Uncertainty in Radiogenic Risks for International Space Station and Mars Missions

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Independent Sources of Uncertainty

- Risk from HN LSS and tumor registry studies, R_{HN}
- Sampling errors in RERF data, $F(R_{HN})$
- Diagnostic misclassification, F(R)
- Errors in DS86, F(D)
- Transfer of Japanese risks to US, F(T)
- Temporal projection of risk, F(P)
- Unknown uncertainties, F(Q)
- DDREF for low-LET and ions, F(E)
- Uncertainty in ion QF/RBE

Requirements for minimizing uncertainty in lifetime risk projections: NASA vs. ground-based approach

Issue	Ground-based	NASA
Vital statistics	Mortality	Incidence
RERF Sampling	Yes	Yes
Diagnostic misclassification	Yes	No
DS86 Error	Yes	Yes
Transfer to US	Yes	Yes
Temporal projection error	Yes	No
Unknown error	Yes	Yes
DREF	Yes	Yes
QF/RBE	Yes(alpha)	Yes(ions, alpha)

Basics: Lifetime Risk Projection

Step 1: Decide if entire approach is based on cancer incidence or mortality. Select appropriate Japanese data.

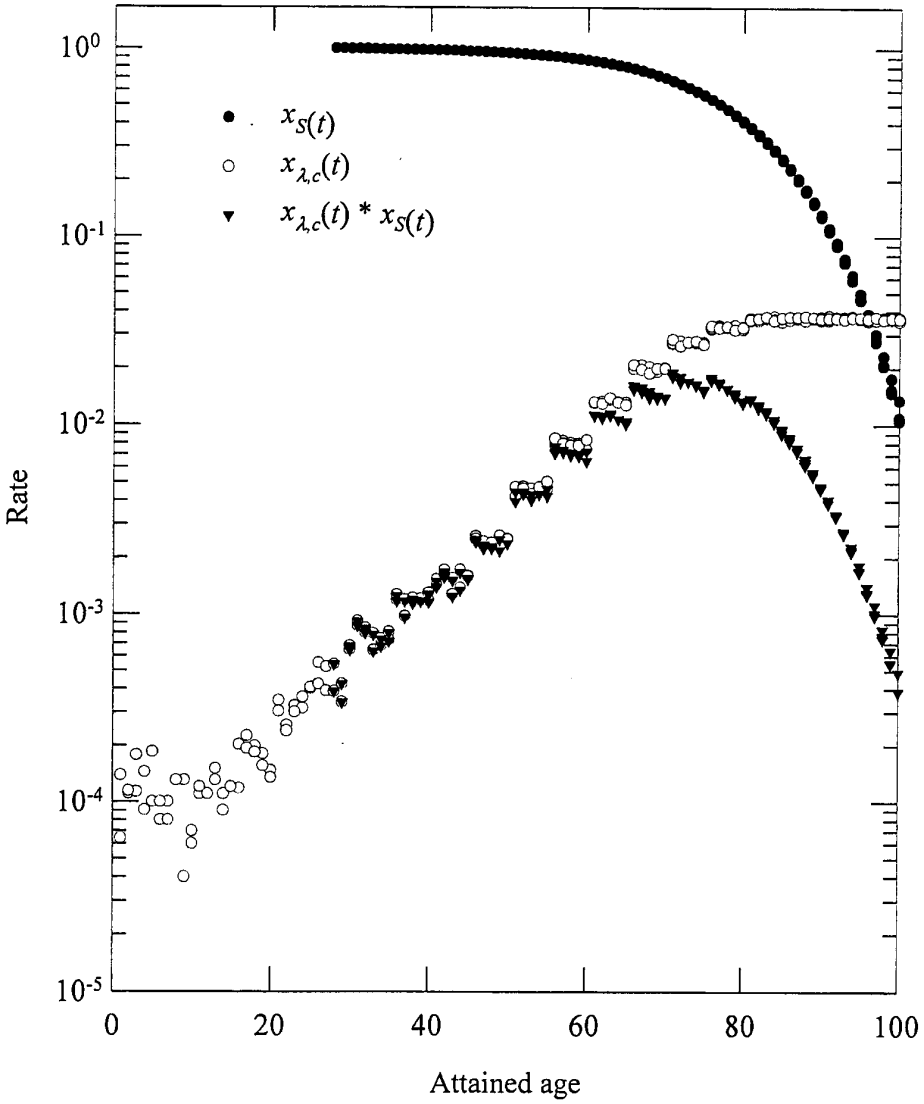
Step 2: Generate Poisson regression coefficients from Japanese data two ways (1) absolute and (2) multiplicative

Step 3: Transfer Japanese risks three ways: (1) absolute, (2) multiplicative, and (3) NIH multiplicative

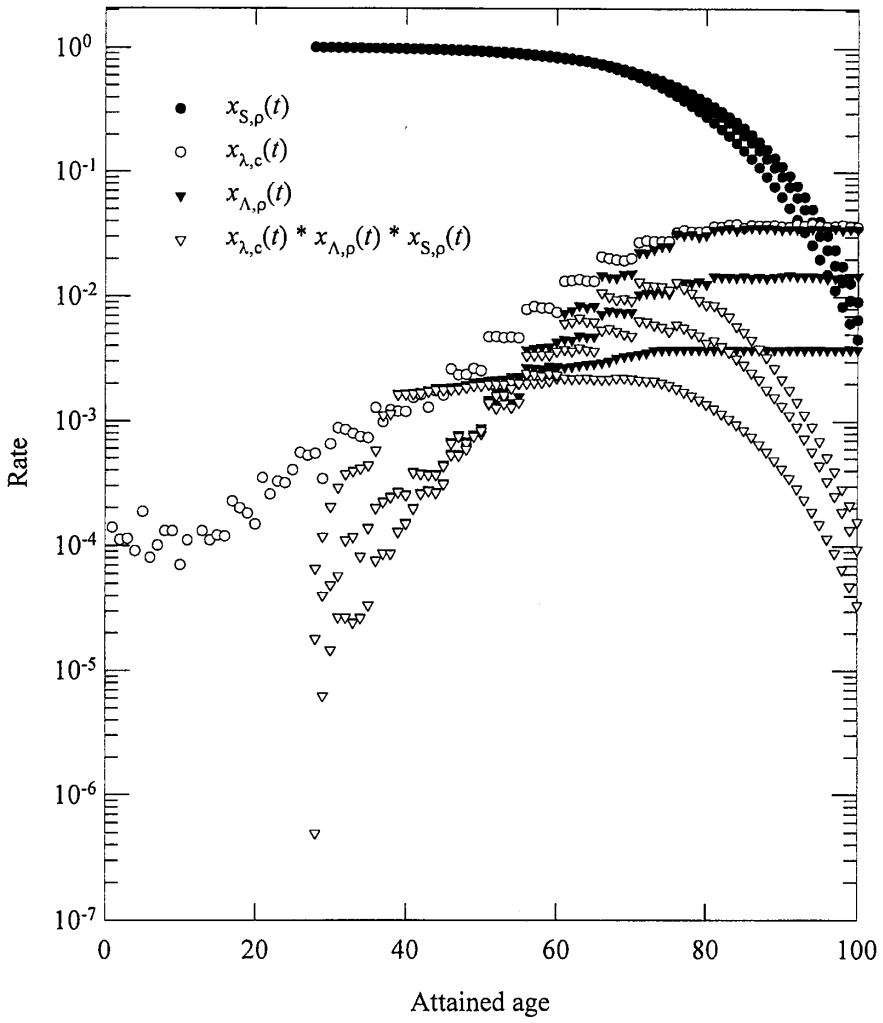
Sources of uncertainty driven by method ("know which committee/commission did what")

Method	Components	Change in bias
"MM" *(Mortality-mortality)*	Mortality-based Poisson regression	Diagnostic misclassification
	US cancer mortality rates	Diagnostic misclassification
"MLI" *(Mortality-lethality-incidence)*	Mortality-based Poisson regression	Diagnostic misclassification
	US cancer mortality rates	Diagnostic misclassification
	Division of mortality risks by lethality fractions	Unknown
"II" *(Incidence-incidence)*	Incidence-based Poisson regression	No diagnostic misclassification
	US cancer incidence rates	No diagnostic misclassification
	No lethality fractions	No unknown uncertainty for lethality fractions

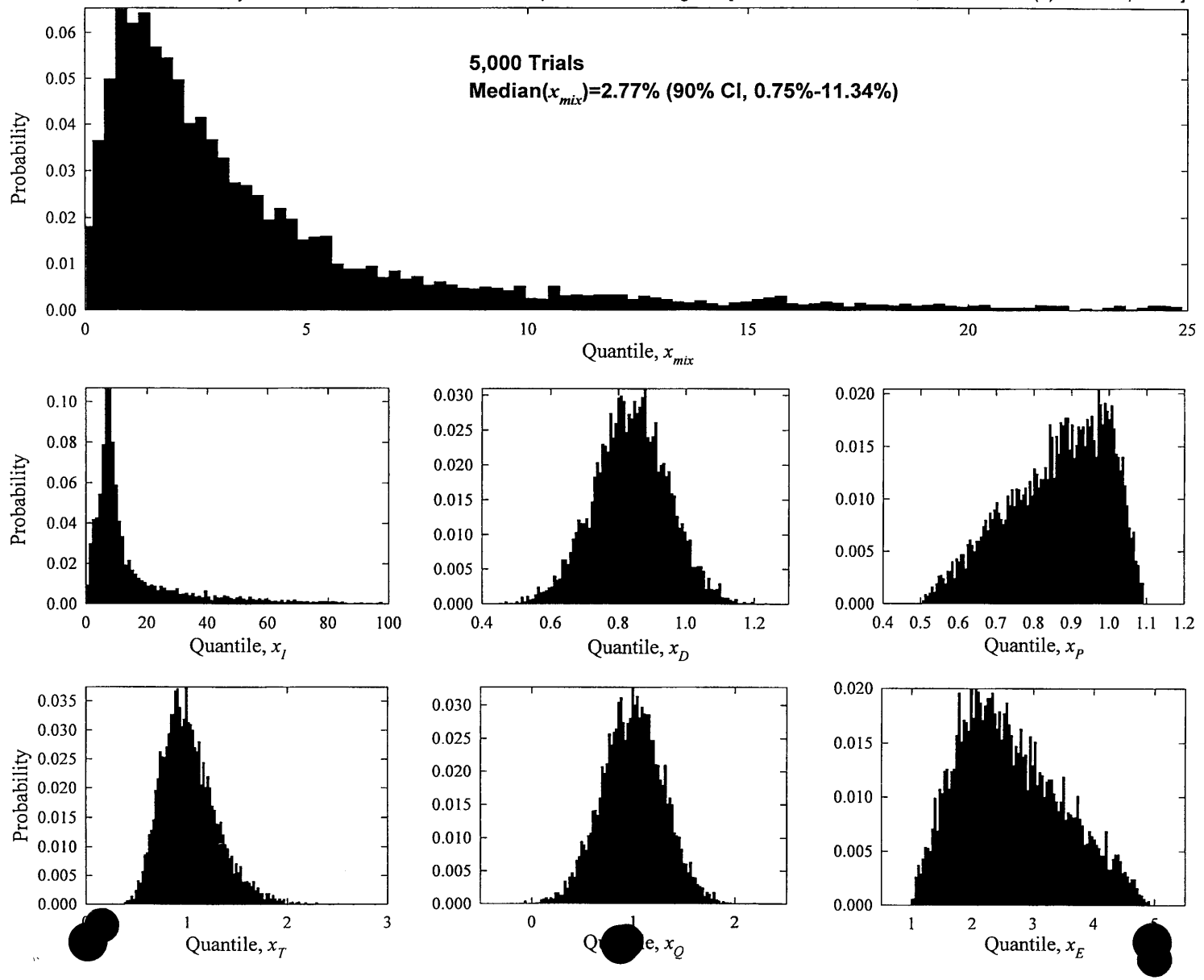
Quantiles of hazard and survivorship functions for baseline cancer incidence



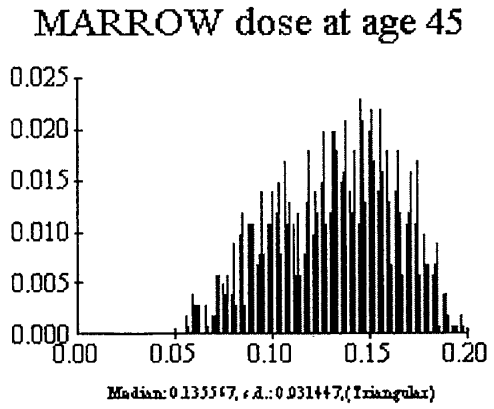
Quantiles of hazard and survivorship functions for excess cancer incidence
(age at exposure 18 to 65 at 0.02 Sv/y)

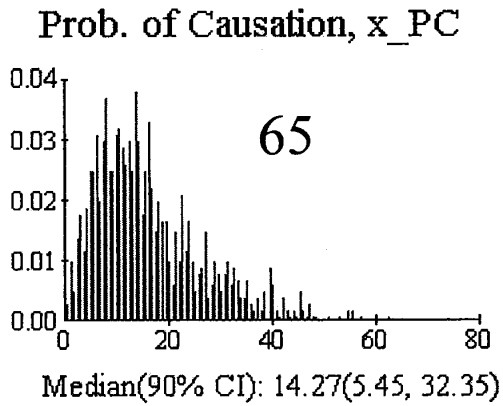


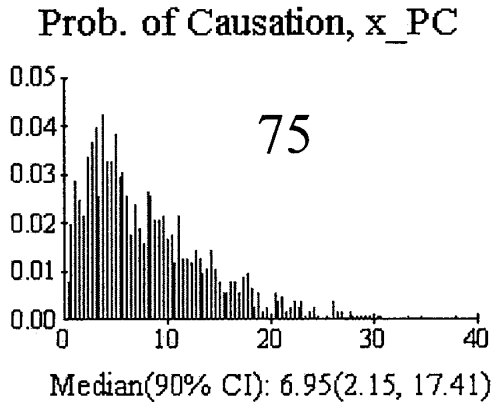
Median and 90% subjective confidence interval for males exposed to 1 Sv at age 45 [Peterson and Cucinotta, Mut. Res. 430(2): 327-334, 1999.]

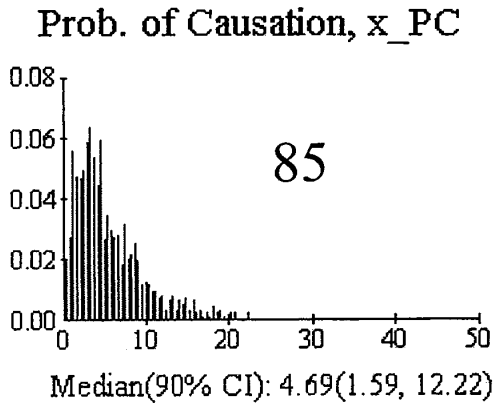


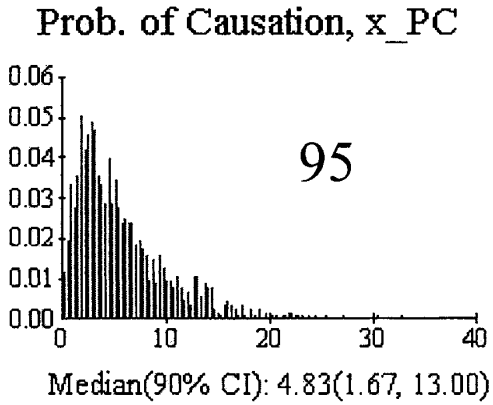
Comparison of leukemia probability of causation for males exposed to 0.15 Sv (6 month ISS mission, 1,000 iterations)

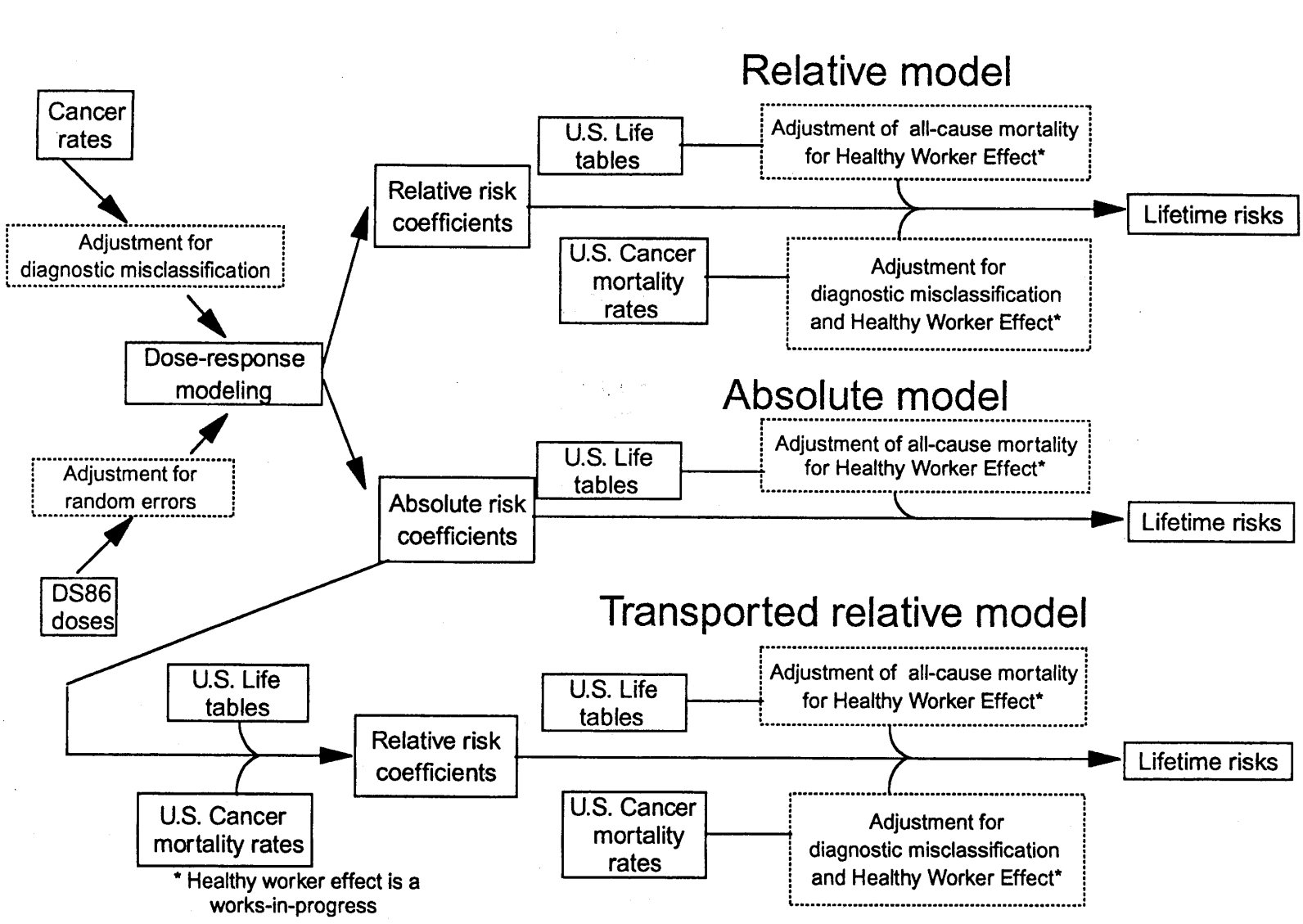




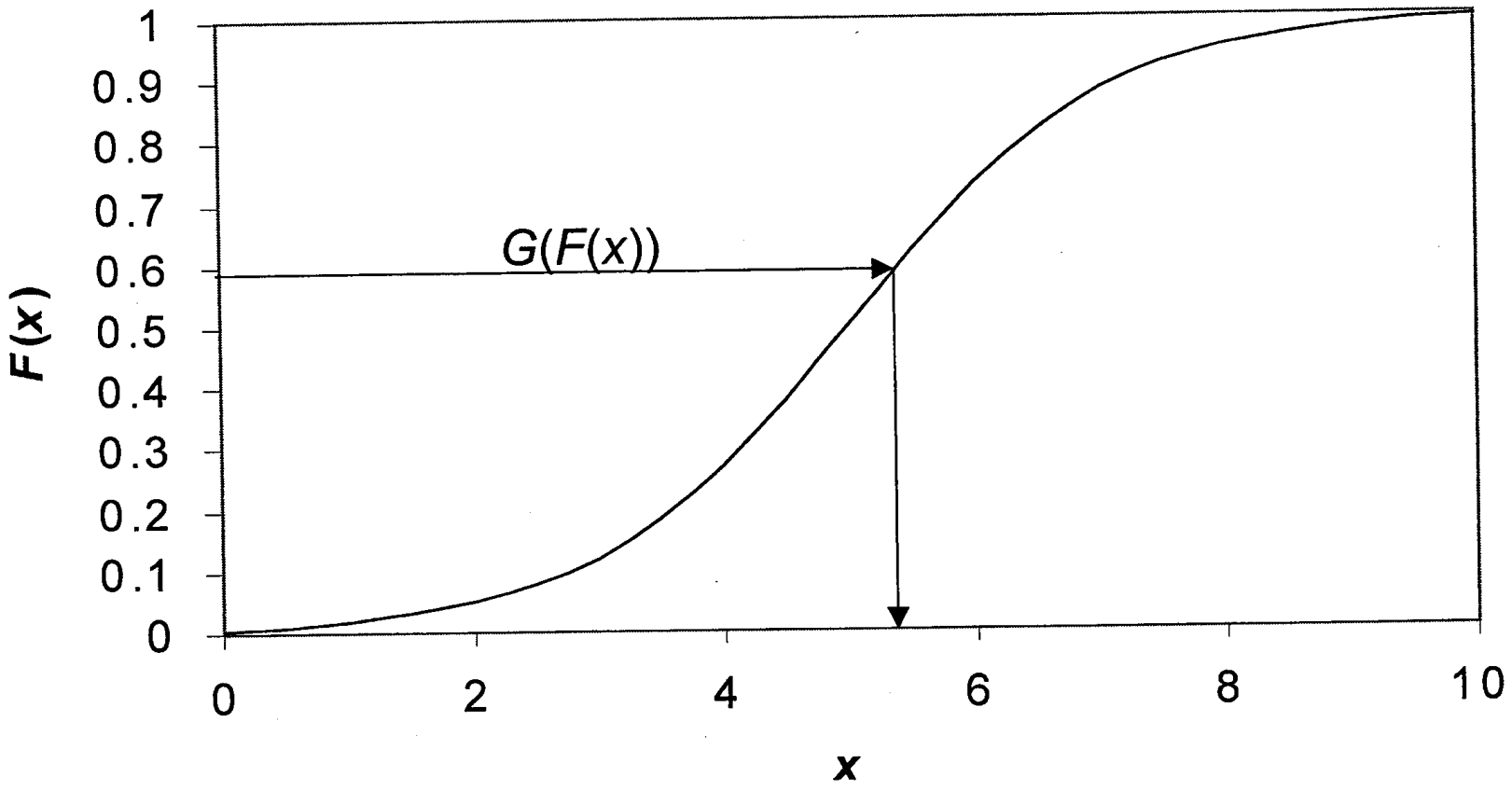







Relative model
Cancer rates
Adjustment for diagnostic misclassification
Dose-response modeling
Adjustment for random errors
DS86 doses
Relative risk coefficients
U.S. Life tables
Adjustment of all-cause mortality for Healthy Worker Effect*
Lifetime risks
U.S. Cancer mortality rates
Adjustment for diagnostic misclassification and Healthy Worker Effect*
Absolute model
Absolute risk coefficients
U.S. Life tables
Adjustment of all-cause mortality for Healthy Worker Effect*
Lifetime risks
Transported relative model
U.S. Life tables
Relative risk coefficients
U.S. Cancer mortality rates
U.S. Life tables
Adjustment of all-cause mortality for Healthy Worker Effect*
Lifetime risks
U.S. Cancer mortality rates
Adjustment for diagnostic misclassification and Healthy Worker Effect*
* Healthy worker effect is a works-in-progress

Relationship between the quantile, x, cumulative distribution, and inverse cumulative distribution function



Frequency distribution resulting from Monte Carlo simulation

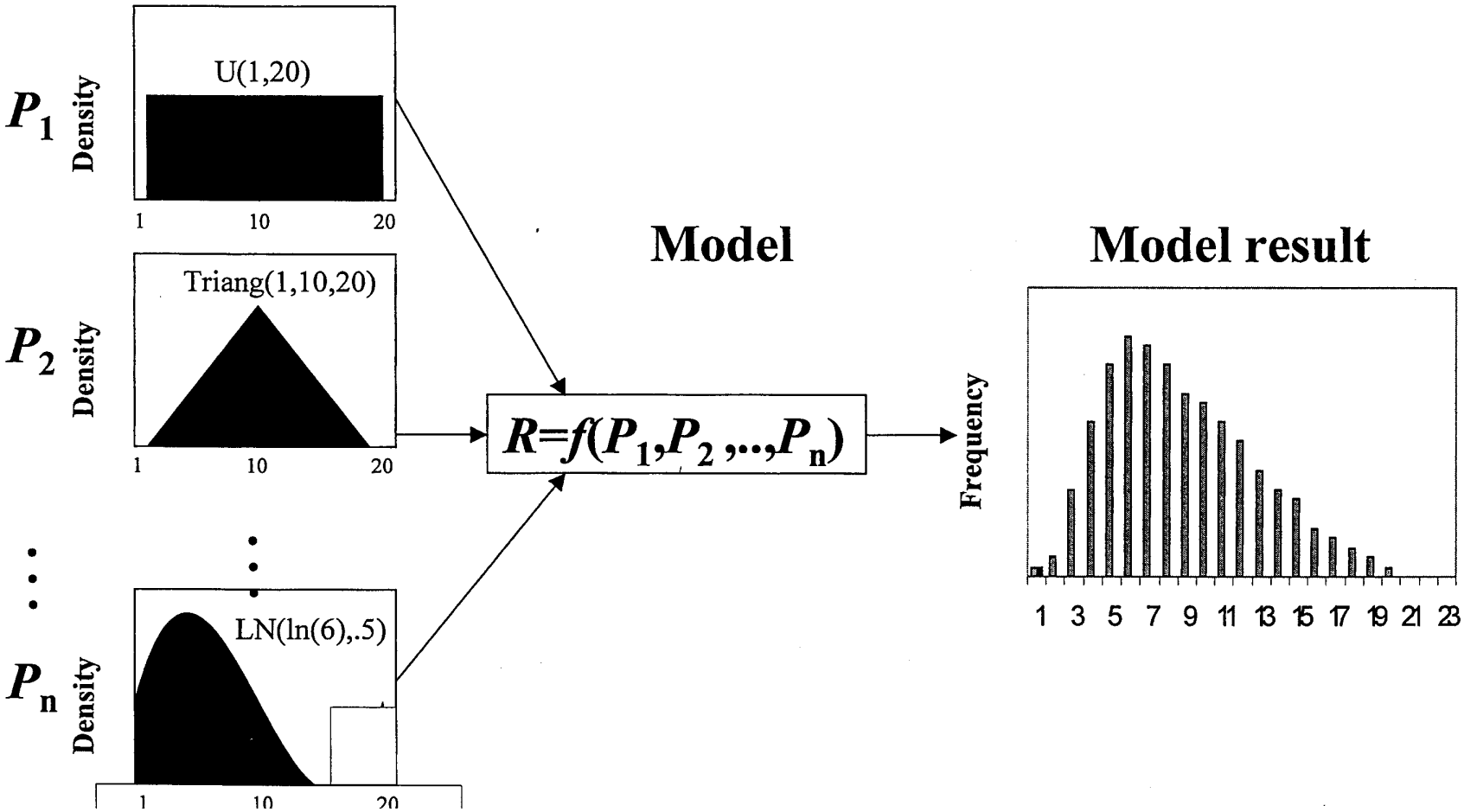


Table 1. Median lifetime incidence risks for the mixture model, $m(x_{mix})$, and 90% subjective confidence intervals of radiation-induced cancer (%) among males exposed to 1 Sv low-LET radiation in Shuttle and ISS orbits.

	Age at exposure	
Site	45	55
Oral cavity	0.02 (0.01,0.16)	0.02 (0.01,0.12)
Digestive	0.95 (0.34,2.59)	0.79 (0.26,2.35)
Esophagus	0.02 (0.01,0.07)	0.02 (0.01,0.06)
Colon	0.16 (0.06,1.30)	0.13 (0.05,1.28)
Rectum	0.04 (0.01,0.11)	0.03 (0.01,0.09)
Liver	0.08 (0.04,0.18)	0.06 (0.03,0.13)
Pancreas	0.02 (0.01,0.08)	0.02 (0.01,0.07)
Lung	0.39 (0.15,3.27)	0.29 (0.11,2.73)
Nonmelanoma	0.05 (0.02,0.10)	0.04 (0.02,0.08)
Prostate	0.05 (0.02,1.45)	0.04 (0.02,1.41)
Bladder	0.11 (0.04,1.22)	0.08 (0.03,1.15)
Kidney	0.17 (0.07,0.51)	0.13 (0.05,0.41)
CNS	0.02 (0.01,0.04)	0.01 (0.00,0.03)
Thyroid	0.08 (0.03,0.17)	0.06 (0.02,0.12)
Nonleukemia	2.77 (0.75,11.34)	2.20 (0.59,10.12)
Leukemia	0.38 (0.19,0.74)	0.34 (0.16,0.65)

Peterson and Cucinotta. Mutation Res. 430(2): 327-334; 1999.

Table 2. Median lifetime incidence risks for the mixture model, $m(x_{mix})$, and 90% subjective confidence intervals of radiation-induced cancer (%) among females exposed to 1 Sv low-LET radiation in Shuttle and ISS orbits.

	Age at exposure	
Site	45	55
Oral cavity	0.03 (0.01,0.08)	0.02 (0.01,0.06)
Digestive	1.09 (0.43,2.56)	0.97 (0.35,2.35)
Esophagus	0.02 (0.01,0.05)	0.02 (0.01,0.04)
Colon	0.20 (0.08,1.36)	0.17 (0.06,1.32)
Rectum	0.04 (0.02,0.09)	0.03 (0.01,0.08)
Liver	0.09 (0.02,0.21)	0.07 (0.02,0.18)
Pancreas	0.03 (0.01,0.09)	0.02 (0.01,0.08)
Lung	0.46 (0.19,1.76)	0.34 (0.14,1.40)
Nonmelanoma	0.05 (0.02,0.13)	0.04 (0.02,0.10)
Breast	0.76 (0.29,6.13)	0.58 (0.22,4.81)
Bladder	0.13 (0.05,0.43)	0.11 (0.04,0.39)
Kidney	0.18 (0.09,0.37)	0.14 (0.07,0.29)
CNS	0.02 (0.01,0.04)	0.01 (0.01,0.03)
Thyroid	0.11 (0.05,0.22)	0.08 (0.04,0.16)
Nonleukemia	2.98 (0.90,11.70)	2.44 (0.70,10.30)
Leukemia	0.37 (0.19,0.73)	0.27 (0.14,0.54)

Peterson and Cucinotta. Mutation Res. 430(2): 327-334; 1999.