

## Radiation-epidemiological analysis of the incidence of non-cancer diseases among the Chernobyl liquidators

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The work is concerned with assessment of radiation risks for non-cancer diseases among the Chernobyl liquidators from 1986 to 1996. As of 1 January 1999 the Russian National Medical and Dosimetric Registry contain medical and dosimetric data for 174 thousand liquidators. The cohort of 68,309 liquidators for whom best verified medical data are available is discussed. The dose dependency of the incidence of non-cancer diseases was estimated by the cohort method and using the software package Epicure. For some classes of non-cancer diseases among liquidators statistically significant estimates of radiation risk were derived for the first time. The highest excess relative risk per 1 Gy was found for cerebrovascular diseases  $ERR/Gy=1.17$  at the 95% confidence interval (0.45; 1.88).

### Introduction

Radiation disaster at 1'23" on 26 April 1986. The largest in human history occurred at the fourth power unit of the Chernobyl NPP.

In June 1986 the Ministry of Health Care of USSR adopted a large-scale program to establish the All-Union Distributed Registry of people exposed to radiation. The Research Institute of Medical Radiology of USSR AMS in Obninsk (today Medical Radiological Research Center) was appointed the lead organization to develop and maintain the Registry.

The Registry basically pursues two goals: first, to evaluate health effects of the disaster in order to develop an optimum strategy for minimizing medical consequences and secondly, to conduct many-years epidemiological studies in order to determine, first of all, actual radiation risks.

By December 1991 (the date of the USSR disintegration) the Registry database contained personal medical and dosimetric information for 659,292 persons including 284,919 emergency workers (liquidators). All republics of the former USSR, many of research and public health institutions have been involved in creating the Registry.

On 22 September 1993 the Government of Russian Federation adopted the Decree «On state registration of persons exposed to radiation as a result of the Chernobyl and other radiation disasters and incidents». By 1 January 1999 the Russian National Medical and dosimetric Registry (RNMDR) included medical and dosimetric data for 530,965 persons exposed to radiation as a result of the Chernobyl accident and residing in the territory of Russian Federation, among them 174,916 liquidators.

By now a lot of papers have been published in the literature on assessment of health effects of the Chernobyl accident. These papers primarily aim to study the dynamics of oncological diseases, in particular thyroid cancer among residents of the most contaminated areas. At the same time, the number of papers dealing with assessment of radiation risks of cancers among the Chernobyl liquidators is still rather

limited [1-5] and there are virtually no papers on estimation of radiation risks for non-cancer diseases among liquidators. The present work, in fact, is the first to provide assessments of dose dependency for non-cancer diseases based on the RNMDR data on the cohort of liquidators.

It should be mentioned the results of RERF researchers [6] concerning estimation of radiation risks of non-cancer diseases in the population affected by the atomic bombing (the AHS cohort), were not published until 1993. Statistically significant estimates of dose dependency (estimates of relative risk per 1 Gy under the assumption of linear relationship) were derived for four non-cancer diseases: thyroid disorders, myoma, chronic hepatitis and cirrhosis of the liver and myocardial infarction (for persons under 40 at the time of atomic bombing).

### Methods and materials

#### Description of the cohort under study

To date the RNMDR contains medical and dosimetric information for more than 174 thousand liquidators living across Russia. The procedure of final verification of the establishment incidence data and of health status data took 95% completeness for those registered in RNMDR takes about 2 years. Therefore, the endpoint of the study was taken 31 December 1996. To enhance the reliability of the study the cohort was formed from the liquidators registered in 6 main regional centers of RNMDR which annually supply best verified medical and dosimetric data: North-West, North-Caucasus, Volgo-Vyatsky, Povolzhsky, Central-Chernozemny and Urals. By the end of 1996 the RNMDR contained information on 95638 liquidators living in the territories of the above regions. This sample of liquidators included 26,557 persons with unknown external dose and therefore they could not be included in the cohort under study. The remaining set included 190 female liquidators who were not included in the cohort under study either. Other 582 liquidators were not entered in the cohort because of the absence of medical examination data and

because they did not ask any medical aid since registration in RNMDR and by the end of 1996 no data on their health were available.

It should be noted that liquidators were not only registered in RNMDR immediately after arrival from the recovery area, but the process still goes on. To exclude possible bias in results due to additional registration in the years after the accident we decided to include only those liquidators who were registered prior to 1 January 1992. Thus, we formed a retrospective cohort consisting of 68,309 male liquidators, for each of which external gamma-radiation dose was known and health information was available in RNMDR (at least one entry from 1986 to 1996). All were registered before 1 January 1992.

Fig. 1 shows coverage by the annual medical checkups of liquidators who arrived to the 30-km zone of the Chernobyl NPP in 1986-1987 and those who arrived to the zone later. It can be seen that starting from 1990 the number of followed-up liquidators with different time of arrival to the zone remains at a constant level which indicates stability in the methods of epidemiological data collection and consequently robustness of the derived estimates concerning the health of the cohort members.

Fig. 2 shows the distribution of the number of liquidators with different time of arrival to the zone by the number of annual checkups registered in RNMDR from 1986 to 1996. As can be seen, the number of liquidators with 1 to 9 examinations is growing steadily and the highest number is 10,023 liquidators.

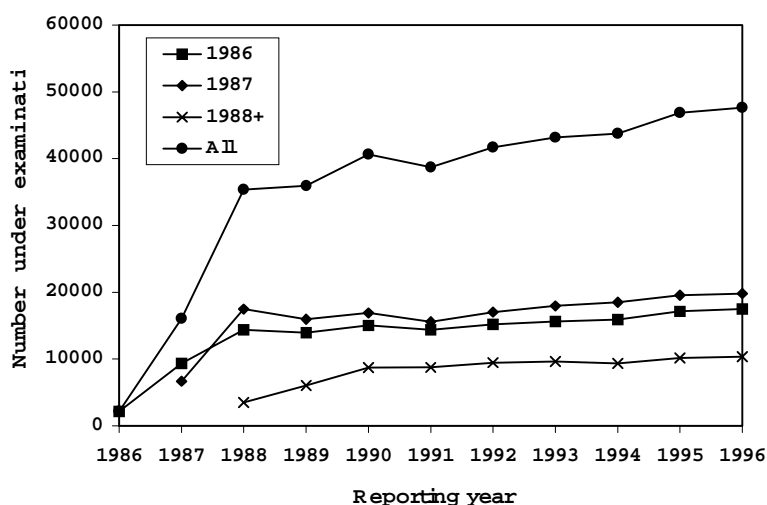


Fig. 1. Dynamics of checkups of liquidators who arrived to the 30-km zone at different times.

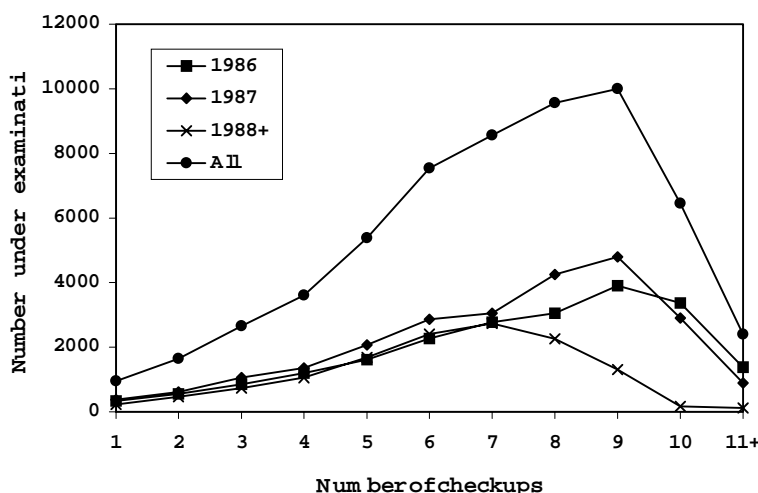


Fig. 2. Distribution of the number of liquidators with different time of arrival to the zone by the number of checkups registered in the registry.

In the present study the term dose means a documentary confirmed external radiation dose for each liquidator. The dosimetric data for liquidators may be classified into three groups:

- radiation or absorbed dose based on readings of an individual dosimeter;
- group dose assigned to members of a group performing an operation in the zone, based on the

readings of an individual dosimeter held by one member of the group;

- itinerary dose estimated from the average dose rate in the zone and duration of stay of the group there.

Fig. 3 illustrates distribution of liquidators of the cohort under study by dose groups. The ranges of dose groups are the same as the values used for radiation-epidemiological analysis. As can be seen from Fig. 3, the most representative (by the number of people) dose group is group 50-150 mGy and it basically consists of the liquidators who arrived to the zone in 1987. The group «above 200 mGy» consists predominantly of liquidators of the who arrived in 1986. The smallest in number is group 150-200 mGy.

As can be seen from Fig. 4, the number of the cohort members aged 35 to 39 at the time of the arrival to the 30-km zone is the largest in the age groups selected for analysis. The number of

liquidators older than 45 years of age was the smallest.

Fig. 5 shows the distribution of liquidators by average dose in different age groups (the age at the time of arrival to the 30-km zone).

As can be seen, the maximum average doses 139 mGy and 135 mGy were received by liquidators who were 18-29 years and older 45 years, respectively.

Figs. 6 and 7 show distributions of the cohort members by the number and mean dose as a function of the time of arrival to the zone. As can be seen from Fig. 6, most of the liquidators entered the zone in 1987 and the smallest from 1988 onwards. In terms of the maximum of the mean dose (Fig. 7), as might be expected; the liquidators of 1986 were exposed to maximum of the mean dose (167 mGy). The liquidators who entered the zone in 1988 and later were exposed to the minimum (31 mGy).

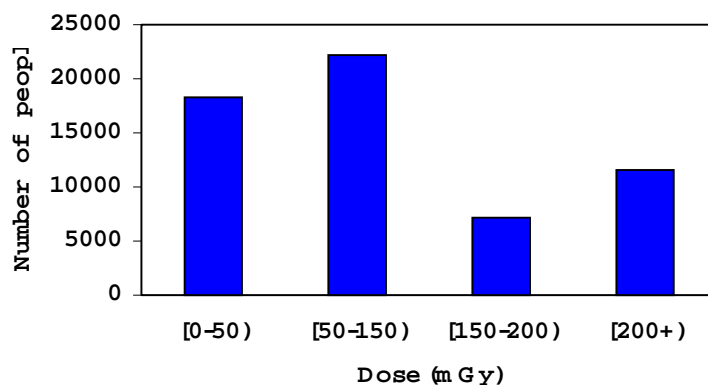


Fig. 3. Distribution of liquidators by radiation dose.

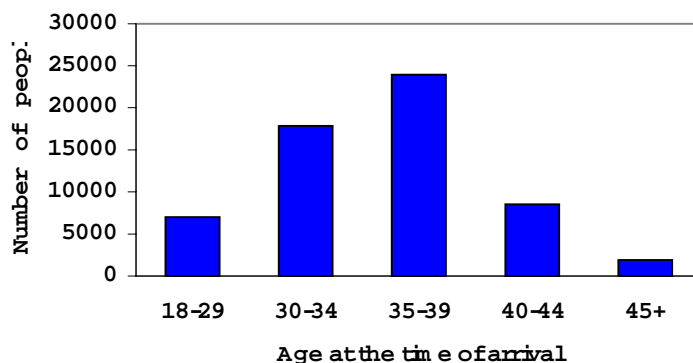


Fig. 4. Distribution of liquidators by age at the time of arrival to the zone.

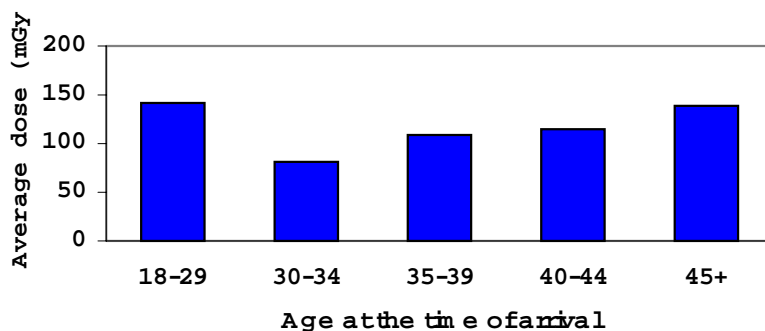


Fig. 5. Distribution of liquidators by the mean dose as a function of age at the time of arrival to the zone.

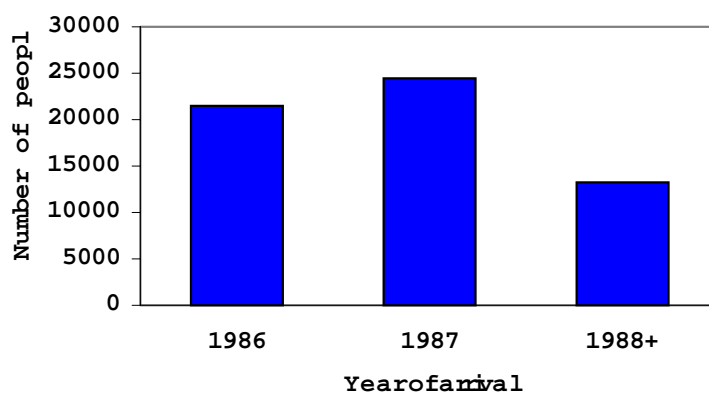


Fig. 6. Distribution of liquidators by the number of people as a function of time of arrival to the zone.

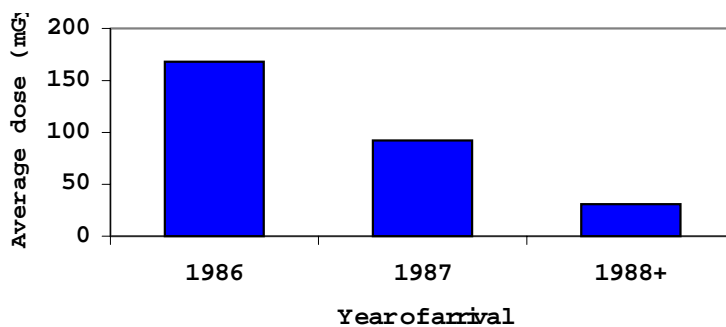


Fig. 7. Distribution of liquidators by the mean dose as a function of time of arrival to the zone.

**Annual medical checkups of liquidators**

In accordance with the decree of Ministry of Health № 171 of 26 July 1993 liquidators are subject

to annual examinations by GP, surgeon, oncologist, endocrinologist and take mandatory laboratory and diagnostic tests for hemoglobin, erythrocytes, leukocytes, thrombocytes, differential blood count,

erythrocyte sedimentation rate (ESR), urinalysis, electrocardiogram (ECG), arterial pressure, ultrasonic screening of thyroid, abdominal and pelvic organs, gastroscopy, colonoscopy (for persons older 50 years) and examinations by indications.

Diseases of the circulatory system are diagnosed using standard diagnostic criteria. We used the criteria recommended by WHO for epidemiological studies, namely the criteria for diseases of the circulatory system are angina of effort, anamnesis myocardial infarction and electrocardiographic symptoms of diseases of the circulatory system (Minnesota code); the criteria of cerebrovascular diseases by the WHO epidemiological protocol are initial manifestation of cerebral circulation insufficiency, temporary disorders in cerebral circulation, insult and discirculatory encephalopathy. Arterial hypertension is understood to be a high-systolic arterial pressure (140 mm and higher) and/or the diastolic arterial pressure 90 mm and higher.

The persons who were diagnosed with diseases of the circulatory system during a checkup are usually taken to hospital for examination.

Results of annual checkups of liquidators are put down in paper records of RNMDR and are then entered in the computer database of the Registry. The coded data on the health status of liquidators on magnetic disks are passed on via the regional centers to state bodies and after verification become available for radiation-epidemiological analysis.

#### Analytical method

The time under risk to develop a disease of the class under study (or specific disease) is calculated as a difference of dates  $T_1$  and  $T_0$ , where  $T_0$  is the time of arrival to the 30-km zone and  $T_1$  is the minimum of the following dates: the date of the first diagnosis for the disease class under study, the date of the latest medical checkup, the death date and the date of termination of follow-up. The incidence rate used in this paper is defined as ratio of the total cases of a disease class and the total time under risk measured in person-years.

To determine the dependence of incidence rates on radiation dose we used the cohort method. A multi-dimensional table was drawn in which the individual data on liquidators were divided into 5 strata by age at the time of arrival to the 30-km zone (18-29, 30-34, 35-39, 40-44, 45 and older), 3 strata by the year of arrival to the zone (1986, 1987, 1988+), 6 strata by belonging to a regional center of RNMDR: North-West, North-Caucasus, Volgo-Vyatsky, Povolzhsky, Central-Chernozemny and the Urals and 4 groups by dose ([0-50), [50-150), [150-200), [200 and higher) mGy). The stratification by age was done to make up for the influence of age peculiarities of the detected diseases. To take into account the specific conditions in the affected zone in different years after the accident stratification by the year of arrival to the zone was introduced. Stratification by belonging to a regional center was done to allow for the differences in the background incidence rates due to different intensity of medical screening in the indicated regions.

Let  $i$  be the age group index and  $j$  is the dose group index.

Let  $Y_{ij}$  be the number of cases,  $P_{ij}$  is person-years,  $M_{ij}$  is the incidence rate in the stratum  $ij$ . In these terms  $M_{ij}$  for a given class of diseases can be determined as follows:

$$M_{ij} = Y_{ij} / P_{ij} . \tag{1}$$

The relative incidence risk  $RR_{ij}$  is determined as the ratio of incidence rates in the study and control groups, i.e.:

$$RR_{ij} = M_{ij} / M_{i0}, \tag{2}$$

and the control group comprises people whose dose lies in the first dose interval (in our case from 0 to 50 mGy).

It is reasonable to assume that the values  $Y_{ij}$  are independent Poisson random values with mathematical expectation  $E(Y_{ij}) = P_{ij}M_{ij}$ . For determination of the dependence of  $M_{ij}$  on the dose  $M_{ij}$  should be presented as parametric function and its parameters are to be determined via maximization of the logarithmic likelihood function:

$$l = \sum \{Y_{ij} \ln(P_{ij}M_{ij}) - P_{ij}M_{ij}\}, \tag{3}$$

where  $M_{ij} = f(D_{ij})$  where  $D_{ij}$  is the average dose in the stratum  $ij$ , the summation is done by all the strata  $ij$ . Simple functions are used in this paper:

$$f(D_{ij}) = \exp(a_j), \tag{4}$$

$$f(D_{ij}) = M_{i0} \exp(b_j \delta_{ij}), \tag{5}$$

$$f(D_{ij}) = M_{i0} + cD_{ij}, \tag{6}$$

$$f(D_{ij}) = M_{i0} (1 + \beta D_{ij}), \tag{7}$$

where  $\delta_{ij} = 0$  for  $j = 0$  and  $\delta_{ij} = 1$  for  $j > 0$ .

Function (4) is used to determine crude incidence rates in the dose groups, function (5) is used to determine relative risk  $RR$  in the dose groups, functions (6) and (7) are used to determine the linear trends of the incidence rate and the relative risk by dose. To estimate the significance of the dose dependence of the relative risk the likelihood ratio test was applied. The 0-50 mGy group was taken as the background dose group (internal control). We also determined the excess relative risk (ERR) equal to the estimate of parameter  $\beta$  in (7).

The estimation of parameters of equations (5-7), the statistical tests and determination of confidence intervals was done using the programming package EPICURE.

## Discussion and results

### Estimation of dose dependency for the main classes of non-cancer diseases

As can be seen from Table 1 and Fig. 8, a dependence upon dose which is statistically significant (with 95% confidence interval) was observed for four classes of non-cancer diseases:

1. endocrine diseases and metabolic disorders (ERR=0.58, 95% CI (0.30, 0.87));

2. mental disorders (ERR=0.40, 95% CI (0.17, 0.63));
3. diseases of the nervous system and sensory organs (ERR=0.35, 95% CI (0.19, 0.52));
4. diseases of the digestive system (ERR=0.24, 95% CI (0.05, 0.43)).

Two other classes of diseases show a dose dependency which is close to being statistically significant.

1. diseases of the circulatory system (ERR=0.23, 95% CI (-0.03, 0.50));
2. diseases of the genitourinary system (ERR=0.43, 95% CI (-0.02, 0.87)).

For other classes of diseases under study no statistically significant dose dependencies were observed.

We also calculated the excess relative risk separately for liquidators with different time of arrival to the emergency zone. It is only the endocrine and metabolic diseases for which we obtained statistically significant estimates of ERR both for 1986 and 1987. The values of ERR for the liquidators of 1986 was 0.57 with 95% CI (0.19, 1.00) and for the liquidators

of 1987 the value of ERR was 0.75 with 95% CI (0.28, 1.22). Below listed are diseases for which statistically significant estimates of ERR as a function of the year of arrival to the zone were obtained:

- mental disorders, 1986 (ERR=0.53, 95% CI (0.21, 0.85));
- diseases of the nervous system and sensory organs, 1986 (ERR=0.45, 95% CI (0.22, 0.68));
- diseases of the digestive system, 1986 (ERR=0.27, 95% CI (0.01, 0.52));
- diseases of the genitourinary system (ERR=0.89, 95% CI (0.10, 1.68)).

Thus, as a result of the radiation-epidemiological analysis of the dose dependency of non-cancer diseases we identified a series of classes of diseases, which show a statistically significant growth with increase in dose. For endocrine and metabolic diseases a statistically significant risk was observed for both the liquidators of 1986 and the liquidators of 1987 (the time of arrival to the zone). For diseases of the genitourinary system the statistically significant relative risk was obtained for the liquidators of 1987.

Table 1

Estimation of parameters of dose dependency of incidence rates for different non-cancer diseases among liquidators

Disease	ICD-9 codes	P	ERR (1/Gy)
Infectious and parasitic diseases	001-139	0.152	-0.49 (-1.12, 0.15)
Endocrine and metabolic diseases	240-279	<0.001	0.58 (0.30, 0.87)
Diseases of blood and blood-forming organs	280-289	0.701	-0.17 (-1.00, 0.67)
Mental disorders	290-319	<0.001	0.40 (0.17, 0.64)
Diseases of the nervous system and sensory organs	320-389	<0.001	0.35 (0.19, 0.52)
Diseases of the circulatory system	390-459	0.077	0.23 (-0.03, 0.50)
Diseases of the respiratory system	460-519	0.893	0.11 (-0.15, 0.18)
Diseases of the digestive system	520-579	0.013	0.24 (0.05, 0.43)
Diseases of the genitourinary system	580-629	0.048	0.43 (-0.02, 0.87)
Diseases of the skin and subcutaneous tissue	680-709	0.377	-0.22 (-0.70, 0.26)
Diseases of the musculoskeletal system and connective tissue	710-739	0.319	0.09 (-0.09, 0.26)
Injuries and poisoning	800-999	0.161	0.24 (-0.11, 0.59)

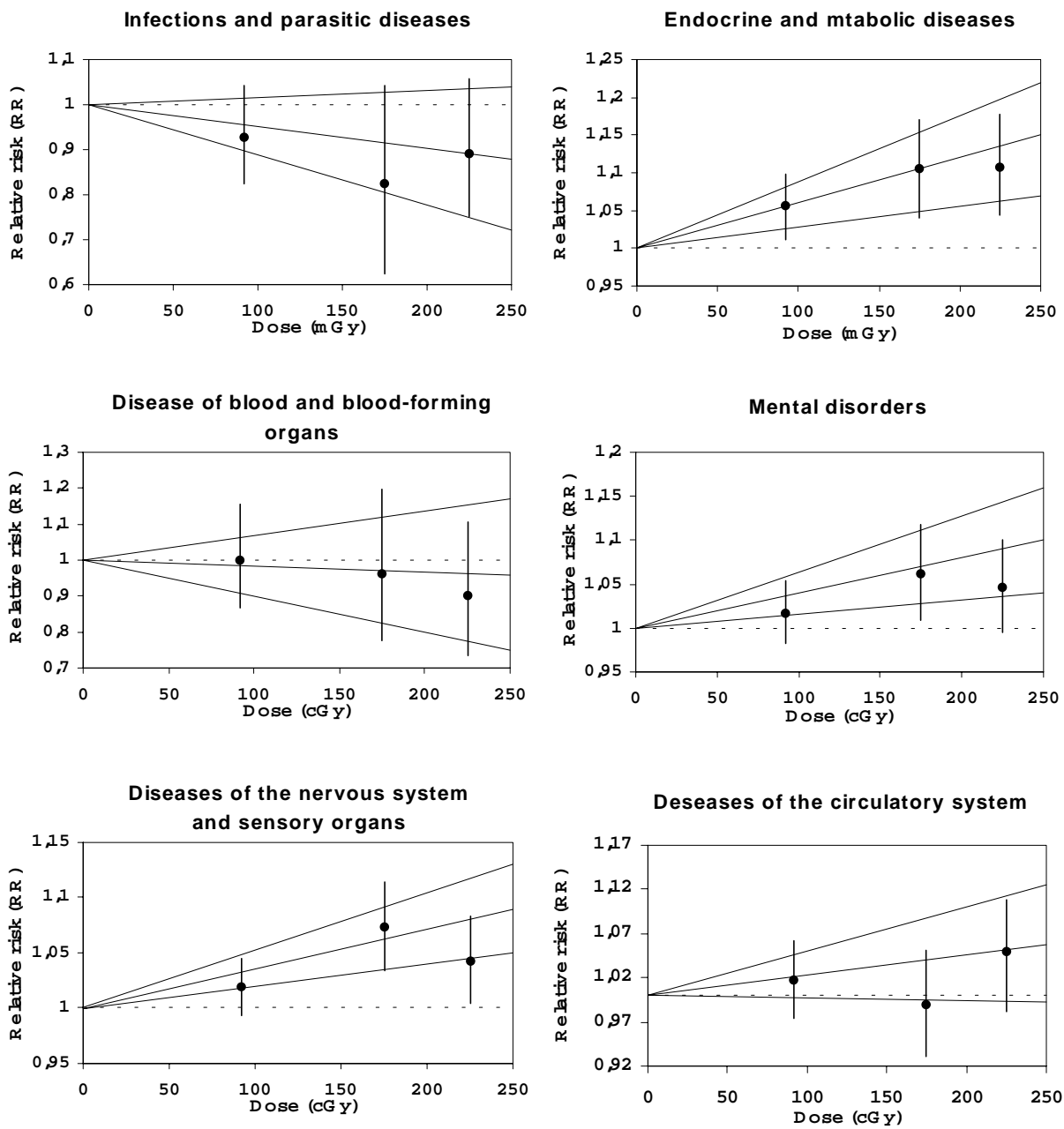
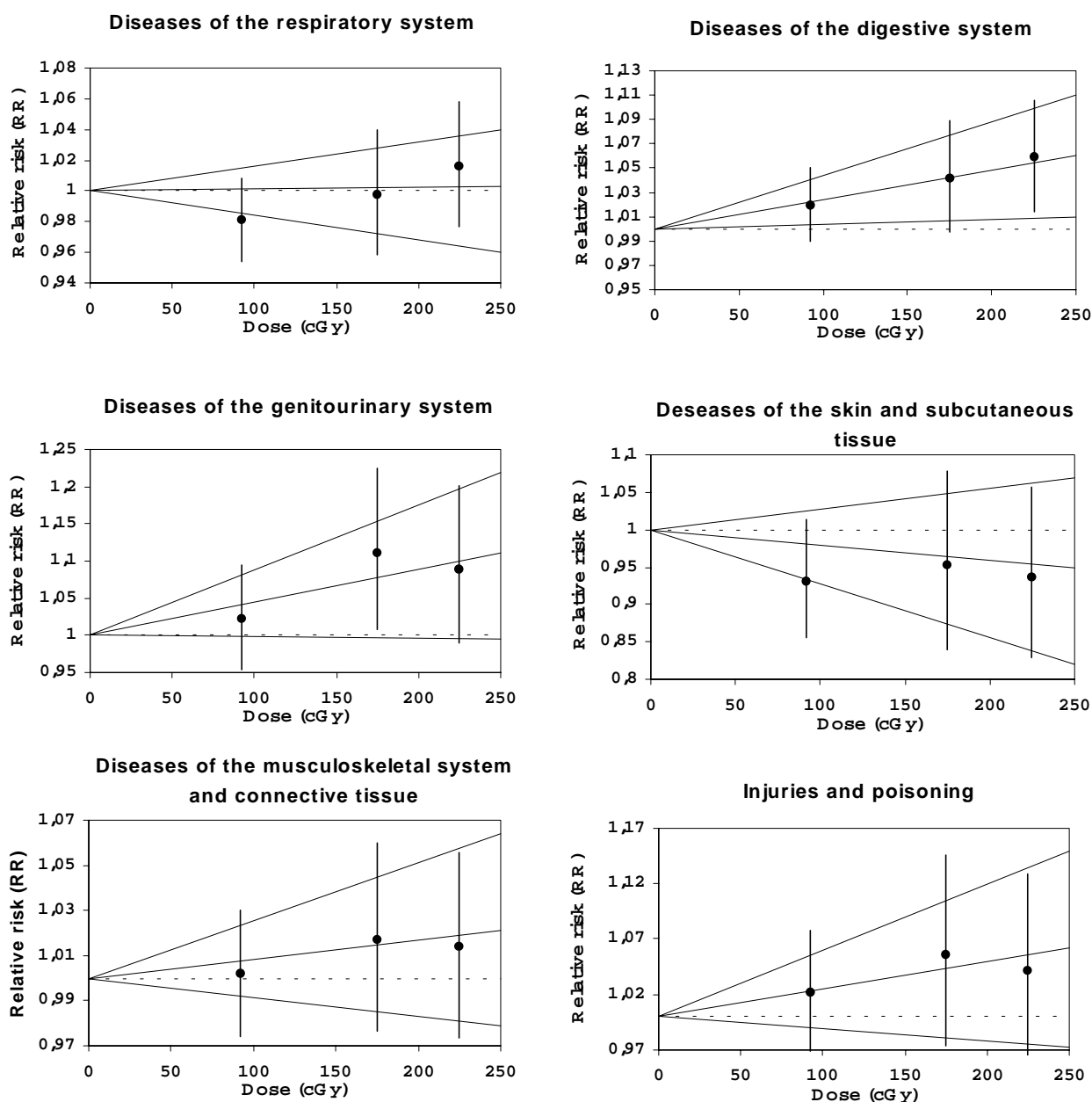


Fig. 8. Relative risk among liquidators with different non-cancer diseases in the dose groups (the line is linear trend corresponding to the regression function (7)).



**Fig. 8 (Continued).** Relative risk among liquidators with different non-cancer diseases in the dose groups (the line is linear trend corresponding to the regression function (7)).

**Estimation of the dose dependency for the proposal diseases of the circulatory system**

This section contains estimates of relative risks for the proposal diseases of the circulatory system. We focus on the analysis of epidemiological characteristics of the liquidators' cohort from the



standpoint of stability and homogeneity of data accumulated in the Registry on diseases of the circulatory system.

Table 2 shows the proposal classes of diseases of the circulatory system, their ICD-9 codes, the number of diseases of a class diagnosed in the time period under study, the number of person-years under risk and values of the crude incidence rate per 100,000 person-years calculated by formula 4. As can be seen from Table 2, in the considered time period from 1986 to the end of 1996 19,542 cases of diseases of the circulatory system (ICD-9 codes 390-459) were reported in the cohort of liquidators under study, with the total number of follow-up person-years being

462,611. The most common circulatory diseases among liquidators are hypertensive disease (ICD-9: 401-405) – 9,316 cases, ischaemic heart disease (ICD-9: 410-414) – 5,383 cases, cerebrovascular diseases (ICD-9: 430-438) – 3,887 cases and diseases of veins, lymphatic vessels and other circulatory diseases (ICD-9: 451-459) – 4,338 cases. The main contribution to the hypertensive disease in liquidators is made by essential hypertension (ICD-9: 401) – 7,741 cases and the hypertensive disease with heart affection (ICD-9: 402) – 2,469 cases. Among the ischaemic heart diseases prevailing is angina pectoris (ICD-9: 413) – 2,714 cases and other forms of chronic IHD (ICD-9: 414) – 3,011 cases.

**Table 2**

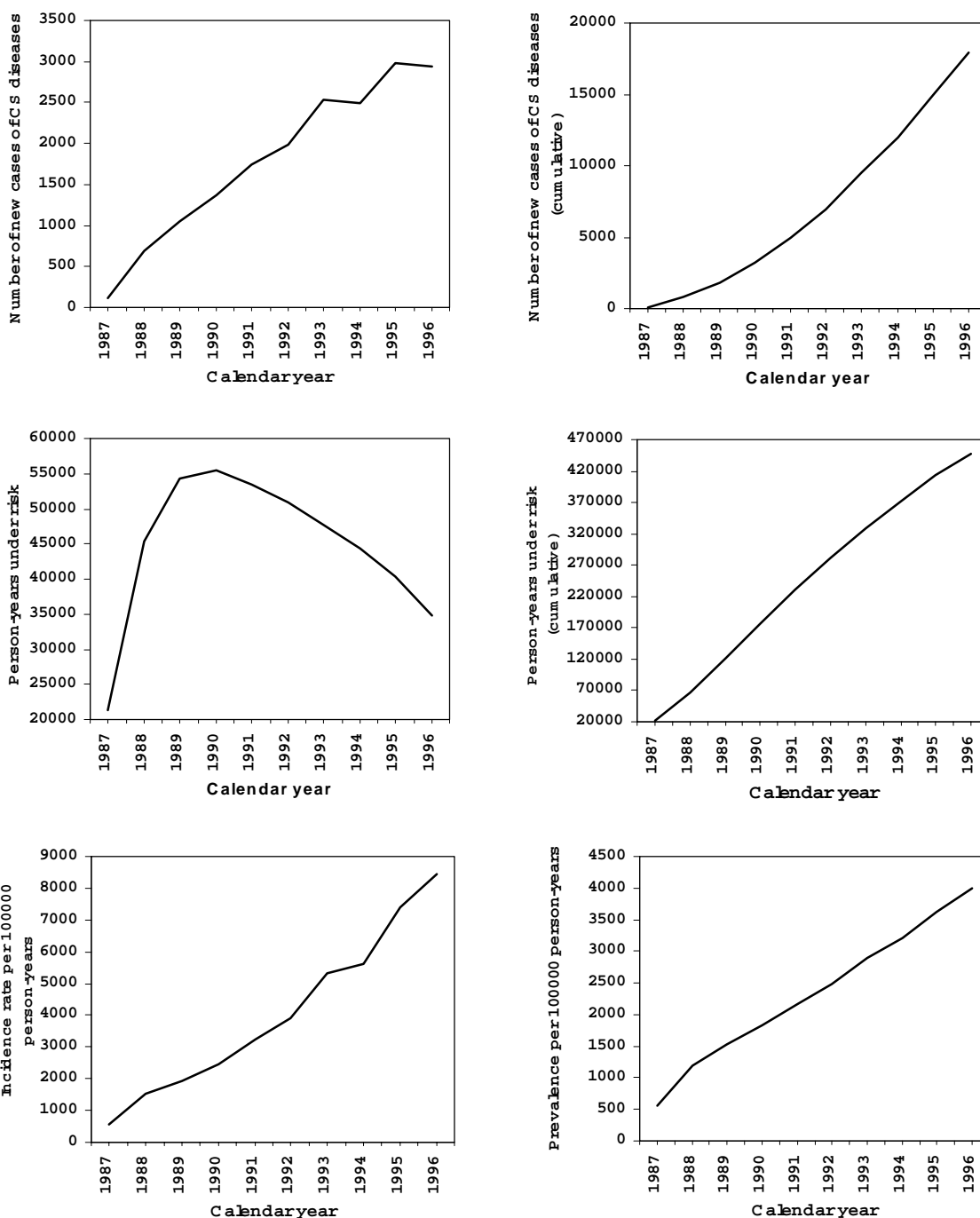
**Incidence rate for diseases of the circulatory system among liquidators in the period 1986-1996**

Disease	ICD-9 codes	Number of cases	Time under risk (person-years)	Crude incidence rate per 100000 person-years
Diseases of the circulatory system	390-459	19,542	462,611	4,224
Hypertensive disease	401-405	9,316	493,029	1,890
Essential hypertension	401	7,741	498,034	1,554
Hypertension heart disease	402	2,469	518,098	477
Ischaemic heart disease (IHD)	410-414	5,383	513,283	1,049
Acute myocardial infarction	410	595	524,325	113
Other acute IHD	411	498	524,881	95
Angina pectoris	413	2,714	519,758	522
Other chronic forms of IHD	414	3,011	518,807	580
Other forms of heart disease	420-429	1,715	521,378	329
Cerebrovascular diseases	430-438	3,887	519,100	749
Diseases of arteries, arterioles and capillaries	440-448	1,963	521,496	376
Diseases of veins, lymphatic vessels and other diseases of the circulatory system	451-459	4,338	511,910	847

Fig. 9 shows the dynamics of detection of diseases of the circulatory system, the time under risk and crude incidence rates per 100,000 person-years by observational years and cumulatively. The dynamics of new cases of diseases of the circulatory system is indicative of a steady increase in the number of newly diagnosed cases, which is only natural, as the cohort is getting older and a minor decrease in the number of diagnosed cases in 1996 is probably explained by a certain delay in obtaining data at the national level. As can be seen from the figure, the maximum of annual time under risk falls on 1990 and then the time under risk is smoothly decreasing to 34,000 additional person-years a year. It should be noted that the trend would continue in the future, as the number of liquidators having no problems with the circulatory system decreases every

year. The year-by-year incidence rate is growing steadily, which is in full agreement with the dynamics of the newly diagnosed cases and is a direct consequence of the aging of the cohort.

The prevalence shows similar behavior from year to year in all the regions. Over the entire time interval of the study the maximum values of incidence rate were reported in the Northwest region and the minimum in the Central-Chernozemny region. Thus the cohort under study is basically homogeneous for 6 regions supplying information on liquidators and the differences in incidence rates for diseases of the circulatory system resulting from regional differences in the background incidence of diseases of the circulatory system and in the methodologies used for diagnosing cardiovascular diseases are taken into account by grouping data by regions.



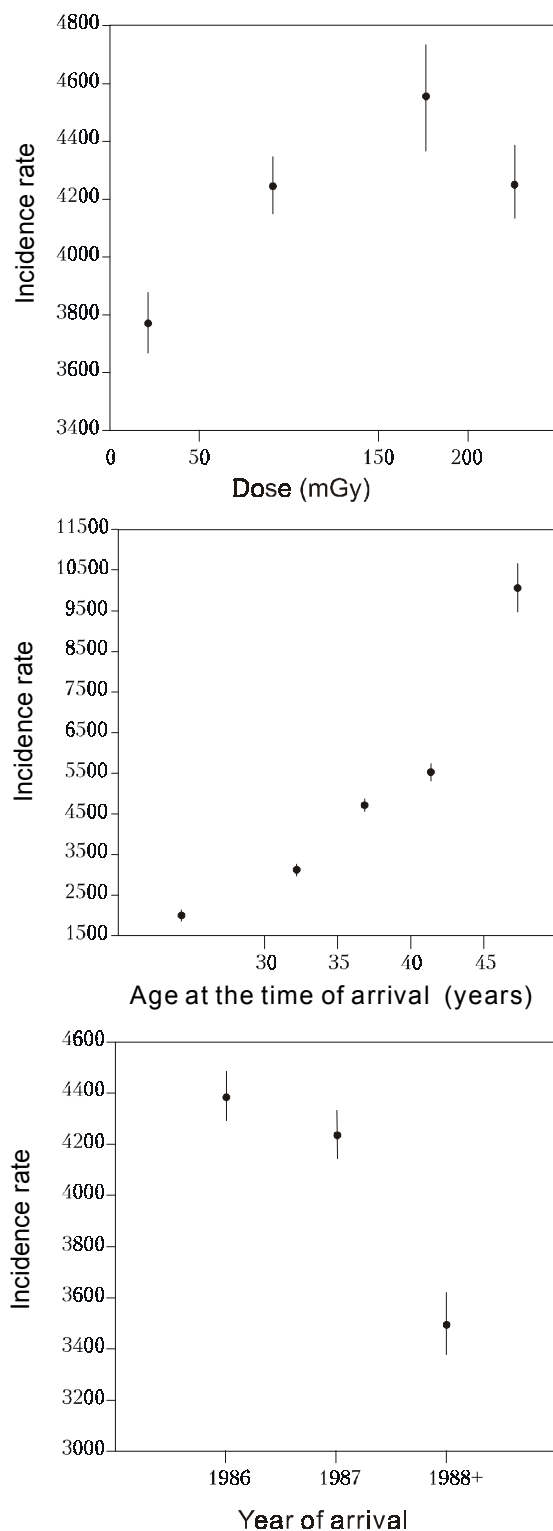
**Fig. 9.** Dynamics of detection of cases of diseases of the circulatory system, time under risk and crude incidence rate per 100,000 person-years: year-by-year (left) and cumulative (right).

Fig. 10 shows estimates of the crude incidence rate for diseases of the circulatory system as a function of dose of liquidators, age at the time of arrival to the zone and the year of arrival to the zone. As can be seen, the incidence rate increases significantly with the growth of external radiation dose ( $p < 0.05$ ) and age ( $p < 0.05$ ) and decreases

significantly ( $p < 0.05$ ) with increase in the year of arrival to the 30-km zone for all diseases of the circulatory system. So, the radiation dose and year of arrival to the 30-km zone are the most important «external» factors influencing the incidence of diseases of the circulatory system among liquidators. These two factors are independent of the natural

increase in the incidence rate, as is the case with age. They are closely interrelated and it would take

more study to understand how they can be treated separately and ranked.



**Fig. 10.** Crude incidence rates per 100000 person-years for diseases of the circulatory diseases as a function of dose, age at the time of arrival to the zone and year of arrival to the zone for liquidators.

Table 3 gives calculated radiation risks of the considered diseases of the circulatory system among liquidators. Fig. 11 shows relative risk in the dose groups calculated by formula 5. It should be noted that the slope of the linear trend in Fig. 11 is the excess relative risk which was calculated by model 7, rather using the well-known least square method.

The conducted studies have revealed, first of all, a statistically significant estimate ERR for cerebrovascular diseases (ERR=1.17, 95% CI (0.45, 1.88)) and essential hypertension (ERR=0.52, 95% CI (0.07, 0.98)). It has also been demonstrated that for the liquidators who arrived to the zone in 1986 the value of ERR for cerebrovascular diseases was higher than for the cohort as a whole and equals 1.29 (95% CI (0.34, 2.24)) and for essential hypertension among the liquidators of 1987 the value ERR is 0.88 with 95% CI (0.10, 1.66).

Among diseases of the circulatory system attention should be paid to the class as a whole, in which the value ERR is 0.23 with 95% CI (-0.03, 0.50) and hypertension (ERR=0.35, 95% CI (-0.05, 0.74)) for both of which the lower boundary is almost 0, i.e. for these diseases there is a clear tendency, even though not statistically significant.

We also studied the robustness of radiation risk estimates depending on dose group ranges and effect of stratification by the arrival year on these estimates.

The study has shown that division into smaller dose groups does not result in noticeable differences in radiation risk estimates.

To investigate the effect of stratification by arrival year on final results we estimated relative risks using the same analytical method, but without stratification by arrival year. The results are:

- The general trends in the dose dependence for the class as a whole and separate diseases remain;
- for cerebrovascular diseases (ERR=1.4, 95% CI (0.73, 2.78)) and essential hypertension (ERR=0.55, 95% CI (0.15, 0.95)) the values remain stable, but the statistical significance has increased;
- the statistical significance has been noticed for the class as a whole (ERR=0.39, 95% CI (0.15, 0.64)) and hypertension (ERR=0.52, 95% CI (0.16, 0.88));
- The statistically significant dose dependence has been revealed for the ischaemic heart disease (ERR=0.53, 95% CI (0.06, 1.00)) and angina pectoris (ERR=1.025, 95% CI (0.29, 1.77)).

Table 3

Estimated parameters of the dose dependency of incidence of different diseases of the circulatory system among liquidators

Disease	ICD-9 codes	P	ERR (1/Gy)
Diseases of the circulatory system)	390-459	0.077	0.23 (-0.03, 0.50)
Hypertensive disease	401-405	0.071	0.35 (-0.05, 0.74)
Essential hypertension	401	0.016	0.52 (0.07, 0.98)
Hypertension heart disease	402	0.814	-0.08 (-0.76, 0.60)
Alchemic heart disease (IHD)	410-414	0.735	0.08 (-0.39, 0.55)
Acute myocardial infarction	410	0.702	0.29 (-1.23, 1.81)
Other acute IHD	411	0.642	-0.35 (-1.74, 1.05)
Angina pectoris	413	0.372	0.31 (-0.40, 1.01)
Other chronic forms of IHD	414	0.970	-0.04 (-0.64, 0.57)
Other forms of heart disease	420-429	0.927	-0.04 (-0.83, 0.90)
Cerebrovascular diseases	430-438	<0.001	1.17 (0.45, 1.88)
Diseases of arteries, arterioles and capillaries	440-448	0.167	0.56 (-0.31, 1.44)
Diseases of veins, lymphatic vessels and other diseases of the circulatory system	451-459	0.341	-0.25 (-0.75, 0.26)

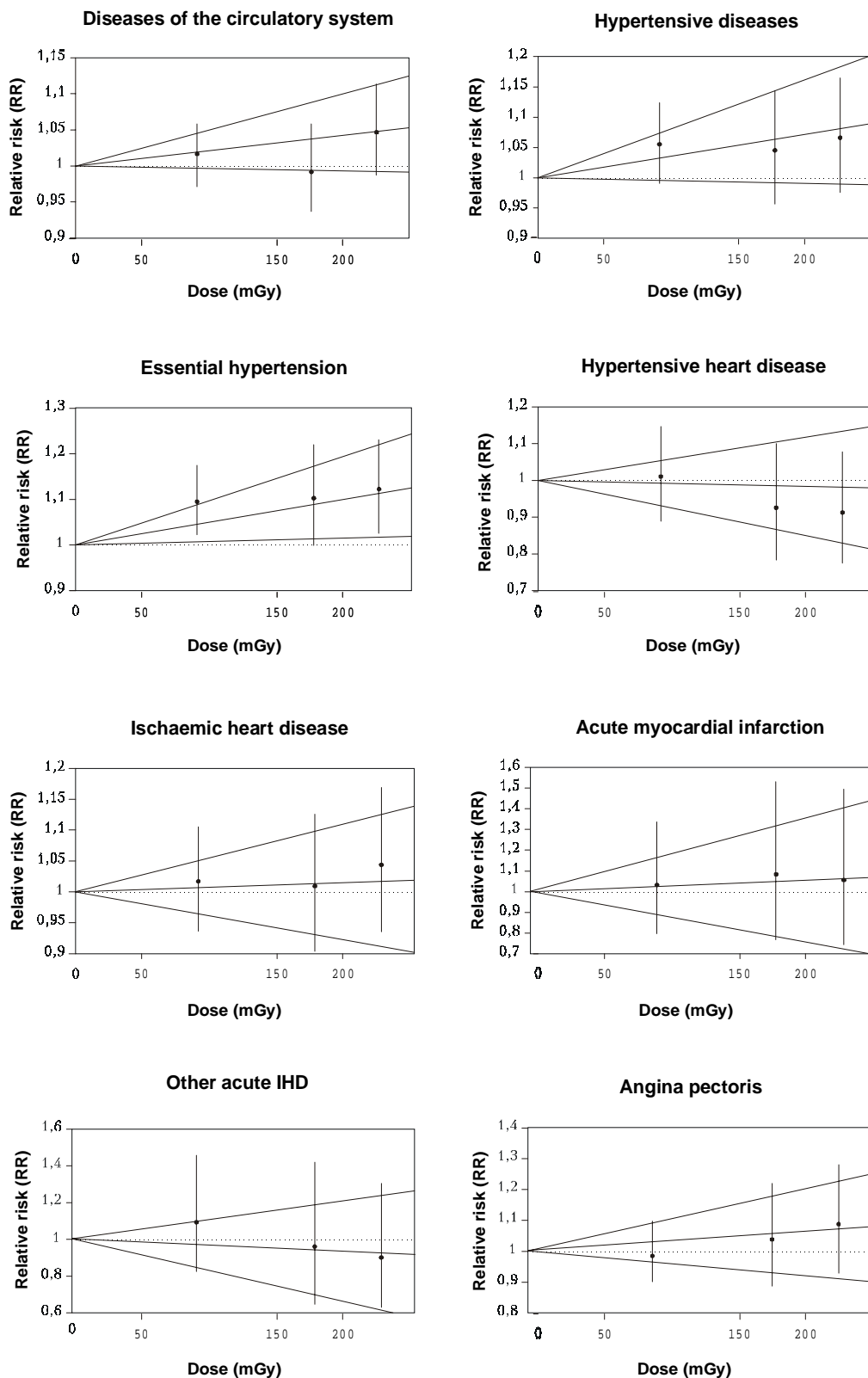
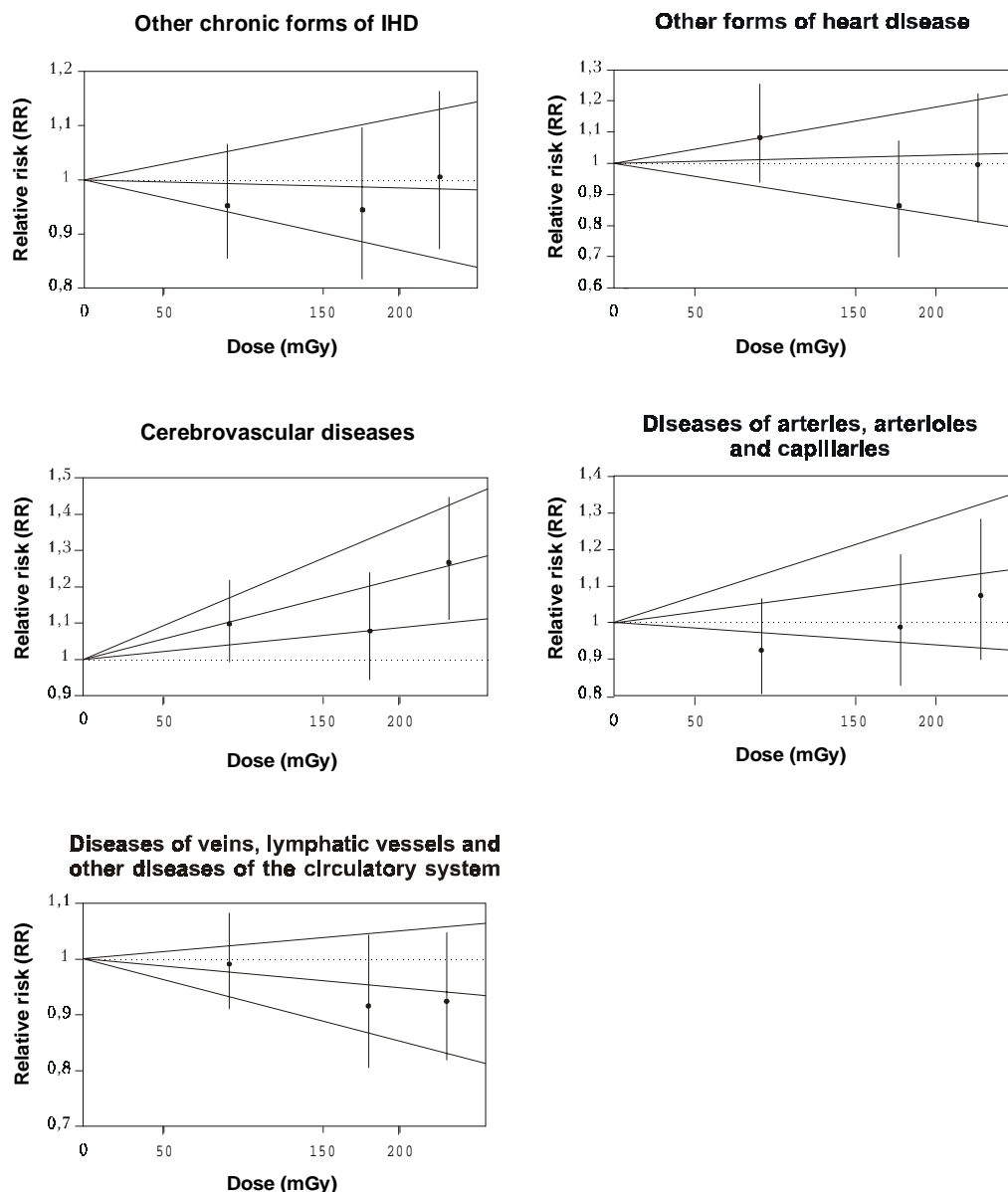


Fig. 11. Relative risk for different diseases of the circulatory system in the dose groups (the line is linear trend corresponding to the regression function (7)).



**Fig. 11 (Continued).** Relative risk for different diseases of the circulatory system in the dose groups (the line is linear trend corresponding to the regression function (7)).

It should be noted that the study did not allow for various recognized risk factors such as excessive weight, hypercholesterolemia, smoking and alcoholism. Therefore, there is no way thus far to single out the radiation component in incidence of diseases of the circulatory system and other somatic diseases among liquidators. This requires in-depth studies considering all risk factors of both radiation and non-radiation nature and conducting detailed questioning of liquidators under study.

Another significant risk factor for cardiovascular and other somatic diseases which was not explored by us is psychological and emotional stress from exposure to ionizing radiation which is the strongest immediately after the exposure.

### Conclusion

The main outcome of this study is establishing a statistically significant dose dependency in the liquidators' cohort as a whole using stratification by age at the time of arrival to the zone, year of arrival to the zone and area of residence with respect to the following non-cancer diseases:

- endocrine diseases and metabolic disorders (ERR=0.58, 95% CI (0.30, 0.87));
- mental disorders (ERR=0.40, 95% CI (0.17, 0.63));
- diseases of the nervous system and sensory organs (ERR=0.35, 95% CI (0.19, 0.52));

- diseases of the digestive system (ERR=0.24, 95% CI (0.05, 0.43));
- cerebrovascular diseases (ERR=1.17, 95% CI (0.45, 1.88));
- Essential hypertension (ERR=0.52, 95% CI (0.07, 0.98)).

When comparing the obtained results with the Japanese data (the AHS cohort) it should be born in mind that the above analysis of incidence among the cohort of liquidators was performed for the 11 year period of the follow-up, whereas collection of data on non-cancer incidence in the Japanese cohort began in 1958, 13 years after the exposure.

The obtained results are tentative and need to be refined. Further follow-up will help to reduce uncertainty in quantitative interpretation of results and enable identifying the radiation constituent in incidence of different diseases, provided all risk factors of radiation and non-radiation origin are taken into account.

In conclusion it should be emphasized that the problem of reliable estimation of radiation risks of non-cancer diseases remains complicated and unresolved both for ICRP and Russian Scientific Commission on Radiation Safety. Therefore further studies on the subject are of highest priority for the radiation-epidemiological studies of RNMDR.

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