

SERUM 2,3,7,8-TCDD CONCENTRATION IN A MICHIGAN, USA POPULATION WITH NO UNUSUAL SOURCES OF EXPOSURE

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The University of Michigan Dioxin Exposure Study

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Outlines

- Background and objectives
- Study population
- Problems and solutions
- Methods
- Results
- Conclusions and discussions

Background and Objective

- Background:
 - There is concern that people's body burdens of dioxins, furans and PCBs are elevated in Midland and Saginaw counties, Michigan, USA, where the Dow Chemical Company operations have led to contamination of soils.
- Objectives:
 - To characterize the background levels of dioxin exposure in residents of a Michigan community who lived in an area with no unusual sources of exposure
 - To compare to the serum dioxin levels observed in Midland and Saginaw counties.

Study Population

- Population in Jackson and Calhoun counties, Michigan, were selected as the control population.
 - It is believed to have had background dioxin, furan and PCB exposures that are typical for residents of Michigan who live in the areas that are not contaminated by dioxin-like compounds from Dow Chemical Company.
 - The samples were collected in summer 2005, and a total of 251 residents have serum dioxin, furan, and PCB measures.
 - Details of the survey design and serum sampling methods and analyses can be found on our study website at: umdioxin.org

Problems and Solutions

- Limit of detection (LOD)
 - **Problem:** Fifty-two (21%) subjects have values below the LODs
 - **Simple solution:** Impute the non-detects with LOD, $\text{LOD}/\sqrt{2}$, or $\text{LOD}/2$, but these approaches do not account for imputation uncertainty.
 - **Better solution:** multiple imputation based on some statistical models (Little and Rubin 2002) to get multiple complete data.
- Serum TCDD levels are positively associated with age
 - **Problem:** Marginal estimates of the background levels depend on the distribution of the age in the reference population
 - **Solution:** estimating age-specific background levels

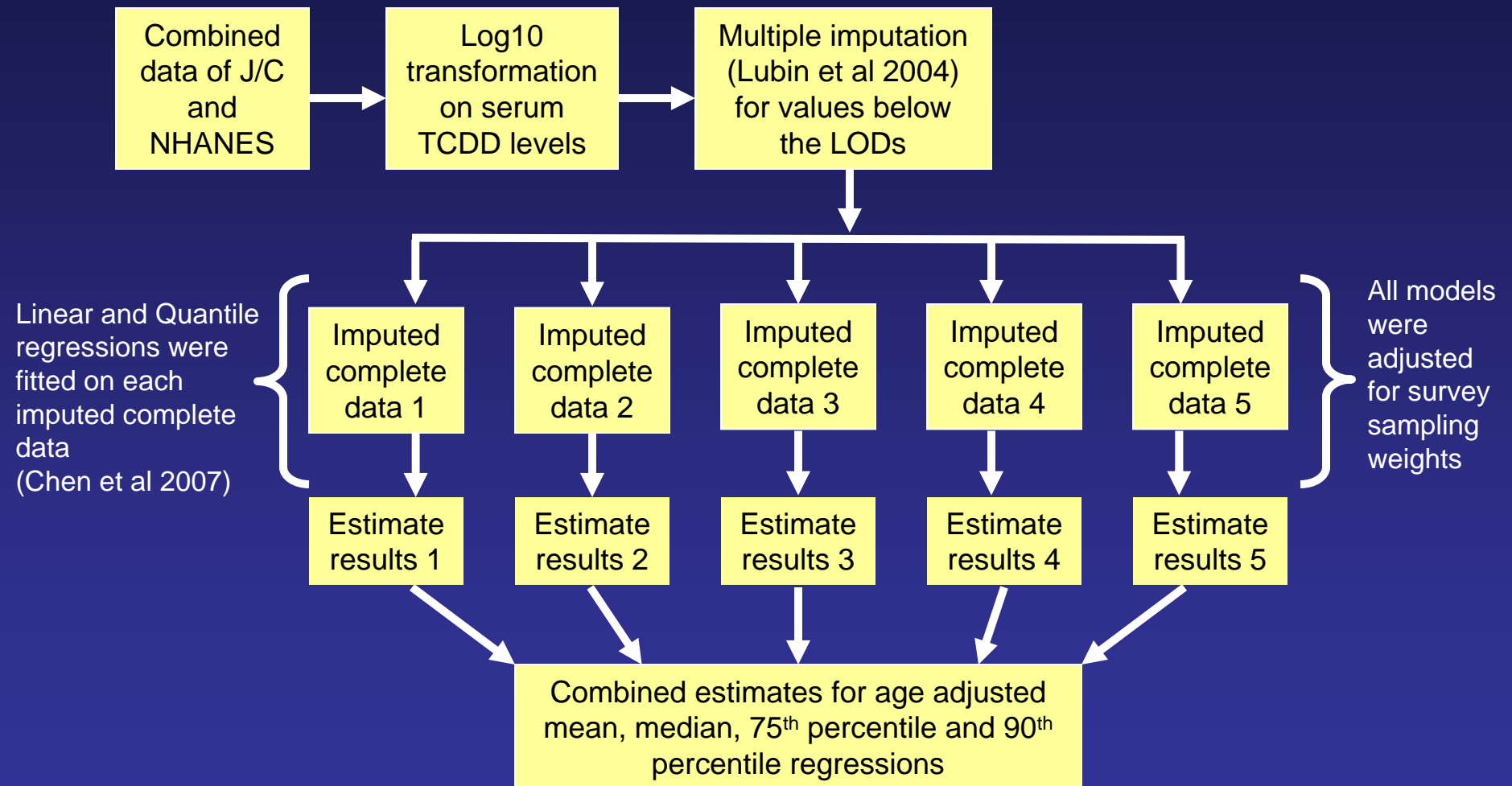
Problems and Solutions (Cont.)

- Relatively few people older than 75 are in the study →
 - **Problem:** It is difficult to estimate the age-specific upper percentiles among old people
 - 2001-2002 National Health and Nutrition Examination Survey (NHANES)
 - The data were drawn from a representative sample of the U.S. population age 20 years and over.
 - The NHANES non-Hispanic whites population are similar with the Jackson/Calhoun population in some important demographic predictors. →
 - *Cons:* the proportion of values below LOD were substantially higher in the NHANES data than in the Jackson/Calhoun data. →
 - *Pros:* Among people older than 75, the NHANES data have enough observations above the LODs. →
 - **Solution:** supplement the analysis by the NHANES data

Methods

- Age-specific background level measures
 - Mean (survey weighted linear regression)
 - Median, 75th percentile, 90th percentile (survey weighted quantile regression)
 - SAS 9.1
- Improving the estimates by using information from the 2001-2002 NHANES, especially among people over age 75.
 - The NHANES data set was concatenated with the UMDES Jackson and Calhoun data.
 - The data source was retained (NHANES=1 and UMDES=0)
 - Survey sampling weights were standardized within each data source by dividing by their respective mean sampling weights
 - Important demographic information was retained

Flow Chart of the Statistical Analysis



Results of mean and quantile regressions of base 10 logarithm of serum TCDD concentrations

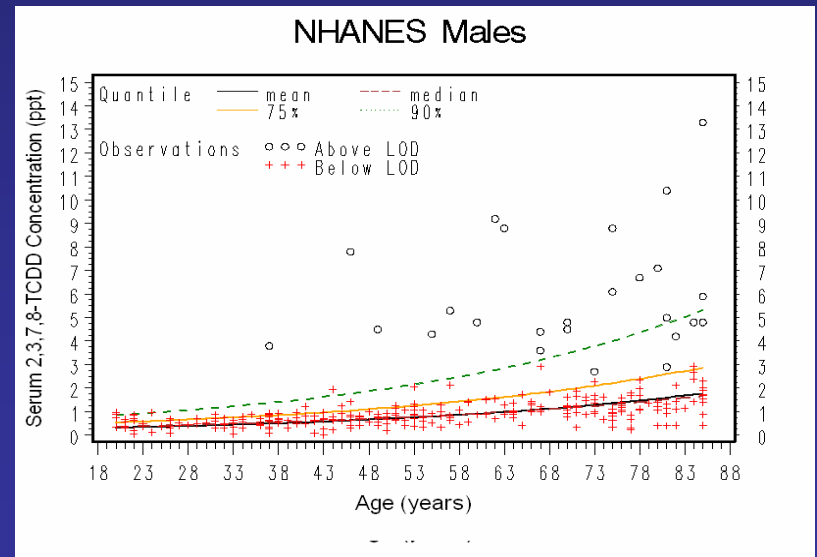
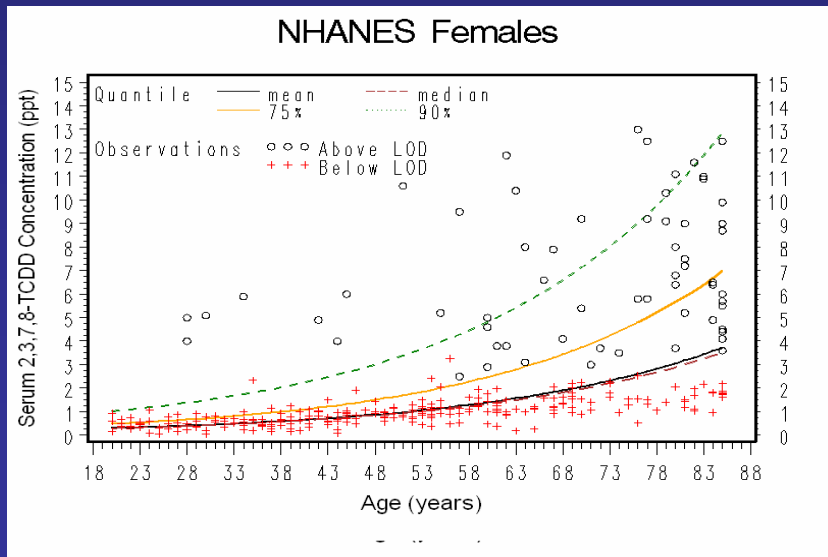
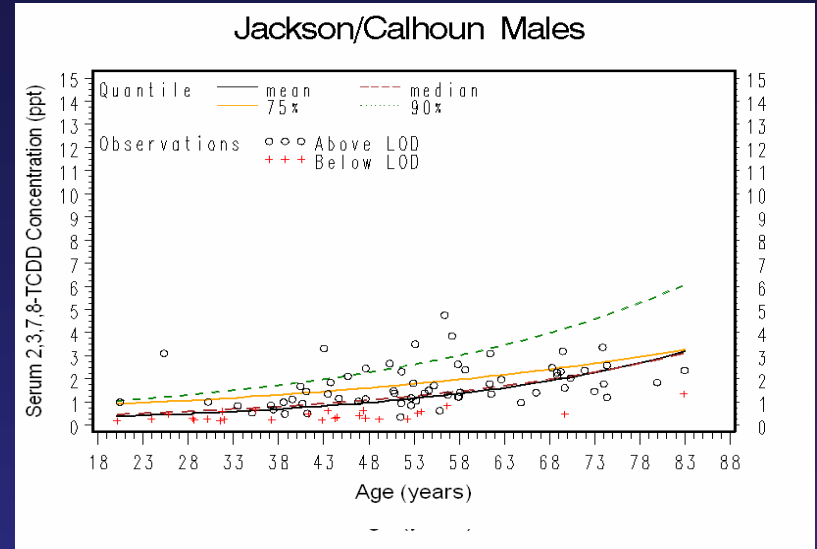
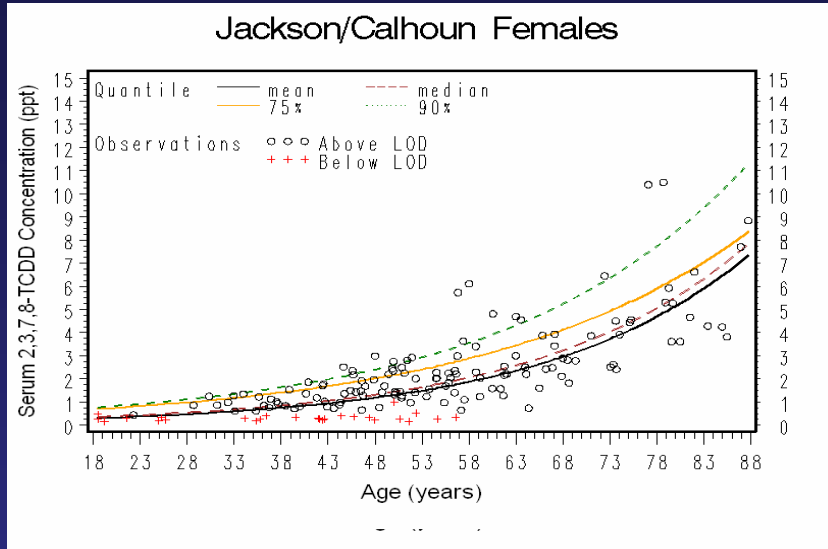
Factor	Linear regression (mean)	Quantile Regression (median)	Quantile Regression (75 th percentile)	Quantile Regression (90 th percentile)
Intercept	0.110 (0.031)***	0.153 (0.029)***	0.334 (0.038)***	0.412 (0.027)***
Age-50 (years)	0.020 (0.002)***	0.020 (0.002)***	0.016 (0.002)***	0.017 (0.003)***
Gender (Male=1)	-0.094 (0.041)**	-0.098 (0.049)**	-0.111 (0.068)	-0.033 (0.069)
source (NHANES=1)	-0.139 (0.049)***	-0.202 (0.052)***	-0.123 (0.073)	0.098 (0.097)
(Age-50)*Gender	-0.005 (0.002)**	-0.006 (0.003)*	-0.007 (0.003)**	-0.005 (0.005)
(Age-50) * Source	-0.003 (0.002)	-0.003 (0.004)	0.002 (0.004)	0.0002 (0.005)
Gender*source	-0.040 (0.084)	-0.005 (0.074)	-0.038 (0.086)	-0.184 (0.138)

Results are reported as estimate + (standard error) + P-value

***P-value<0.01; **P-value<0.05; *P-value<0.1

- 85% of the NHANES data are below the LODs.
- Be cautious in interpreting this significance, since the mean and median regressions for the NHANES data are mostly based on the imputed values.
- the serum TCDD increases more quickly in females than in males
- Neither the interaction term between age and data source nor the interaction term between gender and data source is significant.
- The effects of age and gender are the same for both data sources.

Prediction of the age specific mean, median, 75th percentile, and 90th percentile of TCDD levels



Conclusions

- The mean, median, 75th percentile, and 90th percentile of serum TCDD concentrations increase log-linearly with age, and the rates of increase in the mean, median, and 75th percentile are greater among females than males.
- Using the NHANES data enhanced our understanding of the distribution of serum TCDD values among older people in the Jackson/Calhoun population.
- The Jackson/Calhoun population are similar to the general US population in the serum TCDD exposure. This implies that the Jackson/Calhoun population is a valid reference population for the population in the Midland/Saginaw counties, Michigan.

Discussions

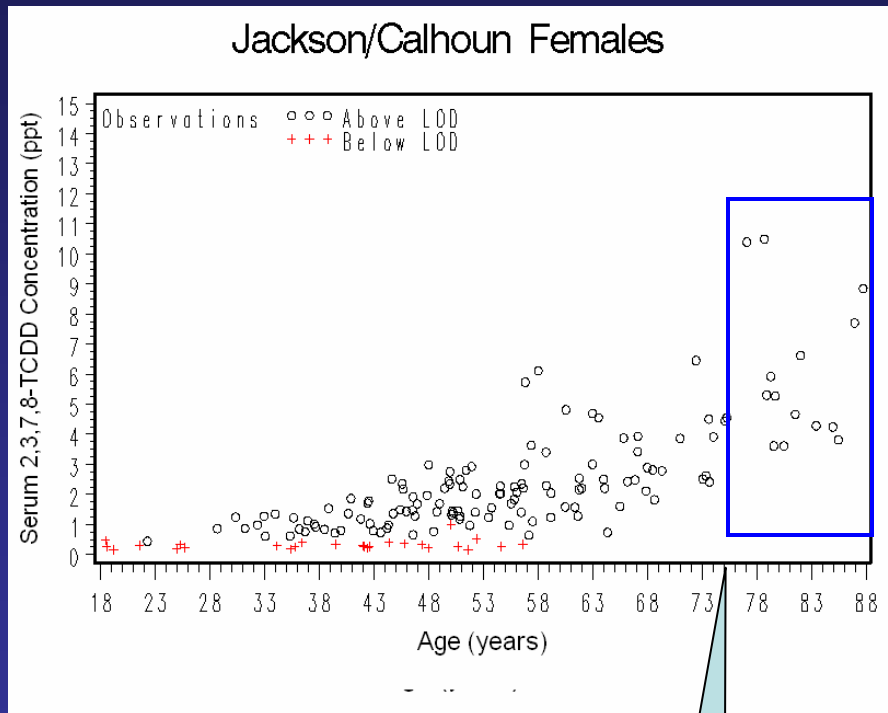
- For each resident in Midland/Saginaw, we can compare the serum TCDD level to the background level of people of the same age and sex in Jackson/Calhoun to see whether their serum TCDD level are elevated.
- With multiple quantile curves, different researchers can define different age-specific-quantile/mean curves as their reference levels according to their research interests.
- Quantile regressions provide better adjustment of the age effect in estimating the quantiles than the traditional method of calculating the population quantiles without adjusting for age, or of adjusting for a limited number of age groups.

References

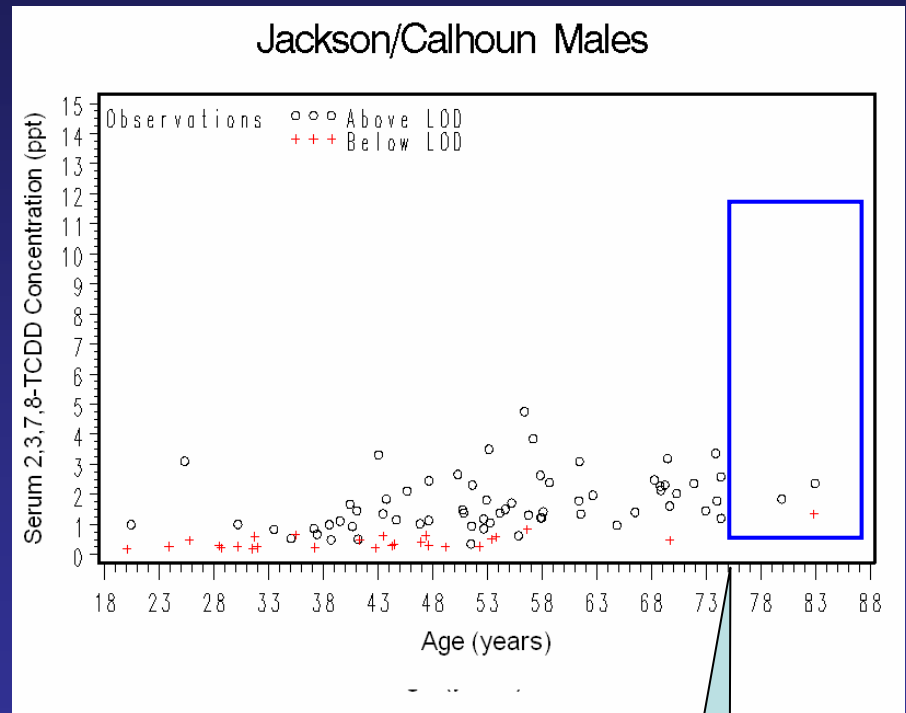
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- **Posters:**
 - For details on the statistical methods in this work, please see our poster **P295**.
 - For the application the results of this work, please see our poster **P288**.

Thank you!

Scatter Plots of the Jackson/Calhoun data



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Demographics Comparisons

Factor	NHANES (n=615)	Jackson/Calhoun (n=251)
Median age (years)	48.2	49.9
Mean BMI (kg/cm ²)	27.9	28.7
Mean Pack-yrs	11.5	12.5
Female only: Mean No. of children breast feeding	1.1	1.0
Proportion of males	48%	38%

- ❑ The Jackson/Calhoun population have higher proportion of females than the general US population.
- ❑ This difference can be overcome by the separate analysis for males and females.
- ❑ Similar in age, BMI, pack-yrs, and breast-feeding among females.



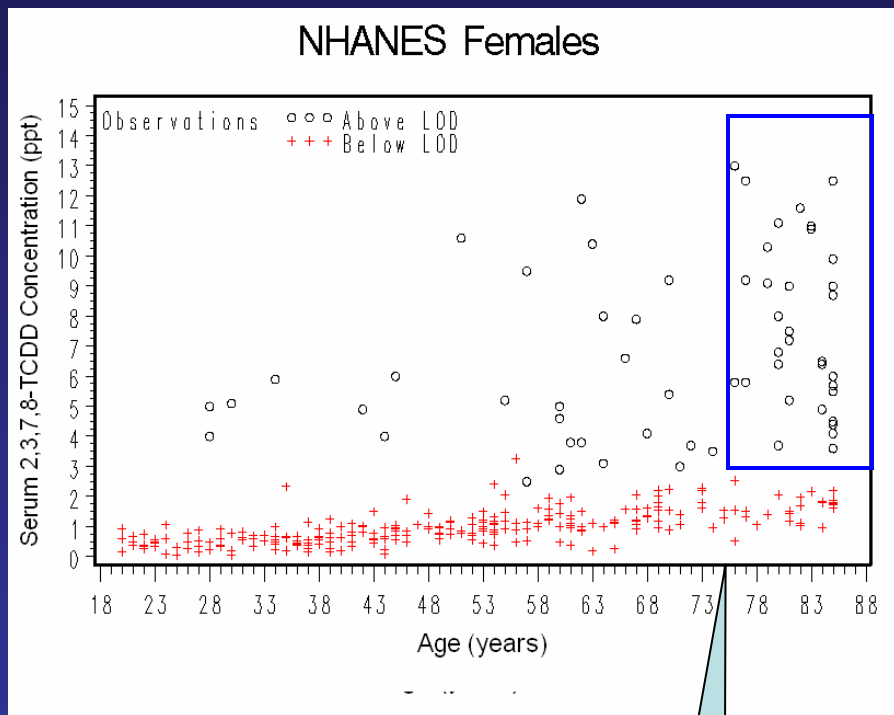
LODs Comparison

Factor	NHANES (n=615)	Jackson/Calhoun (215)
Proportion of below LOD	85.4%	20.7%
Median LOD levels among non-detections	3.0 ppt	0.5 ppt

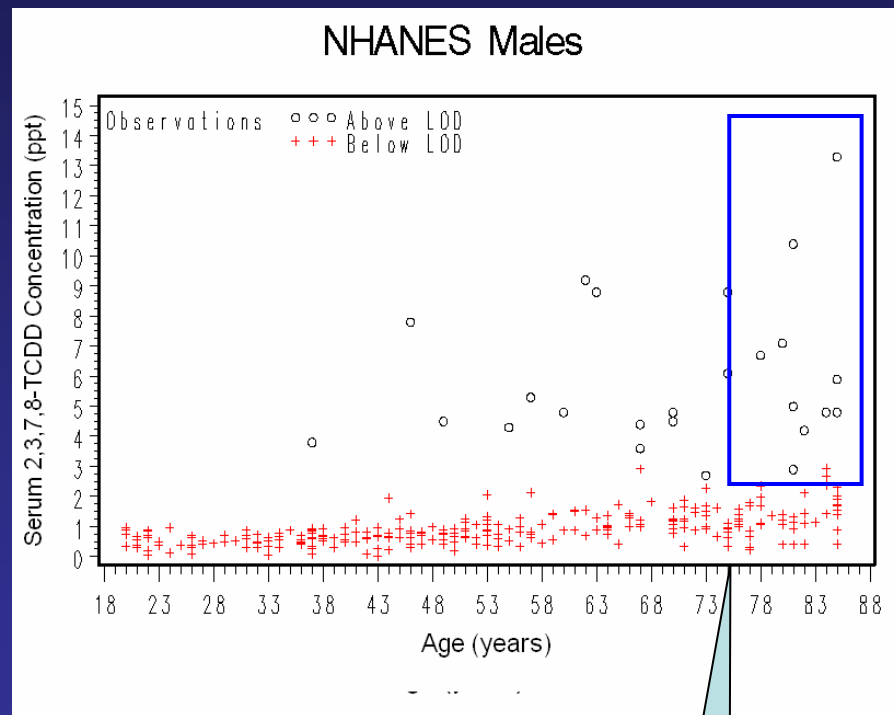
- ❑ The NHANES data have much higher proportion of below the LODs and higher median LOD levels than the Jackson/Calhoun data.



Scatter Plots of the NHANES data



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