## **REVIEW**

# Cancer consequences of the Chernobyl accident: 20 years on

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#### Abstract

26 April 2006 marks the 20th anniversary of the Chernobyl accident. On this occasion, the World Health Organization (WHO), within the UN Chernobyl Forum initiative, convened an Expert Group to evaluate the health impacts of Chernobyl. This paper summarises the findings relating to cancer. A dramatic increase in the incidence of thyroid cancer has been observed among those exposed to radioactive iodines in childhood and adolescence in the most contaminated territories. Iodine deficiency may have increased the risk of developing thyroid cancer following exposure to radioactive iodines, while prolonged stable iodine supplementation in the years after exposure may reduce this risk. Although increases in rates of other cancers have been reported, much of these increases appear to be due to other factors, including improvements in registration, reporting and diagnosis. Studies are few, however, and have methodological limitations. Further, because most radiation-related solid cancers continue to occur decades after exposure and because only 20 years have passed since the accident, it is too early to evaluate the full radiological impact of the accident. Apart from the large increase in thyroid cancer incidence in young people, there are at present no clearly demonstrated radiation-related increases in cancer risk. This should not, however, be interpreted to mean that no increase has in fact occurred: based on the experience of other populations exposed to ionising radiation, a small increase in the relative risk of cancer is expected, even at the low to moderate doses received. Although it is expected that epidemiological studies will have difficulty identifying such a risk, it may nevertheless translate into a substantial number of radiation-related cancer cases in the future, given the very large number of individuals exposed.

#### 1. Introduction

26 April 2006 marks the 20th anniversary of the accident at the Chernobyl nuclear plant in northern Ukraine, the largest nuclear accident in history. As a result of the accident about five million people were exposed to radioactive contamination in Belarus, the Russian Federation and Ukraine. The knowledge gained in the last 20 years provides valuable information on the

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effects of environmental and occupational radiation exposure and will contribute to determining how best to respond to any future accidents of this nature.

#### 2. Methods

In 2003, the WHO convened an Expert Group on Health (EGH) within the UN Chernobyl Forum, an initiative supported by eight UN organisations. After three years of work, the WHO-EGH produced a comprehensive technical report, 'Health effects of the Chernobyl accident and special health care programmes', including detailed critical reviews of published, scientifically valid studies of thyroid cancer, leukaemia and other cancers, as well as non-cancer outcomes (UN Chernobyl Forum 2006). The EGH gave little, if any, weight to anecdotal observations. The present paper, focused on radiation dosimetry and epidemiology, summarises the findings related to cancer, the main long-term effect expected as a result of radiation exposure (UNSCEAR 2000, US NRC 2006).

#### 3. Results

## 3.1. Sources and levels of radiation dose

The greatest sources of radiation dose from Chernobyl were, at different time periods, intake of short-lived radioactive iodines (particularly  $^{131}$ I), external exposure from radionuclides deposited on the ground (particularly  $^{95}$ Zr +  $^{95}$ Nb,  $^{103}$ Ru,  $^{106}$ Ru,  $^{132}$ Te +  $^{132}$ I,  $^{140}$ Ba +  $^{140}$ La,  $^{141}$ Ce and  $^{144}$ Ce) and ingestion of radioactive caesiums (particularly  $^{134}$ Cs and  $^{137}$ Cs).

Three major groups of people were exposed to and, in some cases, are still being exposed to radioactive contamination:

- 1. Workers (liquidators, or emergency and recovery operations workers). Those individuals who were involved in emergency response, containment, clean-up and associated activities at the Chernobyl site and in the contaminated areas, commonly referred to as liquidators. This group consists of approximately 600 000 individuals, of whom about 240 000 worked in 1986 and 1987, when doses were highest, at the reactor site and the surrounding 30 km zone (Cardis *et al* 1996).
- Inhabitants who were evacuated or relocated from contaminated areas. In the months
  following the accident about 116 000 people were evacuated from areas surrounding the
  reactor in Belarus, the Russian Federation and Ukraine. A further 220 000 people were
  relocated after 1986.
- 3. *Inhabitants of contaminated areas who were not evacuated.* About 5 million people continue to live in areas of Belarus, Ukraine and Russia that were contaminated by the accident.

Table 1 presents a summary of the number of persons exposed and the levels of doses received in these population groups. Residents of contaminated areas include residents of strict control zones (where strict measures to monitor and decrease annual whole body doses continue to be implemented) and residents of less contaminated areas.

The liquidators were mainly exposed to external  $\gamma$ - and  $\beta$ -radiation. Internal exposure due to ingestion was negligible, though inhaled radioiodines may have contributed to the dose for a small proportion of the liquidators during the first weeks after the accident. In the first few days after the accident, dose-rates were extremely heterogeneous and those liquidators who worked on the industrial site of the Chernobyl Nuclear Power Plant could receive very high doses (up to

Table 1.	Estimates of mean	effective doses	(mSv) for populati	on groups of int	erest (Cardis et al
1996. UN	SCEAR 2000).				

Population	Approximate size of population	Mean effective dose (mSv)
Liquidators (1986–1987, 30 km zone)	240 000	100
Evacuees of 1986	116 000	33
Persons living in contaminated areas:		
Deposition density of $^{137}$ Cs > 37 kBq m <sup>-2</sup>	5200 000 <sup>a</sup>	10 <sup>b</sup>
Deposition density of $^{137}$ Cs > 555 kBq m $^{-2c}$	270 000	50 <sup>b</sup>

<sup>&</sup>lt;sup>a</sup> Including approximately 1900000 persons from Belarus, 2000000 from Russia and 1300000 from Ukraine (UNSCEAR 2000).

**Table 2.** Distribution of doses to clean-up workers as recorded in state Chernobyl registries (UN Chernobyl Forum 2006).

	Number of clean-up	Percentage for whom dose is	External dose (mSv)			
Country and period	workers	available	Mean	Median	75th (%)	95th (%)
Belarus						
1986-1987	31 000	28	39	20	67	111
1986-1989	63 000	14	43	24	67	119
Russian Federation						
1986	69 000	51	169	194	220	250
1987	53 000	71	92	92	100	208
1988	20 500	83	34	26	45	94
1989	6 000	73	32	30	48	52
1986-1989	148 000	63	107	92	180	240
Ukraine						
1986	98 000	41	185	190	237	326
1987	43 000	72	112	105	142	236
1988	18 000	79	47	33	50	134
1989	11 000	86	35	28	42	107
1986-1989	170 000	56	126	112	192	293

several Sv). In the course of time, due to decay of radionuclides and decontamination activities, dose-rates dropped significantly. This, together with the implementation (from the end of May 1986) of practices to limit exposure, resulted in doses that were generally below permissible levels (250 mSv in 1986; 50–100 mSv in 1987, depending on the work). The distribution of doses available in the State Chernobyl Registries is shown in table 2. The average recorded dose for the liquidators who worked on the reactor site and 30 km zone in 1986–87 is about 100 mSv (table 1), with few individual doses over 250 mSv.

The effective dose estimates for individuals in the general population accumulated over the 20 years following the accident (1986–2005) range from a few mSv to some hundred mSv depending on location, age and lifestyle factors, such as diet, or time spent outdoors. These doses are mainly due to external exposure from a mixture of deposited radionuclides, as well as to internal exposure from intake of <sup>134</sup>Cs and <sup>137</sup>Cs (UNSCEAR 2000). The mean effective dose accumulated up to 2005 among residents in the strict control zones (with <sup>137</sup>Cs deposition density of 555 kBq m<sup>-2</sup> or more) is of the order of 50 mSv, while in less contaminated areas

<sup>&</sup>lt;sup>b</sup> For the period 1986–2005.

<sup>&</sup>lt;sup>c</sup> Strict control zones (included in the areas with deposition density >37 kBq m<sup>-2</sup>).

Table 3. Estimates of thyroid doses (Goulko *et al* 1996, Likhtarov *et al* 2005, Minenko 2000, UNSCEAR 2000).

		Mea	e (Gy)	
Population	Size of population	0–7 years	Adults	Total
Evacuees of 1986, including	116131	1.82	0.29	0.48
villages, Belarus	24 725	3.10	0.68	1.00
Pripyat town	49 360	0.97	0.07	0.17
villages, Ukraine	28 455	2.70	0.40	0.65
Belarus				
Entire country	10 000 000	0.15	0.04	0.05
Gomel region	1 680 000	0.61	0.15	0.22
Ukraine				
Entire country	55 000 000	_	_	0.01
Region around Chernobyl NPP	500 000	_	_	0.38
Kiev city	3 000 000	_	_	0.04
Russian Federation				
Entire country	150 000 000	_	_	0.002
Bryansk region	1 457 500	0.16	0.026	0.04
Kaluga, Orel, Tula regions	4 000 000	_	_	0.01

it is of the order of 10 mSv (table 1). For comparison, the average effective dose from natural background radiation, excluding radon, to an average person is about 1 mSv/year (UNSCEAR 2000), or about 70–80 mSv over a lifetime.

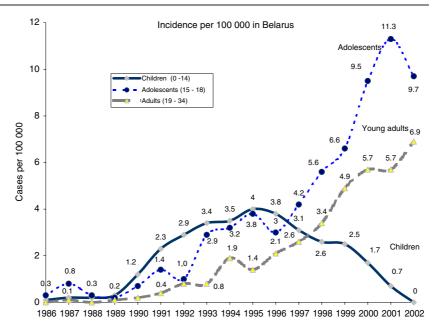
The highest organ-specific dose was to the thyroid gland, primarily from ingestion of milk contaminated with radioactive iodines, particularly <sup>131</sup>I. However, there are other sources of exposure resulting from the Chernobyl accident that contribute to thyroid dose, including intake of short-lived radioiodines (<sup>132</sup>I, <sup>133</sup>I and <sup>135</sup>I) and radiotelluriums (<sup>131</sup>Te and <sup>132</sup>Te), external irradiation from radionuclides deposited on the ground and ingestion of <sup>134</sup>Cs and <sup>137</sup>Cs. These represent, for most individuals, only a small percentage of the thyroid dose due to <sup>131</sup>I.

The estimation of thyroid doses from <sup>131</sup>I is mainly based on the 350 000 direct thyroid exposure-rate measurements made among residents of Belarus, Ukraine and the Russian Federation, within a few weeks of the accident (UNSCEAR 2000, Gavrilin *et al* 1999, Likhtarov *et al* 2005, Zvonova and Balonov 1993). A wide range of thyroid doses was received by the inhabitants of the contaminated areas in the three affected countries. Doses varied with age at the time of the accident, level of ground contamination and rate and source of milk consumption. Reported individual thyroid doses ranged up to several tens of Gy, while average doses range from a few tens of mGy to several Gy (table 3).

Intake of stable iodine tablets during the first 6–30 h after the accident reduced the thyroid dose of the residents of Pripyat by a factor of six to seven on average (Balonov *et al* 2003, Goulko *et al* 1996). Pripyat was the largest city near Chernobyl and close to 50 000 residents were evacuated within 40 h of the accident.

# 3.2. Epidemiological studies

To date, most of the published studies of health consequences have been of the ecological type, where information on dose and health outcomes (and occasionally on potential confounders) is available only at the group or population level. This type of study can be subject to potential bias, in particular the ecological fallacy (the failure of group level data to properly



**Figure 1.** Annual incidence of childhood, adolescent and adult thyroid cancer in Belarus (courtesy of Yu E Demidchik).

(This figure is in colour only in the electronic version)

reflect individual level associations) (Greenland and Morgenstern 1989, Piantadosi *et al* 1988). Analytical studies in which information is collected at the individual level, in particular case—control and cohort studies, are therefore important to evaluate the health risks associated with the Chernobyl accident (UNSCEAR 2000).

3.2.1. Thyroid cancer. The main health effect of radiation from the accident observed to date is a dramatic increase in the incidence of thyroid cancer in persons exposed as young people. This increase was observed first in the early 1990s in Belarus and continues until now in the most contaminated areas of Belarus, Ukraine and the Russian Federation (Jacob et al 2006, Kazakov et al 1992, Stsjazhko et al 1995, UNSCEAR 2000). To illustrate this, figure 1 shows the temporal trends of childhood (0–14 years), adolescent (15–18 years) and adult (19–34 years) thyroid cancer in the general population of Belarus following the accident. By 1995, the incidence of childhood thyroid cancer had increased to four per 100 000 per year compared to 0.03–0.05 cases per 100 000 per year prior to the accident. As those who were children at the time of the accident have aged (by 2002, even the very youngest had reached adulthood), the childhood thyroid cancer rates have declined to near zero and parallel increases in the incidence of thyroid cancer in adolescents and slightly later in young adults have been seen.

The number of thyroid cancer cases diagnosed in Belarus, Ukraine and in the four most contaminated regions of Russia during 1986–2002 among those who were children (<15) or adolescents (15–17) at the time of the Chernobyl accident is presented in table 4. Altogether close to 5000 cases were observed in the three countries. Of these, 15 are known to have been fatal up to now.

At the time of the Chernobyl accident, it was widely held that radioactive iodines were much less carcinogenic than external photon exposure, as little or no experience of the effects

**Table 4.** Number of cases of thyroid cancer diagnosed between 1986 and 2002, by country and age at exposure.

	Number of cases					
Age at exposure (years)	Belarus <sup>a</sup>	Russian Federation (4 most contaminated regions) <sup>b</sup>	Ukraine <sup>c</sup>	Total		
<15	1711	349	1 762	3822		
15-17	299	134	582	1015		
Total	2010	483	2 344	4837		
Population aged less than	n 15 years in 19	86				
	2300 000	1100000	11 000 000	14 400 000		

<sup>&</sup>lt;sup>a</sup> Cancer Registry of Belarus, 2006.

of the isotopes of iodine on the child's thyroid was available (Baverstock and Cardis 1996). Information on radiation induced thyroid cancer came from studies of populations exposed to external radiation, mainly the atomic bomb survivors and patients who received therapeutic exposures in childhood and infancy. The estimate of risk for persons exposed to x- or  $\gamma$ -radiation before age 15, from a combined analysis of these studies (Ron *et al* 1995), is shown in table 5. A number of epidemiological studies of thyroid cancer following exposure to radioactive iodines from the Chernobyl accident have been reported both in the most contaminated countries and in other European countries (UNSCEAR 2000). The most recent and informative studies of persons exposed in childhood and adolescence are also summarised in table 5. The excess relative risks (ERRs) derived in the case—control and cohort studies are all similar, though slightly lower than the estimate from studies of external radiation. The risk estimate from the ecological study is, on the other hand, higher but statistically compatible with that from studies of external radiation. The reasons for the difference in risk estimates for the two study designs are not yet clear, although uncertainties in dose estimates may be partly responsible.

Based on many decades of follow-up of studies of populations exposed to external radiation (Ron *et al* 1995), it is expected that Chernobyl-related thyroid cancers will continue to occur for many more years, although the long-term magnitude of risk cannot yet be quantified.

There is some indication that iodine deficiency at the time of exposure may increase the risk of developing thyroid cancer among persons exposed to <sup>131</sup>I as children (Cardis *et al* 2005a, Shakhtarin *et al* 2003). Conversely, prolonged stable iodine supplementation in the years after exposure may reduce this risk (Cardis *et al* 2005a). Further studies are needed to replicate these findings.

Papillary cancer is the primary pathological type of thyroid cancer found in those exposed as children and adolescents to fallout from the Chernobyl accident. The biology of radiation-induced thyroid cancer does not appear to be fundamentally different from that seen in non-irradiated populations, although a slightly greater percentage of radiation-induced thyroid cancers appear to be papillary in nature (Williams *et al* 2004). Possible differences in the molecular biology of the tumours, particularly with regard to *RET/PTC* rearrangements and *BRAF* mutations, are unclear at this time (Detours *et al* 2005, Powell *et al* 2005).

While the increased risk of thyroid cancer in those exposed in childhood and adolescence is well demonstrated, the effect of exposure on adults remains unclear. In the only study that has evaluated the risk for adults living in the contaminated areas (Ivanov *et al* 2003a), no

<sup>&</sup>lt;sup>b</sup> Cancer subregistry of the Russian National Medical and Dosimetric Registry, 2006.

<sup>&</sup>lt;sup>c</sup> Cancer Registry of Ukraine, 2006.

**Table 5.** Summary of the case–control and cohort studies, and of the most recent ecological study of thyroid cancer following the Chernobyl accident: comparison with a combined analysis of data on populations with external exposures.

Reference	Type of study	Country/ Region	Number of cases (ascertainment period)	Number of controls/size of study population	Type of thyroid dose	ERR at 1 Gy (95% CI)
Ron et al (1995)	Pooled analyses of 5 cohort studies	International	436	119 387	Individual doses from external exposure (x-ray, neutrons)	7.7 (2.1–28.7)
Astakhova et al (1998)	Case–control study (population based)	Belarus	107 (1988–92)	214	Individualised doses from <sup>131</sup> I (inferred from estimated mean adult thyroid dose in the village of residence, accounting for age and place of residence)	ERR: N.A <sup>a</sup> $OR^b \ge 1$ Gy versus <0.3 Gy: 5.0 (1.5–16.7) to 5.8 (2.0–17.3)
Davis <i>et al</i> (2004)	Case–control study (population based)	Russia (Bryansk)	26 (1991–1997)	52	Individual reconstruction of doses from <sup>131</sup> I	N.A
Cardis <i>et al</i> (2005a)	Case–control study (population based)	Belarus (Gomel, Mogilev), Russia (Bryansk, Kaluga, Orel, Tula)	276 (1992–1998)	1300	Individual reconstruction of doses from <sup>131</sup> I, external irradiation, intake of short-lived radioiodines and long-lived radionuclides	4.5 (2.1–8.5) to 7.4 (3.1–16.3)
Jacob <i>et al</i> (2006)	Ecologic	Belarus and Ukraine	1089 (1990–2001)	1620 000	Age-gender -settlement specific doses due to <sup>131</sup> I exposure derived from measurements of thyroid activity	18.9 (11.1–26.7)
Tronko <i>et al</i> (2006)	Cohort (screened)	Ukraine	45 (1998–2000)	13 127	Individual reconstruction of doses from <sup>131</sup> I based on measurements of thyroid activity	Approximately 5

<sup>&</sup>lt;sup>a</sup> N.A.: not available. <sup>b</sup> OR: odds ratio.

dose–response relationship was found. No association with radiation dose was observed in studies of Estonian, Latvian and Russian liquidators (Rahu *et al* 2006, Ivanov *et al* 2002).

3.2.2. Leukaemia. Leukaemia (excluding chronic lymphocytic leukaemia) has been associated with exposure to ionising radiation in a number of populations, including atomic bomb survivors, patients treated with radiotherapy and populations exposed occupationally in medicine and the nuclear industry (UNSCEAR 2000). Increases in leukaemia risk appear within 2 to 5 years after exposure and the ERR per unit of dose (particularly in children) is one of the highest among all radiation-induced cancers (UNSCEAR 2000, US NRC 2006). Leukaemia incidence and mortality are, therefore, often considered 'markers' of radiation risks in exposed populations.

It has been suggested in ecological studies in Europe, particularly in Greece (Petridou *et al* 1996), that *in utero* radiation exposure from Chernobyl may increase the risk of infant leukaemia. These results have not been confirmed in a similar study in Germany (Steiner *et al* 1998) and results of studies in Belarus (Ivanov *et al* 1998) and Ukraine (Noshchenko *et al* 2001), where this has also been investigated, are not consistent. Because the studies had low statistical power and the exposure measures were crude, the association between leukaemia and *in utero* exposure is still unclear.

Several ecological studies have examined the association between leukaemia risk and exposure to radiation from the Chernobyl accident in childhood, including the European Childhood Leukaemia–Lymphoma Study (ECLIS), the largest and most comprehensive study to date (Parkin *et al* 1993, 1996), and national incidence studies in Belarus (Gapanovich *et al* 2001, Ivanov *et al* 1993) and Russia (Ivanov and Tsyb 2002, Ivanov *et al* 2003b). The ECLIS study found no evidence of a radiation-related increase in the incidence of leukaemia in Europe in the first five years after the accident. The national studies (including those in Belarus and the Russian Federation) do not, in general, provide evidence for an increase in the incidence of childhood leukaemia. None of these studies, however, is sufficiently sensitive to detect small changes in the incidence of rare diseases such as childhood leukaemia and all are subject to methodological problems that may limit the interpretation of the findings.

Only two case–control studies of childhood leukaemia have been published to date (Noshchenko *et al* 2002, Davis *et al* 2005). A significant association between leukaemia risk and radiation dose to the bone marrow was found in Ukraine but results are difficult to interpret due to problems in the selection and comparability of controls in Ukraine. No significant increase was seen in Belarus or Russia.

Thus, the current information is scant and conclusions cannot be drawn about possible increases in childhood leukaemia following the Chernobyl accident.

The results of studies of leukaemia risk among adults, conducted both among persons residing in contaminated areas and among liquidators, are equally inconclusive. The studies of leukaemia risk among adult populations living in highly contaminated areas are ecological in nature and generally indicate an increase in leukaemia incidence over time, that does not appear to be related to level of contamination (Bebeshko *et al* 1997, Ivanov *et al* 1997, Prisyazhniuk *et al* 1995). Small studies of Estonian and Russian liquidators provide little information about risks (Rahu *et al* 1997, Shantyr *et al* 1997, Tukov and Dzagoeva 1993, Rahu *et al* 2006), while an apparent increase in incidence of leukaemia in a large cohort of Ukrainian liquidators (Buzunov *et al* 1996) is not related to dose. An approximately twofold increased risk is reported however in a very large cohort of liquidators in Russia with registered radiation doses between 150 and 300 mSv (Ivanov *et al* 2003c). Dose estimates are quite uncertain in these studies. Ongoing case—control studies of liquidators with individual dose estimates are expected to provide additional information on the magnitude of a possible increased risk of leukaemia.

3.2.3. Solid cancers other than thyroid cancer. Although ionising radiation has been shown to increase the risk of cancers at many sites, data from Chernobyl on cancers other than thyroid cancer are very sparse (UNSCEAR 2000).

No significant increase in the incidence of solid cancers (defined as all cancers excluding haematological malignancies) was seen in a cohort of over 55 000 Russian liquidators (Ivanov *et al* 2004) or among residents of the contaminated region of Kaluga in Russia (Ivanov *et al* 1997).

Analyses of rates of breast cancer among subjects included in the Ukrainian Chernobyl registry indicated a significantly increased incidence compared to the general population (Prysyazhnyuk *et al* 2002). Increases in the incidence of breast cancer over time were also reported in the Mogilev region of Belarus (Ostapenko *et al* 1998). Both of these reports are difficult to interpret, as no information about radiation dose level was available. A more detailed ecological study was therefore conducted to describe the spatial and temporal trends in breast cancer incidence in Belarus and Ukraine (Pukkala *et al* 2006). A large increase in breast cancer incidence was found in all areas of Belarus and Ukraine, reflecting improvements in cancer diagnosis and registration. A significant increase in risk was also observed during the period 1997–2001, based on a relatively small number of cases, in the districts with highest average dose levels compared to the least exposed districts. The magnitude of this increase is greater, however, than would be expected based on current risk estimates (US NRC 2006). Due to the public health importance of breast cancer, these findings warrant further investigation.

Increases in rates of other cancers, including cancers of the bladder and kidney, have also been reported (reviewed UN Chernobyl Forum, 2006). Because of various limitations (including small numbers of cases and/or controls, inadequate information on doses and/or on epidemiological methods and lack of information on other common risk factors for these diseases), it is difficult to judge the scientific merits of the findings.

## 4. Discussion

The study of the consequences of the Chernobyl accident has provided important information concerning the magnitude of the risk, and the biology of thyroid cancer following exposure to radioactive iodines in childhood and adolescence.

There remains, however, a lack of evidence of any clearly demonstrated effect of Chernobyl radiation exposures on the risk of leukaemia or solid cancers other than thyroid cancer. There have been reports of an elevated incidence of all solid cancers combined, as well as of specific cancers in Belarus, the Russian Federation and Ukraine, but much of the increase appears to be due to other factors, including improvements in diagnosis, reporting and registration. An increase in the incidence of breast cancer in the most heavily contaminated districts suggests a possible relation to radiation exposure. Recent studies suggest a doubling of leukaemia risk among Chernobyl liquidators. Both of these findings need confirmation in well designed analytical epidemiological studies with careful reconstruction of individual organ doses.

As noted above, studies of cancer risk other than thyroid are few and most have methodological limitations. Doses to most organs outside the thyroid tended to be low and studies lacked statistical power. Further, it is thought that for most solid cancers the latent period is likely to be longer than for leukaemia or thyroid cancer—of the order of 10–15 years or more (Cardis *et al* 2005b). Because studies of external radiation indicate that radiation-related risks of solid cancers remain elevated throughout life, it is too early to evaluate the full radiological impact of the Chernobyl accident.

The fact that no significant increased cancer risk, apart from thyroid cancer, has been conclusively demonstrated to date among populations most exposed to the Chernobyl accident does not therefore imply that no increase in risk has occurred. Indeed, based on the experience of other populations exposed to ionising radiation, it is expected that the low to moderate doses received will have led to a small increase in the relative risk of cancer. Given the large number of individuals exposed, the absolute number of cancer cases caused by a small increase in the relative risk could be substantial, particularly in the future.

The question of estimating the number of cancer cases which could occur due to the Chernobyl accident is important for public health planning purposes. At present, given the lack of demonstrated increases and the relatively short follow-up for solid cancers, any such estimation must be based on risk estimates derived from other populations exposed to radiation, most notably the atomic bomb survivors. This implies a number of uncertainties. Major uncertainties relate to the choice of models used for transfer of risk between populations with different background cancer rates, for projection of risk over time and for extrapolation of risks following primarily external high dose and high dose-rate exposure to very low dose and low dose-rate exposures involving a mixture of external and internal radiation. Unfortunately, these problems limit the accuracy and precision of such projections.

In 1996, Cardis *et al* published predictions of the health effects of Chernobyl radiation, derived from models of radiation-associated risk from epidemiological studies of other populations exposed to radiation, mainly members of the Life Span Study (LSS) of Japanese atomic bomb survivors. The predicted lifetime excess of cancer and leukaemia deaths due to radiation from the Chernobyl accident was of the order of 4000 for liquidators, evacuees and residents of the strict control zones. A further 5000 cancer deaths were predicted among residents of other contaminated areas, for a total of about 9000 deaths among the most exposed persons in Belarus, the Russian Federation and Ukraine. This number is only an indication of the likely impact of the accident and should not be taken at face value because of the important uncertainties listed above. Although the absolute number of predicted deaths is large, it represents only a small fraction (about 1%) of the total number of cancers expected in these populations from other causes.

If these predictions are correct, therefore, it is expected that epidemiological studies will have limited statistical power to detect small increases of risk against much larger background rates of cancer. Further, the absence of high quality disease registers in many of the contaminated regions at the time of the accident, recent changes in the longevity of the populations in the affected countries (both in contaminated and uncontaminated regions) and the absence of individual dose estimates for the majority of exposed persons make it difficult to conduct informative epidemiological studies. On the other hand, well designed studies of carefully selected populations (such as the liquidators) and endpoints (in particular leukaemia, as well as breast cancer in young women) will facilitate the detection of a wider spectrum of health effects and possibly provide important additional information about radiation risks.

# 5. Conclusion

Today, nearly 20 years after the Chernobyl accident, the large increase in thyroid cancer incidence among those exposed in childhood and adolescence continues; fortunately, few of these have been fatal. In contrast, at this time, no clearly demonstrated increase in the incidence of other cancers can be attributed to radiation exposure from the accident.

Of course, the absence of a demonstrated increase in total cancer risk is not proof that no increase has, in fact, occurred. Based on the experience of atomic bomb survivors and of populations with medical and occupational exposures to ionising radiation, a small increase

in the relative risk of cancer is expected, even at the low to moderate doses received. Given the very large number of individuals exposed, even a small increase in the relative risk would result in a substantial number of radiation-related cancer cases in the future. In the coming years, careful studies of selected populations and health outcomes are needed in order to study the full effects of the accident and compare them to predictions.

#### References

- Astakhova L N et al 1998 Chernobyl-related thyroid cancer in children of Belarus: a case–control study Radiat. Res. 150 349–56
- Balonov M, Kaidanovsky G, Zvonova I, Kovtun A, Bouville A, Luckyanov N and Voilleque P 2003 Contributions of short-lived radioiodines to thyroid doses received by evacuees from the Chernobyl area estimated using early in vivo activity measurements *Radiat. Prot. Dosim.* 105 593–9
- Baverstock K F and Cardis E 1996 The WHO activities on thyroid cancer 1st Int. Conf. of the European Commission, Belarus, the Russian Federation and the Ukraine on the Radiological Consequences of the Chernobyl Accident (Minsk, Belarus, March 1996) (Brussels: European Commission) pp 715–26
- Bebeshko V G, Bruslova E M, Klimenko V I, Dyagil I S and Drozdova V D 1997 Leukemia and lymphomas at population of Ukraine exposed to chronic low dose irradiation *Low Doses of Ionizing Radiation: Biological Effects and Regulatory Control* (Vienna: IAEA) pp 337–8 (IAEA-TECDOC-976)
- Buzunov V N, Omelyanetz N, Strapko N, Ledoschick B, Krasnikova L and Kartushin G 1996 Chernobyl NPP accident consequences cleaning up participants in Ukraine—health status epidemiologic study—main results 1st Int. Conf. of the European Commission, Belarus, the Russian Federation and the Ukraine on the Radiological Consequences of the Chernobyl Accident (Minsk, Belarus, March 1996) (Brussels: European Commission) pp 871–8
- Cardis E, Anspaugh L R, Ivanov V K, Likhtarev I A, Mabuchi K, Okeanov A E and Prisyazhniuk A E 1996 Estimated long term health effects of the Chernobyl accident *One decade after Chernobyl—Summing up the Consequences of the Accident (Proc. EU/IAEA/WHO Conf. (Vienna, April, 1996)* (Vienna: IAEA) pp 241–71
- Cardis E et al 2005a Risk of thyroid cancer after exposure to 131I in childhood J. Natl Cancer Inst. 97 724-32
- Cardis E et al 2005b Cancer risk following low doses of ionising radiation—a retrospective cohort study in 15 countries Br. Med. J. 331 77–80
- Davis S et al 2004 Risk of thyroid cancer in the Bryansk oblast of the Russian Federation after the Chernobyl power station accident Radiat. Res. 162 241–8
- Davis S *et al* 2005 Childhood leukaemia in Belarus, Russia, and Ukraine following the Chernobyl power station accident: results from an international collaborative population-based case–control study *Int. J. Epidemiol.* (November) (Epub ahead of print)
- Detours V, Wattel S, Venet D, Hutsebaut N, Bogdanova T, Tronko M D, Dumont J E, Franc B, Thomas G and Maenhaut C 2005 Absence of a specific radiation signature in post-Chernobyl thyroid cancers *Br. J. Cancer* 92 1545–52
- Gapanovich V N, Iaroshevich R F, Shuvaeva L P, Becker S I, Nekolla E A and Kellerer A M 2001 Childhood leukemia in Belarus before and after the Chernobyl accident: continued follow-up *Radiat. Environ. Biophys.* 40 259–67
- Gavrilin Y I, Khrouch V T, Shinkarev S M, Krysenko N A, Skryabin A M, Bouville A and Anspaugh L R 1999 Chernobyl accident: reconstruction of thyroid dose for inhabitants of the Republic of Belarus Health Phys. 76 105–19
- Greenland S and Morgenstern H 1989 Ecological bias, confounding, and effect modification *Int. J. Epidemiol.* **18** 269–74
- Goulko G M, Chumak V V, Chepurny N I, Henrichs K, Jacob P, Kairo I A, Likhtarev I A, Repin V S, Sobolev B G and Voigt G 1996 Estimation of 131I thyroid doses for the evacuees from Pripjat *Radiat. Environ. Biophys.* **35** 81–7
- Inskip P D *et al* 1997 Thyroid nodularity and cancer among Chernobyl cleanup workers from Estonia *Radiat. Res.* **147** 225–35
- Ivanov E P, Tolochko G, Lazarev V S and Shuvaeva L 1993 Child leukaemia after Chernobyl Nature 365 702
- Ivanov E P, Tolochko G V, Shuvaeva L P, Ivanov V E, Iaroshevich R F, Becker S, Nekolla E and Kellerer A M 1998 Infant leukemia in Belarus after the Chernobyl accident *Radiat. Environ. Biophys.* 37 53–5
- Ivanov V K, Gorski A I, Maksioutov M A, Vlasov O K, Godko A M, Tsyb A F, Tirmarche M, Valenty M and Verger P 2003a Thyroid cancer incidence among adolescents and adults in the Bryansk region of Russia following the Chernobyl accident *Health Phys.* 84 46–60
- Ivanov V K, Gorski A I, Tsyb A F, Ivanov S I, Naumenko R N and Ivanova L V 2004 Solid cancer incidence among the Chernobyl emergency workers residing in Russia: estimation of radiation risks *Radiat. Environ. Biophys.* 43 35–42

- Ivanov V K, Gorski A I, Tsyb A F and Khait S E 2003b Post-Chernobyl leukemia and thyroid cancer incidence in children and adolescents in Bryansk region: an evaluation of risks *Vopr. Onkologii* **49** 445–9
- Ivanov V K and Tsyb A F 2002 Medical Radiological Effects of the Chernobyl Catastrophe on the Population of Russia: Estimation of Radiation Risks (Moscow: Meditsina)
- Ivanov V K, Tsyb A F, Gorski A I, Maksyutov M A, Khait S E, Preston D and Shibata Y 2003c Elevated leukemia rates in Chernobyl accident liquidators [electronic letter] *Br. Med. J.*
- Ivanov V K, Tsyb A F, Nilova E V, Efendiev V F, Gorsky A I, Pitkevich V A, Leshakov S Y and Shiryaev V I 1997 Cancer risks in the Kaluga oblast of the Russian Federation 10 years after the Chernobyl accident *Radiat. Environ. Biophys.* 36 161–7
- Ivanov V K, Tsyb A F, Petrov A V, Maksioutov M A, Shilyaeva T P and Kochergina E V 2002 Thyroid cancer incidence among liquidators of the Chernobyl accident. Absence of dependence of radiation risks on external radiation dose *Radiat. Environ. Biophys.* **41** 195–8
- Jacob P *et al* 2006 Thyroid cancer risk in areas of Ukraine and Belarus affected by the chernobyl accident *Radiat. Res.* **165** 1–8
- Kazakov V S, Demidchik E P and Astakhova L N 1992 Thyroid cancer after Chernobyl [letter] Nature 359 21
- Likhtarov I, Kovgan L, Vavilov S, Chepurny M, Bouville A, Luckyanov N, Jacob P, Voilleque P and Voigt G 2005 Post-Chornobyl thyroid cancers in Ukraine. Report 1: estimation of thyroid doses *Radiat. Res.* 163 125–36
- Minenko V 2000 IRPA-10: Proc. Int. Radiation Protection Association (Hiroshima, Japan, May 2000) 5-23-0040
- Noshchenko A G, Moysich K B, Bondar A, Zamostyan P V, Drosdova V D and Michalek A M 2001 Patterns of acute leukaemia occurrence among children in the Chernobyl region *Int. J. Epidemiol.* 30 125–9
- Noshchenko A G, Zamostyan P V, Bondar O Y and Drozdova V D 2002 Radiation-induced leukemia risk among those aged 0-20 at the time of the Chernobyl accident: a case–control study in the Ukraine *Int. J. Cancer* **99** 609–18
- Ostapenko V A, Dainiak K L and Hunting 1998 Breast Cancer Rates Among Women in Belarus Prior to and Following the Chernobyl Cathastrophe (Rotterdam: International Conference on Diagnosis and Treatment of Radiation Injury)
- Parkin D M et al 1993 Childhood leukaemia following the Chernobyl accident: the European Childhood Leukaemia-Lymphoma Incidence Study (ECLIS) Eur. J. Cancer 29A 87–95
- Parkin D M et al 1996 Childhood leukaemia in Europe after Chernobyl: 5 year follow-up Br. J. Cancer 73 1006–12
  Petridou E, Trichopoulos D, Dessypris N, Flytzani V, Haidas S, Kalmanti M, Koliouskas D, Kosmidis H,
  Piperopoulou F and Tzortzatou F 1996 Infant leukaemia after in utero exposure to radiation from Chernobyl Nature 382 352–3
- Piantadosi S, Byar D P and Green S B 1988 The ecological fallacy Am. J. Epidemiol. 127 893-904
- Powell H G, Jeremiah J, Morishita M, Bethel J, Bogdanova T, Tronko M and Thomas G A 2005 Frequency of BRAF T1794A mutation in thyroid papillary carcinoma relates to age to patient at diagnosis and not to radiation exposure J. Pathol. 205 558–64
- Prisyazhniuk A, Gristchenko V, Zakordonets V, Fouzik N, Slipeniuk Y and Ryzhak I 1995 The time trends of cancer incidence in the most contaminated regions of the Ukraine before and after the Chernobyl accident *Radiat. Environ. Biophys.* 34 3–6
- Prysyazhnyuk A E, Gulak L O, Gristchyenko V G and Fedorenko Z P 2002 Cancer incidence in Ukraine after the Chernobyl accident *Chernobyl: Message of the 21st Century. Proc. 6th Chernobyl Sasakawa Medical Cooperation Symp.* (New York: Elsevier)
- Pukkala E, Polyakov S, Ryzhov A, Kesminiene A, Drozdovitch V, Kovgan L N, Kyyronen P, Malakhova I, Gulak L and Cardis E 2006 Breast cancer in Belarus and Ukraine after the Chernobyl accident *Int. J. Cancer* www3.interscience.wiley.com (doi:10.1002/ijc.21885)
- Rahu M, Rahu K, Auvinen A, Tekkel M, Stengrevics A, Hakulinen T, Boice J D Jr and Inskip P D 2006 Cancer risk among Chernobyl cleanup workers in Estonia and Latvia, 1986–1998 Int. J. Cancer 119 162–8
- Rahu M, Tekkel M, Veidebaum T, Pukkala E, Hakulinen T, Auvinen A, Rytomaa T, Inskip P D and Boice J D Jr 1997 The Estonian study of Chernobyl cleanup workers: II. Incidence of cancer and mortality *Radiat. Res.* 147 653–7
- Ron E, Lubin J H, Shore R E, Mabuchi K, Modan B, Pottern L M, Schneider A B, Tucker M A and Boice J D Jr 1995 Thyroid cancer after exposure to external radiation: a pooled analysis of seven studies *Radiat. Res.* 141 259–77
- Shakhtarin V V, Tsyb A F, Stepanenko V F, Orlov M Y, Kopecky K J and Davis S 2003 Iodine deficiency, radiation dose, and the risk of thyroid cancer among children and adolescents in the Bryansk region of Russia following the Chernobyl power station accident *Int. J. Epidemiol.* 32 584–91
- Shantyr I I et al 1997 Cancer Morbidity Among the Emergency Workers of the Chernobyl Accident Int. Conf. on Low Doses of Ionizing Radiation: Biological Effects and Regulatory Control (Seville, Spain) (Vienna: IAEA) IAEA-TECDOC-976
- Steiner M, Burkart W, Grosche B, Kaletsch U and Michaelis J 1998 Trends in infant leukaemia in West Germany in relation to in utero exposure due to Chernobyl accident *Radiat. Environ. Biophys.* 37 87–93

Stsjazhko V A, Tsyb A F, Tronko N D, Souchkevitch G and Baverstock K F 1995 Childhood thyroid cancer since accident at Chernobyl [letter] *Br. Med. J.* **310** 801

- Tronko M D *et al* 2006 A cohort study of thyroid cancer and other thyroid diseases after the Chernobyl accident: thyroid cancer in Ukraine detected during first screening *J. Natl Cancer Inst.* at press
- Tukov A and Dzagoeva L G 1993 Morbidity of Atomic Industry Workers of Russia who Participated in the Work of Liquidating the Consequences of the Chernobyl Accident—Medical Aspects of Eliminating the Consequences of the Chernobyl Accident (Moscow, SSSR: Central Scientific Research Institute)
- UN Chernobyl Forum 2006 Health Effects of the Chernobyl Accident and Special Health Care Programmes (Geneva: WHO)
- UNSCEAR (United Nations Scientific Committee on the Effects of Atomic Radiation) 2000 Sources and Effects of Ionizing Radiation—Volume II: Effects (New York: United Nations)
- US NRC (National Research Council) 2006 Health Risks from Exposure to Low Levels of Ionizing Radiation. BEIR, VII Report, phase II (Washington, DC: NRC)
- Williams E D et al 2004 Thyroid carcinoma after Chernobyl latent period, morphology and aggressiveness Br. J. Cancer 90 2219–24
- Zvonova I A and Balonov M I 1993 Radioiodine dosimetry and forecast for consequences of thyroid exposure of the RSFSR inhabitants following the Chernobyl accident *The Chernobyl Papers. V. I: Doses to the Soviet Population and Early Health Effects Studies* (Richland, WA: Research Enterprises) pp 71–125