BIOLOGICAL REVIEWS
Cambridge Philosophical Society
Biol. Rev. (2013), **88**, pp. 226–254.
doi: 10.1111/j.1469-185X.2012.00249.x

The effects of natural variation in background radioactivity on humans, animals and other organisms

Anders P. Møller[1,*] and Timothy A. Mousseau[2]

[1] *Laboratoire d'Ecologie, Systématique et Evolution, CNRS UMR 8079, Université Paris-Sud, Bâtiment 362, F-91405, Orsay Cedex, France*
[2] *Department of Biological Sciences, University of South Carolina, Columbia, SC 29208, USA*

ABSTRACT

Natural levels of radioactivity on the Earth vary by more than a thousand-fold; this spatial heterogeneity may suffice to create heterogeneous effects on physiology, mutation and selection. We review the literature on the relationship between variation in natural levels of radioactivity and evolution. First, we consider the effects of natural levels of radiation on mutations, DNA repair and genetics. A total of 46 studies with 373 effect size estimates revealed a small, but highly significant mean effect that was independent of adjustment for publication bias. Second, we found different mean effect sizes when studies were based on broad categories like physiology, immunology and disease frequency; mean weighted effect sizes were larger for studies of plants than animals, and larger in studies conducted in areas with higher levels of radiation. Third, these negative effects of radiation on mutations, immunology and life history are inconsistent with a general role of hormetic positive effects of radiation on living organisms. Fourth, we reviewed studies of radiation resistance among taxa. These studies suggest that current levels of natural radioactivity may affect mutational input and thereby the genetic constitution and composition of natural populations. Susceptibility to radiation varied among taxa, and several studies provided evidence of differences in susceptibility among populations or strains. Crucially, however, these studies are few and scattered, suggesting that a concerted effort to address this lack of research should be made.

Key words: adaptation, cancer, disease, DNA repair, hormesis, mutation, radioactivity, radio-resistance, radio-tolerance.

CONTENTS

I. INTRODUCTION

Radiation can be divided into non-ionizing radiation (radio waves, visible light and heat) and ionizing radiation that has sufficient energy to ionize an atom. Ionizing radiation consists of particles that cannot penetrate paper, particles that can penetrate paper, but not an aluminium sheet, and rays that can penetrate paper, aluminium and thin layers

* Address for correspondence (Tel: (+33) 1 69 15 56 88; Fax: (+33) 1 69 15 56 96; E-mail: anders.moller@u-psud.fr)

of lead. Both ionizing and non-ionizing radiation can be damaging for organisms, although ionizing radiation is more damaging because the ions that are generated may directly damage DNA and other molecules. Levels of background ionizing radiation (hereafter radiation) have always varied spatially and temporally on Earth. Levels of background radiation were very high during the Pre-Cambrian period peaking around two billion years ago at a dose rate of 7 mGy per year, but have decreased by a factor of 10 since life first originated (Karam & Leslie, 2005). During the subsequent 2 billion years, radiation levels fluctuated considerably due to large solar flares, nearby supernovae and gamma ray bursts. Large meteor impacts in Mexico, India, Russia and other sites also likely caused the release of vast amounts of radioactive material on Earth (e.g. Alvarez *et al*., 1980). Such fluctuations may have contributed to current levels of resistance to radiation damage in free-living organisms. Today, typical background radiation dose rates vary around a minimum of only 0.01–0.10 with the natural level in Chernobyl before the nuclear accident being 0.01–0.02. By contrast, there are geographic regions where naturally occurring radiation can reach very high levels (3 orders of magnitude above global mean levels). There are equally many sites with high levels of radiation in the oceans, with thermal vents and their associated unique biodiversity being a well-known example (e.g. Fiala-Médioni, Alaysee & Cahet, 1986; Cherry *et al*., 1992; Jollivet *et al*., 1995*a*, *b*, 2003). Maximum terrestrial levels of radioactivity reach as high as 29.7 h in Ramsar, Iran, 22 h in Morro do Ferro, Minas Gerais, Brazil, 12 h in Mombasa, Kenya, 10 /h in Lodeve, France, 4.0 Sv/h in Kerala, India, 4.0 Sv/h in Tamil Nadu, India, and 0.7 /h in Yangjiang, China (Ghiassi-Nejad *et al*., 2002). Such radiation is related to the presence of radionuclides in the rock or in the form of gases like radon that can be trapped inside buildings or caves and increase human exposure to mutagens that subsequently increase rates of cancer (e.g. Lubin & Boice, 1997; Hendry *et al*., 2009). These natural levels of radiation are still 20-fold less than the maximum levels present today at Chernobyl.

Mutations are changes in genomic sequences of DNA that may occur as a consequence of breakage of a single or double strand of DNA. DNA repair can restore sequences of DNA, most readily single-strand, but also double-strand DNA (Lehman, 2006; von Sonntag, 2010). Somatic mutations are sometimes the source of genetic diseases including cancer, while germ-line mutations can be transferred to offspring. Mutations are an important source of novel genetic variation (Hartl & Clark, 1997). That radiation is a powerful mutagen was shown by classical laboratory experiments (Nadson & Philippov, 1925; Muller, 1954; UNSCEAR, 1988; National Academy of Sciences – Natural Resources Council, 1990), but it is less well known that natural variation in levels of background radiation is also a significant cause of mutation (e.g. Forster *et al*., 2002); exposure to natural radon in homes is the second leading cause of lung cancer in the US (e.g. Lubin & Boice, 1997; WHO, 2009). However, we currently do not know the relative importance of radiation and, for example, dietary mutagens as causes of mutations, nor do we understand the average effect of naturally occurring background radiation on mutations.

What are the consequences of natural variation in background radiation for evolution? Given the current 1000-fold difference in natural levels of background radiation such effects should be measurable in both past and current rates of mutations, but we are unaware of any studies investigating such effects. A partial answer may come from a recent study of the relationship between local population density and radiation at Chernobyl arising from the catastrophe on 26 April 1986. Different species of birds in the Chernobyl area vary enormously in their tolerance of radiation; some species have similar local densities at high and low levels of radiation, while other species have dramatically reduced population densities at sites with high radiation levels. Møller *et al*. (2010) showed that historical mitochondrial mutation rates in birds, as reflected by DNA substitution rates, were positively correlated with the impact of radiation from Chernobyl on local population density, independent of all known confounding variables correlated with mitochondrial DNA (mtDNA) substitution rates. Thus, species that were ecologically strongly impacted by radiation around Chernobyl, as shown by reduced densities at high levels of radiation, were also those most strongly impacted by mutagens in the past as reflected by high substitution rates. Although other factors (e.g. variation in historical population sizes, mutational biases related to DNA composition and interactions, and selection) also likely affected historical mtDNA substitution rates (e.g. Gaut *et al*., 2011), we can conclude that current sensitivity to radiation at least in part reflects past sensitivity to mutagens in general.

Very few mutations are beneficial; most are slightly deleterious or neutral (e.g. Lynch *et al*., 1999; Eyre-Walker & Keightley, 2007). If mutation rates are elevated in areas with high natural levels of background radiation, we should be able to demonstrate fitness costs of radiation. For example, it is well known that mutations are the source of many cancers and other diseases (e.g. Valko *et al*., 2004). It is also well known that cancer caused by radon shows enormous spatial variability so that foci of such cancers are concentrated in areas with specific rock substrata (e.g. Lubin & Boice, 1997). Are there effects of such natural variation in radiation on the incidence of diseases such as cancer, and hence intensity of selection to repair mutations more efficiently?

If radiation at 'natural' levels can be shown to have negative fitness consequences for plants and animals, even though such natural levels may be modest, there is a reason to expect that higher doses due to nuclear accidents will have even larger negative fitness consequences. The flipside of negative fitness consequences is evolutionary adaptation to radiation. If organisms are exposed to the negative effects of radiation for long periods of time, we could expect that some individuals may become radio-tolerant, showing normal or even enhanced survival and reproduction in the face of radiation. If such variation in the ability to cope with radiation had a genetic basis, resistance to radiation would

be selected, even if such resistance was associated with a physiological cost. The end point of evolutionary adaptation to radiation is exploitation of radiation to the advantage of the individual. For example, several micro-fungi and bacteria associated with thermal vents and deserts are able to live under extremely high radiation levels (e.g. Brooks & Murray, 1981; Suzuki *et al*., 1988; Jolivet *et al*., 2003, 2004; de Groot *et al*., 2005; Chanal *et al*., 2006; Shravage *et al*., 2007; Charmasson *et al*., 2009; Daly, 2009). Several micro-fungi from irradiated areas are directly attracted by radionuclides (positive radiotropism), being able to grow upon 'hot particles' and even degrade them (Zhdanova *et al*., 2004). Furthermore, in some cases ionizing radiation has a positive stimulatory effect on spore germination (Tugay *et al*., 2006). Finally, exposure to ionizing radiation increases the growth of some melanized fungi while simultaneously transferring electrons to melanin. This has led to speculation that these redox properties might even be used to transduce energy for cell metabolism, thereby enhancing growth (Dadachova *et al*., 2007; Dadachova & Casadevall, 2008).

A slightly different aspect of adaptation to radiation and acquisition of fitness benefits from radiation exposure is hormesis; the suggestion that organisms may benefit from an hypothesised stimulatory effect of low levels of radiation compared to the absence of radiation (e.g. Planel *et al*., 1987; Wolff, 1989). There is an extensive literature on this subject in humans and other organisms [see reviews in Kondo (1993) and Luckey (1991)]. Mossman (2001) emphasized that the evidence is open to alternative interpretations: data purported to provide evidence for radiation hormetic effects in humans are based on epidemiological findings used to test different hypotheses; hormetic effects are weak at best and inconsistent; there is no consensus on how these presumed benefits are defined or quantified; and it remains unclear how hormesis can be classified between the Scylla of beneficial health effects and the Charybdis of requirements for protection of health. Here we suggest that the documented consequences of naturally increased levels of background radiation have important implications for hormesis. In particular, we would expect that radiation hormetic effects should be found in areas with higher levels of natural background radiation because of adaptation to such enhanced levels of radiation, and we predict that on average radiation should have positive effects on the wellbeing of humans and other organisms if hormesis operates at naturally occurring low-dose radiation.

The objectives of this review of the effects of natural variation in radiation levels on free-living organisms were fourfold. (*i*) To review the effects of natural levels of radiation on mutation rates, DNA repair, and other genetic mechanisms. (*ii*) To review the evidence for the effects of natural levels of radiation on physiology, immunology and disease frequency. If there is adaptation to local radiation levels, then the relationship between radiation levels and the measured effect might be weaker than expected based solely on the direct effect of radiation on mutation rates (i.e. there is a confounding variable of the extent to which mutations are repaired). (*iii*) To review the evidence for radiation resistance to assess its prevalence in natural populations. (*iv*) To review the extent to which natural variation in background radiation has positive hormetic effects on health, fecundity and longevity. We emphasize that we do not review literature on the effects of radiation from nuclear accidents, nuclear weapons tests, medical treatments, or similar human-induced exposures, although such studies may prove useful for testing whether radio-resistant organisms predominate in such contaminated sites and whether resistance can change in response to altered background radiation levels.

The information that is derived from this quantitative meta-analysis will help us to understand the role of radiation in the balance between mutation, selection and evolution, a topic of general interest in the field of evolutionary genetics. Information on radio-tolerance may help to focus future research in an attempt to understand the role of radiation in contemporary ecological and evolutionary processes. Finally, this review attempts to provide baseline information concerning the potential consequences of nuclear accidents like those at Chernobyl and Fukushima.

II. METHODS

(1) Literature search

We conducted an extensive search for all scientific papers on natural levels of radiation, radioactivity, radio-tolerance and radio-resistance, using the *Web of Science* and *Google Scholar* and the key words 'radiation', 'radioactivity', 'radio-tolerance', 'radio-resistance' and 'high background radiation' combined with 'natural'. This was followed by subsequent searches for literature concerning natural radioactivity and 'mutation*', 'physiology', 'immunology' and 'disease'. We also attempted to find all papers that cited Grüneberg *et al*. (1966), Gopal-Ayengar *et al*. (1970), Ahuja *et al*. (1973), Barcinski *et al*. (1975), Kochupillai *et al*. (1976) and Pillai, Thangavelu & Ramalingaswami (1976), which are considered seminal papers in this field. We searched all reference lists in the resulting list of publications for further papers that could include relevant information. The inclusion criteria for all publications were that: (*i*) they compared at least one control population with a low level of background radiation and one population with high background radiation; (*ii*) they had test statistics that could be converted into effect sizes; and (*iii*) they reported background radiation levels for both control and irradiated populations. We examined more than 5000 papers to arrive at the 46 publications included in our meta-analysis. These publications had 373 effect sizes, or 8.1 effect sizes per publication. These were reduced to 66 effect sizes because some of the 46 publications reported effects on more than1 species. We excluded the extensive literature on radon because this literature has already been reviewed elsewhere (e.g. Lubin & Boice, 1997; Hendry *et al*., 2009), and its volume would swamp the fewer publications reviewed herein. We located 56 publications on radio-tolerant and radio-resistant

species within the initial 5000 papers. The cut-off date for inclusion of studies was 31 December 2011.

Because many of these papers were difficult to acquire through ordinary libraries, we have made available a directory containing copies of the papers used for this review of natural sources of radiation (http://cricket.biol.sc.edu/papers/natural/).

(2) Extracting data

We extracted test statistics (t, F, c^2) for all studies together with information on the number of populations under study (this was typically one high background radiation area and one control area) and the number of individuals studied. If no statistics were reported, we extracted means (S.E.M.) and conducted standard parametric tests for comparison of means, or we extracted all data and conducted regression analyses. If only a maximum probability value was reported, we conservatively estimated the Pearson correlation coefficient required for the given sample size to achieve the reported probability. If several effects were reported, we used the effect that controlled for confounding variables such as age or smoking in order to be conservative. In five studies included in the mean effect size calculations see Table 2 we conservatively used the number of populations rather than the number of subjects because the latter was not reported; in cases of cancer deaths (Körblein & Hoffmann, 2006) use of the size of the underlying total population would seriously distort our study findings towards the effect size in those studies. Therefore, for these five studies we used the number of populations to be conservative. Effect sizes estimated in the present review therefore are conservative. In total we obtained 373 effect-size estimates (Table 1).

For each effect we also extracted information on the trait involved and classified these into the following categories: disease; fecundity; immunology; morphology including dermatoglyphics; phenodeviants and developmental instability; mutation and DNA repair; physiology; and sex ratio. For each effect size we also extracted information on the mean level of background radiation and report these as mSv per year in Table 1. We assumed that 1 R = 10 mSv (Körblein & Hoffmann, 2006

(3) Meta-analysis

The test statistics were first transformed into Pearson product-moment correlation coefficients, using the equations reported by Rosenthal (1991). These correlation coefficients were then converted to z-transformed correlation coefficients (z_r) using Fisher's transformation. Based on z_r and the sample size of the study, we calculated an effect size for each study and category (see below) using MetaWin 2.1 for meta-analysis (Rosenberg, Adams & Gurevitch, 2000). Thus in a study with 10 effect sizes for 5 species, we calculated 5 effect sizes weighted by sample size using MetaWin as described below. Likewise, if a study reported an effect size for disease and immunology, we included mean and variance in effect size for these two categories in the analyses. We used MetaWin to calculate the mean effect size across all studies using an unstructured, random-effects model by using individual effect sizes and weighting these by sample size, while using resampling tests with 10000 iterations to determine confidence intervals for the mean effect size (Raudenbush, 1994). A random-effects model accounts for the fact that both true random components and sampling error affect effect sizes.

Because effects may differ among categories of study (disease, fecundity, immunology, morphology, mutation, physiology, sex ratio), we conducted a random-effects categorical meta-analysis to compare mean effects for these categories (Rosenberg *et al*., 2000).

We used mean effect size per study for each species relying on sample size N for the species in the study. This is equivalent to setting $r = 1$ (i.e. assuming that effects are not independent within a study) when calculating the mean effect so that the variance is not overly reduced by inflating N (Slatyer *et al*., 2011).

There was no *a priori* reason to expect that there would be any publication bias in the literature because 'negative' effects of radiation would be expected under the mutation hypothesis, while 'positive' effects would be expected under the hormesis hypothesis. We are unaware of any unpublished studies in this area despite having worked on biological effects of radiation for more than 20 years. We conducted four indirect tests of publication bias by estimating the Kendall rank order correlation coefficient between effect sizes and their variances, between effect size and sample size, and between effect size and year of publication (Begg & Mazumdar, 1994; Møller & Jennions, 2001; Jennions & Møller, 2002). Finally, we conducted a trim-and-fill test to estimate the effect of the apparently 'missing' studies that may have caused the asymmetry in effect size distributions (Duval & Tweedie, 2000*a*, *b*). We estimated the number of 'missing' studies using the L_o parameter in the 'trim and fill' method (Duval & Tweedie, 2000*a*, *b*), which assumes that a plot of effect size on sample size should be symmetric if there is no bias. We then re-calculated the mean effect after adding values for putative 'missing' studies.

Effect sizes can be judged using Cohen's (1988) rule of thumb that effects can be considered small, medium or large based on the proportion of variance that they explain in a sample (1, 9, or 25%, respectively). On average, the proportion of variance explained by main effects in meta-analyses in the biological sciences is only 5–10%, but for many published studies it is much lower (Møller & Jennions, 2002).

III. RESULTS

(1) Mean effect size and tests for publication bias

All effect sizes and their attributes are listed in Table 1; mean effect sizes and their confidence intervals are given in Table 2. Mean effect size across all studies was 0.093 (Fig. 1, Table 2;

Table 1. Effect sizes for studies of effects of natural levels of radiation on biological response variables

Species	Kingdom	Effect	Category	References	Confounding variables controlled	Test statistic	Direction of effect	Value of test statistic	r	N	No. populations	Radiation level (mSv/year)
Allium cepa	Plant	DNA damage assessed by comet assay	Mutation	Saghirzadeh *et al.* (2008)	1	r	1	0.936	0.936	13	13	87.60
Calotropis gigantea	Plant	Cytological abnormalities	Mutation	Gopal-Ayengar *et al.* (1970)	0	r	1	0.255	0.255	7	7	82.96
Crotalaria verrucosa	Plant	Cytological abnormalities	Mutation	Gopal-Ayengar *et al.* (1970)	0	r	1	0.894	0.894	5	5	82.96
Crotalaria verrucosa	Plant	Pollen sterility	Mutation	Gopal-Ayengar *et al.* (1970)	0	r	1	0.488	0.488	3	3	82.96
Croton bonplandianum	Plant	Cytological abnormalities	Mutation	Gopal-Ayengar *et al.* (1970)	0	r	1	0.124	0.124	9	9	82.96
Homo sapiens	Animal	Aneuploid cells	Mutation	Barcinski *et al.* (1975)	1	t	−1	0.029	−0.002	349	2	6.40
Homo sapiens	Animal	Chromatid aberrations	Mutation	Barcinski *et al.* (1975)	1	t	−1	1.580	−0.085	349	2	6.40
Homo sapiens	Animal	Deletions	Mutation	Barcinski *et al.* (1975)	1	t	1	2.550	0.136	349	2	6.40
Homo sapiens	Animal	Dicentrics	Mutation	Barcinski *et al.* (1975)	1	t	1	2.380	0.127	349	2	6.40
Homo sapiens	Animal	Rings	Mutation	Barcinski *et al.* (1975)	1	t	1	2.490	0.132	349	2	6.40
Homo sapiens	Animal	Chromatid aberrations	Mutation	Barcinski *et al.* (1975)	1	t	1	1.580	0.085	349	2	6.40
Homo sapiens	Animal	Total number of breaks	Mutation	Barcinski *et al.* (1975)	1	t	1	4.910	0.255	349	2	6.40
Homo sapiens	Animal	Variance smaller for three out of six dermatoglyphic traits in contaminated area	Morphology	Ahuja *et al.* (1973)	0	F	−1	1.450	−0.106	130	2	32.98
Homo sapiens	Animal	Variance smaller for three out of six dermatoglyphic traits in contaminated area	Morphology	Ahuja *et al.* (1973)	0	F	1	1.220	0.097	130	2	32.98
Homo sapiens	Animal	Variance smaller for three out of six dermatoglyphic traits in contaminated area	Morphology	Ahuja *et al.* (1973)	0	F	−1	1.340	−0.102	130	2	32.98
Homo sapiens	Animal	Variance smaller for three out of six dermatoglyphic traits in contaminated area	Morphology	Ahuja *et al.* (1973)	0	F	1	1.620	0.112	130	2	32.98
Homo sapiens	Animal	Variance smaller for three out of six dermatoglyphic traits in contaminated area	Morphology	Ahuja *et al.* (1973)	0	F	1	2.050	0.126	130	2	32.98

Table 1. *(Cont.)*

Species	Kingdom	Effect	Category	References	Confounding variables controlled	Test statistic	Direction of effect	Value of test statistic	r	N	No. populations	Radiation level (mSv/year)
Homo sapiens	Animal	Variance smaller for three out of six dermatoglyphic traits in contaminated area	Morphology	Ahuja *et al.* (1973)	0	F	−1	2.190	−0.130	130	2	32.98
Homo sapiens	Animal	Antioxidant levels reduced	Physiology	Attar *et al.* (2007)	1	t	1	27.990	0.943	100	4	260.00
Homo sapiens	Animal	Neutrophil activity	Immunology	Attar *et al.* (2007)	1	t	1	15.200	0.838	100	4	260.00
Homo sapiens	Animal	Phagocytosis	Immunology	Attar *et al.* (2007)	1	t	1	20.340	0.899	100	4	260.00
Homo sapiens	Animal	Locomotion of peripheral neutrophils	Immunology	Attar *et al.* (2007)	1	t	1	32.650	0.957	100	4	260.00
Homo sapiens	Animal	Interleukine-2	Immunology	Attar *et al.* (2007)	1	t	1	14.150	0.819	100	4	260.00
Homo sapiens	Animal	Interleukine-4	Immunology	Attar *et al.* (2007)	1	t	1	24.190	0.925	100	4	260.00
Homo sapiens	Animal	Interleukine-10	Immunology	Attar *et al.* (2007)	1	t	1	25.710	0.933	100	4	260.00
Homo sapiens	Animal	Interferon-gamma	Immunology	Attar *et al.* (2007)	1	t	−1	11.110	−0.747	100	4	260.00
Homo sapiens	Animal	Proliferation	Immunology	Attar *et al.* (2007)	1	t	−1	2.670	−0.260	100	4	260.00
Homo sapiens	Animal	Whorls, loops and arches	Morphology	Bhasin *et al.* (1980)	1	Chi-square	1	3.315	0.226	65	2	17.52
Homo sapiens	Animal	Whorls, loops and arches	Morphology	Bhasin *et al.* (1980)	1	Chi-square	1	4.304	0.257	65	2	17.52
Homo sapiens	Animal	Whorls, loops and arches	Morphology	Bhasin *et al.* (1980)	1	Chi-square	1	12.818	0.573	39	2	17.52
Homo sapiens	Animal	Whorls, loops and arches	Morphology	Bhasin *et al.* (1980)	1	Chi-square	1	0.480	0.099	49	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al.* (1980)	1	F	1	0.576	0.092	69	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al.* (1980)	1	F	−1	1.526	−0.149	69	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al.* (1980)	1	F	−1	1.017	−0.122	69	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al.* (1980)	1	F	1	0.681	0.100	69	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al.* (1980)	1	F	1	1.748	0.159	69	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al.* (1980)	1	F	−1	1.051	−0.124	69	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al.* (1980)	1	F	1	0.816	0.110	69	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al.* (1980)	1	F	−1	1.530	−0.149	69	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al.* (1980)	1	F	−1	1.069	−0.125	69	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al.* (1980)	1	F	−1	1.023	−0.123	69	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al.* (1980)	1	F	−1	1.100	−0.131	65	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al.* (1980)	1	F	−1	1.085	-0.130	65	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al.* (1980)	1	F	1	0.993	0.125	65	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al.* (1980)	1	F	−1	1.317	−0.143	65	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al.* (1980)	1	F	−1	2.137	−0.181	65	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al.* (1980)	1	F	1	0.724	0.103	69	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al.* (1980)	1	F	1	0.714	0.103	69	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al.* (1980)	1	F	1	0.461	0.083	69	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al.* (1980)	1	F	1	0.576	0.092	69	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al.* (1980)	1	F	1	0.714	0.103	69	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al.* (1980)	1	F	1	0.643	0.131	39	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al.* (1980)	1	F	1	0.484	0.114	39	2	17.52

Table 1. *(Cont.)*

Species	Kingdom	Effect	Category	References	Confounding variables controlled	Test statistic	Direction of effect	Value of test statistic	r	N	No. populations	Radiation level (mSv/year)
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al*. (1980)	1	F	1	0.385	0.101	39	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al*. (1980)	1	F	−1	1.303	−0.184	39	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al*. (1980)	1	F	1	0.415	0.105	39	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al*. (1980)	1	F	1	0.587	0.125	39	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al*. (1980)	1	F	1	0.962	0.159	39	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al*. (1980)	1	F	1	0.646	0.131	39	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al*. (1980)	1	F	1	0.368	0.099	39	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al*. (1980)	1	F	−1	1.188	−0.157	49	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al*. (1980)	1	F	−1	1.043	−0.147	49	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al*. (1980)	1	F	1	0.642	0.116	49	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al*. (1980)	1	F	1	0.565	0.109	49	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al*. (1980)	1	F	1	0.516	0.104	49	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al*. (1980)	1	F	1	0.664	0.118	49	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al*. (1980)	1	F	1	0.548	0.107	49	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al*. (1980)	1	F	1	0.587	0.111	49	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al*. (1980)	1	F	1	0.752	0.125	49	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al*. (1980)	1	F	1	0.575	0.110	49	2	17.52
Homo sapiens	Animal	Finger ridge count	Morphology	Bhasin *et al*. (1980)	1	F	1	0.924	0.139	49	2	17.52
Homo sapiens	Animal	Main line formulae	Morphology	Bhasin *et al*. (1980)	1	Chi-square	1	3.202	0.222	65	2	17.52
Homo sapiens	Animal	Main line formulae	Morphology	Bhasin *et al*. (1980)	1	Chi-square	1	0.241	0.061	65	2	17.52
Homo sapiens	Animal	Main line formulae	Morphology	Bhasin *et al*. (1980)	1	Chi-square	1	5.938	0.390	39	2	17.52
Homo sapiens	Animal	Main line formulae	Morphology	Bhasin *et al*. (1980)	1	Chi-square	1	2.199	0.212	49	2	17.52
Homo sapiens	Animal	Line D distribution	Morphology	Bhasin *et al*. (1980)	1	Chi-square	−1	0.966	−0.122	65	2	17.52
Homo sapiens	Animal	Line D distribution	Morphology	Bhasin *et al*. (1980)	1	Chi-square	−1	0.051	−0.028	65	2	17.52
Homo sapiens	Animal	Line D distribution	Morphology	Bhasin *et al*. (1980)	1	Chi-square	−1	0.702	−0.134	39	2	17.52
Homo sapiens	Animal	Line D distribution	Morphology	Bhasin *et al*. (1980)	1	Chi-square	1	6.365	0.360	49	2	17.52
Homo sapiens	Animal	Hypothenar	Morphology	Bhasin *et al*. (1980)	1	Chi-square	−1	0.024	−0.019	65	2	17.52
Homo sapiens	Animal	Hypothenar	Morphology	Bhasin *et al*. (1980)	1	Chi-square	−1	0.118	−0.043	65	2	17.52
Homo sapiens	Animal	Hypothenar	Morphology	Bhasin *et al*. (1980)	1	Chi-square	−1	2.669	−0.262	39	2	17.52
Homo sapiens	Animal	Hypothenar	Morphology	Bhasin *et al*. (1980)	1	Chi-square	1	5.929	0.348	49	2	17.52
Homo sapiens	Animal	Thenar I	Morphology	Bhasin *et al*. (1980)	1	Chi-square	−1	1.615	−0.158	65	2	17.52
Homo sapiens	Animal	Thenar I	Morphology	Bhasin *et al*. (1980)	1	Chi-square	−1	0.082	−0.036	65	2	17.52
Homo sapiens	Animal	Thenar I	Morphology	Bhasin *et al*. (1980)	1	Chi-square	−1	0.045	−0.034	39	2	17.52
Homo sapiens	Animal	Thenar I	Morphology	Bhasin *et al*. (1980)	1	Chi-square	−1	1.969	−0.200	49	2	17.52
Homo sapiens	Animal	Thenar II	Morphology	Bhasin *et al*. (1980)	1	Chi-square	−1	0.172	−0.051	65	2	17.52
Homo sapiens	Animal	Thenar II	Morphology	Bhasin *et al*. (1980)	1	Chi-square	−1	1.436	−0.149	65	2	17.52
Homo sapiens	Animal	Thenar II	Morphology	Bhasin *et al*. (1980)	1	Chi-square	−1	0.363	−0.096	39	2	17.52
Homo sapiens	Animal	Thenar II	Morphology	Bhasin *et al*. (1980)	1	Chi-square	−1	0.220	−0.067	49	2	17.52
Homo sapiens	Animal	Thenar III	Morphology	Bhasin *et al*. (1980)	1	Chi-square	−1	0.150	−0.048	65	2	17.52
Homo sapiens	Animal	Thenar III	Morphology	Bhasin *et al*. (1980)	1	Chi-square	−1	0.603	−0.096	65	2	17.52
Homo sapiens	Animal	Thenar III	Morphology	Bhasin *et al*. (1980)	1	Chi-square	−1	0.563	−0.120	39	2	17.52
Homo sapiens	Animal	Thenar III	Morphology	Bhasin *et al*. (1980)	1	Chi-square	−1	0.163	−0.058	49	2	17.52

Table 1. *(Cont.)*

Species	Kingdom	Effect	Category	References	Confounding variables controlled	Test statistic	Direction of effect	Value of test statistic	r	N	No. populations	Radiation level (mSv/year)
Homo sapiens	Animal	Thenar IV	Morphology	Bhasin *et al*. (1980)	1	Chi-square	−1	0.090	−0.037	65	2	17.52
Homo sapiens	Animal	Thenar IV	Morphology	Bhasin *et al*. (1980)	1	Chi-square	−1	0.688	−0.103	65	2	17.52
Homo sapiens	Animal	Thenar IV	Morphology	Bhasin *et al*. (1980)	1	Chi-square	−1	1.108	−0.169	39	2	17.52
Homo sapiens	Animal	Thenar IV	Morphology	Bhasin *et al*. (1980)	1	Chi-square	1	4.443	0.301	49	2	17.52
Homo sapiens	Animal	Interdigital ridge count a-b	Morphology	Bhasin *et al*. (1980)	1	*F*	1	0.846	0.115	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count b-c	Morphology	Bhasin *et al*. (1980)	1	*F*	−1	2.120	−0.180	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count c-d	Morphology	Bhasin *et al*. (1980)	1	*F*	1	0.639	0.100	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count a-d	Morphology	Bhasin *et al*. (1980)	1	*F*	1	0.828	0.114	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count d-t	Morphology	Bhasin *et al*. (1980)	1	*F*	−1	1.189	−0.136	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count angle atd	Morphology	Bhasin *et al*. (1980)	1	*F*	1	3.398	0.226	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count distance c-t	Morphology	Bhasin *et al*. (1980)	1	*F*	1	5.035	0.272	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count a-b	Morphology	Bhasin *et al*. (1980)	1	*F*	−1	1.453	−0.150	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count b-c	Morphology	Bhasin *et al*. (1980)	1	*F*	−1	2.053	−0.178	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count c-d	Morphology	Bhasin *et al*. (1980)	1	*F*	−1	1.529	−0.154	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count a-d	Morphology	Bhasin *et al*. (1980)	1	*F*	1	1.010	0.126	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count d-t	Morphology	Bhasin *et al*. (1980)	1	*F*	−1	1.335	−0.144	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count angle atd	Morphology	Bhasin *et al*. (1980)	1	*F*	1	3.172	0.219	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count distance c-t	Morphology	Bhasin *et al*. (1980)	1	*F*	1	3.667	0.235	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count a-b	Morphology	Bhasin *et al*. (1980)	1	*F*	1	0.874	0.117	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count b-c	Morphology	Bhasin *et al*. (1980)	1	*F*	−1	1.613	−0.158	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count c-d	Morphology	Bhasin *et al*. (1980)	1	*F*	−1	0.965	−0.123	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count a-d	Morphology	Bhasin *et al*. (1980)	1	*F*	1	0.511	0.090	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count d-t	Morphology	Bhasin *et al*. (1980)	1	*F*	1	0.396	0.079	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count angle atd	Morphology	Bhasin *et al*. (1980)	1	*F*	−1	0.497	−0.088	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count distance c-t	Morphology	Bhasin *et al*. (1980)	1	*F*	−1	0.371	−0.077	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count a-b	Morphology	Bhasin *et al*. (1980)	1	*F*	−1	2.186	−0.183	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count b-c	Morphology	Bhasin *et al*. (1980)	1	*F*	−1	0.973	−0.123	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count c-d	Morphology	Bhasin *et al*. (1980)	1	*F*	1	0.699	0.105	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count a-d	Morphology	Bhasin *et al*. (1980)	1	*F*	1	0.308	0.070	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count d-t	Morphology	Bhasin *et al*. (1980)	1	*F*	−1	1.043	−0.128	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count angle atd	Morphology	Bhasin *et al*. (1980)	1	*F*	−1	0.653	−0.101	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count distance c-t	Morphology	Bhasin *et al*. (1980)	1	*F*	1	0.736	0.107	65	2	17.52
Homo sapiens	Animal	Interdigital ridge count a-b	Morphology	Bhasin *et al*. (1980)	1	*F*	−1	1.201	−0.177	39	2	17.52

Table 1. *(Cont.)*

Species	Kingdom	Effect	Category	References	Confounding variables controlled	Test statistic	Direction of effect	Value of test statistic	r	N	No. populations	Radiation level (mSv/year)
Homo sapiens	Animal	Interdigital ridge count b-c	Morphology	Bhasin *et al*. (1980)	1	F	−1	1.327	−0.186	39	2	17.52
Homo sapiens	Animal	Interdigital ridge count c-d	Morphology	Bhasin *et al*. (1980)	1	F	1	0.651	0.131	39	2	17.52
Homo sapiens	Animal	Interdigital ridge count a-d	Morphology	Bhasin *et al*. (1980)	1	F	−1	1.027	−0.164	39	2	17.52
Homo sapiens	Animal	Interdigital ridge count d-t	Morphology	Bhasin *et al*. (1980)	1	F	1	0.132	0.060	39	2	17.52
Homo sapiens	Animal	Interdigital ridge count angle atd	Morphology	Bhasin *et al*. (1980)	1	F	1	1.305	0.185	39	2	17.52
Homo sapiens	Animal	Interdigital ridge count distance c-t	Morphology	Bhasin *et al*. (1980)	1	F	−1	0.353	−0.097	39	2	17.52
Homo sapiens	Animal	Interdigital ridge count a-b	Morphology	Bhasin *et al*. (1980)	1	F	1	0.361	0.098	39	2	17.52
Homo sapiens	Animal	Interdigital ridge count b-c	Morphology	Bhasin *et al*. (1980)	1	F	−1	1.378	−0.189	39	2	17.52
Homo sapiens	Animal	Interdigital ridge count c-d	Morphology	Bhasin *et al*. (1980)	1	F	−1	1.311	−0.185	39	2	17.52
Homo sapiens	Animal	Interdigital ridge count a-d	Morphology	Bhasin *et al*. (1980)	1	F	−1	1.073	−0.168	39	2	17.52
Homo sapiens	Animal	Interdigital ridge count d-t	Morphology	Bhasin *et al*. (1980)	1	F	1	0.300	0.090	39	2	17.52
Homo sapiens	Animal	Interdigital ridge count angle atd	Morphology	Bhasin *et al*. (1980)	1	F	1	0.437	0.108	39	2	17.52
Homo sapiens	Animal	Interdigital ridge count distance c-t	Morphology	Bhasin *et al*. (1980)	1	F	1	0.812	0.147	39	2	17.52
Homo sapiens	Animal	Interdigital ridge count a-b	Morphology	Bhasin *et al*. (1980)	1	F	−1	0.983	−0.143	49	2	17.52
Homo sapiens	Animal	Interdigital ridge count b-c	Morphology	Bhasin *et al*. (1980)	1	F	−1	1.741	−0.189	49	2	17.52
Homo sapiens	Animal	Interdigital ridge count c-d	Morphology	Bhasin *et al*. (1980)	1	F	1	0.832	0.132	49	2	17.52
Homo sapiens	Animal	Interdigital ridge count a-d	Morphology	Bhasin *et al*. (1980)	1	F	1	0.735	0.124	49	2	17.52
Homo sapiens	Animal	Interdigital ridge count d-t	Morphology	Bhasin *et al*. (1980)	1	F	1	0.310	0.081	49	2	17.52
Homo sapiens	Animal	Interdigital ridge count angle atd	Morphology	Bhasin *et al*. (1980)	1	F	−1	0.606	−0.113	49	2	17.52
Homo sapiens	Animal	Interdigital ridge count distance c-t	Morphology	Bhasin *et al*. (1980)	1	F	−1	0.566	−0.109	49	2	17.52
Homo sapiens	Animal	Interdigital ridge count a-b	Morphology	Bhasin *et al*. (1980)	1	F	−1	2.179	−0.210	49	2	17.52
Homo sapiens	Animal	Interdigital ridge count b-c	Morphology	Bhasin *et al*. (1980)	1	F	−1	2.462	−0.223	49	2	17.52
Homo sapiens	Animal	Interdigital ridge count c-d	Morphology	Bhasin *et al*. (1980)	1	F	1	0.747	0.125	49	2	17.52
Homo sapiens	Animal	Interdigital ridge count a-d	Morphology	Bhasin *et al*. (1980)	1	F	−1	1.525	−0.177	49	2	17.52
Homo sapiens	Animal	Interdigital ridge count d-t	Morphology	Bhasin *et al*. (1980)	1	F	1	0.601	0.112	49	2	17.52
Homo sapiens	Animal	Interdigital ridge count angle atd	Morphology	Bhasin *et al*. (1980)	1	F	−1	0.682	−0.120	49	2	17.52
Homo sapiens	Animal	Interdigital ridge count distance c-t	Morphology	Bhasin *et al*. (1980)	1	F	−1	0.736	−0.124	49	2	17.52
Homo sapiens	Animal	SRBC right S1	Morphology	Bhasin *et al*. (1982)	1	Chi-square	−1	2.340	−0.190	130	2	15.00
Homo sapiens	Animal	SRBC right S2	Morphology	Bhasin *et al*. (1982)	1	Chi-square	1	1.231	0.134	130	2	15.00
Homo sapiens	Animal	SRBC right S3	Morphology	Bhasin *et al*. (1982)	1	Chi-square	−1	0.062	−0.031	130	2	15.00
Homo sapiens	Animal	SRBC right S4	Morphology	Bhasin *et al*. (1982)	1	Chi-square	1	2.489	0.196	130	2	15.00
Homo sapiens	Animal	SRBC right S5	Morphology	Bhasin *et al*. (1982)	1	Chi-square	−1	0.303	−0.068	130	2	15.00
Homo sapiens	Animal	SRBC left S1	Morphology	Bhasin *et al*. (1982)	1	Chi-square	−1	0.207	−0.056	130	2	15.00

Table 1. *(Cont.)*

Species	Kingdom	Effect	Category	References	Confounding variables controlled	Test statistic	Direction of effect	Value of test statistic	r	N	No. populations	Radiation level (mSv/year)
Homo sapiens	Animal	SRBC left S2	Morphology	Bhasin *et al*. (1982)	1	Chi-square	−1	0.381	−0.077	130	2	15.00
Homo sapiens	Animal	SRBC Left S3	Morphology	Bhasin *et al*. (1982)	1	Chi-square	−1	0.088	−0.037	130	2	15.00
Homo sapiens	Animal	SRBC left S4	Morphology	Bhasin *et al*. (1982)	1	Chi-square	1	1.868	0.170	130	2	15.00
Homo sapiens	Animal	SRBC Left S5	Morphology	Bhasin *et al*. (1982)	1	Chi-square	1	0.000	0.000	130	2	15.00
Homo sapiens	Animal	DRBC right S1	Morphology	Bhasin *et al*. (1982)	1	Chi-square	−1	0.383	−0.108	130	2	15.00
Homo sapiens	Animal	DRBC right S2	Morphology	Bhasin *et al*. (1982)	1	Chi-square	1	0.000	0.000	130	2	15.00
Homo sapiens	Animal	DRBC right S3	Morphology	Bhasin *et al*. (1982)	1	Chi-square	−1	0.992	−0.152	130	2	15.00
Homo sapiens	Animal	DRBC right S4	Morphology	Bhasin *et al*. (1982)	1	Chi-square	−1	0.273	−0.065	130	2	15.00
Homo sapiens	Animal	DRBC right S5	Morphology	Bhasin *et al*. (1982)	1	Chi-square	1	0.000	0.000	130	2	15.00
Homo sapiens	Animal	DRBC left S1	Morphology	Bhasin *et al*. (1982)	1	Chi-square	1	0.000	0.000	130	2	15.00
Homo sapiens	Animal	DRBC left S2	Morphology	Bhasin *et al*. (1982)	1	Chi-square	1	0.000	0.000	130	2	15.00
Homo sapiens	Animal	DRBC left S3	Morphology	Bhasin *et al*. (1982)	1	Chi-square	−1	0.656	−0.050	130	2	15.00
Homo sapiens	Animal	DRBC left S4	Morphology	Bhasin *et al*. (1982)	1	Chi-square	−1	0.004	−0.008	130	2	15.00
Homo sapiens	Animal	DRBC left S5	Morphology	Bhasin *et al*. (1982)	1	Chi-square	1	0.000	0.000	130	2	15.00
Homo sapiens	Animal	DRBC right S6	Morphology	Bhasin *et al*. (1982)	1	Chi-square	1	0.000	0.000	130	2	15.00
Homo sapiens	Animal	DRBC left S6	Morphology	Bhasin *et al*. (1982)	1	Chi-square	1	0.000	0.000	130	2	15.00
Homo sapiens	Animal	TRBC right	Morphology	Bhasin *et al*. (1982)	1	Chi-square	−1	0.010	−0.012	130	2	15.00
Homo sapiens	Animal	TRBC left	Morphology	Bhasin *et al*. (1982)	1	Chi-square	−1	0.010	−0.012	130	2	15.00
Homo sapiens	Animal	Cancer rate	Disease	Binu *et al*. (2005)	1	r	1	0.100	0.100	205	2	82.96
Homo sapiens	Animal	Lymphocyte chromosomal aberrations dicentrics and rings	Mutation	Chen & Wei (1991)	1	t	1	1.867	0.128	210	2	3.30
Homo sapiens	Animal	Lymphocyte chromosomal aberrations dicentrics and rings	Mutation	Chen & Wei (1991)	1	t	1	3.294	0.216	224	2	3.30
Homo sapiens	Animal	Lymphocyte chromosomal aberrations translocations and inversions	Mutation	Chen & Wei (1991)	1	t	1	2.000	0.137	210	2	3.30
Homo sapiens	Animal	Lymphocyte chromosomal aberrations translocations and inversions	Mutation	Chen & Wei (1991)	1	t	1	2.667	0.176	224	2	3.30
Homo sapiens	Animal	Lymphocyte chromosomal aberrations dicentrics and rings	Mutation	Chen & Wei (1991)	1	t	1	0.105	0.007	221	2	3.30
Homo sapiens	Animal	Lymphocyte chromosomal aberrations dicentrics and rings	Mutation	Chen & Wei (1991)	1	t	1	2.933	0.227	161	2	3.30
Homo sapiens	Animal	Lymphocyte chromosomal aberrations translocations and inversions	Mutation	Chen & Wei (1991)	1	t	1	4.210	0.279	212	2	3.30

Table 1. *(Cont.)*

Species	Kingdom	Effect	Category	References	Confounding variables controlled	Test statistic	Direction of effect	Value of test statistic	r	N	No. populations	Radiation level (mSv/year)
Homo sapiens	Animal	Lymphocyte chromosomal aberrations translocations and inversions	Mutation	Chen & Wei (1991)	1	t	1	3.250	0.219	212	2	3.30
Homo sapiens	Animal	Cancer mortality	Disease	Chen & Wei (1991)	1	r	−1	.—	0.000	1035410	2	3.30
Homo sapiens	Animal	Cancer mortality	Disease	Chen & Wei (1991)	1	r	−1	.—	0.001	968429	2	3.30
Homo sapiens	Animal	Mitotic cell divisions	Mutation	Chen & Wei (1991)	1	t	1	2.090	0.135	239	2	3.30
Homo sapiens	Animal	Mitotic cell divisions	Mutation	Chen & Wei (1991)	1	t	1	4.920	0.359	166	2	3.30
Homo sapiens	Animal	Mitotic cell divisions	Mutation	Chen & Wei (1991)	1	t	1	1.600	0.140	130	2	3.30
Homo sapiens	Animal	Unscheduled DNA synthesis	Mutation	Chen & Wei (1991)	1	t	1	0.910	0.133	48	2	3.30
Homo sapiens	Animal	Unscheduled DNA synthesis	Mutation	Chen & Wei (1991)	1	t	1	1.568	0.324	23	2	3.30
Homo sapiens	Animal	Unscheduled DNA synthesis	Mutation	Chen & Wei (1991)	1	t	1	1.242	0.203	38	2	3.30
Homo sapiens	Animal	Unscheduled DNA synthesis	Mutation	Chen & Wei (1991)	1	t	1	1.960	0.359	28	2	3.30
Homo sapiens	Animal	Chromosomal aberrations dicentrics	Mutation	Cheriyan *et al.* (1999)	1	t	−1	0.056	−0.001	10230	2	35.00
Homo sapiens	Animal	Chromosomal aberrations translocations	Mutation	Cheriyan *et al.* (1999)	1	t	1	1.250	0.012	10230	2	35.00
Homo sapiens	Animal	Chromosomal aberrations inversions	Mutation	Cheriyan *et al.* (1999)	1	t	−1	1.000	−0.010	10230	2	35.00
Homo sapiens	Animal	Chromosomal aberrations centric fragments	Mutation	Cheriyan *et al.* (1999)	1	t	1	2.800	0.028	10230	2	35.00
Homo sapiens	Animal	Chromosomal aberrations acentric fragments	Mutation	Cheriyan *et al.* (1999)	1	t	−1	4.060	−0.040	10230	2	35.00
Homo sapiens	Animal	Chromosomal aberrations minutes	Mutation	Cheriyan *et al.* (1999)	1	t	1	0.000	0.000	10230	2	35.00
Homo sapiens	Animal	Chromosomal aberrations multiple aberrations	Mutation	Cheriyan *et al.* (1999)	1	t	1	2.200	0.022	10230	2	35.00
Homo sapiens	Animal	Chromosomal aberrations chromosome breaks	Mutation	Cheriyan *et al.* (1999)	1	t	−1	4.900	−0.048	10230	2	35.00
Homo sapiens	Animal	Chromosomal aberrations chromosome gaps	Mutation	Cheriyan *et al.* (1999)	1	t	−1	3.430	−0.034	10230	2	35.00
Homo sapiens	Animal	Chromosomal aberrations chromatid breaks	Mutation	Cheriyan *et al.* (1999)	1	t	−1	2.000	−0.020	10230	2	35.00
Homo sapiens	Animal	Chromosomal aberrations chromatid gaps	Mutation	Cheriyan *et al.* (1999)	1	t	−1	3.230	−0.032	10230	2	35.00
Homo sapiens	Animal	Chromosomal aberrations polyploids	Mutation	Cheriyan *et al.* (1999)	1	t	1	2.150	0.021	10230	2	35.00
Homo sapiens	Animal	Chromosomal aberrations endoreplications	Mutation	Cheriyan *et al.* (1999)	1	t	−1	0.820	−0.008	10230	2	35.00

Table 1. *(Cont.)*

Species	Kingdom	Effect	Category	References	Confounding variables controlled	Test statistic	Direction of effect	Value of test statistic	r	N	No. populations	Radiation level (mSv/year)
Homo sapiens	Animal	Chromosomal aberrations autosomal trisomies	Mutation	Cheriyan *et al.* (1999)	1	t	−1	1.140	−0.009	16169	2	35.00
Homo sapiens	Animal	Chromosomal aberrations 48 XXY + 21	Mutation	Cheriyan *et al.* (1999)	1	t	1	1.290	0.010	16169	2	35.00
Homo sapiens	Animal	Chromosomal aberrations 48 XXY + 21 + centric fragments	Mutation	Cheriyan *et al.* (1999)	1	t	−1	0.180	−0.001	16169	2	35.00
Homo sapiens	Animal	Chromosomal aberrations sex chromosomal	Mutation	Cheriyan *et al.* (1999)	1	t	1	1.310	0.010	16169	2	35.00
Homo sapiens	Animal	Chromosomal aberrations deletions	Mutation	Cheriyan *et al.* (1999)	1	t	−1	2.760	−0.022	16169	2	35.00
Homo sapiens	Animal	Chromosomal aberrations inversions	Mutation	Cheriyan *et al.* (1999)	1	t	1	1.210	0.010	16169	2	35.00
Homo sapiens	Animal	Chromosomal aberrations Robertsonian translocations	Mutation	Cheriyan *et al.* (1999)	1	t	1	1.210	0.010	16169	2	35.00
Homo sapiens	Animal	Chromosomal aberrations other translocations	Mutation	Cheriyan *et al.* (1999)	1	t	−1	0.140	−0.001	16169	2	35.00
Homo sapiens	Animal	Frequency of micronuclei	Mutation	Das & Karuppasamy (2009)	1	t	−1	0.003	−0.004	271	2	4.00
Homo sapiens	Animal	Telomere length	Physiology	Das *et al.* (2009)	1	t	−1	0.880	−0.050	310	2	4.00
Homo sapiens	Animal	Mitochondrial DNA mutations	Mutation	Forster *et al.* (2002)	1	Chi-square	1	8.983	0.097	795	2	11.00
Homo sapiens	Animal	Surface proteins CD4+/CD69+ on T helper cells unstimulated	Immunology	Ghiassi-Nejad *et al.* (2004)	1	t	−1	1.020	−0.115	80	2	13.00
Homo sapiens	Animal	Surface proteins CD8+/CD69+ on T helper cells unstimulated	Immunology	Ghiassi	1	t	1	0.000	0.000	80	2	13.00
Homo sapiens	Animal	Surface proteins CD4+/CD69+ on T helper cells stimulated	Immunology	Ghiassi	1	t	1	2.200	0.242	80	2	13.00
Homo sapiens	Animal	Surface proteins CD8+/CD69+ on T helper cells stimulated	Immunology	Ghiassi	1	t	1	0.520	0.059	80	2	13.00
Homo sapiens	Animal	Percentage stable cell aberrations	Mutation	Ghiassi	1	t	1	2.690	0.291	80	2	13.00
Homo sapiens	Animal	Percentage unstable cell aberrations	Mutation	Ghiassi	1	t	1	1.762	0.196	80	2	13.00
Homo sapiens	Animal	Chromosomal aberrations	Mutation	Hayata *et al.* (2000)	1	r	−1	0.100	0.100	17	2	3.12

Table 1. *(Cont.)*

Species	Kingdom	Effect	Category	References	Confounding variables controlled	Test statistic	Direction of effect	Value of test statistic	r	N	No. populations	Radiation level (mSv/year)
Homo sapiens	Animal	Chromosomal aberrations dicentric and ring chromosomes	Mutation	Hayata *et al*. (2004)	1	r	1	0.410	0.410	39	2	3.11
Homo sapiens	Animal	Chromosomal aberrations	Mutation	Hayata *et al*. (2004)	1	t	1	5.182	0.544	66	2	3.11
Homo sapiens	Animal	Congenital malformations	Morphology	Jaikrishan *et al*. (1999)	1	Chi-square	1	0.349	0.004	36805	2	2.84
Homo sapiens	Animal	Stillbirths	Mutation	Jaikrishan *et al*. (1999)	1	Chi-square	1	1.040	0.008	36805	2	2.84
Homo sapiens	Animal	Male cancer rate	Disease	Jayalekshmi *et al*. (2005)	1	r	1	0.022	0.022	179810	12	1.72
Homo sapiens	Animal	Female cancer rate	Disease	Jayalekshmi *et al*. (2005)	1	r	−1	0.169	0.169	179810	12	1.72
Homo sapiens	Animal	Chromosomal aberrations with fragments	Mutation	Jiang *et al*. (2000)	1	F	1	5.823	0.365	40	2	149.00
Homo sapiens	Animal	Chromosomal aberrations without fragments	Mutation	Jiang *et al*. (2000)	1	F	1	3.669	0.297	40	2	149.00
Homo sapiens	Animal	Down's syndrome	Disease	Kochupillai *et al*. (1976)	0	Chi-square	1	4.480	0.870	12	2	22.50
Homo sapiens	Animal	Chromatid aberrations	Mutation	Kochupillai *et al*. (1976)	0	Chi-square	1	2.058	0.220	85	2	22.50
Homo sapiens	Animal	Chromosome aberrations	Mutation	Kochupillai *et al*. (1976)	0	Chi-square	1	10.527	0.498	85	2	22.50
Homo sapiens	Animal	Severe mental retardation	Disease	Kochupillai *et al*. (1976)	0	Chi-square	1	4.880	0.613	13	2	22.50
Homo sapiens	Animal	Cancer mortality	Disease	Körblein & Hoffmann (2006)	1	t	1	3.289	0.321	96	96	0.67
Homo sapiens	Animal	Child mortality	Disease	Körblein & Hoffmann (2006)	1	t	1	3.223	0.315	96	96	0.67
Homo sapiens	Animal	Initial DNA damage	Mutation	Masoomi *et al*. (2006)	1	F	1	27.627	0.529	73	3	10.20
Homo sapiens	Animal	Induced DNA damage	Mutation	Masoomi *et al*. (2006)	1	F	1	128.407	0.802	73	3	10.20
Homo sapiens	Animal	Vitamin C in plasma	Physiology	Masoomi *et al*. (2006)	1	t	1	1.200	0.020	73	3	10.20
Homo sapiens	Animal	Vitamin C in urine	Physiology	Masoomi *et al*. (2006)	1	t	−1	1.840	0.046	73	3	10.20
Homo sapiens	Animal	Number of micronuclei before irradiation	Mutation	Mohammadi *et al*. (2006)	0	t	−1	0.832	−0.164	27	2	13.00
Homo sapiens	Animal	No. micronuclei after irradiation	Mutation	Mohammadi *et al*. (2006)	0	t	−1	2.905	−0.502	27	2	13.00

Table 1. *(Cont.)*

Species	Kingdom	Effect	Category	References	Confounding variables controlled	Test statistic	Direction of effect	Value of test statistic	r	N	No. populations	Radiation level (mSv/year)
Homo sapiens	Animal	Cell apoptosis before irradiation	Mutation	Mohammadi *et al.* (2006)	0	t	−1	0.668	−0.132	27	2	13.00
Homo sapiens	Animal	Cell apoptosis after irradiation	Mutation	Mohammadi *et al.* (2006)	0	t	1	4.261	0.649	27	2	13.00
Homo sapiens	Animal	DNA damage before irradiation	Mutation	Mohammadi *et al.* (2006)	0	t	1	10.074	0.896	27	2	13.00
Homo sapiens	Animal	DNA damage after irradiation	Mutation	Mohammadi *et al.* (2006)	0	t	1	8.856	0.871	27	2	13.00
Homo sapiens	Animal	Residual DNA damage after irradiation	Mutation	Mohammadi *et al.* (2006)	0	t	1	8.442	0.860	27	2	13.00
Homo sapiens	Animal	Residual DNA damage after irradiation	Mutation	Mohammadi *et al.* (2006)	0	t	1	5.491	0.739	27	2	13.00
Homo sapiens	Animal	DNA repaired	Mutation	Mohammadi *et al.* (2006)	0	t	1	4.467	0.666	27	2	13.00
Homo sapiens	Animal	Cancer rate	Disease	Monfared *et al.* (2010)	0	r	−1	0.430	−0.430	184	184	0.53
Homo sapiens	Animal	Chromosome aberrations per cell	Mutation	Mortazavi & Karam (2005)	0	t	1	1.725	0.288	35	2	13.00
Homo sapiens	Animal	Chromosome aberrations per cell after exposure to 1.5 Gy	Mutation	Mortazavi & Karam (2005)	0	t	1	5.273	0.676	35	2	13.00
Homo sapiens	Animal	Chromosome aberrations per cell	Mutation	Mortazavi *et al.* (2005)	0	t	1	16.667	0.931	45	2	1.36
Homo sapiens	Animal	Chromosome aberrations per cell after exposure to 2 Gy gamma rays	Mutation	Mortazavi *et al.* (2005)	0	t	−1	15.241	−0.919	45	2	1.36
Homo sapiens	Animal	Chromosome aberrations per cell	Mutation	Mortazavi *et al.* (2005)	0	t	−1	0.625	−0.194	12	2	1.36
Homo sapiens	Animal	Chromosome aberrations per cell after exposure to 1.5 Gy	Mutation	Mortazavi *et al.* (2005)	0	t	−1	9.213	−0.946	12	2	1.36
Homo sapiens	Animal	Cancer rates	Disease	Nair *et al.* (1999)	0	r	−1	0.068	0.068	195962	2	2.03
Homo sapiens	Animal	Cancer rates women	Disease	Nair *et al.* (1999)	0	r	−1	0.057	0.057	198848	2	2.03
Homo sapiens	Animal	Chromosomal and Down syndrome	Mutation	Padmanabhan *et al.* (2004)	1	Chi-square	1	4.310	0.008	62914	2	5.63
Homo sapiens	Animal	Autosomal dominant anomalies	Mutation	Padmanabhan *et al.* (2004)	1	Chi-square	1	6.270	0.010	62914	2	5.63
Homo sapiens	Animal	De novo cases of autosomal dominant anomalies	Mutation	Padmanabhan *et al.* (2004)	1	Chi-square	1	0.940	0.004	62914	2	5.63
Homo sapiens	Animal	Autosomal and X-linked recessives	Mutation	Padmanabhan *et al.* (2004)	1	Chi-square	1	9.096	0.012	62914	2	5.63

Table 1. *(Cont.)*

Species	Kingdom	Effect	Category	References	Confounding variables controlled	Test statistic	Direction of effect	Value of test statistic	r	N	No. populations	Radiation level (mSv/year)
Homo sapiens	Animal	Congenital anomalies	Morphology	Padmanabhan *et al.* (2004)	1	Chi-square	1	0.600	0.003	62914	2	5.63
Homo sapiens	Animal	Multifactorial anomalies	Morphology	Padmanabhan *et al.* (2004)	1	Chi-square	1	7.010	0.011	62914	2	5.63
Homo sapiens	Animal	All thyroid swellings	Disease	Pillai *et al.* (1976)	0	Chi-square	1	0.128	0.023	250	2	15.00
Homo sapiens	Animal	All nodular swellings	Disease	Pillai *et al.* (1976)	0	Chi-square	−1	2.777	0.023	250	2	15.00
Homo sapiens	Animal	Uninodular swellings	Disease	Pillai *et al.* (1976)	0	Chi-square	1	0.128	0.001	250	2	15.00
Homo sapiens	Animal	Number of copies of the sex determining SRY gene	Mutation	Premi *et al.* (2009)	1	r	1	0.579	0.579	21	2	2.03
Homo sapiens	Animal	Gene expression of sex determining SRY gene	Mutation	Premi *et al.* (2009)	1	r	1	0.526	0.526	21	2	9.00
Homo sapiens	Animal	Number of micro-deletions	Mutation	Premi *et al.* (2009)	1	Chi-square	1	1052.971	0.945	1180	3	2.03
Homo sapiens	Animal	DBY1 and DBY2 genes on the Y chromosome	Mutation	Premi *et al.* (2009)	1	Chi-square	1	227.780	0.439	1180	3	2.03
Homo sapiens	Animal	Microdeletions	Mutation	Premi *et al.* (2009)	1	Chi-square	1	583.790	0.703	1180	3	2.03
Homo sapiens	Animal	Extra amplicons for parts of their genomes	Mutation	Premi *et al.* (2009)	1	Chi-square	1	1144.208	0.985	1180	3	2.03
Homo sapiens	Animal	Gene duplication of Y chromosome	Mutation	Premi *et al.* (2009)	1	Chi-square	1	643.246	0.738	1180	3	2.03
Homo sapiens	Animal	Loss of Y chromosome	Mutation	Premi *et al.* (2009)	1	Chi-square	1	15.550	0.115	1180	3	2.03
Homo sapiens	Animal	Sex ratio	Sex ratio	Saadat (2003)	1	Chi-square	1	0.950	0.007	21857	2	13.00
Homo sapiens	Animal	Sex ratio	Sex ratio	Saadat (2003)	0	Chi-square	−1	0.130	0.001	261509	2	13.00
Homo sapiens	Animal	Down's syndrome	Disease	Sundaram (1977)	1	Chi-square	1	2.800	0.483	12	2	22.50
Homo sapiens	Animal	Down's syndrome	Disease	Tao & Wei (1986)	1	Chi-square	1	2.821	0.010	26512	2	3.36
Homo sapiens	Animal	T-lymphocyte count	Immunology	Tao & Wei (1986)	1	t	1	0.129	0.000	168	2	3.36
Homo sapiens	Animal	Cell proliferation	Immunology	Tao & Wei (1986)	1	t	1	1.661	0.016	168	2	3.36
Homo sapiens	Animal	Morphological transformation rate of lymphocytes	Immunology	Tao & Wei (1986)	1	t	1	3.835	0.024	592	2	3.36
Homo sapiens	Animal	31 hereditary diseases	Disease	Tao & Wei (1986)	1	Chi-square	1	0.002	0.000	26512	2	3.36
Homo sapiens	Animal	B-lymphocyte count	Immunology	Tao & Wei (1986)	1	t	1	2.150	0.012	166	2	3.36
Homo sapiens	Animal	Cancer rates	Disease	Tao *et al.* (2000)	1	t	−1	0.145	0.000	393	2	6.40
Homo sapiens	Animal	Down's syndrome	Disease	Thampi *et al.* (2005)	1	Chi-square	1	6.085	0.098	632	2	82.96
Homo sapiens	Animal	Malformations	Mutation	Thampi *et al.* (2005)	1	Chi-square	−1	2.080	−0.033	1869	2	82.96
Homo sapiens	Animal	Stillbirths	Mutation	Thampi *et al.* (2005)	1	Chi-square	−1	0.000	−0.003	470	2	82.96
Homo sapiens	Animal	Karyotype anomalies	Mutation	Thampi *et al.* (2005)	1	t	−1	0.282	−0.002	23844	2	82.96

Table 1. *(Cont.)*

Species	Kingdom	Effect	Category	References	Confounding variables controlled	Test statistic	Direction of effect	Value of test statistic	r	N	No. populations	Radiation level (mSv/year)
Homo sapiens	Animal	Age-adjusted liver cancer incidence linear model for men	Disease	Ujeno (1983)	1	r	1	0.659	0.659	13	13	1.05
Homo sapiens	Animal	Standardized mortality ratio of leukemia for men	Disease	Ujeno (1983)	1	r	−1	0.211	−0.211	46	46	1.05
Homo sapiens	Animal	Stomach cancer mortality in male population aged more than 40 years	Disease	Ujeno (1983)	1	r	1	0.802	0.802	649	649	1.05
Homo sapiens	Animal	Age-adjusted liver cancer incidence exponential model for men	Disease	Ujeno (1983)	1	r	1	0.694	0.694	13	13	1.05
Homo sapiens	Animal	Standardized mortality ratio of leukemia for women	Disease	Ujeno (1983)	1	r	1	0.110	0.110	46	46	1.05
Homo sapiens	Animal	Cancer as a cause of death	Disease	Veiga & Koifman (2005)	0	t	1	0.000	0.000	479	2	2.40
Homo sapiens	Animal	Oesophagus cancer as a cause of death	Disease	Veiga & Koifman (2005)	0	t	−1	2.119	−0.480	17	2	2.40
Homo sapiens	Animal	Stomach cancer as a cause of death	Disease	Veiga & Koifman (2005)	0	t	−1	1.524	−0.234	42	2	2.40
Homo sapiens	Animal	Larynx cancer as a cause of death	Disease	Veiga & Koifman (2005)	0	t	−1	0.091	−0.034	9	2	2.40
Homo sapiens	Animal	Lung cancer as a cause of death	Disease	Veiga & Koifman (2005)	0	t	−1	1.372	−0.226	37	2	2.40
Homo sapiens	Animal	Female breast cancer as a cause of death	Disease	Veiga & Koifman (2005)	0	t	−1	1.156	−0.245	23	2	2.40
Homo sapiens	Animal	Prostrate cancer as a cause of death	Disease	Veiga & Koifman (2005)	0	t	1	1.206	0.205	35	2	2.40
Homo sapiens	Animal	Leukaemia as a cause of death	Disease	Veiga & Koifman (2005)	0	t	1	0.000	0.000	19	2	2.40
Homo sapiens	Animal	Cancer as a cause of death	Disease	Veiga & Koifman (2005)	0	t	1	10.045	0.287	1122	2	3.40
Homo sapiens	Animal	Oesophagus cancer as a cause of death	Disease	Veiga & Koifman (2005)	0	t	1	2.541	−0.421	32	2	3.40
Homo sapiens	Animal	Stomach cancer as a cause of death	Disease	Veiga & Koifman (2005)	0	t	−1	3.121	0.263	133	2	3.40
Homo sapiens	Animal	Larynx cancer as a cause of death	Disease	Veiga & Koifman (2005)	0	t	1	0.761	0.172	21	2	3.40
Homo sapiens	Animal	Lung cancer as a cause of death	Disease	Veiga & Koifman (2005)	0	t	1	2.660	0.245	113	2	3.40
Homo sapiens	Animal	Female breast cancer as a cause of death	Disease	Veiga & Koifman (2005)	0	t	1	3.155	0.340	78	2	3.40

Table 1. *(Cont.)*

Species	Kingdom	Effect	Category	References	Confounding variables controlled	Test statistic	Direction of effect	Value of test statistic	r	N	No. populations	Radiation level (mSv/year)
Homo sapiens	Animal	Prostrate cancer as a cause of death	Disease	Veiga & Koifman (2005)	0	t	1	1.089	0.145	57	2	3.40
Homo sapiens	Animal	Leukaemia as a cause of death	Disease	Veiga & Koifman (2005)	0	t	1	2.117	0.295	49	2	3.40
Homo sapiens	Animal	Cancer as a cause of death	Disease	Veiga & Koifman (2005)	0	t	1	1.764	0.081	468	2	6.40
Homo sapiens	Animal	Oesophagus cancer as a cause of death	Disease	Veiga & Koifman (2005)	0	t	1	2.100	0.315	42	2	6.40
Homo sapiens	Animal	Stomach cancer as a cause of death	Disease	Veiga & Koifman (2005)	0	t	1	3.468	0.347	90	2	6.40
Homo sapiens	Animal	Larynx cancer as a cause of death	Disease	Veiga & Koifman (2005)	0	t	1	0.104	0.039	9	2	6.40
Homo sapiens	Animal	Lung cancer as a cause of death	Disease	Veiga & Koifman (2005)	0	t	1	2.814	0.309	77	2	6.40
Homo sapiens	Animal	Female breast cancer as a cause of death	Disease	Veiga & Koifman (2005)	0	t	1	0.762	0.148	28	2	6.40
Homo sapiens	Animal	Prostrate cancer as a cause of death	Disease	Veiga & Koifman (2005)	0	t	1	2.971	0.401	48	2	6.40
Homo sapiens	Animal	Leukaemia as a cause of death	Disease	Veiga & Koifman (2005)	0	t	−1	0.035	−0.008	19	2	6.40
Homo sapiens	Animal	Other abnormalities	Disease	Wang *et al*. (1990)	1	t	−1	2.053	−0.046	2006	2	3.30
Homo sapiens	Animal	All nodular disease	Disease	Wang *et al*. (1990)	1	t	1	1.325	0.030	2006	2	3.30
Homo sapiens	Animal	Thyroxine-free serum (T4)	Disease	Wang *et al*. (1990)	1	t	−1	0.417	−0.018	550	2	3.30
Homo sapiens	Animal	Tiiodo-thryroxine-free serum (T3)	Disease	Wang *et al*. (1990)	1	t	1	0.400	0.017	550	2	3.30
Homo sapiens	Animal	Anti-mitochondrial antibody serum (AMA)	Disease	Wang *et al*. (1990)	1	t	1	0.600	0.026	550	2	3.30
Homo sapiens	Animal	Urinary iodine-creatinine	Disease	Wang *et al*. (1990)	1	t	1	6.842	0.380	279	2	3.30
Homo sapiens	Animal	Urinary iodine	Disease	Wang *et al*. (1990)	1	t	−1	3.231	−0.191	279	2	3.30
Homo sapiens	Animal	Translocations	Mutation	Wang *et al*. (1990)	1	t	1	0.571	0.041	200	2	3.30
Homo sapiens	Animal	Inversions	Mutation	Wang *et al*. (1990)	1	t	1	0.800	0.057	200	2	3.30
Homo sapiens	Animal	Deletions	Mutation	Wang *et al*. (1990)	1	t	1	2.800	0.195	200	2	3.30
Homo sapiens	Animal	Unstable chromosomal aberrations	Mutation	Wang *et al*. (1990)	1	t	1	3.333	0.230	200	2	3.30
Homo sapiens	Animal	Prevalence of 31 hereditary diseases	Disease	Wei *et al*. (1990)	1	Chi-square	1	0.002	0.000	26572	2	3.37
Homo sapiens	Animal	Cancer mortality	Disease	Wei *et al*. (1990)	1	r	−1	0.002	0.002	632280	2	3.37
Homo sapiens	Animal	Down's syndrome	Disease	Wei *et al*. (1990)	1	Chi-square	1	2.820	0.010	26572	2	3.37
Homo sapiens	Animal	Down's syndrome	Disease	Wei *et al*. (1990)	1	Chi-square	1	5.624	0.011	47095	2	3.37
Homo sapiens	Animal	Nodular disease	Disease	Wei *et al*. (1990)	1	Chi-square	1	0.017	0.003	2006	2	3.37

Table 1. *(Cont.)*

Species	Kingdom	Effect	Category	References	Confounding variables controlled	Test statistic	Direction of effect	Value of test statistic	r	N	No. populations	Radiation level (mSv/year)
Homo sapiens	Animal	Chromosomal translocations	Mutation	Zhang *et al*. (2003)	1	F	1	0.004	0.010	40	2	2.75
Homo sapiens	Animal	Chromosomal translocations	Mutation	Zhang *et al*. (2004)	1	F	1	6.117	0.330	52	2	2.71
Homo sapiens	Animal	Cancer rates	Disease	Zou *et al*. (2005)	1	t	1	0.000	0.000	1202	2	6.37
Homo sapiens	Animal	Non-cancer mortality	Disease	Zou *et al*. (2005)	1	t	1	1.960	0.020	10038	2	6.37
Ipomoea pes-caprae	Plant	Cytological abnormalities	Mutation	Gopal-Ayengar *et al*. (1970)	0	r	1	0.751	0.751	6	6	82.96
Ipomoea pes-caprae	Plant	Pollen sterility	Mutation	Gopal-Ayengar *et al*. (1970)	0	r	1	0.414	0.414	6	6	82.96
Launaea pinnatifida	Plant	Cytological abnormalities	Mutation	Gopal-Ayengar *et al*. (1970)	0	r	1	0.983	0.983	5	5	82.96
Launaea pinnatifida	Plant	Pollen sterility	Mutation	Gopal-Ayengar *et al*. (1970)	0	r	1	0.751	0.751	5	5	82.96
Lochnera rosea	Plant	Cytological abnormalities	Mutation	Gopal-Ayengar *et al*. (1970)	0	r	1	0.934	0.934	11	11	49.06
Lochnera rosea	Plant	Cytological abnormalities	Mutation	Gopal-Ayengar *et al*. (1970)	0	r	1	0.749	0.749	11	11	49.06
Lochnera rosea	Plant	Cytological abnormalities	Mutation	Gopal-Ayengar *et al*. (1970)	0	r	1	0.896	0.896	11	11	82.96
Lochnera rosea	Plant	Pollen sterility	Mutation	Gopal-Ayengar et al. (1970)	0	r	1	0.538	0.538	11	11	82.96
Rattus rattus	Animal	Standardized variance in tooth measurements	Morphology	Grüneberg *et al*. (1966)	1	t	−1	0.159	−0.005	855	16	8.53
Rattus rattus	Animal	Mean skeletal character value	Morphology	Grüneberg *et al*. (1966)	1	t	1	1.997	0.068	855	16	8.53
Rattus rattus	Animal	Variance in skeletal character values	Morphology	Grüneberg *et al*. (1966)	1	t	−1	0.612	−0.021	855	16	8.53
Rattus rattus	Animal	Fossa olecrani perforata	Morphology	Grüneberg *et al*. (1966)	1	Chi-square	−1	38.494	−0.212	855	16	8.53
Rattus rattus	Animal	Foramen hypoglossi double	Morphology	Grüneberg *et al*. (1966)	1	Chi-square	−1	19.926	−0.153	855	16	8.53
Rattus rattus	Animal	Maxillary foramen double	Morphology	Grüneberg *et al*. (1966)	1	Chi-square	1	0.600	0.026	855	16	8.53
Rattus rattus	Animal	Metoptic roots abnormal	Morphology	Grüneberg *et al*. (1966)	1	Chi-square	−1	74.558	−0.295	855	16	8.53
Rattus rattus	Animal	Pregancy rate	Fecundity	Grüneberg *et al*. (1966)	1	Chi-square	1	0.025	0.007	469	16	8.53
Rattus rattus	Animal	Dead embryos	Mutation	Grüneberg *et al*. (1966)	1	Chi-square	−1	0.018	−0.007	399	16	8.53
Rattus rattus	Animal	Pre-implantation loss	Mutation	Grüneberg *et al*. (1966)	1	Chi-square	−1	1.258	−0.064	307	16	8.53

Table 1. *(Cont.)*

Species	Kingdom	Effect	Category	References	Confounding variables controlled	Test statistic	Direction of effect	Value of test statistic	r	N	No. populations	Radiation level (mSv/year)
Rattus rattus	Animal	Post-implantation loss	Mutation	Grüneberg *et al.* (1966)	1	Chi-square	1	0.001	0.002	372	16	8.53
Rattus rattus	Animal	Standardized variance in tooth measurements females	Morphology	Grüneberg *et al.* (1966)	1	t	−1	0.718	−0.025	855	16	8.53
Rattus rattus	Animal	Metoptic roots abnormal	Morphology	Grüneberg *et al.* (1966)	1	t	−1	0.721	−0.025	855	16	8.53
Tradescantia sp.	Plant	Stamen hair mutations	Mutation	de Azevedo Gomes *et al.* (2002)	1	t	1	4.004	0.853	20	2	7.89
Tradescantia sp.	Plant	Stamen hair mutations	Mutation	de Azevedo Gomes *et al.* (2002)	1	t	1	1.692	0.568	20	2	31.56
Tradescantia sp.	Plant	Stamen hair mutations	Mutation	de Azevedo Gomes *et al.* (2002)	1	t	1	2.661	0.736	20	2	52.60
Tradescantia sp.	Plant	Stamen hair mutations	Mutation	de Azevedo Gomes *et al.* (2002)	1	t	1	1.434	0.505	20	2	110.46
Tradescantia sp.	Plant	Stamen hair mutations	Mutation	de Azevedo Gomes *et al.* (2002)	1	t	1	3.277	0.801	20	2	215.66
Tradescantia sp.	Plant	Stamen hair mutations	Mutation	de Azevedo Gomes *et al.* (2002)	1	t	1	3.587	0.826	20	2	263.00
Tradescantia sp.	Plant	Stamen hair mutations	Mutation	de Azevedo Gomes *et al.* (2002)	1	t	1	0.772	0.300	20	2	526.00
Tradescantia sp.	Plant	Stamen hair mutations	Mutation	Nayar *et al.* (1970)	1	r	1	0.784	0.784	4	2	95.09
Tyto alba	Animal	Intensity of pheomelanin colour	Physiology	Galván & Alonso-Alvarez (2011)	0	t	1	2.250	0.030	376	18	1.40

Confounding variables controlled: 0 – no, 1- yes; direction of effect: −1 implies decrease with increasing radiation level, 1 implies increase with increasing radiation level; r, Pearson r; N, sample size. Note that radiation levels are estimates based on maximum dose rates.

bootstrap 95% CI = 0.039–0.171, $N = 66$ effects from 46 studies). Therefore, natural background radiation accounted for 0.9% of the variance. Variation in individual effect sizes was larger than expected from sampling error ($Q_T = 952.41$, d.f. = 65, $P < 0.0001$). We did find significant evidence of publication bias when analyzing the relationship between effect size and year of publication in a regression weighted by sample size [$F = 20.457$, d.f. = 1,64, $P < 0.0001$, slope (S.E.) = 0.0035 (0.0008)], and we did find a significant correlation between standardized effect size estimates and their variance ($r_{bias} = 0.441$, $N = 66$, $P < 0.0001$) and study sample size ($r_{bias} = 0.446$, $N = 66$, $P < 0.0001$). A funnel plot of the 66 effect sizes indicated asymmetry in distribution of effect sizes (Fig. 2A). There was similar asymmetry if the funnel plot was restricted to studies of animals, mutational effects or disease effects (Fig. 2B–D). A trim and fill analysis indicated that there were 11 missing studies (according to the L_o estimator = 11.25), and estimated mean effect size after inclusion of these 11 studies revealed a mean effect size across all studies of 0.014 ($P = 0.0012$, bootstrap 95% CI = 0.006–0.022).

There was a weakly increasing effect size with year of publication [slope (S.E.) = 0.0038 (0.0008), $P < 0.0001$, bootstrap 95% CI = 0.038–0.167], with a heterogeneous difference among studies ($Q_T = 25.09$, d.f. = 1, $P < 0.0001$), suggesting that more recent studies showed stronger effects. However, the difference in predicted effect size across the 46 years of publication only accounted for an increase in effect size by 0.17, and the positive relationship is contrary to expectations based on publication bias (Jennions & Møller, 2002).

(2) Effect size and explanatory variables

There was a significant difference in effect size between studies of animals (which were nearly exclusively humans) and plants, with mean weighted effect for plants being almost an order of magnitude greater than that for studies of animals (Table 2).

When effects were categorized with respect to predictor variables, we found a significant difference in effect size among categories (Table 2). Mean effect size was large for immunology, decreasing to intermediate in studies of physiology and small in studies of mutation, disease and morphology (Table 2). When only considering studies of disease, there was no significant heterogeneity between studies of cancer and studies of other types of disease, with both effects being small (Table 2).

Because effect sizes for plants only consisted of studies of mutation, we also compared plant and animal studies only based on mutations. In this case mean effect size for plants remained 0.749 (bootstrap 95% CI = 0.570–0.878), while it was 0.017 (bootstrap 95% CI = 0.019–0.053) for animals; a non-significant difference ($Q_T = 1.72$, d.f. = 1, $P = 0.18$).

We found no significant evidence of study quality as estimated from effects being controlled for potentially confounding variables affecting mean effect sizes (Table 2). There was large overlap in confidence intervals between studies that controlled or did not control for potentially confounding variables.

A test for the importance of the number of study populations as a basis for the individual studies suggested no significant weighted effect [slope (S.E.) = −0.0009 (0.0216), $P = 0.97$, bootstrap 95% CI = 0.035–0.161], with a heterogeneous difference among studies ($Q_T = 0.002$, d.f. = 1, $P = 0.97$), suggesting no clear effects of replication level.

Finally, we tested if the level of radiation predicted mean weighted effect size as expected if radiation was the underlying factor. There was a significant positive effect [slope (S.E.) = 0.0583 (0.0170), $P = 0.0006$, bootstrap 95% CI = 0.038–0.167], with a heterogeneous difference among studies ($Q_T = 11.71$, d.f. = 1, $P < 0.0001$), suggesting that higher levels of radiation were associated with stronger effects.

(3) Variation in radiation resistance among natural populations

There are numerous examples of differences in radio-resistance among strains, lines or populations since the first studies on *Drosophila melanogaster* by Strømnæs (1955) (Table 3). Evidence for strain differences in radio-sensitivity has been replicated for fruitflies *Drosophila melanogaster* and domestic mice *Mus musculus* by different laboratories (Table 3).

We are only aware of a single negative result: Varanda, Takahashi & Soares (1985) were unable to show radio-resistance in *Melittobia hawaiiensis* exposed to high levels of gamma radiation for many generations. Many studies have shown that selection in the laboratory for radio-resistance is effective (e.g. Wallace, 1952). We do not discuss such studies further here.

By far the largest majority of studies showing radio-tolerance or radio-resistance are concerned with bacteria (Table 3). *Deinococcus deserti* were able to survive levels of radiation up to 15000 Gy (de Groot *et al*., 2005). Daly (2009) showed that manganese-based protein complexes could provide protection to DNA repair machinery thus permitting survival at very high radiation levels. Fungi constitute the other major group showing extreme radio-tolerance, even growing within the sarcophagus at Chernobyl (Zhdanova *et al*., 2000). Experimental studies have shown hyphal growth directed towards radiation sources (Zhdanova *et al*., 2004).

Some metazoan bdelloid rotifers (Gladyshev & Meselson, 2008) and tardigrades (Horikawa *et al*., 2006) show an ability to survive high radiation doses, although this is accompanied by sterility. *Drosophila* spp., silkworm *Bombyx mori* and mouse *Mus musculus* show differences in resistance to radiation, although tolerance levels are many orders of magnitude lower than in bacteria and fungi (Table 3).

Table 2. Mean effect sizes weighted by sample size, their confidence intervals, number of studies, heterogeneity (Q_T) among studies (global test) or among categories, degrees of freedom (d.f.) for the heterogeneity test and probability (P) for this heterogeneity test for different groupings of the data set listed in Table 1

Category	Mean effect size	Bootstrap 95% confidence interval	No. studies	Q_T	d.f.	P
All studies	0.093	0.039, 0.171	66	952.41	65	<0.0001
Animals	0.089	0.071, 0.108	57	39.45	1	<0.0001
Plants	0.749	0.570, 0.878	9	—	—	—
Immunology	0.451	0.018, 0.750	3	70.86	4	<0.0001
Physiology	0.278	−0.029, 0.767	4	—	—	—
Mutation	0.177	0.059, 0.376	31	—	—	—
Disease	0.054	0.004, 0.124	19	—	—	—
Morphology	−0.005	−0.049, 0.006	6	—	—	—
Cancer	0.057	−0.017, 0.158	11	1.49	1	0.22
Other diseases	0.026	0.010, 0.063	8	—	—	—
Confounding variables not controlled	0.056	−0.079, 0.199	17	2.08	1	0.15
Confounding variables controlled	0.098	0.041, 0.184	49	—	—	—

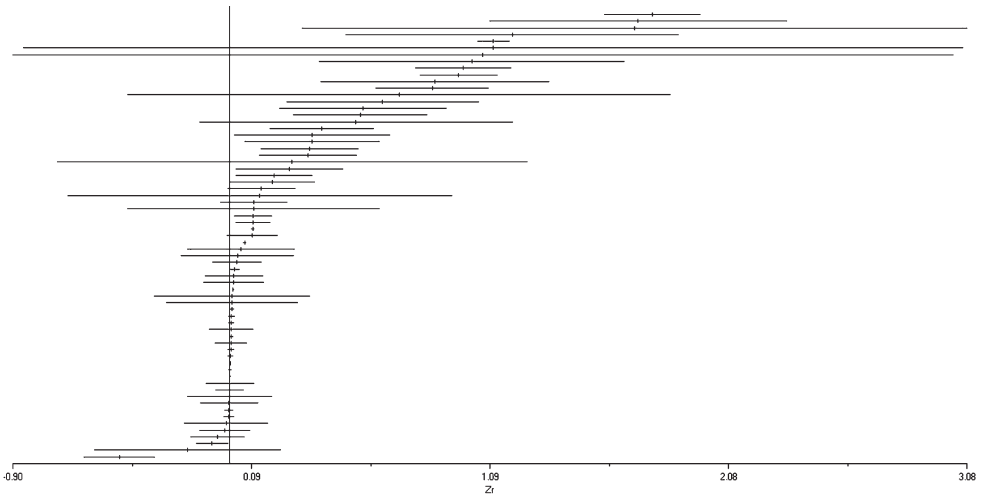

Fig. 1. Plot of the 66 effect size estimates of the relationship between level of natural background radiation and biological response variables, ordered by increasing effect size. Effect sizes are z-transformed Pearson product-moment correlation coefficient estimates (Z_r), shown here with 95% confidence intervals. Vertical line indicates overall mean effect size of 0.093.

IV. DISCUSSION

The objectives of this review were to examine the effects of radiation on DNA, health, and radiation resistance, and to investigate evidence for the presence of hormesis (positive effects of radiation). We found extensive evidence of small, but significant negative effects of natural variation in background radiation on immunology, mutation and disease across a range of different species of animals and plants. This significant effect was robust to indirect tests for effects of publication bias as provided by the trim and fill procedure (Duval & Tweedie, 2000*a*, *b*). The effects for plants were much stronger than for animals, and studies conducted at higher natural radiation levels showed stronger effect sizes. Numerous studies have shown evidence of radio-resistance, mainly in bacteria and fungi, but also in Metazoa including fruitflies and mice; the extent of this radio-resistance differs among taxa.

The studies reviewed herein generally had a design that compared one or more control populations with a 'normal' level of background radiation with one or more populations that had a 'high' level of background radiation. More than 75% of all effect sizes consisted of comparisons of one control and one high-radiation population. If effects were entirely due to chance alone, we should expect equally many 'positive' and 'negative' effect sizes, with an expected mean of zero, which was clearly not the case. An explicit test for effects of level of replication showed no significant confounding effects. Typically the level of radiation in the high-radiation population was an order of magnitude above the level in the control population. Because such population comparisons are correlational in nature, they may be confounded by uncontrolled third variables. As

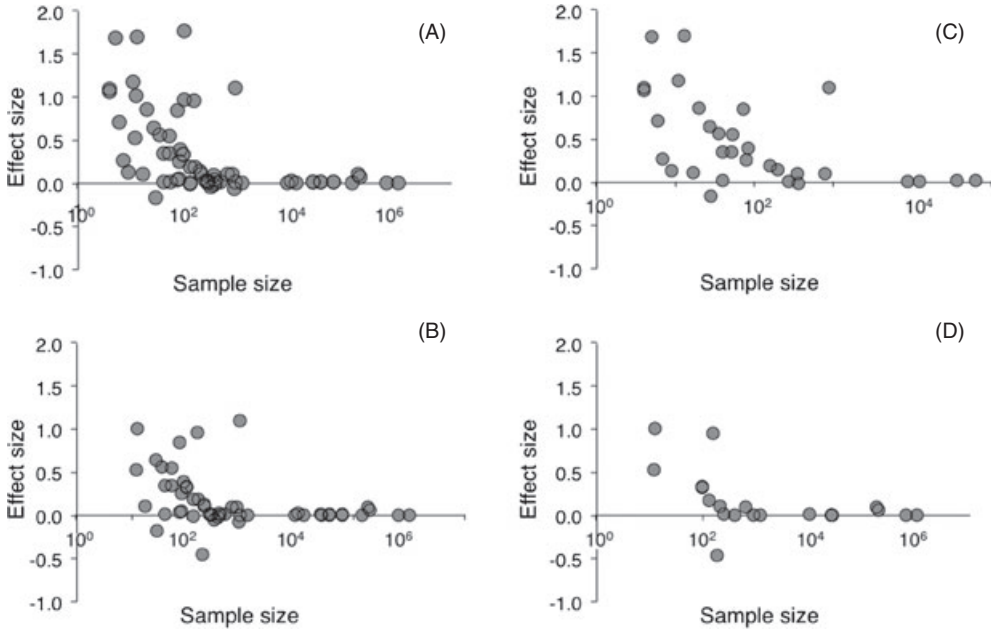

Fig. 2. Funnel plots of *z*-transformed effect size in relation to $\log_{10}$-transformed sample size for (A) all 66 effect sizes, (B) animal studies, (C) mutation studies and (D) disease studies.

a case in point, one of the first studies of the effects of high background radiation in Kerala, India, by Kochupillai *et al*. (1976) was subsequently criticised for not having properly controlled the incidence of Down's syndrome for differences in age of mothers in the control population and the high-radiation-level population (Sundaram, 1977). However, subsequent studies of the incidence of Down's syndrome in Kerala corrected for such confounding effects, and studies in other areas also have confirmed the initial observation. Subsequent studies have carefully tested and controlled study design for the confounding effects of age, sex, ethnicity, religion, consanguinity, smoking, unemployment rate and other factors. In fact, most studies of humans in high-radiation areas are characterized by extreme ethnic homogeneity because populations have been living in the study area for many generations. A case in point is the study of effects of radiation in the Guangdong Province in Southern China, where the study populations consist of homogeneous Han Chinese that have lived in the region for many centuries (Wang *et al*., 1990). Many studies report effects before and after statistical control for confounding variables, and we consistently used such robust effect sizes in this review. When testing for a difference in mean effect size between more and less rigorous studies, we found no significant difference.

The distribution of effect sizes in relation to sample size is usually assumed to be funnel-shaped with larger variance around the true mean effect size at smaller sample sizes (the so-called funnel plot) (Light & Pillemer, 1984; Begg, 1994). Asymmetric plots may be due to publication bias, heterogeneity in effect sizes or other factors (e.g. Egger *et al*., 1997; Thornhill, Møller & Gangestad, 1999). We found evidence of asymmetric funnel plots (Fig. 2), but also showed that elimination of such asymmetry by adoption of the 'trim and fill' procedure (Duval & Tweedie, 2000*a*, *b*) did not eliminate an overall significant mean effect size.

Radiation causes mutations even at the modest levels of natural radiation. There is extensive evidence for naturally high levels of radiation being associated with increased rates of genetic damage, including mutations. This effect was the predominant finding in most studies, showing a small, but highly significant effect size (Tables 1 and 2). In other words, effects of natural radiation are reported at a much higher frequency than would be expected by chance alone. This implies that natural radiation effects like those reported here are frequent and significant. The magnitude of the overall effect was 'only' small, accounting for less than 1% of the variance. However, in an evolutionary context even a small effect may have large consequences when considered across the large number of generations of evolutionary time scales. It is important to notice that we found a mean difference in effect size of almost an order of magnitude between animals and plants, suggesting that the sessile habits of plants subject them to chronic radiation. However, the difference in effect size for mutations between animals and plants was not statistically significant, although the difference in mean effects was large, probably due to low statistical power. More studies are required to assess this effect. In addition, reduced levels of migration in plants compared to mammals should result in greater levels of local adaptation in plants. Indeed, recent studies of DNA repair and gene expression in plants in Chernobyl seem to be consistent with such an interpretation (Boubriak *et al*., 2008; Danchenko *et al*., 2009; Klubicová *et al*., 2010). Despite this expectation we still found stronger negative effects of radiation on plants than on animals. Therefore, we can conclude that there is current selection for local adaptation in plants to cope with

Table 3. Studies of genetic variation in radiation tolerance and resistance in different taxa

Species	Evidence	Comments	References
Fungi:			
Penicillium hirsutum, *P. lanosum*, *P. westlingii*, *Cladosporium cladosporiodes*	Hyphal growth directed towards radioactive source. Three other taxa from uncontaminated areas showed no similar directed growth	No distinction between β- and γ-radiation	Zhdanova *et al*. (2004)
19 genera of fungi	Melanized genera predominant inside the containment structure of the Chernobyl Nuclear Power Plant	Could partly be an effect of reduced interspecific competition from non-melanized fungi	Zhdanova *et al*. (2000)
Stachybotrys, *Ulocladium*, *Preussia*, *Plenodomus*, *Humicola*, *Aureobasidium*, *Alternaria*	Melanized genera predominant after 1986, but not before, and only in contaminated areas around Chernobyl	Could partly be an effect of reduced interspecific competition from non-melanized fungi	Zhdanova *et al*. (1994)
Curvularia geniculatan Alternaria alternata	Resistance to γ-radiation	Maximum of 1.7 megarad	Saleh *et al*. (1988)
Saccharamysis cerevisiae	Resistance to γ-radiation	—	Kimura *et al*. (2006)
Ustilago maydis	Resistance to γ-radiation	Maximum of 6000 Gy	Holliday (1971) and Leaper *et al*. (1980)
Cyanobacteria:			
Chroococcidiopsis spp.	Resistance to γ-radiation source	4000 Gy	Billi *et al*. (2000)
Bacteria:			
Escherichia coli	Two radio-resistant loci identified	—	Greenberg (1964*a*, *b*)
Azotobacter	Resistance to high γ-radiation source	Soil populations more resistant than laboratory populations	Vela & Wyss (1965)
Bacillus subtilis	Resistance to γ-radiation source	Mechanisms unknown	Setlow (2006)
Methylobacterium radiotolerans	Resistance to γ-radiation source	1000 Gy	Ito & Iizuka (1971) and Green & Bousfield (1983)
Locurio rosea	Resistance to γ-radiation source	2000 Gy	Rainey *et al*. (1997) and Brooks & Murray (1981)
Acinetobacter radioresistens	Resistance to γ-radiation source	2000 Gy	Nishimura *et al*. (1994)
Kineococcus radiotolerans	Resistance to γ-radiation source	2000 Gy	Phillips *et al*. (2002)
Thermococcus gammatolerans	Resistance to γ-radiation source	—	Jolivet *et al*. (2003, 2004)
Thermococcus marinus	Resistance to γ-radiation source	—	Jolivet *et al*. (2004)
Thermococcus stetteri	Resistance to γ-radiation source	>1000 Gy	Kopylov *et al*. (1993)
Rubrobacter radiotolerans	Resistance to γ-radiation source	Resistance to 11000 Gy	Suzuki *et al*. (1988) and Ferreira *et al*. (1999)
Rubrobacter xylanophilus	Resistance to γ-radiation source	Resistance to 5500 Gy	Ferreira *et al*. (1999)
Desulfurococcus amyloliticus	Resistance to γ-radiation source	> 2500 Gy	Kopylov *et al*. (1993)
Deinococcus radiodurans	Resistance to γ-radiation source	10000 Gy	Brooks & Murray (1981) and Ito *et al*. (1983)
Deinococcus deserti	Resistance to γ-radiation source	15000 Gy	De Groot *et al*. (2005)
Deinococcus radiopugnans	Extremely efficient DNA repair	1500 rad	Minton (1994)
Deinococcus proteolyticus	Extremely efficient DNA repair	1500 rad	Minton (1994)
Deinococcus radiophilus	Extremely efficient DNA repair	1500 rad	Minton (1994)
Deinococcus geothermalis	Resistance to γ-radiation	7300 Gy	Ferreira *et al*. (1997)
Deinococcus murrayi	Resistance to γ-radiation	3700 Gy	Ferreira *et al*. (1997)
Deinococcus	Nine new species	Resistance to 30000 Gy	Rainey *et al*. (2005)
Deinobacter grandis	—	—	Minton (1994)
Cryptococcus neoformans	Resistance to γ-radiation source	Resistance to 4000 Gy	Dadachova *et al*. (2004)
Histoplasma capsulatum	Resistance to γ-radiation source	Resistance to 4000 Gy	Dadachova *et al*. (2004)
Pyrococcus abyssi	Resistance to γ-radiation source	Maximum of 2500 Gy	Gérard *et al*. (2001)
Pyrococcus furiosus	Resistance to high γ-radiation source	Chromosome fully restored following fragmentation caused by 2500 Gy	DiRuggiero *et al*. (1997)
Geodermatophilus sp.	Resistance to γ-radiation source	Resistance to 30000 Gy	Rainey *et al*. (2005)
Hymenobacter actinosclerus	Resistance to γ-radiation source	Resistance to 3500 Gy	Collins *et al*. (2000)

Table 3. *(Cont.)*

Species	Evidence	Comments	References
Hymenobacter sp.	Resistance to γ-radiation source	Resistance to 30000 Gy	Rainey *et al*. (2005)
Metazoa:			
Caenorhabditis elegans	Resistance to irradiation, but subsequently sterile	Resistance to 5000 Gy	Johnson & Hartman (1988)
Bdelloid rotifers *Adineta vaga* and *Philodina roseola*	Resistance to irradiation, but subsequently sterile	Survives 1120 Gy, which is much higher than in a desiccation-intolerant rotifer	Gladyshev & Meselson (2008)
Milnesium tardigradum	Resistance to γ-radiation source and heavy ions	Resistance up to 6200 Gy in hydrated animals and 5200 Gy in anhydrobiotic animals. Survival dose-dependent, but sterility complete above 1000 Gy	Horikawa *et al*. (2006)
Drosophila melanogaster	Differences between two strains in maturation rates and mutation frequency linked to radiation	—	Strømnæs (1955, 1959)
Drosophila melanogaster	Differences in radio-resistance among three strains due to dominant effects	—	Ogaki & Nakashima-Tanaka (1966)
Drosophila melanogaster	Mortality analysis of iso-female lines showed significant strain and strain-by-dose effects. Additive differences from a 4 × 4 diallelic cross, but low dominance and inter-chromosomal interaction effects	90000 and 110000 rads γ-radiation	Parsons *et al*. (1969)
Drosophila nebulosa	Mortality and reproductive performance differed among iso-female lines, and diallelic crosses showed evidence of additive differences	90000 rad	Kratz (1975)
Drosophila willistoni	Egg eclosion and reproductive performance differed significantly among areas ranging from 0.05 to 3.5 mR/h	1000 rad	Cordeiro *et al*. (1973)
Bombyx mori	Differences among lines	—	Tazima (1957)
Bombyx mori	Differences among lines	—	Murakami & Tazima (1966)
Mus musculus	LD_{50} was affected by a recessive genetic factor	—	Kohn & Kalman (1956)
Mus musculus	Difference among strains in number of offspring and duration of the fertile period	—	Ehling (1964)
Mus musculus	Variance in sensitivity is additive with a heritability of 0.55	—	Grahn (1958)

LD_{50} is the dose at which 50% of the individuals have died.

elevated levels of background radiation. Forster *et al*. (2002) showed that human mutation rates in naturally radioactive areas were seven times higher than in control regions, at a background radiation level ten times higher than the worldwide average. This is a typical level of radiation in so-called high-level radiation areas across the world, and this level of radiation is typically what is reported in the studies reviewed here (Table 1). In addition, Forster *et al*. (2002) showed that mutations were strongly aggregated at specific locations on the chromosomes that have had an evolutionary history of high mutation rates. This observation provides evidence that these radiation-associated point mutations are associated with a radiation-induced increase in the cell's normal mutation mechanisms or a decrease in repair mechanisms at these particular sites (Dubrova *et al*., 1997).

Chronic exposure to radiation is associated with significant costs in terms of health. Here we have shown evidence of significant negative effects on immunology, mutation and disease frequency in a large number of studies (Tables 1 and 2). The observed high frequency of negative effects

is very unlikely to reflect random chance. The findings reviewed here include reduced levels of antioxidants, weakened immune responses and elevated frequencies of disease including cancer. Antioxidant levels are typically suppressed in irradiated individuals as commonly reported from radiation accidents (e.g. Yablokov, Nesterenko & Nesterenko, 2009). Attar, Kondolousy & Khansari (2007) showed a similar effect on a number of different measures of immunity in humans in Iran exposed to elevated background radiation levels. This implies that elevated incidence of disease in contaminated areas may be caused by effects of radiation on the immune system rather than being a consequence of increased mutation rates directly causing disease. Three epidemiological studies link cancer to elevated levels of background radiation, even after controlling for potentially confounding variables (Ujeno, 1983; Tao *et al*., 2000; Körblein & Hoffmann, 2006). These findings about disease incidence and natural variation in background radiation have implications for studies of the effects of radiation accidents such as Chernobyl, Fukushima Daiichi and Three Mile Island. Given that natural levels of radiation typically are much lower than those reported for areas subjected to radiation accidents we can predict that the significant effects reported here for natural radiation will be even stronger in areas that are accidentally contaminated with high levels of radiation.

There is extensive evidence of radiation-resistance in bacteria and fungi, but also in higher organisms such as *Caenorhabditis elegans*, bdelloid rotifers, tardigrades, insects and mice (Table 3). Some of these results, such as the tardigrades, can be explained by an absence of replicating cells after birth. While bacteria and fungi can survive exposure to even 15000 Gy, sustainable levels for Metazoa are much lower. However, it remains interesting that there is significant variation in radio-resistance even in mammals. Our review showed clear evidence of interspecific differences in resistance to radiation. Resistance to ionizing radiation in *Dinococcus radiodurans* and bdelloid rotifers appears to be derived from their desiccation resistance (Mattimore & Battista, 1996; Gladyshev & Meselson, 2008). A recent study showed that bacterial biofilms resistant to desiccation and ultraviolet radiation are pre-adapted to cope with ionizing radiation from Chernobyl (Ragon *et al*., 2011), apparently because the same underlying mechanisms are responsible for resistance in both cases. In *Deinococcus radiodurans* there seems to have been an accumulation of genes involved in resistance to radiation that allowed it to cope successfully with different kinds of environmental stresses (or *vice versa*) compared to a closely related radio-susceptible bacterium (Omelchenko *et al*., 2005). Even large amounts of DNA damage in *D. radiodurans* can be repaired without leaving any obvious trace of mutations through homologous recombination, use of single-strand DNA for recombination, regulated DNA replication, and export of damaged nucleotides from the cell for mutation avoidance (Battista *et al*., 1999; Cox & Battista, 2005).

The underlying mechanisms responsible for radiation resistance were originally thought to be efficient DNA repair; the current focus has switched towards mechanisms of repair of DNA damage caused by reactive oxygen species. Both desiccation and irradiation result in oxidative stress (França, Panek & Eleutherio, 2007). High levels of reactive oxidative species cause damage to DNA and proteins that require correction through repair (Minton, 1994, 1996; DiRuggiero *et al*., 1997; Battista *et al*., 1999). Daly *et al*. (2004) showed that *Deinococcus radiodurans* and other radio-resistant bacteria differ from non-radio-resistant species in their level of accumulation of intracellular manganese and low levels of iron; melanin may play a similar role in fungi (Dadachova *et al*., 2007 and trehalose in cyanobacteria (Shirkey *et al*., 2003). In experimental settings manganese seems to facilitate recovery from radiation injury. When manganese combines with ligands, the resulting products can act as powerful scavengers of free radicals arising as a consequence of ionizing radiation (Daly, 2009). Because such bacterial cells rely on homologous recombination for rejoining double-strand breakage of DNA, the presence of multiple copies of the genome in combination with antioxidant protection would allow cells to survive even with multiple double-strand breakages. It is interesting that it appears that protection mechanisms against reactive oxygen species rather than DNA repair as such is the basis for radio-resistance in bacteria such as *Deinococcus radiodurans*. Differences among bacterial taxa in their level of radio-resistance appear to be related to the importance of manganese in such antioxidant defence (Daly, 2009). Thus, it is probably not a coincidence that interspecific differences in the ability to survive the impact of radiation at Chernobyl are associated with ecological factors closely linked to antioxidant status (Møller & Mousseau, 2007). The antioxidant status of individuals (Bonisoli-Alquati *et al*., 2010), and the amount of pheomelanic plumage in birds (Galván, Mousseau & Møller, 2011) predicts the ability to sustain radiation, apparently due to the action of the powerful antioxidant glutathione. The effects of low-dose radiation reported here emphasise a significant role of oxidative stress at even very low levels of natural background radiation. We hypothesise that limited availability of antioxidants and the associated physiological problems in terms of reduced ability to repair damage to DNA and other molecules may account for such effects.

Hormesis is defined as a beneficial effect of normal background radiation on life-history traits such as fecundity and longevity compared to levels achieved in the complete absence of radiation (reviews in Kondo, 1993; Luckey, 1991). If hormetic effects of radiation on fitness exist, we should expect that the optimal level of radiation should increase with background radiation level. If hormesis has evolved as a consequence of local adaptation to specific levels of radiation, we might even find that all populations should perform best at some local level of radiation; exceeding their performance in the absence of radiation. The latter scenario would suggest that fitness should be independent of level of natural background radiation. In either case,

we should not expect to find increased mutation rates, impaired immune function, increased incidence of disease and increased mortality in areas with higher levels of normal background radiation. Our findings are clearly inconsistent with a general role for hormesis in adaptation to elevated levels of natural background radiation. We note that some effect sizes reported herein were negative, thereby deviating from this expectation. However, these effects were of a level that would be expected by chance, inconsistent with expectations for a hormesis hypothesis.

In conclusion, reported rates of mutation caused by natural variation in radiation levels are almost exclusively restricted to studies of humans with only a few studies on other species available. Information on physiology, immunology and disease associated with radiation again are restricted almost exclusively to studies of humans. Note, however, that there is no evidence of radio-tolerance or radio-resistance in humans, and there are still no studies of disease and mutation rates in species in which radio-tolerance or radio-resistance has been documented. The present review provides evidence for interspecific variation in radio-tolerance and radio-resistance in a large number of taxa, suggesting that there has been selection for and evolution of such characteristics. The scarcity of studies on mutations and disease in organisms other than humans clearly should be addressed.

V. CONCLUSIONS

(1) We reviewed the literature on responses to natural variation in background radiation. There was evidence of a significant, but small effect of natural variation in background radiation on mutation rates, DNA damage and DNA repair.

(2) There were significant effects of natural variation in background radiation on immunology and disease including cancer.

(3) The findings reported here are inconsistent with a general role of hormesis from low levels of natural background radiation.

(4) There was strong evidence for the existence of radio-resistance in different taxa, with differences among taxa recorded in a variety of studies.

(5) These findings concerning the relationship between natural variation in background radiation and various biological response variables have important implications for assessment of the biological effects of radiation accidents.

(6) Future studies should address the underlying mechanisms accounting for interspecific differences in susceptibility to radiation.

VI. ACKNOWLEDGEMENTS

P. Lopez helped with references S. Randic, M. D. Jennions and two anonymous referees provided helpful suggestions for the meta-analysis.

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(*Received 6 February 2012; revised 26 September 2012; accepted 5 October 2012; published online 8 November 2012*)