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Basic Considerations in Meta-analysis for DDREF Derivation

Heechan Lee [a], Donghyun Lee [a], Seunghee Lee [a,b], Eun-Hee Kim [a*]
[a]*Dept of Nuclear Engineering, Seoul National Univ., 1 Gwanak-ro, Gwanak-gu, Seoul, Korea*
[b]*FNC Technology Co., Ltd., 32F, 13, Heungdeok 1-ro, Giheung-gu, Yongin-si, Gyeonggi-do, Korea*
∗Corresponding Author: eunhee@snu.ac.kr

1. Introduction

The risk of cancer from exposure to low-dose radiation has been estimated mainly by extrapolating from the risk data observed at acute exposure to high-dose radiation. Epidemiologic studies and experiments indicate that the excess risk per unit dose may be smaller at low doses than at high doses.[1] The risk would be reduced even further when the radiation exposure proceeds at a low dose rate.[1] The low-dose-effectiveness-factor (LDEF) and the dose-rate-effectiveness-factor (DREF) have been suggested to correct the difference of excess risk per unit dose attributed to the dose level and dose rate, respectively.[2] The dose and dose-rate effectiveness factor (DDREF) is a correction factor integrating the dose and dose-rate effectiveness both in one.

The correction factors LDEF, DREF and DDREF have been published by different research groups with different sources of epidemiological statistics in radiation workers, atomic bomb survivors, and other exposed groups. In this study, we investigated the methodology of integrating diverse resources of epidemiological data and reviewed the parametric considerations to be taken in the integration.

2. Methods

2.1 Review of Kocher's work

The most recent suggestion of DDREF was made by Kocher et al.[3] They derived the distributions of LDEF by using risk coefficients from different sources of epidemiological studies. Each distribution was derived by conducting Monte Carlo uncertainty propagation with coefficients fitted in Weibull distributions. They integrated LDEF distributions by assigning them different weights to estimate 50th percentiles and 90% confidence intervals (CIs) of LDEF. The 50th percentiles and 90% CIs of DREF were estimated following the same scheme. They integrated different combinations of LDEF and DREF distributions to derive DDREF distributions. They assigned the same weights to both LDEF and DREF distributions of each combination to derive the corresponding DDREF distribution. The Kocher's work has been challenged by Wakeford et al. in regard to the vague basis of weight assignments to DREF data from different sources.[4]

2.2 Reference Distributions and Weight Assignments

Kocher et al. chose the Weibull distribution to represent the reported maximum likelihood estimates (MLEs) and CIs of risk coefficients considering the features of estimates that were highly skewed in frequencies. The UNSCEAR 2012 report,[5] suggested several reference distributions, including normal, uniform, beta, and gamma distributions, available for representing probabilistic data. Considering the skewness of data distribution, we chose log-normal distribution and triangle distribution to present the variations of coefficient data instead of any single reference distribution suggested by the UNSCEAR. Data fitting was conducted also with the Weibull distribution as a reference function to verify our schemes by comparing with the results of Kocher et al.

Different weights can be assigned to each of data elements under integration considering the variance or sample size of each data element.[6] Since variance tends to be inversely proportional to sample size, similar weight assignments are expected by any choice. However, as Kocher et al. asserted in their response to Wakeford et al.,[7] for some cases the inverse-variance weighting is not a good option due to large statistical variance of the integrated result. Kocher et al. did not clarified what basis they took in weight assignment. In this study, inverse-variance weighting and sample size weighting were conducted for meta-analysis purposes. The reference function for data fitting was Weibull distribution.

3. Results

3.1 Difference by reference distributions

Our estimates of DDREF for solid cancer are listed in Table 1 in comparison with Kocher et al.'s work and depicted in Fig. 1. Our data based on Weibull distribution showed very similar feature to Kocher et al.'s work (Table 1), which confirms our scheme of deriving DDREF. The similarity was maintained regardless of the reference function employed for data fitting.

3.2 Difference by weight assignments

Fig. 2 depicts our DDREF estimates derived from LDEF and DREF data that were obtained by assigning weights to different source elements according to sample size or inverse variance. Sample size-based weight assignment resulted in DDREF distribution that was very close to Kocher et al.'s. The inverse variance-based weight assignment gave a far different result.

Table I: DDREFs for solid cancer derived from LDEF and DREF data fitted to different reference functions.

Reference functions	percentile				
	2.5th	5th	50th	95th	97.5th
Weibull by Kocher et al.	0.39	0.47	1.3	3.6	5.6
Weibull	0.39	0.47	1.3	3.6	5.2
Log-normal	0.39	0.47	1.3	3.3	4.7
Triangular	0.39	0.46	1.3	3.8	5.7

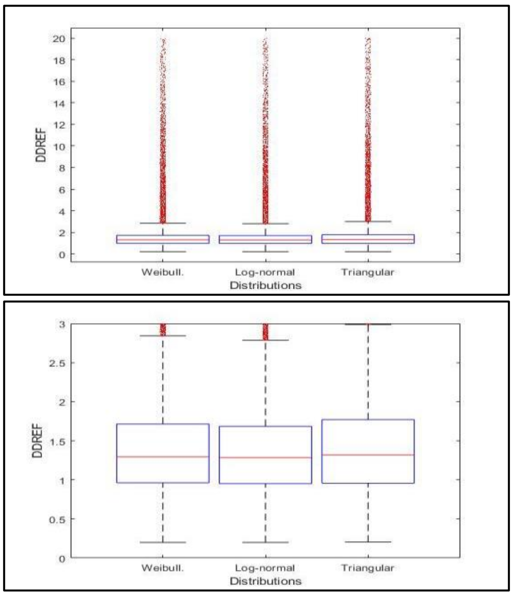

Fig. 1. Box-and-whisker plot of DDREFs based on different reference functions: extended range (upper) and range from 0 to 3 (lower).

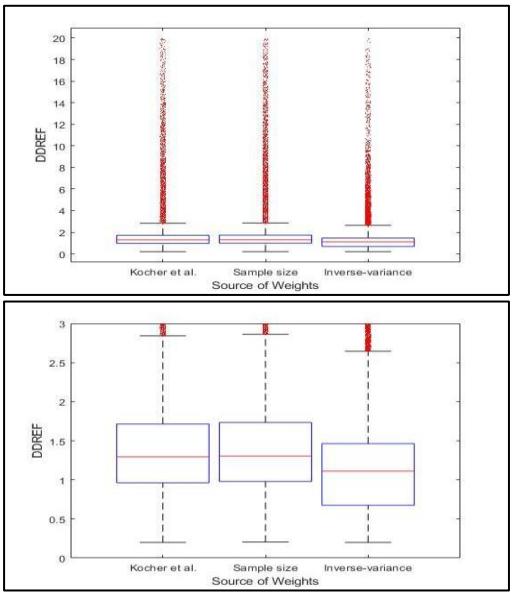

Fig. 2. Box-and-whisker plot of DDREFs fitted to Weibull distribution with different bases of weight assignment: extended range (upper) and range from 0 to 3 (lower).

4. Conclusion

Weibull, log-normal, and triangular distributions would make proper reference functions for fitting LDEF and DREF data of significant statistical variation originating from diverse studies. Sample size would be preferred as a basis of weight assignment to multiple source elements for integrating them.

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