The status of herd immunity to measles in Russia: A systematic review and meta-analysis of epidemiological studies

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Introduction. The comprehensive assessment of the herd immunity to measles in Russia can be challenging, as Russian subject-related studies tend to focus on seroprevalence in various cohorts of different sizes. The systematic review and subsequent meta-analysis of different research findings increase the total number of observations and statistical significance of the studies, thus enhancing the reliability of conclusions.

The **purpose** of the study is to assess the status of herd immunity to measles in Russia by analyzing the findings of studies published by Russian researchers.

Materials and methods. The conducted systematic review and meta-analysis covered 13 Russian studies (the total number of the examined was 15,353, from birth to 79 years of age) published in 2011–2020 and addressing the assessment of herd immunity to measles in population of different regions in Russia.

Results. It was found that the principal approach in all the studies was assessment of herd immunity through examination of adult people, including healthcare workers, with no regard for their vaccination history. The proportion of seronegative cases among young people (18–30 years) — 27.3% (95% CI 25.7–27.3%) and among children under 17 — 38.3% (95% CI 35.8–40.8%), who were born after the two-time vaccination had been included in the National Immunization Calendar, was larger than in older age groups — 19.8% (95% CI 17.8–21.8%). The level of herd immunity among healthcare workers representing a decreed group — 84.5% (95% CI 83.7–85.3%) was higher than that of relatively healthy population — 75.4% (95% CI 74.1–76.6%), which can be explained by stricter vaccination requirements.

Conclusion. The high proportion of seronegative cases among children and young adults of under 30 years of age is a risk factor associated with measles spread among the population and can be seen as the result of insufficient vaccination coverage.

Keywords: *herd immunity; measles; systematic review; meta-analysis.*

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Состояние популяционного иммунитета к кори в России: систематический обзор и метаанализ эпидемиологических исследований

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Введение. Комплексная оценка состояния популяционного иммунитета населения России к кори затруднена, т.к. отечественные работы по указанной тематике, как правило, ограничены изучением серопревалентности в отдельных группах разной численности. Систематический обзор и последующий метаанализ результатов работ разных авторов позволяют увеличить общий объем наблюдений и статистическую значимость исследований, что повышает достоверность выводов.

Цель работы — оценка состояния популяционного иммунитета населения России к кори на основании анализа результатов опубликованных научных работ отечественных авторов.

Материалы и методы. Проведен систематический обзор и метаанализ результатов 13 отечественных научных работ (обследовано 15 353 лица в возрасте от рождения до 79 лет), опубликованных в период с 2011 по 2020 г. и посвященных оценке состояния популяционного иммунитета к кори у населения разных регионов России.
Результаты. Установлено, что при проведении исследований основным подходом к оценке популяционного иммунитета является обследование взрослых лиц, в том числе медицинских работников, без учета прививочного анамнеза. Доля серонегативных среди лиц молодого возраста (18–30 лет) — 27,3% (95% ДИ 25,7–27,3%) и детей до 17 лет — 38,3% (95% ДИ 35,8–40,8%), родившихся после введения двукратного режима вакцинации в Национальный календарь профилактических прививок, была больше, чем в старших возрастных группах — 19,8% (95% ДИ 17,8–21,8%). Уровень коллективного иммунитета у медицинских работников как декретированного контингента — 84,5% (95% ДИ 83,7–85,3%) — оказался выше, чем среди условно здорового населения — 75,4% (95% ДИ 74,1–76,6%), что связано с более жесткими требованиями к проведению вакцинации.
Заключение. Наличие значительной доли серонегативных лиц среди детей и молодых взрослых до 30 лет в пределах, показанных в работе, является фактором риска распространения вируса кори среди населения и может быть следствием недостаточного охвата вакцинацией.

Ключевые слова: *популяционный иммунитет; корь; систематический обзор; метаанализ.*

Источник финансирования. Авторы заявляют об отсутствии финансирования при проведении исследования.

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Introduction

Prevention and control of infectious diseases, including vaccine-preventable diseases, remain critically important. Prior to immunization, measles was a common disease among children under six years of age, who accounted for 80% of measles cases. According to the World Health Organization (WHO), major measles epidemics occurred every 2–3 years and measles caused an estimated 2.6 million deaths each year [1, 2].

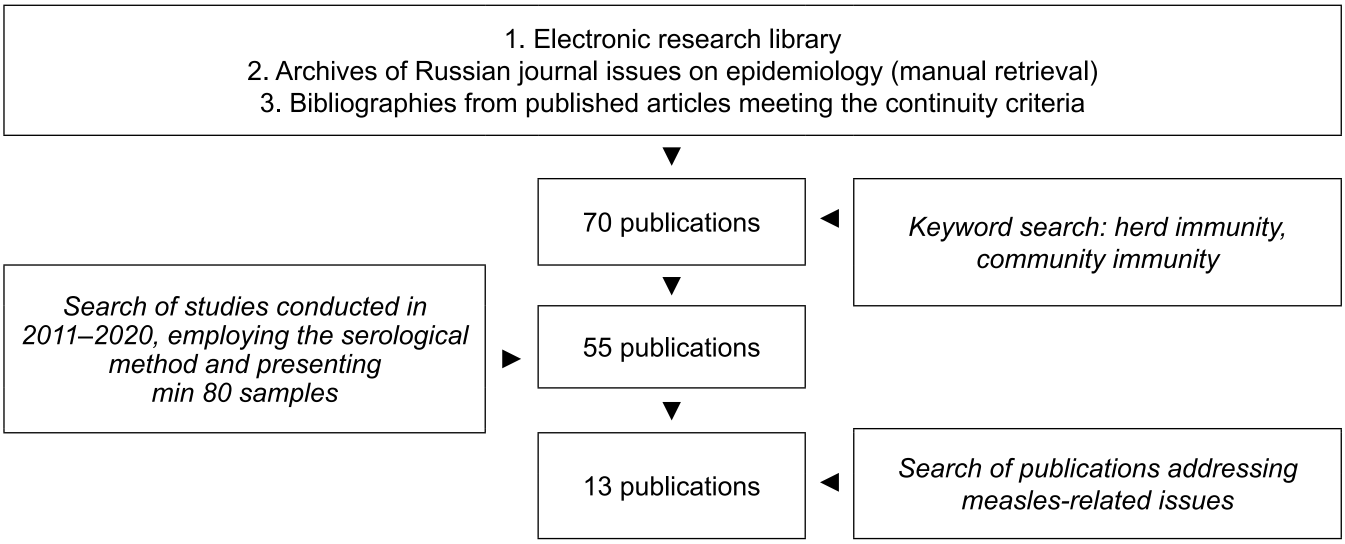
After the vaccination against measles had been included in Russia's National Immunization Calendar (1968), the measles-related morbidity and mortality rates went steadily down [3–5]. The successful implementation of mass immunization against measles resulted in establishing a high level of herd (or community) immunity (HI) through the increased proportion of individuals immune to the infection after being vaccinated [6, 7]. HI is acquired specific protection of the population; it is a totality of naturally acquired and vaccine-based immunity of individuals of the population [8, 9]. The fact that measles can be eliminated through vaccination of the population was backed up by theoretical studies as well as by fundamental changes in its epidemic behavior, thus encouraging WHO to declare the Measles Elimination Program targeting at measles eradication in five regions of the world by 2010 [10, 11]. In the meantime, the changing (weakening) herd immune protection of the population is one of the main factors increasing the risk of measles spread in future [12–14].

The importance of assessment of measles-related HI as the principal factor preventing the infection spread is driven by the need to resolve the controversy occurring in the present-day infection-related epidemiological situation. Along with high rates of vaccination coverage (more than 90%), since 2010 measles resurgence has been reported in many countries worldwide (in North and South America, Africa, and Europe), including Russia and post-Soviet countries. Despite implementation of extensive additional preventive measures, including vaccination of the previously unvaccinated population, the measles incidence rates continued to rise in 2019 [15].

HI assessment employs serological surveillance laboratory methods to estimate the proportion of individuals who are seronegative (non-immune) and seropositive (immune) to a certain pathogen [16]. The group of examined people is divided into those who are seronegative and seropositive to the measles virus. The division is based on the results of the individual serological examination and their conformity/non-conformity to the threshold levels specified by manufacturers of test systems used in laboratory diagnostics[1].

Thus, seroepidemiological studies are an efficient tool for assessment of risk associated with spread of infectious diseases and for monitoring of the effectiveness of specific preventive programs. The scientific value and practical significance of such studies

[1] MU 3.1.2943-11 Organizing and conducting of serological monitoring of the herd immunity to infections controllable by means of specific prevention (diphtheria, tetanus, whooping cough, measles, rubella, mumps, polio, hepatitis B) (adopted on 15/7/2011). URL: http://docs.cntd.ru/document/1200088401



The protocol of collection of research studies addressing assessment of the population's herd immunity to the measles virus (the criteria for study entry are italicized).

are universally recognized. An increasing number of studies addressing the population's HI to preventable infections involve screening assays based on materials of national serum banks [17–19]. This approach makes it possible to create a representative sample of a sufficient size and, thus, to achieve the adequate statistical reliability of the research results. At present, the comprehensive assessment of HI of the Russian population poses a challenge, as subject-specific Russian studies are generally limited to individual groups characterized by certain epidemiological significance. For example, healthcare workers (HCWs) are a risk group in terms of many infections, including measles. Therefore, the vaccination requirements applicable to them are significantly stricter (according to the National Immunization Calendar, all individuals belonging to this professional group and being under 55 years of age must be vaccinated against measles[2]).

Another risk group in terms of infection includes hospital patients who can be a source of infection for HCWs and can be involved in the measles epidemic process after their contact with a diseased HCW. Furthermore, in some cases, chronic diseases can result in contraindications to vaccination against measles and may aggravate the disease caused by infection. Thus, the examination and evaluation of the herd immunity of HCWs and inpatients helps assess the risk associated with the spread of nosocomial measles.

Pregnant women and infants under one year of age, i.e. younger than the age at which routing MMR vaccination is recommended, fall into higher risk groups, as they may develop measles-induced complications. The assessment of herd immunity in these groups makes it possible to measure the risk of increased incidence rates among infants.

However, the HI assessment is not limited to examination of risk groups and should include evaluation of immunological protection in different age groups of the relatively healthy population (RHP). Note that the reliability of serological studies tends to increase with higher coverage of the population across different groups and larger numbers of the examined, which is a difficult task for research groups. In this regard, the systematic review and the subsequent meta-analysis of different research findings are instrumental in increasing the total number of observations, statistical power of the studies, and, consequently, reliability of the assessment [20, 21].

The purpose of the study is assessment of measles-related HI of the Russian population by analyzing the results of published studies conducted by Russian researchers.

Materials and methods

The systematic review included only Russian studies addressing assessment of measles-related HI of the Russian population and was performed in compliance with the protocol outlining the sequence of operations required for data collection (**Figure**).

The primary search of published studies was conducted by key words (herd immunity, community immunity) from 26/4/2020 to 30/4/2020 in accordance with the following strategies:

- at the electronic research library;
- through manual retrieval at archiving sites for Russian journal issues on epidemiology (Journal of Microbiology, Epidemiology and Immunobiology, Epidemiology and Preventive Vaccination, Epidemiology and Infectious Diseases.

[2] The Decree of the Ministry of Health of the Russian Federation, dated 21/3/2014, No. 125n "On adoption of the national immunization calendar and the epidemic-related preventive vaccination calendar." URL: http://docs.cntd.ru/document/499086215

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Current Issues, Infection and Immunity, Bulletin of the Russian Academy of Sciences);
- through bibliographies in published articles meeting the continuity criteria.

After duplicates had been removed, the source list of research articles included 70 subject-related publications. The task of the next stage was to remove publications that did not meet the study entry criteria listed in the Figure. The final list contained 13 research articles [26–38] addressing assessment of HI to the measles virus and based on studies using the serological method; the articles were published in 2011-2020.

Studies were conducted among residents of the following territories: Moscow, St. Petersburg, Republic of Tatarstan, Republic of Buryatia, Petrozavodsk, Samara, Perm, and Tver Region.

During the next stage of the study, all the relevant information about the design and groups of the examined was summarized in **Table 1**. A total of 13 studies were conducted and the total number of the examined was 15,353 individuals, from birth to 79 years. The smallest number of participants in the study was 80 people, while the largest number was 4,444 people.

The research articles were used to retrieve data on specific approaches and criteria for selection of individuals in conducting serological studies as well as data on percentage distribution of seronegative individuals in different age groups of the population. The data were summarized and analyzed by using a meta-analysis.

Methods of elimination of biased data during the meta-analysis

To prevent publication bias (some results that do not have, in researchers' opinion, any scientific value or statistical significance are not included in the Study Results section), the research articles were thoroughly studied to retrieve only the information that was present in each article. To exclude any biased representation and data omission (for example, if there are different criteria for dividing the examined into age groups), the missing information was regained through mathematical calculations based on the source variables given in the Materials and Methods section.

Thus, the following variables were used in the meta-analysis:
- the age of the examined;
- the data on their previous vaccination against measles;
- the distribution of seronegative and seropositive individuals in the groups.

Criteria for summarizing data

The results presented in research articles were consistent both methodologically (estimating the percentage distribution of seronegative and seropositive cases among the examined individuals) and statistically (presented as average values and their standard deviation or 95% confidence interval), thus providing ground for their summarizing and conducting of a meta-analysis in compliance with the guidelines specified in the manual for medical statistics [20].

Table 1. General information about the examined individuals according to the data of 13 Russian research articles published in 2011–2020 and addressing assessment of measles-related HI of residents of different regions in Russia

Parameter	Number of studies in compliance with the selection criteria applicable to individuals participating in serological studies	Number of the examined	
		abs.	%
Age			
Infants	2	898	5.8
Preschool children	3	829	5.4
Children/adolescents (7–17 years)	2	714	4.7
Adults 18–60 years	12	11,571	75.4
Over 60 years	6	1,341	8.7
Cohort			
Healthcare workers	8	7,450	48.5
Inpatients	1	80	0.5
Mother–newborn pairs	2	898	5.9
УЗН Relatively healthy population	6	6,925	45.1
Vaccination history of the examined			
Availability of vaccination history	5	4,000	26.1
Absence of vaccination history	8	11,353	73.9
Serological methods of study			
The enzyme-linked immunosorbent assay (ELISA) using test systems manufactured by *Vector-Best, CJSC*	13	11,570	75.4
out of them, the cut-offs for positive samples			
≥0.18 IU/ml	11	10,162	87.8
≥0.2 IU/ml	2	1,408	12.2
Passive hemagglutination assay	1	3,783	24.6
Total	13	15,353	100

Statistical methods of processing of meta-analysis results

The meta-analysis was performed with the help of the Statistica 12.0 software package (StatSoft) in accordance with the guidelines for statistical processing of research results [21]. The average proportion of seronegative cases among the examined and its 95% confidence interval (CI) were calculated. The significance of differences across the groups was estimated by using the Student *t*-test at the confidence of 95% and higher ($p \leq 0.05$).

Results

Analysis of approaches to organization of serological studies

Examined cohorts. The study found that the highest priority in assessment of measles-related HI should be given to estimation of the percentage distribution of seronegative and immune individuals in the HCW group (48.5% of the examined), among RHP (45.1%) as well as infants and their mothers (5.9%) (Table 1). The selection of the above groups is explained by the specifics of the present-day epidemic process of measles: involvement of HCWs and inpatients during disease outbreaks at the site of treatment and preventive care facilities and a rapidly increasing number of cases among infants and young children (under 2 years). In the meantime, studies of herd immunity in the children population (not including infants) are sparse (the related data were found in 3 out of 13 studies). The status of immunological protection against the measles virus among infants (accounting for 5.8% of the examined) was assessed by using serological testing of umbilical cord blood serum samples. The most frequent participants of studies were adult individuals aged 18–60 years (75.4% of the examined).

Methods of serological studies. In Russia, ELISA, together with using test systems from Russian manufacturers ((Vector-Brest CJSC), is the main method of laboratory examination of serum materials. Most of the articles showed 0.18 IU/ml (in 2 articles — 0.2 IU/ml) as the minimum positive level of antibodies. Only the article of M.A. Belopolskaya et al. [32] referred to two methods of serological examination: ELISA (661 samples) and a passive hemagglutination assay (PHAA) (3,783 samples). In conducting PHAA (by using test kits from Russian manufacturers), the minimum positive antibody titer was 1:10. The average portions of seropositive cases among the examined were calculated by using the results of the two above-mentioned tests and amounted to 75.3% (ELISA) and 85.0% (PHAA).

Statistical analysis of the data. The studies addressing assessment of herd immunity in RHP, pregnant women and infants were randomized. Blood serum samples were collected during outpatient visits of the examined individuals and during their regular medical checkups. The HCW groups were created by job functions at treatment and preventive care facilities where the examination was conducted. The aspects referring to compliance of the conducted studies with the Russian legislation in personal data protection, including the informed consent signed by participants of the studies, as well as study inclusion/exclusion criteria were specified only in two articles [36, 38].

Most of the obtained results were processed by using Microsoft Office Excel; in 6 cases, researchers used special-purpose software packages (Biostat IBM, SPSS 96 Statistics 11.0, Statistica). The distribution of individuals seronegative and seropositive to the measles virus is given as a percentage value, including the standard deviation or 95% CI. The rules used for distribution of variables and constituting the criterion for selection of parametric and non-parametric tests were defined only in one article (the study results are presented as a mean value and its 95% CI) [38].

The vaccination and infection status of the examined individuals

The analyzed research articles presented two approaches to assessment of the HI status: through examination of people with the available vaccination history and without such history. When conducting studies employing blood serum samples from adult individuals with available vaccination history, special attention should be paid to the reliability of the sources of subject-specific medical data. The information is seen as reliable is it is supported by the records in the outpatient's personal registration form; the records must specify the vaccination date, series and dose of the vaccine. In this respect, the examination of HCWs representing a decreed group is most informative, as in compliance with the applicable laws, HCWs must be vaccinated against measles till they reach 55 years. In a number of cases, it may be difficult to get reliable information about the vaccination status of the examined; therefore, researchers may use alternative ways of obtaining information (questionnaires and survey). Based on the results of the studies, the estimated vaccination coverage of HCWs ranged from 37.8% [29] to 92.5% [31] (**Table 2**).

As for other groups of population (which should be vaccinated against measles before they reach the age of 35 years), the data on vaccination history of the examined were collected from three sources: records in the outpatient's chart, anamnestic information, official statistics on coverage of the children population by preventive vaccination when the examined individuals reached 12 months and 6 years of age (the age of the first and second vaccine dose). Due to difficulties associated with obtaining reliable information, in 8 out of 13 research articles (73.9% of the examined) the serological assessment of HI to the measles virus did not include vaccination history of the examined. Four out of 5 articles presenting data on vaccination and infection history of the examined focused on assessment of the herd immunity level in HCWs. In the study [36] the vaccination coverage (588%) was estimated only in the seronegative cases (68%) among RHP.

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Table 2. Results of the serological examination of HCWs, based on data from research articles

Year and place of the study	Source	Cohort	Number of the examined	Age, years	Vaccination coverage[1], %	Average proportion of seronegative cases[2], %	Age group with the highest proportion of seronegative cases	
							age, years	%
2011, Perm	[31]	Healthcare workers	896	18–56	18–35 years — 92.5	13.7 ± 1.1	18–35	19.3
2011, Republic of Buryatia	[37]	Healthcare workers	200	18–65	Unavailable	5.0	18–29	8.9
2011, Tver Region			393			18.6	18–29	22.9
2015–2017, Republic of Tatarstan	[26]	Healthcare workers	480	18–60	84.38 ± 1.66	36.03 ± 2.4	20–29	47.0
		Medical students	619	18–22		45.07 ± 3.0		
2018, Moscow	[34]	Healthcare workers	1899	19–68	Unavailable	16.7	18–23	38.5
							19–33	24.8
2018, St. Petersburg	[32]	Healthcare workers	2077	18–65	Unavailable	9.1	<14	26.1
							18–25	52.3
The year is not specified, Samara	[30]	Healthcare workers	1503	18–79	77.58	27.5	Young adults	
Not specified	[28]	Patients from the lung transplant waiting list	80	17–65	Unavailable	16.3	17–30	22.2–28.6
2014, 2016, 2018, 2019, Petrozavodsk	[29]	Healthcare workers and outpatients[3]	402	36–71	20.9[4]	12.7	36–50	22.6

Note. [1]The vaccination coverage was estimated by summarizing data from medical documentation, questionnaires and surveys.
[2]The average proportion of seronegative cases is presented in the format used in the source articles (only the average value, the average value and standard deviation or 95% CI).
[3]Outpatients were seen as RHP.
[4]The vaccination coverage is estimated only by using data from medical documentation.

Analysis of the herd immunity status

Relatively healthy population. Based on the results published in the research articles, the proportion of seronegative cases among RHP of under 60 years of age ranged from 23.4% [35] to 29.0% (95% CI 26.3–31.8%) [38] (**Table 3**). Within the narrower age range (under 43–44 years), the above proportion accounted for 20.1% [34] to 26.1 ± 2.9% [33].

All authors of the analyzed studies obtained results indicating the increasing proportion of seronegative cases among younger adults (under 30 years) who were born after the two-time vaccination had been included in the National Immunization Calendar. The highest proportions of seronegative cases were identified among the youngest adults participating in each of the studies (Table 3).

On average, the meta-analysis of the study results identified 27.3% (95% CI 25.7–27.3%) seronegative cases among the examined individuals aged 18–30 and 19.8% (95% CI 17.8–21.8%) seronegative cases in the group of 31–70-year-olds (**Table 4**). Five studies used Spearman's non-parametric correlation coefficient and Smirnov's criterion to show the existence of a negative correlation relationship between the age of the examined and the proportion of seronegative cases among them. Thus, the average level of herd immunity (the proportion of immune individuals) among adult residents of Russia was 75.4% (95% CI 74.1–76.6%).

In assessment of preventive vaccination effectiveness, great importance is given to distribution of seronegative cases among the children population whose herd immunity was mainly built up under the influence of vaccination. Based on the results of the meta-analysis, the proportion of such individuals among children under 17 years of age was significantly ($p \leq 0.05$) higher than among adult residents of this country (24.6%; 95% CI 23.4–25.9%) and averaged 38.3% (95% CI 35.8–40.8%). In the meantime, infants and young children, who demonstrated the highest frequency of occurrence of seronegative cases, were a risk group in terms of measles incidence. For example, in the group of children aged one year to 2 years, according to A.P. Toptygina et al. [35], in 2018 there were 41.8% of seronegative cases; according to T.A. Semenenko et al. [38] in 2019 there were 51%. The results of the meta-analysis show that among infants, the proportion of seronegative cases was 20.5% (95% CI 17.9–23.3%), which was lower than among their mothers [33, 34] and among RHP of different age groups. Similar data can be found in other articles [22, 23]. Such results can be explained by the specifics of the transplacental transport of IgG [24, 25].

Healthcare workers. Eight out of 13 research articles address assessment of herd immunity in HCWs. The age of the individuals participating in the study ranged from 20 to 76 years. According to different authors, the proportion of seronegative cases among HCWs widely ranged from 5% [37] to 36.03 ± 2.4% [26] (Table 2).

As expected, differences in the vaccination coverage among HCWs affected the results of serological studies. At the low vaccination coverage of HCWs (20.9%) [29], the average proportion of seronegative cases was higher (22.6% in the group of 36–50-year-olds) than in the study [31] where the vaccination coverage was quite high (92.5%) and the average proportion of seronegative cases was 13.7 ± 1.1%. Among the vaccinated HCWs, there were 34.16% of seronegative cases (aged 18–55 years) [30] and 19.3 ± 4.3% (aged 18–35 years) of individuals having no antibodies [31]. As in case of RHP, all the researchers point out the prevalence of non-immune individuals in the youngest age groups of HCWs. The meta-analysis identified 12.7% (95% CI 11.9–13.6%) of seronegative cases among HCWs aged 31–70 years and 22.7% (95% CI 21.0–24.5%) aged 18–30 years (Table 4).

On average, the level of herd immunity among HCWs representing a decreed group was significantly ($p \leq 0.05$) higher (the immune individuals accounted for 84.5%; 95% CI 83.7–85.3%) than among RHP (75.4%; 95% CI 74.1–76.6%).

The data on specific humoral immunity to measles among medically ill patients were found only in the article [28] presenting the examination of patients from the lung transplant waiting list. The obtained results were similar to the values presented by other researchers for the HCW group (the average proportion of seronegative cases was 16.3% and in the group of 17–30-year-olds it varied from 22.2 to 28.6%). However, the number of individuals participating in the study (80 people) was too small for statistically reliable comparison that would include the measles-related immune responses of patients from the transplant waiting list and similar responses of individuals from other cohorts.

Discussion

The conducted systematic review of the articles addressing assessment of measles-related HI of the Russian population showed that approaches should be unified and standardized. First of all, it refers to the Materials and Methods section, which gave insufficient attention to ethical and regulatory matters as well as to the procedure and criteria of inclusion (exclusion) of the participants of the study. In addition, the criteria used for dividing the examined individuals into age groups varied significantly, thus making it difficult to compare results obtained by different authors. In our opinion, the problem could be resolved through division of the examined individuals into age groups in accordance with their vaccination history (creating groups of individuals who were born prior to the vaccination against measles, during one-time and two-time vaccination) and the National Immunization Calendar (till the age of 35, all adults must be vaccinated; till the age of 55 – all HCWs).

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Table 3. Results of the serological examination of RHP, based on data from research articles

Year and place of the study	Source	Cohort	Number of the examined	Age, years	Vaccination coverage, %	Average proportion of seronegative cases[2], %	Age group with the highest proportion of seronegative cases	
							age, years	%
2011–2012, Moscow	[34]	Maternity patients (umbilical cord blood)	672	16–43	Unavailable	20.1	16–35	25.0
The year is not specified, Moscow and Moscow Region	[33]	Maternity patients	226	15–44	Unavailable	26.1 ± 2.9	15–23	36.8
		Infants	226			21.7 ± 2.7		
		Relatively healthy females	149	15–44		22.1 ± 3.4		
2013, Moscow and Moscow Region	[35]	Relatively healthy population	654	0–60	Unavailable	36.2	1–2	41.8
				18–60		23.4	18–30	45.3
2018, different regions of Russia	[36]	Relatively healthy population	100	19–30	58.8%[1]	68.0		
2016–2017, Moscow	[38]	Relatively healthy population	2,410	0–17	Unavailable	38.8 (35.5–41.1)	1–2	51.0
				18–60		29.0 (26.3–31.8)	18–19	40.4
2018, St. Petersburg	[32]	Outpatients	2,367	0–65	Unavailable	28.1	<14	26.1
							18–25	52.3

Note. [1]The vaccination coverage is estimated only among the identified seronegative cases.
[2]The average proportion of seronegative cases (not including infants under one year of age) is presented in the format used in the source articles (only the average value, the average value and standard deviation or 95% CI).

Table 4. Percentage distribution of seronegative cases in different age groups of RHP and HCWs

Group	The proportion of people seronegative to the measles virus, % (95% CI)		
	18–30 years	31–70 years	total
Relatively healthy population	27.3 (25.7–27.3)	19.8 (17.8–21.8)	24.6 (23.4–25.9)
Healthcare workers	22.7 (21.0–24.5)	12.7 (11.9–13.6)	15.5 (14.7–16.3)

Approaches to assessment of the vaccination status of the examined, the herd immunity of the vaccinated and unvaccinated individuals need systematization. The identification of a substantial proportion of seronegative cases among the vaccinated individuals is alarming and calls for explanation. Besides, the quality of the source information about vaccination history of the examined is of critical importance. In our opinion, only the data obtained through analysis of vaccination records in personal registration forms can be seen as reliable. Other sources of information (anamnestic information, official statistics on vaccination coverage of decreed age groups) can be used exclusively for reference. However, even taking into consideration anamnestic information about vaccination and infection status, the vaccination coverage of HCWs exceeded 90% only in one study [31]. The study [29] points out that reliable information about vaccination obtained only from 20.9% HCWs. Such comments imply the existence of problems regarding organization of preventive vaccination, namely, regarding the registration of the vaccinated individuals and individuals who must be vaccinated. Such problems affect the reliability of the official statistical information about the preventive vaccination coverage of the population. On the whole, the herd immunity of HCWs (the proportion of immune individuals was 84.5%; 95% CI 83.7–85.3%) was higher than the herd immunity of RHP (75.4%; 95% CI 74.1–76.6%), which can be explained by more stringent requirements for vaccination.

The fact that there are problems related to organizing and performing preventive vaccination against measles is backed up by the results of assessment of HI among RHP in different age groups. Based on the study results, the highest proportion of individuals seronegative to measles virus was identified among children who have their first vaccine dose (at the age of one year to 2 years). On average, the level of herd immunity of the children population (the proportion of immune individuals was 38.3%; 95% CI 35.8–40.8%), which was generally built under the influence of vaccination, was lower as compared to the adult population (the proportion of immune individuals was 24.6%; 95% CI 23.4- 25.9%). At the same time, among the adults (aged 18–30 years), who were born after the two-time vaccination had been included in the National Immunization calendar, the proportion of immune individuals (72.7%; 95% CI 72.7–74.3%) was significantly ($p \leq 0.05$) lower than in older (31–70 years) age groups (80.2%; 95% CI 78.2–82.2%).

Thus, the meta-analysis of the results presented in research articles showed that among the Russian population, the proportion of individuals immune to the measles virus averaged 75.4%; 95% CI 74.1–76.6%. The existence of the substantial proportion of seronegative cases among children and young adults under 30 years of age is a risk factor relating to measles spread among the population and can be seen as a consequence of insufficient vaccination coverage. In such conditions, the priority should be given to assessment of HI of the population without taking into consideration the vaccination history of the examined. This approach was used by most of the authors of the research articles.

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