

# GLOBAL INFLUENZA HOSPITAL SURVEILLANCE NETWORK

## RESULTS OF SEASON 2015-16



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Ankara, TURKEY

# Barriers to adult immunization – Turkey

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COMMENTARY

OPEN ACCESS

## Barriers to adult immunization and solutions: Personalized approaches

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### ABSTRACT

Immunization is an important component of preventive healthcare services aiming to prevent and eventually eradicate infectious diseases by immunizing people before they become infected. Although immunization is an integral part of children's healthcare, this fact is underrated, even ignored in adults. In Turkey, adult immunization is available only for certain high risk groups such as health care professionals and populations aged > 65 y and under certain conditions including pregnancy, military service, travel-pilgrimage, and employment procedures. The fact that diseases such as pneumococcal pneumonia, influenza, rubeola, varicella, hepatitis A, and tetanus, which could be associated with severe complications in adults, are vaccine-preventable indicates the importance of adult immunization. In addition to the healthcare providers' knowledge about immunization, effective policies of related professional associations and the management of this issue by regulatory authorities, people's awareness in protecting their own health is of utmost importance in achieving the targeted level of adult immunization. This article focuses on the characteristics of the individuals as one of the 3 main cornerstones (individual, healthcare providers, regulatory authorities and supporting organizations) of immunization practices and discusses barriers to adult immunization and recommends solutions.

### ARTICLE HISTORY

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### KEYWORDS

adults; barriers;  
Immunization; solutions;  
vaccination



# ABOUT THE FOUNDATION

## Mission of the Foundation

The Foundation for Influenza Epidemiology was created in September 2015 by [Sanofi Pasteur](#) under the auspices of [Fondation de France](#) to formalize several years of commitment to epidemiological research on severe influenza.

This funding mechanism was established to facilitate additional funding from other donors for this world-scale active surveillance project.

All donations collected through this foundation are dedicated to epidemiological research in the field of severe influenza and other respiratory viral diseases through the Global Influenza Hospital Surveillance Network (GIHSN).

Not -for- profit institutions with proposals aligned with the GIHSN scope and study design are eligible to apply for a grant from this foundation.

# ABOUT THE STUDY

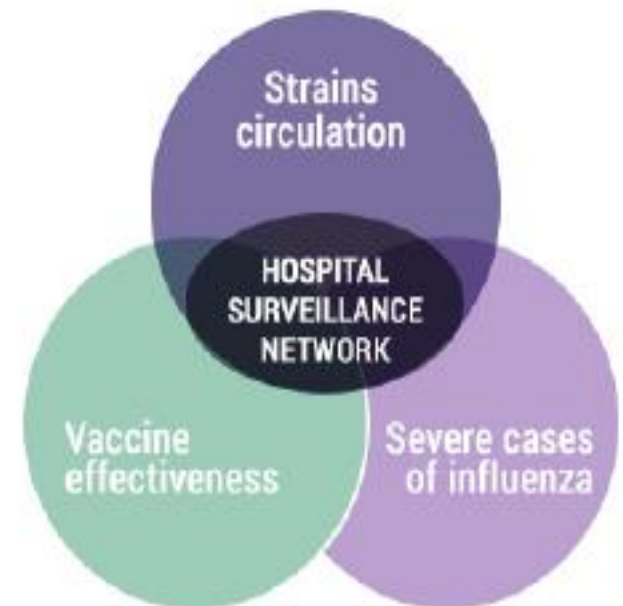
## Rational and Scientific objectives

Severe cases of influenza requiring hospitalization are probably the most influential factors in term of flu vaccination advocacy and cost-benefit evaluation of vaccination. In addition, little is known about the effect of influenza vaccine on the prevention of severe disease. Indeed, previously published studies are prone to various biases.

A design based on a network of hospitals is easier to standardize for quality insurance reasons and easier to coordinate than a General Practitioners (GP) network approach. Finally the availability of diagnostic capacities at hospital make influenza case ascertainment more reliable.

### The GIHSN has three main objectives:

- I. Evaluate the burden of severe influenza disease, defined as hospitalization related to community-acquired influenza or complications following an influenza infection;
- II. Quantify the distribution of the different influenza viruses (A(H1N(H3N2)), B/Yamagata, and B/Victoria) among these severe cases; and
- III. Measure the effectiveness of influenza seasonal vaccines to prevent these hospitalizations using a test-negative design.





# **Institution:** **Turkish Society of Internal Medicine**

**Primary Investigator:** Prof Serhat Unal, MD

**Project Coordinator:** Prof Mine Durusu Tanriover, MD

**Epidemiologist:** A. Tulay Bagci Bosi, MSc, PhD

- A non-profit organization for continuing medical education of internists and improvement of public health.
- Founded in 1995 as a non-profit organization.
- Turkish Society of Internal Medicine is a member of the European Federation of Internal Medicine and takes the lead in the ADVICE-Adult Vaccination Campaign in Europe-Working Group.

# Background



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Hospital Surveillance  
Network

- A national Sentinel Influenza Surveillance Network that is based on primary health care system has been established in 2005 in Turkey.
- Turkey has been involved in the network since 2012-13 season as a partner in GIHSN.

# Objectives



## Primary Objective

- Determine the frequency of influenza infections among acute admissions with influenza like illness in selected hospitals in Turkey and determine the burden of disease during the 2015-2016 season.

## Secondary Objectives

- Determine the economical burden of influenza.
- Determine the vaccine effectiveness.

# Methods



- Ethical Approval was taken from Hacettepe University, Faculty of Medicine Ethics Committee (GO 15/809-39). Good clinical practices and good laboratory practices were followed throughout the study.
- Fieldwork,
  - started on December 21, 2015 (52nd week)
  - ended on April 01, 2016 (13th week).



# The catchment area and the study centers



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2815  
beds

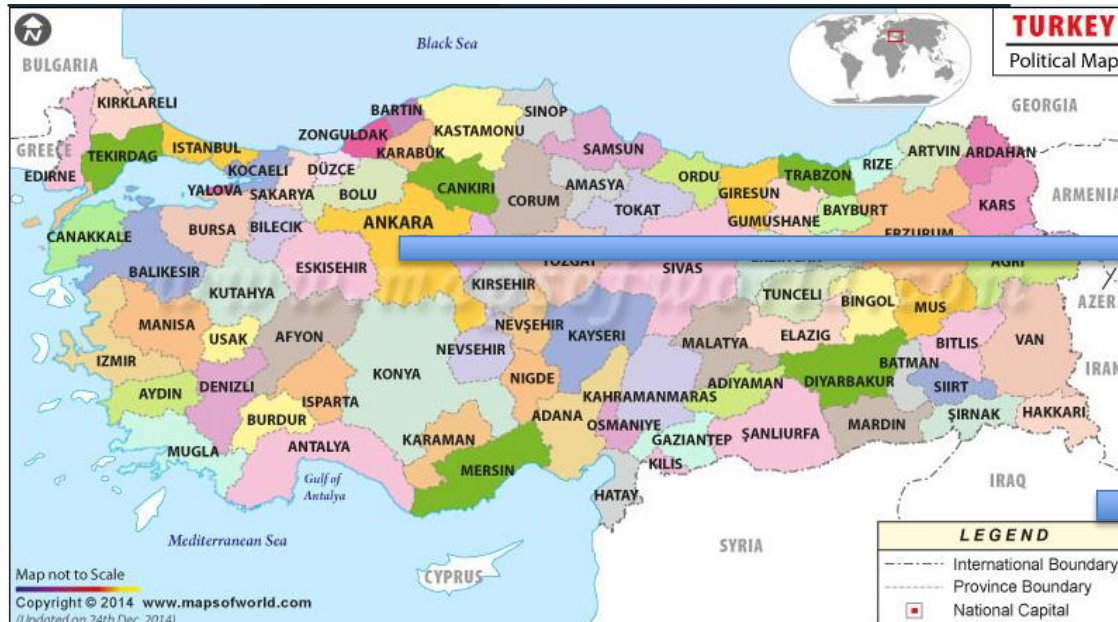
15.1%

18,641  
beds

5,270,575  
inhabitants

6.7%

78,741,053  
inhabitants



Turkish Statistical Institution for year 2015.

# Participating hospitals



Name of Hospitals	Type of ward	Total # of beds per hospital	# beds for each ward
01-Hacettepe University Adult Hospital	Adult Emergency	689	35
	Acute Care		10
	Medical Intensive Care		9
02-Hacettepe University İhsan Doğramacı Children's Hospital	Pediatric Emergency	270	12
	Pediatric Infectious Diseases		18
	Pediatric Intensive Care		16
03-Gazi University Hospital, Adult	General Pediatric Wards	1117	148
	Adult Emergency		30
	Hematology		38
	Hematologic Intensive Care Unit		4
04-Gazi University Hospital, Children's	Medical Intensive Care Unit	1117	12
	Stem Cell Transplant Unit		8
	Pediatric Emergency		8
	Pediatrics Ward		64
	Infectious Diseases		10
05-Ankara Training and Research Hospital	Pediatric Intensive Care	468	5
	Adult Emergency		16
	Acute Care		10
	Intensive Care		34
06-Ankara Hematology Oncology Children's Training and Research Hospital	Infectious Diseases	271	22
	Pediatric Infectious Disease Unit		28
06-Ankara Hematology Oncology Children's Training and Research Hospital	Emergency Unit	271	13
Total number of beds screened		2815	550



# Recruitment

Hospital admission registries, charts or available records were screened and *all* patients hospitalized in the previous 24-48 hours or overnight in the predefined wards or emergency room were identified.



Admission diagnoses were evaluated and resident patients whose indication for admission was any of a predefined set of conditions, described as possibly associated with a recent influenza infection were eligible for further evaluation. International Classification of Diseases Code version (ICD)-10 was used to report diseases.



A patient was considered as a resident if (s)he has been living in Turkey as a citizen for the last 6 months.



Screening took place on weekdays between 8 am Monday and 5 pm on Friday.

# Recruitment



- Diagnoses
- Exclusion & inclusion criteria

Per protocol

If the patient was eligible in terms of admission date and the clinical condition, the patient or the guardian was further interviewed for consent and the inclusion and exclusion criteria and to record other data.

# Swabbing and sample procedures



- A nasopharyngeal swab or a pharyngeal swab for adults (14 years of age or older) or a nasal sample for children (less than 14 years old) were obtained from each patient.
- Each swab was tagged using a standardized coding (number of the patient, followed by medical record number and date of swabbing).
- Nasal swabs were collected using Virocult (Medical Wire & Equipment, UK) and the courier of DÜZEN laboratory gathered the swabs from each participating hospital each day. Swabs were sent to the laboratory in 1-3 days.
- Upon arrival in the laboratory, all samples were transferred to cryo-tubes and, if not tested on arrival date, stored in  $-20^{\circ}\text{C}$  freezer.

# Laboratory procedures



- EZ1 Virus mini kit V2.0 (Catalog number: 955134, Qiagen, Germany) was used for total nucleic acid extraction. Real-time PCR based, multiplex FTD<sup>®</sup> Respiratory Pathogens 21 kit (Fast-track diagnostics Ltd. Malta) was used for detection of respiratory pathogens on RotorGene Q platform (Qiagen, Germany).
- For detection of Influenza H1, H3 subtype, Influenza B Yamagata and Victoria lineages real-time RT-PCR method was performed using a RotorGene Q platform with CDC primers and probes according to the CDC protocol.

# Number of patients screened and enrolled



	Number of patients (%)		
	5 years and older	Under 5 years	Total
<b>Screened</b>	<b>883</b>	<b>468</b>	<b>1351</b>
<b>Exclusion criteria</b>			
Non-resident	3 (0.3)	7 (1.5)	10 (0.7)
Institutionalized	23 (2.6)	2 (0.4)	25 (1.9)
Discharged in 30 days	207 (23.4)	59 (12.6)	266 (19.7)
Unable to communicate	86 (9.7)	10 (2.1)	96 (7.1)
Language	2 (0.2)	8 (1.7)	10 (0.7)
Discharged	71 (8.0)	1 (0.2)	72 (5.3)
No deputy	10 (1.1)	0 (0)	10 (0.7)
Neurological impairment	3 (0.3)	0 (0)	3 (0.2)
Others	0 (0)	1 (0.2)	1 (0.1)
No consent	6 (0.7)	5 (1.1)	11 (0.8)
<b>Enrollment</b>	<b>558</b>	<b>385</b>	<b>943</b>
Not fulfilling ILI clinical criteria	99 (11.2)	-----	103 (7.6)
Not fulfilling ILI time	60 (6.8)	10 (2.1)	72 (5.3)
<b>Enrollment</b>	<b>399 (45.2)</b>	<b>375 (80.1)</b>	<b>774 (57.3)</b>



# Laboratory test results

	Number of patients (%)		
	5 years and older	Under 5 years	Total
<b>Included with valid laboratory results</b>	<b>399</b>	<b>375</b>	<b>774</b>
<b>RT-PCR result</b>			
Influenza negative	308 (77.2)	324 (86.4)	632 (81.6)
Influenza positive*	91 (22.8)	51 (13.6)	142 (18.4)
<b>Subtype and lineage</b>	<b>Number of patients (%) within the influenza positive cases</b>		
A(H1N1) pdm09**	49 (53.8)	19 (37.3)	68 (47.9)
A(H3N2)	35 (38.5)	22 (43.1)	57 (40.1)
A not subtyped	3 (3.3)	3 (5.9)	6 (4.2)
B Yamagata	4 (4.4)	7 (13.7)	11 (7.8)
B Victoria	0	0	0
B not subtyped	0	0	0

RT-PCR, reverse transcriptase-polymerase chain reaction

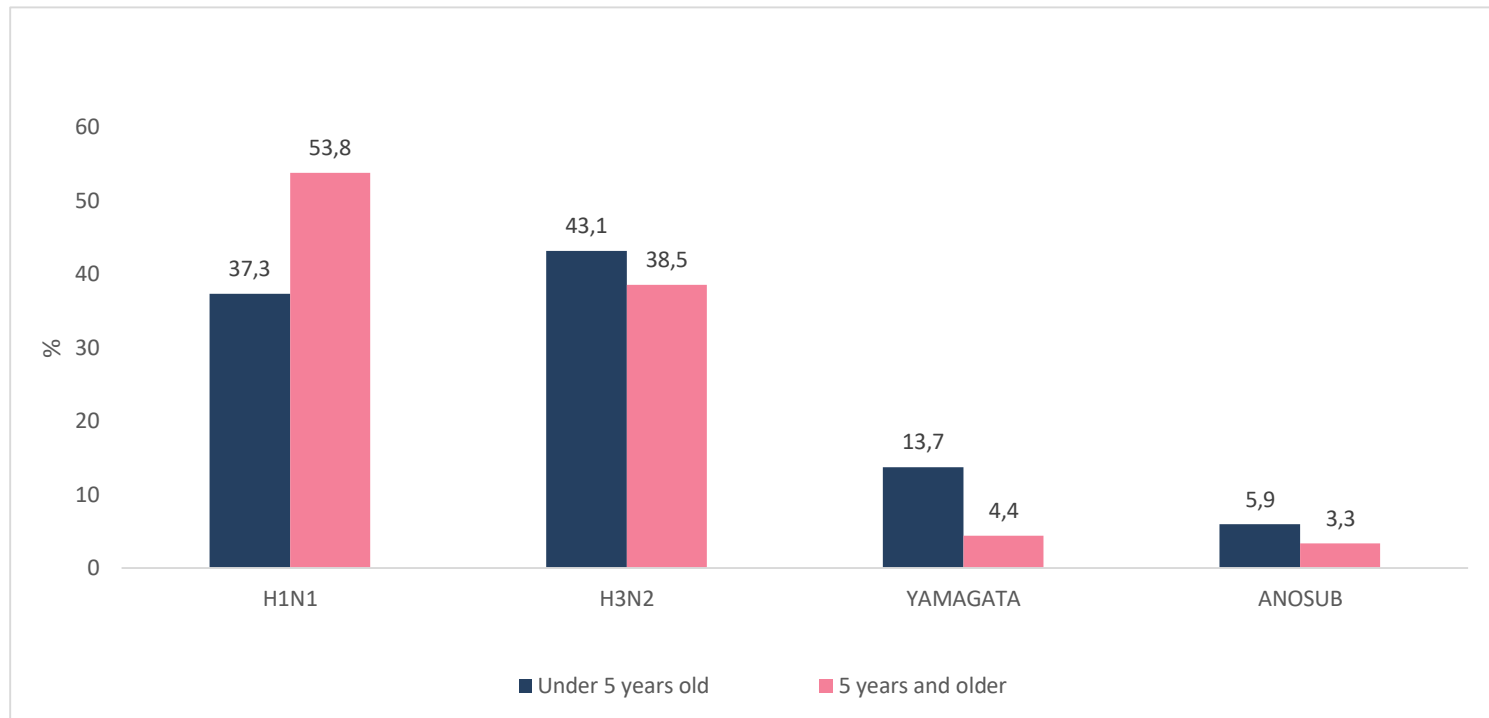
\*p =0.001

\*\* p <0.001





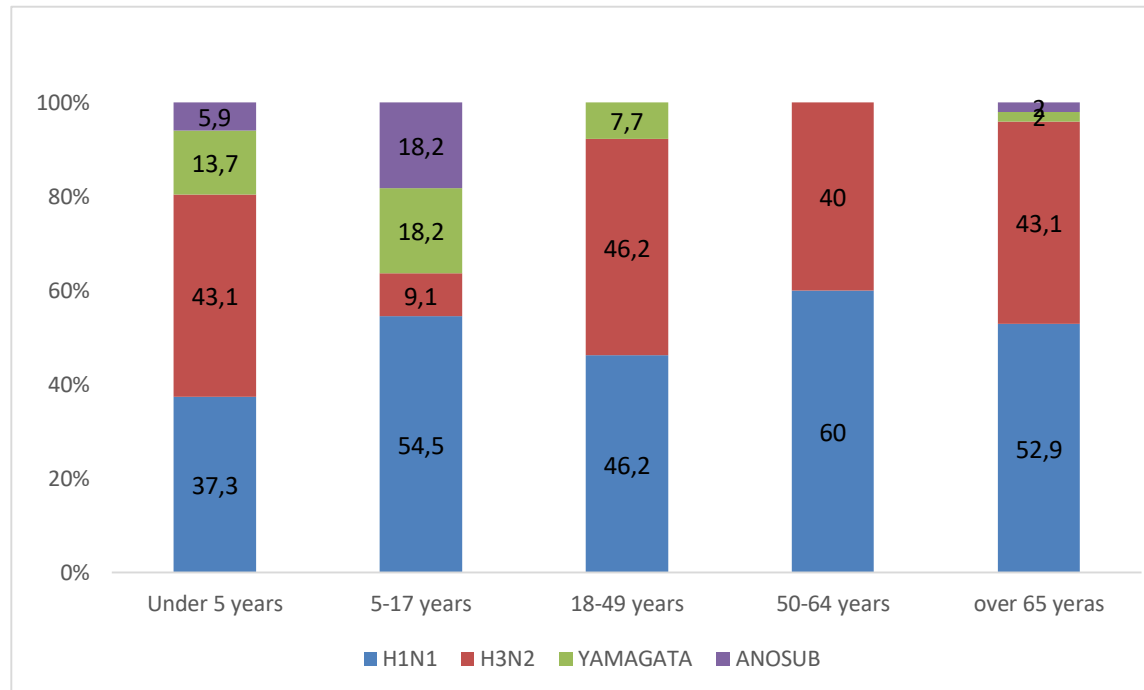
# Laboratory test results



**Percentage distribution of viruses by groups under 5 years old & 5 years and older.**



# Laboratory test results



**Distribution of virus types in different age segments**



# Laboratory test results

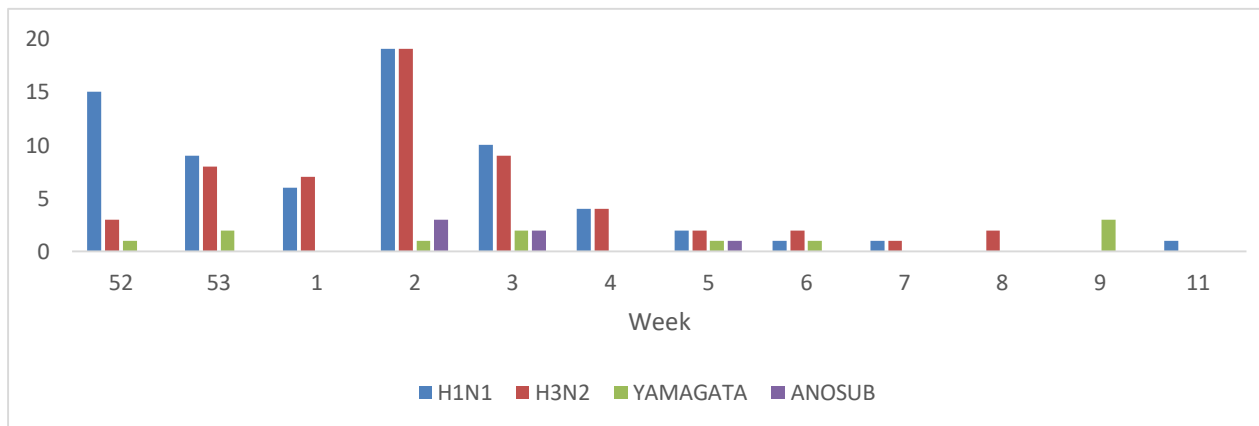
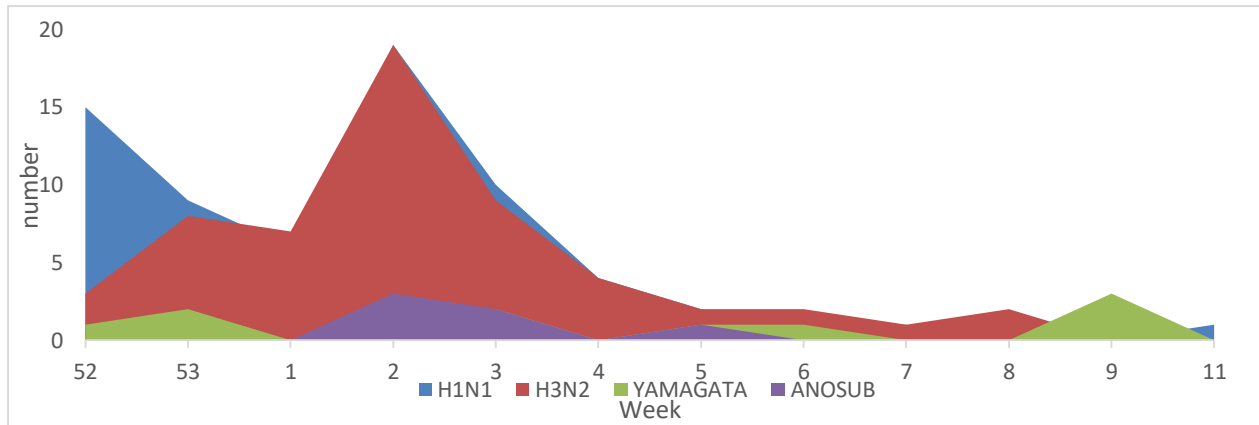


Figure 4. Weekly distribution of number of influenza viruses during the study period.

# Laboratory test results

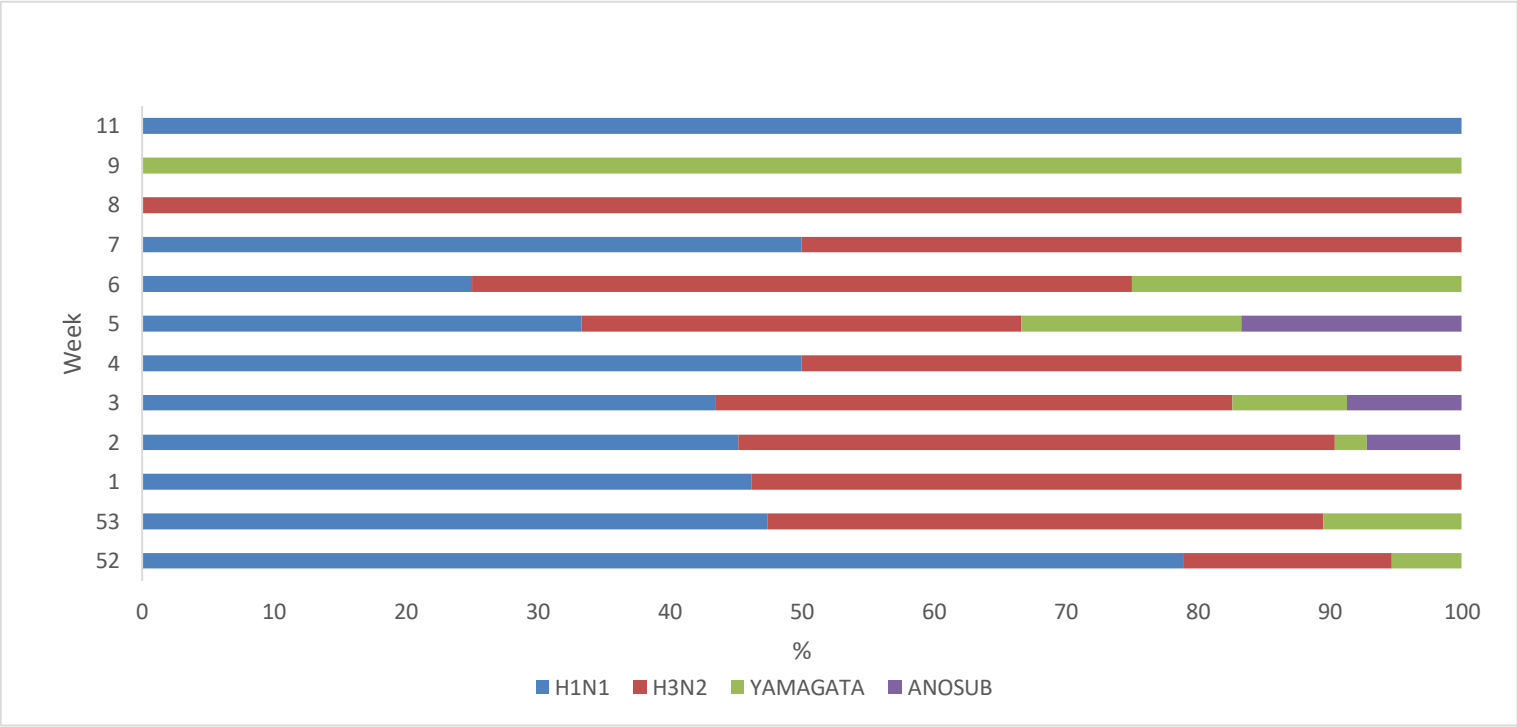
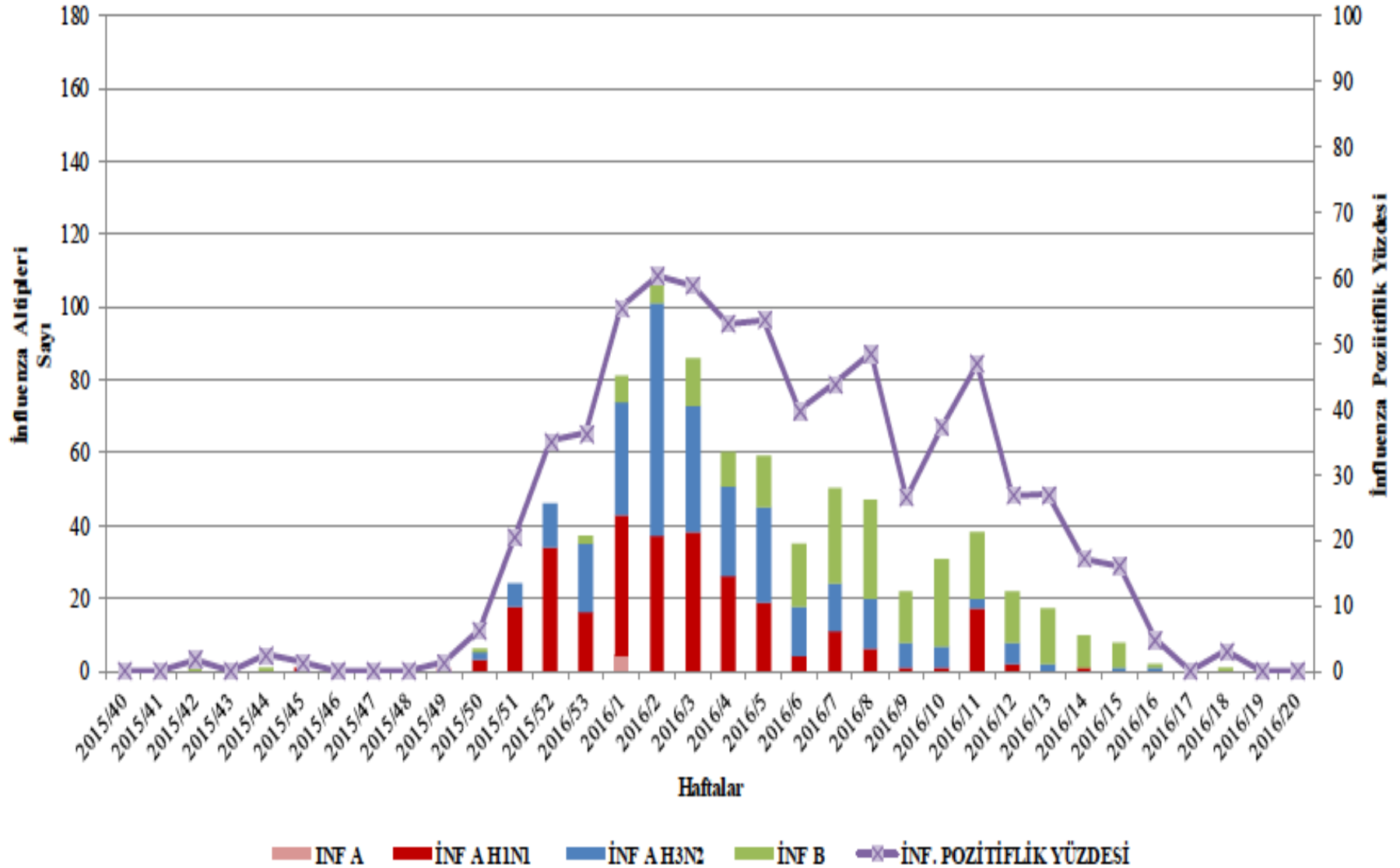


Figure 5. Weekly distribution of viruses during the study period.

## Haftalık İnfluenza Alt tipleri Sayısı ve İnfluenza Pozitiflik Yüzdesi



Grafik-2: Ülkemizde Sentinel Grip Benzeri Hastalık Sürveyansı kapsamında haftalık tespit edilen İnfluenza alt tipleri sayısı ve İnfluenza pozitiflik yüzdesi.

# Turkey; Influenza Surveillance (2015-2016)



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	T.H.S.K. VİROLOJİ LAB.		İSTANBUL ÜNi.		İSTANBUL H.S.L.		ADANA H.S.L.		SAMSUN H.S.L.		ERZURUM H.S.L.		TOPLAM	
	Sayı	%	Sayı	%	Sayı	%	Sayı	%	Sayı	%	Sayı	%	Sayı	%
Çalışılan Numune	7457		1964		3545		4718		2466		1578		21728	
Toplam Pozitiflik*	2881	38,6	612	31,2	2077	58,6	2509	53,2	1037	42,1	766	48,5	9882	45,5
İnf A	14		1		0		0		6		13		34	
İnf A H1N1	1646		313		986		1638		581		344		5508	
İnf A/H3	792		205		702		582		289		250		2820	
İnf B	429		93		389		289		161		159		1520	
Adenovirus	52		3		27		40		28		33		183	
Birden fazla etken	104		16		29		52		50		75		326	
Coronavirüs	154		22		47		50		78		39		390	
Enterovirüs	0		0		2		0		0		0		2	
Hum.Metapneumovirüs	56		16		25		56		34		19		206	
Human Bocavirüs	30		8		20		33		8		6		105	
Parainfluenza	76		5		4		24		18		4		131	
Rhinovirüs	266		11		11		34		27		68		417	
RSV	322		47		95		203		109		50		826	
DiĞER	6		3		0		3		8		5		25	
TOPLAM	3947		743		2337		3004		1397		1065		12493	

# Turkey; Influenza Surveillance (2012-2016)



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Sezon	Numune Sayısı	İnfluenza A (H1N1)	İnfluenza A (H3N2)	İnfluenza B	Toplam	Pozitiflik Oranı
2012-2013	6.109	951	48	28	1.027	<b>%17</b>
2013-2014	5.329	26	824	219	1.069	<b>%20</b>
2014-2015	10.266	1.012	245	1.406	2.663	<b>%26</b>
2015-2016	21.728	5508	2820	1520	9882	<b>%45,3</b>

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# Turkey; Influenza Surveillance (2012-2016)



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Sezon	influenza A (H1N1)	influenza A (H3N2)	influenza B
2012-2013	<b>%92,5</b>	%4,6	%2,7
2013-2014	%2,5	<b>%77</b>	%20,5
2014-2015	%38,0	%9,2	<b>%52,8</b>
2015-2016*	<b>%55,7</b>	%28,5	%15,4



# Patient characteristics, comorbidities and functional status



- 85.7% of the patients 5 years and older had at least one chronic disease condition, the most prevalent one being cardiovascular disease followed by chronic obstructive lung diseases
- The mean Barthel index among women was  $64.5 \pm 3.36$ , while it was  $75.5 \pm 3.36$  among men ( $p = 0.02$ ).

# Patient characteristics, comorbidities and functional status



	Number of patients (%)		
	5 years and older n=399	Under 5 years n=375	Total n=774
<b>Gender (female)</b>	196 (49.1)	162 (43.2)	
<b>At least one chronic condition</b>	342 (85.7)	63 (16.8)	405 (52.3)
<b>Smoking status*</b>			
Current smoker	46 (12.6)	163 (43.6)	331 (42.8)
Ex-smoker	102 (27.9)	20 (5.3)	122 (15.8)
Never smoked	218 (54.6)	191 (51.1)	409 (52.8)
<b>Health care utilization</b>			
At least one outpatient visit in the last 3 months	310 (77.7)	290 (77.3)	600 (77.5)
At least one hospitalization in the last 12 months	215 (53.9)	134 (35.7)	349 (45.1)
<b>Underlying diseases</b>			
Cardiovascular disease	218 (54.6)	17 (4.5)	235 (30.4)
COPD	103 (25.8)	1 (0.3)	104 (13.4)
Asthma	50 (12.5)	10 (2.7)	60 (7.8)
Immunodeficiency/transplant	29 (7.3)	7 (1.9)	36 (4.7)
DM	93 (23.3)	1 (0.3)	94 (12.1)
Malignancy	58 (14.5)	4 (1.1)	62 (8.0)
Renal diseases	56 (14.0)	0	56 (7.2)
Chronic liver disease	6 (1.5)	3 (0.8)	9 (1.2)
Rheumatismal disease	19 (4.8)	6 (1.6)	25 (3.2)
Autoimmune disease	9 (2.3)	3 (0.8)	12 (1.6)
Neuromuscular disease	50 (12.5)	17 (4.5)	67 (8.7)
<b>Barthel for ≥ 65 years</b>			
Total disability (0–15 points)	22 (11.3)		
Severe disability (20–35 points)	17 (8.8)		
Moderate disability (40–55 points)	15 (7.7)		
Mild disability (60–90 points)	76 (39.2)		
Minimal disability (95–100 points)	64 (33.3)		

5-17 y/o            14.0 %  
 18-49 y/o           3.4 %  
 50-64 y/o           20.6 %  
≥ 65 y/o            62.0 %

# Vaccination status



	Number of patients (%)		
	5 years and older n=399	Under 5 years n=375	Total n=774
Flu vaccine 2015-16	48 (12.0)	8 (2.1)	56 (7.2)
Flu vaccine 2014-15	68 (17.4)	3 (0.8)	71 (9.2)
Flu vaccine 2013-14	63 (15.8)	1 (0.3)	64 (8.3)
Antiviral drug prescribed	86 (21.6)	31 (8.3)	117 (15.1)



# Outcome

The mean length of hospital stay (max. 171 days)

**12.52±0.89 days**  
among patients 5  
years and older

$p < 0.001$

**6.77±0.33 days**  
among patients under  
5 years

**12.99±0.89 days**  
among patients with  
at least one  
comorbidity

$p < 0.001$

**6.17±0.27 days**  
among patients  
without any  
comorbidity

# Outcome



	Number of patients (%)		
	5 years and older n=399	Under 5 years n=375	Total n=774
Admission the intensive care unit	130 (32.6)	10 (2.7)	140 (18.1)
Mechanical ventilation	90 (22.6)	3 (0.8)	93 (12.0)
Death	59 (14.8)	0	59 (7.6)

Patients over 65 years of age had:

A higher chronic disease burden,  
Longer mean length of stay,  
Higher mortality.



## Discussion

1351 patients were screened

774 patients were swabbed

142 samples yielded influenza

Doubling influenza  
positive sample  
number compared to  
previous year's study

Scarcity of influenza B viruses  
Early ending of the season

# Discussion



- The study population was composed of patients with a high chronic disease burden and high utilization of healthcare services.
- Despite the high chronic disease burden only 12% of the patients over 5 years of age was vaccinated in the current season whereas this rate was only 2.1% for those children below 5 years.
- The rate of influenza vaccine was only 15.9% among those patients over 65 years of age.

# Discussion



- There was a high mortality rate among patients admitted to the hospital with ILI symptoms.
- The outcomes were worse and length of hospital stay was longer among adults, particularly over 65 years of age.
- Interestingly, there was no difference between the influenza positive and influenza negative groups with regard to outcome.





## Conclusion

- In 2015-16 hospital based influenza surveillance study, an influenza virus was detected in nearly one in five patients screened for ILI and swabbed during the study period.
- The influenza vaccination rate was extremely low.
- The outcomes were particularly worse among those patients over 65 years of age, regardless of the presence of the influenza virus positivity.
- Vaccine effectiveness and the multitude of factors affecting worse outcomes should be analyzed on collated data to yield reliable findings.

## For the 2016-2017 season



- Better described resident criterion
- Two swabs per protocol
- Better communication with the lab and closer data management
- Financial burden estimates
- Collated data analysis

# Special thanks to..



Global Influenza  
Hospital Surveillance  
Network



**FISABIO**

**Sanofi Pasteur**

**Fondation de France**

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