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**Epidemiological assessment of the peculiarities of the development of non-tumor diseases residents of the radioactively contaminated areas aged 18-47 years old, born before the Chernobyl accident.
The observation period 1988-2016.**

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Abstract

An epidemiological assessment of changes in the health status of RCA residents under 18 years old at the time of the Chernobyl accident for the period 1988-2016 was conducted.

The main source of information was the database of medical data of the State Register of Ukraine (SRU) of victims of the Chernobyl accident. The cohort consisted of 33,684 residents of RCA aged 18 to 47 years old (as of the date of the Chernobyl accident under the age of 18), of whom men - 16,757, women - 16,927.

The state of health of the offspring was assessed based on the information from the Ukraine State Register (USR).

45417 cases (100%) of non-tumoral diseases were identified in eight classes of ICD-10, which is 103.46 ± 0.46 cases per 1000 person-years of follow-up. 21,148 diseases were diagnosed in men (96.32 ± 0.63 per 1000 person-years), and 24,269 in women ($110.60 \pm$

0.67). Epidemiological analysis of non-tumoral morbidity and disability was conducted over five-year observation periods: 1988-1992, 1993-1997, 1998-2002, 2003-2007, 2008-2012, and 2013-2016.

The dynamics of non-tumoral morbidity of the subjects show a gradual decrease in morbidity from the highest in the first period (the first six years after the accident) to the lowest in the last period (2013-2016).

Thyroid diseases (97.60%) are the main component among the nosological forms of the endocrine system, eating disorders and metabolic disorders (18.97 ± 0.20 cases per 1000 man-years) of the total number for 1988-2016 epidemiological observation.

In the structure of the causes of disability, the largest components are diseases of the nervous system and mental and behavioral disorders, which together account for 51.75%.

According to the indicators of the structure, the residents born before the Chernobyl accident (April 26, 1986) aged 0 to 18 years, showed the highest incidence of non-tumoral diseases of the respiratory, digestive, endocrine system (almost 80%).

Men (1.1-1.4 times) were more likely to suffer from diseases of the respiratory system, digestive system, circulatory system, musculoskeletal system, mental and behavioral disorders. In women, the incidence of non-tumoral diseases was higher (1.1-3.4 times) in the endocrine, nervous and genitourinary systems.

Against the background of a gradual decrease in the incidence from the first to the last five-year observation period, there is an increase in the disability of the subjects in the three disability groups; thus, there was synchronization in different directions.

Keys words: residents of the radioactively contaminated areas; radiation exposure; non-tumor diseases

About 20% of the entire territory of Ukraine, which is 12 regions with a population of up to 3 million people, belongs to the radioactively contaminated areas (RCA) due to the Chernobyl accident [1]. One of the significant negative consequences of the Chernobyl catastrophe was the increase in the incidence of the population living in RCA, where the leading place is occupied by non-tumoral morbidity [2, 3, 4]. In the publications of the post-accident period, many scientists have demonstrated the influence of small doses of radiation on the development of non-tumoral diseases and the role of unmodified factors, such as gender and age at the time of the Chernobyl accident [5, 6]. The results of epidemiological studies performed at the Institute of Radiation Hygiene and Epidemiology (IRHE) NRCRM NAMS of Ukraine for the post-accident years until 2016 indicate the development of non-

tumoral diseases in people living with RCA, both in adulthood and in children and adolescents. Often leads to early disability and mortality [7-10].

Goal

To determine the features of the development of non-tumoral diseases of RCA residents under the age of 18 on the date of the Chernobyl accident for 1988-2016 based on epidemiological research methods.

Materials and methods

The main source of information was the database of medical data of the State Register of Ukraine (SRU) of victims of the Chernobyl accident. The cohort consisted of 33,684 (100%) residents of RCA aged 18 to 47 years old (as of the date of the Chernobyl accident under the age of 18), of whom men - 16,757 (49.75%), women - 16,927 (50.25%).

The cohort was formed, taking into account the total (internal and external radiation) effective doses of ionizing radiation accumulated from 1986 to 2012, which are 14.31 ± 8.69 mSv ($M \pm \delta$). The cohort includes persons from the settlements of Zhytomyr, Kyiv, Chernihiv, Rivne regions, respectively Ovruch, Ivankiv, Kozelets, Rokytno districts.

Epidemiological analysis of non-tumoral morbidity and disability was conducted over five-year observation periods: 1988-1992, 1993-1997, 1998-2002, 2003-2007, 2008-2012, and 2013-2016.

The calculation of indicators was performed using Excel-2016 software packages.

Results

45417 cases (100%) of non-tumoral diseases were identified in eight classes of ICD-10, which is 103.46 ± 0.46 cases per 1000 person-years of follow-up. 21,148 diseases were diagnosed in men (96.32 ± 0.63 per 1000 person-years), and 24,269 in women (110.60 ± 0.67).

The study of the structure of non-tumoral morbidity in RCA residents under 18 years of age on the date of the Chernobyl accident for 1988-2016 observation made it possible to establish priorities for the development of non-tumoral diseases among those determined by classes ICD-10 (Fig. 1).

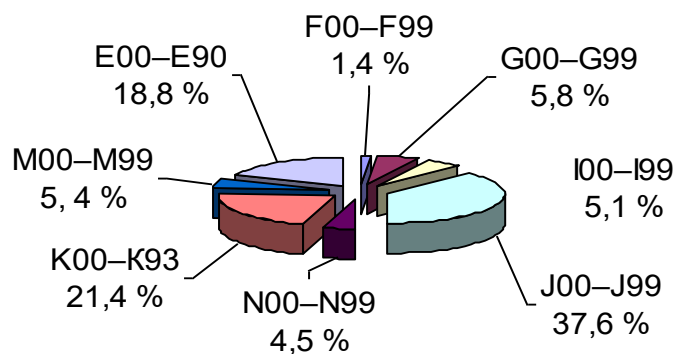


Figure 1 - The structure of the incidence of non-tumoral diseases in residents of RCA under the age of 18 on the date of the Chernobyl accident for the post-accident period for 1988-2016 epidemiological surveillance

Legend:

E00 - E90 - diseases of the endocrine system, eating disorders and metabolic disorders; F00 - F99 - mental and behavioral disorders; G00 - G99 - diseases of the nervous system; I00 - I99 - diseases of the circulatory system; J00 - J99 - respiratory diseases; K00 - K93 - diseases of the digestive system; N00 - N99 - diseases of the genitourinary system; M00 - M99 - diseases of the musculoskeletal system.

In the structure of non-tumoral morbidity, respiratory diseases occupy the first place in terms of specific weight, among other diseases. In second place are diseases of the digestive system, in third place - diseases of the endocrine system, eating disorders, and metabolic disorders. Together, they account for 77.8% and only 22.2% of other diseases, including diseases of the nervous system, circulatory system, genitourinary and musculoskeletal systems. The smallest class of "Mental and behavioral disorders." The study of these classes of non-tumoral diseases was carried out, mainly taking into account the development of chronic diseases.

Respiratory diseases are represented by chronic diseases of the upper respiratory tract (rhinitis, nasopharyngitis, pharyngitis, sinusitis, laryngotracheitis) and diseases of the lower respiratory tract (simple chronic bronchitis, chronic obstructive pulmonary disease, bronchial asthma).

Digestive diseases are diseases of the gallbladder, biliary tract, gastritis and duodenitis, gastric and duodenal ulcers, liver fibrosis and cirrhosis, chronic hepatitis, and duodenitis, diseases of the pancreas. Diseases of the endocrine system, eating disorders, and metabolic disorders are mainly thyroid disease (97.60%) and diabetes. Diseases of the thyroid

gland were mainly formed by diseases associated with iodine deficiency and similar conditions (E01.0-E01.8), endemic diffuse, multinodular and unspecified goiter, as well as other forms of non-toxic goiter (E04.0-E04.9), thyrotoxicosis (hyperthyroidism) (E05.0-E05.9), thyroiditis (E06.0-E06.9), other diseases of the thyroid gland (E07.0-E07.9).

Of the diseases of the nervous system, mainly disorders of the autonomic nervous system have been registered (G90.9-E09.9).

Among diseases of the circulatory system, other heart diseases, cardiomyopathy, were most often diagnosed; among diseases of the musculoskeletal system - dorsopathy, osteopathy and chondropathy, osteochondrosis of the spine; among diseases of the genitourinary system - diseases of the urinary system, inflammatory diseases of the pelvic organs, non-inflammatory diseases of the female genital organs and others.

The structure of the incidence of non-tumoral diseases depending on gender shows that men have a higher proportion than women of diseases of the circulatory system (0.8%), mental and behavioral disorders (0.34%), digestive organs (1.63%), musculoskeletal system (1.85%), respiratory system (2.63%), and women have more of diseases of the endocrine (1.09%), nervous (1.58%) and urogenital (4, 73%) systems (Table 1).

Table - 1. The structure of non-tumoral morbidity of residents of RCA under the age of 18 on the date of the Chernobyl accident article during 1988-2016 observations in absolute numbers, percentages

Classes of Diseases	Code by ICD –10	Male		Female	
		absolute number	%	absolute number	%
Respiratory diseases	J00 – J99	8243	38,98	8821	36,35
Digestion diseases	K00 – K93	4719	22,31	5019	20,68
Endocrine system diseases, eating disorders and metabolic disorders	E00 – E90	3865	18,28	4666	19,37
Nervous system diseases	G00 – G99	1044	4,94	1581	6,51
Blood circulation system diseases	I00 – I99	1163	5,50	1137	4,68
Bone and muscle system related diseases and of connection tissue	M00 – M99	1357	6,42	1109	4,57
Diseases of the genito-urinary system	N00 – N99	424	2,01	1636	6,74
Psychological and behavioural disorders	F00 – F99	333	1,57	300	1,24
Total	A00 – N99	21148	100 %	24269	100 %

Thus, the largest share (about 80%) in the structure of the incidence of non-tumoral diseases of RCA residents under the age of 18 on the date of the Chernobyl accident take diseases of the respiratory, digestive and endocrine systems.

1. Morbidity

Analysis of the dynamics of post-accident non-tumoral morbidity in RCA residents under 18 years of age on the date of the accident and depending on their sex made it possible to establish changes in levels over five-year periods during 1988-2016 epidemiological surveillance (Fig. 2).

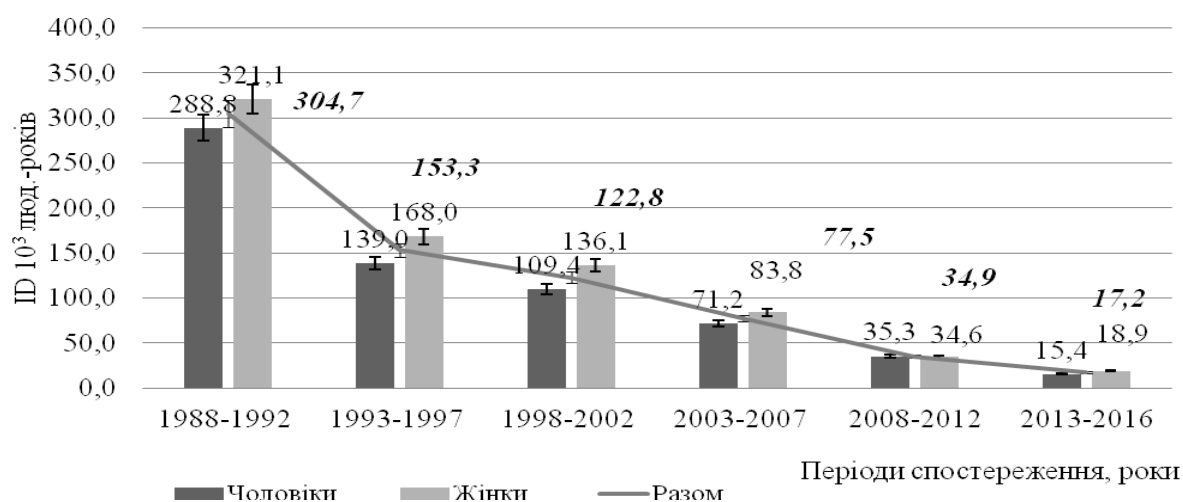


Figure 2 - Dynamics of the incidence of non-tumoral diseases in residents of RCA under the age of 18 on the date of the Chernobyl accident for post-accident five-year observation periods during 1988-2016.

Residents of this age group have the highest incidence in the first five-year follow-up period. The incidence rate registered in the second period (1993-1997) decreased by 1.99 times compared to the first period. In each subsequent period, the indicator decreased against the previous one (1998-2002) by 1.25 times, in 2003-2007 by 1.58 times, in 2008-2012 by 2.22 times, in 2013-2016 by 2.03 times times. For men and women, the identity of the dynamics of the incidence of the general cohort is traced. For women, the incidence exceeded the incidence of men during 1988-2007 (19 years in a row after the accident), but later, the identified features of the incidence between males and females were not recorded.

Thus, the dynamics of non-tumoral morbidity of the subjects show a gradual decrease in morbidity from the highest in the first period (the first six years after the accident) to the lowest in the last period (2013-2016).

Thyroid diseases (97.60%) are the main component among the nosological forms of the endocrine system, eating disorders and metabolic disorders (18.97 ± 0.20 cases per 1000 man-years) of the total number for 1988-2016 epidemiological observation. Such a high thyroid involvement in the subjects was the basis for studying the structure and dynamics of the disease. All groups of nosological forms of thyroid disease were analyzed. The group of diseases with the manifestation of iodine hypothyroidism (E00-E03) consisted of diseases associated with iodine deficiency, subclinical hypothyroidism, and other forms of hypothyroidism. The group of diseases other forms of non-toxic goiter (E04) includes diffuse, single-nodular, multinodular, refined, and unspecified forms of non-toxic goiter. Thyrotoxicosis (hyperthyroidism) (E05) forms diffuse goiter, toxic single-nodular and multinodular goiter and other forms. The group of nosologies of thyroiditis (E06) includes acute, subacute, chronic thyroiditis, autoimmune thyroiditis, and other forms. Thyroid diseases also include "other thyroid diseases (E07)".

The study of the structure of thyroid diseases in the subjects showed that the largest proportion by a group of diseases "other forms of non-toxic goiter (E04)", significant - by group "other diseases of the thyroid gland (E07)" (Table 2).

Table 2 - The structure of non-tumoral thyroid diseases by groups of diseases ICD -10 in the cohort and depending on the sex of the inhabitants of RCA under the age of 18 on the date of the Chernobyl accident for 1988-2016,%

Endocrine system diseases, eating disorders and metabolic disorders by ICD –10	Total	Male	Female
Other forms of non-toxic goiter (E04)	88,42	89,04	87,89
Other diseases of the thyroid gland (E07)	9,46	9,94	9,11
Diseases associated with iodine deficiency (hypothyroidism) and other forms of hypothyroidism (E00–E03)	1,26	0,56	1,85
Thyrotoxicosis (hyperthyroidism) (E05)	0,47	0,32	0,59
Thyroiditis (E06)	0,37	0,13	0,57

The rest of the thyroid disease has a small percentage.

In the structure of diseases of the thyroid gland, it was found that of the studied men and women, the most numerous in nosological forms is the group "other forms of non-toxic goiter (E04)".

At the same time, men have higher percentages for the group of diseases "other forms of non-toxic goiter (E04)" and "other diseases of the thyroid gland (E07)", and women - for

the group "thyroiditis (E06)", "iodine hypothyroidism (other forms of hypothyroidism)" E00-E03)", "thyrotoxicosis (hyperthyroidism) (E05) (see Table 2).

The study of the dynamics of certain thyroid diseases of the studied cohort during the epidemiological period of observation showed that the highest incidence rate falls on the first five-year observation period (the first seven years after the accident), Fig. 3.

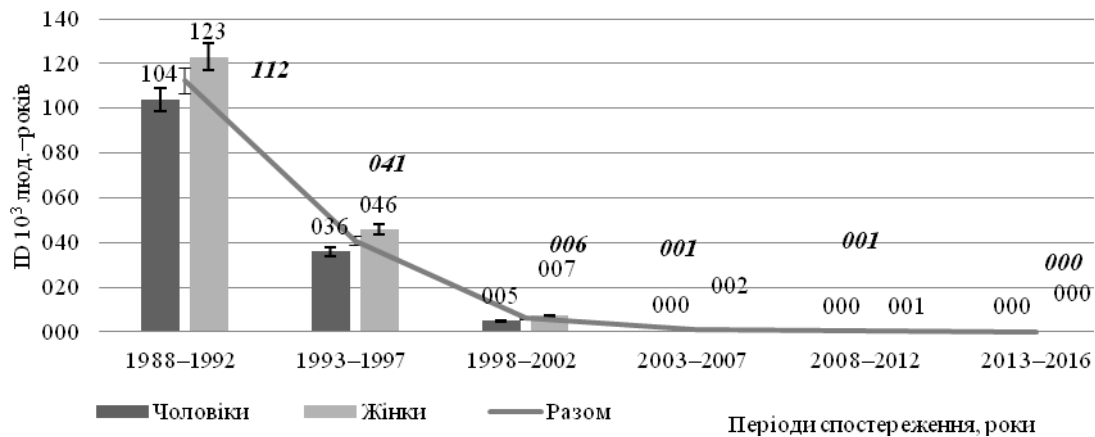


Figure 3 - Dynamics of thyroid disease in residents of RCA under the age of 18 on the date of the Chernobyl accident and by sex in the five-year post-accident observation periods during 1988-2016.

In the second five-year follow-up period, there was a sharp decrease (almost 3 times) in the incidence of disease compared to the first period. In each subsequent period, a significant decrease in the indicator continued (2-6 times). The incidence of women and men is identical to the cohort. However, for women in each five-year period, except the last, there is a significant excess of morbidity compared to men.

Thus, the structure of thyroid disease is mainly formed by the nosological group "other forms of non-toxic goiter (E04)" both in the cohort and by sex.

Also, the group of diseases "thyroiditis (E06)", "iodine hypothyroidism (other forms of hypothyroidism) (E00-E03)" "thyrotoxicosis (hyperthyroidism) (E05)" has a higher proportion in the structure of non-tumoral thyroid diseases among women freely.

The dynamics of certain thyroid diseases of residents under the age of 18 on the date of the Chernobyl accident was characterized by a gradual decrease in morbidity from the first five-year period (peak incidence in the first seven years after the accident) to the last observation period. The incidence rate in the second period of observation (7-11 years after

the accident) is 2.77 times lower than in the first period. In subsequent follow-up periods (17-30 years after the accident), the incidence decreased to insignificant levels.

2. Disability from non-tumoral diseases

According to the results of a cohort epidemiological study of the health of RCA residents under the age of 18 on the date of the Chernobyl accident in 1988-2016, the observation revealed 2541 cases of disability of the first, second and third groups from non-tumoral diseases, including men - 1285, women - 1256.

In the structure of the causes of disability, the largest components are diseases of the nervous system and mental and behavioral disorders, which together account for 51.75%.

Table 4. The structure of the causes of disability from non-tumoral diseases in residents of RCA under the age of 18 on the date of the Chernobyl accident and by sex for the post-accident period (1988-2016), %

Classes of Diseases by ICD –10	Male	Female	Total
Mental and behavioral disorders (F00–F99)	27,39	16,56	22,04
Nervous system diseases (G00–G99)	26,61	32,88	29,71
Blood circulation system diseases (I0–I99)	11,05	12,34	11,69
Bone and muscle system related diseases (M00–99)	9,26	8,12	8,70
Diseases of the digestive system (K00–K93)	8,95	9,39	9,17
Diseases of the endocrine system (E00 –E90)	8,25	10,51	9,37
Respiratory diseases (J00–J99)	7,16	7,17	7,16
Diseases of the genito-urinary system (N00–N99)	1,32	3,03	2,16

Of the nosological forms of diseases of the nervous system, the main contribution to the formation of disability in demyelinating diseases and diseases of the peripheral nervous system. The third place belongs to diseases of the circulatory system (diseases with high blood pressure, coronary heart disease, other heart diseases, cerebrovascular diseases). The fourth place has diseases of the musculoskeletal system, mainly osteochondrosis. The fifth place is shared by diseases of the endocrine system and digestive organs. In the class of diseases of the endocrine system, disability is established in diseases of the thyroid gland (mainly hypothyroidism) and diabetes. Disability due to diseases of the digestive system has been established for: gastric and duodenal ulcers, liver fibrosis and cirrhosis, chronic liver disease. Other significant causes of disability are respiratory diseases (chronic obstructive

pulmonary disease, asthma) and musculoskeletal system. The smallest manifestation of disability is in diseases of the genitourinary system (renal failure).

The analysis shows that the structure of the causes of disability from non-tumoral diseases in men and women is identical to the structure of the cohort. Men have a higher disability than women with mental and behavioral disorders (10%), diseases of the musculoskeletal system (1.14%). For women, the most common causes of disability than for men are diseases of the nervous system (6.27%, thyroid disease (2.26%), diseases of the genitourinary system (1.61%).

2.2 Dynamics of disability development

A study of the dynamics of disability in a mixed cohort of residents under 18 years old during the epidemiological observation showed that disability increases almost twice with each five-year observation period until 2008 due to disability of both sexes, but with a slight excess in men (Fig. 4).

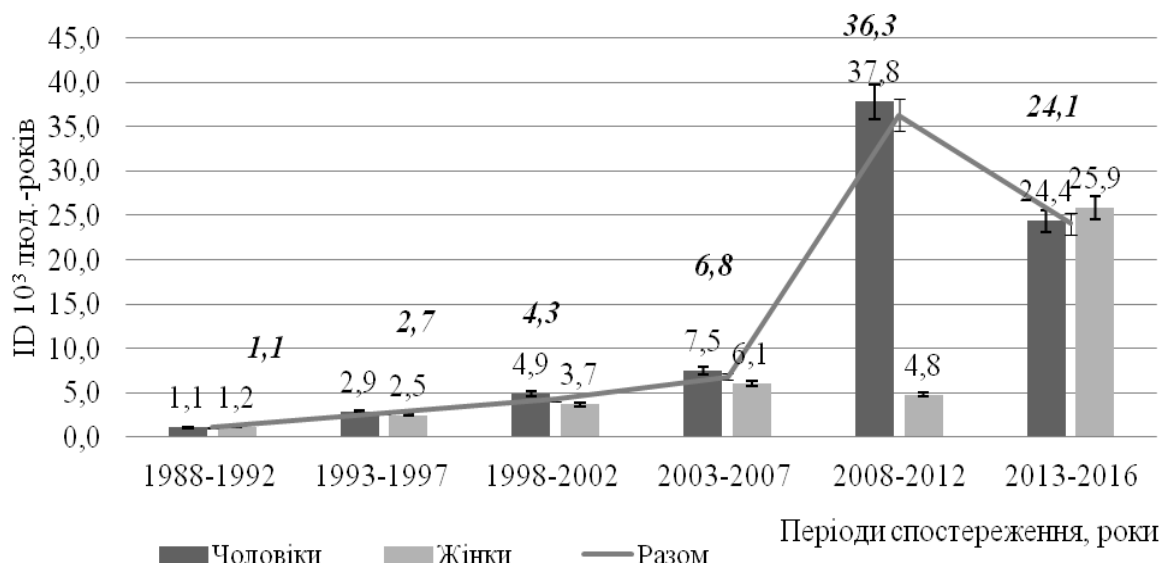


Figure 4 - Dynamics of causes of disability from non-tumoral diseases in residents of RCA under the age of 18 on the date of the Chernobyl accident during 1988-2016 observation

The peak of the disability level occurred in 2008-2012 due to the significant disability of men. During 2013-2016, disability rates were significantly higher compared to 1988-2012.

Men during twelve years (from 1988 to 2012) have higher disabilities than women, but in the last five years the figures do not differ.

Depending on the severity of the disease during 1988-2016, the first, second and third groups of disability were established (Fig. 5).

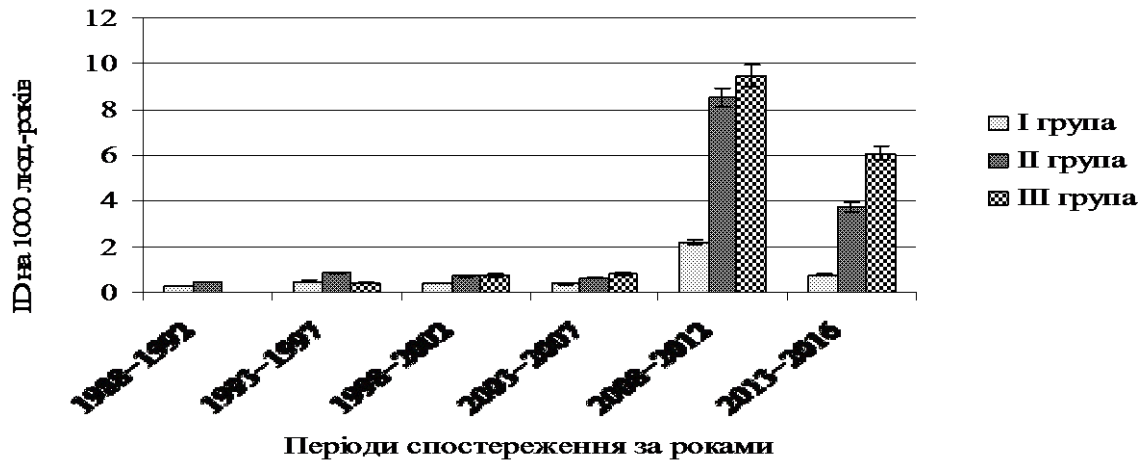


Figure 5 - Establishment of disability in the first, second and third groups, depending on the severity of the disease during 1988-2016 medical examination of residents of RCA under 18 years on the date of the Chernobyl accident

The number of residents for each of the disability groups changed almost equally over the years of observation. In the second five-year period, the number of disabled people significantly increases compared to the first period. During 1998-2007, no significant changes in the indicators for establishing disability were revealed. During 2008-2012, there was a significant increase in the number of residents with disabilities compared to all previous years of observation. Such a high disability continued in 2013-2016 but was significantly lower than in the previous five-year period. In the five-year periods from 2003 to 2016, the number of disabled people with the first group is the smallest, and with the third group - the largest.

Thus, the main reasons for the disability of RCA residents under the age of 18 on the date of the Chernobyl accident, regardless of gender and age, were diseases of the nervous system, circulatory system, respiratory system, urogenital system. For some diseases, disability was higher in men, for some - in women. In men, the main role in disability was played by mental and behavioral disorders, osteochondrosis of the spine, fibrosis and cirrhosis of the liver, chronic liver disease, gastric and duodenal ulcers, coronary heart disease. In women, disability was more often diagnosed by demyelinating diseases, hypothyroidism, renal tubulointerstitial disease, glomerular disease, cardiomyopathy, cerebrovascular diseases, diseases of arteries, arterioles, capillaries, veins, and lymphatic system.

The dynamics of disability development indicated a gradual increase in the disability of victims (almost twice) in each five-year follow-up (from 1988 to 2007), both in men and in women with a slight excess in men. From 2008 to 2016, the disability of both male and

female residents increased. An epidemiological study of the dynamics of non-tumoral diseases for the period 1988-2016 showed complications of nosological forms of lung disease at the beginning of the post-accident period to more severe thirty years after the accident, which lead to disability of RCA residents (18-47 years).

Conclusions

According to the indicators of the structure, the residents born before the Chernobyl accident (April 26, 1986) aged 0 to 18 years, showed the highest incidence of non-tumoral diseases of the respiratory, digestive, endocrine system (almost 80%).

Men (1.1-1.4 times) were more likely to suffer from diseases of the respiratory system, digestive system, circulatory system, musculoskeletal system, mental and behavioral disorders. In women, the incidence of non-tumoral diseases was higher (1.1-3.4 times) in the endocrine, nervous and genitourinary systems.

Of these classes of diseases, the victims most often suffered: respiratory diseases, chronic obstructive pulmonary disease, chronic bronchitis, bronchial asthma, laryngitis, laryngotracheitis; for diseases of the digestive system for diseases of the gallbladder, biliary tract, gastritis and duodenitis, gastric and duodenal ulcers, liver fibrosis and cirrhosis, diseases of the pancreas; for diseases of the endocrine system, eating disorders and metabolic disorders for thyroid disease (97.60%) and diabetes mellitus; for diseases of the nervous system for disorders of the autonomic nervous system; for diseases of the circulatory system for heart disease, cardiomyopathy; for diseases of the musculoskeletal system in dorsopathy, osteopathy, chondropathy, osteochondrosis of the spine; for diseases of the genitourinary system for diseases of the urinary system, inflammatory diseases of the pelvic organs in women, etc.

A study of the dynamics of non-tumoral diseases of RCA residents under 18 years of age on the date of the Chernobyl accident during 1988-2016 showed that there was a gradual decline in morbidity from the highest in the first six years after the accident to the lowest in the last period (30 years after the accident).

The high incidence in the first five-year period compared to the following years of the study may be related to the impact, first of all, of the "screening effect," significant coverage in the first years after the Chernobyl accident by medical examinations of the RCA population and high disease detection. There are no data on the incidence of non-tumoral diseases before the accident in the USSR.

Against the background of a gradual decrease in the incidence from the first to the last five-year observation period, there is an increase in the disability of the subjects in the three

disability groups; thus, there was synchronization in different directions. This feature of changes in health was manifested in the results of medical examinations in 2008-2016. The main causes of disability were mainly diseases of the nervous system and mental and behavioral disorders, circulatory system (diseases characterized by high blood pressure, heart disease, cerebrovascular disease, coronary heart disease), respiratory system (due to obstructive pulmonary disease), genitourinary system (renal tubulointerstitial diseases and glomerular disease). The study of the dynamics of disability showed the development of complications of nosological forms from lung at the beginning of the post-accident period to more severe forms of the disease with the registration of disability for thirty years of life of RCA residents after the accident (18-47 years old).

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