



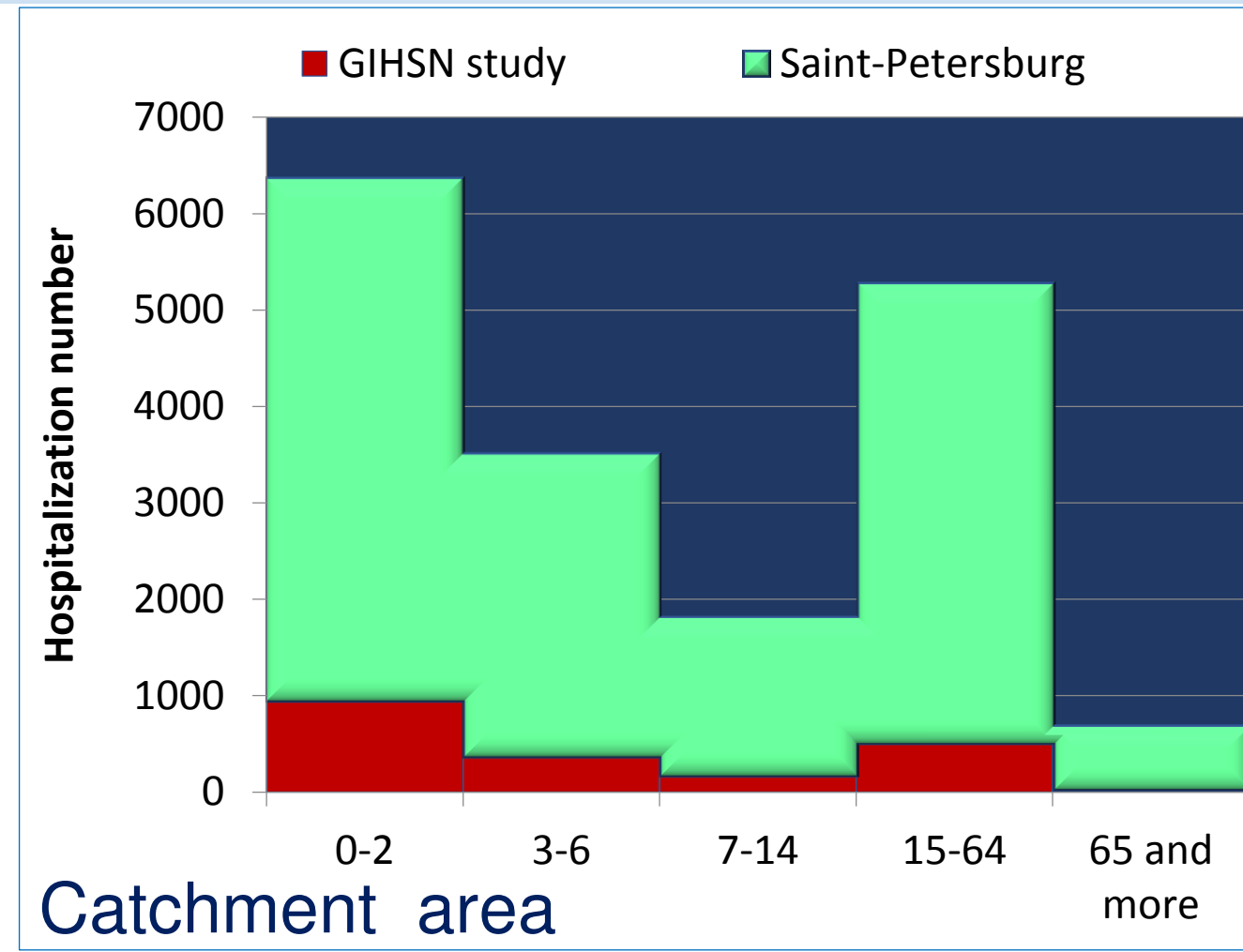
**SAINT-PETERSBURG GIHSN SITE'S EXPERIENCE AND RESULTS OF 2016-2017 SEASON**

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**Site presentation**

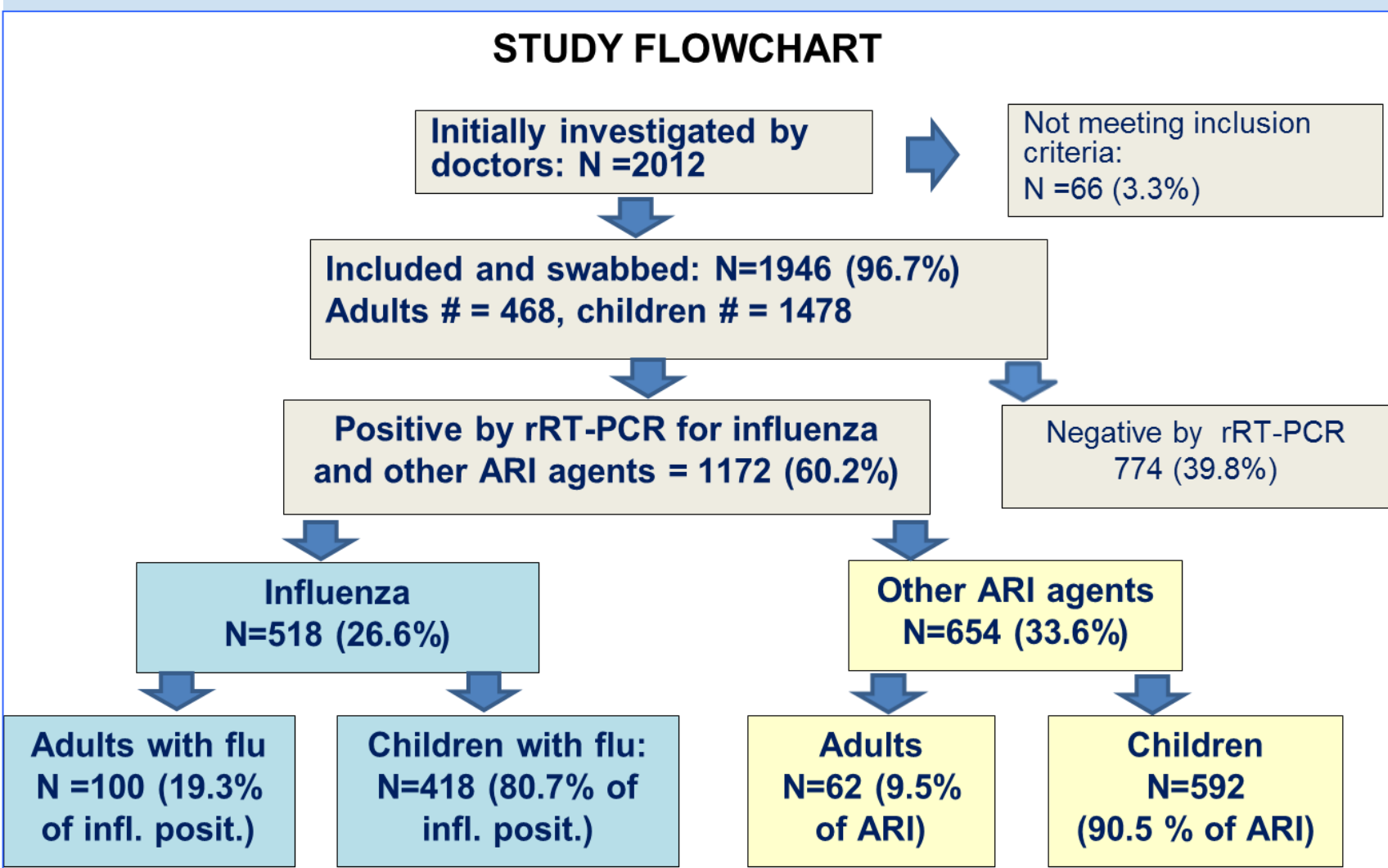
**Three hospitals:** Municipal Infectious Diseases Hospital # 30 (code #1), the ward for adults aged > 17 years (60 beds); Children's Infectious Hospital # 5 (code # 2): five wards for children aged from 0 to 17 years (60 beds each); Children's City Hospital # 4 (code # 3): two wards for children aged from 0 to 17 years (60 beds each); **Regions covered:** Number of patients in GIHSN study was estimated as 12.8% of total number of patients hospitalized in the city (15 696); **Study period:** from 19 December 2016 to 3 June 2017.



**Methods**

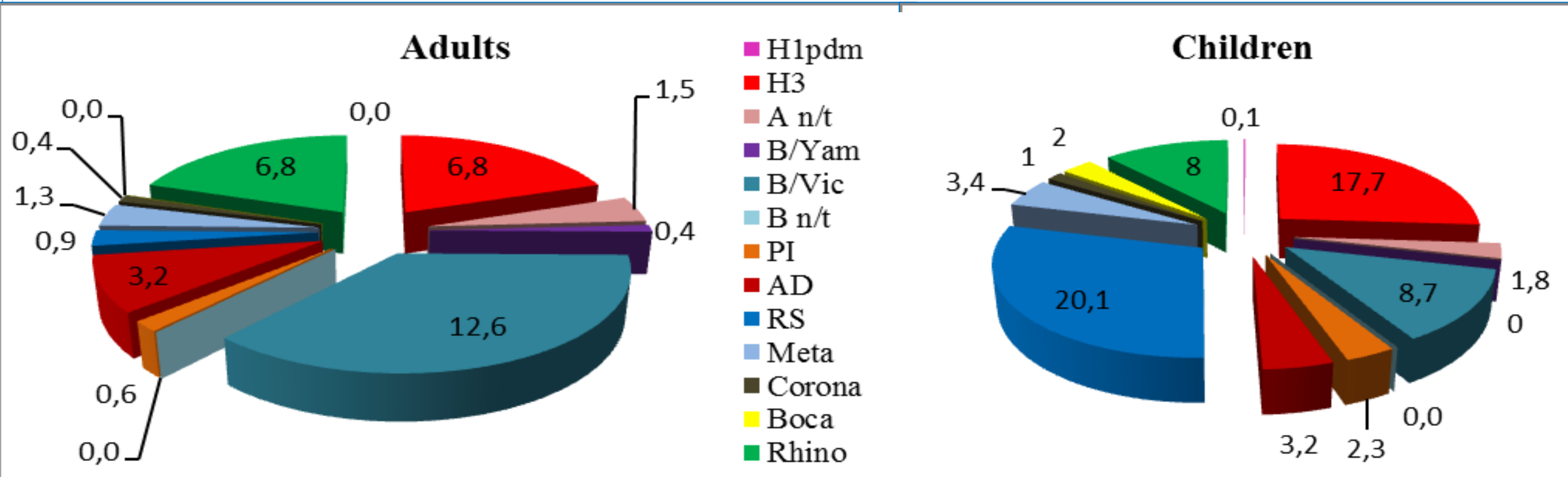
The reported data included hospitalized adults and children with ILI selected according to criteria of inclusion in the GIHSN study. All procedures were performed according to GIHSN Protocol. Nasopharyngeal swabs were collected in UTM (Copan) and tested for influenza viruses A&B; Flu A positive samples were used for subtyping of H1N1pdm09 and H3N2; Flu A&B negative samples were tested for human RSV, metapneumovirus, parainfluenza (types 1-4), coronavirus, RhV, adenovirus and bocavirus (AmpliSense, Russia). Flu B positive samples were used for determining of Yamagata or Victoria lineage (CDC primers & probes, USA). Virus isolation, genetic and antigenic analyses were performed according to the "Manual for the laboratory diagnosis and virological surveillance of influenza" (WHO Global Influenza Surveillance Network, WHO, 2011) with some modifications.

**Results**

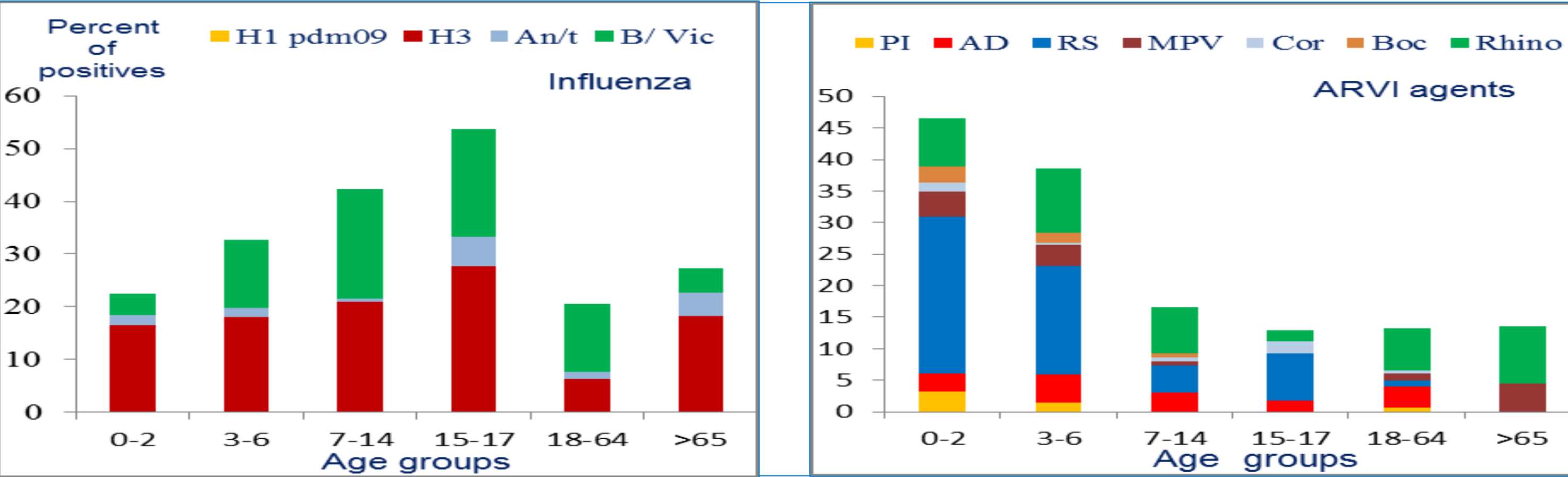


Age group (years)	Primarily investigated	Included in the study	Percent
0-2	944	906	46.6
3-6	367	355	18.2
7-14	170	163	8.4
15-17	54	54	2.8
18 - 64	451	446	22.9
≥65	26	22	1.1
Total	2012	1946 (96.7%)	100.0%

Influenza A(H3N2), B/Victoria and RSV prevailed in 2016-2017 season. Percentage of patients infected by influenza B virus was the highest in adults (p=0.01) and by RSV – in children (p<0.00001). Rhinovirus was the significant causative agent of admission in all age groups (p<0.00001).

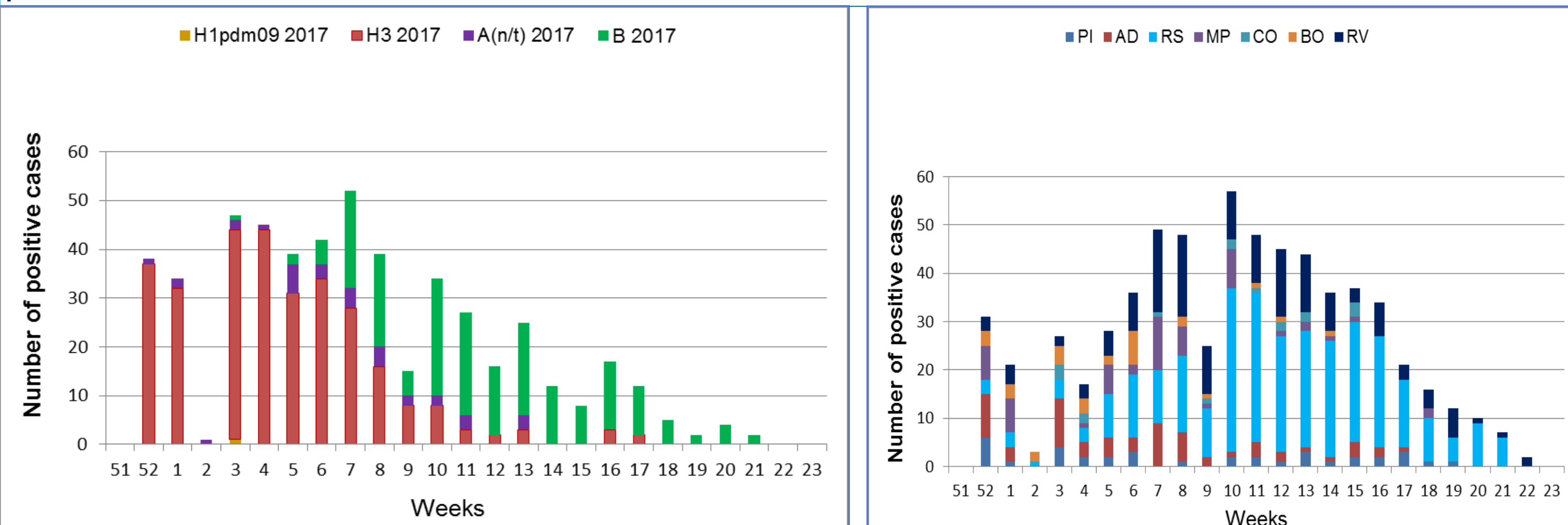


**Etiological structure of respiratory virus infections in adults and children (percentage of positive cases)**



**Age dependent rate of influenza and other ARI agents in hospitalized patients**

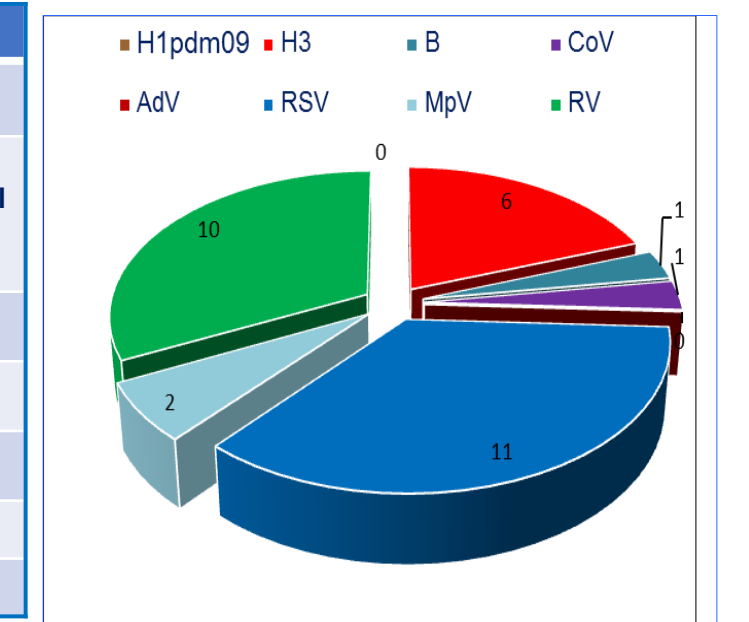
The tendency to increase of influenza A(H3N2) and B(Vic) viruses percentage was observed among children by age. RSV infected more frequently young children aged 0-2 and 3-6 yrs (p=0.002). MpV infection was registered mostly in young children and elderly patients.



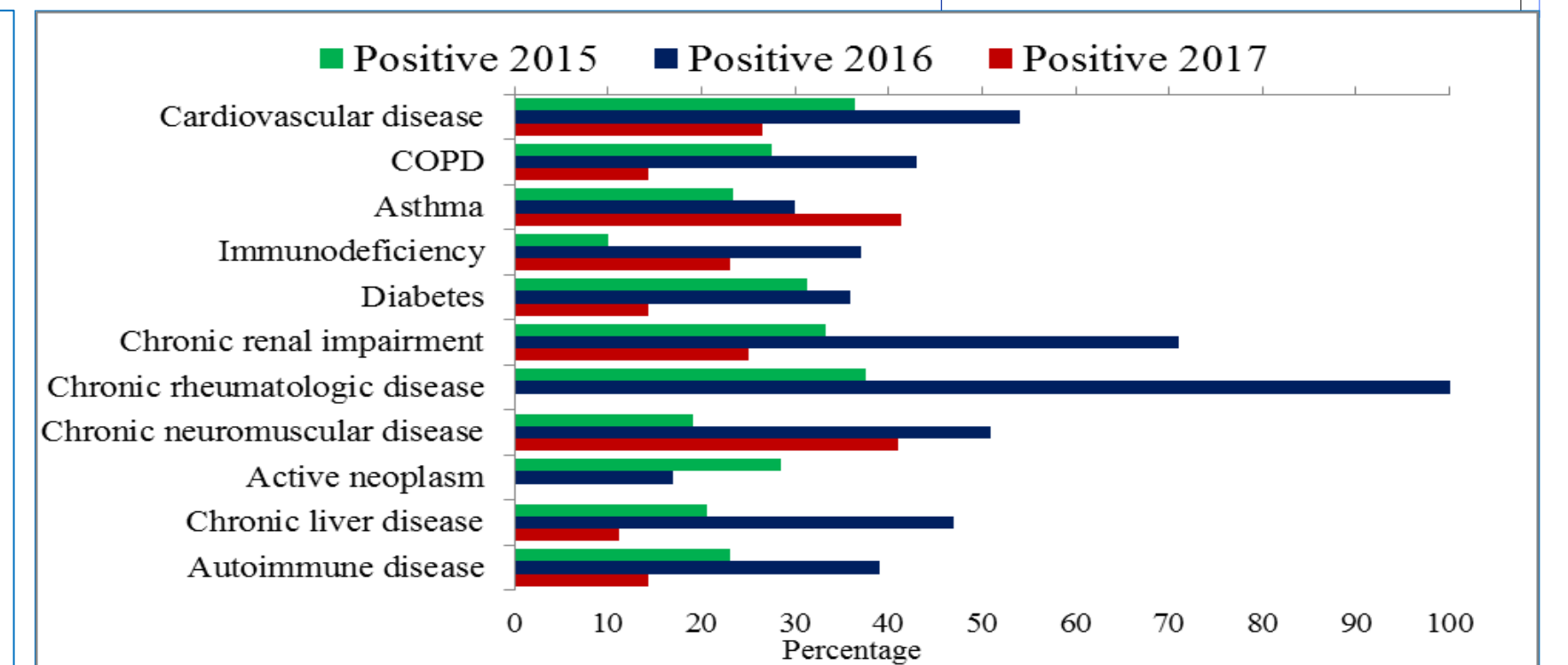
**Monitoring of influenza and other respiratory viruses activity in 2016-2017**

A total 53 ICU patients (98% children). The most often causative agents were RSV (11 cases), RhV (10 cases) and A(H3N2) (6 cases). One child (2 month) with RhV died.

Age group (years)	Number of ICU patients	Positive cases	Virus detected										Total ARI
			H3	A n/t	B/Vic	Total Flu	RSV	MpV	CoV	RhV			
0-2	34	20	3	0	0	3	11	1	1	4	17		
3-6	11	8	2	1	0	3	0	1	0	4	5		
7-14	7	4	1	0	1	2	0	0	0	2	2		
≥65	1	0	0	0	0	0	0	0	0	0	0		
Total	53	32	6	1	1	8	11	2	1	10	24		



Percentage of patients with comorbidity among influenza positive in 2016-2017 season was lower compared to 2015-2016 season excluding asthma, which together with chronic neuromuscular disease was the most often (p<0.00001).

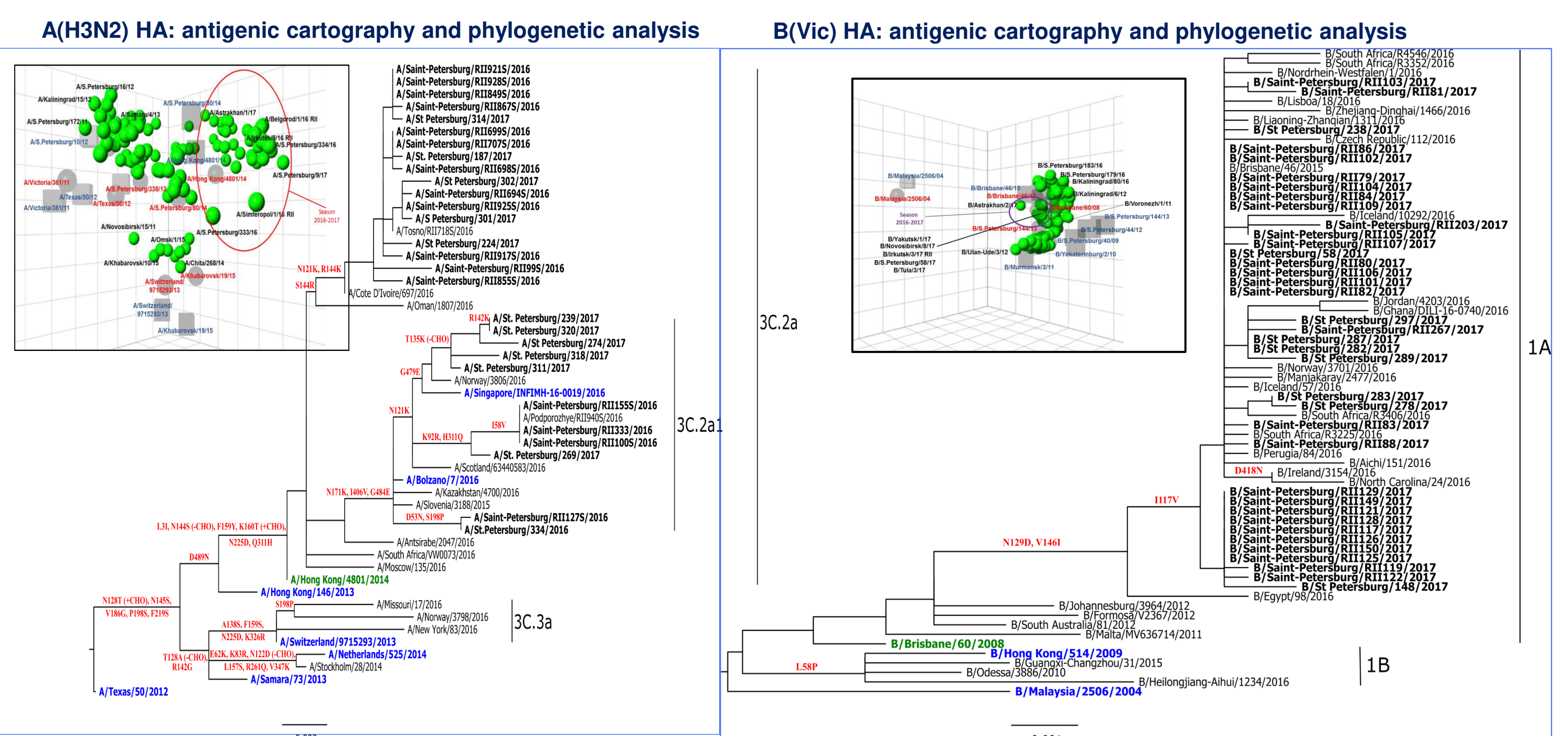


Influenza vaccination is included in the National Calendar of Vaccination and paid from Federal Budget. "Sovigripp", "Grippol" and "Ultrix" vaccines were mainly used for immunization in Russia (about 47 mln doses). Other vaccines available in the country: "Vaxigrip" (Sanofi Pasteur), "Begrivac" (Novartis), "Fluarix" (SmithKline Beecham), "Influvac" (Abbott) etc. The number of vaccinated among hospitalized in GIHSN study in 2016-2017 season was 85 (4.4%) patients. Among them 31 (36.5%) patients were influenza positive.

76 pregnant women were included in GIHSN study additionally. Significantly higher rate of flu positive cases was observed among pregnant women compared to the adjusted control group of not pregnant (p=0.01). Influenza B virus was detected in pregnant women more often (35.5%) compared to other respiratory agents (p=0.04). RhV infection was registered in 13.2% of pregnant women.

	Pregnant		Not pregnant	
	N	%	N	%
N	76		45	
Age	18-43		16-45	
Influenza all	34	44.7	9	20
H3	5	6.6	1	2.2
A	2	2.6	0	0
B	27	35.5	8	17.8
ARVI all	11	14.5	8	17.8
RhV	10	13.2	3	6.7

According to HA gene phylogenetic analysis influenza A(H3N2) viruses were represented by clade 3C2a and genetic subgroup 3C2a.1 (39%). Most of the aa substitutions in viruses of 3C2a clade occurred in antigenic site A. The most affected antigenic sites from subgroup 3C2a.1 were also A (R142G in 44% of sequences) and E (K92R in 33% of sequences). All sequenced viruses had S245N in NA (+ potential N-glycosylation site with S247N substitution). NGS sequencing revealed deletion in segment 2 of some 3C2a.1 viruses resulting in 11 aa truncated PB1-F2 protein. The PB1-F2 truncated viruses clustered together on phylogenetic trees for all segments of genome. According to EpiFlu GISAID database 11 aa PB1-F2 truncation is untypical for A(H3N2) viruses, but all influenza A(H1N1)pdm09 viruses have truncated PB1-F2. All influenza B viruses (except two) belonged to Victoria lineage. Phylogenetic analysis of HA gene showed that influenza B(Vic) viruses isolated in St. Petersburg belonged to the genetic subgroup 1A (B/Brisbane/60/2008 - like) and were genetically homogenous. Two viruses of Yamagata lineage belonged to clade 3 (B/Phuket/3073/2013 - like). Results of antigenic cartography correlated with phylogenetic data.



**Key aspects & challenges**

1. High proportion of young children (46.6%) and low proportion of elderly patients (1.1%) in St. Petersburg site (p<0.00001);
  2. Influenza epidemic of the 2016-2017 season caused by A(H3N2) and B(Vic) viruses was characterized by early start, moderate intensity and prolonged duration in both St. Petersburg and in the whole country;
  3. Last season influenza A and B viruses matched the vaccine strains by results of genetic and antigenic analysis;
  4. Risk factors for hospitalization in adults were cardiovascular diseases caused by influenza A(H3N2) virus and in children chronic neuromuscular disease caused by RSV, RhV or influenza A(H3N2) virus.
  5. 31 influenza positive cases were detected among 85 vaccinated patients.
- Challenges:** Expansion of geography of GIHSN study in the country for future surveillance enhancement and influenza vaccines effectiveness estimation; Development and evaluation of new approaches for IVE estimation.

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