Global Influenza Hospital Surveillance Network

Influenza Hospital Surveillance Results in Moscow, Russia. Season 2018-2019

Svetlana Trushakova[1], Lidiya Kisteneva[1,2], Elena Burtseva[1]

K Krasnoslobodtsev[1,2], E Morozova[1], E Mukasheva[1] A.Rosatkevich[1], L Merkulova[1,2], R Vartanyan[1,2], I Kruzhkova[2], L Kolobukchina[1,2]

[1]FSBI "N.F. Gamaleya NRCEM" Ministry of Health of Russian Federation, Moscow, Russia; [2]Emergency Clinic #1 for Infectious Diseases, Moscow, Russia

Site presentation

District	% admitted
1	6,4%
2	12,5%
3	11,5%
4	6,5%
5	14,6%
6	11,0%
7	11,9%
8	10,9%
9	9,9%
10	0,7%
11	3,0%
12	0,1%

Hospital is located in North-Western District population 1 001 346 (2018)
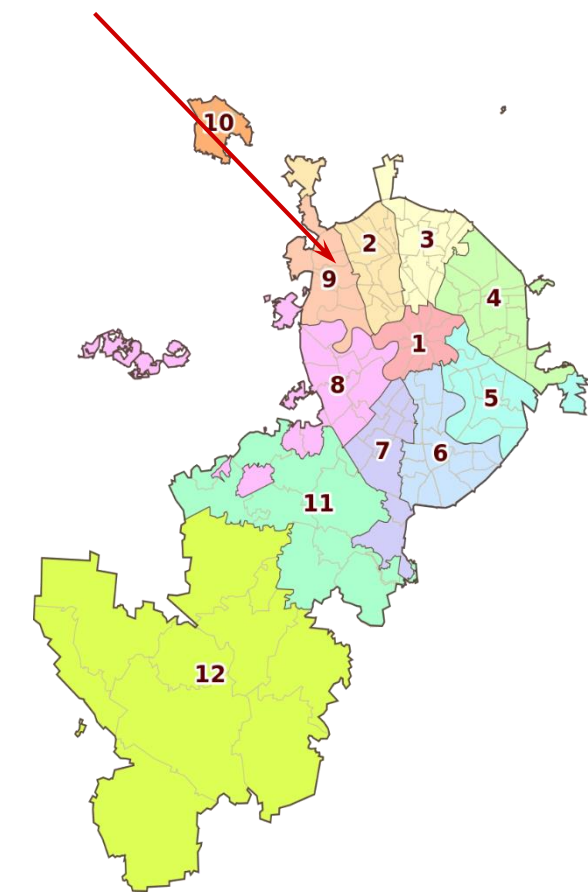
- Catchment area – Moscow
- Population – 12 615 882 (2019)
- Hospital – Emergency Clinic #1 for Infectious Diseases
- Specialty of Hospital – any infectious diseases
- Patients – Moscow residents and guests from 0 to 90 y.o.
- Hospital capacity – 706 beds
- GIHSN participated beds:120 adults, 113 children, 69 obstetric, 12 ICU
- Influenza seasonality – from December to May

Methods

The Hospital conducts screening and sampling of patients. The laboratory (N.F. Gamaleya NRCEM) conducts swabs test and process of the received results. Design of the study is based on the core protocol of the GIHSN. The patients are screened 3 days a week – Tuesday, Wednesday and Thursday.

Russian commercial diagnostic PCR kits have been used: «Ribosorb» and «Riboprep» (AmpliSens, Russia), «DNA-prep» (DNA-technology, Russia); «Reverta-L» (AmpliSens, Russia), «Reagent kit for reverse transcription» (DNA-technology, Russia); AmpliSens Influenza virus A/B, AmpliSens Influenza virus A-type (H1N1 and H3N2), AmpliSens Influenza virus A/H1-swine-FL (H1N1pdm09), influenza B virus (DNA-technology, Moscow), in-house reagents for type B-lineages. Also "ARVI Amplisence PCR kit" was used for detection of respiratory viruses (hRSv, HMPv, hRv, etc.). CDC&P (USA) primers and probes have been used for detection of influenza A/B, H1/H3, B/Yam/Vic.

Results

Flow-chart of screened patients 2018-2019. Patients were included in the GIHSN study from December 2018 to May 2019. Totally, 1278 samples were tested for influenza, 379 of them were positive. Also, 32 specimens were tested for acute respiratory infections (ARI): 29 from children under 5 years old (all were positive for any respiratory virus) and 3 cases from old patients with SARI (1 - MpV, 1 – Piv, 1 – neg)
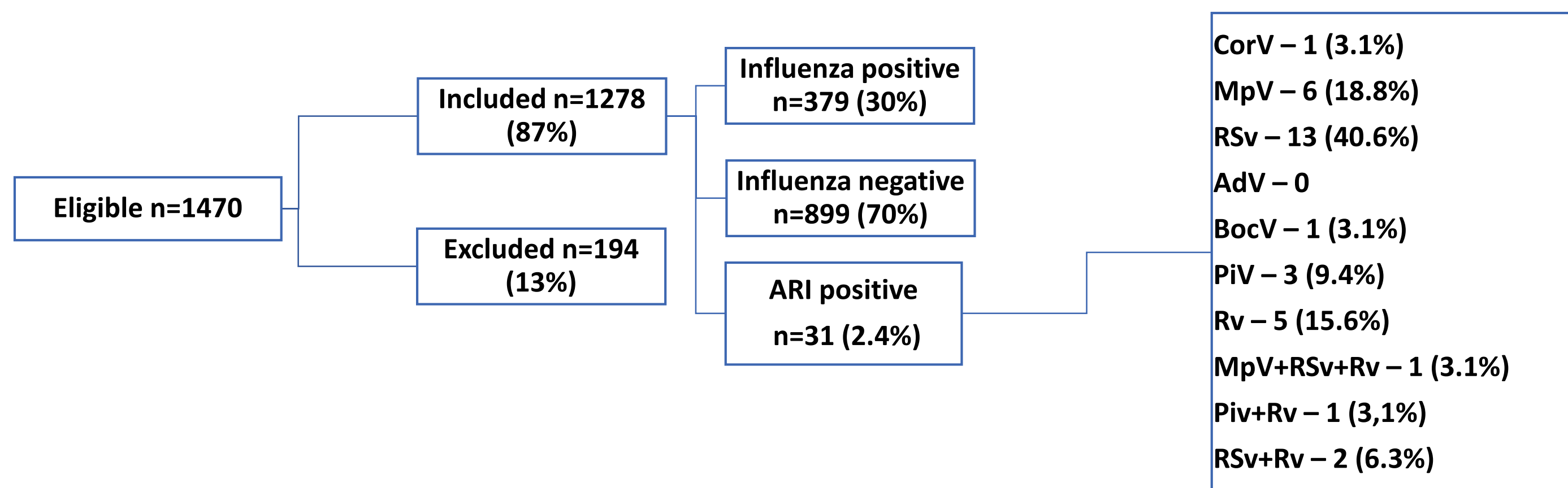
Flow-chart:
- Eligible n=1470
  - Included n=1278 (87%)
    - Influenza positive n=379 (30%)
    - Influenza negative n=899 (70%)
    - ARI positive n=31 (2.4%)
  - Excluded n=194 (13%)

ARI positive breakdown:
- CorV – 1 (3.1%)
- MpV – 6 (18.8%)
- RSv – 13 (40.6%)
- AdV – 0
- BocV – 1 (3.1%)
- PiV – 3 (9.4%)
- Rv – 5 (15.6%)
- MpV+RSv+Rv – 1 (3.1%)
- Piv+Rv – 1 (3,1%)
- RSv+Rv – 2 (6.3%)

Table 1. Influenza results in patients divided by age and pregnancy status. Pregnants and elderly patients were groups the most prone to influenza hospitalizations. Dominant virus was A(H3N2) followed by A(H1N1), while influenza B was registered just in a few cases.

	Children 0-4 N=298	Children 5-14 N=21	Adults 15-64 N=365	Elderly 65+ N=118	Pregnants 15-45 N=476	Total N=1278
N cases (%)						
RT-PCR result						
Positive	45 (15.1)	5 (23.8)	80 (21.9)	34 (28.8)	215 (45.2)	379 (29.7)
Negative	253 (84.9)	16 (76.2)	285 (78.1)	84 (71.2)	261 (54.8)	899 (70.3)
Influenza type						
A(H1N1)pdm09	24 (8.1)	1 (4.8)	25 (6.8)	6 (5.1)	58 (12.2)	114 (8.9)
A(H3N2)	18 (6.0)	3 (14.3)	41 (11.2)	25 (21.2)	148 (31.1)	235 (18.4)
B/Yamagata	0	0	5 (1.4)	1 (0.8)	0	6 (0.5)
B/Victoria	0	0	3 (0.8)	0	2 (0.4)	5 (0.4)
A not subtyped	2 (0.7)	0	6 (1.6)	2 (1.7)	5 (1.1)	15 (1.2)
B not subtyped	1 (0.3)	1 (4.8)	0	0	2 (0.4)	4 (0.3)

Table 2. Severity of influenza positive cases. There was no death in this season. Support oxygen and ICU were needed mainly in children under 5 yo due to their bronchopulmonary obstruction. Pneumonia and bronchitis were more often diagnosed in risk groups.

Outcome	Children 0-4	Children 5-14	Adults 15-64	Elderly 65+	Pregnants 15-45	Total
N cases/positive (%)						
ICU treatment	4/1 (25)	0	2/0	2/1 (50)	0	8/2 (25)
Mechanical ventilation	0	0	3/0	2/1 (50)	0	5/1 (20)
Support oxygen	76/4 (5)	0	8/2 (25)	6/3 (50)	0	90/9 (10)
Death	0	0	0	0	0	0
Hypoxia	64/3 (4.7)	0	22/1 (4.6)	9/2 (22)	0	95/6 (6)
Pneumonia	51/3 (5.9)	1/1 (100)	104/16 (15.4)	41/31 (75.6)	4/3 (75)	201/54 (26.9)
Bronchitis	134/45 (33.6)	4/1 (25)	133/40 (30.1)	50/18 (36)	43/25 (58.1)	364/129 (35.4)

Figure 1. Hospital admissions and influenza results by week 2018-2019. The season lasted 14 weeks. Middle activity of circulating viruses was observed without any untypical manifestations.

Start of the study 16 December 2018. End of the study 6 May 2019.

Legend: A(H1N1)pdm09, A(H3N2), B/Yamagata, B/Victoria, A unsubtyped, B unsubtyped, Admitted tested patients
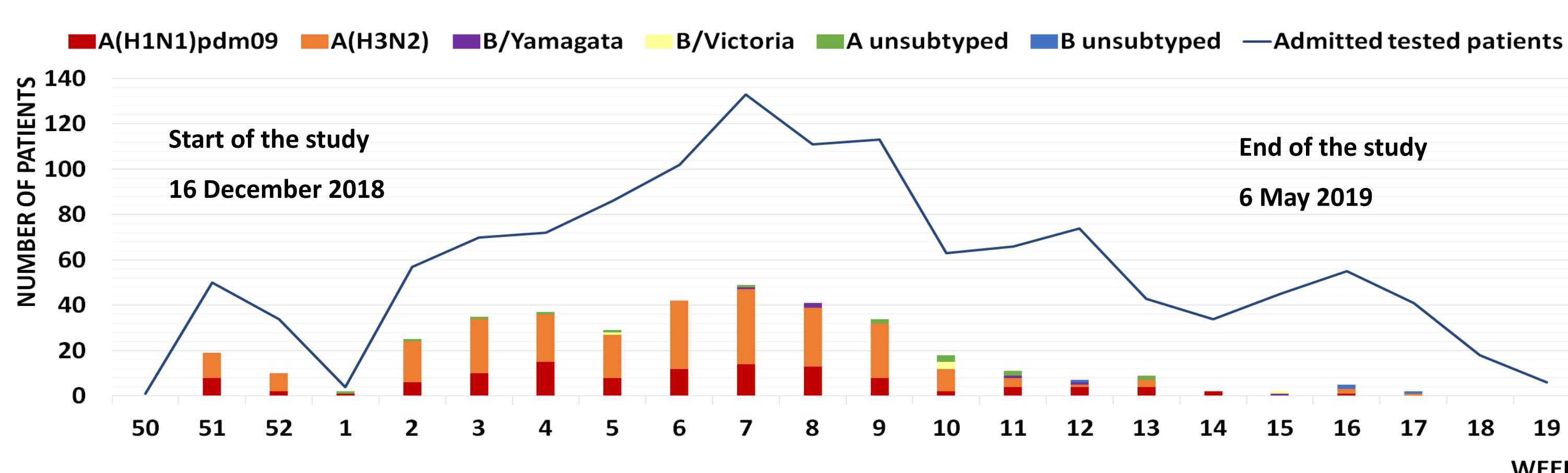
Table 3. Information and sequencing data of HA from GIHSN patients/strains 2018-2019. Sequencing data of 10 influenza strains which were isolated from GIHSN patients showed their cluster representation. Two H1N1pdm09 strains contain S183P substitution in HA1 associated with high susceptibility to host cell receptors. All H3N2 strains represent one clade 3C.2a and contain mutation K176T related to host specificity shift. Influenza B virus belongs to subgroup 3 with mutation D211N which creates a new potential N-glycosylation site.

Name of strain	Type	Sex	Age	Vaccination	Comorbidities	Severity	Treatment	Saturation /resp rate	Clade	Mutations identified in HA
A/Moscow/250/18	H1N1	f	43	no	no information			98/18	6B1.A	T15A, I240V, I286L, K302T,I404M, N496S, E506D
A/Moscow/2/19	H1N1	f	3	no	no				6B1.A	S183P, N129D, N260S
A/Moscow/3/19	H1N1	f	30	no	pregnancy 32w				6B1.A	S183P, T120A, N455T
A/Moscow/236/18	H3N2	m	72	vaccinated 01.11.2018	CVD, COPD, neoplasm	bronchitis		97/22	3C.2a	E78G, K108R, T147K, K176T, P210L, S235F, H327Q, V363M, E495G, V545I
A/Moscow/238/18	H3N2	m	81	no	no (?)	bronchitis		98/18	3C.2a	E78G, K108R, T144A, T151K, K176T, P210L, H327Q, E495G
A/Moscow/1/19	H3N2	f	35	no	Diabetes, Obesity		Ingavirin	98/18	3C.2a	E78G, K108R, T144A, T151K, K176T, P210L, H327Q, E495G
A/Moscow/119/19	H3N2	m	85	no	CVD, COPD, prostate adenoma	SARI, Hypoxia, pneumonia	ICU, mechanical ventilation	78/22	3C.2a	D69N, E78G, K108R, T144A, T151K, K176T, P210L, S214P, H327Q, E495G, I538T
A/Moscow/121/19	H3N2	m	0,3	no	no				3C.2a	E78G, K108R, T147K, K176T, P210L, S235F, H327Q, V363M, E495G, V545I
A/Moscow/122/19	H3N2	f	27	no	pregnancy 16 w				3C.2a	Q73K, E78G, K108R, T147K, K176T, P210L, S235F, H327Q, V363M, E495G, V545I
B/Moscow/5/19	B/Yamagata	m	55	no	no information	SARI, pneumonia	Oseltamivir	88/22	Y3	L187Q, D211N, M266V

Table 4. Characteristics of influenza positive pregnant women and test-negative controls enrolled in GIHSN. Pregnant women are a risk group for influenza hospitalizations, despite the small number of complications identified. ARI along with influenza cause threatened abortion.

Characteristics N=476	Positive pregnants N cases =215 (%)	Negative pregnants N controls=261 (%)	P value
Gestational age			
First trimester	59 (27.4)	85 (32.6)	0.23
Second trimester	77 (35.8)	96 (36.8)	0.83
Third trimester	79 (36.7)	80 (30.7)	0.16
Symptoms			
Fever	214 (99.5)	256 (98.1)	0.23
37-38	49 (22.8)	122 (46.7)	<0.01
38-39	127 (59.1)	102 (39.1)	<0.01
39-40	40 (18.6)	30 (11.5)	0.03
Headache	160 (74.4)	184 (70.5)	0.34
Malaise	203 (94.4)	236 (90.4)	0.11
Myalgia	131 (60.9)	118 (45.2)	0.0006
Cough	185 (86.0)	170 (65.1)	<0.01
Sore throat	145 (67.4)	207 (79.3)	0.0033
Breath	25 (11.6)	45 (17.2)	0.09
Pneumonia	3 (1.4)	1 (0.4)	0.33
Bronchitis	25 (11.6)	18 (6.9)	0.07
Threatened abortion at admission	29 (13.5)	59 (22.6)	0.01
Vaccinated 18-19	3 (1.4)	1 (0.4)	0.33
Comorbidities ≥1	57 (26.5)	72 (27.6)	0.79
Other data			
Blood RH+	159 (74.0)	169 (64.8)	0.03
Blood RH-	24 (11.2)	43 (16.5)	0.09

Figure 2. Patients with comorbidities. Most common comorbidity was CVD (along with other unidentified underlying conditions). However, influenza was more often registered in patients with neoplasm, obesity and renal disorders
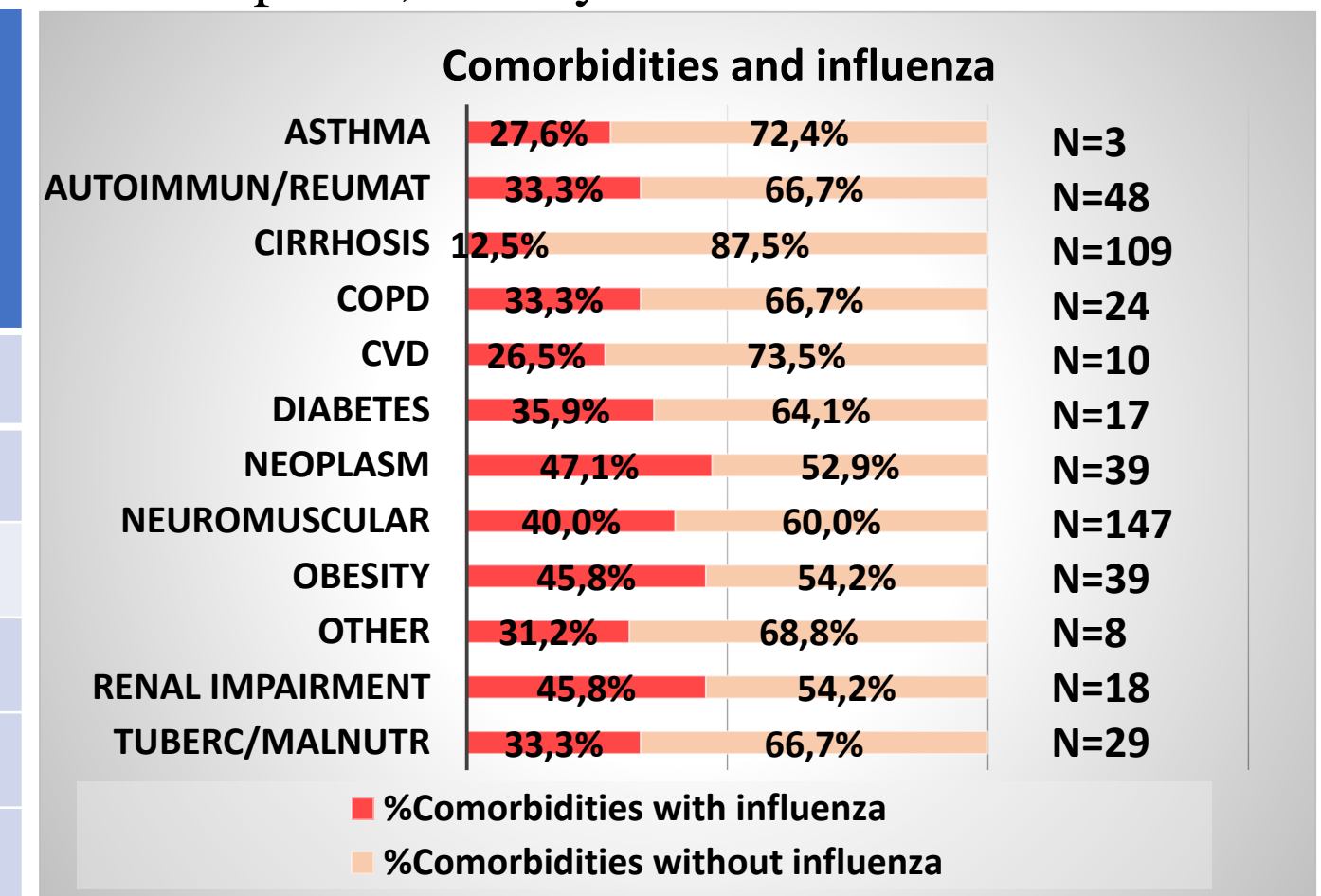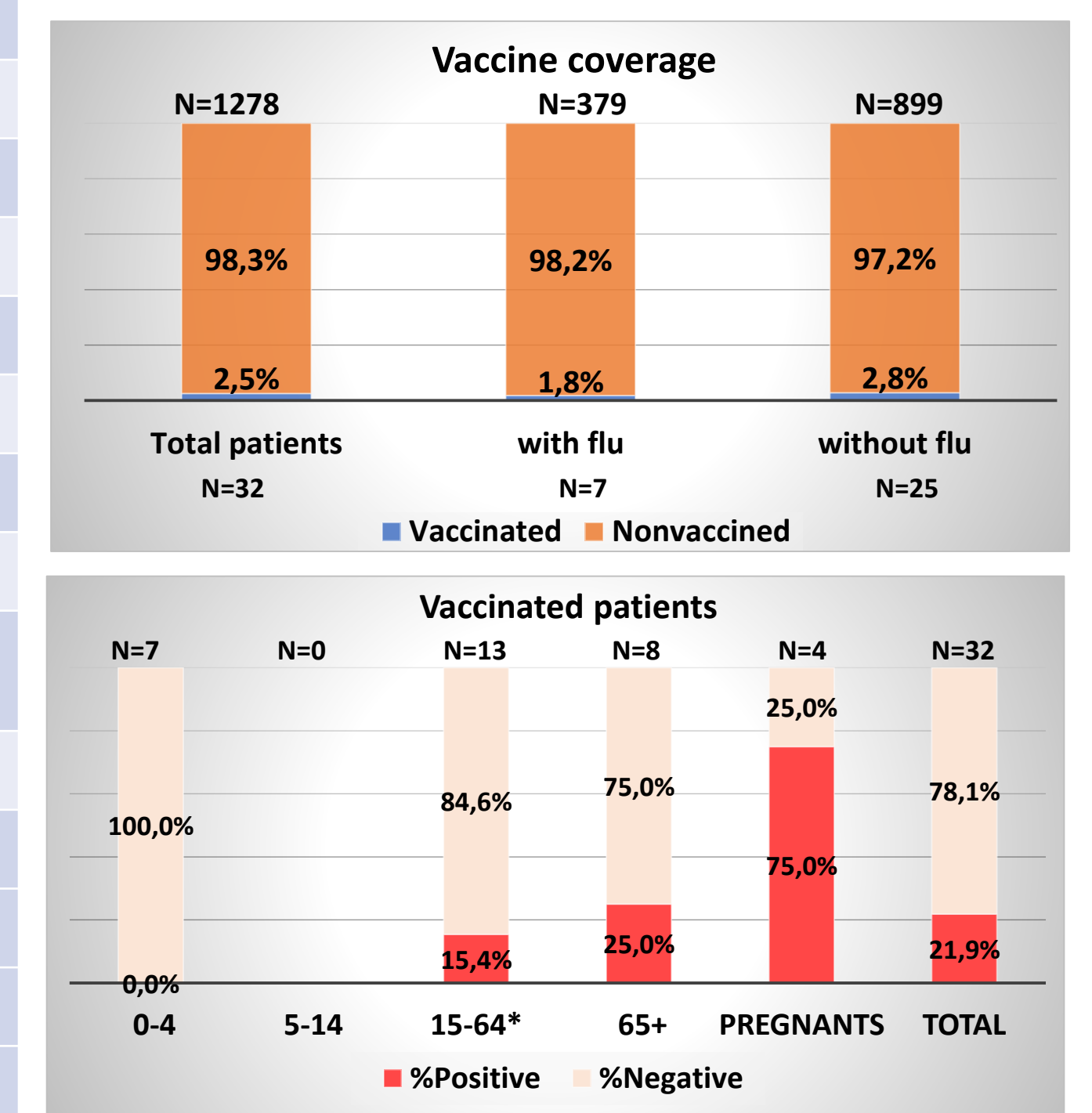
Comorbidities and influenza:
- ASTHMA: 27,6% / 72,4% — N=3
- AUTOIMMUN/REUMAT: 33,3% / 66,7% — N=48
- CIRRHOSIS: 12,5% / 87,5% — N=109
- COPD: 33,3% / 66,7% — N=24
- CVD: 26,5% / 73,5% — N=10
- DIABETES: 35,9% / 64,1% — N=17
- NEOPLASM: 47,1% / 52,9% — N=39
- NEUROMUSCULAR: 40,0% / 60,0% — N=147
- OBESITY: 45,8% / 54,2% — N=39
- OTHER: 31,2% / 68,8% — N=8
- RENAL IMPAIRMENT: 45,8% / 54,2% — N=18
- TUBERC/MALNUTR: 33,3% / 66,7% — N=29

%Comorbidities with influenza / %Comorbidities without influenza

Figure 3. Influenza vaccine coverage in cases and controls. Vaccine coverage of hospitalized patients was very low. It is impossible to assess vaccine effectiveness.

Vaccine coverage:
- Total patients N=1278: 98,3% Nonvaccinated / 2,5% Vaccinated
- with flu N=379: 98,2% / 1,8%
- without flu N=899: 97,2% / 2,8%

Vaccinated patients:
- 0-4 N=7: 0,0% / 100,0%
- 5-14 N=0
- 15-64 N=13: 15,4% / 84,6%
- 65+ N=8: 25,0% / 75,0%
- PREGNANTS N=4: 75,0% / 25,0%
- TOTAL N=32: 21,9% / 78,1%

%Positive / %Negative

Key aspects & challenges

2017-2018	2018-2019
Late start of the influenza season on 3 wk of Jan 2018	Usual start of the influenza season on 51 wk of Dec 2018
Duration of the influenza season – 18 weeks	Duration of the season – 14 weeks
Approximately equal percentage of influenza virus A(H3N2) - 36% A(H1N1)pdm09 - 30% B/Yamagata-lineage - 24% 4 cases of influenza B/Victoria-lineage	**Dominant influenza** virus – A(H3N2) - 62% A(H1N1)pdm09 - 30% **Low level of influenza B** B/Yamagata-lineage - 2% B/Victoria-lineage – 2%
2 elderly deaths (1 with flu) / 6 cases of ICU (1 with flu)	No deaths / 8 case of ICU (2 with flu) Support oxygen and ICU were needed mostly in children under 5 y.o.
Pregnants and elderly patients are most prone to influenza hospitalizations. Bronchitis and pneumonia caused by influenza are commonly registered in these groups	
63 vaccinated patients	32 vaccinated patients
Increase in female admissions: 318 pregnants/ 345 nonpregnants Elderly: 34	476 pregnants/ 204 nonpregnants Increase in elderly admissions: 118

Challenges

- Missing some significant data in view of heavy workload during the peak period of the influenza season.
- Difficulty in taking swabs and gathering data from SARI patients
- Losing data from patients transferred from another hospital
- Shortage of high-skilled and motivated staff to carry out comprehensive and appropriate data collection.

Contact: Influenza Etiology and Epidemiology Laboratory, Moscow
s.trushakova@gmail.com, lidia.kisteneva@gmail.com, elena-burtseva@yandex.ru