Attachment 7

Anniston Community Health Survey: Follow-up Study and Dioxin Analyses

**Sample Size and Power Estimation for Exposure Assessment**

**Part A.** Sample size estimation for change in PCB congener value between Time 1 and Time 2

**Study Design:** One-time cross-sectional follow-up study seven years after baseline

**Assumption 1:** Metabolism and elimination of PCB congener follows an exponential decay model

**Assumption 2:** Additional individual exposure to PCB congener between Time 1 and Time 2 is minimal

**Assumption 3:** Change in PCB congener variable is lognormal

**Null Hypothesis (*HO*):** PCB congener concentration follows an exponential decay model (Seegal et al., 2011) where half-life (HL) = 14 years (for PBCs 118, 153, 206 based on Knobeloch et al., 2009).

**Alternative Hypothesis (*HA*):** PCB congener concentration follows and exponential decay model, where half-life (HL) = 20 years or longer.

$C\_{(t)}=C\_{\left(0\right)}e^{-Kt}$, where $K= \frac{ln(2)}{HL}$

Let *x1, . . . ., xn* denote the data at Time 1. Then *x1*$e^{-Kt}$, . . . . , *xn*$e^{-Kt}$ are the data at Time 2.

The change in PCB level for individual, *i*, is given by:

Change = *xi – x*i $e^{-Kt}$ = *xi* (1*–* $e^{-Kt}$).

Since we assume these variables are lognormal, we use a log-transformation to make the distribution normal.

g(*x*)$≡$ln (Change) = ln [*xi*$ (1–e^{-Kt})$] = ln (*xi*)+ ln (J),

where J is the constant, (1*–* $e^{-Kt}$).

We can use a 2nd order Taylor series around the mean, $\overline{x}$ = $μ,$ to approximate Var (g(x)). [See Dudewicz & Mishra, p263, Theorem 5.5.18]

Var (g(*x*)) $≈$ [g’ ($μ$)]2 $σ$2,

where $μ$ and $σ$2 are the mean and the variance of the individual data. It follows that

Var (g(*x*)) $=$ Var [ln (*xi*) + ln (J)] $= \frac{σ^{2}}{μ^{2}}$.

The standard deviation of g(*x*) is approximated by $\frac{σ}{μ}$.

Restated, the standard deviation of the natural log of the change in PCB level is approximately equal to the standard deviation of the individual data divided by their mean.

Before calculating a sample size, it is worth noting that the mean change in PCB level is equal to the change in the mean.

Mean Change in PCB Level = *x1* (1*–* $e^{-Kt}$) + . . . . . . + *xn* (1*–* $e^{-Kt}$)

 n

= (1*–* $e^{-Kt}$)( *x1* + *. . . .* + *xn*)

n

= (1*–* $e^{-Kt}$) $\overline{x}$ = Change in Mean PCB Level

Thus on the natural log scale,

Mean ln (Change in PCB Level) = ln ($μ$) + ln (J)

Example for representative low, moderately, and highly chlorinated PCB congeners using NCSS Power Analysis and Sample Size (PASS) 2008 Software, Kayesville, UT:

**Test for One-Sample T-Test:** *HO*: HL = 14 years vs. *HA*: HL ≥ 20 years

1. Under *HO*, $K= \frac{ln(2)}{14}$ = 0.04951 and J = (1*–* $e^{-Kt}$) = 0.2929
2. Under *HA*, $K= \frac{ln(2)}{20}$ = 0.03466 and J = (1*–* $e^{-Kt}$) = 0.2154

**For PCB 118:**

From Time 1, based on serum PCBs from n=765 ACHS participants, assume $μ$ = 70, σ = 177, and Var [ln (Change)] = 177/70 = 2.5286.

*HO*: Mean ln (Change in PCB Level) = ln ($μ$) + ln (J) = ln (70) + ln (0.2929)

= 3.0206

*HA*: Mean ln (Change in PCB Level) = ln ($μ$) + ln (J) = ln (70) + ln (0.2154)

= 2.7132

A sample size of 420 achieves 80% power to detect a difference of 0.3 between the null hypothesis mean of 3.0 and the alternative hypothesis mean of 2.7 with an estimated standard deviation of 2.5 and $α$ = 0.05, using a one-sided one-sample t-test.

**For PCB 153:**

From Time 1, based on serum PCBs from n=765 ACHS participants, assume $μ$ = 218, σ = 409, and Var [ln (Change)] = 409/218 = 1.8761.

*HO*: Mean ln (Change in PCB Level) = ln ($μ$) + ln (J) = ln (218) + ln (0.2929)

= 5.3845 - 1.2279 = 4.1566

*HA*: Mean ln (Change in PCB Level) = ln ($μ$) + ln (J) = ln (218) + ln (0.2154)

= 5.3845 - 1.5352 = 3.8492

A sample size of 232 achieves 80% power to detect a difference of 0.3 between the null hypothesis mean of 4.2 and the alternative hypothesis mean of 3.8 with an estimated standard deviation of 1.9 and with a significance level (alpha) of 0.05 using a one-sided one-sample t-test.

**For PCB 206:**

From Time 1, based on serum PCBs from n=764 ACHS participants, assume $μ$ = 40, σ = 98, and Var [ln (Change)] = 98/40 = 2.4500.

*HO*: Mean ln (Change in PCB Level) = ln ($μ$) + ln (J) = ln (40) + ln (0.2929)

= 3.68887945 - 1.22792403 = 2.4610

*HA*: Mean ln (Change in PCB Level) = ln ($μ$) + ln (J) = ln (40) + ln (0.2154)

= 3.68887945 - 1.53525851 = 2.1536

A sample size of 395 achieves 80% power to detect a difference of 0.3 between the null hypothesis mean of 2.5 and the alternative hypothesis mean of 2.2 with an estimated standard deviation of 2.5 and with a significance level (alpha) of 0.05 using a one-sided one-sample t-test.

**References:**

Dudewicz, E.J., Mishra, S.N., 1988. Modern Mathematical Statistics. John Wiley & Sons, Inc., New York.

Knobeloch, L., Turyk, M., Imm, P., Schrank, C., Anderson, H., 2009. Temporal changes in PCB and DDE levels among a cohort of frequent and infrequent consumers of Great Lakes sportfish. Environ. Res. 109(1), 66-72.

Seegal, R.F., Fitzgerald, E.F., Hills, E.A., Wolff, M.S., Haase, R.F., Todd, A.C., Parsons P., Molho, E.S., Higgins, D.S., Factor, S.A., Marek, K.L., Seiby, J.P., Jennings, D.L., McCaffrey, R.J., 2011. Estimating the half-lives of PCB congeners in former capacitor workers measured over a 28-year interval. J. Exposure Sci. Environ. Epi. 21, 234–246.

**Part B. Power estimation to detect difference in PCB levels between incident diabetes cases and non-diabetics**

**Method:** Two-Sample T-Test Power Analysis

**Estimated number of incident diabetes cases:**

We estimate to enroll 365 persons without diabetes (out of 500 total). To estimate the total number of incident diabetes cases we used combined average rate of 9.5 /1,000 per year for 255 normoglycemic individuals and 50/1,000 for 110 pre-diabetics over the average of 7 years of follow up (See Section B.1 – Sample Size).

**Supplemental Table 1.** Estimated number of incident diabetes cases.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Year** | **No. Available** | **Rate per Year** | **No. Incident Cases** |  | **No. Available** | **Rate per Year** | **No. Incident Cases** |
|  | Normoglycemic |  | Pre-Diabetic |
|  |  |  |  |  |  |  |  |
| 1. | 255.0 | 0.0095 | 2.42 |  | 110.0 | 0.050 | 5.50 |
| 2. | 252.6 | 0.0095 | 2.40 |  | 104.5 | 0.050 | 5.23 |
| 3. | 250.2 | 0.0095 | 2.38 |  | 99.3 | 0.050 | 4.96 |
| 4. | 247.8 | 0.0095 | 2.35 |  | 94.3 | 0.050 | 4.72 |
| 5. | 245.4 | 0.0095 | 2.33 |  | 89.6 | 0.050 | 4.48 |
| 6. | 243.1 | 0.0095 | 2.31 |  | 85.1 | 0.050 | 4.26 |
| 7. | 240.8 | 0.0095 | 2.29 |  | 80.9 | 0.050 | 4.04 |
| **Total** |  |  | **16.48** |  |  |  | **33.18** |

The calculations suggest that we can assume to detect an estimated 16 cases of incident diabetes in normoglycemic individuals and about 33 cases in pre-diabetic individuals in 7 years of follow up for a total of 49 cases.

**Report Definitions:**

Power is the probability of rejecting a false null hypothesis. Power should be close to one.

N1 (non-diabetics) and N2 (incident diabetics) are the number of items sampled from each population.

Alpha is the probability of rejecting a true null hypothesis. It should be small.

Beta is the probability of accepting a false null hypothesis. It should be small.

Mean1 is the mean of populations 1 and 2 under the null hypothesis of equality.

Mean2 is the mean of population 2 under the alternative hypothesis. The mean of population 1 is unchanged.

S1 and S2 are the population standard deviations. They represent the variability in the populations.

**Numeric Results for Two-Sample T-Test:**

**Null Hypothesis:** Mean1=Mean2. Alternative Hypothesis: Mean1<Mean2.

**Assumptions:** The standard deviations were assumed to be unknown and unequal.

**Power N1 N2 Ratio Alpha Mean1 Mean2 S1 S2**

0.865 316 49 0.155 0.05000 6.1 6.6 1.3 1.2

**Summary Statements:**

Group sample sizes of 316 and 49 achieve 86.5% power to detect a difference of -0.5 between the null hypothesis that both group means are 6.1 and the alternative hypothesis that the mean of group 2 is 6.6 with estimated group standard deviations of 1.3 and 1.2 and with a significance **level (alpha) of 0.0500 using a one-sided two-sample t-test.**

**References:**

Machin, D., Campbell, M., Fayers, P., Pinol, A., 1997. Sample Size Tables for Clinical Studies, second edition. Malden, MA, Blackwell Science.

Zar, J.H., 1984. Biostatistical Analysis, second edition. Englewood Cliffs, NJ, Prentice-Hall.