

National Institute for Public Health and the Environment Ministry of Health, Welfare and Sport

Annual report Surveillance of influenza and other respiratory infections in the Netherlands: winter 2014/2015



## Annual report Surveillance of influenza and other respiratory infections in the Netherlands: winter 2014/2015

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### Colophon

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## Synopsis

## Surveillance of influenza and other respiratory infections in the Netherlands: winter 2014/2015

Lasting a total of 21 weeks, the influenza epidemic in the Netherlands in the winter of 2014/2015 had the longest duration since more than 40 years.

The high number of influenza cases has probably led to more pneumonia cases, which is a known complication of influenza, and to higher mortality. During the epidemic period, more than 65,000 persons died in the Netherlands; this is approximately 8,600 persons more than the expected number of deaths in this 21-week period. This winter, the vaccine effectiveness was lower than expected. It remains unclear whether this contributed to the long duration of the epidemic.

These are results of the annual report 'Surveillance of influenza and other respiratory infections in the Netherlands: winter 2014/2015', by the Dutch National Institute for Public Health and the Environment (RIVM). Together with its partners, the RIVM continuously surveys epidemiological and microbiological developments in respiratory infections. Persons aged over 60 or belonging to a medical risk group, such as asthma patients, are offered the influenza vaccination each autumn by their general practitioner.

Starting from December 2014 up to the end of April 2015, more than 51 patients per 100,000 inhabitants consulted their general practitioner with influenza-like symptoms. An epidemic is defined as an incidence above this threshold for at least two consecutive weeks. The actual incidence of influenza cases is considerably higher, because only a proportion of the patients with influenza-like symptoms consult the general practitioner.

At the start of the season, influenza virus A(H3N2) dominated, while later in the season, influenza virus B was most prevalent. A part of the circulating influenza A-viruses appeared to mismatch with the influenza A-strain in the vaccine.

Currently, no registration exists for hospital admissions due to influenza complications. Therefore, a research collaboration has been started in 2015 between the RIVM and two Dutch hospitals, aiming to map and provide good estimations of hospital admissions due to severe acute respiratory infections.

#### Other respiratory infections

In 2014, two patients were diagnosed with the MERS-Coronavirus. These patients had been infected while travelling in the Middle East. There were no important elevations during the calendar year 2014 in the notifiable respiratory infectious diseases tuberculosis, legionellosis, psittacosis, and Q fever, with 823, 348, 41 and 25 notifications respectively. These infectious diseases are notifiable, since timely measures, such as source- and contact-tracing are crucial to prevent outbreaks or dissemination of the diseases.

Keywords: respiratory infections, flu, influenza, pneumonia, Legionnaires' disease, Legionella, parrot fever, psittacosis, Q fever, tuberculosis

## Publiekssamenvatting

#### Surveillance van influenza en andere luchtweginfecties: winter 2014/2015

De griepepidemie van 2014/2015 duurde 21 weken en was daarmee de langstdurende in meer dan 40 jaar. Waarschijnlijk heeft het hoge aantal griepgevallen tot meer longontstekingen, een bekende complicatie van de griep, en meer sterfgevallen geleid. Tijdens de griepepidemie stierven ruim 65.000 mensen, dat is ruim 8.600 meer dan in deze 21 weken was verwacht. De griepprik bleek dit seizoen minder effectief dan verwacht. Het is niet duidelijk of dit de oorzaak van de lange duur van de epidemie is geweest.

Dit blijkt uit het jaarverslag influenza en andere luchtweginfecties van het RIVM. Het RIVM voert met partners continue surveillance uit om ontwikkelingen in luchtweginfecties tijdig te signaleren. Zestigplussers en mensen die tot de medische risicogroep behoren, zoals astmapatiënten, worden elk najaar door de huisarts uitgenodigd om een griepprik te halen.

Tussen begin december 2014 en eind april 2015 meldden zich wekelijks meer dan 51 patiënten per 100.000 inwoners met griepverschijnselen bij de huisarts. Er is sprake van een epidemie als dit aantal in twee opeenvolgende weken wordt overschreden. Het werkelijke aantal griepgevallen is veel hoger omdat lang niet iedereen met griepverschijnselen naar de huisarts gaat. Van de twee typen van het influenzavirus die voor de mens van belang zijn (A en B), is in het begin van het seizoen vooral het influenzavirus A (H3N2) aangetroffen. Later was dat vooral het influenzavirus B. Een deel van het circulerende influenza A-virus bleek af te wijken van het A-virus dat in het griepvaccin was opgenomen.

Tot dusver kan nog niet worden geregistreerd hoeveel mensen in ziekenhuizen worden opgenomen vanwege complicaties van de griep. Het RIVM is daarom in 2015 in samenwerking met twee ziekenhuizen een onderzoek gestart om dit in kaart te brengen en de schattingen hiervan beter cijfermatig te onderbouwen.

#### Andere luchtweginfecties

In 2014 zijn in Nederland twee patiënten gediagnostiseerd met het MERS-Coronavirus. De patiënten hadden deze infectie opgelopen tijdens een reis naar het Midden Oosten. Wat betreft de meldingsplichtige luchtweginfectieziekten tuberculose, legionellose, papegaaienziekte (psittacose) en Q-koorts zijn er in het kalenderjaar 2014 geen zorgwekkende uitbraken of veranderingen in het aantal zieken waargenomen. Van deze infecties kwamen respectievelijk 823, 348, 41 en 25 meldingen binnen; de aantallen zijn in lijn met de voorgaande jaren. De genoemde infecties zijn meldingsplichtig, omdat tijdige maatregelen, zoals de besmettingsbron of contacten opsporen, belangrijk kunnen zijn om uitbraken of verdere verspreiding van de ziekte te voorkomen.

Kernwoorden: luchtweg infecties, griep, influenza, longontsteking, pneumonie, legionellose, papegaaienziekte, Psittacose, Q-koorts, tuberculose

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## Chapter 1 Introduction

## 1.1 Aim and focus of this report

This report describes the current trends and epidemiology of various respiratory infectious diseases and pathogens in the Netherlands. This is an annual report, targeting policymakers, epidemiologists, microbiologists, staff of public health services and others working or interested in the field of respiratory infectious diseases. Previous annual reports were written in Dutch. National surveillance of respiratory infectious diseases that are considered in this report is the responsibility of the Department for Respiratory Infectious Disease, Centre for Infectious Diseases, Epidemiology and Surveillance (EPI), Centre for Infectious Disease Control (Clb) of the National Institute for Public Health and the Environment (RIVM) in the Netherlands, in collaboration with other partners, within and outside RIVM.

Chapter 2 of this report describes the data sources and methods used for surveillance of the different diseases or pathogens. Chapters 3 and 4 show the surveillance data for influenza virus infection, influenza-like illness (ILI), acute respiratory infections (ARI), and pneumonia. The term 'influenza-like illness' is based on the fact that symptoms of influenza may be caused by several other pathogens than influenza viruses. Since influenza virus infection, ILI and ARI, as well as pneumonia show winter seasonality, data are reported for the respiratory winter season 2014/2015, i.e. week 40 of 2014 through week 20 of 2015. This surveillance is important because of the high burden of disease, in terms of patient numbers, impact on the health care system, and mortality. The causative pathogen remains unknown in the majority of patients because most infections are not laboratory-confirmed, but only clinically diagnosed. The surveillance of ILI, ARI and pneumonia is currently mainly based on the registration of consultations by general practitioners (GPs) participating in NIVEL Primary Care Database (in Dutch: NIVEL Zorgregistraties eerste lijn). Elderly care physicians provide data within the context of the national sentinel surveillance network for infectious diseases in nursing homes (SNIV). Laboratory-confirmed influenza in these two networks is assessed by the National

Influenza Centre (NIC), location RIVM (at the Centre for Infectious Disease Research, Diagnostics and Screening (IDS) of CIb) and at NIC, location Erasmus Medical Centre.

Respiratory infectious diseases such as influenza and pneumonia are important causes of death. As direct and real-time data on deaths from respiratory infectious diseases are not available, there is surveillance of all-cause mortality, as reported in chapter 5. Surveillance of mortality is based on data collected by Statistics Netherlands (CBS).

The notifiable respiratory infectious diseases legionellosis, tuberculosis, Q fever and psittacosis are described in separate reports. However, a summary of the results of the surveillance of these diseases in key points for the calendar year 2014 is included in chapter 6 of this report. Other notifiable respiratory diseases that are part of the National Immunisation Programme, like pertussis and invasive pneumococcal disease, are described in the annual RIVM publication 'The National Immunisation Programme in the Netherlands' and are not reported here.

In chapter 7, diagnoses of respiratory infections reported in the virologic laboratory surveillance are described, either for the respiratory season 2014/2015 or for 2014, depending on their seasonality.

Finally, chapter 8 describes the international developments with respect to the emergence of new respiratory pathogens as part of preparedness for threats that are relevant for the Netherlands.

## 1.2 Collaborations: national and international

For the surveillance of respiratory infectious diseases, the Centre for Infectious Disease Control collaborates with many partners: the Netherlands institute for health services research (NIVEL), including the network of sentinel general practices, coordinated by NIVEL, the surveillance network in nursing homes (SNIV), the National Influenza Centre (NIC), location Erasmus MC, Influenzanet, the KNCV Tuberculosis Foundation, the Regional Public Health Laboratory Kennemerland, Haarlem (national reference laboratory for legionellosis), and Statistics Netherlands (CBS). The collaboration with the Municipal Health Services (in Dutch: GGD) is the basis for the surveillance of notifiable infectious diseases. For zoonoses (psittacosis and Q fever), collaboration with the Netherlands Food and Consumer Product Safety Authority (NVWA) is in place, and for psittacosis also with the Orbis Medical Centre in Sittard. The laboratories delivering the data for the virologic laboratory surveillance are all members of the Working group for Clinical Virology of the Dutch Society for Medical Microbiology (NVMM).

A part of the data in this report is also reported internationally. The notifiable infectious diseases legionellosis, Q fever and tuberculosis are reported annually to the European Centre for Disease Prevention and Control (ECDC). Travel-related legionellosis is reported daily to the European Legionnaires Disease Surveillance Network (ELDSNet) of the ECDC. Moreover, the RIVM (CIb/IDS and CIb/EPI) are participating together with NIVEL and Erasmus MC in the

European Influenza Surveillance Network (EISN) of ECDC, in FluNet and FLuID of the WHO (World Health Organization) in Geneva, and in EUROFLU of WHO-EURO in Copenhagen. Data on influenza is reported on a weekly basis. All-cause mortality is reported weekly to EuroMoMo, a European consortium that weekly publishes the mortality data of nineteen European countries.

# Chapter 2 Methods of respiratory surveillance

## 2.1 Respiratory season or calendar year

The aim of this annual report is to describe the surveillance of influenza and other respiratory infections in the Netherlands. Since influenza, influenza-like illness (ILI), acute respiratory infections (ARI), pneumonia, respiratory syncytial virus (RSV) infection, and all-cause mortality mainly occur in winter, data is usually presented for the respiratory year. A respiratory year is defined as the period from week 40 through week 39 of the next year. In this report, data on the respiratory year 2014/2015 is limited to the winter period only (week 40 of 2014 through week 20 of 2015), to allow a timely reporting. These respiratory infections may occur outside this winter period in a limited way. Because the notifiable diseases legionellosis, tuberculosis, Q fever and psittacosis as well as the majority of pathogens monitored in the virologic laboratory surveillance occur without typical winter seasonality, the results of these diseases refer to the calendar year 2014 (weeks 1-52).

### 2.2 Data sources

#### **NIVEL Primary Care Database**

In 2012, the Netherlands institute for health services research (NIVEL), initiated the integral monitoring and information services for primary care, called 'NIVEL Primary Care Database' (Verheij, 2015). The NIVEL Primary Care Database holds longitudinal data registered by general practitioners (GP) and other primary health care providers. For the surveillance of respiratory infectious diseases, the following data of NIVEL is used:

Near real-time (weekly) surveillance data concerning pneumonia and acute respiratory
infections, based on consultation data in electronic medical records from general practices
[http://www.nivel.nl/NZR/wekelijkse-surveillance-gezondheidsproblemen]. In the
respiratory season 2014/2015, the coverage increased to about 1.2 million persons (7% of the
Dutch population). These GPs do not actively report patients and do not take laboratory

samples for surveillance purposes but make their electronic patient information systems available for automatic, anonymised, data extraction (Hooiveld et al., 2013).

• A proportion of the GPs participating in NIVEL-Primary Care Database take part in 'sentinel surveillance'. These GPs actively report on the number of patients who consult them for ILI. From a subset of patients they collect a throat swab and nose swab and send it to RIVM for virologic laboratory diagnostics. The population of these sentinel practices covers approximately 0.7% of the Dutch population and is representative for age, sex, regional distribution and population density (Donker, 2015).

#### National sentinel surveillance network for infectious diseases in nursing homes (SNIV)

The nursing homes participating in this network serve as sentinels for the national surveillance of infectious diseases in nursing homes. The participating nursing homes weekly report the number of residents with ILI and pneumonia and annually report the total bed capacity in the nursing home. Due to reporting delay in the weekly reports, the incidence measures for the current calendar year are not yet complete and should be considered preliminary data. The annual total bed capacity is reported retrospectively, i.e. after closure of the calendar year. Therefore, the total bed capacity of the current calendar year is not yet definite and based on the number reported in the previous calendar year. We assume 100% coverage of the total number of beds for every week that data has been registered. From a subset of ILI patients, or if not available/possible from patients with another acute respiratory infection (ARI), a throat swab and nose swab is collected for virologic laboratory diagnostics.

#### Influenzanet

Influenzanet (in Dutch: De Grote GriepMeting) is a system to monitor the incidence of ILI based on self-reported symptoms by volunteers via the internet. Since 2003, yearly press releases have encouraged people from the Dutch general population to fill in a web-based baseline questionnaire asking for demographical, medical and lifestyle data. Participants receive a weekly e-mail with a link to a short questionnaire asking about ILI symptoms experienced since their previous visit to the website. The incidence of ILI is determined on the basis of a uniform case definition. Influenzanet is operational in several other European countries, including Belgium, Portugal, Italy and the United Kingdom. In this report, we only use the data of the Dutch participants (on average 10,500 active participants every day in the respiratory season 2014/2015).

#### Statistics Netherlands (CBS)

Statistics Netherlands (In Dutch: Centraal Bureau voor de Statistiek: CBS) is responsible for the official Dutch national statistics, that are available on CBS-Statline [http://statline.cbs.nl]. The mortality data in this report is derived from an aggregated dataset of all-cause mortality in the Netherlands. This data is sent to the RIVM weekly, allowing for a real-time monitoring of mortality.

#### Virologic laboratory surveillance

On a weekly basis, about 20 virologic laboratories, all members of the Working Group for Clinical Virology of the Dutch Society for Medical Microbiology (NVMM), report the number of diagnoses of several viral pathogens and certain obligatory intracellular (i.e. only growing within a cell) bacteria to RIVM. Data are reported by week of laboratory diagnosis. No distinction can be made between samples originating from primary care or hospital care, or between the used diagnostic methods, such as culture, molecular diagnostic, serology or rapid tests. Data are therefore reported in an aggregated format. Although no background information concerning patient status, clinical data and type of diagnostic method is available, the weekly laboratory surveillance can be used as an additional source to follow trends of respiratory infections over a prolonged period because of their relative robust reporting history.

#### Osiris

According to Dutch legislation, legionellosis, psittacosis, Q fever, tuberculosis, Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and human infections with an animal influenza virus are notifiable diseases. Medical doctors and medical-microbiological laboratories notify cases to the Municipal Health Services, who subsequently report these to the RIVM via the online registration program Osiris. Tuberculosis is reported to the Dutch Tuberculosis Registry (NTR), which is integrated in Osiris. Furthermore, latent tuberculosis infections (LTBI) are reported voluntarily by the Municipal Health Services and registered in Osiris-NTR. Osiris is a dynamic system and due to corrections and additions of the Municipal Health Services, small differences may exist between the data reported here and earlier reported data. Osiris notifications consist of anonymous patient data, date of disease onset, diagnostic information (dates, diagnostic methods, outcome) and information on source finding and contact tracing. For tuberculosis, Osiris furthermore registers information regarding treatment and treatment outcome.

#### New respiratory virus infections

In case of a suspected human infection with animal influenza, such as influenza A(H5N1) virus or influenza A(H7N9) virus, or infection with the Middle East Respiratory Syndrome Coronavirus (MERS-CoV), diagnostics are performed by the RIVM (Clb/IDS). If necessary, confirmation is performed by the virologic diagnostic laboratory at Erasmus MC. Both human infection with animal influenza and MERS-CoV are notifiable in the Netherlands.

Alerts concerning respiratory infectious disease outbreaks that occur outside the Netherlands but that can pose a potential hazard to the Netherlands, are monitored using website sources like those of the World Health Organization (WHO, Geneva: http://www.who.int/csr/don/en/), ECDC, Stockholm: http://ecdc.europa.eu/en/publications/surveillance\_reports/Communicable-Disease-Threats-Report/Pages/default.aspx and international alerting systems (e.g. ProMed mail, EWRS, IHR).

### 2.3 Data analysis

#### Influenza-like illness (ILI)

ILI incidence is calculated using three data sources: 1) NIVEL Primary Care Database - sentinel GP practices; 2) SNIV nursing homes; and 3) Influenzanet. These three data sources all use different ILI case definitions.

In the NIVEL Primary Care Database - sentinel GP practices, ILI is defined according to the 'Pel-criteria' (Pel, 1965):

- Sudden onset of symptoms
- Fever (at least 38 °C, rectal temperature)
- At least one of the following symptoms:
  - cough
  - rhinorrhoea
  - sore throat
  - frontal headache
  - retrosternal pain
  - myalgia

ILI incidence is calculated as the number of patients with a new episode of ILI, divided by the total number of enlisted patients of the participating Sentinel GP Practices (Donker, 2015). The influenza epidemic threshold is set at an ILI incidence of 5.1 per 10,000 persons per week, based on historical data (Vega Alonso et al., 2004). An influenza epidemic is defined as a period of at least two consecutive weeks with ILI incidence above the influenza epidemic threshold, during which influenza virus is detected in nose swabs and throat swabs of ILI patients.

The ILI incidence in SNIV nursing homes is calculated using the number of residents with ILI as nominator, and the number of observed resident weeks as denominator. The case definition of ILI used by SNIV surveillances is according to the ECDC case definition for ILI and is as follows:

• Sudden onset of symptoms

And at least one of the following four systemic symptoms:

- Fever or feverishness
- Malaise
- Headache
- Myalgia

And at least one of the following three respiratory symptoms:

- Cough
- Sore throat
- Shortness of breath

The case definition of ILI measured by Influenzanet is as follows: At least one of the four systemic symptoms:

- Fever and/or chills
- Feeling tired or exhausted
- Headache
- Muscle pain

And at least one of the three respiratory symptoms:

- Cough
- Sore throat
- Shortness of breath (dyspnoea).

The weekly ILI incidence is defined as the number of participants who reported the onset of ILI in that week, divided by the person-time of active participation during the same week. The person-time of active participation per week is defined as the number of participants who were active during that week multiplied by the percentage of the week each participant was active.Data is downloaded from the website http://www.influenzanet.eu.

#### Acute respiratory infections (ARI)

Weekly numbers on patients consulting for an acute respiratory infection (including acute/ chronic sinusitis, acute laryngitis/tracheitis, acute bronchitis/bronchiolitis or influenza) are extracted from NIVEL Primary Care Database. Although ARI is less specific for an influenza virus infection than ILI, seasonal data are highly correlated. ARI surveillance figures are calculated as the number of patients consulting their GP in a given week, divided by the total number of enlisted patients. This produces weekly prevalence figures. To allow for cumulation of weekly surveillance data we report the results as 'number of consultations', rather than prevalence.

#### Influenza virus and other respiratory viruses

#### Surveillance of circulating viruses

At the NIC location RIVM the respiratory specimens are analysed that are taken for the influenza virus surveillance at the GP sentinel practices and the SNIV sentinel nursing homes. Additionally, Dutch laboratories submit a subset of their influenza virus isolates or clinical specimens that are positive for influenza virus to the NIC location Erasmus MC, for further subtyping, lineage determination and antigenic characterization.

The GP sentinel practices from NIVEL Primary Care Database are requested to take specimens (combined throat swabs and nose swabs) of at least two ILI patients per week, of which one patient should be a child below the age of ten years. If no ILI patients are encountered or willing to participate, specimens should be taken from patients with an acute respiratory infection other than ILI, defined as:

sudden onset of symptoms;

• at least one respiratory symptom, e.g. cough, rhinorrhoea, sore throat.

These other respiratory infections are further classified as upper respiratory tract infections (URI) or lower respiratory tract infections (LRI) based on reported clinical diagnosis.

Elderly care physicians participating in SNIV surveillance receive the same instructions, obviously without the special request for sampling children.

The GP and SNIV specimens are analysed by NIC location RIVM for influenza viruses, RSV, rhinoviruses and enteroviruses. The reason to test for RSV is that the clinical presentation is similar for RSV and influenza and that RSV infections can have a severe progression, both in young children and in the elderly. Rhino- and enteroviruses are important causes of acute respiratory infections, and the clinical presentation often resembles that of ILI. Influenza virus and RSV are genetically typed as influenza virus A, influenza virus B, RSV type A and RSV type B. Influenza virus type A is subsequently subtyped, and for influenza virus type B the phylogenetic lineage is assessed. The type of enterovirus is also determined.

#### Influenza virus antigenic and genetic characterization

Antigenic characterization of a subset of influenza viruses and influenza virus positive clinical specimens, submitted by peripheral laboratories and from the sentinel GP surveillance, is performed by NIC location Erasmus MC in Rotterdam. This provides an indication of the degree of antigenic match between the circulating influenza viruses and the vaccine virus. Furthermore, a subset of influenza viruses are characterized genetically by sequence analysis of the haemagglutinin genome segment at both NIC locations. This phylogenetic analysis gives information about the evolution of influenza viruses and changes that might lead to the emergence of potential antigenic variants. In addition, this type of information complements the antigenic analysis, especially when antigenic characterization is cumbersome, as was the case with A(H<sub>3</sub>N<sub>2</sub>) viruses during the 2014/2015 season.

#### Antiviral susceptibility of influenza viruses

Infection with an influenza virus with a reduced susceptibility for an antiviral agent can lead to a reduced effectiveness of treatment. The antiviral susceptibility of influenza viruses is systematically monitored. Of the influenza virus isolates obtained in the NIVEL and SNIV influenza surveillance, the phenotypic antiviral susceptibility for neuraminidase inhibitors (oseltamivir and zanamivir) is determined by NIC location RIVM. For virus isolates derived from specimens sent to NIC location Erasmus MC, the phenotypic antiviral susceptibility for neuraminidase inhibitors is determined at that location. Of viruses that appear reduced susceptible, the neuraminidase genome segment is sequenced to determine the amino acid substitution that explains the reduced susceptible phenotype. Molecular markers for resistance to adamantanes (M2 ion channel blockers: amantadine and rimantadine) are assessed in a subset of influenza virus type A positive clinical specimens with a high viral load by sequencing at NIC location RIVM. For all influenza virus type A positive specimens, the most important molecular markers for reduced sensitivity for neuraminidase-inhibitors are determined by a rapid molecular test at both NIC locations. From the influenza virus clinical specimens with a high viral load, the neuraminidase gene is sequenced in order to screen for new molecular markers for reduced sensitivity for neuraminidase inhibitors. In case of mutations with previously unknown impact on antiviral susceptibility, the phenotypical neuraminidase inhibition test is the final proof for the degree of inhibition. This is done at both locations of the NIC for their own set of viruses.

Data from viruses analysed at location RIVM and data from viruses analysed at location Erasmus MC are combined on a weekly basis to achieve one overall picture of the current situation.

#### Influenza vaccine effectiveness

The influenza vaccine effectiveness (VE) for the season 2014/2015 is calculated using data from patients of the NIVEL sentinel surveillance. For this goal, the test-negative (case control) design is used (Jackson and Nelson, 2013). Cases are defined as influenza virus positive patients with ILI or another acute respiratory infection, controls as influenza virus negative patients. Only samples that were taken within 6 days after day of onset were included in the analysis. Using this method, the odds of being vaccinated as a case is divided by the odds of being vaccinated as a control. With logistic regression this odds ratio (OR) is adjusted for confounding factors such as age group and presence of comorbidity. The vaccine effectiveness is calculated as (1-OR) x 100%. The vaccine effectiveness is calculated per influenza virus type, and per subtype or lineage.

VE is also calculated against ILI, without laboratory tests, for the season 2014/2015 using data from participants of Influenzanet. For this purpose, the cohort method is used. When participants met the Influenzanet case definition, they were considered as cases; participants who did not meet the case definition were considered as controls. Not everyone who met the case definition will have experienced an influenza virus infection. Therefore, a seasonal baseline [baseline = 275 + 75 cos ((week number - 2) / 52) x 360) ] incidence for non-epidemic ILI is determined. Only the cases above the baseline are included in the analysis, in the weeks that the ILI is above the Influenzanet threshold. The relative risk (RR) is calculated by the formula [A/ (A+B)] / [C/(C+D)]. In this formula is A the number of participants which are vaccinated against influenza and did develop ILI symptoms; B is the number of participants which are vaccinated against influenza and did not develop ILI symptoms; C is the number of participants which did not receive the influenza vaccination and did develop ILI symptoms; and D is the number of participants which did not receive influenza vaccination and did not develop ILI symptoms. The 95% confidence intervals are calculated with the LaMorte Biostatistics tool (Source: medlib.bu.edu/busm/LaMorte.xls). The VE is calculated as (1-RR) x 100%. The analysis was performed for all Dutch participants. In addition, the analysis is stratified for participants of 60 years and older and for participants with a chronic illness.

#### All-cause mortality

In the Netherlands, deaths are notified to municipalities and then reported to 'Statistics Netherlands' (CBS), which collects and monitors all Dutch vital statistics. On a weekly basis, RIVM analyses CBS data that includes date of death, report-delay, age-group and region. The report-delay is the number of days between the date of death and the date that the death notification was received by CBS. Every Thursday the number of reported deaths is checked for the presence of significant excess deaths above the expected mortality level (the baseline), at two different time-lags: deaths reported within one week (43% of all deaths) and deaths reported within two weeks after date of death (93% of all deaths). The baselines and prediction limits are calculated using a Serfling type algorithm on historical mortality data from the five previous years. In the historical data, any weeks with extreme underreporting were removed. Also periods with high excess mortality in winter and summer were removed

as not to influence the calculated baseline with previous outbreaks. When the observed number of deaths exceeds the upper limit of the prediction interval, mortality is considered to be significantly increased (excess deaths being the number of deaths above the baseline).

#### Pneumonia

Pneumonia data are obtained from NIVEL Primary Care Database, in a similar way as acute respiratory infections described above and is defined as the weekly number of patients consulting their GP for pneumonia (ICPC code R81), regardless of being a new or already existing pneumonia episode. The total practice population of participating GP practices serves as the denominator. Pneumonia data are also obtained from nursing homes (SNIV), in which the incidence of pneumonia is based on the weekly number of residents with new clinical diagnosis pneumonia, registered by the SNIV nursing homes. The denominator is the number of observed resident weeks.

#### Virological laboratory surveillance

To describe trends over time in adenovirus, bocavirus, coronavirus, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, para-influenza virus, RSV, rhinovirus and human metapneumovirus (hMPV), we used the weekly number of positive diagnoses reported in the virological laboratory surveillance. The trend for RSV is reported for the respiratory season 2014/2015. Other trends are reported for the calendar year 2014. The RSV season is defined as the period in which the number of RSV-diagnoses is over 20 per week. Number of diagnoses of psittacosis, Q fever and influenza as reported in virologic laboratory surveillance are given in their dedicated chapters.

# Chapter 3 Influenza and Influenza-like illness

## 3.1 Key points

- In the 2014/2015 season, the influenza epidemic lasted 21 weeks, which was the longest since 1970.
- The highest peak in weekly influenza-like illness (ILI) incidence was 16.1/10,000 inhabitants, which was higher than the peak incidence of the four previous seasons. Also the cumulative seasonal ILI incidence (264.8/10,000 inhabitants) was higher compared to the previous four seasons.
- Among nursing home residents, there was a peak in weekly ILI incidence of 72/10,000, which was lower compared to the 2011/2012 and 2012/2013 seasons, but higher than the 2010/2011 and 2013/2014 seasons.
- There were more consultations in primary care for acute respiratory infections (ARI) than in the 2013/2014 season, but fewer than in the 2010/2011 through 2012/2013 seasons.
- Both the weekly ILI incidence and the weekly number of ARI consultations were highest in the o-4 year olds, followed by people aged 65 years or older.
- Subtype A(H<sub>3</sub>N<sub>2</sub>) was the dominating influenza virus in the 2014/2015 epidemic. During the first half A(H<sub>3</sub>N<sub>2</sub>) dominated. In the second half of the epidemic, the proportion of type B viruses (Yamagata-lineage) increased and was dominant in the last weeks of the epidemic.
- Approximately half of the A(H3N2) viruses characterized showed genetic evidence of antigenic difference from the virus included in the 2014/2015 northern hemisphere influenza vaccine. Also the detected B viruses did not show optimal antigenic match with the influenza B virus component of the vaccine. The detected A(H1N1)pdmog viruses were antigenically comparable with the respective component of the vaccine.
- The vaccine effectiveness against laboratory confirmed influenza virus infection was estimated low for the subtype A(H<sub>3</sub>N<sub>2</sub>): -<sub>31</sub>% (95% Cl: -<sub>122</sub>% to 22%), and for the type B viruses: 16% (95% Cl: -81 to 61%), and high for the subtype A(H<sub>1</sub>N<sub>1</sub>)pdmo9: 60% (95% Cl: -<sub>72</sub>% to 91%), however the 95% confidence intervals were very broad.

- No protective effect of influenza vaccination on self-reported ILI in Influenzanet could be demonstrated. However, in the group of Influenzanet participants of 60 years of age and older with chronic underlying illness, vaccination seemed to be protective with a VE of 62% (95% CI 40%-76%).
- Except for one A(H1N1)pdmo9 virus with highly reduced inhibition by oseltamivir, there were no indications of reduced inhibition of influenza A and B viruses by neuraminidase inhibitors oseltamivir and zanamivir.

## 3.2 Background

Influenza is an acute respiratory infection, which is caused by influenza viruses. Most people recover quickly, although an influenza virus infection can cause severe illness in the elderly and people with an underlying condition. There are several types of influenza virus and the viruses constantly change and mutate (antigenic drift). Influenza viruses cause yearly epidemics, mostly in the winter. The major part of the influenza infections in humans are caused by the influenza virus types A and B. Influenza type A viruses are divided into subtypes based on proteins on the surface of the virus: hemagglutinin (HA) and neuraminidase (NA). Many different combinations of HA and NA proteins are possible, for example H1N1 and H3N2. In contrast, influenza type B viruses are divided into lineages based on their HA only. Currently circulating influenza B viruses belong to the lineage B/Yamagata/16/88 or B/Victoria/2/87. Sometimes a new influenza virus subtype is introduced from animal sources in the human population, for which humans have no or low pre-existing immunity (antigenic shift). Therefore, worldwide pandemics can occur, like the A(H1N1)pdmog pandemic in 2009.

## 3.3 Epidemiological situation, season 2014/2015

#### Influenza-like illness (ILI)

From week 49 of 2014 through week 17 of 2015 there was a 21-week lasting influenza epidemic in the Netherlands. The maximum peak of weekly ILI incidence as reported by sentinel GPs was high (16.1/10,000) compared to the previous four seasons. Additionally, the cumulative seasonal incidence was 264.8/10,000 inhabitants, this was also higher compared to the previous four seasons. The ILI incidence was highest among children 4 years of age and younger, followed by the elderly (65 years and older). The ILI incidence of the general population measured by Influenzanet using self-reported symptoms showed the same trend as the medically attended ILI incidence measured by the sentinel GPs. However, the peak of self-reported ILI incidence of 87 per 10,000 participants in the 2014/2015 season, measured by Influenzanet, was not higher compared to all previous four seasons. The peak incidence of the seasons 2010/2011 (104 per 10,000 participants), and 2012/2013 (124 per 10,000 participants) were higher. Among nursing home residents, there was a high peak in weekly ILI incidence of 72/10,000, which was lower compared to the peaks in the 2011/2012 and 2012/2013 seasons, but higher than the peaks in the 2010/2011 and 2013/2014 seasons.

#### Acute respiratory infections (ARI)

Weekly numbers of patients consulting a GP participating in NIVEL Primary Care Database for an acute respiratory infection (excluding pneumonia) peaked in week 2 of 2015 (49 per 10,000 inhabitants). This peak was higher compared to seasons 2011/2012 and 2013/2014, but lower compared to the 2010/2011 and the 2012/2013 seasons. The seasonal cumulative weekly number of GP consultations for ARI was higher (994/10,000 inhabitants) than in 2013/2014, but lower than the 2010/2011 through 2012/2013 seasonal estimates. The weekly number of ARI consultations was highest for children of 4 years of age and younger, followed by people 65 years of age and older.

#### Virus surveillance

In the respiratory season 2014/2015, 389 influenza viruses were detected in 1,244 samples taken by sentinel GPs. In addition, 2,648 positive influenza specimens were submitted by the Dutch laboratories for further investigation, excluding samples taken for sentinel GP surveillance and the SNIV nursing home surveillance. These specimens were mainly from patients aged 65 years or older (65%). Only eight samples were taken from nursing home residents. In the 2014/2015 season, influenza virus type  $A(H_3N_2)$ , type  $A(H_1N_1)$ pdmog and type B viruses (mainly Yamagata lineage) circulated. Type A(H3N2) predominated, but increasing proportions of type B viruses were detected in the last weeks of the epidemic. In the 2014/2015 season, two clades (3C.3b and 3C.2a) of the type A(H3N2) co-circulated in the Netherlands. Type A(H<sub>3</sub>N<sub>2</sub>) viruses of HA genetic clade 3C.3b did not differ from the vaccine strain, however the clade 3C.2a showed evidence of antigenic difference from the A(H3N2) virus included in the 2014/2015 northern hemisphere influenza vaccine. Also the detected B viruses (clade 3) were not optimally antigenic comparable with the B virus component of the vaccine (clade 2). The detected A(H1N1)pdmo9 viruses were antigenic comparable with the A(H1N1)pdmo9 component of the vaccine. Except for one A(H1N1)pdmo9 virus with highly reduced inhibition by oseltamivir, there were no indications of reduced inhibition of influenza A and B viruses by neuraminidase inhibitors oseltamivir and zanamivir in the 2014/2015 season.

#### Vaccine effectiveness

For the 2014/2015 season, we found very broad confidence intervals for the vaccine effectiveness (VE) against laboratory confirmed influenza virus infection. The VE was low for subtype A(H3N2) virus infection (-31%, 95% CI: -122% to 22%) and for the type B virus infection (16%, 95% CI: -81% to 61%), and high for subtype A(H1N1)pdmog virus infection (60%, 95% CI: -72% to 91%). The number of samples does not allow for stratification of VE by age or risk group. There was no difference in incidence of self-reported ILI in Influenzanet between the vaccinated and the non-vaccinated participants and therefore no protective effect of influenza vaccination could be demonstrated. However, in the group of Influenzanet participants of 60 years of age and older with chronic underlying illness, vaccination seemed to be protective with a VE of 62% (95% CI 40%-76%).

## 3.4 Discussion

The 2014/2015 influenza season lasted long, with a higher peak incidence compared to the previous four seasons. In this season, half of the circulating A(H3N2) viruses (of HA genetic clade 3C.2a) showed antigenic differences with the vaccine A(H3N2) virus. Also the B viruses that circulated in higher proportions later in the season were not optimally comparable with the vaccine components. In addition, these viruses were also antigenic drifted compared with the viruses circulating in previous seasons, resulting in reduced immune protection in the general - not vaccinated - population. Both observations might have contributed to the long influenza season. The WHO has adapted the H3N2 component for the 2015/2016 northern hemisphere influenza vaccine; an A/Texas/50/2012 (H3N2)-like virus (clade 3.C1) that was included in the 2014/2015 vaccine is changed into an A/Switzerland/9715293/2013 (H3N2)-like virus (clade 3C.3a) in the 2015/2016 vaccine. The WHO also adapted the B component for the 2015/2016 northern hemisphere influenza vaccine; a B/Massachusetts/2/2012 virus (clade 2) that was included in the 2014/2015 vaccine is changed into a B/Phuket/3073/2013 virus (clade 3) in the 2015/2016 vaccine. The mismatch of clade 3C.2a might have caused the lower vaccine effectiveness for the A(H3N2) and type B viruses, which was also shown in other countries (D'Mello et al., 2015; Pebody et al., 2015; Skowronski et al., 2015). Despite the high number of specimens taken by the sentinel GPs, the influenza vaccine effectiveness estimate still had a broad 95% confidence interval. For the first time, we reported the ILI vaccine effectiveness against self-reported ILI in Influenzanet. The larger number of cases allowed stratification by age. However, to be able to accurately interpret these results, virological endpoints are needed.

In addition to weekly ILI incidence from sentinel GP practices, we report for the first time weekly numbers for all acute respiratory infections including influenza, as measured by a much larger group of GPs participating in NIVEL Primary Care Database. ARI data can be of added value for stratification by smaller age groups or geographic regions in the future. Differences between ARI weekly numbers and ILI incidence can be explained by the contribution of viruses other than influenza in causing ARI.

In the SNIV nursing home surveillance, a low number of specimens were taken from residents with ILI or another acute respiratory infection, despite the higher ILI incidence. To be able to monitor the influenza burden in this patient group, a higher number of specimens are needed. A more active approach to encourage nursing homes to send in specimens might be necessary to improve this surveillance.

## 3.5 Tables and figures

#### ILI incidence: sentinel GP practices

**Figure 3.1** Seasonal cumulative ILI incidence in the respiratory seasons 2010/2011 - 2014/2015 (through week 20 of 2015) (Source: NIVEL Primary Care Database).



Footnote: ILI = influenza-like illness; GP = general practitioner.

**Figure 3.2** Weekly ILI incidence during the respiratory seasons 2010/2011 - 2014/2015 (through week 20 2015) (Source: NIVEL Primary Care Database).



Footnote: ILI = influenza-like illness; GP = general practitioner.



**Figure 3.3** Weekly ILI incidence per age category, for the respiratory season of 2014/2015, week 40 2014 through week 20 2015 (Source: NIVEL Primary Care Database).

Footnote: ILI = influenza-like illness; GP = general practitioner.

#### ILI incidence: in nursing homes

**Figure 3.4** Weekly ILI incidence in SNIV nursing homes in the respiratory season 2014/2015 and trend lines for the respiratory seasons 2010/2011 through 2014/2015 (Source: SNIV, RIVM).



Footnote: Trend lines are based on 5-week moving averages.

No epidemic threshold for this data is calculated. ILI = influenza-like illness; SNIV = national sentinel surveillance network for infectious diseases in nursing homes.

#### ILI incidence: self-reported in Influenzanet

**Figure 3.5** Weekly self-reported ILI incidence, seasons 2010/2011 through 2014/2015 (Source: Influenzanet, the Netherlands: http://www.influenzanet.eu).



Footnote: ILI = influenza-like illness

#### GP consultations for ARI

**Figure 3.6** Seasonal cumulative weekly numbers of patients consulting their GP because of ARI in the respiratory seasons 2010/2011 - 2014/2015 (through week 20) (Source: NIVEL Primary Care Database).



**Footnote:** ARI = acute respiratory infection; GP = general practitioner

**Figure 3.7** Weekly number of patients consulting their GP because of ARI per 10,000 inhabitants in 2014/2015 (through week 20 2015) and the trend lines for 2010/2011 - 2014/2015 (through week 20) (Source: NIVEL Primary Care Database).



**Footnote:** Trend lines indicate a 5-week moving average. ARI = acute respiratory infection; GP = general practitioner

**Figure 3.8** Weekly number of patients consulting their GP because of ARI per 10,000 inhabitants per age category, for the respiratory season of 2014/2015 (through week 20 2015) (Source: NIVEL Primary Care Database).



Footnote: ARI = acute respiratory infection; GP = general practitioner

#### Virus surveillance

**Table 3.1** Characteristics of ILI, URI, and LRI patients, who are sampled by sentinel GPs and by elderly care physicians/nurses in the 2014/2015 season (Source: NIC location RIVM).

Characteristics	NIVEL sentinel GPs			SNIV nursing homes			
	ILI	URI	LRI	ILI	URI	LRI	
	patients	patients	patients	patients	patients	patients	
	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)	
Gender =male	295/631	250/563	25/50	0/7	0/1	0/0	
	(47)	(44)	(50)	(0)	(0)	(0)	
Vaccinated against	146/630	141/563	17/49	6/7	0/1	0/0	
influenza	(23)	(25)	(35)	(86)	(0)	(0)	
Respiratory allergy	74/631	66/563	11/49	0/6	0/1	0/0	
	(12)	(12)	(22)	(0)	(0)	(0)	
Immunosuppression	11/631	9/563	1/49	0/6	0/1	0/0	
	(2)	(2)	(2)	(0)	(0)	(0)	
Chronic disease/	90/631	96/563	15/50	3/7	0/1	0/0	
condition	(14)	(17)	(30)	(43)	(0)	(0)	
Delay in sampling, in daysª	4 (2-7)	5 (3-9)	5 (3-12)	1 (0-2)	_ b	_ b	

**Footnote:** <sup>a</sup> Number of days between the first day of illness and the day of sampling (median, 1<sup>st</sup>, and 3<sup>rd</sup> quartile) <sup>b</sup> For the URI and LRI specimens, which were taken from nursing home residents, no delay in sampling could be calculated because of the low number of specimens.

n = the number in the corresponding group; N = total number of patients, for whom the information was available; SNIV = national sentinel surveillance network for infectious diseases in nursing homes; ILI =influenza-like illness; URI = acute upper respiratory tract infection; LRI = acute lower respiratory tract infection **Figure 3.9** Age distribution of ILI, URI and LRI patients, sampled by NIVEL sentinel GPs, and the ILI cumulative seasonal incidence per age category in the respiratory season 2014/2015 (Source: NIVEL Primary Care Database, NIC location RIVM).



**Footnote:** ILI =influenza-like illness; URI = acute upper respiratory tract infection; LRI = acute lower respiratory tract infection. All sampled SNIV nursing homes residents were aged 65 years or older (n=8).

**Figure 3.10** Number of detected respiratory pathogens among ILI, URI, and LRI patients, who were sampled in the NIVEL GP sentinel surveillance or the SNIV nursing home surveillance in the respiratory season 2014/2015 (Source: NIC location RIVM).



Footnote: ILI =influenza-like illness; URI = acute upper respiratory tract infection; LRI = acute lower respiratory tract infection; SNIV = national sentinel surveillance network for infectious diseases in nursing homes.

**Figure 3.11** Percentage of positive ILI specimens, taken by sentinel GPs, and ILI incidence with epidemic threshold during the respiratory season 2014/2015, displayed by week of sampling (Source: NIVEL Primary Care Database, NIC location RIVM).



Footnote: ILI = influenza-like illness; GP = general practitioner Note: the numbers above the bars are the total number of tested samples.

**Figure 3.12** Subtyping of influenza viruses submitted by Dutch laboratories to the NIC location Erasmus MC during the 2014/2015 season, displayed by week of specimen collection, excluding samples taken for sentinel GP surveillance and the SNIV nursing home surveillance (Source: NIC location Erasmus MC).



**Table 3.2** Genetic characterisation of influenza viruses, week 40 of 2014 through week 20 of2015 (Source: NIC location RIVM, NIC location Erasmus MC)

Virus	Clade Antigenic match with		Source				
(sub)type		2014/2015 vaccine strains <sup>a</sup>	Sentinel GP <sup>b</sup>	Virology labs '	Aruba <sup>b</sup>	Hadj pilgrims <sup>b</sup>	Nursing home outbreak <sup>b</sup>
A(H1N1)pdm09 (n=8)	6b	good	12	2			
A(H3N2) (n=57)	3C.2a	bad	23	3	1	4	4
	3C.3	good			11		
	3C.3a	bad				1	
	3C.3b	good	18	5			
B-Yamagata (n=22)	3	moderate	28	3			

<sup>a</sup> Composition 2014/2015 vaccine: A/California/7/2009 (H1N1)pdm09; A/Texas/50/2012 (H3N2); B/Massachusetts/2/2012 Yamagata lineage

<sup>b</sup> Source NIC location RIVM

<sup>c</sup> Source NIC location Erasmus MC

Footnote: GP = general practitioner

**Figure 3.13** Phylogenetic analysis of A(H3N2) influenza viruses from specimens collected week 40 of 2014 through week 20 of 2015 (Source: NIC location RIVM, NIC location Erasmus MC).



#### Influenza diagnostics in virological laboratories

**Figure 3.14** Weekly number of influenza virus type A and B diagnoses, reported by the virological laboratory surveillance in the period week 1 of 2005 through week 20 of 2015 (Source: Virological laboratory surveillance, RIVM).



**Figure 3.15** Weekly number of influenza virus type A and B diagnoses reported in the virological laboratory surveillance, for the period week 40 2014 through week 20 2015 (Source: Virological laboratory surveillance, RIVM).



#### Antiviral resistance influenza viruses

**Table 3.3** (Highly) reduced inhibition of influenza viruses by neuraminidase inhibitors and M2 ion-channel blockers, 2012/2013 – 2014/2015 (Source: NIC location RIVM, NIC location Erasmus MC)<sup>a</sup>

	2012/2013 n/N (%)	2013/2014 n/N (%)	2014/2015⁵ n/N (%)
Neuraminidase inhibitor		1/150/.114	1/170/.10
A(H1N1)pdm09	3/125 (2) <sup>c</sup>	1/150 (<1) <sup>a</sup>	1/130 (<1) <sup>e</sup>
Influenza virus type	0/156 (0)	2/220 (<1) <sup>f</sup>	0/718 (0)
A(H3N2) Influenza virus type B	0/8 (0)	0/4 (0)	0/26 (0)
M2 ion-channel blocker			
Influenza virus type	10/10 (100)	20/20 (100)	10/10 (100)
A(HTNT)pam09 Influenza virus type A(H3N2)	15/15 (100)	31/31 (100)	48/48 (100)

<sup>a</sup> Combined results obtained with phenotypic (virus isolates) and genotypic (clinical specimens) assays. Season defined as week 40 of the first year to week 39 of the following year.

<sup>b</sup> Preliminary data 2014/2015.

<sup>c</sup> Three viruses with highly reduced inhibition by oseltamivir due to the H257Y amino acid substitution. Two isolated from epidemiological unlinked immunocompromised hospitalised patients treated with oseltamivir. No details available for the third patient.

<sup>d</sup> One clinical specimen with A(H1N1)pdmo9 virus with highly reduced inhibition by oseltamivir due to the H257Y amino acid substitution in the neuraminidase. No patient characteristics or viral exposure data available.

<sup>e</sup> One virus A(H1N1)pdmo9 virus isolate with highly reduced inhibition by oseltamivir from a patient treated with oseltamivir.

<sup>f</sup> Two clinical specimens from two patients with A(H3N2) viruses with mixed 292R and 292K amino acid composition in the neuraminidase; R292K is associated with highly reduced inhibition by oseltamivir and zanamivir. No patient characteristics or viral exposure data available.

#### Influenza vaccine effectiveness

**Figure 3.16** Overview of influenza vaccine effectiveness in the 2014/2015 season, measured in GP sentinel surveillance (against laboratory confirmed influenza virus infection) and in Influenzanet (against not-laboratory confirmed ILI) (Source: NIVEL Primary Care Database, Influenzanet).



Footnote: Green box indicate a point estimate of the VE above zero, red box indicate a point estimate of the VE below zero.

**Table 3.4** Estimation of vaccine effectiveness against laboratory confirmed influenza for all ages, based on influenza positive and influenza negative ILI, URI, and LRI samples, which were collected for the sentinel GP surveillance in the 2014/2015 season.

	Number of used observations	Vaccine effectiveness % (95% CI) <sup>a</sup>
All influenza virus subtypes	692	-11% (-77% to 31%)
Influenza virus type A(H1N1)pdm09	414	60% (-72% to 91%)
Influenza virus type A(H3N2)	577	-31% (-122% to 22%)
Influenza virus type B	475	16% (-81% to 61%)

<sup>a</sup> Corrected for age (spline) and chronic diseases (indications for influenza vaccination).

Footnote: ILI = influenza-like illness; URI = acute upper respiratory tract infection; LRI = acute lower respiratory tract infection; GP = general practitioner; CI = confidence interval
**Table 3.5** Estimation of vaccine effectiveness against ILI for all participants, and stratified for participants 60 years or older, and chronic ill patients based on self-reported ILI to Influenzanet (the Netherlands) in the 2014/2015 season.

	Number of used observations	Vaccine effectiveness % (95% Cl)
All participants	10,867	2.1% (-17% to 18%)
60+ with no chronic illness	1,438	ND <sup>1</sup>
60+ with chronic illness	2,747	62% (40% to 76%)
60- with chronic illness	1,595	-9.7% (-51 to 20%)

**Footnote:** ILI = influenza-like illness; CI = confidence interval.

1 In the risk group '60+ with no chronic illness', the number of vaccinated persons that reported ILI was zero. The VE could therefore not be calculated for this risk group.

# Chapter 4 Community-acquired pneumonia

## 4.1 Key points

- In 2014/2015, the highest peak (8.4 per 10,000 inhabitants) in pneumonia weekly GP consultations was observed since respiratory season 2010/2011.
- After this peak, the number of pneumonia consultations rapidly declined, resulting in overall seasonal cumulative pneumonia estimate for 2014/2015 (through week 20) higher than in 2013/2014 (respectively 153 and 114 per 10,000 inhabitants), but lower than earlier seasons since 2010 (range: 155 to 184 per 10,000 inhabitants).
- The SNIV nursing homes reported the highest peak in the weekly incidence for pneumonia since the 2010/2011 season (108 patients per 10,000 residents).
- The cumulative incidence of pneumonia in these nursing homes in 2014/2015 (1931 per 10,000 residents) was the highest reported since the 2010/2011 season (range: 1172-1444 per 10,000 residents).

## 4.2 Background

Pneumonia is a common clinical disorder of the lower respiratory tract with high morbidity and mortality, especially in elderly. Pneumonia is an inflammatory condition of the lungs affecting primarily the microscopic air sacs known as alveoli. Typical symptoms include a cough, chest pain, fever, and difficulty breathing.

Infection with microorganisms, mainly bacteria and viruses, is the most common cause of community-acquired pneumonia (CAP). Many studies in the Netherlands and other countries show that *Streptococcus pneumoniae* is the predominant aetiological agent of CAP. In daily clinical care, a general practitioner (GP) diagnosis of CAP is based on clinical symptoms, usually without confirming the presence of infiltrative abnormalities on a chest x-ray and without laboratory diagnosis (Verheij et al., 2011). Also in hospital settings, causative pathogens remain unknown in the majority of CAP patients, since microbiological tests are not routinely

used and are usually limited to blood and sputum cultures for bacterial causes. Antibiotic treatment is therefore usually empirical, guided by the clinical presentation of the patient. The pneumonia surveillance in this report includes both the registration of GP consultations because of pneumonia (NIVEL Primary Care Database) and the registration of pneumonia in nursing homes (SNIV).

# 4.3 Epidemiological situation, season 2014/2015

The highest number of weekly pneumonia consultations was reported in week 2 of 2015 (8.4 per 10,000 inhabitants). This was the highest peak since respiratory season 2010/2011 (6.9 per 10,000 in week 2/2012). The seasonal cumulative weekly number of pneumonia consultations in 2014/2015 (through week 20) was higher (153 per 10,000 inhabitants) compared to the previous season (114 per 10,000 inhabitants), but lower compared to the seasons 2010/2011-2012/2013 (range: 155-184 per 10,000 inhabitants). As in previous seasons, the cumulative weekly number of pneumonia consultations was the highest for patients aged 65 years and older.

In the SNIV-nursing homes, the cumulative incidence of pneumonia in 2014/2015 (through week 20: 1931 per 10,000 residents) was higher compared to this incidence in earlier seasons (range: 1172-1444 per 10,000 residents in the seasons 2010/2011 through 2013/2014). The highest incidence was reported in week 4 2015 (108 per 10,000 residents), which was the highest peak since 2010/2011 (93 per 10,000 residents in week 8 2013).

# 4.4 Discussion

In 2014/2015, both GP consultations as nursing homes reported the highest peaks for pneumonia since season 2010/2011. Since pneumonia is a common complication of influenza, these high peaks may be explained by the influenza epidemic, with the highest peak in ILI incidence of the previous five seasons.

Following the peak number of GP consultations for pneumonia in week 2 of 2015, the number of pneumonia consultations rapidly declined. This resulted in overall cumulative number of weekly pneumonia consultations for 2014/2015 higher than in 2013/2014, but lower than earlier seasons since 2010. In the SNIV nursing homes, cumulative incidence of pneumonia was the highest reported since 2010. This is probably explained by the fact that influenza subtype A(H3N2), which is known to have higher burden of disease in the elderly, was the dominating influenza virus in the 2014/2015 season.

Like previous seasons, the number of pneumonia patients in nursing homes is higher than that in general practice. This can largely be explained by the high rate of comorbidity and the high average age of nursing home residents compared the population of GP patients. Additionally, differences in data sampling by the two surveillance systems might contribute to this difference in patient numbers, such as the active case finding in the SNIV surveillance compared to the passive surveillance within the NIVEL Primary Care Database.

## 4.5 Figures

### GP consultations because of pneumonia

**Figure 4.1** Cumulative weekly numbers of patients consulting their GP for pneumonia per 10,000 inhabitants in the seasons 2010/2011 - 2014/2015 (through week 20) (Source: NIVEL Primary Care Database).



**Figure 4.2** Weekly numbers of patients consulting their GP per 10,000 inhabitants in 2014/2015 (through week 20) and the trend lines for 2010/2011 - 2014/2015 (through week 20). (Source: NIVEL Primary Care Database)



Footnote: Trend lines are based on a 5-week moving average.

**Figure 4.3** Cumulative weekly number of GP consultations for pneumonia per 10,000 inhabitants by age group in the seasons 2010/2011 – 2014/2015 (through week 20) (Source: NIVEL Primary Care Database).



## Incidence pneumonia (nursing homes)

**Figure 4.4** Pneumonia incidence in SNIV nursing homes per 10,000 residents in the seasons 2010/2011 - 2014/2015 (through week 20) (Source: SNIV, RIVM).



**Figure 4.5** Weekly incidence of pneumonia patients in SNIV nursing homes per 10,000 residents in 2014/2015 (through week 20) and trend lines for the seasons 2010/2011 – 2014/2015 (through week 20). The trend lines indicate a 5-week moving average (Source: SNIV, RIVM).



# Chapter 5 Weekly mortality monitoring

## 5.1 Key Points

- An average of 2,656 deaths occurred weekly in the Netherlands since 2010.
- Deaths above the expected weekly level are defined as excess deaths: excess mortality was estimated at 8,608 excess deaths occurring during the 21 weeks of the 2014/2015 influenza epidemic (on a total of 65,103 deaths during this period).
- Increased mortality occurred during the entire influenza epidemic (week 49 of 2014 week 17 of 2015).
- Excess mortality during the 2014/2015 influenza epidemic was higher than during the previous four influenza epidemics.
- Excess mortality was observed in the 75+ age group. In some weeks of the influenza epidemic slight increases were also observed in 65-74 year age group.
- Throughout Europe, excess mortality was seen in almost all (14 out of 16) of the European countries participating in EuroMoMo.

# 5.2 Background

The Dutch weekly mortality monitoring system was initiated in August 2009 during the influenza A(H1N1) pandemic. It is a collaboration between the RIVM Centre for Infectious Disease Control (RIVM CIb) and Statistics Netherlands (CBS). The system monitors nation-wide reported number of deaths (population size of 16.9 million in 2015) from all causes, as the cause of death information is not available in real-time.

Weekly, the death notification data is checked for the presence of any excess mortality (i.e. mortality levels above a pre-defined threshold). Excess mortality gives an indication of the impact of any expected and unexpected events that potentially affect population health. Examples of expected events are heat and cold snaps and seasonal influenza epidemics, for

which the morbidity and mortality burden varies due to variations in the circulation of influenza types and strains.

# 5.3 Epidemiological situation, season 2014/2015

Mortality (number of deaths reported within two weeks) was statistically significantly increased from the start of the influenza epidemic in week 49 of 2014 and remained increased during the entire influenza epidemic period until week 17 of 2015. Excess mortality was observed in the 75+ age group. In some weeks of the influenza epidemic slight increases were also observed in 65-74 year age group. There were no cold snaps in the 2014/2015 winter season.

While the previous 2013/2014 season was a very mild influenza season with no excess deaths, in the current season (2014/2015), significant excess deaths were observed from week 49 of 2014 with an estimated 181 excess deaths in that week (there were 2,780 deaths observed against a baseline of 2, 599 – reported within 2 weeks). Excess mortality further increased over time (except for a decrease in excess in week 52 and week 1, coinciding with the two weeks of Christmas school holidays) until excess mortality peaked in week 3 of 2015 with 780 excess deaths in that week (3,430 observed deaths against a baseline of 2,650).

During the 21 weeks of the influenza epidemic and based on deaths reported within three weeks (99% complete), the cumulative total excess mortality (summing up all deaths observed above the expected baseline) was estimated at 8,608 cases (56,495 expected baseline deaths compared to 65,103 deaths reported within three weeks after death). This is higher than the cumulative excess mortality in any of the four previous influenza epidemics (2010/2011 to 2013/2014). However, cumulative excess deaths were also high two years earlier, during the 2012/2013 18-week long influenza epidemic, with an estimated 6,320 excess deaths (of deaths reported within three weeks). Excess deaths were much lower for the other shorter influenza epidemics: 2013/2014 with no excess deaths and 2010/2011 and the 2011/2012 influenza epidemics with 418 and 600 estimated excess deaths respectively (based on numbers of deaths reported within three weeks).

## **Excess Mortality in Europe**

The Netherlands participates in weekly mortality monitoring at a European level in the EuroMoMo collaboration [www.EuroMOMO.eu]. Excess deaths were also significantly higher than in the previous four seasons in 14 of 16 European countries participating in a study of the 2014/2015 winter season. With the EuroMoMo method, an excess above baseline was first observed in England, the Netherlands and Portugal (week 50 using the EuroMoMo algorithm). Excess mortality was observed in the 65+ age group but pooled analyses also showed some excess mortality in the age group of 15–64 years. (Mølbak et al., 2015).

The rise in excess mortality (observed in 65+ year old persons) coincided with increased proportion of influenza detections in the European influenza surveillance schemes with a main predominance of influenza A(H3N2) viruses seen throughout Europe in the current season, though cold snaps and other respiratory infections may also have had an effect ((Mølbak et al., 2015).

## 5.4 Discussion

Weekly mortality monitoring is currently performed using unspecified mortality data. Using cause of death specific data to estimate the impact of influenza circulation on mortality is currently not an option as 1) deaths notified as influenza reflect only a small part of the mortality attributable to influenza since laboratory diagnosis is usually not performed; 2) in the elderly underlying chronic conditions are often recorded as the cause of death on the death certificate; and 3) crude mortality data is available in a much more timely fashion than death-cause-specific data, the latter not being available per week in the Netherlands.

The influenza epidemic often coincides with increases in mortality. It is assumed that influenza plays a role in the increased mortality observed in winter in the Northern Hemisphere (Mølbak et al., 2015). Also other typical winter pathogens can play a role in mortality such as RSV and norovirus (Van Asten et al., 2012). Estimates of influenza attributable deaths have been made using statistical models. Although estimates vary hugely between season (due to influenza virus strain variability) for the Netherlands on average 1389 deaths per year were estimated to be attributable to influenza A and B infections in the 65+ age group (1999-2007) (Van Asten et al., 2012) and on average 1956 yearly deaths (all ages) were estimated to be attributable to influenza-like illness data instead of influenza laboratory diagnoses (Van den Wijngaard et al., 2012).

# 5.5 Tables and figures



**Figure 5.1** Weekly number of deaths from 2010-2015 by date of death at three different levels of notification delay (notified within one, two, and three weeks since date of death).

**Footnote**: Bottom blue line: deaths notified within one week; orange line: notified within two weeks; top green line: notified within three weeks.

**Figure 5.2** Observed and expected ('baseline') weekly number of deaths (reported within two weeks, 93% complete) in 2014/2015 with the influenza epidemic weeks depicted by blue shading.



Footnote: Black line: number of deaths per week reported within two weeks.

Blue line: expected number of deaths (calculated using historical data in which extremes were excluded). Red line: upper prediction limit (based on the 95% confidence interval).

**Table 5.3** Weekly observed, expected, and excess numbers of deaths (of deaths reported within two weeks).

		Observed deaths	Expected deaths	Estimated	Significant
Year	Week*	(reported within 2 weeks)	(baseline)	excess**	excess***
2014	40	2455	2482	- 27	no
2014	41	2576	2505	71	no
2014	42	2542	2526	16	no
2014	43	2592	2544	48	no
2014	44	2506	2560	- 54	no
2014	45	2567	2572	- 5	no
2014	46	2669	2581	88	no
2014	47	2703	2588	115	no
2014	48	2666	2594	72	no
2014	49	2780	2599	181	y es
2014	50	2839	2604	235	y es
2014	51	3047	2610	437	y es
2014	52	2903	2617	286	y es
2015	1	2855	2628	227	y es
2015	2	3230	2638	592	y es
2015	3	3430	2650	780	y es
2015	4	3230	2661	569	y es
2015	5	2900	2671	229	y es
2015	6	3217	2679	538	y es
2015	7	3235	2685	550	y es
2015	8	3241	2687	554	y es
2015	9	3161	2686	475	y es
2015	10	3108	2682	426	y es
2015	11	3181	2674	507	y es
2015	12	3011	2663	348	y es
2015	13	2909	2651	258	y es
2015	14	2806	2637	169	y es
2015	15	2795	2622	173	y es
2015	16	2803	2608	195	y es
2015	17	2767	2594	173	y es
2015	18	2547	2581	- 34	no
2015	19	2676	2569	107	no
2015	20		2557		

\* weeks running from Thursday to Wednesday

\*\* Excess is calculated as: observed - expected (negative numbers indicate that observed mortality was below the baseline). Differences of 1 are due to rounding.

\*\*\* Above the upper limit Prediction Interval (based on 95CI on restricted historical data)

Blue shaded area: number of excess death in weeks with significant excess mortality

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# Chapter 6 Other respiratory infectious diseases

## 6.1 Legionnaires' disease

## **Key points**

- In 2014, 348 cases of confirmed or probable Legionnaires' disease were notified. The number of notifications per 100,000 inhabitants in 2014 was 2.1, which is higher than the incidence in the years 2011 through 2013, but lower than the incidence in 2010.
- The increase in cases was observed in domestic cases only (22% increase compared to 2011-2013). The number of cases with a history of travel abroad was within the range of the previous three years (range 128-138).
- The usual seasonal pattern with most cases reported in the warm months (June-October) was observed.
- The number of domestic cases with onset in June, July, August, and December was higher than expected based on the average of 2009-2013, while less than expected domestic cases with onset in September were observed. This pattern could possibly be explained by the weather, with abundant precipitation in July and August, while September was an exceptionally dry month.
- Travel Associated Legionnaires' disease (TALD) accounted for 45% of notifications. Most TALD were associated with travel abroad (39%) and 6% with domestic travel.
- Like other years only a few genotypic matches were made between patients' clinical isolates and sampled environmental sources. The four matches found in 2014 identified respectively a camper vehicle, potting soil, a sauna and a hospital ward as probable source of infection.

#### **Tables and figures**

**Figure 6.1** Notifications of Legionnaires' disease acquired abroad or acquired in the Netherlands (domestic), by month of disease onset in 2014 and the monthly average from 2009-2013 (source: Osiris).



**Table 6.1** Number of legionellosis notifications in 2010 – 2014, incidence, clinical and epidemiological background, mortality and diagnostics (source: Osiris).

Year of onset disease <sup>a</sup>	2010 n (%)	2011 n (%)	2012 n (%)	2013 n (%)	2014 n (%)
Number of legionellosis notifications <sup>b</sup>	473	314	308	310	370
Confirmed Legionnaires' disease <sup>b</sup>	413	266	265	288	327
Probable Legionnaires' disease <sup>b</sup>	25	27	25	13	21
Possible Legionnaires' disease <sup>c</sup>	28	19	14	7	12
Excluded from analysis <sup>d,e</sup>	7 <sup>d</sup>	2 <sup>d</sup>	4 <sup>d</sup>	2 <sup>d</sup>	10 <sup>d</sup> +12 <sup>e</sup>
n (%) unless otherwise specified	n (%)				
Legionnaires' Disease (LD) (100%)	466 (100)	312 (100)	304 (100)	308 (100)	348 (100)
Incidence (per 100,000 residents)	2,8	1,9	1,8	1,8	2,1
Gender (male)	323 (69)	218 (70)	214 (70)	203 (66)	255 (73)
Median age (Q1-Q3)	62 (53-71)	62 (54-69)	62 (53-72)	63 (54-72)	61 (53-71)
Hospital admission <sup>f</sup>	452 (97)	300 (97)	294 (97)	299 (97)	342 (98)
X-thorax confirmed pneumonia <sup>f</sup>	448 (96)	293 (97)	287 (98)	290 (99)	328 (94)
Deaths	17 (4)	18 (6)	16 (5)	17 (6)	13 (4)

Year of onset disease <sup>a</sup>	2010 n (%)	2011 n (%)	2012 n (%)	2013 n (%)	2014 n (%)
Setting of infection:					
Travel abroad <sup>g</sup>	144 (31)	138 (44)	130 (43)	128 (42)	134 (39)
Domestic (acquired in The Netherlands)	322 (69)	174 (56)	173 <sup>h</sup> (57)	180 (58)	214 (61)
Domestic categories:					
Domestic travel <sup>g</sup>	26 ( 6)	15 ( 5)	17 (6)	12 (4)	20 (6)
Nosocomial	2 (<1)	1 (<1)	1 (<1)	1 (<1)	4 (1)
Healthcare Associated	7 ( 2)	2 (<1)	4 (1)	-	6 (2)
Community Acquired assumed	268 (58)	149 (48)	138 (45)	157 (51)	180 (52)
Community Acquired definite	16(3)	6 (2)	13 (4)	10 (3)	4 (1)
No information/ other	3 (<1)	1 (<1)	1 <sup>h</sup> (<1)	-	-
Diagnostics					
Legionella cultured performed (=yes)	209 (45)	134 (42)	133 (44)	124 (40)	156 (45)
Positive culture	93 (20)	71 (23)	59 (19)	49 (16)	67 (19)
Proportion L.pneumophila sg1 <sup>i</sup>	91%	86%	85%	96%	90%
Positive urine antigen test	400 (86)	253 (81)	257 (85)	283 (92)	314 (90)
Positive PCR	41 (9)	45 (14)	40 (13)	43 (14)	54 (16)
Significant titre rise	14 (3)	12 (4)	6 (2)	5 (2)	5 (1)
Direct immunofluorescence	-	1(<1)	2 (<1)	-	-
Median diagnostic delay in days (Q1-Q3)	6 (4-8)	6 (4-9)	6 (4-9)	6 (4-8)	6 (4-8)
Median notification delay in days (90% notified)	0 (3)	0 (3)	0 (3)	0 (3)	0 (2)

<sup>a</sup> If date of onset disease was unknown, date of diagnosis minus the median diagnostic delay was used to estimate onset. <sup>b</sup> Legionellosis is an infection with *legionella* spp, and is a notifiable disease according to Dutch legislation.

Legionnaires' Disease (LD) is a severe form of legionellosis which includes pneumonia. European definition for surveillance is limited to Legionnaires disease. Confirmed and probable LD according to the European case definition (Commission Implementing Decision, 2012: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2012:262:0001 :0057:EN:PDF).

<sup>c</sup> Single high titre (not specific for *L. pneumophila* serogroup1) as diagnostic confirmation.

<sup>d</sup> Notifications without pneumonia or notifications from non-residents are excluded.

<sup>e</sup> Cases of possible Legionnaires' Disease (only single high titre) are excluded starting from 2014.

<sup>f</sup> Percentage based on the number of patients for which this specific information was available.

<sup>g</sup> Travel Associated Legionnaires Disease (TALD) is defined as travel (including at least one overnight stay) in the period of 2-14 days before disease onset. This differs from the TALD cases that are reported to the surveillance network ELDSNet [http://ecdc.europa.eu/en/activities/surveillance/ELDSNet/Pages/index.aspx] which is limited to travel 2-10 days before onset. In 2014, four cases were included with travel at day 11-14 before onset.

<sup>h</sup> Country of infection was unknown for one case in 2012.

<sup>i</sup> Proportion based on the number of patients for whom clinical specimens (culture of PCR) were available for typing at the reference lab.

## 6.2 Psittacosis

## **Key points**

- In 2014, 41 patients with psittacosis were notified. This number is comparable with the number of notifications in 2013 and 2012.
- Since 2012, the number of notification is substantially lower compared to the years 2008 to 2011.
- Almost all patients who were notified in 2014 were hospitalised (93%). This percentage is higher than in the previous years.
- The percentage of notified cases in which the diagnosis was confirmed with PCR has increased to 66%.
- Genotyping has been performed for most of the cases (89%) for whom diagnostic material is available (i.e. who are diagnosed by PCR).
- Like in 2013, genotype A (known to be associated with parrot-like birds), and genotype B (known to be associated with doves) were most prevalent among patients in 2014.
- Furthermore, the genotyping and supplementary diagnostics revealed some less common (geno)types, namely C. *psittaci* genotype C, E/B, and a new genotype most similar to C. As a result of the national genotyping service a case of C. *caviae* infection (a closely related *Chlamydia* species) was detected.
- In 2014, the Netherlands Food and Consumer Product Safety Authority (NFCPSA) was contacted by a municipal health service for source tracing 45 times. As a result of that, the NFCPSA took samples on 33 possible source locations. 14 locations tested positive for *C. psittaci*.

## Tables and figures



**Figure 6.2** Number of notifications of human psittacosis by year and mode of confirmation of laboratory diagnosis, 2005 through 2014 (Source: Osiris).

**Table 6.2** Demographical, clinical and diagnostic characteristics of notified patients with psittacosis and positive diagnoses in the virological laboratory surveillance, in 2010 up to 2014 (Source: Osiris and virological laboratory surveillance).

N (%), unless otherwise specified	2010	2011	2012	2013	2014
Osiris (notifications):					
Number of notifications <sup>a</sup>	73	70	45	54	41
Incidence (per 100,000 inhabitants)	0.44	0.42	0.27	0.32	0.24
Median age in years (Q1-Q3)	59 (48 – 66)	59 (51 – 70)	57 (45 - 65)	59 (43 – 70)	58 (47 -71)
Sex = male	50 (68.5)	49 (70.0)	28 (62.2)	36 (66.7)	32 (78.1)
Hospitalised	53 (73.6) <sup>b</sup>	52 (74.3)	32 (71.1)	41 (75.9)	38 (92.7)
Deaths	0	2 (2.9)	0	0	1 (2.4)
Infected abroad	3 (4.2) <sup>c</sup>	0 <sup>b</sup>	1 (2.2)	2 (3.7)	1 (2.4)
Notification delay in days median (Q1-Q3) <sup>d</sup>	1 (0 – 7)	1 (0 – 3)	0 (0 - 2)	0 (0 - 2)	0 (0 - 1)
Diagnostics used for notifications:					
Diagnostic delay in days median (Q1-Q3) <sup>e</sup>	32 (21 – 50)	18.5 (11 – 41)	28 (11 – 45)	18 (9 – 29)	12 (7 – 21)
Mode of confirmation of laboratory diagnosis:					
Serological	66 (90.4)	37 (52.9)	32 (71.1)	22 (40.7)	14 (34.2)
'Demonstrating pathogen' (PCR)	7 (9.6)	29 (41.4)	13 (28.9)	32 (59.3)	27 (65.9)
Serological and 'demonstrating pathogen' (PCR)	0	4 (5.7)	0	0	0

N (%), unless otherwise specified	2010	2011	2012	2013	2014
Notified patients for whom diagnostic material for genotyping was received by Orbis MC <sup>f</sup>			3	31 <sup>g</sup> (96.9)	24 (88.9) <sup>h</sup>
Typing outcomes:					
C. psittaci genotype A:			3 (100)	16 (51.6)	9 (37.5)
C. psittaci genotype B:				11 (35.5)	11 (45.8)
C. psittaci genotype C:					1 (4.2)
C. psittaci genotype E/B:					1 (4.2)
New C. <i>psittaci</i> genotype most similar to C (93% homology)					1 (4.2)
Negative for any C. <i>psittaci</i> genotype				2 (6.5)	1 (4.2)
Of which further diagnostics revealed:					
C. caviae				1 (3.2)	1 (4.2)
No outcome				2 (6.5)	
Virological laboratory surveillance:					
Number of positive diagnoses	29	37	23	23	16

Date used for statistics = date of onset of disease or, if missing, date of notification or date of laboratory confirmation (depending on which of these dates was first)

Both notifications with status 'definite' and 'authorised' (i.e. not definite) are included.

- b. Information is missing or reported to be unknown from one notification.
- c. Information is missing or reported to be unknown from two notifications.
- d. Notification delay = number of days between date of laboratory confirmation and date of notification at the Municipal Health Service. Negative delays and delays of more than a year are excluded.
- e. Diagnostic delay = number of days between onset of disease illness and date of laboratory confirmation. Negative delays and delays of more than a year are excluded.
- f. Genotyping of notified patients was started as a pilot project on 27 Augustus 2012. In this project, C. *psittaci* isolates of notified psittacosis patients are genotyped at the OrbisMC in Sittard using ompA genotyping. This method distinguishes nine avian genotypes of C. *psittaci* (A F,E/B, MC56, and WC). Each genotype is relatively bird type specific. This method can furthermore identify C. *abortus*. Genotyping is only possible if diagnosis is based on PCR. In the table, the number of notified patients confirmed with PCR is used for denominator to calculate the percentage.
- g. Apart from the notified patients, diagnostic material from one non-notified patient was submitted for genotyping (the outcome was C. *psittaci* genotype B).
- h. Apart from the notified patients, diagnostic material from four non-notified patients was submitted for genotyping (outcomes were two times C. *psittaci* genotype A and two times C. *psittaci* genotype B).
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# 6.3 Q fever

## **Key points**

- In 2014, 25 patients with acute Q fever were notified. This number is comparable to the number of notifications in 2013 and the years before the outbreak that started in 2007.
- The percentage of hospitalised patients was in 2014 somewhat lower than in 2013 (64% versus 75%).
- The diagnostic delay has decreased from a median of 33 days in 2013 to a median of 24 days in 2014.
- As in previous years, the number of diagnoses of Q fever reported in the laboratory surveillance was considerable higher than the number of notifications. It is unknown whether this is due to under reporting in Osiris or to over reporting in the laboratory surveillance.
- In 2014, one new farm was found positive in the bulk milk monitoring by the Netherlands Food and Consumer Product Safety Authority (NFCPSA). This concerned a milk-producing goat farm in the east of the Netherlands.
- As of 7 April 2015, eight farms (all milk-producing goat farms) still had an 'infected' status based on the bulk milk monitoring. This concerned two farms that were declared infected since 2009, four since 2010, one since 2013 and one since 2014.
- In addition to the bulk milk monitoring, six farms (four sheep and two goat farms) were sampled for *C. burnetii*, following human notifications. All farms tested negative.



## Tables and figures

Figure 6.3 Number of notifications of acute Q fever by year, 2005 through 2014 (Source: Osiris).

**Table 6.3** Demographic, clinical and diagnostic characteristics of notified acute Q fever patients and positive diagnoses in the laboratory surveillance, 2010-2014 (Source: Osiris and virological laboratory surveillance).

N (%), unless otherwise specified	2010	2011	2012	2013	2014
Osiris (notifications):					
Number of notifications <sup>a</sup>	411	77	63	20	25
Of which confirmed	382 (92.9)	73 (94.8)	62 (98.4)	18 (90.0)	21 (84.0)
Of which probable <sup>b</sup>	29 (7.1)	4 (5.2)	1 (1.6)	2 (10.0)	4 (16.0)
Incidence (per 100,000 inhabitants)	2.48	0.46	0.38	0.12	0.15
Median age in years (Q1-Q3)	49 (39 - 59)	50 (40 - 64)	52.0 (43 - 64)	51.5 (38.5 - 64)	55 (39 - 70)
Sex = male	220 (53.5)	49 (63.6)	48 (76.2)	13 (65.0)	20 (80.0)
Hospitalised	96 (23.6) <sup>c</sup>	42 (54.6)	33 (52.4)	15 (75.0)	16 (64.0)
Deaths					
Notified in Osiris	0	1 (1.3)	0	0	0
Total number reported to RIVM <sup>d</sup>	11	5	1	0	0
Infected abroad	8 <sup>e</sup> (2.0)	6 <sup>f</sup> (8.3)	5 <sup>g</sup> (8.1)	3 (15.0)	4 (16.0)
Notification delay in days median (Q1-Q3) <sup>h</sup>	4 (0 - 12.5)	1 (0 - 5.5)	1 (0 - 4.5)	1 (0 - 2.0)	1 (0 - 6.0)
Diagnostic delay in days median (Q1-Q3) <sup>i</sup>	23.0 (13.0 - 25.0)	22.5 (14.5 - 38.5)	27.5 (14.5 - 46.5)	33.0 (8.0 - 52.0)	24.0 (13.0 - 47.0)
Virological Laboratory surveillance:					
Number of positive diagnoses	417	136	83	89	130

<sup>a</sup> Date used for statistics = date of onset of disease or, if missing, date of notification or date of laboratory confirmation (depending on which of these dates was first). Both notifications with status 'definite' and 'authorized' (i.e. not definite) are included.

<sup>b</sup> Confirmed case = a patient with a clinical and laboratory diagnostic confirmation, and a period of maximum ninety days between the laboratory outcome and the day of onset of illness. Probable case = a clinical confirmed case with a single high IgG-titre, or single high complement binding reaction (CBR). The distinction between confirmed and probable notifications has been made since 1 July 2008.

<sup>c</sup>Information on this variable was missing for four patients.

<sup>d</sup> This includes deaths caused by Q fever that are notified in Osiris as well as deaths that are reported to RIVM/LCI outside Osiris.

<sup>e</sup> Information on this variable was missing for nine patients.

<sup>f</sup> Information on this variable was missing for five patients.

<sup>g</sup> Information on this variable was missing for one patient

<sup>h</sup> Notification delay = number of days between date of laboratory confirmation and date of notification at the Municipal Health Service. Negative delays and delays of more than a year are excluded.

<sup>i</sup> Diagnostic delay = number of days between onset of disease illness and date of laboratory confirmation. Negative delays and delays of more than a year are excluded.

# 6.4 Tuberculosis

## **Key points**

- In 2014, 823 TB patients were reported in the Netherlands Tuberculosis Register (NTR) compared to 844 in 2013.
- The incidence rate was 4.9 per 100,000 population.
- 451 TB patients (55%) had pulmonary TB in 2014.
- In 2014, the majority of TB patients were foreign born (73%).
- Like in previous years the largest group of foreign TB patients came from Somalia (n=105), followed by TB patients born in Morocco (n=82) and Eritrea (n=53).
- 49 children (age <15) with TB were reported in 2014 (50 in 2012, 33 in 2013).
- A previous TB episode was recorded for 20 TB patients.
- The proportion of TB-patients in risk groups was 42% in 2014 (37% in 2013). Especially the number of asylum seekers shorter than 2.5 years in the Netherlands was higher (93 in 2014, 44 in 2013). Also the number of immigrants less than 2.5 years in the Netherlands was slightly higher (89 in 2014, 76 in 2013).
- In 2014, six patients with MDR-TB were registered; all were foreign born.
- The proportion TB patients tested for HIV was 51% in 2014.
- The HIV test was positive for 23 TB patients (2.8%).
- In 2013, 91% of all TB patients with rifampicin susceptible tuberculosis completed treatment successfully (85% in 2012).
- Of 14 patients with rifampicin resistant tuberculosis, diagnosed in 2012, ten patients (71%) completed treatment successfully.

## Tables and figures

Figure 6.4 Tuberculosis incidence (per 100,000 population) by postal code area.



	2012	2013	2014
	N (%)	N (%)	N(%)
Number TB patients notified	956	844	823
Incidence per 100,000 population	5.7	5.0	4.9
Mean age (years)	41	42	41
Age <15 years	50 (5.2)	33 (3.9)	49 (6.0)
Age >65 years	150 (15.7)	132 (15.6)	128 (15.6)
Sex ratio (man versus woman)	1.3	1.5	1.6
Foreign born	700 (73)	623 (74)	602 (73)
Residence in 1 of 4 largest cities	326 (34)	270 (32)	239 (29)
Previous episode of TB (treatment)	49 (5.1)	43 (5.1)	20 (2.4)
HIV status known	460 (48)	477 (57)	424 (52)
HIV co-infection	30 (3.1)	17 (2.0)	23 (2.8)
Active case finding	146 (15)	128 (15)	137 (17)
Pulmonary tuberculosis (PTB & EPTB) <sup>a</sup>	497 (52)	458 (54)	451 (55)
Sputum positive PTB <sup>a</sup>	234 (24)	197 (23)	201 (24)
Culture confirmed TB	658 (69)	607 (72)	519 (63)
MDR TB <sup>b,c</sup>	11 (1.7)	17 (2.8)	6 (1.2)
Isoniazid resistance <sup>b</sup>	37 (5.6)	32 (5.3)	32 (6.1)
TB patients in risk groups	387 (40)	312 (37)	343 (42)
-TB contacts	103 (11)	68 (8)	68 (8)
-Immigrant <2.5 yrs. in the Netherlands	103 (11)	76 (9)	89 (11)
-Asylum seeker <2.5 yrs. in the Netherlands	69 (7)	44 (5)	93 (11)
Latent tuberculosis Infection	1,308	1,344	1,244

**Table 6.4** Summary tuberculosis data the Netherlands, 2012, 2013 and 2014.

<sup>a</sup> PTB= pulmonary TB; EPTB= combination of pulmonary and extrapulmonary TB

<sup>b</sup> MDR= Multi Drug Resistant

<sup>c</sup> percentage of culture confirmed TB



Figure 6.5 Number of TB patients and incidence per 100,000 population, 1994-2014.

More detailed information about surveillance of tuberculosis in the Netherlands and the latest surveillance report 'Tuberculose in Nederland, 2013' is available at the RIVM website (only available in Dutch). The next surveillance report 'Tuberculose in Nederland, 2014' will be published in December 2015.

The web-based application TBC-online [http://www.tbc-online.nl] provides information about tuberculosis in the Netherlands. TBC-online offers the opportunity to make tables and graphs of selected variables in the NTR.

# Chapter 7 Virological laboratory surveillance

## 7.1 Key points

- As in previous years RSV, rhinovirus and adenovirus were the most frequently reported positive diagnoses in the virological laboratory surveillance.
- The RSV season, defined as the period of consecutive weeks during which at least 20 positive RSV diagnoses were reported, started in week 49 of 2014 and lasted for a total of 20 weeks.
- The peak in the number of positive RSV diagnoses occurred in week 8 of 2015 (n=177), which is late compared to previous seasons.
- The number of positive RSV diagnoses in 2014/2015 (n=1742; through week 20) was higher than 2013/2014 (n=1645), but lower that the earlier seasons (range: 1838-3075 in 2005/2006-2012/2013; through week 20).
- In the final weeks of 2014 an increasing number of positive *Mycoplasma pneumoniae* diagnoses were reported.
- The number of positive hMPV diagnoses in the first two months of 2014 was low compared to previous years.
- The number of positive parainfluenza virus diagnoses in April-May 2014 was low compared to that period in earlier years.

# 7.2 Discussion

The respiratory surveillance is supplemented by weekly data on the number of positive diagnoses of respiratory pathogens reported by virological laboratories. This virological laboratory surveillance includes data from both primary care and hospitals. Patient's background and information on clinical presentation is lacking in the virological laboratory surveillance, and no distinction can be made between the data from primary care and hospital. It is plausible that patient population and disease severity in primary care and hospital are

different. Therefore, the trends from the virological laboratory surveillance can differ from those in the sentinel practices of the NIVEL Primary Care Database.

Changes in the number of positive diagnoses in the virological laboratory surveillance data are not necessarily caused by actual changes in the incidence of infection, but can also be caused by changes in the policy of testing by the physicians and/or microbiological laboratories. Nevertheless, the virological laboratory surveillance is a valuable source for monitoring longterm trends in the viral diagnostics because of the relatively stable history of this surveillance.

## 7.3 Tables and figures

**Table 7.1** Number of reported positive diagnoses of parainfluenza virus, rhinovirus,Mycoplasma pneumoniae, coronavirus, human metapneumovirus (hMPV) and Chlamydiapneumoniae, bocavirus and adenovirus in the virological laboratory surveillance for the period2005 - 2014.

	Number of positive diagnoses:								
Year:	Parainfluenza	Rhinovirus	Mycoplasma Pneumoniae	<b>Coronavirus</b> <sup>a</sup>	hMPVª	Chlamydia	Bocavirus⁵	<b>Adenovirus</b> <sup>a</sup>	
	virus		Pheumoniae			pheumonide			
2005	512	419	749	-	-	-	-	-	
2006	298	665	588	82	87	40	-	1072	
2007	412	770	626	133	127	40	-	1058	
2008	272	899	458	200	205	30	-	1028	
2009	772	1994	414	192	221	64	-	1325	
2010	528	1906	541	429	419	35	-	1513	
2011	605	1987	917	288	389	43	107	1121	
2012	438	1780	775	307	298	60	136	1060	
2013	632	2045	324	376	467	27	111	1209	
2014	431	2190	435	318	385	20	107	1141	

<sup>a</sup> Coronavirus, hMPV, Chlamydia pneumoniae and adenovirus are registred since 2006.

<sup>b</sup> Bocavirus is registerd since 2011.

**Table 7.2** Number of reported positive diagnoses of respiratory syncytial virus (RSV) in the Virological laboratory surveillance for the period 2005/2006 - 2014/2015.

	Positive diagnoses weeks 40-20 (N)	Positive diagnoses weeks 21-39 (N)	Positive diagnoses weeks 40-39 (N)
2005/2006	2225	19	2244
2006/2007	1939	32	1971
2007/2008	2128	43	2171
2008/2009	2416	35	2451
2009/2010	3075	34	3109
2010/2011	2702	27	2729
2011/2012	1838	51	1889
2012/2013	2197	12	2209
2013/2014	1629	16	1645
2014/2015	1742ª	_b	_b

<sup>a</sup> Data for weeks 40 of 2014 through week 39 of 2015 are preliminary.

<sup>b</sup> Data for weeks 21-39 of 2015 are not yet available.

**Table 7.3** RSV seasonal trends in the virological laboratory surveillance for the period2005/2006 - 2014/2015: season onset, duration and peak.

			Peak:	
	Onset week (week number)	Season duration (N weeks)	Timing (week number-year)	Positive diagnoses (N)
2005/2006	46	17	51-2005	252
2006/2007	43	17	51-2006	225
2007/2008	43	17	51-2007	239
2008/2009	43	22	50-2008	278
2009/2010	45	21	4-2010	297
2010/2011	45	22	3-2011	264
2011/2012	45	23	51-2011	125
2012/2013	46	22	2-2013	182
2013/2014	48	19	6-2014	130
2014/2015	49	20	8-2015	177

**Figure 7.1** Number of weekly reported positive diagnoses of respiratory syncytial virus (RSV) in the virological laboratory surveillance for the period 2005/2006-2014/2015 (through week 20).



#### Weekly number of positive diagnoses

**Figure 7.2** Number of weekly reported positive diagnoses of rhinovirus in the virological laboratory surveillance for the calendar years 2010-2014.







**Figure 7.4** Number of weekly reported positive diagnoses of human metapneumovirus (hMPV) in the virological laboratory surveillance for the calendar years 2010-2014.



**Figure 7.5** Number of weekly reported positive diagnoses of coronavirus in the virological laboratory surveillance for the calendar years 2010-2014.



**Figure 7.6** Number of weekly reported positive diagnoses of parainfluenza virus in the virological laboratory surveillance for the calendar years 2010-2014.







**Figure 7.8** Number of weekly reported positive diagnoses of adenovirus in the virological laboratory surveillance for the calendar years 2010-2014.







# Chapter 8 Emerging infections

## 8.1 MERS-CoV

In 2012, a new type of coronavirus was discovered in the Kingdom of Saudi Arabia (KSA): the Middle East respiratory syndrome corona-virus (MERS-CoV). This virus can cause Acute Respiratory Distress Syndrome (ARDS). Most common symptoms are fever, cough and shortness of breath. There is no evidence of sustained human-to-human transmission. Dromedary camels have been identified as the most probable host, but the mode of transmission has not been identified yet. Between April 2012 and 18 May 2015, 1118 laboratoryconfirmed cases of Middle East Respiratory Syndrome coronavirus (MERS-CoV) including at least 423 related deaths have been reported (WHO 18 May 2015: http://www.who.int/csr/ don/18-may-2015-mers-are/en/). Most MERS-CoV infections occur in Middle East countries, but travel-related cases have been reported in Europe, Asia and the United States.

Since July 2013, MERS-CoV is a group A notifiable disease for hospital care providers in the Netherlands, meaning that a specialist is obliged to immediately report a patient suspected of being infected with the MERS-CoV to the Municipal Health Service [http://www.rivm.nl/en/Topics/M/MERS\_Coronavirus]. This enables the Municipal Health Service to take immediate appropriate action aimed at preventing further transmission by tracing and follow-up of potential contacts. In case of suspected MERS-CoV infection in the Netherlands, diagnostics are performed at RIVM (Clb/IDS), with confirmation by ErasmusMC.

In 2014, 76 suspect cases were tested for MERS-CoV infection and four suspect cases in 2015 (through March). In May 2014 two suspected cases were found positive. These two Dutch residents had returned from a pilgrimage to Medina and Mecca, KSA (Kraaij-Dirkzwager et al., 2014). They had travelled with a group of 29 other people. Contact tracing of these patients followed and 131 contacts were tested for MERS-CoV infection, of which none were positive. An epidemiological assessment of the travel group was conducted to identify likely source(s) of infection and presence of potential risk factors. Although the exact source of infection

remained difficult to identify, exposure to MERS-CoV during a hospital visit was considered a likely source of infection for Case 1. For Case 2, the most likely source could not be determined. This study revealed the complexity of MERS-CoV outbreak investigations wherein multiple potential exposures to MERS-CoV were reported such as healthcare visits, exposure to camels, and exposure to untreated food products (Fanoy et al., 2014).

## 8.2 Animal influenza viruses

### Situation world-wide

Influenza A viruses are found in many different animals, including ducks, chickens, pigs. Sometimes these animal viruses infect humans. World-wide, sporadic human infections with swine influenza viruses, like A(H1N1)v, A(H1N2)v, and A(H3N2)v were reported to the WHO in 2014 and 2015. Additionally, sporadic human infections with avian influenza viruses in the same years, like A(H5N6), A(H9N2), A(H10N8), were reported to the WHO. Of the human animal influenza cases in 2014 and 2015, most were caused by either A(H5N1) or A(H7N9).

### Influenza A(H5N1)

Highly pathogenic avian influenza A(H5N1) virus is highly contagious among birds, and potentially deadly to birds. Infections in birds with this avian flu virus occurred most in the South-East Asia Region. Though relatively rare, sporadic human infections with this virus have occurred and caused serious illness and death, mostly in the South-East Asia Region, Middle East Region and in the African Region. From 2003 onwards, 840 human cases and 447 deaths have been reported in humans, most of which had had contact with poultry or poultry markets. In Egypt, the number of laboratory-confirmed human cases of avian influenza A(H5N1) virus infection with onset of illness sharply increased since December 2014, totalling 132 cases for the first four months of 2015 combined, which is higher than in earlier years. Compared to previously circulating avian flu, major genetic changes (circulating either in humans of in animals) were not detected in the 2014 and 2015 strains, but further in depth analysis is on-going. Continuous increase of virus circulation in backyard poultry and exposure to infected poultry are most probably contributing to the recently observed increase in human cases. No evidence of sustained person-to-person spread of A(H5N1) has been found.

#### Influenza A(H7N9)

A low pathogenic influenza virus A(H7N9) for poultry also causes infections in humans. Human infections with a new avian influenza A (H7N9) virus were first reported in China in March 2013. Since then through 18 May 2015, 663 influenza A(H7N9) infections and 263 deaths were reported to the WHO by authorities in mainland China, Hong Kong, Taiwan, Malaysia, and Canada. Most human infections occurred in Eastern China. No evidence of sustained personto-person spread of A(H7N9) has been found.
#### Situation in the Netherlands

In the Netherlands, human infections with an animal influenza virus, like A(H5N1), A(H7N9), and A(H3N2)v is a notifiable disease group B1, meaning that the attending physician and the laboratory are obliged to report a patient suspected of being infected with an animal influenza virus to the Municipal Health Service within 24 hours. This makes it possible to implement legal measures if necessary, such as forced hospitalisation or isolation, forced investigation, and prohibition of profession as possible options for containment. In case of suspicion of human infection, diagnostics are performed by NIC location RIVM with confirmation by NIC location ErasmusMC. At the end of 2014, five poultry farms were infected with the high pathogenic avian influenza virus type A(H5N8). In the context of outbreaks of avian influenza on poultry farms in the Netherlands, and in the context of returning travellers from countries where possible exposure to avian influenza viruses occurred, seven patients with respiratory illness from 2014 and none from 2015 (through May 2015) were tested for avian influenza virus infection. None of them had an infection with avian influenza virus. However, two patients had an infection with human influenza virus, one with type B and one with A(H1N1)pdmog influenza virus. Both patients were exposed to poultry possibly infected with avian influenza, when they visited mainland China. The other five patients with exposure to infected poultry in the Netherlands were negative for influenza virus.

#### 8.3 Enterovirus D68

Human enterovirus D68 (EV-D68) is generally associated with mild to severe respiratory infections. However, in 2014, case reports with EV-D68 human infections suggested an association with serious neurological complaints, like acute flaccid paralysis of arms and legs. A causal relation has not been proven, since no direct evidence of EV-D68 infection in the central nervous system has been found. In the summer of 2014, this virus caused a large outbreak of acute respiratory infections with shortness of breath in the USA. The outbreak caused a high hospitalisation rate. A few children died and a number of children were affected with acute flaccid paralysis (CDC website: http://www.cdc.gov/ncird/investigation/viral/ sep2014/investigation.html).

In 2010, an EV-D68 outbreak of acute respiratory infections was detected in the NIVEL primary care sentinel surveillance in the Netherlands. (Meijer et al., 2012) Since that outbreak, the RIVM monitors this virus with two surveillance systems: the NIVEL Primary Care sentinel surveillance for acute respiratory infections and the enterovirus surveillance in the context of polio eradication. After the outbreak in 2010, EV-D68 continued to circulate in a seasonal pattern. Like in the USA, the detections of EV-D68 in the Netherlands generally start in the late summer and continue until the early winter, with a total of 33 infections detected in both surveillance systems together in 2014. In the reported patients only acute respiratory infections were reported and no neurological complaints.

#### 8.4 Tables and figures

**Table 8.1** International summary of the total number human infections with Middle EastRespiratory Syndrome coronavirus (MERS-CoV) and animal influenza viruses A(H5N1),A(H7N9), and A(H3N2)v in 2012, 2013, 2014, and 2015 (through to week 20 of 2015).

Infectious disease	Total number of human infections (deaths) <sup>a,b</sup>				
	2012	2013	2014	2015	Total <sup>g</sup>
MERS-CoV <sup>c</sup>	9 (5)	172 (72)	773 (275)	164 (71)	1118 (423)
Influenza A(H5N1) <sup>d</sup>	32 (20)	39 (25)	52 (22)	139 (40)	840 (447)
Influenza A(H7N9) <sup>e</sup>	-	157 (46)	337 (119)	169 (98)	663 (263)
Influenza A(H3N2)v <sup>f</sup>	309 (1)	19 (0)	3 (0)	0 (0)	343 (1)

<sup>a</sup> Where the date of onset is unknown, the date of reporting has been used.

<sup>b</sup> The number of deaths might be higher, as not all deaths might be reported retrospectively.

<sup>c</sup> Reported through 18 May 2015 (source: http://www.who.int/csr/don/en/)

<sup>d</sup> Reported through 18 May 2015 (source: http://www.who.int/influenza/human\_animal\_interface/H5N1\_cumulative\_ table\_archives/en/).

<sup>e</sup> Reported through 18 May 2015 (source: http://www.who.int/csr/don/en/ and http://www.who.int/influenza/ human\_animal\_interface/HAI\_Risk\_Assessment/en/)

<sup>f</sup> Reported through 18 May 2015 (source: http://www.cdc.gov/flu/swineflu/hʒnzv-case-count.htm).

<sup>g</sup> Total number is calculated by including the numbers before 2012.



**Figure 8.1** Number of EV-D68 detections in the NIVEL Primary Care sentinel surveillance for acute respiratory infections and the enterovirus surveillance in 2014 in the Netherlands.

Footnote: EV-D68 = enterovirus D68

# Chapter 9 General discussion and conclusion

The most striking observation from the 2014/2015 respiratory season was the exceptionally long duration of the influenza epidemic. The incidence of influenza-like illness (ILI) as reported by sentinel general practitioners (GPs) was above the epidemic threshold of 5.1 per 10,000 inhabitants from week 49 of 2014 to week 17 of 2015. During this 21-week period influenza virus was detected in nose swabs and throat swabs taken from ILI patients. This was the longest lasting influenza epidemic since the start of the national ILI registration in 1970. The peak ILI incidence (16.1 per 10,000 inhabitants) did not reach the level of 20 ILI cases per 10,000 inhabitants, which is defined as the level above which the epidemic is 'moderate'. The overall impact of the 2014/2015 epidemic was, however, considerable. Currently, we have no real-time data on numbers of severe acute respiratory infections (SARI) patients admitted to the hospital, which could serve as a proxy for severe influenza infections. However, in January 2015 the pneumonia surveillance in GP as well as nursing homes showed highest peaks for pneumonia since the winter of 2010/2011. Moreover, the mortality monitoring system that is in place, showed excess mortality during the entire duration of the influenza epidemic with a total number of excess deaths of 8,608. A large proportion of these deaths is likely to be associated with influenza. Interestingly, the number of excess deaths during this regular influenza season is higher than the number of excess deaths from pandemic influenza in the 'base scenario' of the Dutch National Risk Assessment (Mennen, 2012).

During most of the epidemic, influenza A(H3N2) dominated in swabs from ILI patients in primary care sentinel surveillance as well as in non-sentinel swabs that mostly originate from hospitalised patients. The circulating A(H3N2) virus was a drift variant with genetic and antigenic differences compared to the A(H3N2) vaccine virus. Towards the end of the season influenza B dominated. Robust estimates of vaccine effectiveness specific for the Netherlands are not available because the number of samples from sentinel surveillance is too low. Increasing the number of samples from ILI patients in sentinel surveillance would be costly and not essential for the primary objective of monitoring the circulation of influenza viruses in the general population, and obtaining virus isolates for genetic and antigenic characterization. For the purpose of estimating vaccine effectiveness as early in the season as possible, RIVM and NIVEL therefore participate in

the European I-MOVE (influenza monitoring vaccine effectiveness) network so that results from individual countries can be pooled and robust estimates can be obtained (Valenciano et al., 2012; Kissling et al., 2014). Reports from other European countries show low vaccine effectiveness (Pebody et al., 2015). Except for one A(H1N1)pdmo9 virus with highly reduced inhibition by oseltamivir, there were no indications of reduced inhibition of influenza A and B viruses by neuraminidase inhibitors oseltamivir and zanamivir. The lower than expected vaccine effectiveness prompted public health agencies from some countries, but not in the Netherlands, to advice physicians a liberal prescribing of antiviral medication. This gave rise to some controversy such as reflected in different opinions of the US Centers for Disease Control and Food and Drug Administration (Lenzer, 2015).

For the present report we used pneumonia data that were extracted weekly from information systems of a much larger group of GPs than those participating in sentinel surveillance. Sentinel GPs in the Netherlands also actively record pneumonia patients. In January 2015 a pilot study was started in which aetiology of community-acquired pneumonia patients in primary care is assessed through urinary antigen tests for *Streptococcus pneumoniae* and *Legionella pneumophila*. Results are not yet available. Despite the exceptionally long influenza epidemic, consultations for acute respiratory infections (ARI), that may include infections caused by many different viruses, remained at a relatively low level. Research on possible viral interactions is on-going.

Swabs from sentinel GPs are analysed for influenza virus, RSV, rhinovirus and enterovirus. For other respiratory pathogens, the only information available is the weekly number of positive tests in a number of virological laboratories. Although clinical and patient information is lacking, these weekly reports are an important component of respiratory surveillance and have been used extensively in studies that required data on circulating respiratory pathogens (Van Asten et al., 2012). Some of the laboratories have started reporting the number of laboratory tests performed. This provides a denominator for the positive test results, thereby greatly increasing the value for surveillance. Hopefully, this additional information can be used for the 2015/2016 surveillance report.

As already mentioned, this season we still had no real time insight in severe influenza infections, as there is no surveillance system covering severe acute respiratory infections (SARI). However, next season the feasibility of setting up of such a SARI surveillance system will be investigated in collaboration with two Dutch hospitals. Also, the use of intensive care data for SARI surveillance (NICE registration (Koetsier et al. 2013)) is being investigated.

Notifiable infectious disease presenting as pneumonia are underreported because in most cases of community acquired pneumonia that are managed in primary care, no specific diagnostic laboratory tests will be done. Almost all patients who were notified with psittacosis in 2014 were hospitalised (93%). This percentage is higher than in the previous years. It could be speculated that less diagnostics for psittacosis is performed for milder cases of community acquired pneumonia and therefore more cases are missed compared to previous years.

As in previous years, the number of diagnoses of Q fever reported in the virological laboratory surveillance was considerable higher than the number of notifications. In the virological laboratory surveillance no clinical and patient information is available. Therefore, it is unknown what the reason for this difference is. Probably, many cases with a positive laboratory diagnosis do not fulfil the notification criteria and are therefore not notified in Osiris as acute Q fever cases.

Response to suspected MERS-CoV cases was evaluated in 2014. Positive points were good interdisciplinary collaboration, good communication and clear division of tasks. A constraint was the contact investigation. Overall, the response structure appeared to be well organized. As far as we know, the outbreaks of highly pathogenic avian influenza A(H5N8) on poultry farms in 2014, did not result in any human infections.

An overall objective of RIVM is to make as much surveillance information as possible publicly available. The RIVM website already provides weekly updated information on influenza trends and all-cause mortality. Information on tuberculosis is updated every quarter, data on psittacosis, and Q fever monthly, or more frequently if indicated, such as during the 2007-2010 Q fever epidemic. For some subjects including legionellosis and pneumonia this has to be further developed.

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#### Abbreviations

ARDS	Acute Respiratory Distress Syndrome
ARI	acute respiratory infections
BEL	Legionella Source Identification Unit
	(NL: Bronopsporingseenheid legionellapneumonie)
CAP	community-acquired pneumonia
CBR	complement binding reaction
CBS	Statistics Netherlands
	(NL: Centraal Bureau voor de Statistiek)
Clb	Centre for Infectious Disease Control (Centre of RIVM)
	(NL: Centrum Infectieziektebestrijding)
CIb/EPI	Centre for Infectious Diseases, Epidemiology and Surveillance of CIb
	(NL: Centrum Epidemiologie en Surveillance van Infectieziekten)
CIb/IDS	Centre for Infectious Disease Research, Diagnostics and Screening of Clb
	(NL: Centrum Infectieziekteonderzoek, Diagnostiek en Screening)
CIb/LCI	National Coordination Centre for Communicable Disease Control of CIb
	(NL: Landelijke Coördinatie Infectieziektebestrijding)
ECDC	European Centre for Disease Prevention and Control
EISN	European Influenza Surveillance Network
ELDSNet	European Legionnaires Disease Surveillance Network
EPTB	combination of pulmonary and extrapulmonary TB
ETB	extrapulmonary tuberculosis
EV-D68	Human enterovirus D68
GGD	Municipal Health Services
	(NL: Gemeentelijke Gezondheidsdienst)
GP	general practitioner
HIV	Human Immunodeficiency Virus
hMPV	human metapneumovirus
ILI	influenza-like illness
LD	Legionnaires' Disease
LRI	lower respiratory tract infections
LTBI	latent tuberculosis infection
MDR-TB	Multi Drug Resistant tuberculosis
MERS-CoV	Middle East Respiratory Syndrome Coronavirus
NFCPSA	the Netherlands Food and Consumer Product Safety Authority
	(NL: Nederlandse Voedsel- en Waren Autoriteit: NVWA)
NIC	National Influenza Centre
NIVEL	Netherlands institute for health services research
	(NL: Nederlands instituut voor onderzoek van de gezondheidszorg)
NTR	Dutch Tuberculosis Registry
NVMM	Dutch Society for Medical Microbiology
PCR	Polymerase Chain Reaction
ЫВ	pulmonary tuberculosis

- RIVM National Institute for Public Health and the Environment
- RSV respiratory syncytial virus
- SARI severe acute respiratory infections
- SNIV national sentinel surveillance network for infectious diseases in nursing homes
- TALD Travel Associated Legionnaires' disease
- URI upper respiratory tract infections
- VE vaccine effectiveness
- WHO World Health Organization

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