



# Ozone Clinical Studies and Dose-Response

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# Human Clinical Studies



- These studies measure physiological effects, primarily respiratory function (forced expiratory volume in 1 second - FEV<sub>1</sub>)
- They take into account 3 parameters, which make up O<sub>3</sub> *dose*:
  - O<sub>3</sub> concentration (in ppm)
  - Duration of exposure (in min)
  - Ventilation rate (ie. Exercise level; in L/min)

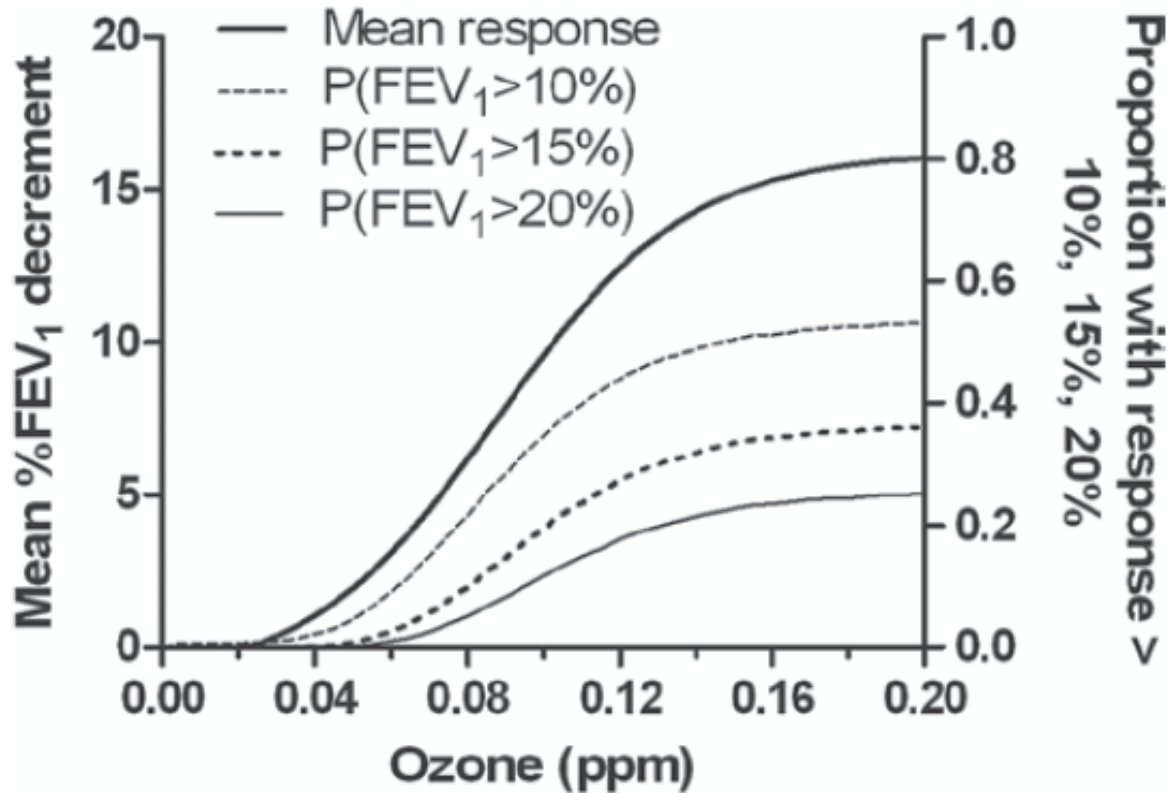


# Adverse Effects – FEV<sub>1</sub>

- ATS, 2000 - “reversible loss of lung function in combination with the presence of symptoms should be considered adverse.”
- ATS/ERS, 2005 - “two-point, short-term changes of >12% and >0.2L in the FEV<sub>1</sub> are usually statistically significant and may be clinically important” (Pellegrino 2005)
- US EPA 2014b - “...a focus on the mid- to upper-end of the range of moderate levels of functional responses and higher (FEV<sub>1</sub> decrements  $\geq$  15%) is appropriate for estimating potentially adverse lung function decrements in active healthy adults, while for people with asthma or lung disease, a focus on moderate functional responses (FEV<sub>1</sub> decrements down to 10%) may be appropriate”



# McDonnell 2012 Dose-Response Curve

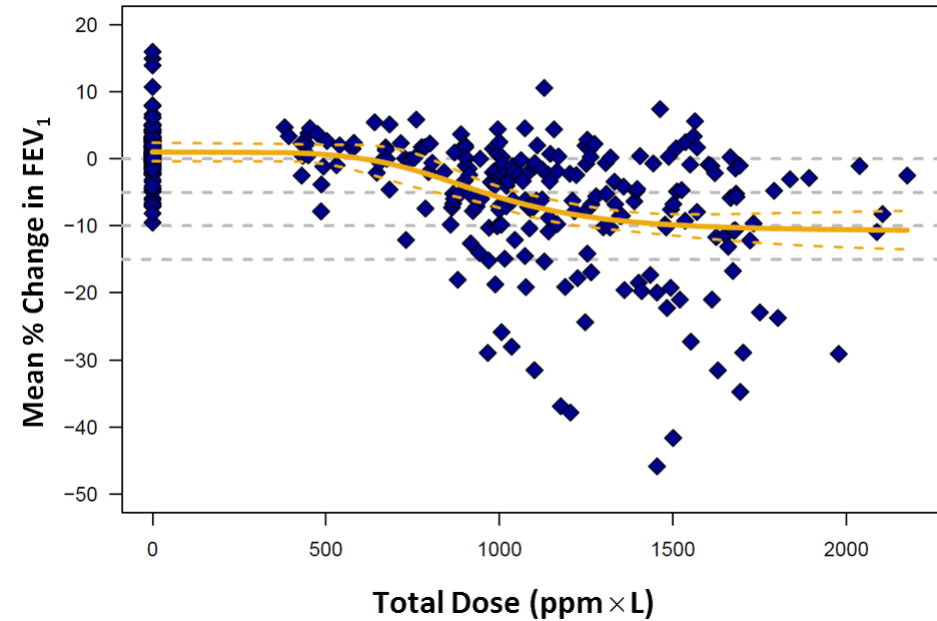


Assuming an exercise ventilation rate of 20 L/min m<sup>2</sup> body surface area (~34 – 40 L/min) and a duration of 6.6 hours

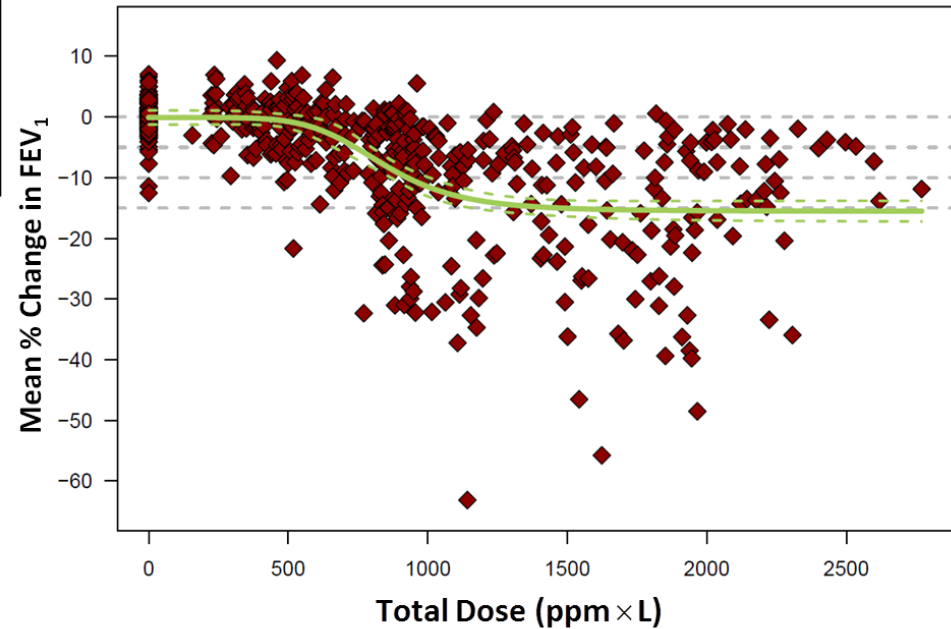


# O<sub>3</sub> Dose-Response Curves

Longer Exposure (6-8 hours)



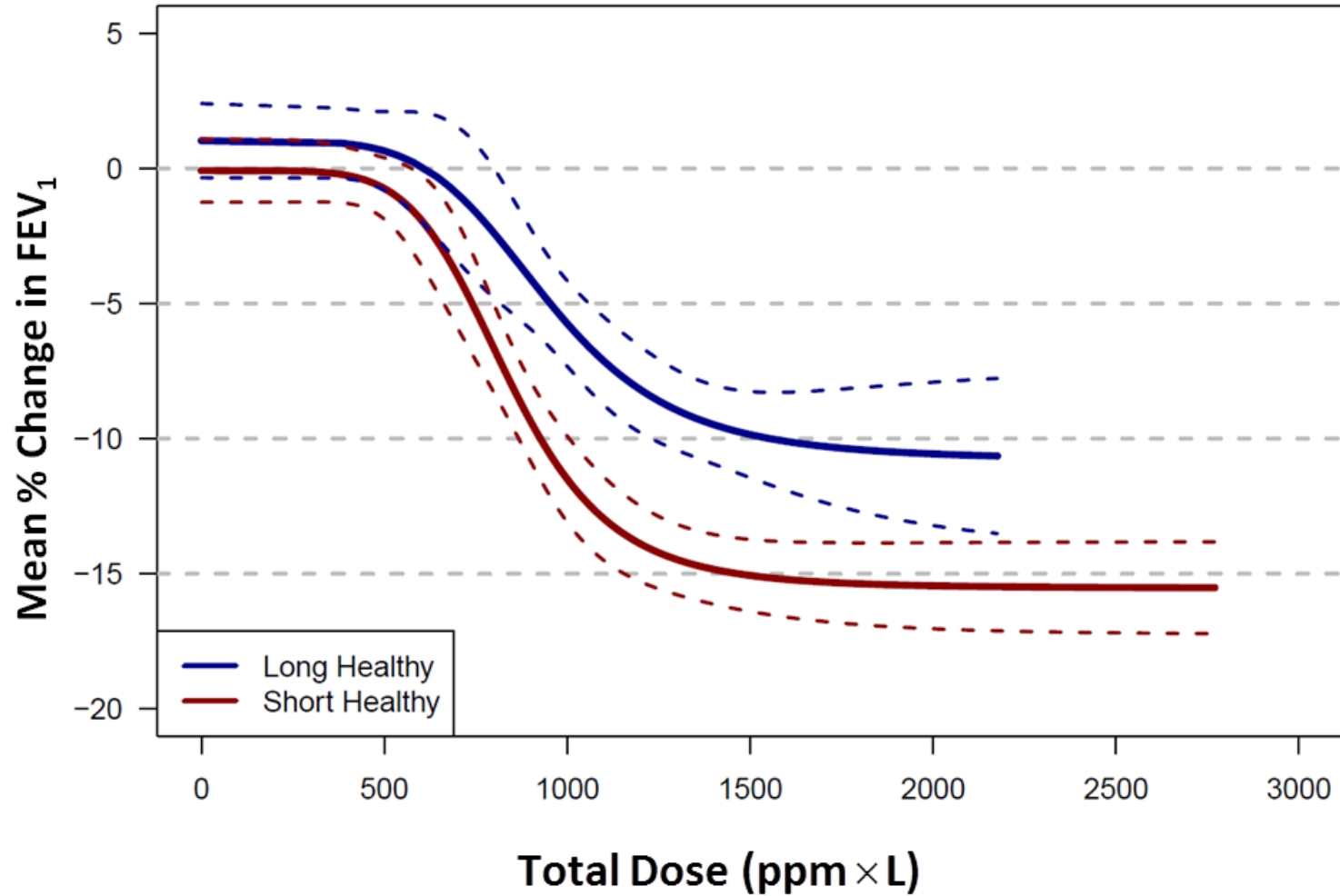
Shorter Exposure (≤ 3 hours)



With M. Honeycutt from TCEQ; G. Tao, L. Rhomberg & J. Goodman from Gradient; M. Dourson from TERA

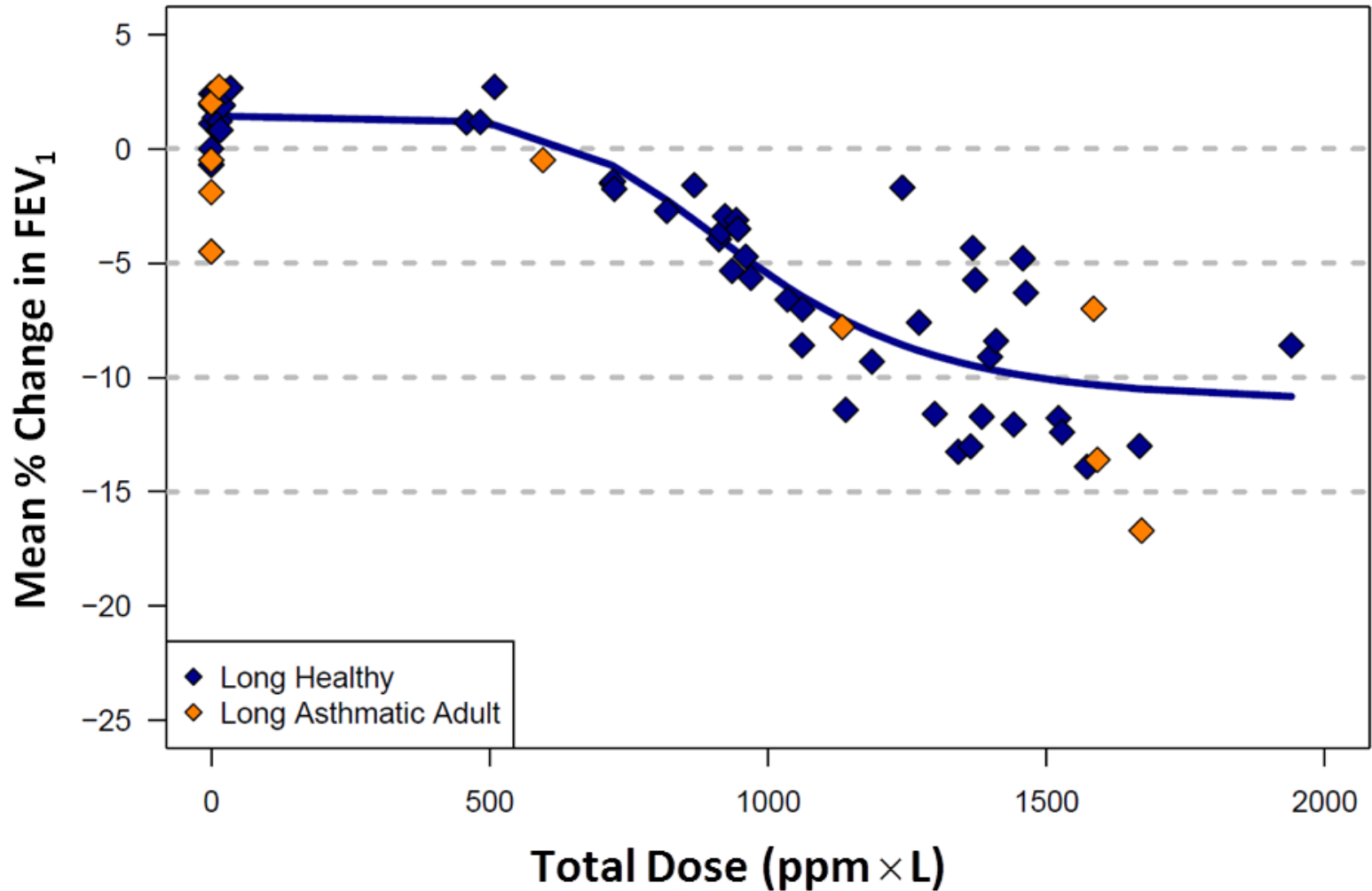


# O<sub>3</sub> Dose-Response Curves



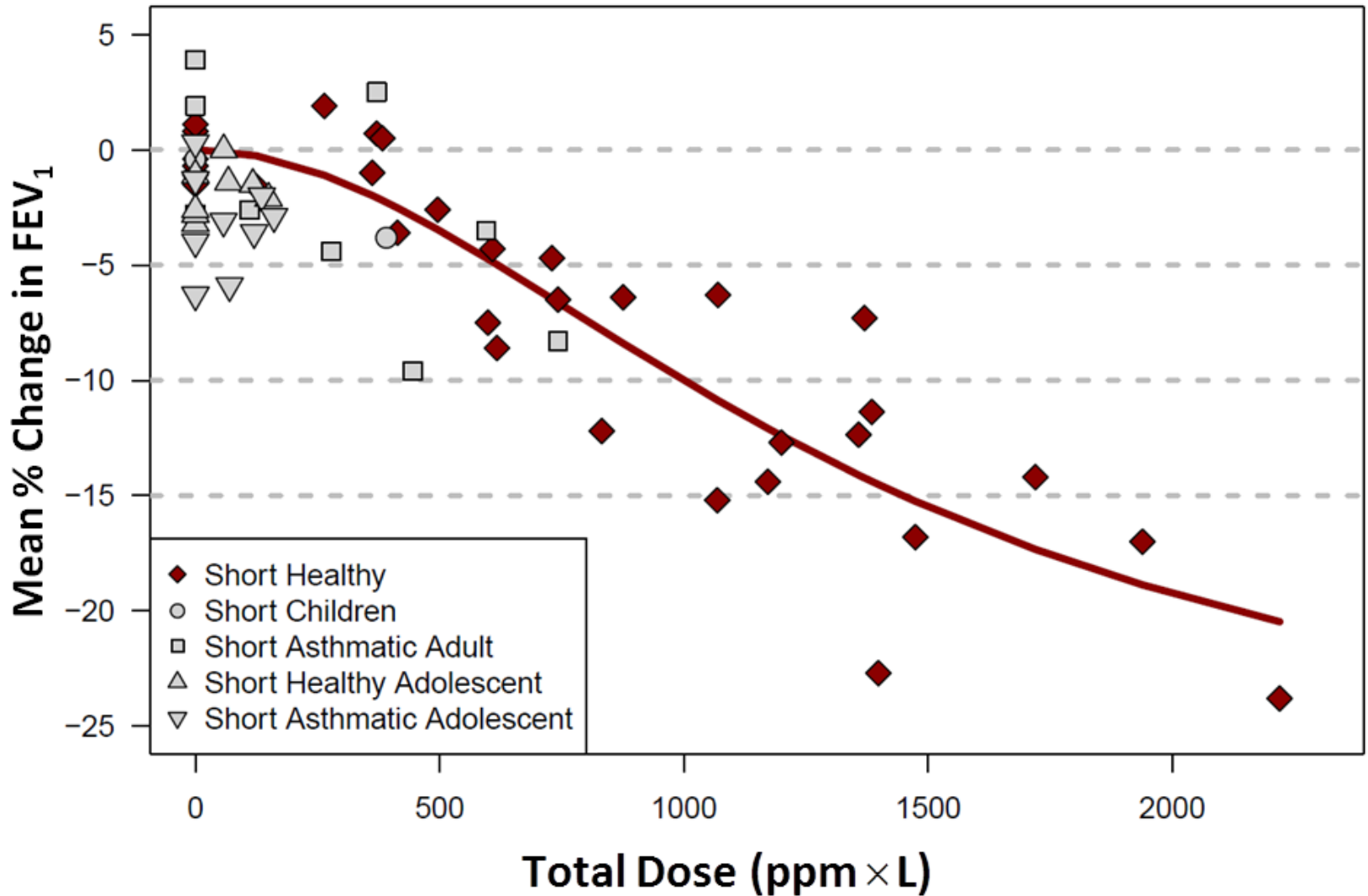


# D-R Curves with Sensitive Populations





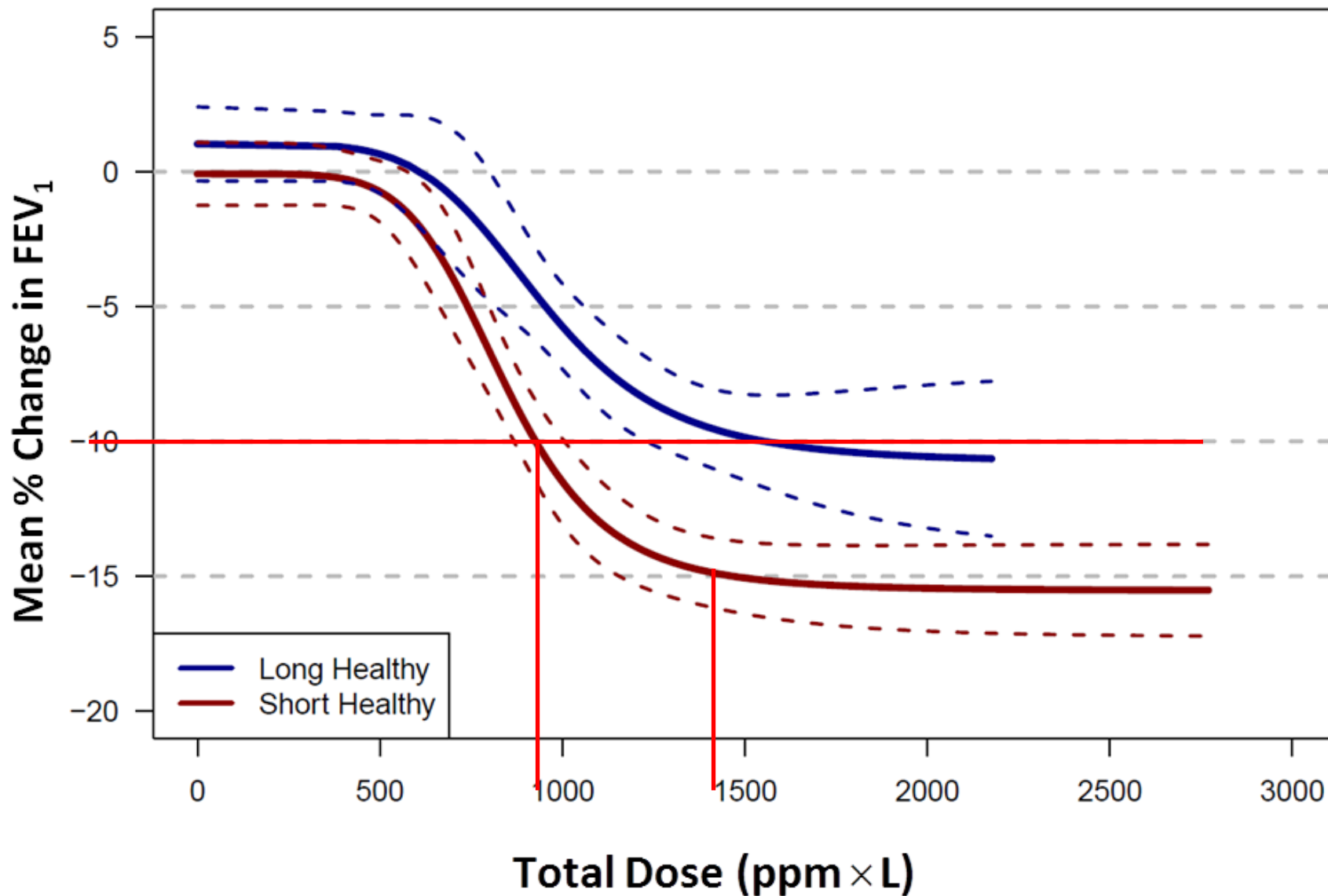
# D-R Curves with Sensitive Populations







# Ozone Dose Thresholds





# O<sub>3</sub> FEV<sub>1</sub> Dose Thresholds

## Individual Data Dose-Response Curves

| Mean % Change in FEV <sub>1</sub> | Short exposure dose (ppm•L) | Long exposure dose (ppm•L) |
|-----------------------------------|-----------------------------|----------------------------|
| 0                                 | N/A                         | 608.5                      |
| -5                                | 740.2                       | 953.5                      |
| -10                               | 926.7                       | 1553.8                     |
| -15                               | 1467.4                      | N/A                        |
| -20                               | N/A                         | N/A                        |



# Exercise Ventilation Rates & Durations

| Source               | Population                    | Exercise Intensity                        | Ventilation Rate (L/min)* | Duration (hours)* |
|----------------------|-------------------------------|---|---------------------------|-------------------|
| <b>US EPA 2009</b>   | Children (6 - < 11 years old) | Sedentary                                 | 4.8 (3.7-6)               | 13.7 (13-15)      |
|                      |                               | Light                                     | 11.3 (9.2-14)             | 7.4 (5.5-9.6)     |
|                      |                               | Moderate                                  | 21.6 (17-26.8)            | 2.6 (0.9-4.1)     |
|                      |                               | High                                      | 41.5 (31.4-53.5)          | 0.3 (0.02-0.9)    |
|                      | Adult (21 - < 31 years old)   | Sedentary                                 | 5.3 (3.6-5.9)             | 12.5 (11.2-13.8)  |
|                      |                               | Light                                     | 11.8 (9.2-14.9)           | 6.3 (3.8-9.7)     |
|                      |                               | Moderate                                  | 26.1 (18.8-34.4)          | 5 (1.8-7.6)       |
|                      |                               | High                                      | 49.8 (34.6-67.2)          | 0.3 (0.05-0.6)    |
| <b>US EPA 1994</b>   | Non-occupational              | 24 hr Ventilation with 8 hrs Manual labor | 14                        | 24                |
|                      | Occupational                  | Manual labor                              | 22                        | 8                 |
| <b>Zuurbier 2003</b> | Adult                         | Bicycle commute                           | 23.5 (11-47.7)            | 2                 |
| <b>Samet 1993</b>    | Child                         | Outdoor play                              | 16 (12.1-17.4)            | 1.9               |
|                      | Child                         | Bicycling                                 | 27.1 (16.7-34.8)          | 2.1               |
|                      | Adult                         | Vigorous bicycling                        | 65 (40.8-87.8)            | 0.8               |

\* Mean ventilations and times, and where available, the 10<sup>th</sup> and 90<sup>th</sup> percentiles in parentheses.



# Ozone Concentrations

| 1 Hour Measurements | 8 hr Max Ave | 4 hr Max Ave | 12 hr Max Ave | 24 Hr Ave |
|---------------------|--------------|--------------|---------------|-----------|
| 19.4                |              |              |               |           |
| 30.9                |              |              |               |           |
| 40.4                |              |              |               |           |
| 57.4                |              | 37.0         |               |           |
| 70.5                |              | 49.8         |               |           |
| 81.0                |              | 62.3         |               |           |
| 87.5                |              | 74.1         |               |           |
| 81.3                | 58.6         | 80.1         |               |           |
| 72.2                | 65.2         | 80.5         |               |           |
| 72.2                | 70.3         | 78.3         |               |           |
| 69.7                | 74.0         | 73.9         |               |           |
| 62.1                | 74.6         | 69.1         | 62.1          |           |
| 58.1                | 73.0         | 65.5         | 65.3          |           |
| 50.2                | 69.2         | 60.0         | 66.9          |           |
| 43.0                | 63.6         | 53.4         | 67.1          |           |
| 43.3                | 58.9         | 48.7         | 65.9          | 49.1      |



# Ozone Concentrations

Ozone concentrations on days with maximum eight-hr concentrations of 75, 70 or 65 ppb.

| Concentration Metric | 75 ppb Days (ppb) | 70 ppb Days (ppb) | 65 ppb Days (ppb) |
|----------------------|-------------------|-------------------|-------------------|
|                      | mean (SD)         | mean (SD)         | mean (SD)         |
| 1-hr max             | 85.8 (3.5)        | 77.4 (5.7)        | 72.4 (4.7)        |
| 2-hr max average     | 84.2 (3.2)        | 76.2 (5.2)        | 71.3 (4.1)        |
| 3-hr max average     | 82.8 (2.7)        | 75.3 (4.8)        | 70.3 (3.7)        |
| 4-hr max average     | 80.8 (2.2)        | 74.3 (4.2)        | 69.6 (3.4)        |
| 5-hr max average     | 79.4 (1.7)        | 73.3 (3.2)        | 68.6 (2.6)        |
| 6-hr max average     | 78.2 (1.3)        | 72.4 (2.1)        | 67.6 (1.9)        |
| 7-hr max average     | 76.8 (0.9)        | 71.4 (1.4)        | 66.6 (1.1)        |
| 8-hr max average     | 75.4 (0.6)        | 70.2 (0.7)        | 65.6 (0.8)        |
| 9-hr max average     | 72.6 (4.5)        | 69 (0.7)          | 64.5 (1.2)        |
| 10-hr max average    | 71.5 (3.2)        | 97.6 (1.6)        | 63.2 (2.0)        |
| 11-hr max average    | 70.4 (2.2)        | 66.2 (2.4)        | 61.9 (2.9)        |
| 12-hr max average    | 69.2 (1.8)        | 64.9 (3.2)        | 60.6 (3.5)        |
| 13-hr max average    | 68 (1.8)          | 63.8 (4.0)        | 59.2 (4.2)        |
| 14-hr max average    | 66.9 (2.1)        | 62.7 (4.7)        | 57.9 (4.8)        |
| 24-hr average        | 52.2 (5.5)        | 51.4 (8.5)        | 46.2 (6.5)        |

Note: provided are the mean maximum averages using different time metrics from 10 days with eight-hour maximum averages of 75, 70 or 65 ppb (standard deviation in parentheses). Shaded is the measured eight-hour maximum average.



# O<sub>3</sub> Dose Calculation

## Example: A child exercising at moderate intensity

Ventilation Rate: **21.6 L/min**

Duration: **2.6 hours** (156 minutes)

Ozone concentration at **3 hour** maximum average:

| <b>8 hr Max Ozone</b> | <b>75 ppb</b> | <b>70 ppb</b> | <b>65 ppb</b> |
|-----------------------|---------------|---------------|---------------|
| 3 hr Max Ozone        | 82.8 ppb      | 75.3 ppb      | 70.3 ppb      |

### Dose Calculation:

75 ppb: 21.6 L/min x 156 minutes x 0.0828 ppm = **279 ppm x L**

70 ppb: 21.6 L/min x 156 minutes x 0.0753 ppm = **254 ppm x L**

65 ppb: 21.6 L/min x 156 minutes x 0.0703 ppm = **237 ppm x L**

### **Compare to short exposure (< 4 hours) thresholds:**

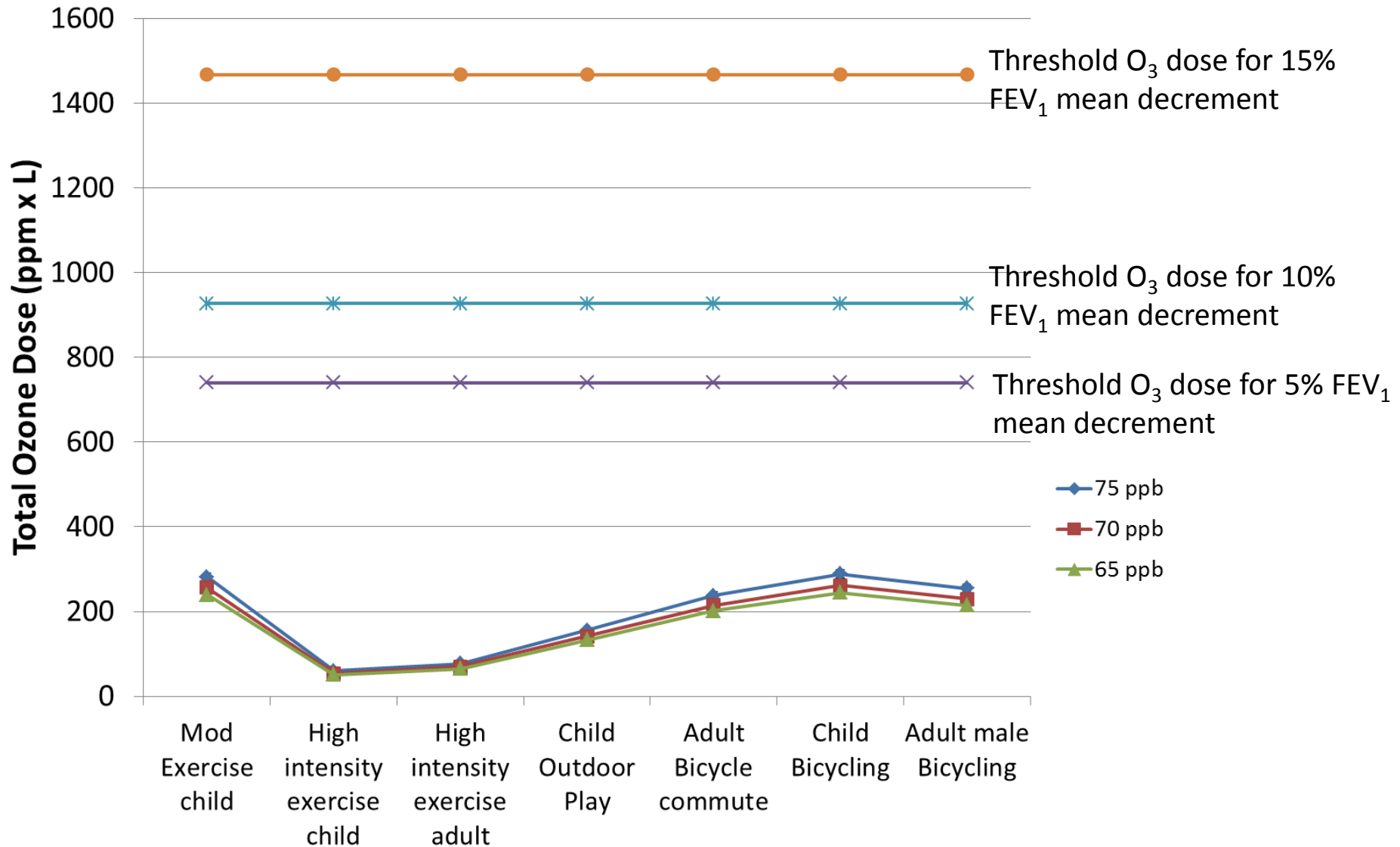
5% FEV<sub>1</sub> decrement: 740 ppm x L

10% FEV<sub>1</sub> decrement: 927 ppm x L

15% FEV<sub>1</sub> decrement: 1467 ppm x L

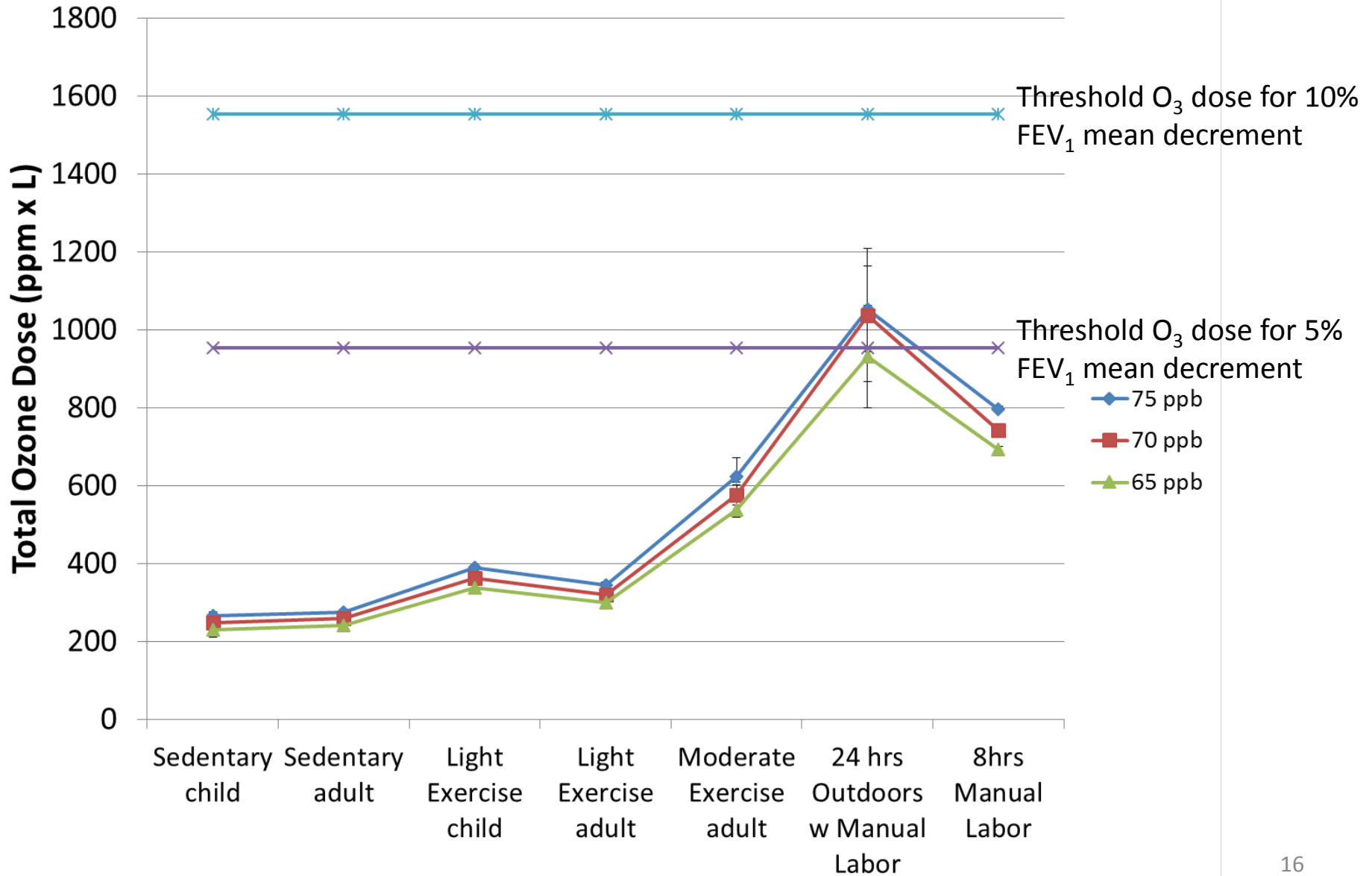


# Short Exposure Scenarios





# Longer Exposure Scenarios







# References

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