Virological Surveillance of Influenza in Belgium
Season 2015-2016

VIRAL DISEASES
National Influenza Centre (WHO)
Isabelle Thomas, Cyril Barbezange, Anneleen Hombrouck, Steven Van Gucht
Jeannine Weyckmans, Laura Ullens, Mona Abady, Ilham Fdillate

T +32 2 373 32 43
E-mail: isabelle.thomas@wiv-isp.be

EPIDEMIOLOGY OF INFECTIOUS DISEASES
Nathalie Bossuyt

HEALTH SERVICES RESEARCH
Viviane Van Casteren, Yolande Pirson

Scientific Institute of Public Health
Reference number : D/2016/2505/40

Influenza surveillance in Belgium is financed by the Federal Public Service Health, food chain safety and environment, the “Fédération Wallonie Bruxelles” and the “Vlaams Agentschap Zorg en Gezondheid”.

© Institut scientifique de Santé publique | Wetenschappelijk Instituut Volksgezondheid, Bruxelles 2014.
This report may not be reproduced, published or distributed without written authorization of WIV-ISP.
## TABLE OF CONTENTS

A. ABSTRACT ........................................................................................................................................ 3

B. BACKGROUND.................................................................................................................................. 3-4

C. METHODS ........................................................................................................................................ 4

D. RESULTS ........................................................................................................................................... 11

D.1 SENTINEL SURVEILLANCE OF ILI.............................................................................................. 11

D.1.1 Clinical surveillance ......................................................................................................................... 11

D.1.2 Virological surveillance .................................................................................................................... 12-14

D.2 SENTINEL SURVEILLANCE OF SARI .............................................................................................. 14

D.2.1 Virological surveillance .................................................................................................................... 14-16

D.3 NON-SENTINEL SURVEILLANCE .................................................................................................... 16

D.4 SUSPECTED CASES OF AVIAN INFLUENZA ............................................................................... 16

D.5 SUSPECTED CASES OF MERS-CoV ................................................................................................. 16

D.6 OTHER RESPIRATORY VIRUSES .............................................................................................. 17

D.6.1 ILI Surveillance ............................................................................................................................... 17-18

D.6.2 SARI Surveillance ............................................................................................................................ 18-20

D.7 CHARACTERISATION OF INFLUENZA VIRUSES ............................................................................. 21

D.7.1 A(H1N1)pdm2009 .......................................................................................................................... 21-23

D.7.2 A(H3N2) ........................................................................................................................................ 23-25

D.7.3 B Yamagata ..................................................................................................................................... 25-26

D.7.4 B Victoria ....................................................................................................................................... 26-28

D.8 ANTIVIRAL MONITORING .............................................................................................................. 28

D.9 COMPOSITION OF INFLUENZA VIRUS VACCINES FOR USE IN THE 2013-2014 NORTHERN HEMISPHERE SEASON .............................................................................................................. 29

D.10 VACCINE EFFECTIVENESS ............................................................................................................ 29

E. CONCLUSION ...................................................................................................................................... 30

F. ACKNOWLEDGEMENTS .................................................................................................................... 30

G. REFERENCES ..................................................................................................................................... 31-33
A. Abstract

The influenza epidemic during the 2015-2016 season had a medium intensity and lasted 10 weeks. In Belgium, the epidemic threshold was exceeded from week 4 (25 - 31 January 2016) to week 13 (25 March - 3 April 2016).

The epidemic was of medium intensity. The peak of the epidemic was observed in week 9-2016, with an incidence of 734 consultations for influenza-like syndromes per 100,000 inhabitants. After week 9-2016, the number of influenza-like syndromes declined and was below the threshold after week 14.

Based on ILI surveillance, we estimated that approximately 380,000 Belgians presented with clinical influenza infections this season, one third of whom were children (between 0 and 14 years). This proportion was higher than it had been in the previous five seasons.

There is no indication that severity was increased except for at-risk patients within the 45-64 years age bracket; a larger proportion of severe infections was observed in these patients in comparison with the previous four seasons. Unlike the previous year, there was no excess mortality (all causes combined) during the influenza epidemic.

The first positive sample was diagnosed in week 42-2015 and increasingly large numbers of positive influenza cases were detected from week 53-2015 onwards, reaching a proportion of 80% positive samples in week 10-2016. These were mainly A(H1N1)pdm2009 viruses and B viruses of the Victoria lineage, which circulated together.

All respiratory samples were also analysed for other respiratory viruses. In the ILI population, 35% of the influenza negative patients were positive for one or more other respiratory viruses, whereas in the SARI population, this percentage reached 51%. This suggest an important role of other respiratory viruses in hospitalized patients during the flu season.

The preliminary data for VE are 41% when considering all influenza strains.

All tested viruses were sensitive to Oseltamivir and Zanamivir, except one sample from an immunocompromised patient treated with Oseltamivir, for which the H275Y mutation was detected.

B. Background

Influenza virus is a leading cause of human morbidity and mortality worldwide. On average, influenza viruses infect 5 to 15% of the global population, resulting in ~500,000 deaths annually (1). Each year, a flu epidemic occurs usually during the winter period, and three or four times per century a new influenza virus emerges. The type of influenza virus circulating and the vulnerability of the population determine the severity of the epidemic or pandemic.

The major objectives of the surveillance are to monitor influenza activity (intensity, duration, severity, ...) all over the year, to determine the type and subtypes of circulating strains and their antigenic and genetic characterization, to contribute to the annual determination of influenza vaccine content, to assess the overall vaccine effectiveness, to monitor resistance to antivirals and to detect new potentially pathogenic influenza viruses. Since the A(H1N1) 2009
pandemic, special attention has been given to closer monitoring the severity of influenza cases. Following WHO and ECDC recommendations, the Belgian National Influenza Center (NIC) has extended, since 2010, its surveillance to SARI (Severe Acute Respiratory Infection) cases. The main objectives were 1) to build a clinical and virological database of hospital cases permitting to rate the severity across seasons and pandemics; 2) to detect signals of severity during the course of an epidemic or a pandemic; 3) to describe genotypic and phenotypic characteristics of influenza viruses associated with severe forms of infection; 4) to test clinical samples for other respiratory viruses. Furthermore, there is always a risk of emergence of new pathogenic viruses. In 2013, for example, two new highly lethal respiratory viruses emerged (influenza A(H7N9) in Asia and MERS-CoV in the Middle East), demonstrating the importance of the surveillance of respiratory pathogens for the public health. This report is mainly focusing on the virological results.

C. Methods

C.1. Surveillance

C.1.1. Sentinel Surveillance of ILI

Network of Sentinel General Practices
In Belgium, the influenza surveillance is performed by the NIC, in collaboration with the Unit of Health Services Research and the Unit of Epidemiology of Infectious Diseases of the Scientific Institute of Public Health in Brussels. A network of sentinel general practices (SGPs) has been involved since 2007 in the clinical and virological influenza surveillance. The main purposes of the surveillance are the early detection of an influenza epidemic, the study of the intensity and duration of the epidemic, the identification and characterisation of circulating viruses and the participation to the selection of next-season influenza vaccine strains. The development of capability to detect new emerging viruses, the estimation of vaccine effectiveness and the monitoring of the antiviral susceptibility are also important tasks.

Clinical surveillance
The SGPs network is geographically representative of all GPs in Belgium. Besides the number of acute respiratory infections by age group, the GPs reported weekly, on a standardised form, every patient with an influenza-like illness (ILI). The general criteria for ILI were: sudden onset of symptoms, high fever, respiratory (i.e. cough, sore throat) and systemic symptoms (headache, muscular pain). For every patient, age group (<5, 5-14, 15-64, 65-84, 85+), hospitalisation, antiviral treatment, and vaccination status were recorded.

Virological surveillance
A subset of these SGPs were also involved in the virological surveillance. They were invited to collect 2 nasopharyngeal swabs/week (each week, the first two patients presenting for ILI belonging to different households).
Sampling kits were sent to all physicians. Each kit contained the materials required to collect nasopharyngeal swabs (2 nostrils + 1 throat) in patients with influenza-like illness. The material consisted of tubes containing 3 ml of transport medium [UTM (COPAN)], swabs [flocked Swabs (COPAN)] and patient registration forms. Samples and forms were returned to the National influenza Centre by mail (postage paid) and new kits were regularly sent depending on the shipment of samples.

**C.1.2. Sentinel Surveillance of SARI**

**Network of sentinel hospitals**

Following the A(H1N1)2009 pandemic, WHO and the European Centre for Disease Prevention and Control (ECDC) recommended hospital-based surveillance of severe acute respiratory infections (SARI) as a tool to monitor severe disease caused by influenza (3). This can complement outpatient surveillance of influenza like illness (ILI) or acute respiratory illness (ARI) to cover the full spectrum of influenza-related disease. As a result, the Belgian NIC has extended, since 2010, its surveillance to SARI cases. The main objectives were 1) to build a clinical and virological database of hospital cases permitting to rate the severity across seasons and pandemics; 2) to detect signals of severity during the course of an epidemic or a pandemic; 3) to describe genotypic and phenotypic characteristics of influenza viruses associated with severe forms of infection; 4) to test clinical samples for other respiratory viruses.

During the 2015-2016 influenza season, six hospitals located in the three regions of the country participated to the surveillance. The SARI case definition was: an acute respiratory illness with onset within the last seven days, fever of ≥ 38°C, cough or dyspnea, and that required hospitalisation (for 24h or more). As we are mostly interested in severe influenza cases, the surveillance was carried out only during the epidemic period of seasonal influenza. Pediatric and adult units collected both clinical data and nasopharyngeal swabs from patients who corresponded to the case definition. Sampling kits contained the materials required to collect 2 nasopharyngeal swabs (nostrils and throat) per patient responding to the SARI case definition. The material consisted of tubes containing 3 ml of transport medium [UTM (COPAN)], swabs [flocked Swabs (COPAN)] and patient registration forms. Samples and forms were returned to the NIC by mail (postage paid) and new kits were sent regularly to hospitals depending on the shipment of samples. Patients information, clinical data and laboratory results were encoded in a dedicated web based database protected by a login and password.

The following hospitals participated in the SARI surveillance during season 2015-2016:

- CHU UCL (Mont-Godinne) (Yvoir)
- CHU Saint-Pierre (Brussels)
- AZ St Jan (Brugge)
- UZ Brussel
- Jessa Ziekenhuis (Hasselt)
- Grand hôpital de Charleroi (Charleroi)
C.1.3. Non Sentinel Surveillance

Each year, a letter is sent to hospitals and laboratories across the country to encourage them to collect samples from patients presenting with severe acute respiratory diseases in particular specific conditions: ARDS (acute respiratory distress syndrome), ECMO (extracorporeal membrane oxygenation), death, suspicion of antiviral resistance, returning from abroad. Monitoring of clusters of Influenza cases is also an important task. This surveillance is carried out throughout the year.

C.1.4. Suspected cases of Avian Influenza H5N1 and H7N9

Influenza A (H5N1)

Since 2003, and till 13 June 2016, 851 human infections with highly pathogenic H5N1 viruses have been reported to WHO by 16 countries (4). About 50% (450) of the laboratory confirmed people died from their illness. Regularly, new cases are reported in different countries, especially in Asia but also in Egypt. Human cases and fatalities due to influenza A(H5N1) virus continue to increase in Egypt, with cases from the country now accounting for the highest number of human cases reported worldwide. In 2016, A(H5N1) cases were only reported in Egypt. Since December 2005, an emergency procedure has been developed in Belgium to assure rapid diagnosis in case of suspicion of a human case of influenza A/H5N1. The Belgian NIC at the Scientific Institute of Public Health was appointed as reference laboratory for testing of the H5N1 suspected cases, which are mainly cases returning from affected countries.

Influenza A (H7N9)

On 31 March 2013, the first human cases of an avian influenza A (H7N9) virus, not previously described as causing disease in humans, were reported in China. Most of the cases resulted in severe respiratory illness, with a mortality rate of about 30 percent (5). From February 2013 until 20 July 2016, 795 laboratory-confirmed cases of human infection with the avian A(H7N9) were reported to WHO including 314 deaths. Most of the cases were from China. One case in a Chinese traveler was reported by Malaysia and 2 in travelers returning from China were reported by Canada. Phylogenetic analysis of the eight genes indicate that the new influenza A (H7N9) virus is a combination of genomic fragments originating from two avian influenza A (H9N2) viruses previously detected in chickens and domestic and wild birds, influenza A/H7 and A/N9 viruses (6). Genetic analysis detected diversity in the HA gene showing that influenza A (H7N9) viruses had already started to evolve. The virus appears to be sensitive to Oseltamivir. The main routes of transmission to humans, and the distribution and prevalence of this virus among people and animals (including the distribution in wild birds) appears to be associated with exposure to infected live poultry or contaminated environments, including markets where live poultry are sold. Information to date does not support sustained human-to-human transmission, although limited human-to-human transmission cannot be excluded in a very few clusters of cases. As the extent of virus circulation in animals is not clear, epidemiological and virological surveillance and follow up of suspected human cases should remain high. WHO advises countries to continue strengthening influenza surveillance and reporting human infections.
The Belgian NIC has developed molecular tests for the detection of A(H7N9) virus in suspected cases. The same surveillance strategy applies as for human infections with highly pathogenic avian influenza A(H5N1) virus.

C.1.5. Suspected Cases of MERS CoV

The Middle East Respiratory Syndrome (MERS) coronavirus (CoV) is a newly emerging betacoronavirus that causes a severe acute respiratory infection in the deep airways and lungs. The first human cases were identified in April 2012. As of 23 June 2016, 1700 laboratory-confirmed cases of human infection with Middle East Respiratory Syndrome coronavirus (MERS-CoV) have been reported to WHO since 2012, including at least 600 deaths. To date, 27 countries have reported cases, including countries in the Middle East: Egypt, Iran, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia (KSA), United Arab Emirates (UAE) and Yemen; in Africa: Algeria, and Tunisia; in Europe: Austria, France, Germany, Greece, Italy, the Netherlands, Turkey and the United Kingdom; in Asia: China, the Republic of Korea, Malaysia and Philippines; and in North America: the United States of America (USA). The majority of cases (>85%) have been reported from KSA. Since May 2015, two new countries have been affected (China and Republic of Korea). From 20 May 2015 until 21st of July, 185 laboratory-confirmed cases including 36 deaths have been identified in the Republic of Korea. There is evidence of tertiary transmission. This is the largest outbreak of MERS-CoV outside the Middle East (7).

So far, all cases have been linked to countries in and near the Arabian Peninsula. The epidemiological pattern of human infections is highly suggestive of a zoonotic infection. The animal vector or reservoir seems to be dromedary camels but infection acquired by exposure to camels represent a minority of all cases. Human-to-human transmission is amplified among household contacts and in healthcare settings. In Belgium, we could not find evidence for coronavirus infection in bats (8). Based on the current situation and available information, WHO encourages all Member States to continue their surveillance for severe acute respiratory infections (SARI) and to carefully review any unusual patterns (9).

C.1.6. Surveillance of other respiratory viruses

In addition to flu viruses, several other respiratory viruses can also circulate during the flu season and can cause symptoms and illness similar to those seen with flu infection. Respiratory infections are very common. They may be associated with significant morbidity and even mortality in young children and elderly patients. In about 30-50% of cases with influenza-like symptoms, no influenza virus can be detected, and in at least 20% of influenza-negative ILI cases, other respiratory viruses (such as RSV, rhinovirus, parainfluenza viruses, … ) seem to be involved (20). Also, a preliminary study (unpublished results) showed that samples from SARI patients are sometimes co-infected by other respiratory viruses. Furthermore, severe influenza cases often seem to be complicated by co-infections with other respiratory viruses (22). We have developed 4 quadruplex Real time PCRs for the detection of 16 different respiratory viruses: respiratory syncytial virus (RSVA and RSVB), parainfluenza viruses (PIV 1, 2, 3, 4), rhinoviruses/enterovirus (HRV/ENV), human metapneumoviruses (hMPV), paraechoviruses (HPeV), bocaviruses (HBoV), adenoviruses (ADV) and different coronaviruses (CoOC43, CONL63, Co229E, MERS-CoV).
C.2. Laboratory tests

C.2.1. Real-time RT-PCR Influenza

Nasopharyngeal swabs received at the NIC are tested with different real-time RT-PCRs: A/B typing followed by subtyping (for influenza A) or determination of the lineage (for influenza B). The sequence of tests is presented in Figure 1.

Typing A/B
A triplex Real-time RT-PCR Influenza A/B/RP: adapted protocols (10,11); primers and probes for the matrix gene (influenza A) and hemagglutinin gene (influenza B). The RNaseP (RP) primers and probe target the human RNase P gene and serves as an internal positive control for human nucleic acid.

Subtyping A (H1, H3, N1, N2)
For influenza A positive samples, the subtype is determined.
- RTPCR Influenza A/H1 sw: adapted protocol from CDC (10); primers and probes are chosen in the hemagglutinin gene.
- RTPCR Influenza A/H3: adapted protocol from RIVM (12); primers and probes in the hemagglutinin gene.
For a subset of samples:
- RT-PCR N1: adapted protocol from RIVM (12); primers and probes in the neuraminidase gene.
- RT-PCR N2: adapted protocol from Pasteur Institute Paris (13); primers and probes in the neuraminidase gene.

Lineage B (Yamagata, Victoria)
For influenza B positive, the lineage (Yamagata or Victoria) is determined.
- Duplex RT-PCR B YAM-VIC: adapted protocol from Olav Hungnes (14).

In case of un-subtypable influenza A, if the Ct value is < 36, primers and probe specific for the Nucleoprotein of animal influenza (SWA) are used (protocol CDC ) (10): This test allows to determine if the influenza strain is of animal origin and to continue with complementary tests.
Subtyping (H5, H7, …)
Samples from suspected cases of avian influenza are submitted to real-time RT-PCR A/B for typing and, in case of positivity, to different real-time RT-PCR for subtyping depending on the epidemiological and clinical context.

RT-PCR H5N1
Two different sets of primers and probes H5 are used following two different protocols: adapted protocol from Spackman et al. 2002 (15) and adapted protocol from the Health Protection Agency, 2006 (16).

RT-PCR H7N9
Protocol adapted from WHO (17).

C.2.2 PCR tests for MERS CoV
Samples from suspected cases for MERS-CoV are submitted to specific real-time RT-PCRs for MERS-CoV (screening and confirmation); protocol from Corman et al. (18).
C.2.3 PCR tests for other respiratory viruses

Respiratory samples from the different surveillance networks (ILI, SARI, Hospital) were additionally submitted to 4 quadruplex Real-time RT-PCRs detecting 16 other respiratory viruses (Respiratory syncytial virus (RSVA and RSVB), parainfluenza viruses (PIV 1, 2, 3, 4), rhinoviruses/enterovirus (HRV/ENV), human metapneumoviruses (hMPV), paraechoviruses (HPeV), bocaviruses (HBoV), adenoviruses (ADV) and different coronaviruses (CoOC43, CONL63, Co229E, MERS-CoV)) (Table 1).

Table 1. Multiplex RT PCR tests for respiratory viruses

<table>
<thead>
<tr>
<th>MIX 1</th>
<th>MIX 2</th>
<th>MIX 3</th>
<th>MIX 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>RSV A</td>
<td>HEX</td>
<td>PIV 1</td>
<td>ROK</td>
</tr>
<tr>
<td>RSV B</td>
<td>ROK</td>
<td>PIV 2</td>
<td>HEX</td>
</tr>
<tr>
<td>hMPV</td>
<td>Cy5</td>
<td>PIV 3</td>
<td>FAM</td>
</tr>
<tr>
<td>EV</td>
<td>FAM</td>
<td>Adenó</td>
<td>Cy5</td>
</tr>
</tbody>
</table>

The protocols have been adapted from those of the Statens Serum institute (19) with some modifications (primers for rhinoviruses as described by Hombrouck et al. (20), and primers for MERS CoV as described by Corman et al. (18). Rhinoviruses and enteroviruses were considered together as rhinovirus/enterovirus (HRV/ENV).

C.2.4 Genetic characterisation

Genetic characterisation is performed by sequencing of the HA and NA genes of influenza viruses. Sequencing of PCR products is realized with ABI 3130xl (ABI) using Big Dye Terminator v 3.1 Cycle Sequencing kit. Sequence comparison, alignments and phylogenetic trees are realized using ClustalX, MEGALIGN (DNASTAR) en MEGA 7 programs. Influenza sequences are compared to reference strains and vaccine strains. Based on evolutionary models, influenza strains can be classified in clusters characterised by common and specific mutations.

C.2.5 Resistance to antivirals

An important task of the centre is the monitoring of antiviral resistance of circulating influenza viruses. The most commonly used antivirals are neuraminidase inhibitors [oseltamivir (Tamiflu ®) and zanamivir (Relenza ®)]. Influenza strains may develop phenotypic resistance to these antivirals, and thus become less susceptible to their inhibitory activity. Phenotypic resistance is often associated with mutations in the viral target of the inhibitor, causing reduced binding to the antiviral. For example, the Y275H mutation in N1 was associated with resistance to oseltamivir. Other mutations associated with resistance to antivirals were also described for A(H3N2) and influenza B.

Resistant strains can be detected by phenotypic tests based on IC₅₀ measurement or genotypic tests based primarily on sequencing techniques to highlight NA mutations compared to reference sequences.
C.2.6. Sending of strains to London WHO CC

Each year, about fifty representative Belgian strains are sent to the WHO Collaborating Centre in London to undergo additional tests: antigenic and genetic characterization and monitoring of antiviral resistance. The characterization of circulating strains in Belgium contributes to the determination by WHO of the strains to be included in flu vaccines for the next season.

D. Results

D.1 Sentinel surveillance of ILI

D.1.1 Clinical surveillance

In Belgium, the epidemic threshold for the 2015-2016 season was set at 140 ILI/100,000 inhabitants. The threshold was crossed from week 4 (25-31 January 2016) and the epidemic was declared in week 5-2015 (2 consecutive weeks above threshold). From week 4-2015, the number of consultations for ILI increased to reach the level of 734 ILI/100,000 inhabitants in week 9-2015. After week 9-2015, the number of ILI gradually fell and was below the threshold after week 14 (Figure 2). The epidemic lasted 10 weeks.

![Weekly incidence of influenza-like syndromes per 100,000 inhabitants, 2015-2016 season, Belgium (Source: Sentinel general practices)](image-url)
D.1.2 Virological surveillance

The influenza surveillance period started in week 40-2014 (September 29, 2014) and continued through week 20-2015 (May 17, 2015).

Origin of samples
A total of 90 general practices (47 for Flanders, 43 for Wallonia-Brussels Federation) took part in the virological surveillance and sent 744 nasopharyngeal swabs to the NIC among which 743 samples were suitable for analysis.

Number of nasopharyngeal swabs
Flanders: 410 (55.1%)
Wallonia-Brussels: 333 (44.8%)
Total: 743

Typing and subtyping results
The first positive sample was diagnosed in week 42-2015 and increasingly large numbers of positive influenza cases were detected from week 53-2015 onwards, reaching a proportion of 80% positive samples in week 10-2016 (Figure 3). From week 40-2015 to week 20-2016, 743 respiratory samples were sent by the sentinel GPs network and analysed at the NIC. Of these samples, 381 (51%) were positive for influenza with 186 (25%) positive for influenza A and 197 (27%) positive for influenza B (Figure 3). One sample was co-infected with influenza A and B. Among the influenza A samples that were subtyped, 93% (173/186) were A(H1N1)pdm2009 and 1% (2/186) were A(H3N2). Eleven samples (6%) could not be subtyped due to their low viral load. Of the 197 influenza B samples analysed, 96% (190/197) belonged to the Victoria lineage and 3% (6/197) to the Yamagata lineage (Table 2-3).

![Figure 3. Weekly detection of influenza viruses in Belgium from week 40-2015 to week 20-2016 in the network of sentinel GPs](image)

Influenza 2015-2016
Table 2. Numbers and proportion of the different types and subtypes analysed during the 2015-2016 season

<table>
<thead>
<tr>
<th></th>
<th>FLU</th>
<th>FLU A</th>
<th>FLU B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>total</td>
<td></td>
</tr>
<tr>
<td>Total (week 40/2015-19/2016)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of positive samples</td>
<td>381</td>
<td>186</td>
<td>173</td>
</tr>
<tr>
<td>Number of tested samples</td>
<td>743</td>
<td>743</td>
<td>186</td>
</tr>
<tr>
<td>Percentage (%)</td>
<td>51</td>
<td>25</td>
<td>93</td>
</tr>
</tbody>
</table>

*Subtyping only realized on a part of positive samples
NT: not subtyped/non subtypable
NL: no lineage determined

Table 3. repartition of the different types and subtypes during the influenza season 2015-2016 ILI surveillance .

<table>
<thead>
<tr>
<th>Type</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>A(H1N1)</td>
<td>173</td>
<td>45.2</td>
</tr>
<tr>
<td>A(H3N2)</td>
<td>2</td>
<td>0.5</td>
</tr>
<tr>
<td>A(NT)</td>
<td>11</td>
<td>2.9</td>
</tr>
<tr>
<td>B Victoria</td>
<td>190</td>
<td>49.6</td>
</tr>
<tr>
<td>B Yamagata</td>
<td>6</td>
<td>1.6</td>
</tr>
<tr>
<td>B NL</td>
<td>1</td>
<td>0.3</td>
</tr>
</tbody>
</table>

**Influenza viruses according to age group**

The NIC received a higher number of samples from the age group 15 to 44 year old. The percentage of positivity for influenza varied between the different age groups. There were less positive samples in the age groups 15-44 and 45-64 years old than in the age groups <15 and 65-84 years old. (Figure 4). There were few samples in the age group >85.

The distribution of influenza types (and subtypes) also varied with age as shown in Figure 4. Influenza B Victoria was the predominant virus detected in samples from children <15 years old, while A(H1N1)pdm2009 was the predominant virus in samples from patients >45 years old .
D.2 Sentinel Surveillance of SARI

D.2.1 Virological surveillance

SARI Surveillance started week 1-2016 after the first influenza cases were recorded by the sentinel GPs, and ended week 17-2016, about one month after the end of the epidemic.

Origin of samples
A total of 1077 patients were registered in the database, among which 1064 (98%) corresponded to the case definition and were suitable for analysis.

Typing and subtyping results
From week 1-2016 to week 16-2016, 1064 respiratory samples from the sentinel network of hospitals were analysed by the NIC, among which 489 (46%) were positive for influenza. Among the influenza positive samples, 276 (56%) were positive for influenza A(H1N1)pdm2009, 3 (0.6%) for A(H3N2), 176 (36%) for influenza B Victoria, and 2 (0.4%) for influenza B Yamagata. Due to the low viral load, 26 (6%) of the influenza A and 2 (0.4%) of influenza B samples were not subtyprable (Figure 5, 6, 7) (table 4). From week 4, the percentage of positivity increased (15%) to reach a peak of 30% in week 8. From week 17, no more samples were sent to the NIC.
Figure 5. Weekly detection of influenza viruses in Belgium in the SARI network from week 1-2016 to week 17-2016

Table 4. Repartition of the different types and subtypes during the influenza season 2015-2016 SARI surveillance.

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>A(H1N1)</td>
<td>276</td>
<td>56</td>
</tr>
<tr>
<td>A(H3N2)</td>
<td>3</td>
<td>0.6</td>
</tr>
<tr>
<td>A NT</td>
<td>29</td>
<td>6</td>
</tr>
<tr>
<td>B Victoria</td>
<td>17</td>
<td>36</td>
</tr>
<tr>
<td>B Yamagata</td>
<td>2</td>
<td>0.4</td>
</tr>
<tr>
<td>B NL</td>
<td>2</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Age distribution of influenza viruses by types and subtypes
A higher number of samples was collected from children under five years old and from adults of the 65-84 age group. The proportion of positive samples was significantly lower in the 45-64 age group (two-tailed chi-square tests). Age group 5-14 was characterised by the predominance of influenza B Victoria among the positive samples. In all the other age groups, both A(H1N1)pdm2009 and B Victoria viruses co-circulated with a slight predominance of A(H1N1)pdm2009 (Figure 6).
Figure 6. Influenza viruses according to age group SARI surveillance season 2015-2016

**Positivity and subtype distribution of influenza viruses by surveillance scheme**

During the SARI surveillance period (week 1 to week 17 of 2016), the samples from ILI patients (61% positive; 95% CI: 57% - 66%) were significantly more frequently positive than those from SARI patients (46% positive; 95% CI: 43% - 49%).

During that period, Influenza A(H1N1) and B Victoria circulated in both surveillances. However, the proportion of A(H1N1) was higher in the SARI surveillance than in the ILI surveillance 62% A(H1N1) vs 48%. These differences were significant.

**D.3 Non sentinel surveillance**

Fifty five respiratory samples from patients with severe influenza were sent from hospitals around the country during the 2015-2016 season and inter-season, and were analysed at the NIC for confirmation and subtyping. Twenty seven were influenza A positive, among which there were 24 A(H1N1)pdm2009, two A(H3N2), and one non-subtypable due to low viral load. Nine samples were positive for influenza B (all of the Victoria lineage).

**D.4 Suspected cases of Avian Influenza**

No sample was sent for diagnosis of Avian flu during this season.

**D.5 Suspected cases of MERS CoV**

No sample was sent for diagnosis of MERS CoV during this season.
D.6 Other Respiratory viruses

All respiratory samples submitted to influenza diagnosis were also analysed for 16 other respiratory viruses: RSV A and B, PIV 1-2-3-4, HRV/ENV, hMPV, HPeV, HBoV, ADV and different Coronaviruses (Co229E, CoOC43, CoNL63, MERS CoV).

D.6.1 ILI surveillance

Between weeks 40-2015 and 20-2016, the 743 respiratory samples analysed for influenza were also submitted to the diagnosis of the other respiratory viruses. Overall, the positivity rate for influenza in the ILI surveillance was 51.4%, i.e. 48.6% of the samples were negative for influenza viruses. The analyses of positive and negative samples for the other respiratory viruses showed that, during the flu epidemic season, other respiratory viruses were also circulating in varying proportions. Among the samples negative for influenza viruses, 126/361 (35%) were positive for one or more other respiratory viruses. Overall, 68% of the patients were positive for at least one respiratory virus (including influenza alone or in co-infections). The most prevalent other respiratory viruses were HRV/ENV (8.3%), CoOC43 (4.7%), hMPV (2.4%) followed by RSVB (1.5%), RSVA (1.3%) and ADV (1.5%). For the other viruses, the percentages were lower and varied from 0.4% for CoNL63 to 0.1% for HPeV (Figure 7). The percentage of co-infection was 4.8% (36/743). Among influenza positive samples, co-infection with other viruses was observed for influenza A in 10/186 (5%) and for influenza B in 16/197 samples (8.12%). Regarding co-infection by respiratory viruses other than influenza, the percentage of co-infection was 7.1% (9/126) and no particular combination of viruses was highlighted.

Figure 7. Proportion of the different respiratory viruses in the ILI surveillance season 2015-2016
Figure 8 shows the weekly proportion of respiratory viruses that were laboratory-confirmed during the 2015-2016 flu season. From week 53 to week 15, most of the respiratory infections were caused by influenza. HRV/ENV were the following most prevalent viruses detected during all the surveillance period with percentages varying from 0 to 55% positive samples per week. RSV (A and B) were detected from week 46 to week 6, at percentages varying from 2 to 21% positive samples per week (week 51). Coronaviruses were detected from week 49 at percentages varying from 0 to 21% positive samples per week. The hMPV, HBoV and ADV viruses were detected more sporadically. We did not observe the RSV peak that usually appears around week 51. This is probably due to the fact that the case definition used for ILI cases is very specific for influenza, but also mainly because the proportion respiratory samples from young children and elderly, who are more susceptible to RSV, is very low in the ILI population.

Figure 8. Weekly proportion of respiratory viruses during the 2015-2016 ILI surveillance

D.6.2 SARI surveillance

From week 1 to week 16-2016, the 1064 respiratory samples analysed for influenza were also submitted to the diagnosis of the other respiratory viruses. Among the influenza viruses negative samples, 295/574 (51%) were positive for another respiratory viruses. Overall, 783/1064 (73%) of the patients were positive for at least one respiratory viruses (including influenza alone or in co-infections). This percentage reached 87% (56/436) in children below the age of 5 years old, although in elderly this percentage was only 55.3%. The most prevalent respiratory viruses were Influenza A (29.5%), influenza B (17.3%), HRV/ENV viruses (12.9%), hMPV (8%), ADV (7.2%), CoOC43 (3.9%), Boca 3.6% followed by RSVA (3%), RSVB (2%). For the other viruses, the percentages were lower and varied from 0.6% for HPeV to 0.4% for CoNL63 and PIV (Figure 9). The proportion of the different viruses varied between age groups (Figure 10 and Figure 11). For all viruses except influenza A and coronaviruses, the percentage was higher in children below 15 years old in comparison with adults (Figure 11).
Overall, the percentage of co-infection (two to 5 viruses) was 14% (148/1064). Most of these co-infections 115/148 (78%) were observed in patients below the age of 5 years old. Among influenza A positive samples, co-infection with other viruses were observed in 52/309 (17%) with the most frequent association being A/HRV/ENV found for 16/52 (30%) samples. Among influenza B positive samples, co-infection with other viruses were observed in 29/179 (17%) with the most frequent association being also with HRV/ENV (9/29, i.e. 31%). Regarding co-infections by respiratory viruses other than influenza, the most common viral co-infections were HRV/ENV with ADV 17/71 (24%) followed by HRV/ENV with hMPV 10/71 (14%).

Figure 9. Proportion of the different respiratory viruses in the SARI surveillance season 2015-2016

Figure 10. Proportion of the different Respiratory viruses in the SARI surveillance season 2015-2016
Figure 11. Proportion of the different Respiratory viruses in the SARI surveillance season 2015-2016

Figure 12 shows the weekly proportion of respiratory viruses that were laboratory-confirmed during the 2015-2016 SARI surveillance period. All tested respiratory viruses (with the exception of MERS-CoV) were detected during the surveillance period (week 1-2016 to 16-2016). Influenza viruses were the most prevalent with percentage of 46% (11 to 75%) positive samples per week, followed by HRV/ENV 13.6% (9 to 24%), hMPV 8% (0 to 11%), and ADV 7.5 (0 to 16%) positive samples per week. The other viruses were detected more sporadically. Although, the number of young children is high in the SARI population, the number of RSV were quite low and we did not observe the RSV peak which usually occurs before the peak of influenza, but this was not surprising since the surveillance began only in week 1-2016, so too late to detect the peak. It is possible that the SARI case definition is also more specific for influenza. It is known that RSV infection has a different clinical presentation, age distribution, risk factors, and seasonality compared to influenza infection. It was thus reported that a case definition requiring fever like that used for ILI and SARI may underestimate the incidence of RSV by 50-80% (21).

Figure 12 Weekly evolution of respiratory viruses during the 2015-2016 ILI surveillance
D.7. Characterisation of the influenza viruses

D.7.1 A(H1N1)pdm2009

Genetic characterisation

Since its appearance in 2009, nine genetic groups of A(H1N1)pdm2009, defined by specific amino acid substitutions in HA1, have emerged and circulated to various extents. In recent months, viruses of the genetic group 6 B have predominated.

The hemagglutinin genes (HA 1 fragment) of 23 influenza A(H1N1)pdm2009 Belgian samples were sequenced. A phylogenetic tree showing the vaccine strain, reference strains and A(H1N1)pdm2009 isolates is presented in Figure 13 A/B. Figure 13 B shows strains circulating in Belgium and other European countries. All the sequenced viruses belonged to the group 6 B1, a new genetic subgroup characterised by substitutions S84N, S162N and I216T in HA1.

Vaccine virus
Reference virus
Circulating virus Belgium
Figure 13 A/B. Phylogenetic analysis of influenza A(H1N1)09 strains

**Antigenic characterisation**

Two isolated A(H1N1)pdm2009 viruses that were sent to WHO CC-London were successfully propagated in cell culture. They were recognised well by the antiserum raised against the current vaccine virus A/California/7/2009 and were also recognised well by antisera against most of the other reference viruses. The two tested viruses were not recognised as well by the antiserum raised against A/Christchurch/16/2010 (Table 5).
### Antigenic analyses of influenza A(H1N1)pdm09 viruses (2016-01-13)

#### Table 5. Antigenic analyses of influenza H1N1pdm09 viruses

<table>
<thead>
<tr>
<th>Viruses</th>
<th>Other information</th>
<th>Genetic group</th>
<th>Collection date</th>
<th>Passage history</th>
<th>Antigenic analyses</th>
<th>Post-infection ferret antisera</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Egg</td>
<td>MDCK</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ferret number</td>
<td>F01/15</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Genetic group</td>
<td>7</td>
</tr>
<tr>
<td><strong>REFERENCE VIRUSES</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A/Christchurch/16/2010</td>
<td>4</td>
<td>2010-07-12</td>
<td>E1/E3</td>
<td>1280</td>
<td>2560</td>
<td>2560</td>
</tr>
<tr>
<td>A/St. Petersburg/27/2011</td>
<td>6</td>
<td>2011-02-14</td>
<td>E1/E3</td>
<td>1280</td>
<td>2560</td>
<td>2560</td>
</tr>
<tr>
<td>A/St. Petersburg/16/2011</td>
<td>7</td>
<td>2011-03-14</td>
<td>E1/E3</td>
<td>1280</td>
<td>2560</td>
<td>2560</td>
</tr>
<tr>
<td>A/Hong Kong/30/2012</td>
<td>6A</td>
<td>2012-02-25</td>
<td>MDCK4/MDCK1</td>
<td>160</td>
<td>320</td>
<td>320</td>
</tr>
<tr>
<td>A/South Africa/30/2013</td>
<td>6B</td>
<td>2013-02-05</td>
<td>E1/E3</td>
<td>320</td>
<td>640</td>
<td>640</td>
</tr>
<tr>
<td><strong>TEST VIRUSES</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A/Belgium/2015G0741/2015</td>
<td>GB.1</td>
<td>2015-10-20</td>
<td>SIAT1/MDCK1</td>
<td>320</td>
<td>640</td>
<td>640</td>
</tr>
<tr>
<td>A/Belgium/2015G0778/2015</td>
<td>GB.1</td>
<td>2015-11-24</td>
<td>MDCK2</td>
<td>1280</td>
<td>2560</td>
<td>2560</td>
</tr>
</tbody>
</table>

* Superscripts refer to antiserum properties (≥ relates to the lowest dilution of antiserum used) Vaccines:
  - 1: G155E
  - 2: G155E-G, D222G
  - 3: S 162N, I216T

### D.7.2 A(H3N2)

#### Genetic characterisation

Few A(H3N2) circulated during this season, and only four samples were characterised. One sample belonged to subgroup 3C.3a, which is close to the vaccine strain A/Switzerland/97/15293/2013, the other three belonging to subgroup 3C.2a that is closer to the A/Hong Kong/5738/2014 reference strain.

A phylogenetic tree showing the vaccine strain, reference strains and the four Belgian A(H3N2) isolates is presented in Figure 14A. Figure 14B shows strains circulating in Belgium and other European countries. Amino acid substitutions that define subgroups 3C.2a and 3C.3a are as follow:

3C.2a: **N144S** (resulting in the loss of potential glycosylation motif), **F159Y**, **K160T** (resulting in the gain of a potential glycosylation site), **N225D**, **Q311H**, all in **HA1** and as found in e.g. A/Hong Kong/5738/2014 and A/Hong Kong/4801/2014.

3C3a: **A138S**, **F159S** and **N225D** in **HA1**. Some also carry **K326R** in **HA1**, e.g. A/Switzerland/9715293/2013;
Influenza 2015-2016

Figure 14A/B. Phylogenetic analysis of circulating influenza A(H3N2) strains
Antigenic characterisation

Antigenic characterisation of A(H3N2) viruses by HI assay continues to be difficult due to variable capacities of HA agglutination of guinea pig, turkey and human red blood cells, and to non-specific red blood cell agglutination mediated by the NA. No A(H3N2) viruses were submitted to antigenic characterisation this season.

D.7.3 B Yamagata

Genetic characterisation

Very few influenza B viruses that have circulated this season were from the Yamagata lineage. The two viruses characterized genetically belonged to the clade 3 represented by the reference strain B/Phuket/3073/2013. A phylogenetic tree showing the vaccine strain, reference strains and the two B Yamagata isolates is presented in Figure 15A. Figure 15B shows strains circulating in Belgium and other European countries.

Figure 15 A/B. Phylogenetic analysis of circulating influenza B Yamagata strain
**Antigenic characterisation**

The two antigenically characterised samples were recognised as well by the antiserum raised against the previously-recommended egg-propagated vaccine virus B/Phuket/3073/2013, the antiserum raised against egg-propagated B/Hong Kong/3417/2014 and that raised against the egg-propagated B/Wisconsin/1/2010. All these three antisera recognised the tested viruses at titres equal to or within 2-fold of the titre for the homologous virus.

**Table 6. Antigenic analyses of influenza B Yamagata viruses**

<table>
<thead>
<tr>
<th>Antigenic analyses of influenza B viruses (Yamagata lineage) Date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Viruses</strong></td>
</tr>
<tr>
<td>-------------</td>
</tr>
<tr>
<td>B/Phuket/3073/2013</td>
</tr>
<tr>
<td>B/Hong Kong/3417/2014</td>
</tr>
</tbody>
</table>

* Superscripts refer to antiserum properties (= relates to the lowest dilution of antiserum used)

**Genetic characterisation**

Sixteen influenza B viruses of the Victoria lineage were sequenced this season, the viruses all belonging to clade 1A, the B/Brisbane/60/2008 clade. A phylogenetic tree showing the vaccine strain, reference strains and influenza B isolates is presented in Figure 16A. Figure 16B shows strains circulating in Belgium and other European countries.
Figure 16 A/B. Phylogenetic analysis of circulating influenza B Victoria strain
Antigenic characterisation

Six viruses were submitted to HI test for antigenic characterisation. HI analysis showed that none of the viruses was recognised by the antiserum raised against the currently-recommended egg-propagated vaccine virus B/Brisbane/60/2008. Similarly, none of the six viruses was well recognised by the antisera raised against other reference viruses propagated in eggs (B/Malta/63714/2011, B/Johannesburg/3964/2012 or B/South Australia/81/2012). However, the six tested viruses were better recognised by antisera raised against viruses exclusively propagated in cell culture and genetically related to B/Brisbane/60/2008.

Table 7. Antigenic analyses of influenza B Victoria viruses

<table>
<thead>
<tr>
<th>Viruses</th>
<th>Genetic group</th>
<th>Passage history</th>
<th>Collection date</th>
<th>HI titer</th>
<th>Post-infection ferret antisera</th>
<th>Vaccine NH 2015-16</th>
</tr>
</thead>
<tbody>
<tr>
<td>B/Malaysia/2506/2004</td>
<td>1A</td>
<td>2004-12-06</td>
<td>E3/E7</td>
<td>320</td>
<td>20</td>
<td>&lt;40</td>
</tr>
<tr>
<td>B/Brisbane/65/2006</td>
<td>1A</td>
<td>2000-08-04</td>
<td>E5/E5</td>
<td>640</td>
<td>160</td>
<td>&lt;40</td>
</tr>
<tr>
<td>B/Paris/17/2009</td>
<td>1A</td>
<td>2000-02-09</td>
<td>C2/MDCK2</td>
<td>640</td>
<td>&lt;10</td>
<td>&lt;40</td>
</tr>
<tr>
<td>B/Malta/E671/2011</td>
<td>1A</td>
<td>2011-03-07</td>
<td>E5/E1</td>
<td>640</td>
<td>160</td>
<td>&lt;40</td>
</tr>
<tr>
<td>B/Johannesburg/3964/2012</td>
<td>1A</td>
<td>2012-08-03</td>
<td>E5/E2</td>
<td>2500</td>
<td>160</td>
<td>&lt;40</td>
</tr>
<tr>
<td>B/Formentos/V357/2012</td>
<td>1A</td>
<td>2012-08-06</td>
<td>MDCK1/MDCK2</td>
<td>640</td>
<td>20</td>
<td>&lt;40</td>
</tr>
<tr>
<td>B/South Australia/81/2012</td>
<td>1A</td>
<td>2012-11-20</td>
<td>E4/E2</td>
<td>640</td>
<td>160</td>
<td>&lt;40</td>
</tr>
<tr>
<td>B/Odessa/3996/2010</td>
<td>1B</td>
<td>2015-11-10</td>
<td>MDCK2/MDCK4</td>
<td>640</td>
<td>&lt;10</td>
<td>&lt;40</td>
</tr>
</tbody>
</table>

* Superscripts refer to antiserum properties ( relates to the lowest dilution of antiserum used)
1 = <40
2 = <10
3 = hyperimmune sheep serum
4 = <20
B: Victoria lineages virus recommended for use in quadrivalent vaccines

D.8. Antiviral monitoring

We performed the sequencing of the neuraminidase gene of four A(H1N1)pdm2009 in order to detect mutations known to be associated with resistance to neuraminidase inhibitors. One mutation H275Y was identified in an immune-deficient patient treated with Oseltamivir.

Furthermore, phenotypic in vitro testing for antiviral resistance was performed in house for one A(H3N2), two A(H1N1)pdm2009 and five B VIC and two B YAM isolates of the season. They were all sensitive to Oseltamivir and Zanamivir.
D.9 Composition of influenza virus vaccines for use in the 2016-2017 northern hemisphere influenza season

The WHO has published its recommendation for the vaccine composition that should be used in the 2016-2017 season in the Northern hemisphere.

**Trivalent vaccine**
- A/California/7/2009 (H1N1)pdm09-like virus;
- A/Hong Kong/4801/2014 (H3N2)-like virus;
- B/Brisbane/60/2008-like virus.

**Quadrivalent (additional strain)**
- B/Phuket/3073/2013-like virus.

<table>
<thead>
<tr>
<th>Saison</th>
<th>A(H1N1)</th>
<th>H3N2</th>
<th>B</th>
<th>Quadrivalent</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002-2003</td>
<td>&quot;</td>
<td>&quot;</td>
<td>B/Hong Kong/330/2001</td>
<td></td>
</tr>
<tr>
<td>2003-2004</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
<td></td>
</tr>
<tr>
<td>2006-2007</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
<td></td>
</tr>
<tr>
<td>2007-2008</td>
<td>A/Solomon Island/3/2008</td>
<td>&quot;</td>
<td>&quot;</td>
<td></td>
</tr>
<tr>
<td>2009-2010</td>
<td>&quot;</td>
<td>&quot;</td>
<td>B/Brisbane/60/2008(VIC)</td>
<td></td>
</tr>
<tr>
<td>2010-2011</td>
<td>A/California/7/2009</td>
<td>A/Pert/16/2009</td>
<td>&quot;</td>
<td></td>
</tr>
<tr>
<td>2011-2012</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
<td></td>
</tr>
<tr>
<td>2013-2014</td>
<td>&quot;</td>
<td>A/Texas/50/2012,</td>
<td>B/Massachusetts/2/2012 (YAM)</td>
<td>B/Phuket/3073/2013(YAM)</td>
</tr>
<tr>
<td>2014-2015</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
<td></td>
</tr>
<tr>
<td>2015-2016</td>
<td>&quot;</td>
<td>A/Switzerland/971529/2013</td>
<td>B/Phuket/3073/2013(YAM)</td>
<td>B/Brisbane/60/2008(VIC)</td>
</tr>
<tr>
<td>2016-2017</td>
<td>&quot;</td>
<td>A/Hong Kong/4801/2014</td>
<td>B/Brisbane/60/2008(VIC)</td>
<td>B/Phuket/3073/2013(YAM)</td>
</tr>
</tbody>
</table>

Figure 17. Evolution of the composition of the trivalent influenza vaccine 2000 – 2017

D.10 Vaccine effectiveness

By pooling data of ILI and SARI patients, we estimated vaccine effectiveness (VE) using a logistic regression model that models influenza positivity in function of vaccination status (adjusted for age group, sex and month of sampling). For the first time in Belgium, a quadrivalent vaccine, including the two lineage of influenza B, was available for the 2015-2016 influenza season. Irrespective of the vaccine used, the preliminary data for VE are 41% when considering all influenza strains, 50% for A(H1N1)pdm2009 and 32% for influenza B.
E. Conclusion

The 2015–2016 influenza season was of medium intensity and lasted for 10 weeks. During the epidemic peak, a total number of 734 ILI per 100,000 inhabitants was reached. Two viruses, A(H1N1)pdm2009 and B Victoria, predominantly circulated during this season. The percentage of positivity was higher in the ILI surveillance as compared to the SARI surveillance, which was probably due to a better specificity of the case definition in the ILI surveillance. The distribution of the different A(H1N1)pdm2009 and B viruses differed in the two surveillance networks, with a higher proportion of A(H1N1)pdm2009 in the SARI surveillance.

All sequenced A(H1N1)pdm2009 viruses were from group 6B.1, a new subgroup, and were antigenically similar to the vaccine strain A/California/7/2009. Most of influenza B viruses that circulated this season were from the Victoria lineage, and all the sequenced influenza B viruses belonged to clade 1A represented by the reference strain B/Brisbane/60/2008. It was the first time since several seasons that the B Victoria lineage has circulated in predominance. The trivalent vaccine included a B Yamagata strain. For the first time in Belgium, a quadrivalent vaccine which included both lineages of influenza B was available this season. It is not well clear what percentage of the population was vaccinated with which type of vaccine. Given the mismatch between the trivalent vaccine and the influenza B Victoria that circulated, it is likely that the efficacy against influenza B would have been reduced. All tested viruses were sensitive to Oseltamivir and Zanamivir, except one sample from an immunocompromised patient treated with Oseltamivir, for which the H275Y mutation was detected.

During this season, all respiratory samples were also analysed for other respiratory viruses. In the ILI population, 35% of the influenza negative patients were positive for one or more other respiratory viruses, whereas in the SARI population, this percentage reached 51%. This suggest an important role of other respiratory viruses in hospitalized patients during the flu season with symptoms relevant to the chosen case definition. It will be important to continue this surveillance over several seasons to be able to analyse the impact of the different respiratory viruses on public health (correlation with severity, ...).

F. Acknowledgements

The influenza surveillance in Belgium is financially supported by the Federal Public Service Health, Food Chain Safety and Environment, the “Fédération Wallonie Bruxelles” and the “Agentschap Zorg en Gezondheid“. The National Influenza Centre (national reference centre) is partly financially supported by RIZIV Federal Institute for Health Insurance. The SARI surveillance is supported by the Federal Public Service Health, Food Chain Safety and Environment, DG1.

We would like to acknowledge all our partners of the different surveillance networks (the sentinel GPs and the different sentinel hospitals involved in the SARI surveillance). We also want to acknowledge the WHO Collaborating Centre in London for their analyses and their support.
G. References


4. WHO, Cumulative number of confirmed human cases for avian influenza A (H5N1) reported to WHO, 2003-2015

5. WHO risk Assessment of Human infection with avian influenza A (H7N9) virus, 23 February 2015


