5

Application to Inhalation Rates

The treatment of long-term inhalation rates relies on Francis and Feder (1997), who provide a thorough review of available data sources for estimation of long-term and short-term inhalation rate distributions. The authors identify several areas where data are lacking or are out of date and make several recommendations for improving data sources. As Francis and Feder (1997) point out, a potentially important technique for estimating long-term breathing rate distributions is to combine activity pattern distributions with short-term activity-specific breathing rate distributions. Because activity pattern distributions have not yet been developed, this approach is not yet applicable.

Computation of risk for a defined population typically involves sums of products of random variables. The summation is over exposure pathways. For a given pathway, the risk is typically a product of factors. The estimation of distributions for inhalation rates is somewhat similar to a risk assessment, because inhalation rates are themselves the product of component factors.

The approach used to address inhalation rates is considered reasonable when very limited data, such as only estimated means and standard deviations, are available. The method used is motivated by Rai et al. (1996). Assuming independence of the factors within each subpopulation, the mean and standard deviation of the product can be estimated. Since distributional information for the individual factors is not available, model uncertainty is present. Therefore, it is recommended that the lognormal and at least one of the gamma and Weibull distributions with the same estimated product mean and standard deviation be used in risk assessment. In some cases (e.g., if the coefficient of variation [CV] of the product is on the order of 50% or less), these distributions may be sufficiently similar that risk assessment can be reasonably based on any one of them. "For small variance it is likely to be difficult to discriminate between lognormal models and gamma models" (McCullagh and Nelder, 1983).

5.1 Data

Layton (1993) is the only study referenced in the Exposure Factors Handbook (EFH) that allows direct calculation of long-term breathing rate (expressed as cubic meters [m^3] per day) without combining activity distributions with short-term breathing rate distributions. Layton's methods are based on oxygen consumption associated with energy expenditures. The general equation for a metabolically based determination of ventilation rate is:

$$V_E = E * H * VQ \quad (5.1)$$

where

V_E = ventilation rate (inhalation rate) (m^3/day)
E = energy expenditure rate in megajoules/day (MJ/day)
H = oxygen uptake factor, the volume of oxygen (at standard temperature and pressure, dry air) consumed in the production of 1 MJ energy expended (m^3/MJ)
VQ = ventilatory equivalent, the ratio of minute volume to oxygen uptake (unitless).

Layton (1993) presented three approaches for the calculation of V_E based on different methods for estimating the energy expenditure rate. Layton's first method estimates food energy intake from the 1977-1978 National Food Consumption Survey (NFCS) and the National Health and Nutrition Examination Survey (NHANES II). Layton argues that the NFCS and NHANES II estimates are biased low and develops a correction factor of 1.2.

Layton's second method is based on the relationship E=BMR * A, where BMR is the basal metabolic rate (MJ/day) and A is the ratio of the total daily energy expenditure to the daily BMR. BMR values for specific gender/age cohorts are provided by Layton as means and standard deviations that can be used to develop energy expenditure distributions. Sample sizes for each gender/age group range from 38 to 2,879 and are based on Schofield (1985).

Layton's third method is to combine activity pattern distributions with short-term activity-specific breathing rate distributions. For reasons given in the introduction to this section, this approach is

not pursued at this time. The second approach is used here. The first approach is not used because of the arbitrariness of the bias correction factor 1.2.

To apply Layton's second method, the basic equation (5.1) becomes

$$V_E = BMR * A * H * VQ \quad (5.2)$$

where:

BMR = basal metabolic rate (MJ/day)

A = (aka, PAI or MET) ratio of total daily energy expenditure to daily BMR.

Table 5-1 contains the statistical summaries that were used to estimate the distribution of V_E. This is essentially the same information as given by EFH Table 5-12, supplemented by population variance estimates for each quantity. The derivation of the estimated means and standard deviations in Table 5-1 for ventilation rate (V_E) were as follows:

- The mean of oxygen uptake factor (H) was a weighted average from NFCS and NHANES II. We assumed a 10% CV for H based on the idea that any human biochemical attribute must have at least this much variability. However, larger values (10%-20%) may be more reasonable in some situations.

- Ventilatory equivalent (VQ) estimates for ages 0-3 were pooled estimates from Stahlman and Meece (1957) and Cook et al. (1955). A log transformation of the geometric mean and geometric standard deviations reported in the EFH was used to obtain means and standard deviations of log (VQ). A weighted average of the means and variances of log (VQ) was used to obtain pooled estimates. These pooled estimates were then transformed to obtain the mean and variance of an assumed underlying lognormal distribution. (VQ statistics for ages greater than 3 are from Layton, 1993; five studies pooled).

- BMR estimates of the mean were obtained from Table 5-12 in the EFH. EFH Table 5A-4 provided CVs for the same age categories, so the means from Table 5-12 and CVs from Table 5A-4 were used to calculate the standard deviations. Values of BMR and VQ were

chosen to reflect "average" people and are not intended to represent population extremes (e.g., marathon runners).

Ratio of total daily energy expenditure (A) for ages 0-10 was obtained from Griffiths and Payne (1976). A weighted average of the CVs for A from the 10-60 age groups for males and females to obtain a CV for ages 0-10 was used. Estimates of A for ages 10-60 were obtained from Basiotis et al. (1989). Estimates for ages >60 were obtained from James et al. (1989), who summarized five studies for ages >60. Means were calculated from the three estimates for females and four estimates for males. CVs were assumed to be the same as for ages 10-60.

5.2 Statistical Methods

Since the available data consist of means and standard deviations, the only applicable non-Bayesian estimation technique is the method of moments.

The following calculations were carried out for each of the 12 groups defined by gender and the six age ranges (0-3, 3-10, 10-18, 18-30, 30-60, >60 years). Using the estimated means and standard deviations from Table 5-1, the mean and variance of inhalation rate (BMR*A*H*VQ) were estimated, assuming the four factors are statistically independent within each subpopulation. Since independence is assumed only within each subpopulation, this allows for some dependence among the factors (i.e., does not assume overall independence of these factors). Independence implies that the mean of the product is the product of the means. If X and Y are two independent random variables with means MX, MY, and variances VX, VY, then the variance of the product of X*Y is given by

$$\text{variance of } X*Y = VX*VY + VX*MY^2 + MX^2 * VY.$$

The variance of a product of more than two terms can be obtained by repeatedly applying this relation. Finally, the gamma and lognormal distributions with the given product means and variances were calculated and compared.

Since only moment information was available, the standard goodness-of-fit tests are not applicable.

To obtain parameter distributions for uncertainty analysis, the following two approaches are possible. Under the assumption that each of the four factors has a specific distribution (e.g., lognormal), distributions for the individual factor means and variances could be obtained by using a normal or t distribution for the mean and a chi-square distribution for the variance. However, this would be a questionable approach if gamma distributions were assumed for the factors. A bootstrap method would be applicable for either the gamma or lognormal assumption.

The bootstrap method using the gamma case is described for illustration. One thousand simulated copies of Table 5-1 would be generated by assuming gamma distributions with the tabulated means and standard deviations for each factor and group. For each of these 1,000 tables, the 12 estimated means and variances of the products of Equation 5.2 would be calculated. This would yield a bootstrapped distribution for the gamma parameters.

This uncertainty analysis requires special methods based on the method of moments and is planned for a future manuscript.

5.3 Results

Table 5-2 contains estimated means and CVs for inhalation rates, using the methods of Section 5.2 for calculating the mean and variance of a product of independent random variables. Except for ages <3, most of the CVs are on the order of 30%. Because the CVs are of moderate size, the quantiles of the estimated gamma (XG50, XG90, XG95, XG99) and lognormal (XL50, XL90, XL95, XL99) distributions are reasonably similar. The %Diff measure was calculated as the average absolute percent discrepancy between the four gamma and lognormal estimated quantiles, that is, as $|XG99 - XL99| / [(XG99 + XL99) / 2]$, using the average of the two estimated quantiles as the nominal value.

5.4 Conclusions

For most purposes, the difference between the gamma and lognormal distributions would probably be negligible, and the lognormal distributions could be used. If the CVs had been larger (e.g., CV>100%), the difference between gamma and lognormal distributions would have been much more

evident. It thus appears that lack of knowledge of distributional form for the individual factors is not a serious drawback, because the individual factors and the product do not have large CVs.

However, the values assumed for the means and standard deviations of individual factors are important determinants of the product distribution. Francis and Feder (1997) have reviewed the available data sources, including those used here and have made a number of recommendations for updating and improving estimates based on more recent and more relevant data.

The results presented in this analysis are based on the Layton (1993) study in which inhalation rates were determined indirectly, based primarily on the BMR and energy expenditures. BMR values were determined based on the literature, and energy expenditures were calculated based on the USDA 1977-78 NFCS. Therefore, this distribution may be used when conducting an assessment where the U.S. national population is of concern. These values also represent daily average inhalation rates and are not applicable to activity-specific inhalation rates (short-term).

Table 5-1. Parameter Estimates for Individual Factors Affecting Long-Term Inhalation Rates (m^3/day)

Parameter	Age Group	Gender	Mean	Standard Deviation	Coefficient of Variant	Sample Size
H	ALL	Both	0.05	0.005	10.0	51,092
VQ	0-3	Both	28.01	7.44	26.6	61
VQ	>3	Both	27.37	4.56	16.7	75
BMR	0-3	Male	3.40	2.07	60.9	162
BMR	3-10	Male	4.30	0.52	12.1	338
BMR	10-18	Male	6.70	1.34	20.0	734
BMR	18-30	Male	7.70	0.92	11.9	2,879
BMR	30-60	Male	7.50	0.98	13.1	646
BMR	>60	Male	6.10	1.04	17.0	50
BMR	0-3	Female	2.60	1.53	58.8	137
BMR	3-10	Female	4.00	0.52	13.0	413
BMR	10-18	Female	5.70	0.86	15.1	575
BMR	18-30	Female	5.90	0.83	14.1	829
BMR	30-60	Female	5.80	0.64	11.0	372
BMR	>60	Female	5.30	0.64	12.1	38
A	0-10	Both	1.58	0.30	19.6	12
A	10-60	Male	1.59	0.33	20.8	13
A	10-60	Female	1.38	0.24	17.4	16
A	>60	Male	1.52	0.32	20.8	14
A	>60	Female	1.44	0.25	17.4	14

Table 5-2. Estimated Mean, Coefficient of Variation, and Quantiles for Inhalation Rate (m^3/day), Assuming Gamma or Lognormal Distribution

Age	Sex	Mean	CV	XG50	XL50	XG90	XL90	XG95	XL95	XG99	XL99	%Diff
00-03	M	7.52	73	6.2	6.1	14.9	14.1	18.2	17.8	25.7	27.9	4.61
00-03	F	5.75	71	4.8	4.7	11.2	10.7	13.7	13.4	19.2	20.8	4.47
03-10	M	9.30	30	9.0	8.9	13.0	13.0	14.3	14.5	17.0	17.7	1.54
03-10	F	8.65	31	8.4	8.3	12.2	12.1	13.4	13.5	16.0	16.6	1.57
10-18	M	14.58	36	14.0	13.7	21.5	21.4	24.0	24.2	29.2	30.6	1.94
10-18	F	10.76	31	10.4	10.3	15.1	15.1	16.7	16.8	19.9	20.7	1.57
18-30	M	16.75	31	16.2	16.0	23.7	23.7	26.2	26.5	31.3	32.6	1.63
18-30	F	11.14	30	10.8	10.7	15.6	15.6	17.2	17.3	20.4	21.2	1.53
30-60	M	16.32	32	15.8	15.6	23.2	23.2	25.7	25.9	30.8	32.0	1.66
30-60	F	10.95	29	10.7	10.5	15.1	15.1	16.6	16.7	19.6	20.3	1.43
>60	M	12.69	34	12.2	12.0	18.4	18.4	20.5	20.7	24.8	25.9	1.83
>60	F	10.44	29	10.2	10.0	14.5	14.5	15.9	16.0	18.8	19.5	1.46