creased (>20%) level of HLA-DR+ lymphocytes was observed in 60% (n=18) vs 33,3% (n=14) of the comparison group ($\chi 2$ = 5, p=0,03). An increased (>6%) level of CD3+HLA-DR+ lymphocytes was observed in 86,7% (n=36) patients vs 58,3% (n=18) of the comparison group. There was an increase in the CD95+ lymphocyte level by 3,2 times on average in the group of patients with COVID-19 relative to the comparison group (p=0,05) (Table 2).

Conclusion. Against the background of severe lymphopenia and neutrophilia during infection with SARS-CoV-2, multidirectional changes in the studied indicators of cellular immunity were revealed, including a decrease in the absolute level of CD3+-, CD3+CD4+–, CD3+CD8+ – and CD16+CD56+-lymphocytes; an increase in the % level of CD3+HLA-DR+ and CD95+ lymphocytes, the severity and dynamics of which can be determined by the initial type of immune system response. It is promising to study the initial "immunological passport" of a person to identify personal predictors of the course of the disease when infected with coronavirus infection.

Reference

1. Abdullaev R.YU., Komissarova O.G. Laboratornye proyavleniya koronavirusnoj infekcii COVID-19 [Laboratory manifestations of coronavirus infection]. Vrach (The Doctor). 2020; 31(5):3-5 (In Russ.).]
2. Vdoushkina E.S., Borodulina E.A., Povalyaeva L.V., Sukhanova A.V., Zhilinskaya K.V., Sutyagin A.V. Sroki obrashcheniya i tyazhest' sostoyaniya pacientov s porazheniem legkih i podozreniem na novuyu koronavirusnuyu infekciyu pri postuplenii v stacionar v period nachala pandemii [Terms of treatment and severity of the condition of patients with lung damage and suspected new coronavirus infection upon admission to the hospital during the onset of the pandemic]. Vrach (The Doctor). 2020:31(11):60-63 (In Russ.).]
3. Sizyakina L.P., Zakurskaya V.Ya., Skripkina N.A., Antonova E.A. Uroven' ferritina kak prediktor tyazhelogo techeniya COVID-19. Immunologiya [Immunology. 2021;42(5):518-25 (In Russ.).]
4. Baazim H., Schweiger M, Moschinger M. [et al.] CD8+ T cells induce cachexia during chronic viral infection. Nat Immunol. 2019; 20 (6): 701-710.
5. Chen G., Wu D., Guo W [et al.] Clinical and immunological features of severe and moderate coronavirus disease 2019. Clin.Invest. 2020; 130 (5): 2620–2629.
6. Golovkin A., Kalinina O., Bezrukikh V. [et al.] Imbalanced immune response of T – cell and B – cell subsets in patients with moderate and severe COVID-19. Viruses. 2021; 13: 1966.
7. Guan W., Ni Z., Hu Y. [et al.] Clinical Characteristics of Coronavirus Disease 2019 in China. Engl. J. Med. 2020; 382 (18): 1708-1720.
8. Li G., Fan Y, Lai Y [et al.] Coronavirus infections and immune responses. J. Med. Virol. 2020; 92 (4): 424–32.
9. Li Y.X., Wu W., Yang T. [et al.] Characteristics of peripheral blood leukocyte differential counts in patients with COVID-19. Chinese Medical Association Publishing House Ltd. 2020; 59 (5): 372-374.
10. Qin C., Zhou L., Hu Z. [et al.] Dysregulation of immune response in patients with COVID-19 in Wuhan, China. Clin Infect Dis. 2020; 71 (15): 762-768.
11. Ruan Q., Yang K., Wang W. [et al.] Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan. China Intensive CareMed. 2020; 46 (6):1294-1297.
12. Saghazadeh A, Rezaei N. Immune-epidemiological parameters of the novel coronavirus – a perspective. Expert Rev. Clin. Immunol. 2020; 16 (5): 465-470.

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EXCESS MORTALITY IN THE REPUBLIC OF SAKHA (YAKUTIA) DURING THE COVID-19 PANDEMIC (2020-2021)

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Excess mortality is defined as an increase in all-cause mortality over expected mortality (historical baseline for previous years). In the context of COVID-19, excess mortality may reflect the overall impact of the pandemic on mortality, including not only the number of confirmed deaths from COVID-19, but also deaths from COVID-19 when they were not correctly diagnosed and reported, and deaths from other diseases due to pandemic-related causes.

The purpose of the study: to assess the indicators of excess mortality during the COVID-19 pandemic (2020-2021) in the Republic of Sakha (Yakutia). For the analysis, data from the Federal State Statistics Service for 2015-2022 were used. For 2 years of the spread of a new coronavirus infection in the Republic of Sakha (Yakutia), 19556 people died. 7.8% of deaths in 2020 and 21.5% in 2021 were related to COVID-19. The number of all deaths was 22% and 44% respectively higher than the expected number of deaths. The proportion of excess deaths in 2020 was 19% of all deaths, in 2021 - 31%. Of the excess deaths, 42% and 69%, respectively, were related to COVID-19. The excess mortality rate reached 333 per 100,000 population in 2021. The high correlation coefficients (0.94-0.95) between COVID-19-related deaths and additional deaths suggest that excess deaths during the period 2020-2021 will largely be due to the spread of COVID-19.

The decline in mortality underreporting in 2021 against the background of an increase in excess mortality reflects improved diagnosis and correct identification of the causes of death. Research into the causes of excess mortality is needed to assess the impact of the pandemic and other factors on various aspects of mortality in the population.

Keywords: new coronavirus infection, COVID-19, pandemic, excess mortality, Republic of Sakha (Yakutia).

Introduction. Excess mortality is defined as an increase in all-cause mortality over expected mortality (historical baseline for previous years). The increase in mortality is associated with the emergence of some new factors, emergencies that affect the health of the population. In the context of COVID-19, excess mortality may reflect the overall impact of the pandemic on mortality, including not only the number of confirmed deaths from COVID-19, but also deaths from

Table 1

Number of deaths from various causes in 2020-2021 compared to expected (Rosstat)

Causes of death	Expected *	2020		2021	
		official	increase / decrease %	official	increase / decrease %
all causes	7340	8956	22.0	10600	44.4
diseases of the circulatory system	3344	3956	18.3	4003	19.7
neoplasms	1396	1286	-7.9	1241	-11.1
external causes	1011	1206	19.3	1098	8.6
respiratory diseases	321	400	24.6	466	45.2
diseases of the digestive system	376	437	16.0	428	13.8

Note: *-calculated based on 2015-2019 years (linear regression).

COVID-19 when they were not correctly diagnosed and reported, and deaths from other diseases due to pandemic-related causes. For example, due to a decrease in the availability and quality of medical care, the impact of stressful factors, the influence of other conditions during the spread of the infection [2, 5, 6].

Karlinsky A. and Kobak D., creators of the World Mortality Dataset database, based on data on deaths from all causes in 103 countries, showed that in some countries (Peru, Ecuador, Bolivia, Mexico), excess mortality during the COVID-19 pandemic exceeded 50% expected annual mortality. While in other countries (Australia, New Zealand), mortality during the pandemic was below normal levels, which may be due to social distancing measures that reduce infectious mortality not associated with COVID-19 [6]. Accounting for COVID-19 deaths is affected by: COVID-19 death case definition, availability of testing, and fairness of reporting.

In this regard, it is of interest to study excess mortality during this period in a region located on a vast territory, where transport distance from the center affects the availability of medical care.

The purpose of the study: to assess the indicators of excess mortality during the COVID-19 pandemic (2020-2021) in the Republic of Sakha (Yakutia).

Materials and methods. For the analysis, data from the Federal State Statistics Service for 2015-2022 were used. [3]. The expected number of deaths for each month of 2020 was calculated using linear regression analysis in IBM SPSS Statistics 26 based on monthly mortality data in 2015-2019. Further, using the actual data of 2020, the excess mortality for the month was calculated as the difference between the observed number of deaths and the predicted value. The final

Table 2

Number of deaths associated with COVID-19 (Rosstat)

Period	COVID-19 – main cause of death			COVID-19 is not the main cause of death, but has had a significant impact on the development of fatal complications of the disease
	total	virus identified	virus not identified	
2020				
March	0	0	0	0
April	0	0	0	0
May	7	7	0	0
June	26	24	2	0
July	47	42	5	0
August	35	31	4	0
September	58	53	5	6
October	98	93	5	9
November	223	206	17	8
December	179	170	9	5
Total in 2020	**673**	626	47	**28**
2021				
January	83	81	2	7
February	57	56	1	11
March	44	40	4	0
April	41	38	3	7
May	90	86	4	3
June	158	156	2	6
July	151	150	1	7
August	190	186	4	9
September	278	269	9	4
October	418	411	7	20
November	439	430	9	18
December	231	223	8	7
Total in 2021	**2180**	2126	54	**99**

estimate of excess mortality for the year was determined as the sum of excess mortality for all months, starting from March 2020. This approach, according to the researchers, considers both seasonal fluctuations in mortality and the annual trend, and is not inferior in efficiency to more complex methods [6]. To avoid further extrapolation, the same expected mortality rate was taken for 2021.

COVID-19-related deaths included cases where COVID-19 was the primary cause (regardless of virus identification), as well as cases where COVID-19 was not the primary cause of death but had a significant impact on the development of deaths. complications of the disease.

The ratio of the number of excess deaths in the study period to the number of registered deaths associated with COVID-19 in the same period was used as the death underreporting coefficient. This index is called by Russian researchers the "Covid mortality multiplier" in view of the fact that the increase in mortality during this period is due not only to mortality from COVID-19, but also to mortality associated with the overload of the medical care system and the stress experienced by the population [2].

Results and discussion. Excess mortality during the pandemic includes direct COVID-19 deaths and non-COVID-19 indirect deaths. The causes of non-COVID-19 deaths are diverse and include behavioral factors, changes in the healthcare delivery system, the negative effects of social restrictions, economic factors, and others [5]. For example, this can be a change in behavior regarding seeking medical care in cases of occurrence or exacerbation of diseases due to the risk of contracting COVID-19, prioritizing cases of COVID-19 in the provision of care by reducing services for people with chronic noncommunicable diseases, and others. WHO, in a survey conducted in 155 countries, showed that 42% of the countries surveyed have partially or completely discontinued services for the treatment of cancer, 49% for the treatment of diabetes and its complications, 31% for urgent cardiovascular diseases. This indicates that the impact of the pandemic on the healthcare system is global [8]. According to the researchers, excess mortality during the COVID-19 pandemic may reflect the following causes of death: deaths directly caused by COVID-19 infection; deaths caused by the collapse of the healthcare system due to the pandemic; excess mortality from other natural causes; excess mortality from external causes; excess mortality from extreme events (wars, natural disasters, etc.) [5].

Retrospective analysis of the situation in the RS(Y) in 2020-2021 showed that during the summer periods in the republic there were a series of forest fires that caused air pollution by combustion products. For example, according to IQAir, as of August 12, 2021, the content of PM2.5 particles in the air was 2473 μg/m3, while the WHO recommended rate is 25 μg/m3. Long-term exposure to PM2.5 has been associated with an increased long-term risk of cardiopulmonary mortality, according to studies in various countries. Particularly vulnerable groups are people with lung or heart disease, the elderly, and children [7, 9].

For the period 2015-2019. in the Republic of Sakha (Yakutia), as in the whole of the Russian Federation, there was a downward trend in mortality. Thus, the indicators of general mortality in the republic over this period decreased from 8.5 to 7.8 per 1000 population (in the Russian Federation from 13.1 to 12.5, respectively).

Since the beginning of the pandemic of a new coronavirus infection, the situation has changed dramatically. In 2020, 8956 people died in the Republic of Sakha (Yakutia), which is 22% higher than the expected number of deaths (Table 1). The overall mortality rate was 9.2 per 1000 population. A pronounced increase in mortality has been observed since July 2020. During the year, the number of deaths from diseases of the circulatory system (by 18%), respiratory diseases (by 25%), diseases of the digestive system (by 16%) and external causes (by 19%) increased significantly against the background of a decrease in deaths from neoplasms (- eight%). Similar trends were noted in other regions of the Russian Federation [1].

In 2021, 10,600 people died, which is 44% more than the expected number of deaths. The overall mortality rate was 10.8 per 1000 population. The largest number of deaths occurred in September-November 2021. The number of deaths from diseases of the circulatory system for the year was 20% more than expected, from diseases of the respiratory system - by 45%, from diseases of the digestive system - by 14%, from external

Table 3

Excess mortality in the Republic of Sakha (Yakutia) in 2020-2021

Period	Expected *	Mortality 2020				Mortality 2021			
		factual	excess	related to COVID-19**	undercount	factual	excess	related to COVID-19**	undercount
January	698	678	-20	0	-	816	118	90	1.3
February	589	593	4	0	-	726	137	68	2.0
March	590	573	-17	0	-	804	214	44	4.9
April	584	594	10	0	-	657	73	48	1.5
May	730	735	5	7	0.7	702	-28	93	-0.3
June	541	508	-33	26	-1.3	831	290	164	1.8
July	661	803	142	47	3.0	835	174	158	1.1
August	632	748	116	35	3.3	890	258	199	1.3
September	592	860	269	64	4.2	1011	420	282	1.5
October	636	876	240	107	2.2	1190	554	438	1.3
November	548	1010	462	231	2.0	1206	658	457	1.4
December	539	978	439	184	2.4	932	393	238	1.7
Total	7340	8956	1682	701	2.4	10600	3288	2279	1.4

Note: *-calculated based on 2015-2019 data; ** - mortality associated with COVID-19 (the main cause of COVID-19, or COVID-19 is not the main cause of death but had a significant impact on the development of fatal complications of the disease).

causes by 8.6%, respectively. The number of deaths from neoplasms decreased by 11% compared to expected.

The increase in mortality from diseases of the circulatory system, respiratory diseases, and digestive diseases probably reflects both the unaccounted-for mortality from COVID-19 and the high vulnerability of people with chronic diseases in a pandemic. Analysis of the causes of deaths from external causes requires a separate study.

In 2020, 673 people died from COVID-19, in 47 (7%) deaths from COVID-19 the virus was not identified (Table 2). In 28 of the deceased, COVID-19 was not the main cause of death but had a significant impact on the development of fatal complications of the disease. Thus, according to official statistics from Rosstat, in 2020, 7.8% (701) of deaths in the republic were associated with a new coronavirus infection, including 7.5% (673) of cases, COVID-19 was the main cause of death. In 0.3% (28) of deaths, COVID-19 had a significant impact on the development of fatal complications of the disease. When calculating the intensive indicator, the mortality rate associated with COVID-19 was 71.8 per 100,000 population.

In 2021, 2180 people died from COVID-19, in 54 (2.5%) cases the virus was not identified (Table 2). In the deaths of 99 people, COVID-19 was not the main cause of death but had a significant impact on the development of fatal complications of the disease. Thus, in 2021, 21.5% (2279) of deaths were related to COVID-19, of which 20.6% (2180) of cases had COVID-19 as the leading cause of death. In 0.9% (99) of cases, COVID-19 had a significant impact on the development of fatal complications of the disease. The death rate associated with COVID-19 was 230.9 per 100,000 population in 2021.

During the 2 years of the pandemic in the republic, the death of 2980 people was associated with COVID-19. In 2021, 3.25 times more people died from this cause than in 2020, which is associated with a more severe course of the infection, with the delta variant of the virus prevailing in this year.

Comparison of the actual number of deaths with expected levels separately by months showed that since July 2020, excess mortality rates have increased sharply, in just 1682 more people died than expected (Table 3). The excess mortality rate was 172 per 100,000 population. Its share in the structure of total mortality was 18.8%. If all deaths reported as related to COVID-19 are considered, then 42% of excess deaths were due to this cause. The number of deaths associated with COVID-19 was positively correlated with the excess mortality rate, Pearson's correlation coefficient was 0.94, $p<0.001$. The undercount rate in September 2020 was 4.2. In general, for the period March-December, the underestimation rate was 2.4. As shown in studies, underreporting values above 1.0 are mainly due to underreporting of deaths from COVID-19 infection [6].

In 2021, excess mortality was 3288 cases (31% in the structure of total mortality), i.e. 333 per 100,000 population. 69% of them were related to COVID-19. Based on an analysis of all-cause mortality reports from 74 countries over the same period (January 1, 2020 to December 31, 2021), the global excess death rate was 120.3 deaths (113.1–129.3) per 100,000 population. In 21 countries, it exceeded 300 deaths per 100,000 population [4]. According to researchers, excess mortality during an epidemic outbreak can be considered as an indicator of mortality from COVID-19 [5].

The correlation coefficient between the number of deaths associated with COVID-19 and excess mortality in the republic was 0.95, $p<0.001$. The underestimation rate was the highest in March (4.9), for the period January-December 2021 it was 1.4.

In general, for 2020-2021. in the Republic of Sakha (Yakutia) 19556 people died, of which 4970 cases were classified as excess mortality. The number of excess deaths in 2021 was 1.95 times the number in 2020.

According to Goroshko N.V. with co-authors in 2020, excess mortality was observed in 82 out of 85 subjects of the Russian Federation. The increase in the number of deaths in 2020 amounted to 288.0 thousand people compared to the average number of deaths in 2015-2019. When compared with the data of 2019 - 340.3 people [1].

Conclusion. Thus, over 2 years of the spread of a new coronavirus infection (2020-2021) in the Republic of Sakha (Yakutia), 19556 people died. 7.8% of deaths in 2020 and 21.5% in 2021 were related to COVID-19. The number of all deaths was 22% and 44% respectively higher than the expected number of deaths. The proportion of excess deaths in 2020 was 19% of all deaths, in 2021 - 31%. Of the excess deaths, 42% and 69%, respectively, were related to COVID-19. Therefore, the causes of the 1990 excess deaths need to be clarified. The excess mortality rate reached 333 per 100,000 population in 2021. The high correlation coefficients (0.94-0.95) between COVID-19-related deaths and additional deaths suggest that excess deaths during the period 2020-2021 will largely be due to the spread of COVID-19. The decline in mortality underreporting in 2021 against the background of an increase in excess mortality reflects improved diagnosis and correct identification of the causes of death. Research into the causes of excess mortality is needed to assess the impact of the pandemic and other factors on various aspects of mortality in the republic's population.

Reference

1. Goroshko N.V., Patsala S. V. Izbytochnaya smertnost' v period pandemii COVID-19: regiony Rossii na fone strany [Excess mortality during the COVID-19 pandemic: russian regions against the backdrop of the country]. Social'no-trudovye issledovaniya [Social and Labour Research. 2022; 46 (1): 103-116 (In Russ.).] DOI: 10.34022/2658-3712-2022-46-1-103-116.

2. Kashepov A.V. Kovidnyj mul'tiplikator smertnosti ili novyj metodicheskij podhod k analizu izbytochnoj smertnosti naseleniya v 2020-2021 gg. [COVID mortality multiplier and a new methodological approach to the analysis of excess mortality in 2020-2021]. Social'no-trudovye issledovaniya [Social and Labour Research [Federal'naya sluzhby gosudarstvennoj statistiki. Arhiv operativnyh dannyh po EDN (In Russ.).] https://rosstat.gov.ru/storage/mediabank/edn_03-2022.htm

3. Federal State Statistics Service. Archive of operational data on vital statistics. https://rosstat.gov.ru/storage/mediabank/edn_03-2022.htm (In Russ.).]

4. COVID-19 Excess Mortality Collaborators. Estimating excess mortality due to the COVID-19 pandemic: a systematic analysis of COVID-19-related mortality, 2020-21. COVID-19 Excess Mortality Collaborators // Lancet (London, England). 2022; 399(10334): 1513-1536. doi.org/10.1016/S0140-6736(21)02796-3

5. Beaney T, Clarke J. M., Jain V [et al.] Excess mortality: the gold standard in measuring the impact of COVID-19 worldwide? Journal of the Royal Society of Medicine. 2020; 113 (9): 329-334. DOI: 10.1177/0141076820956802

6. Karlinsky A., Kobak D. Tracking excess mortality across countries during the covid-19 pandemic with the world mortality dataset. eLife. 2021; 10: 1-21. DOI: https://doi.org/10.7554/eLife.69336

7. R. Beelen, G. Hoek, P. A. van den Brandt [et al.] Long-term effects of traffic-related air pollution on mortality in a Dutch cohort (NLCS-AIR study). Environmental Health Perspectives. 2008; 116 (2): 196-202. doi:10.1289/ehp.10767

8. WHO. COVID-19 significantly impacts health services for noncommunicable diseases. https://www.who.int/news/item/01-06-2020-covid-19-significantly-impacts-health-services-for-noncommunicable-diseases

9. World Health organization. Health Effects of Particulate Matter. Policy implications for countries in eastern Europe, Caucasus and central Asia. / World Health organization. – 2013. – 15 p. https://www.euro.who.int/__data/assets/pdf_file/0006/189051/Health-effects-of-particulate-matter-final-Eng.pdf