



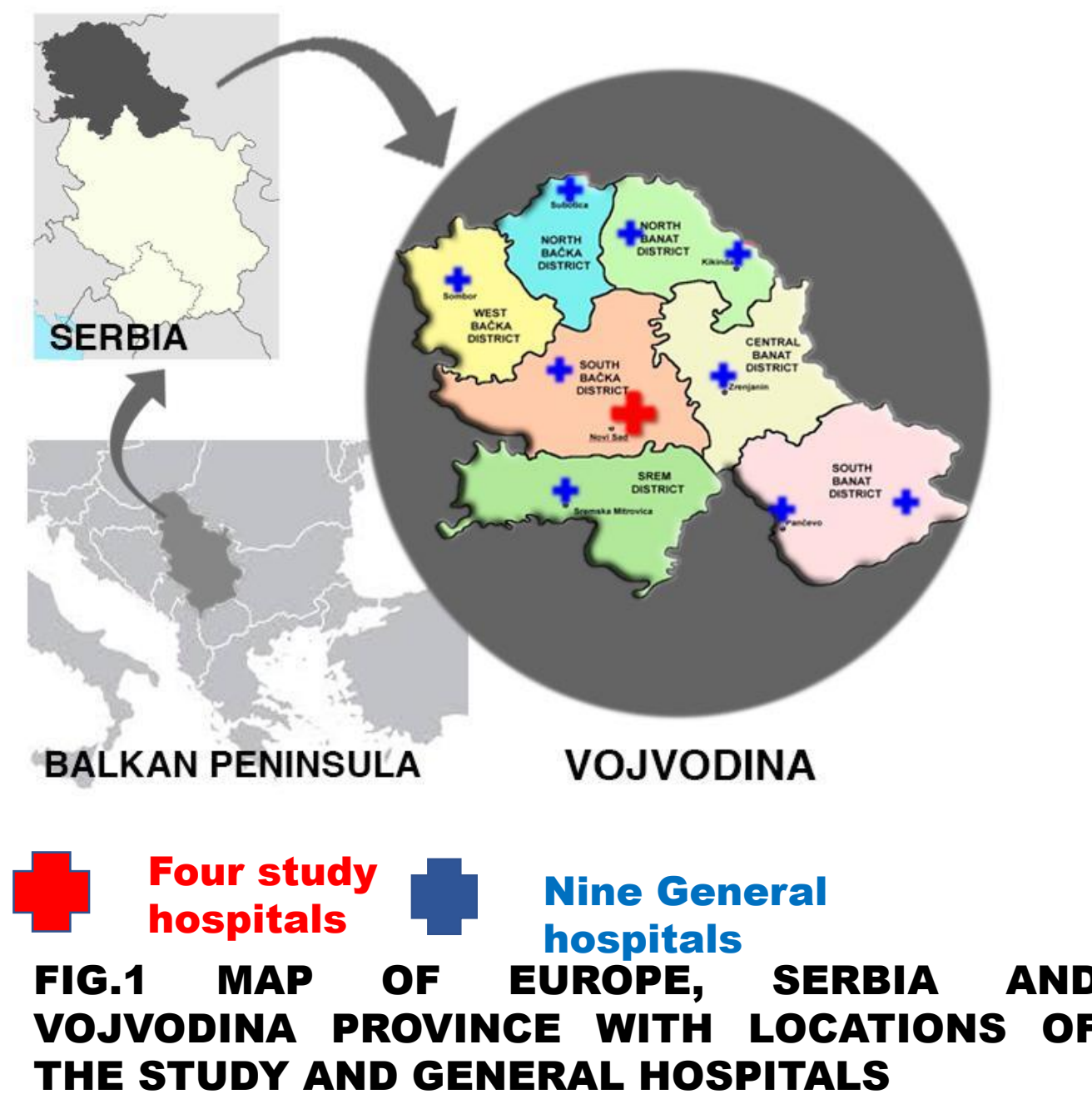
ENHANCED HOSPITAL-BASED SURVEILLANCE OF INFLUENZA AND OTHER RESPIRATORY VIRUSES IN THE AUTONOMOUS PROVINCE OF VOJVODINA, SERBIA, 2017-2018

Snežana Medić^{1,2}, Miodjub Ristić^{1,2}, Vesna Milošević^{1,2}, Jelena Radovanov¹, Vladimir Petrović^{1,2}

¹ Institute of Public Health of Vojvodina, Novi Sad, Serbia, ² Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia

Site presentation

Surveillance is implemented in cooperation of the Institute of Public Health of Vojvodina (IPH) and four tertiary care (study) hospitals (total capacity 954 beds: 350 for pediatric and 604 for adults). Study hospitals regularly admit patients with severe acute respiratory disease from nine general hospitals throughout Vojvodina province, Serbia. **Catchment area** is equal to the population of the Autonomous Province of Vojvodina: 1,931,809 people ($\approx 27\%$ of Serbian population)(Fig.1). We present hospital based surveillance data for the influenza season 2017-2018 in the study area corresponding to the GIHSN site in Vojvodina, Serbia, calendar weeks 40 (2017) -20 (2018).



Methods

Study design: Multi-centre, prospective, active surveillance. **Inclusion&exclusion criteria:** according to GIHSN Protocol. Specific questionnaire for eligible patients of all ages was filled on the spot by health care worker. **Sample collection:** according to GIHSN Protocol. Samples were transported in UTM and tested within 48 hours in the virology laboratory of IPH of Vojvodina. **Molecular diagnostics:** Swab samples were tested for the presence of influenza virus type A; and subtypes A (H1N1)pdm09 and (H3N2) and influenza virus type B (with further determination of B/Yamagata and B/Victoria lineages) using real-time RT-PCR assays. Reverse transcription and amplification were performed using one-step AgPath ID™ One-Step RT-PCR Reagents and oligonucleotide primers and probes (CDC, USA). All influenza negative samples of the patients with acute respiratory distress syndrome (ARDS) and severe acute respiratory infection (SARI) were tested for the presence of other respiratory viruses (MERS-CoV, human meta pneumovirus, human parainfluenza viruses 1, 2, 3 and 4, human rhinovirus, adenoviruses, boka virus and respiratory syncytial virus). **Data analysis:** A descriptive analysis of the obtained results was conducted with aim to evaluate the burden of severe influenza disease among hospitalized patients in study hospitals in Vojvodina.

Results

Dedicated hospital-based surveillance for severe influenza (SARI/ARDS) has been conducted since 2010/11 in all hospitals in Vojvodina. Under the auspices of GIHSN, enhanced hospital-based surveillance was introduced in the influenza season 2017-2018, additionally involving community-acquired influenza-like-illness (ILI) at the hospital admission, according to GIHSN criteria. Data on the number of screened, eligible, tested and laboratory-confirmed influenza cases are shown in Table 1. Virological results by influenza virus type&subtype are presented in Fig. 2.

Table 1. Screening, eligibility, inclusion and laboratory test results, Serbian GIHSN site, 2017-2018

Patient's status	n	%
Screened	2366	100
Eligible	1808	76.4
Included	636	26.9
Influenza virus positive	274	11.6
Other respiratory viruses positive	29	1.2

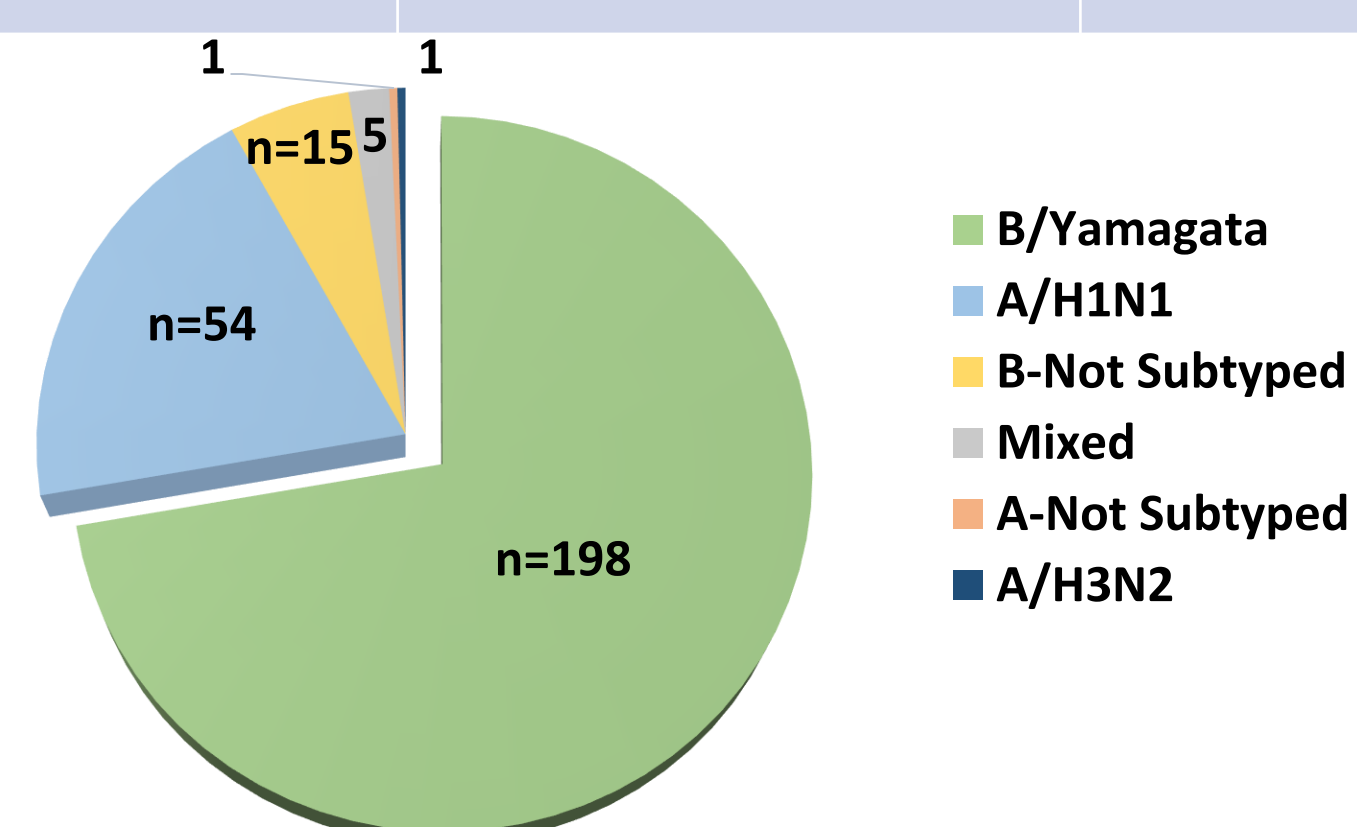


Fig 2 : Influenza virus positive patients by influenza virus type&subtype , Vojvodina, Serbia, 2017-2018

Influenza virus activity in Vojvodina (all types of surveillance) lasted from week 50, 2017, to week 15, 2018. Outbreak of influenza lasted from 4th until 7th calendar week with the highest incidence of ILI recorded in the 5th calendar week of 2018. Epidemic curve that present hospitalized patients according to GIHSN criteria, follow the similar pattern (Fig. 3)

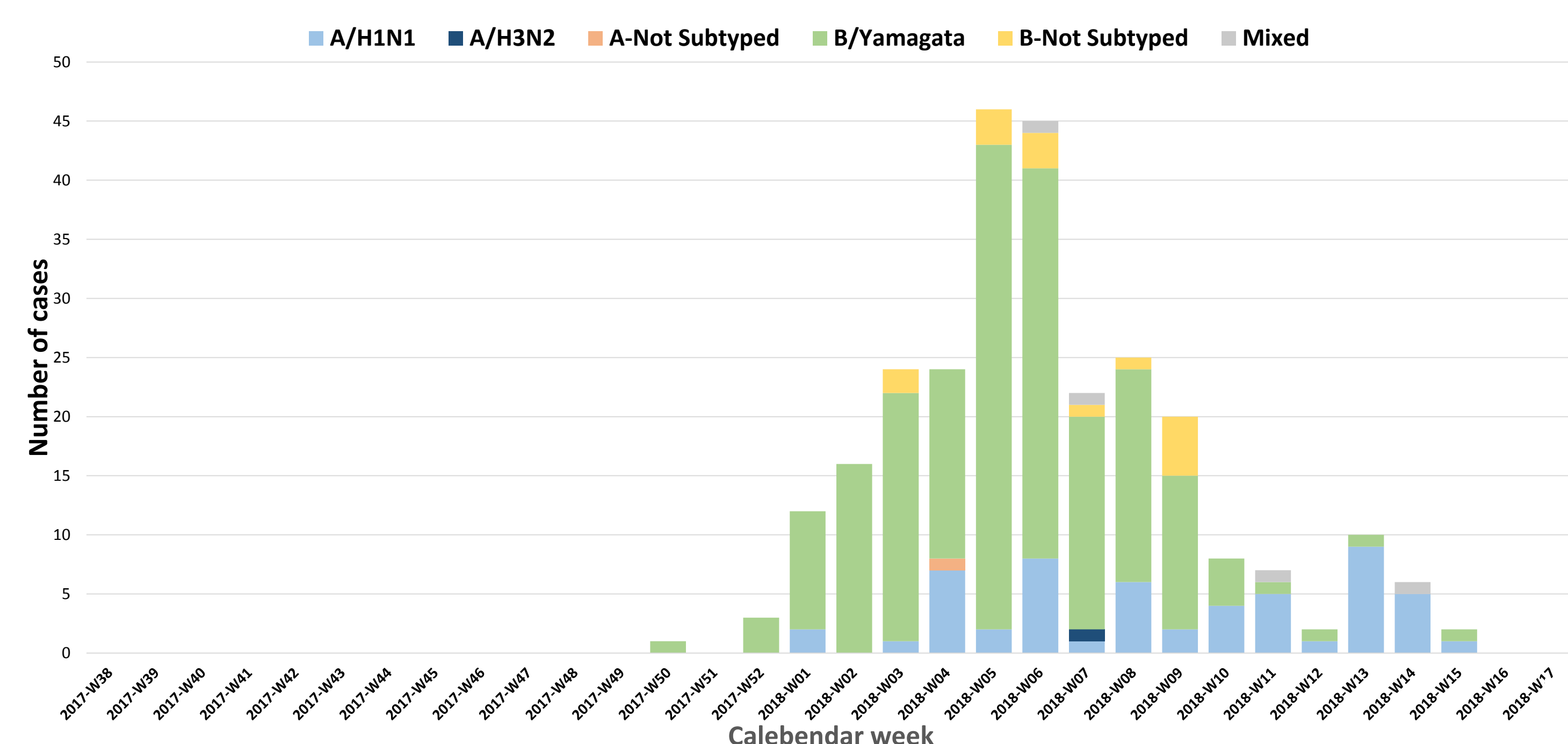


Fig 3 : Influenza virus distribution by calendar week, Vojvodina, Serbia, 2017-2018

There were no significant differences between the influenza virus positive and negative patients in terms of the ICU utilization, mechanical ventilation or in-hospital death (Table 2, Fig. 4).

Table 2: Influenza hospital-related burden in Vojvodina, Serbia,2017-2018

	Total n	Influenza negative n (%)	Influenza positive n (%)	Respiratory virus infections n (%)
ICU admission	257	122 (47.5%)	119 (46.3%)	16 (6.2%)
Mechanically ventilated	209	98 (46.9%)	97(46.4%)	14 (6.7%)
Death outcome	75	36 (48.0%)	37 (49.3%)	2 (2.7%)

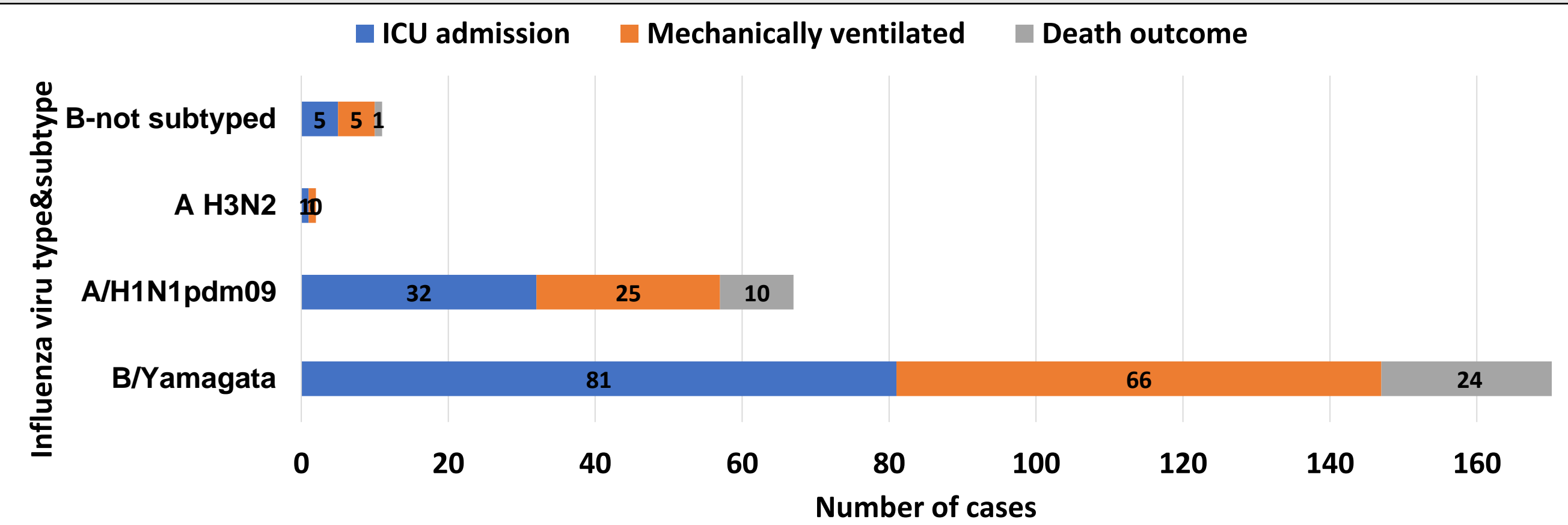


Fig 4. Influenza hospital-related burden in Vojvodina by virus type&subtype, Serbia,2017-2018

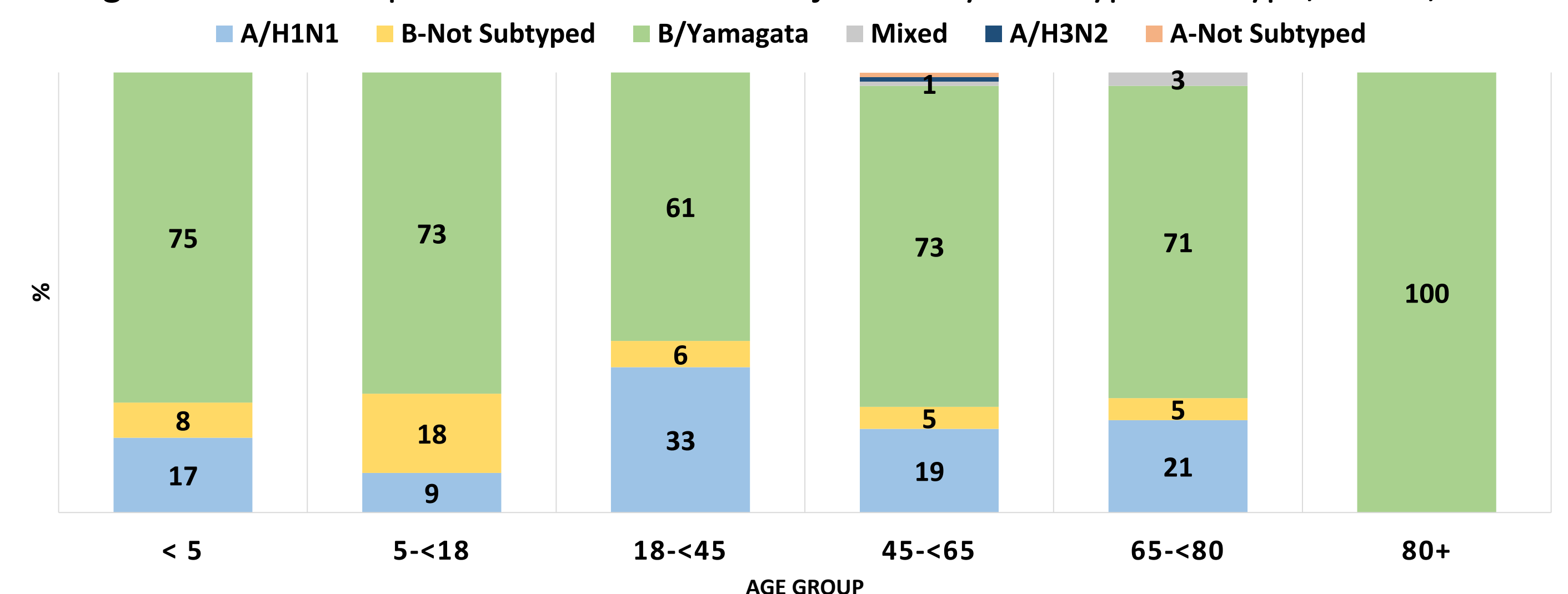


Fig 5. Influenza virus type&subtype by patients age group (%) n=274

We also present age-dependent structure of different influenza strains (Fig. 5). Influenza disease severity and ratio of community-acquired vs. hospitaly- acquired ILI among hospitalized patients are shown in Table 3.

Table 3. Influenza hospital related burden in Vojvodina, Serbia,2017-2018

Hospitalized patients in study hospitals (overall in the influenza season 2017-2018)	Total	Community acquired influenza (GIHSN)	In-hospital acquired influenza	Influenza severity		
				ILI	SARI	ARDS
Tested n (%)	899	636 (70.7)	263 (29.3)	593	210	96
Influenza positive n (%)	393	274 (69.7)	119 (30.3)	260 (43.8)	94 (44.8)	39 (40.6)

Key aspects & challenges

- Key aspects:** The distribution of influenza virus types&subtypes, timing and peak of the influenza season obtained though the GIHSN and national surveillance were similar. The circulation pattern of influenza virus was characterized by the strong predominance of the influenza virus type B-Yamagata lineage (72,3%) followed by influenza virus type A(H1N1)pdm09 (19,7%) and negligible share of undifferentiated A and B influenza virus types. Influenza virus type B-Victoria lineage was not established among included patients. Other respiratory viruses have been confirmed in only 4,6% of all hospitalized and tested GIHSN patients in Vojvodina, Serbia.
- High share of influenza associated deaths (37) and ICU admissions observed in the last season may be explained by older age of patients and co-morbidities as well as criteria for admission to ICU in the study hospitals. In the majority of deceased patients (65%) influenza virus subtype B Yamagata lineage was confirmed. Most influenza related deaths (38%) were recorded in the second half of February.
- The majority of flu-related hospitalizations were recorded in elderly patients aged +65 years with the highest burden among those aged +80 years and patients with cardiovascular and chronic obstructive pulmonary disease. At the time of hospital admission, $\approx 2/3$ of all tested and laboratory confirmed cases of influenza were presented as ILI and $\approx 1/3$ as SARI or ARDS. Pneumonia was commonly registered among influenza positive hospitalized patients.
- The negligible share of included patients (27/636) was vaccinated (4.4% of LCI + 4.3% of LCI-). Virus influenzae type B, Yamagata lineage was confirmed in the majority (10/12) of influenza virus positive vaccinated patients. Significant vaccine vs. circulating influenza virus type B lineage antigenic mismatch was established in the influenza season 2017-2018, highlighting the importance of quadrivalent influenza vaccine introduction in Serbia.
- Conclusion:**Community-acquired influenza was the main trigger for increased hospitalizations, ICU admissions and deaths, especially in elderly patients with comorbidities. Enhanced hospital-based surveillance has increased the number of screened and tested patients, compared to the previous influenza seasons and allow better understanding of influenza related hospital disease burden in Vojvodina, Serbia. **Challenges:** Influenza vaccine coverage rates need to be increased. Lack of data on influenza vaccine effectiveness in Serbia, mainly due to the low national influenza immunization coverage (3,3%). The high share of influenza-related hospitalizations, including ICU admissions and substantial mortality during influenza season, pose additional challenges.