Dose-response relationship and its impact on leukemia risk

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http://www.alfred-koerblein.de/cancer/downloads/dose-response.pdf

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The comparison of radiation effects from nuclear power plants with the effects from background radiation relies on the implicit assumption of the validity of a linear dose-response relationship. With this assumption, the effect depends on average dose only, irrespective of the time pattern and the spatial distribution of dose rates.

If, however, the dose-response curve is curvilinear, the average dose to the population cannot be used to determine the effect. In fact a curvilinear shape of the dose-response was found in data of perinatal mortality in Germany [1] (Figure A1) and in infant mortality data from Poland (Figure A2) after the Chernobyl accident. But perinatal mortality is considered a teratogenic radiation effect, while for cancers a linear dose response is generally accepted. This assumption, however, might not be true for cancers induced in utero. In a University of Leipzig publication [2] (see Figure A3), cancer induction during organogenesis is listed under teratogenic risks, together with congenital malformations and stillbirths. Today most scientists believe that cancers/leukaemias in children below age 5 have a prenatal origin.

Emissions from NPPs are characterised by short-term peaks and not by a constant low dose rate. Figure A4 shows 3-month averages of C-14 releases from a German NPP over a period of about 9 years. Rather regularly, about once a year, peak values are registered which might occur during periodic revision and refuelling. The differences between quarterly releases are greater than a factor of ten. And these are just 3-month averages; the variations between 24-hour intervals could be much larger.
There are also differences of up to 3 orders of magnitude (a factor of 1000) in releases from one reactor to another; this is shown in Figure A5. The differences in spatial distribution of radiation from aerial discharges are still greater. Figure A6 shows elliptic lines of equal radionuclide deposition (isolines) in the fallout plume of NPPs. The innermost isoline denotes a 10,000 times higher value than the outermost isoline, ie the spatial distribution is extremely inhomogeneous.

Let us assume that the extra annual dose from NPP releases is 0.1 mSv in an average, ie 10 to 100 times higher than the calculated values of some µSv (see Figure A7). This is well below the legal dose limit of 0.3 mSv per year. For ease of calculation let us further assume that this dose is delivered in 1/10 of a year, ie the extra dose rate will be 10-times the average dose rate, and zero during the rest of the year. This dose adds to the natural background radiation of about 1 mSv per

year (without the radon contribution). The total dose rate will be 2 mSv per year in 1/10 of a year and 1 mSv per year in 9/10 of a year. With a power of dose of 3.5 as found for perinatal mortality in Germany, the radiation risk will be 2^3.5=11.3-times greater in one tenth of the time. The overall increase of radiation risk will be 11.3*0.1+1*0.9 = 2.03. Thus, a 10 % increase of average dose above background will lead to a 103 % increase of risk.

A mathematical derivation of the shape of the dose-response dependency

Leukaemia induction likely originates from events in the critical period of foetal development, during major organogenesis, when the embryo is extremely sensitive to ionising radiation. The radiosensitivity varies from one individual to another in a human cohort, and also the individual doses will show considerable variation. Adverse health effects might be expected at mean doses generally considered safe from experience with experimental animals. But, contrary to the situation considered here, animal experiments are usually conducted on genetically homogeneous species, irradiated with well-defined radiation doses.

The distribution of individual doses as well as radio-sensitivities in a human population shall be described by lognormal distribution functions, characterised by median dose μ and standard deviation σ. Then the proportion of individuals with doses ranging from x to x+dx is f(x)*dx, where f(x) is a lognormal density function, and the probability of an individual, exposed to dose x, to experience a radiation damage is given by a cumulated lognormal function g(x).

Figure A8 shows dose distributions for median dose rates μ of 1.0, 1.2, 1.4, 1.6, 1.8 mSv/y and with sigma=0.30 (blue lines). The sensitivity distribution is defined by a cumulated lognormal distribution with median μ=4 mSv/y and σ=0.40 (green line). The proportion of affected individuals in the cohort is the integral ∫f(x)*g(x)*dx. The red lines in Figure 1 are the product terms f(x)*g(x); the areas under the red lines are proportional to the number of affected individuals.

Figure A9 shows the results of numerical integrations of f(x)*g(x) for median dose rates of 1.0, 1.2, 1.4, 1.6, 1.8 mSv/y (black squares). The dose-response curve is curvilinear. A regression of the first 3 data points, ie for μ = 1.0, 1.2, and 1.4 mSv/y, yields a best estimate of 4.9 for the power of dose. The extrapolation to higher doses, however, does not fit the other two data points at μ=1.6 and 1.8 mSv/y whereas a cumulated lognormal function with σ=0.50 fits the two data points perfectly well (see Figure A10).

To summarize, a curvilinear form of the dose response dependency follows from the assumption that exposures and radio-sensitivities are randomly distributed in a population. The shape of the dose response curve is a cumulated lognormal distribution function which is characterised by a strong upward curvature at very low doses.

References

1. Körblein A, Küchenhoff H. Perinatal Mortality in Germany following the Chernobyl accident. Radiat Environ Biophys 1997; 36 (1): 3-7, available at: http://www.alfred-koerblein.de/chernobyl/downloads/KoKu1997.pdf

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4. Deutscher Bundestag Drucksache 16/6835. Umweltradioaktivität und Strahlenbelastung im Jahr 2006. http://dip21.bundestag.de/dip21/btd/16/068/1606835.pdf

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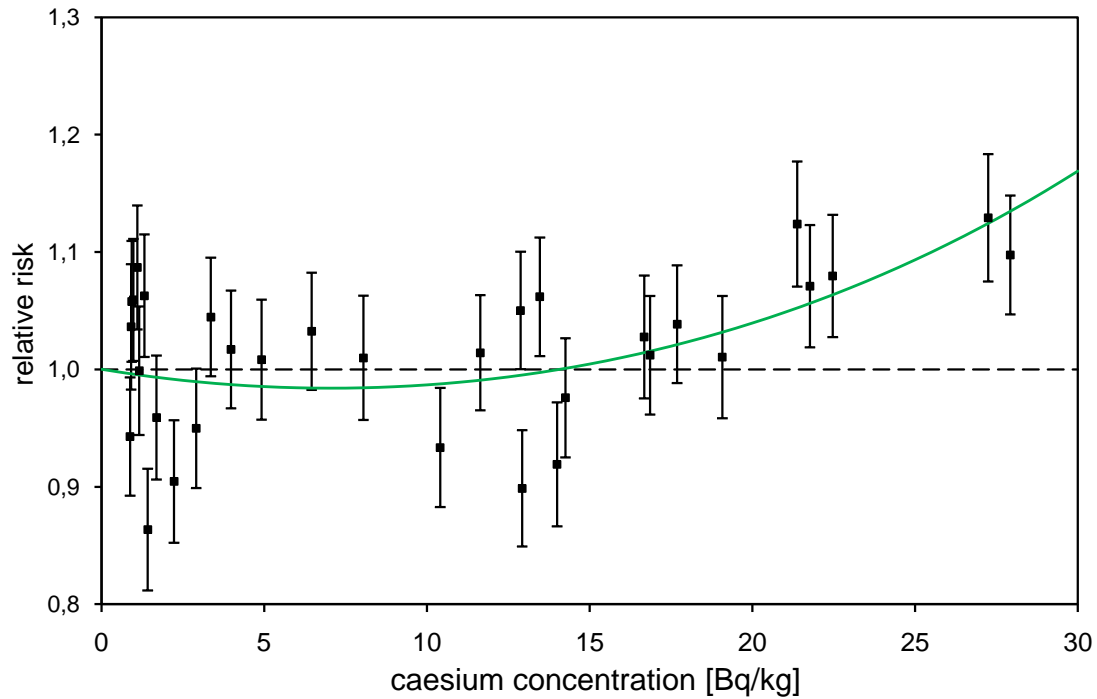
Figure A1: Perinatal mortality risk in Germany as a function of the calculated caesium concentration in pregnant women following the Chernobyl accident and trend line. The dose-response is curvilinear (data analysis by A. Körblein).
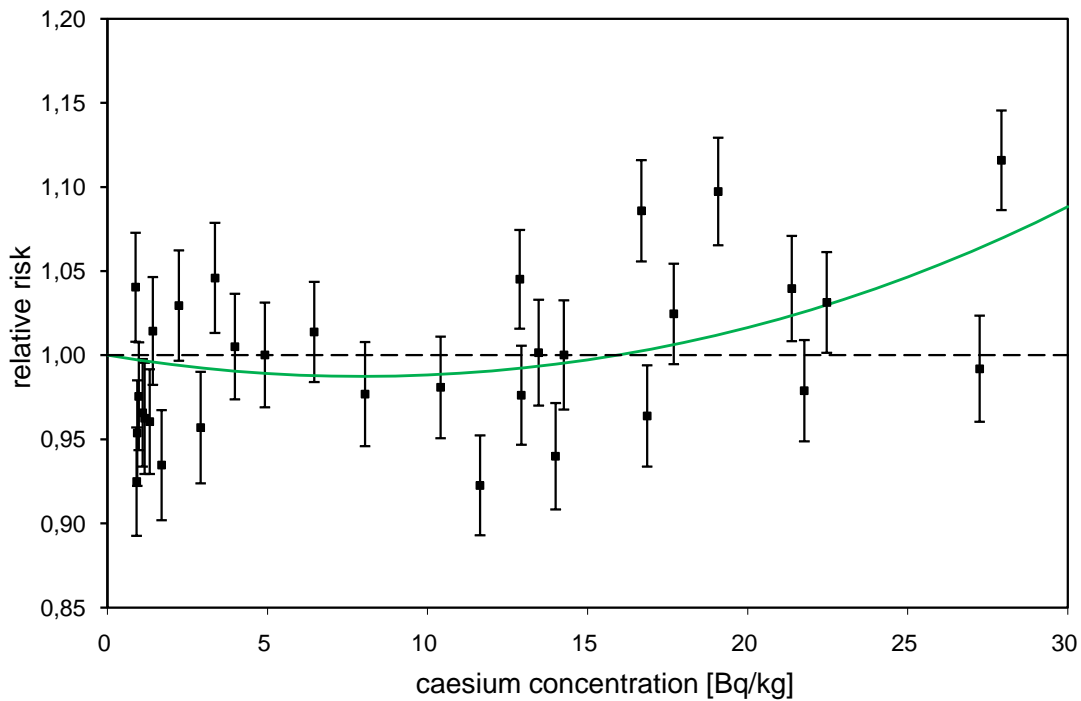

Figure A2: Infant mortality risk in Poland as a function of the calculated caesium concentration in pregnant women following the Chernobyl accident and trend line. The dose-response is curvilinear (data analysis by A. Körblein).
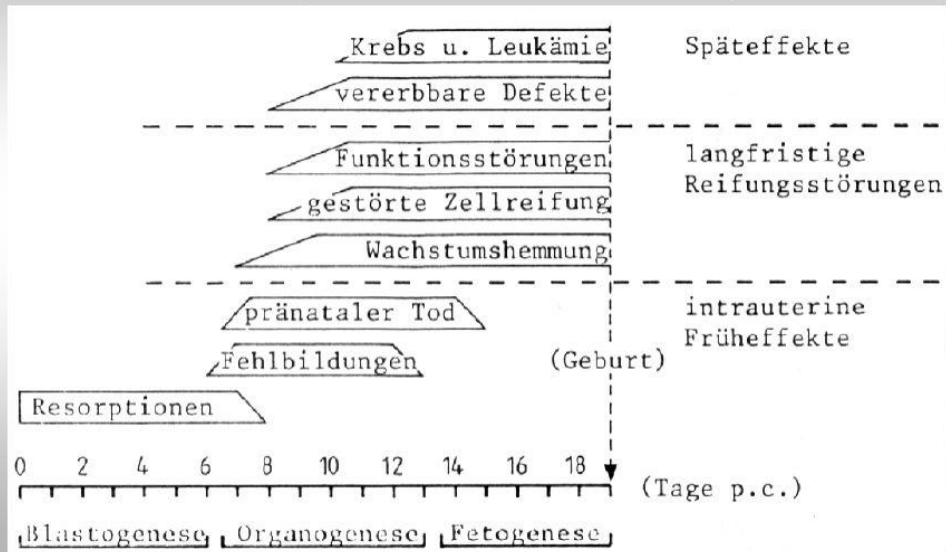
Figure A3:
In-utero cancer induction during pregnancy is listed under teratogenic risk (from [2]).
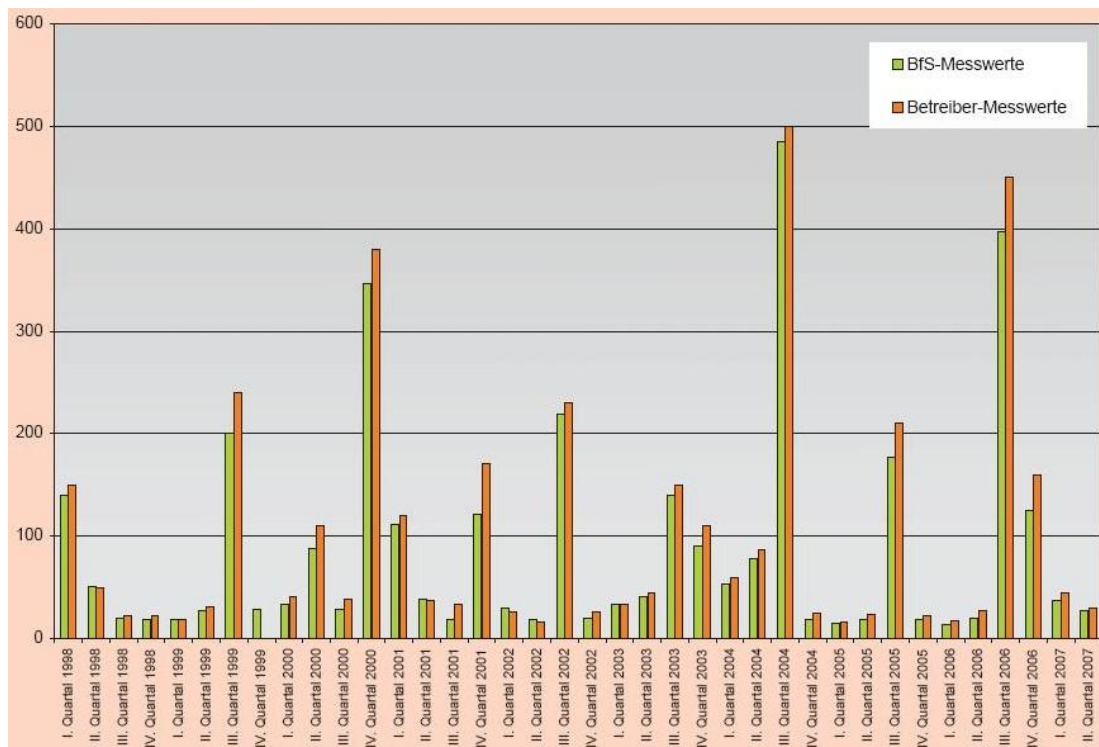

Figure A4:
Quarterly C-14 air concentrations near the Neckarwestheim nuclear power station. The columns are measurements by BfS (green) and by the utility (orange) (from [3]).
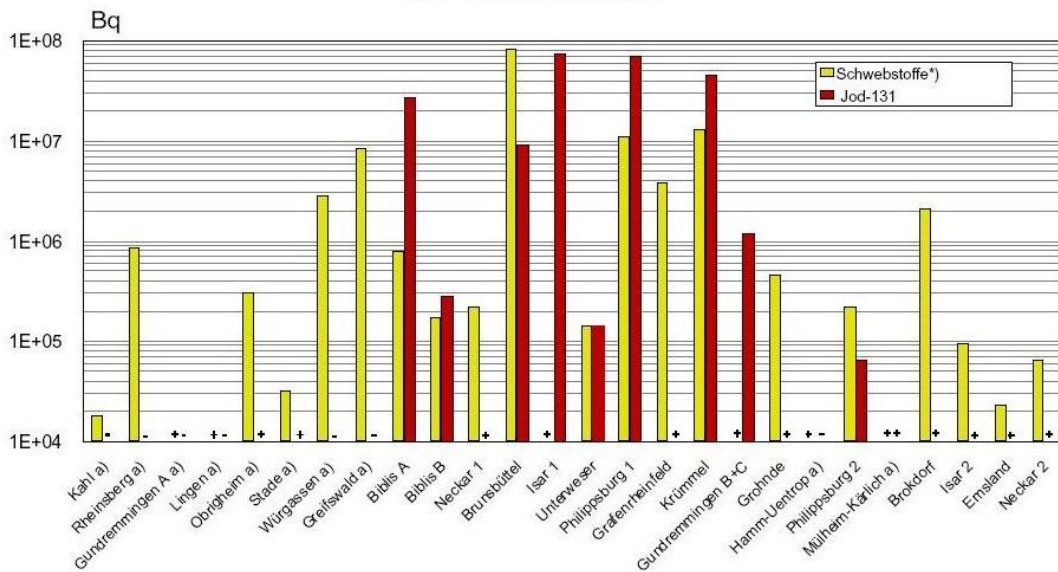
Figure A5:
Annual releases of aerosols (yellow columns) and iodine-131 (red columns) by German nuclear power plants. The releases vary by several orders of magnitude (from [4]).
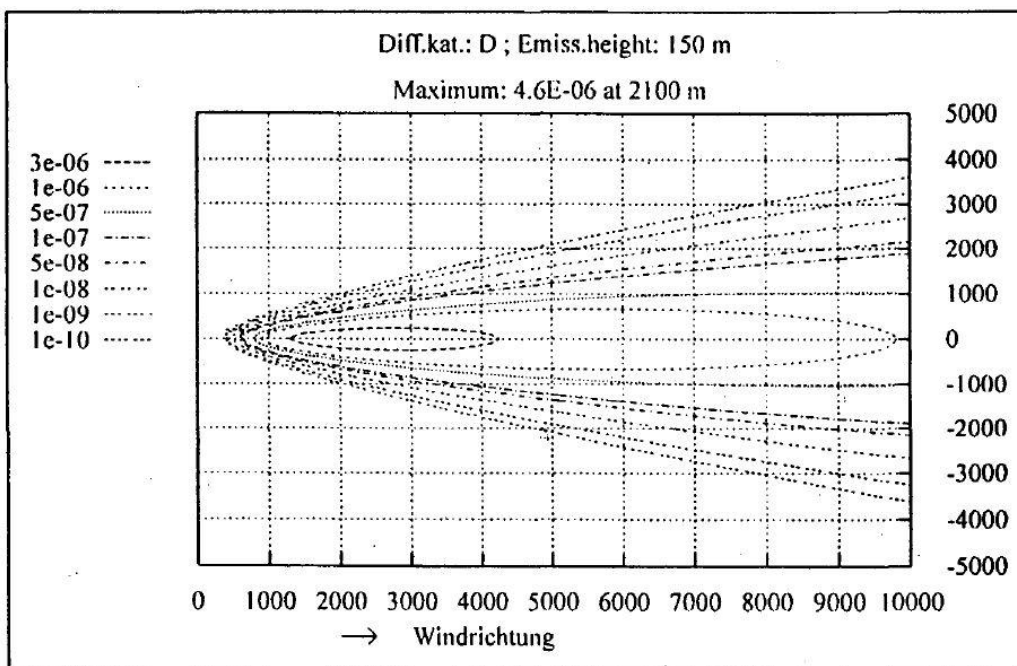

Figure A6:
Calculated isolines of the fallout dispersion coefficient for diffusion category D and stack height 150 meters. The calculated maximum fallout occurs at a distance of 2100 m from the NPP (from [5]).

Strahlenexposition im Jahr 2006 in der Umgebung von Kernkraftwerken durch die Ableitung radioaktiver Stoffe mit der Fortluft

* kleiner als 0,0001 mSv

a) Berechnet für eine Referenzperson an den ungünstigsten Einwirkungsstellen
b) Die Strahlenexposition konnte für Expositionspfade, bei denen Radionuklide in den Vorjahren akkumuliert wurden, nur unvollständig berechnet werden, da bei diesen Kernkraftwerken Werte für die Ableitung radioaktiver Stoffe mit der Fortluft aus den Jahren vor 1990 (Greifswald) bzw. vor 1984 (Rheinsberg) nicht vorliegen
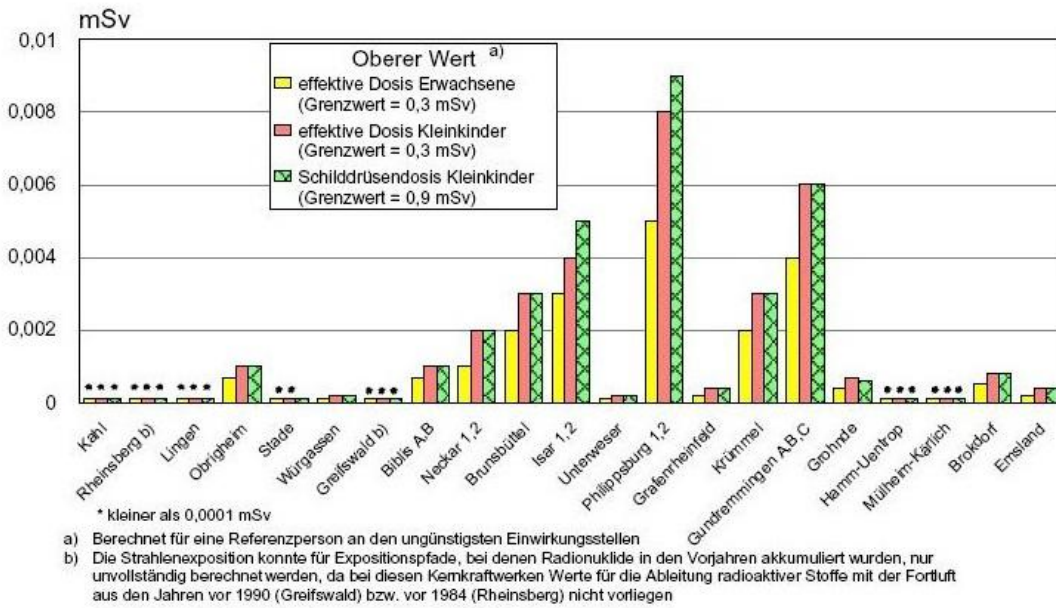
Figure A7: Calculated annual effective doses for young children (*Kleinkinder*) in the vicinity of German nuclear power plants (red columns). The asterisks denote dose values smaller than 0.0001 mSv. The doses vary considerably from one reactor to another (from [4])
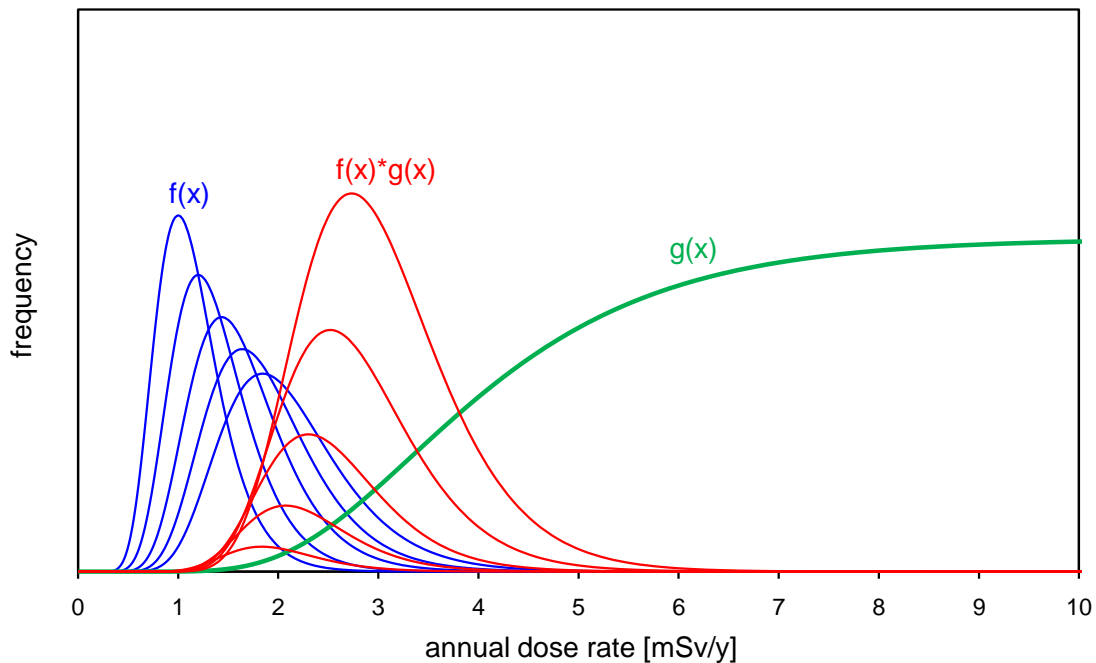

Figure A8: Frequency distribution for 5 values of the median dose rates (1.0, 1.2, 1.4, 1.6, 1.8 mSv/y, blue lines) und probability of a radiation damage (green line). The area below the red lines is proportional to the number of affected individuals.
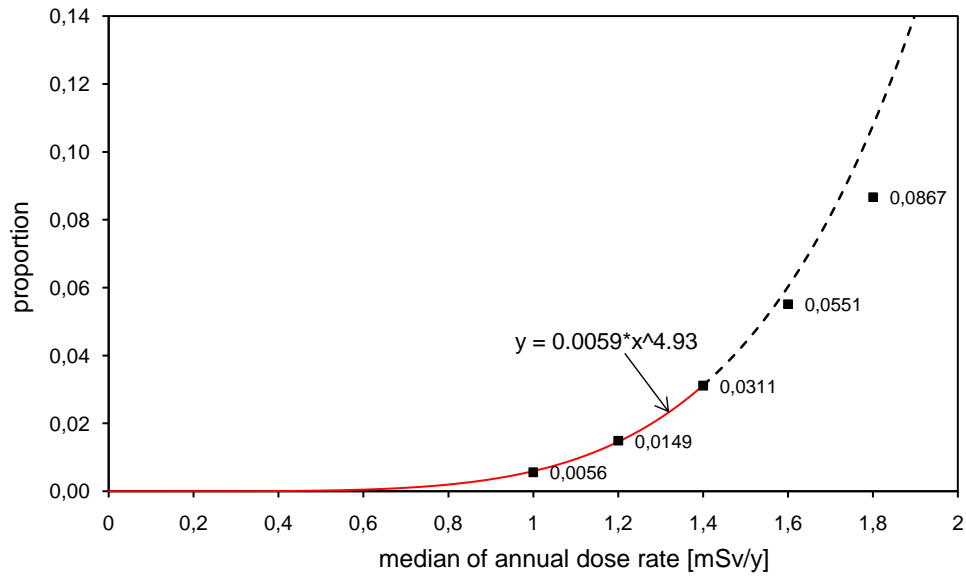
Figure A9: Proportion of affected individuals for 5 values of median dose rates (1.0, 1.2, 1.4, 1.6, 1.8 mSv/y). The solid line is the result of a regression of the first 3 data points with a power-of-dose model, the dotted line is the extrapolation to higher dose rates.
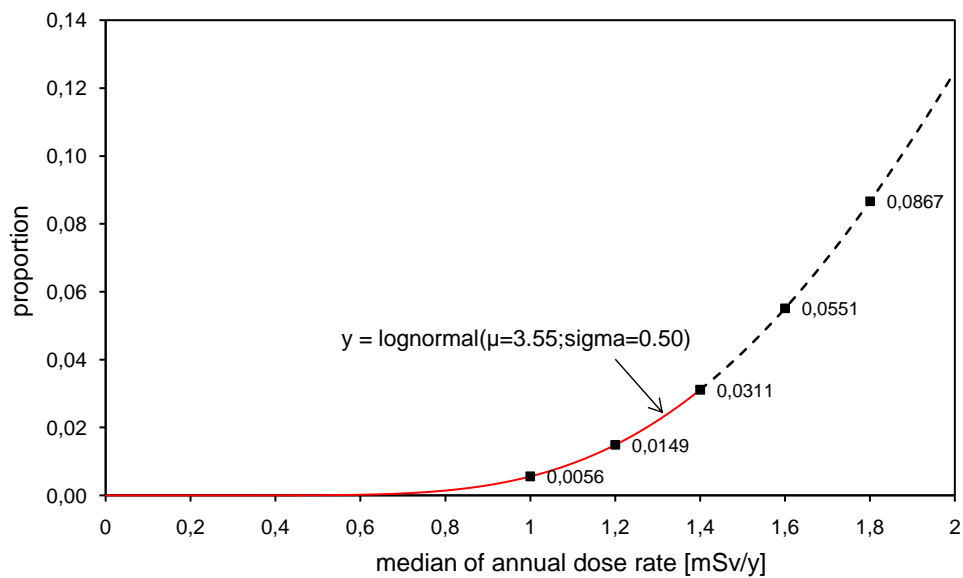

Figure A10: Proportion of affected individuals for 5 values of median dose rates (1.0, 1.2, 1.4, 1.6, 1.8 mSv/y). The solid line is the result of a regression model of the first 3 data points with a lognormal distribution function; the dotted line is the extrapolation to higher dose rates.