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| --- | --- | --- | --- | --- | --- |
| **Supplemental Table 1. CMV infection classification by IgG, IgM, shedding, and IgG avidity among individuals aged 6-49 years, NHANES 1999-2004** | | | | | |
| **CMV Classification** | **IgG** | **IgM** | **Shedding** | **IgG Avidity** | **Unweighted N** |
| Seronegative | Negative | Missing | Missing | Missing | 5,990 |
| Primary infection | Positive | Positive | Positive | Low | 14 |
| Positive | Positive | Negative | Low | 10 |
| Positive | Negative | Positive | Low | 8 |
| Positive | Positive | Missing | Low | 2 |
|  |  |  |  |  | 34 (total) |
| Latent infection | Positive | Negative | Negative | Missing | 5,418 |
| Positive | Negative | Negative | Low | 156 |
| Positive | Negative | Negative | High | 4 |
|  |  |  |  |  | 5,578 (total) |
| Recurrent infection | Positive | Negative | Positive | High | 152 |
| Positive | Positive | Negative | High | 46 |
| Positive | Positive | Positive | High | 16 |
| Positive | Positive | Missing | High | 10 |
|  |  |  |  |  | 224 (total) |

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| **Supplemental Table 2. Summary of laboratory methods used to determine CMV IgG and IgM seropositivity, detect CMV DNA in urine, and measure CMV IgG avidity in NHANES 1999-2004.** | | | | | |
| **CMV Parameter** | **Specimen** | **Testing Method** | **Interpretation** | **Eligible Sample** | **Unweighted N (Weighted %)** |
| IgG | Sera | Commercial ELISA (Quest International, Inc.) | Positive if optical density values exceeded the manufacturer’s suggested cutoff value.  Note: For a small number of samples near the cutoff, a second commercial ELISA (bioMérieux Inc.) was performed with specimens classified as positive if optical density values from both ELISAs exceeded the respective manufacturers’ suggested cutoff values. If these two tests disagreed, a commercial IFA (Bion International, Inc.) was performed with fluorescent intensities exceeding a cutoff value reported as positive. | Participants aged 6 to 49 years with stored sera | 7,698 positive of 13,688 eligible (50.8%) |
| IgM | Sera | Commercial ELISA (Diamedix) | Optical density ratios <0.90 as negative, ≥0.90 to <1.10 as equivocal, and ≥1.10 as positive.  Note: Confirmatory testing was performed on specimens near the test cutoff values using the commercial Vidas ELISA test (bioMerieux, Inc.) with results interpreted according to the manufacturers’ instructions. | Participants who were CMV IgG seropositive with stored sera | 101 positive of 7,070 eligible (1.9%) |
| IgG avidity | Sera | Commercial Vidas ELISA (bioMerieux, Inc.) | Avidity indexes ≥ 0.8 were interpreted as high avidity (suggestive of past infection), >0.7 and <0.8 as indeterminate, and <0.7 as low avidity (suggestive of recent infection). | 1. Participants who were CMV IgG and IgM seropositive with stored sera 2. A similar number of randomly selected CMV IgG seropositive and IgM seronegative participants with stored sera | 38 low avidity of 418 eligible (10.8%) |
| CMV shedding | Urine | RT-PCR | PCR testing was performed in duplicate for all specimens, with two positive results required for specimens to be reported as positive. | Participants who were CMV IgG seropositive with stored urine | 483 shedding of 6,129 eligible (5.3%) |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Supplemental Table 3. Prevalence ratios (95% CI) of CMV IgG seropositivity by toxic metal biomarker and age group, NHANES 1999-2004 (N=13,688)** | | | | | | | | | | | | | | | | | | |
|  |  | **6-19 years (N = 7,465)** | | |  | **20-29 years (N = 2,113)** | | | | |  | | **30-49 years (N = 4,110)** | | | | | |
| **Blood cadmium** | **Unweighted**  **N** | **Unadjusted** | **Minimally adjusteda** | **Fully adjustedb** |  | **Unweighted**  **N** | **Unadjusted** | **Minimally**  **adjusteda** | **Fully adjustedb** |  | | **Unweighted**  **N** | | **Unadjusted** | **Minimally adjusteda** | **Fully adjustedb** | ***Pinteraction*b** |
| **<0.30 μg/Lc** | 4,695 | 1.00  (reference) | 1.00  (reference) | 1.00  (reference) |  | 821 | 1.00  (reference) | 1.00  (reference) | 1.00  (reference) |  | | 1,223 | | 1.00  (reference) | 1.00  (reference) | 1.00  (reference) | 0.36 |
| **0.21-0.30 μg/L** | 1,184 | 1.11  (1.01-1.22) | 1.04  (0.94-1.15) | 1.04  (0.94-1.15) |  | 365 | 1.12  (0.93-1.34) | 1.03  (0.89-1.29) | 1.03  (0.89-1.20) |  | | 606 | | 1.08  (0.94-1.23) | 0.97  (0.85-1.10) | 0.96  (0.95-1.09) |  |
| **0.31-0.50 μg/L** | 1,095 | 1.16  (1.04-1.30) | 1.02  (0.90-1.15) | 1.02  (0.90-1.15) |  | 473 | 1.27  (1.09-1.48) | 1.13  (1.00-1.29) | 1.14  (1.00-1.30) |  | | 1,009 | | 1.27  (1.13-1.42) | 1.07  (0.95-1.19) | 1.06  (0.95-1.19) |  |
| **0.51-8.50 μg/L** | 491 | 1.09  (0.91-1.29) | 1.09  (0.87-1.35) | 1.09  (0.87-1.35) |  | 454 | 1.01  (0.86-1.19) | 1.03  (0.86-1.24) | 1.03  (0.86-1.24) |  | | 1,272 | | 1.30  (1.18-1.44) | 1.08  (0.97-1.21) | 1.08  (0.97-1.20) |  |
| ***Ptrend*** |  | 0.03 | 0.47 | 0.46 |  |  | 0.47 | 0.39 | 0.36 |  | |  | | <0.01 | 0.11 | 0.12 |  |
| **Blood lead** | **Unweighted**  **N** | **Unadjusted** | **Minimally adjusteda** | **Fully adjustedb** |  | **Unweighted**  **N** | **Unadjusted** | **Minimally adjusteda** | **Fully adjustedb** |  | | **Unweighted**  **N** | | **Unadjusted** | **Minimally adjusteda** | **Fully adjustedb** | ***Pinteraction*b** |
| **<0.80 μg/dL** | 1,672 | 1.00  (reference) | 1.00  (reference) | 1.00  (reference) |  | 580 | 1.00  (reference) | 1.00  (reference) | 1.00  (reference) |  | | 506 | | 1.00  (reference) | 1.00  (reference) | 1.00  (reference) | 0.06 |
| **0.81-1.20 μg/dL** | 2,559 | 1.08  (0.96-1.21) | 1.06  (0.93-1.19) | 1.06  (0.93-1.19) |  | 707 | 1.05  (0.88-1.26) | 1.03  (0.86-1.23) | 1.03  (0.86-1.23) |  | | 1,007 | | 0.89  (0.78-1.02) | 0.93  (0.81-1.08) | 0.94  (0.81-1.08) |  |
| **1.21-1.89 μg/dL** | 1,621 | 1.22  (1.09-1.38) | 1.12  (0.99-1.27) | 1.12  (0.99-1.27) |  | 398 | 1.27  (1.04-1.56) | 1.23  (1.02-1.48) | 1.23  (1.03-1.48) |  | | 1,055 | | 0.97  (0.85-1.11) | 1.01  (0.88-1.15) | 1.01  (0.89-1.16) |  |
| **1.90-68.90 μg/dL** | 1,613 | 1.28  (1.14-1.45) | 1.08  (0.96-1.21) | 1.08  (0.96-1.21) |  | 428 | 1.58  (1.34-1.86) | 1.25  (1.04-1.52) | 1.25  (1.04-1.51) |  | | 1,542 | | 0.95  (0.83-1.09) | 1.00  (0.87-1.15) | 1.00  (0.87-1.16) |  |
| ***Ptrend*** |  | <0.01 | 0.10 | 0.10 |  |  | <0.01 | <0.01 | <0.01 |  | |  | | 0.96 | 0.48 | 0.46 |  |
| a Adjusted for age (years, continuous), gender, race/ethnicity (non-Hispanic White, non-Hispanic Black, Mexican American, other Hispanic, other race), education (less than high school diploma, high school diploma or equivalent, more than high school), family income: poverty line (continuous), nativity (born in the 50 U.S. or elsewhere), and serum cotinine (ng/mL, continuous) with mutual adjustment for blood cadmium and lead categories. Prevalence ratios were weighted to account for the complex survey design and 95% confidence intervals were estimated using Taylor series linearization.  b Adjusted for all variables listed above, in addition to crowding index (residents per room, continuous)  **c** Below the highest limit of detection across NHANES cycles 1999-2000, 2001-2002, and 2003-2004 | | | | | | | | | | | | | | | | | |

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| **Supplemental Table 4. Prevalence ratios (95% CI) of CMV recurrence by toxic metal biomarker, NHANES 1999-2004 (N=5,802)** | | | | | |
| **Blood cadmium** | **Unweighted N** | **Unadjusted** | **Minimally adjusteda** | **Fully adjustedb** |  | |
| **<0.30 μg/Lc** | 2,598 | 1.00 (reference) | 1.00 (reference) | 1.00 (reference) |  | |
| **0.21-0.30 μg/L** | 912 | 0.73 (0.43-1.24) | 0.83 (0.48-1.45) | 0.83 (0.48-1.45) |  | |
| **0.31-0.50 μg/L** | 1,192 | 0.69 (0.44-1.07) | 0.88 (0.55-1.40) | 0.88 (0.55-1.40) |  | |
| **0.51-8.50 μg/L** | 712 | 0.49 (0.30-0.80) | 0.67 (0.38-1.18) | 0.67 (0.39-1.18) |  | |
| ***Ptrend*** |  | <0.01 | 0.24 | 0.24 |  | |
| **Blood lead** | **Unweighted N** | **Unadjusted** | **Minimally adjusteda** | **Fully adjustedb** |  | |
| **<0.80 μg/dL** | 1,067 | 1.00 (reference) | 1.00 (reference) | 1.00 (reference) |  | |
| **0.81-1.20 μg/dL** | 1,678 | 1.16 (0.73-1.84) | 1.22 (0.75-1.98) | 1.22 (0.75-1.99) |  | |
| **1.21-1.89 μg/dL** | 1,389 | 0.95 (0.53-1.71) | 1.25 (0.64-2.43) | 1.24 (0.64-2.43) |  | |
| **1.90-68.90 μg/dL** | 1,668 | 0.60 (0.34-1.06) | 0.93 (0.43-2.03) | 0.93 (0.43-2.03) |  | |
| ***Ptrend*** |  | 0.04 | 0.92 | 0.91 |  | |
| a Adjusted for age (years, continuous), gender, race/ethnicity (non-Hispanic White, non-Hispanic Black, Mexican American, other Hispanic, other race), education (less than high school diploma, high school diploma or equivalent, more than high school), family income: poverty line (continuous), nativity (born in the 50 U.S. or elsewhere), and serum cotinine (ng/mL, continuous) with mutual adjustment for blood cadmium and lead categories. Prevalence ratios were weighted to account for the complex survey design and 95% confidence intervals were estimated using Taylor series linearization.  b Adjusted for all variables listed above, in addition to crowding index (residents per room, continuous)  **c** Below the highest limit of detection across NHANES cycles 1999-2000, 2001-2002, and 2003-2004 | | | | | |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Supplemental Table 5. Mean differences (95% CI) in CMV IgG ELISA optical density values by toxic metal biomarker and age group, NHANES 1999-2004 (N=5,802)** | | | | | | | | | | | | | | | | |
|  | **6-19 years (N = 2,717)** | | | |  |  | **20-29 years (N = 977)** | |  | | **30-49 years (N = 2,108)** | | | | | |
| **Blood cadmium** | **Unweighted**  **N** | **Unadjusted** | **Minimally**  **adjusteda** | **Fully adjustedb** |  | **Unweighted**  **N** | **Unadjusted** | **Minimally**  **adjusteda** | **Fully adjustedb** |  | | **Unweighted**  **N** | **Unadjusted** | **Minimally**  **adjusteda** | **Fully adjustedb** | ***Pinteraction*b** |
| **<0.30 μg/Lc** | 1,653 | 0.00 (reference) | 0.00 (reference) | 0.00 (reference) |  | 376 | 0.00 (reference) | 0.00 (reference) | 0.00 (reference) |  | | 569 | 0.00 (reference) | 0.00 (reference) | 0.00 (reference) | <0.01 |
| **0.21-0.30 μg/L** | 450 | 0.13 (0.03, 0.24) | 0.09 (-0.01, 0.19) | 0.09 (-0.01, 0.19) |  | 174 | 0.13 (-0.10, 0.36) | 0.10 (-0.11, 0.30) | 0.09 (-0.11, 0.30) |  | | 288 | 0.12 (-0.03, 0.26) | 0.02 (-0.12, 0.17) | 0.03 (-0.12, 0.17) |  |
| **(0.31-0.50 μg/L** | 420 | 0.11 (0.00, 0.22) | 0.07 (-0.05, 0.19) | 0.07 (-0.05, 0.19) |  | 233 | 0.07 (-0.07, 0.21) | -0.01 (-0.15, 0.13) | -0.01 (-0.15, 0.13) |  | | 539 | 0.09 (-0.07, 0.24) | -0.05 (-0.19, 0.08) | -0.05 (-0.19, 0.08) |  |
| **0.51-8.50 μg/L** | 194 | 0.06 (-0.03, 0.16) | 0.06 (-0.09, 0.21) | 0.06 (-0.09, 0.21) |  | 194 | -0.07 (-0.24, 0.10) | -0.08 (-0.30, 0.14) | -0.08 (-0.30, 0.14) |  | | 712 | 0.37 (0.24, 0.50) | 0.05 (-0.10, 0.21) | 0.05 (-0.10, 0.21) |  |
| ***Ptrend*** |  | 0.02 | 0.15 | 0.15 |  |  | 0.50 | 0.45 | 0.46 |  | |  | <0.01 | 0.85 | 0.83 |  |
| **Blood lead** | **Unweighted**  **N** | **Unadjusted** | **Minimally**  **adjusteda** | **Fully adjustedb** |  | **Unweighted N** | **Unadjusted** | **Minimally**  **adjusteda** | **Fully adjustedb** |  | | **Unweighted N** | **Unadjusted** | **Minimally**  **adjusteda** | **Fully adjustedb** | ***Pinteraction*b** |
| **<0.80 μg/dL** | 576 | 0.00 (reference) | 0.00 (reference) | 0.00 (reference) |  | 238 | 0.00 (reference) | 0.00 (reference) | 0.00 (reference) |  | | 253 | 0.00 (reference) | 0.00 (reference) | 0.00 (reference) | 0.51 |
| **0.81-1.20 μg/dL** | 907 | -0.02 (-0.13, 0.08) | 0.01 (-0.09, 0.12) | 0.01 (-0.09, 0.12) |  | 287 | -0.07 (-0.25, 0.10) | 0.03 (-0.14, 0.21) | 0.04 (-0.14, 0.21) |  | | 484 | 0.00 (-0.18, 0.18) | 0.06 (-0.12, 0.23) | 0.05 (-0.12, 0.22) |  |
| **1.21-1.89 μg/dL** | 611 | -0.11 (0.20, -0.01) | -0.02 (-0.13, 0.09) | -0.02 (-0.13, 0.09) |  | 203 | -0.01 (-0.20, 0.18) | 0.27 (0.08, 0.46) | 0.27 (0.08, 0.46) |  | | 575 | -0.03 (-0.21, 0.15) | 0.10 (-0.07, 0.27) | 0.10 (-0.08, 0.27) |  |
| **1.90-68.90 μg/dL** | 623 | -0.10 (-0.19, -0.01) | 0.00 (-0.12, 0.11) | 0.00 (-0.12, 0.11) |  | 249 | -0.04 (-0.23, 0.15) | 0.30 (0.08, 0.52) | 0.30 (0.08, 0.52) |  | | 796 | -0.10 (-0.30, 0.09) | 0.09 (-0.12, 0.30) | 0.09 (-0.12, 0.30) |  |
| ***Ptrend*** |  | 0.01 | 0.87 | 0.87 |  |  | 0.81 | <0.01 | <0.01 |  | |  | 0.22 | 0.31 | 0.33 |  |
| a Adjusted for age (years, continuous), gender, race/ethnicity (non-Hispanic White, non-Hispanic Black, Mexican American, other Hispanic, other race), education (less than high school diploma, high school diploma or equivalent, more than high school), family income: poverty line (continuous), nativity (born in the 50 U.S. or elsewhere), and serum cotinine (ng/mL, continuous) with mutual adjustment for blood cadmium and lead categories. Mean differences were weighted to account for the complex survey design and 95% confidence intervals were estimated using Taylor series linearization.  b Adjusted for all variables listed above, in addition to crowding index (residents per room, continuous)  **c** Below the highest limit of detection across NHANES cycles 1999-2000, 2001-2002, and 2003-2004 | | | | | | | | | | | | | | | | |

**Stata Code**

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*DATA CLEANING AND SAMPLING WEIGHTS DERIVATION\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

//Import dataset

use "NHANES9904.dta", clear

//Install packages

ssc install groups

ssc install estout

net install gr0002\_3, from(http://www.stata-journal.com/software/sj4-3)

ssc install coefplot

//Cleaning + recoding data

\*Creating male indicator variable

gen male = .

replace male = 1 if riagendr == 1

replace male = 0 if riagendr == 2

\*Health insurance (set refused to answer or don't know to missing)

replace hid010 = . if hid010 == 7 | hid010 == 9

\*Number of rooms in house (set refused to answer or don't know to missing)

replace hod050 = . if hod050 == 777 | hod050 == 999

\*Education

gen education = .

replace education = dmdhredu if ridageyr < 25 // use household reference person

replace education = dmdeduc2 if ridageyr >= 25 // use participant

recode education 7 = . // refused to missing

recode education 9 = . // don't know to missing

recode education 2 = 1 // collapse w/ less than 9th grade

recode education 5 = 4 // collapse w/ some college

\*US Foreign

gen us\_foreign = .

replace us\_foreign = 0 if dmdborn == 1

replace us\_foreign = 1 if dmdborn == 2 | dmdborn == 3

\*Household crowding index

gen crowding = dmdhhsiz/hod050

\*Limits of Detection

\*For lead, the LOD across all cycles was 0.3 ug/dL

\*For cadmium, the LOD for cycles 1999-2002 was 0.3 ug/L, for 2003-2004,

\* it was 0.2 ug/L;

\*For cotinine, the detection limits in each two year cycle from 1999 to 2002 has changed.

\*For 1999-2000 the detection limit was .05 and the below the limit of detection value was .035.

\*For 2001-2002 there were two detection limits and below the limit of detection values.

\*One of the detection limits was .05 and the below the limit of detection value was .035.

\*The other detection limit was .015 and the below the limit of detection value was .011.;

\*For 2003-2004 the detection limit was .015 and the below the limit of detection value was .011.;

\*Flag values < LOD - use the highest across the 3 cycles:

gen cadmium\_lod = .

replace cadmium\_lod = 0 if !missing(lbxbcd) & lbxbcd >= 0.3

replace cadmium\_lod = 1 if !missing(lbxbcd) & lbxbcd < 0.3

gen lead\_lod = .

replace lead\_lod = 0 if !missing(lbxbpb) & lbxbpb >= 0.3

replace lead\_lod = 1 if !missing(lbxbpb) & lbxbpb < 0.3

gen cotinine\_lod = 0

replace cotinine\_lod = 1 if !missing(lbxcot) & lbxcot < 0.05

replace cotinine\_lod = . if missing(lbxcot)

\*Rename variables

gen cadmium = lbxbcd

gen lead = lbxbpb

gen cotinine = lbxcot

\*Rescale the MEC weights since combining 3 cycles

gen wtmec6yr = wtmec4yr\*(2/3) if sddsrvyr == 1 | sddsrvyr == 2 // NHANES 1999-2002

replace wtmec6yr = wtmec2yr\*(1/3) if sddsrvyr == 3 // NHANES 2003-2004

\*Create 3 age groups (6-11, 12-19, and 20-49 years)

gen agegroup = .

replace agegroup = 1 if ridageyr >= 6 & ridageyr <= 11

replace agegroup = 2 if ridageyr >= 12 & ridageyr <= 19

replace agegroup = 3 if ridageyr >= 20 & ridageyr <= 49

\*Create 30 age/sex/racial groups

egen agesexracegroup = group(agegroup ridreth1 male)

\*Create a flag for participants with stored surplus sera or urine available for CMV testing

gen cmvspecimenflag = 0

replace cmvspecimenflag = 1 if !missing(sscmvod) | !missing(ssucysh)

\*Save NHANES dataset

save "/NHANES9904.dta", replace

\*Calculate weighted proportion of available CMV serum samples for each age/sex/racial group (n=30)

//setting sampling weights, clustering and strata variables

svyset sdmvpsu[pweight=wtmec6yr], strata(sdmvstra)

forval i = 1/30 {

qui estpost svy, subpop(if agesexracegroup==`i'): tab cmvspecimenflag

qui esttab ., cell("b(f(4))") nostar noobs nonumber not nomtitle collabel(none)

mat percent=e(b)

di percent[1,2]

eststo clear

}

\*Input proportions of non-missing CMV serum data

clear

input wtcmvserum

.76027739

.79762496

.64997402

.59082428

.6709199

.74329468

.69178479

.73495199

.56838764

.77577281

.87601133

.87540671

.84669303

.88244396

.86359995

.85486537

.87043562

.88353762

.79554003

.83957656

.93693979

.91514309

.92425305

.9639366

.93243411

.94261215

.89807375

.90189461

.89269602

.95091689

end

gen agesexracegroup = \_n

\*Merge with NHANES dataset

merge 1:m agesexracegroup using "NHANES9904.dta"

drop \_merge

\*Re-weight MEC weights:

gen wtmec6yr\_cmvs = wtmec6yr\*wtcmvserum

\*Create new variables

gen cmv\_igg = .

replace cmv\_igg = 0 if sscmv == 2

replace cmv\_igg = 1 if sscmv == 1

gen cmv\_igm = .

replace cmv\_igm = 0 if sscmigm == 2

replace cmv\_igm = 1 if sscmigm == 1

gen lowavidity = .

replace lowavidity = 0 if sscmigga == 2

replace lowavidity = 1 if sscmigga == 1

gen shedding = .

replace shedding = 0 if ssucysh == 2

replace shedding = 1 if ssucysh == 1

gen viralload = ssuctvl

replace viralload = 80 if missing(ssuctvl) & !missing(shedding)

\*Eligiblity

gen eligible = 0

replace eligible = 1 if lbdhi != 1 & !missing(agegroup) & !missing(sscmv) & sscmv != 3 & ///

!missing(lbxbcd) & !missing(lbxbpb) & !missing(education) & !missing(indfmpir) & ///

dmdborn != 7 & dmdborn != 9 & !missing(lbxcot) & !missing(hod050) & hod050 != 777 & ///

hod050 != 9999 & !missing(wtmec6yr\_cmvs) & wtmec6yr\_cmvs != 0

egen cmv\_category = group(cmv\_igg sscmigm ssucysh sscmigga)

groups cmv\_category cmv\_igg sscmigm ssucysh sscmigga if eligible==1, missing

replace cmv\_category = 0 if cmv\_igg == 0 // not infected (susceptible)

\*1 = primary; 2 = recurrence; 3 = latent;

recode cmv\_category 3 = . // active but missing low avidity (n=3)

recode cmv\_category 4 = 1 // primary (n=10)

recode cmv\_category 5 = 2 // recurrence (n=46)

recode cmv\_category 6 = 1 // primary (n=1)

recode cmv\_category 7 = 1 // primary (n=8)

recode cmv\_category 8 = 2 // recurrence (n=152)

recode cmv\_category 9 = . // active but equivocal low avidity (n=2)

recode cmv\_category 10 = . // active but missing low avidity (n=283)

recode cmv\_category 11 = 3 // latent (n=4)

recode cmv\_category 12 = 3 // latent (n=156)

recode cmv\_category 13 = 3 // latent (n=2)

recode cmv\_category 14 = 3 // latent (n=5,416)

recode cmv\_category 15 = . // not producing IgM, equivocal urine CMV PCR (n=23)

recode cmv\_category 16 = . // missing low avidity (n=4)

recode cmv\_category 17 = . // equivocal CMV IgM serology, not shedding (n=6)

recode cmv\_category 18 = . // equivocal CMV IgM serology, equivocal PCR (n=1)

replace cmv\_category = 1 if cmv\_igg == 1 & sscmigm==1 & missing(ssucysh) & sscmigga==1 // primary (n=1)

replace cmv\_category = 2 if cmv\_igg==1 & sscmigm==1 & missing(ssucysh) & sscmigga==2 // recurrence (n=10)

gen cmv\_reac = .

replace cmv\_reac = 0 if cmv\_category == 3 // latent

replace cmv\_reac = 1 if cmv\_category == 2 // recurrence

\*Create new age groups (6-11, 12-19, 20-29, 30-39, 40-49 years)

drop agegroup

gen agegroup = .

replace agegroup = 1 if ridageyr >= 6 & ridageyr <= 11

replace agegroup = 2 if ridageyr >= 12 & ridageyr <= 19

replace agegroup = 3 if ridageyr >= 20 & ridageyr <= 29

replace agegroup = 4 if ridageyr >= 30 & ridageyr <= 39

replace agegroup = 5 if ridageyr >= 40 & ridageyr <= 49

\*Label variables

label define male 1 "Male" 0 "Female"

label values male male

label define us\_native 0 "Born in US territory or other country" 1 "Born in 50 US States or Washington, DC"

label values us\_native us\_native

label define us\_foreign 0 "Born in 50 US States or Washington, DC" 1 "Born in US territory or other country"

label values us\_foreign us\_foreign

label define ridreth1 1 "Mexican American" 2 "Other Hispanic" 3 "Non-Hispanic white" 4 "Non-Hispanic black" 5 "Other Race - Including Multi-Racial"

label values ridreth1 ridreth1

label define education 1 "Less than high school" 3 "High school" 4 "More than high school"

label values education education

\*Selection criteria for CMV IgG serostatus analyes

gen sel\_1 = 0

replace sel\_1 = 1 if eligible==1 & !missing(cmv\_igg)

\*Selection criteria for CMV recurrence analyses

gen sel\_2 = 0

replace sel\_2 = 1 if sel\_1==1 & !missing(cmv\_reac)

\*Create quartiles for blood cadmium, blood lead, and urine cadmium

\_pctile cadmium if sel\_1==1 & cadmium\_lod==0 [pweight=wtmec6yr\_cmvs], p(33.33 66.67)

return list

gen cadmium\_q = .

replace cadmium\_q = 1 if cadmium < 0.3 // below highest LOD

replace cadmium\_q = 2 if cadmium >= 0.3 & cadmium < 0.4000000059604645

replace cadmium\_q = 3 if cadmium >= 0.4000000059604645 & cadmium < 0.6000000238418579

replace cadmium\_q = 4 if cadmium >= 0.6000000238418579 & !missing(cadmium)

summarize cadmium

\_pctile lead if sel\_1==1 [pweight=wtmec6yr\_cmvs], p(25 50 75)

return list

gen lead\_q = .

replace lead\_q = 1 if !missing(lead) & lead < 0.800000011920929

replace lead\_q = 2 if !missing(lead) & lead >= 0.800000011920929 & lead < 1.200000047683716

replace lead\_q = 3 if !missing(lead) & lead >= 1.200000047683716 & lead < 1.899999976158142

replace lead\_q = 4 if !missing(lead) & lead >= 1.899999976158142

summarize lead

\_pctile urxucd if sel\_1==1 [pweight=wtmec6yr\_cmvs], p(25 50 75)

return list

gen ucadmium\_q = .

replace ucadmium\_q = 1 if !missing(urxucd) & urxucd < 0.09

replace ucadmium\_q = 2 if !missing(urxucd) & urxucd >= 0.09 & urxucd < 0.18

replace ucadmium\_q = 3 if !missing(urxucd) & urxucd >= 0.18 & urxucd < 0.35

replace ucadmium\_q = 4 if !missing(urxucd) & urxucd >= 0.35

summarize urxucd

\*Re-define age groups

gen agegroup\_3 = .

replace agegroup\_3 = 1 if ridageyr >= 6 & ridageyr <= 19

replace agegroup\_3 = 2 if ridageyr >= 20 & ridageyr <= 29

replace agegroup\_3 = 3 if ridageyr >= 30 & ridageyr <= 49

\*Save NHANES dataset

save “NHANES9904.dta", replace

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*ANALYSIS\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

//Survey set the data

svyset [w=wtmec6yr\_cmvs], psu(sdmvpsu) strata(sdmvstra)

//CMV seroprevalence

svy, subpop(if sel\_1==1): tab sscmv, percent ci // 50.8% (48.3-55.4%)

//Table 1

foreach v of varlist agegroup\_1 agegroup\_3 education us\_foreign {

svy, subpop(if sel\_1==1): tab `v' cmv\_igg, col percent ci

svy, subpop(if sel\_2==1): tab `v' cmv\_reac, col percent ci

}

foreach v of varlist indfmpir crowding {

svy, subpop(if sel\_1==1 & cmv\_igg==0): mean `v'

svy, subpop(if sel\_1==1 & cmv\_igg==1): mean `v'

svy, subpop(if sel\_2==1 & cmv\_reac==0): mean `v'

svy, subpop(if sel\_2==1 & cmv\_reac==1): mean `v'

}

foreach v of varlist cotinine\_ln cadmium\_ln lead\_ln {

qui svy, subpop(if sel\_1==1 & cmv\_igg==0): mean `v'

nlcom exp(\_b[`v'])

qui svy, subpop(if sel\_1==1 & cmv\_igg==1): mean `v'

nlcom exp(\_b[`v'])

qui svy, subpop(if sel\_2==1 & cmv\_reac==0): mean `v'

nlcom exp(\_b[`v'])

qui svy, subpop(if sel\_2==1 & cmv\_reac==1): mean `v'

nlcom exp(\_b[`v'])

}

svy, subpop(if sel\_1==1 & cmv\_igg==1): tobit sscmvod, ul(3.001)

svy, subpop(if sel\_2==1 & cmv\_reac==0): tobit sscmvod, ul(3.001)

svy, subpop(if sel\_2==1 & cmv\_reac==1): tobit sscmvod, ul(3.001)

svy, subpop(if sel\_1==1): tab shedding cmv\_igg, col percent ci

svy, subpop(if sel\_2==1): tab shedding cmv\_reac, col percent ci

\*Proportion < LOD

svy, subpop(if sel\_1==1): tab cadmium\_lod

svy, subpop(if sel\_1==1): tab lead\_lod

svy, subpop(if sel\_1==1): tab cotinine\_lod

\*Correlations between cadmium and lead:

egen pb\_rank = rank(lead)

egen cd\_rank = rank(cadmium)

pwcorr pb\_rank cd\_rank if sel\_1==1 [aweight=wtmec6yr\_cmvs], sig

//Regression models

global minimum c.ridageyr i.ridreth1 i.male c.cotinine c.indfmpir i.education i.us\_foreign

global full c.ridageyr i.ridreth1 i.male c.cotinine c.indfmpir i.education i.us\_foreign c.crowding

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*CMV Seropositivity\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

//Cadmium x Lead interaction assessment

forval i = 1/3 {

qui svy, subpop(if sel\_1==1 & agegroup\_3==`i'): poisson cmv\_igg c.cadmium\_q##c.lead\_q $full, eform

testparm c.cadmium\_q#c.lead\_q

}

//Cadmium/Lead x Age interaction assessment

qui svy, subpop(if sel\_1==1): poisson cmv\_igg i.cadmium\_q##i.agegroup\_3 i.lead\_q##i.agegroup\_3 $full, eform

testparm cadmium\_q#agegroup\_3

testparm lead\_q#agegroup\_3

//Final seroprevalence models - stratified by age 6-19 years, 20-29 years, 30-49 years

forval i = 1/3 {

svy, subpop(if sel\_1==1 & agegroup\_3==`i'): poisson cmv\_igg i.cadmium\_q i.lead\_q, eform

qui svy, subpop(if sel\_1==1 & agegroup\_3==`i'): poisson cmv\_igg c.cadmium\_q c.lead\_q, eform

testparm cadmium\_q

testparm lead\_q

svy, subpop(if sel\_1==1 & agegroup\_3==`i'): poisson cmv\_igg i.cadmium\_q i.lead\_q $minimum, eform

qui svy, subpop(if sel\_1==1 & agegroup\_3==`i'): poisson cmv\_igg c.cadmium\_q c.lead\_q $minimum, eform

testparm cadmium\_q

testparm lead\_q

svy, subpop(if sel\_1==1 & agegroup\_3==`i'): poisson cmv\_igg i.cadmium\_q i.lead\_q $full, eform

estimates store cmv\_igg\_`i'

qui svy, subpop(if sel\_1==1 & agegroup\_3==`i'): poisson cmv\_igg c.cadmium\_q c.lead\_q $full, eform

testparm cadmium\_q

testparm lead\_q

}

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*CMV IgG Levels\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

//Cadmium x Lead interaction assessment

forval i = 1/3 {

qui svy, subpop(if sel\_2==1 & agegroup\_3==`i'): tobit sscmvod c.cadmium\_q##c.lead\_q $full, ul(3.001)

testparm c.cadmium\_q#c.lead\_q

}

//Cadmium/Lead x Age interaction assessment

qui svy, subpop(if sel\_2==1): tobit sscmvod i.cadmium\_q##i.agegroup\_3 i.lead\_q##i.agegroup\_3 $full, ul(3.001)

testparm cadmium\_q#agegroup\_3

testparm lead\_q#ageagroup\_3

//Final CMV IgG level models - stratified by age 6-19 years, 20-29 years, 30-49 years

forval i = 1/3 {

svy, subpop(if sel\_2==1 & agegroup\_3==`i'): tobit sscmvod i.cadmium\_q i.lead\_q, ul(3.001)

qui svy, subpop(if sel\_2==1 & cmv\_igm==0 & agegroup\_3==`i'): tobit sscmvod c.cadmium\_q c.lead\_q, ul(3.001)

testparm cadmium\_q

testparm lead\_q

svy, subpop(if sel\_2==1 & agegroup\_3==`i'): tobit sscmvod i.cadmium\_q i.lead\_q $minimum, ul(3.001)

qui svy, subpop(if sel\_2==1 & agegroup\_3==`i'): tobit sscmvod c.cadmium\_q c.lead\_q $minimum, ul(3.001)

testparm cadmium\_q

testparm lead\_q

svy, subpop(if sel\_2==1 & agegroup\_3==`i'): tobit sscmvod i.cadmium\_q i.lead\_q $full, ul(3.001)

estimates store igg\_level\_`i'

qui svy, subpop(if sel\_2==1 & agegroup\_3==`i'): tobit sscmvod c.cadmium\_q c.lead\_q $full, ul(3.001)

testparm cadmium\_q

testparm lead\_q

}

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*CMV Recurrence\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

//Cadmium x Lead interaction assessment

forval i = 1/3 {

qui svy, subpop(if sel\_2==1 & agegroup\_3==`i'): poisson cmv\_reac c.cadmium\_q##c.lead\_q $full, eform

testparm c.cadmium\_q#c.lead\_q

}

//Cadmium/Lead x Age interaction assessment

qui svy, subpop(if sel\_2==1): poisson cmv\_reac i.cadmium\_q##i.agegroup\_3 i.lead\_q##i.agegroup\_3 $full, eform

testparm cadmium\_q#agegroup\_3

testparm lead\_q#agegroup\_3

//Final CMV recurrence models - not age-stratified

svy, subpop(if sel\_2==1): poisson cmv\_reac i.cadmium\_q i.lead\_q, eform

qui svy, subpop(if sel\_2==1): poisson cmv\_reac c.cadmium\_q c.lead\_q, eform

testparm cadmium\_q

testparm lead\_q

svy, subpop(if sel\_2==1): poisson cmv\_reac i.cadmium\_q i.lead\_q $minimum, eform

qui svy, subpop(if sel\_2==1): poisson cmv\_reac c.cadmium\_q c.lead\_q $minimum, eform

testparm cadmium\_q

testparm lead\_q

svy, subpop(if sel\_2==1): poisson cmv\_reac i.cadmium\_q i.lead\_q $full, eform

estimates store cmv\_reac

qui svy, subpop(if sel\_2==1): poisson cmv\_reac c.cadmium\_q c.lead\_q $full, eform

testparm cadmium\_q

testparm lead\_q

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*Sensitivity Analysis: Urinary Cadmium\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

//Final seroprevalence models - stratified by age 6-19 years, 20-29 years, 30-49 years

forval i = 1/3 {

svy, subpop(if sel\_1==1 & agegroup\_3==`i'): poisson cmv\_igg i.ucadmium\_q i.lead\_q, eform

qui svy, subpop(if sel\_1==1 & agegroup\_3==`i'): poisson cmv\_igg c.ucadmium\_q c.lead\_q, eform

testparm ucadmium\_q

testparm lead\_q

svy, subpop(if sel\_1==1 & agegroup\_3==`i'): poisson cmv\_igg i.ucadmium\_q i.lead\_q $minimum urxucr, eform

qui svy, subpop(if sel\_1==1 & agegroup\_3==`i'): poisson cmv\_igg c.ucadmium\_q c.lead\_q $minimum urxucr, eform

testparm ucadmium\_q

testparm lead\_q

svy, subpop(if sel\_1==1 & agegroup\_3==`i'): poisson cmv\_igg i.ucadmium\_q i.lead\_q $full urxucr, eform

qui svy, subpop(if sel\_1==1 & agegroup\_3==`i'): poisson cmv\_igg c.ucadmium\_q c.lead\_q $full urxucr, eform

testparm ucadmium\_q

testparm lead\_q

}