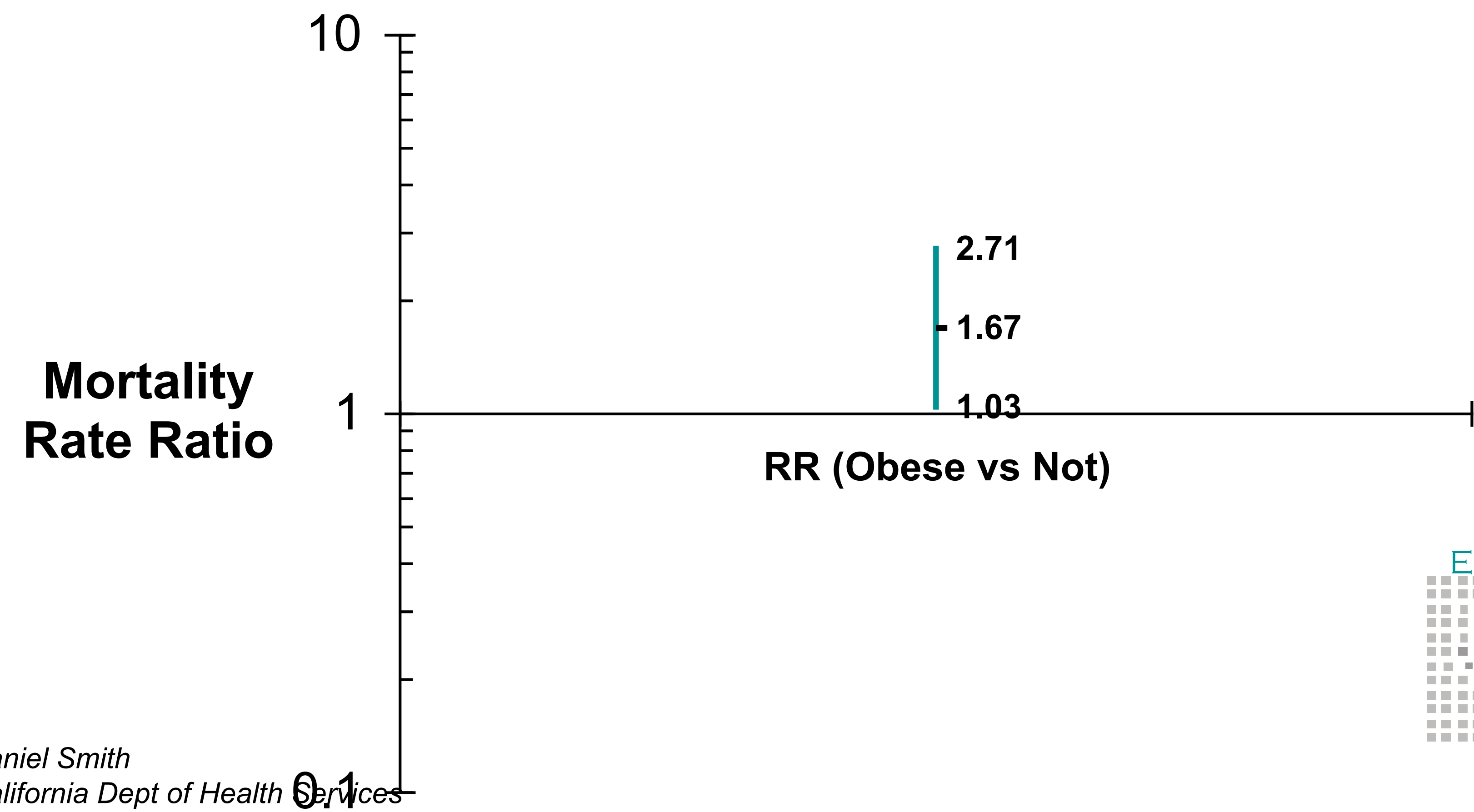
This is also OK…

Confidence limits for a *comparative* measure, versus the null hypothesis value



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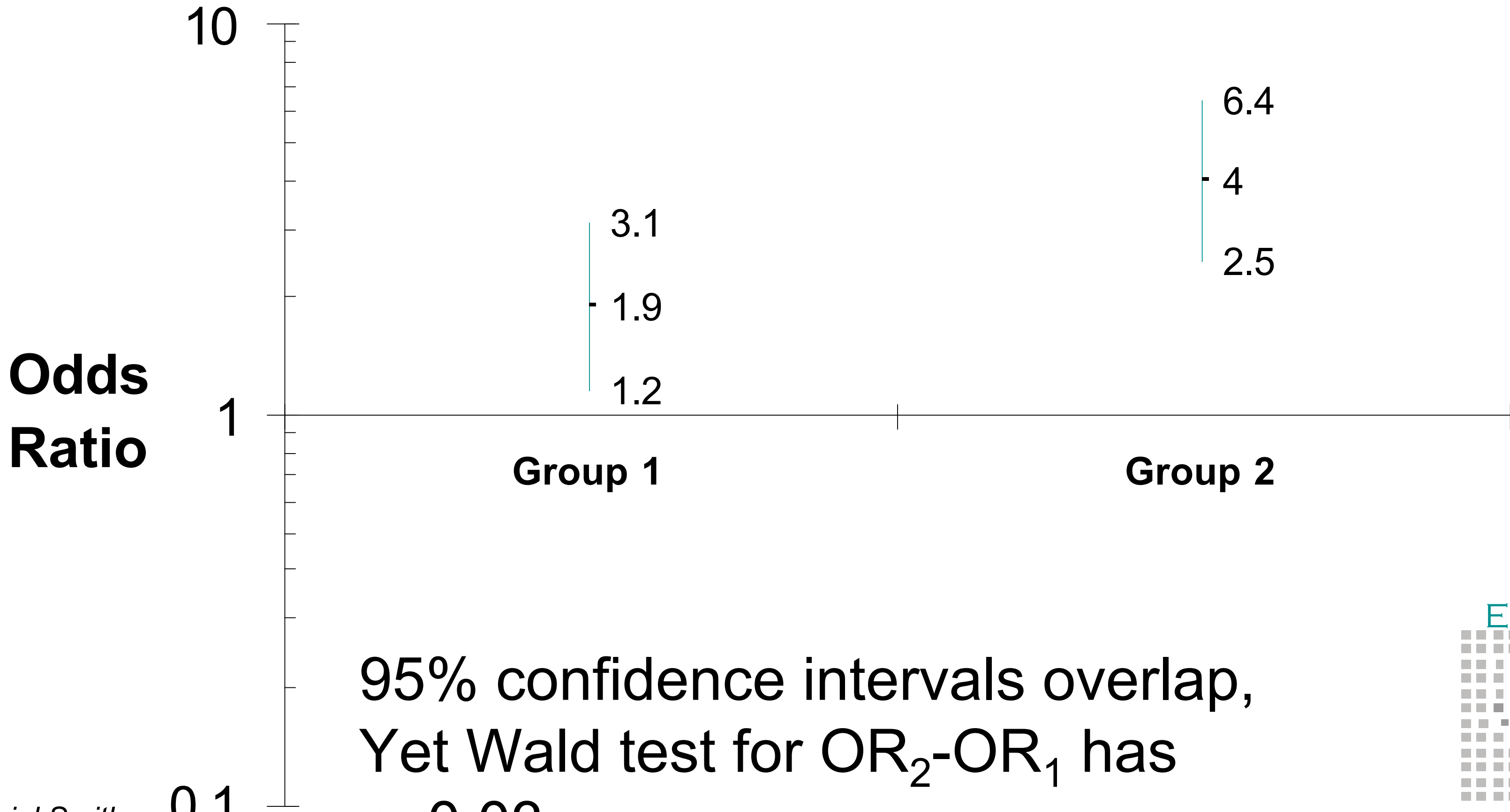
But it is *not* OK to use intervals to compare OR_1 to OR_2…

Confidence interval around *one* OR is not a comparative measure between *two* ORs



95% confidence intervals overlap, Yet Wald test for OR_2-OR_1 has p=0.03

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So what to do?

- Be careful about use of overlap criterion:
  - –Overlap of 1-α % intervals means *p* could still be < α
  - –Intervals can overlap as much as 29% and rates can still be different at the 0.05 level (van Belle, 2001)
  - –Non-overlap of 1-α % confidence intervals means that *p* << α
- Show confidence intervals, but don't use them for testing between two groups
- Show LSD-type intervals, but don't call them confidence intervals

Epilogue

What to do for *adjusted* or *standardized* rates?
(Previous examples have been crude rates)

- It has yet to be worked out how to construct the LSD intervals for *weighted averages…*
- But provisionally, you might try this approach:
  - Note that, for crude rates, the LSD-type interval is narrower than the standard confidence interval by the factor of √1/2
  - Can create an LSD-type interval by multiplying standard CI by √1/2 :

    Width of interval = +/- Z*SE*(√1/2), where SE is the standard error of the standardized rate.

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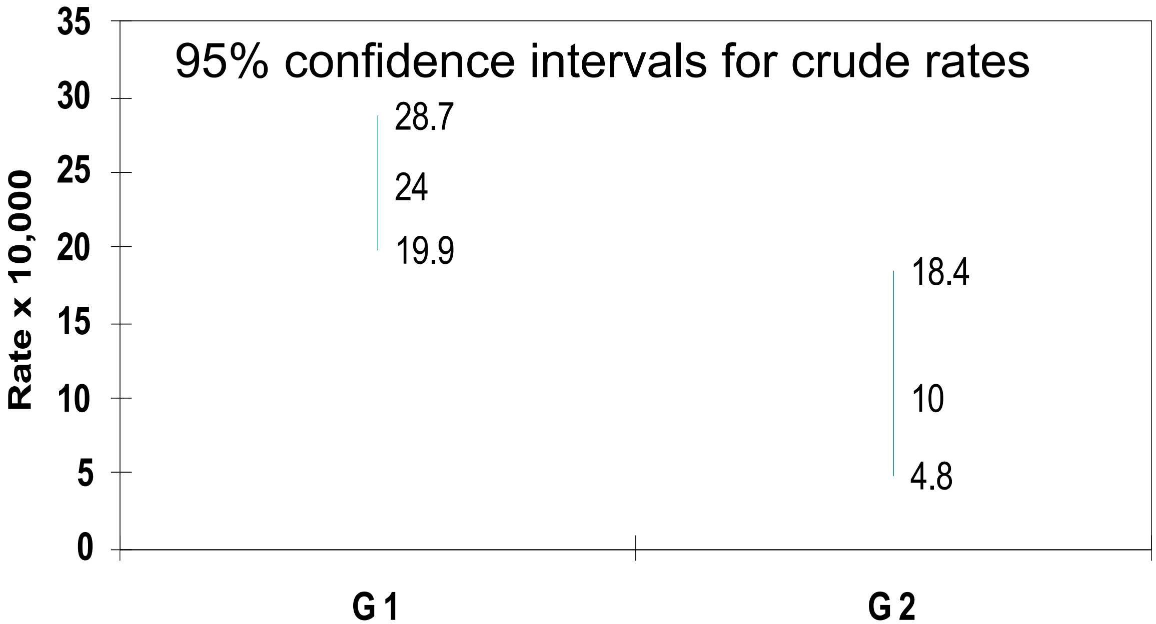
Example of stratified data with confounding

	Group 1	Group 2	$RR_{stratum}$
Stratum 1	20/15,000	5/6,000	1.60
Stratum 2	100/35,000	5/4,000	2.29
Crude totals	120/50,000	10/10,000	2.40

Crude χ^2
p=0.006



Confidence intervals don't overlap, but rates are confounded (crude RR is greater than either stratum RRs)

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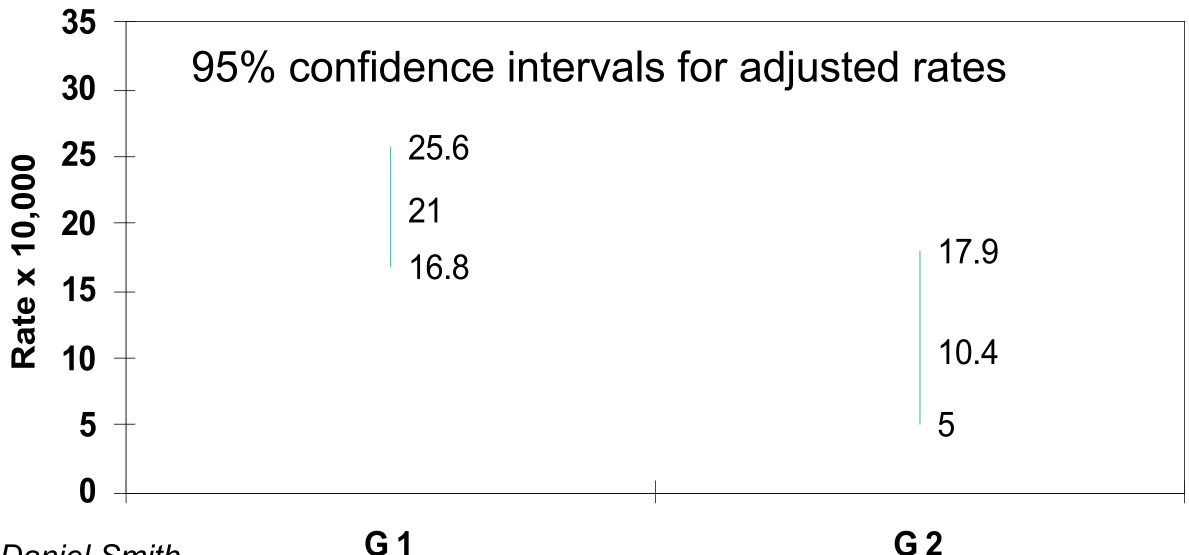
Standardized rates
(“direct adjustment,” using weights)

	Group 1	Group 2	Weight
Stratum 1	20/15,000	5/6,000	0.5
Stratum 2	100/35,000	5/4,000	0.5
Standardized rate	21.0/10,000	10.4/10,000	

Standardized RR = 2.01 (95% CL 1.02 – 4.24)
Mantel-Haenszel χ^2 p-value = 0.039



As expected, the 95% confidence intervals for the standardized rates inappropriately overlap

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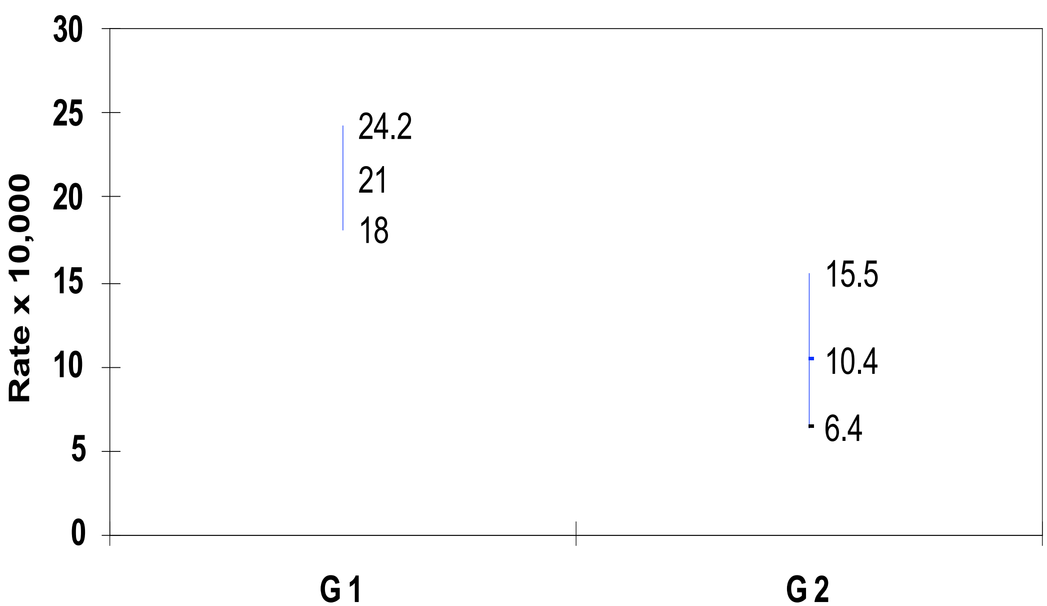
Try the correction factor…

Calculate intervals using $Z * SE_{(\text{standardized rate})} * \sqrt{1/2}$



- Error bars don’t overlap
- Now they’re consistent with Mantel-Haenszel χ^2 test controlling for stratum

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  – Schenker N, Gentleman JF. On judging the significance of differences by examining the overlap between confidence intervals. *American Statistician* 2001; 55(3):182-186
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