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 2019/2020*

Annual report Surveillance of influenza and other respiratory infections in the Netherlands: *winter 2019/2020*

D.F.M. Reukers[1]
L. van Asten[1]
P.S. Brandsema[1]
F. Dijkstra[1]
J.M.T. Hendriksen[2]
W. van der Hoek[1]
M. Hooiveld[1,2]
M.M.A. de Lange[1]
F.A. Niessen[1]
A.C. Teirlinck[1]
A. Meijer[3]
A.B. van Gageldonk-Lafeber[1]

[1] Infectious Diseases, Epidemiology and Surveillance, Centre for Infectious Disease Control, National Institute for Public Health and the Environment (RIVM), Bilthoven
[2] Nivel (Netherlands institute for health services research), Utrecht
[3] Infectious Disease Research, Diagnostics and Laboratory Surveillance, Centre for Infectious Disease Control, National Institute for Public Health and the Environment (RIVM), Bilthoven

Colophon

RIVM report number: 2020-0177

DOI 10.21945/RIVM-2020-0177

Contact:
Daphne Reukers: Daphne.Reukers@rivm.nl

Cover picture: Thinkstock

This investigation has been performed by order and for the account of the Ministry of Health, Welfare and Sport (VWS), within the framework of the project 'Epidemiologie en surveillance van Respiratoire infecties', project number V/150207/20/RI, and 'Labfunctie Respiratoire Virologie', project number V/150304/20/RE.

Report prepared by: Centre for Infectious Disease Control, National Institute for Public Health and the Environment with contributions of:
National Influenza Centre - Erasmus Medical Centre
Netherlands institute for health services research (Nivel)
Statistics Netherlands (CBS)
Legionella Source Identification Unit (BEL) at Regional Public Health Laboratory Kennemerland
Jeroen Bosch hospital (JBZ)

A publication by the
National Institute for Public Health and the Environment (RIVM)
P.O. Box 1
3720 BA Bilthoven
The Netherlands
www.rivm.nl/en

Synopsis

Surveillance of influenza and other respiratory infections: Winter 2019/2020

Influenza

The flu epidemic in the winter of 2019/2020 was mild and lasted for 5 weeks. That is shorter than the ten-week average over the past 25 years. The last two weeks of the flu epidemic, the first half of March 2020, coincided with the start of the COVID-19 epidemic in the Netherlands. An estimated 400,000 people have had the flu between October 2019 and May 2020. About 74,000 people went to their general practitioner with flu-like illness.

People have mainly become ill with type A influenza virus. During the influenza epidemic, 600 more people died than would normally be the case. This "excess mortality" is probably related to influenza. Influenza vaccination prevented 48 percent of vaccinated persons from getting the flu. The effectiveness of the vaccine is about the same as in previous flu seasons.

COVID-19 epidemic in the Netherlands

This report includes the COVID-19 data for the duration of the flu season, up to and including May 17. The first COVID-19 patient in the Netherlands was confirmed on February 27, 2020. Since then, many people have been infected with the new coronavirus (SARS-CoV-2) that causes the disease COVID-19. Between February 27 and May 17, 2020, the Public Health Services reported 43,993 people with COVID-19, with a peak of 7,794 reports in the week of April 6. During this first wave, 11,095 patients were hospitalised and 9,600 more people died than expected in this period.

Notifiable respiratory infections

Some respiratory infections have to be reported to the Public Health Services in order to prevent any further spread. The number of reports of psittacosis rose sharply in 2019 to 91, the highest number since 2010. The number of reported cases of legionella (566), tuberculosis (759) and Q fever (18) remained stable. Q fever, psittacosis and legionella usually manifest themselves in the form of pneumonia. The actual numbers are higher than the reported. People with pneumonia are often not tested, so the causative pathogen remains unknown.

Keywords: respiratory infections, flu, influenza, RS virus, pneumonia, SARS-CoV-2, COVID-19, coronavirus, legionella, Parrot fever, psittacosis, Q fever, tuberculosis

Publiekssamenvatting

Surveillance van griep en andere luchtweginfecties: winter 2019/2020

Griepepidemie

De griepepidemie in de winter van 2019/2020 was mild en duurde 5 weken. Dat is korter dan het gemiddelde van tien weken in de afgelopen 25 jaar. De laatste twee weken van de griepepidemie, de eerste helft van maart 2020, vielen samen met het begin van de COVID-19-epidemie in Nederland. Naar schatting hebben tussen oktober 2019 en mei 2020 400.000 mensen de griep gehad. Ongeveer 74.000 mensen gingen naar de huisarts met griepachtige klachten.
Mensen zijn vooral ziek geworden van het type A-griepvirus. Tijdens de epidemie stierven er 600 mensen meer dan verwacht in deze periode. Deze 'oversterfte' hangt waarschijnlijk samen met de griep. Mensen die een griepprik hebben gekregen, hadden in het griepseizoen 48 procent minder kans om griep te krijgen. De effectiviteit van het vaccin is ongeveer hetzelfde als in vorige griepseizoenen.

COVID-19 epidemie in Nederland

In deze rapportage zijn de gegevens over COVID-19 meegenomen voor de duur van het griepseizoen, tot en met 17 mei. Op 27 februari 2020 is de eerste COVID-19-patiënt in Nederland bevestigd. Sindsdien zijn veel mensen besmet met het nieuwe coronavirus (SARS-CoV-2) dat de ziekte COVID-19 veroorzaakt. Tussen 27 februari en 17 mei 2020 heeft de GGD 43.993 mensen met COVID-19 gemeld, met een piek van 7794 meldingen in de week van 6 april. In deze eerste golf zijn 11.095 patiënten opgenomen in het ziekenhuis en zijn er 9600 mensen meer overleden dan normaal.

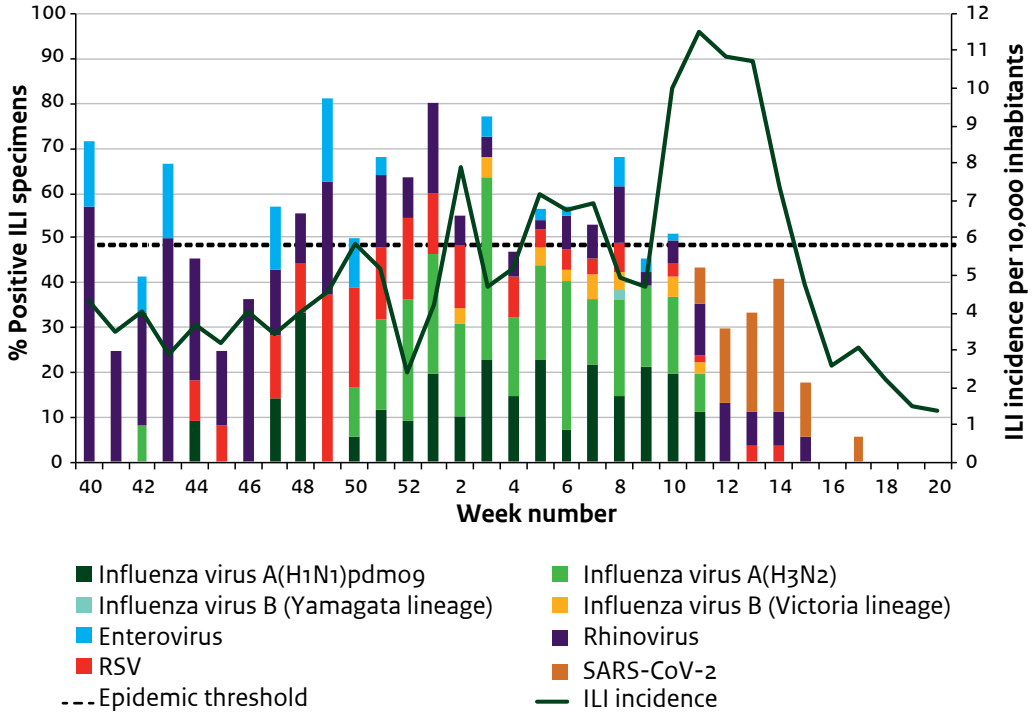
Meldingsplichtige luchtweginfecties

Sommige luchtweginfecties moeten bij de GGD worden gemeld. De GGD kan ze dan intensief volgen en als het nodig is op tijd actie nemen om te voorkomen dat ze zich verder verspreiden. Het aantal meldingen van psittacose is in 2019 sterk gestegen naar 91, het hoogste aantal sinds 2010. Het aantal gemelde gevallen van legionella (566) tuberculose (759) en Q-koorts (18) bleef stabiel. Q-koorts, psittacose en legionella uiten zich meestal in de vorm van longontstekingen. De werkelijke aantallen liggen hoger dan de gemelde. Mensen met een longontsteking worden vaak niet getest, waardoor de ziekteverwekker niet bekend is.

Kernwoorden: luchtweginfecties, griep, influenza, RS-virus, longontsteking, pneumonie, SARS-CoV-2, COVID-19, coronavirus, legionella, papegaaienziekte, psittacose, Q-koorts, tuberculose

Influenza like-illness surveillance at a glance

Figure 1 Percentage of specimens from patients with influenza-like illness positive for influenza virus, RSV, rhinovirus, enterovirus or SARS-CoV-2 taken by sentinel GPs, and ILI incidence with epidemic threshold during the 2019/2020 respiratory season (week 40 of 2019 through week 20 of 2020), displayed by week of sampling (Source: Nivel Primary Care Database; RIVM).



Footnote: ILI = influenza-like illness; GP = general practitioner; RSV = respiratory synsytial virus; SARS-CoV-2 = severe acute respiratory coronavirus 2
The numbers above the bars are the total number of tested specimens.

Contents

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 that is meant for policy-makers, epidemiologists, microbiologists, staff of public health services and others working or interested in the field of respiratory infectious diseases. The national surveillance of respiratory infectious diseases considered in this report is the responsibility of the Department for Respiratory Infections (RES) at the Centre for Infectious Diseases, Epidemiology and Surveillance (EPI), a part of the Centre for Infectious Disease Control (CIb) 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 describes the different syndromic surveillance systems used: influenza-like illness (ILI), acute respiratory infections (ARI), pneumonia, severe acute respiratory infections (SARI) and mortality. The term 'influenza-like illness' is based on the notion that this clinical syndrome may be caused by influenza virus, but also by a range of other pathogens. The causative pathogen remains unknown in the majority of patients with respiratory infections, because most infections are not laboratory-confirmed but based on clinical diagnosis only. This surveillance is important because of the high burden of disease in terms of patient numbers, mortality and the impact on the health care system. 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 the Nivel Primary Care Database is assessed by the National Influenza Centre (NIC), location RIVM (at the Centre for Infectious Disease Research, Diagnostics and Laboratory Surveillance(IDS) of CIb). Laboratory-confirmed influenza cases reported by hospital and peripheral laboratories are monitored at NIC, location Erasmus Medical Centre. As real-time, cause-specific data on deaths are not available, mortality surveillance is based on all-cause mortality, using weekly data from Statistics Netherlands (CBS). Chapters 3 and 4 show the surveillance data for influenza virus

infection and respiratory syncytial virus (RSV) infection. Since the respiratory syndromes as well as influenza virus and RS-virus infections show winter seasonality, data in the Chapters 2-4 are reported for the 2019/2020 respiratory season, i.e. week 40 of 2019 through week 20 of 2020.

Chapter 5 provides results of the surveillance of the notifiable respiratory infectious diseases legionellosis, psittacosis, Q fever, tuberculosis, animal influenza virus infections and MERS-CoV infections for the 2019 calendar year. In the present edition of the report, results of the surveillance of a new notifiable respiratory infectious disease, COVID-19, were added for the 2019/2020 respiratory season up to week 20 2020. Q fever and psittacosis will be described in greater detail in the report 'State of Zoonotic Diseases 2019' (Vlaanderen, Cuperus et al. 2020). More details on tuberculosis will be described in the next surveillance report on tuberculosis, (Slump, van Beurden et al. 2020). Other notifiable respiratory diseases that are targeted by the National Immunization Programme, such as pertussis and invasive pneumococcal disease, are described in the annual RIVM publication 'The National Immunization Programme in the Netherlands' and are not reported here.

Chapter 6 describes diagnoses of respiratory infections reported in the virological laboratory surveillance for the 2019 calendar year. Chapter 7 provides an update on the burden of disease from five respiratory diseases: influenza, legionellosis, tuberculosis, Q fever and psittacosis. In Chapter 8, the main findings of this report are discussed and put into perspective. Finally, Chapter 9 describes the data sources and methods used for surveillance of the different diseases or pathogens.

1.2 Collaborations: national and international

For the surveillance of respiratory infectious diseases, the CIb collaborates with many partners: Nivel (Netherlands institute for health services research), including the network of sentinel general practices; the surveillance network in nursing homes (SNIV); the National Influenza Centre (NIC), location Erasmus MC; the Regional Public Health Laboratory Kennemerland, Haarlem (national reference laboratory for legionellosis); and Statistics Netherlands (CBS). The collaboration with the Public 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 with the Zuyderland Medical Centre in Sittard. The laboratories that report the data for the virological laboratory surveillance are all members of the Working Group for Clinical Virology of the Dutch Society for Medical Microbiology (NVMM). SARI surveillance has been piloted previously at Jeroen Bosch hospital (JBZ), Leiden University Medical Centre (LUMC) and University Medical Centre Utrecht (UMC Utrecht). We are currently developing a more automated SARI surveillance system in these and other hospitals.

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. COVID-19 data is reported weekly to the ECDC. Moreover, the RIVM (CIb/IDS and CIb/EPI) participates together with Nivel and Erasmus MC in the European Influenza Surveillance Network (EISN) of ECDC. The Dutch data are reported weekly in the joint ECDC/WHO regional office for Europe FluNews Europe Bulletin, and in FluNet and FLuID of the WHO (World Health Organization) headquarters in Geneva. All-cause mortality is reported weekly to EuroMoMo, a European consortium that weekly publishes the mortality data of 19 European countries. For the purpose of estimating vaccine effectiveness at a European level, RIVM and Nivel participate in the European I-MOVE (influenza monitoring vaccine effectiveness) network.

Chapter 2
Syndrome surveillance

2.1 Acute respiratory infections (ARI) and influenza-like illness (ILI)

Authors: Marit de Lange, Adam Meijer, Mariëtte Hooiveld
Contributors: Daphne Reukers, Anne Teirlinck, Marjolein Korndewal, Janneke Hendriksen

2.1.1 Key points

- In the 2019/2020 winter season, the influenza epidemic lasted for 5 weeks (week 5 through week 7 and week 10 and 11 of 2020), which is shorter than the average duration of 10 weeks in the last 25 years.
- Additionally, the 2019/2020 seasonal ILI incidence reported by GPs was low compared to four preceding seasons.
- The seasonal number of patients with ILI in nursing homes and patients with ARI that were reported by GPs in 2019/2020 was comparable to the four preceding seasons.
- The weekly number of ARI consultations and ILI incidence reported by GPs was highest in young children (0-4 years), followed by the elderly (65 years or older), which is in line with the four previous seasons.
- The ILI incidence and ARI consultations reported by GPs and the ILI incidence of nursing home residents peaked relatively late in the season compared to the four previous seasons (between week 11-14 2020), which coincided with the start of the COVID-19 pandemic and the last week of the influenza epidemic. The influenza epidemic ended in week 11, as almost no influenza virus was detected in the weeks 12-14, while SARS-CoV-2 was more frequently detected in the ILI specimens in those last three weeks (see chapter 5.7 and 3).
- Besides the peak in week 11 of 2020, the number of ARI consultations in children aged 0-4 years peaked in week 51 of 2019, which coincided with RS virus circulation (see chapter 4).

2.1.2 Background

Acute respiratory infections (ARI) and the subgroup of influenza-like illness (ILI) are clinical diagnoses caused by a range of viruses and bacteria. However, the case definition for ILI is more specific for influenza virus infection, which is defined according to the 'Pel criteria' (Pel 1965): sudden onset of symptoms, fever ≥ 38°C and at least one of the symptoms cough,

rhinorrhoea, sore throat, frontal headache, retrosternal pain, or myalgia. ILI surveillance performed by sentinel general practitioners (GPs) of the Nivel Primary Care Database forms the basis of the influenza surveillance in the Netherlands. Since 1992, it combines the clinical syndrome ILI with virological testing of a combined nose/throat swab of a subset of the ILI patients, to give insights in the main causes of ILI and the influenza virus circulation. Based on these data and using the MEM method, the start of an influenza epidemic was defined for the 2019/2020 season, as an ILI incidence above 5.8/10,000 inhabitants during two consecutive weeks in combination with at least 10% influenza virus detections in at least 20 specimens of patients with ILI (Vega, Lozano et al. 2013, Hooiveld, Donker et al. 2019). This epidemic threshold is reconsidered every season.

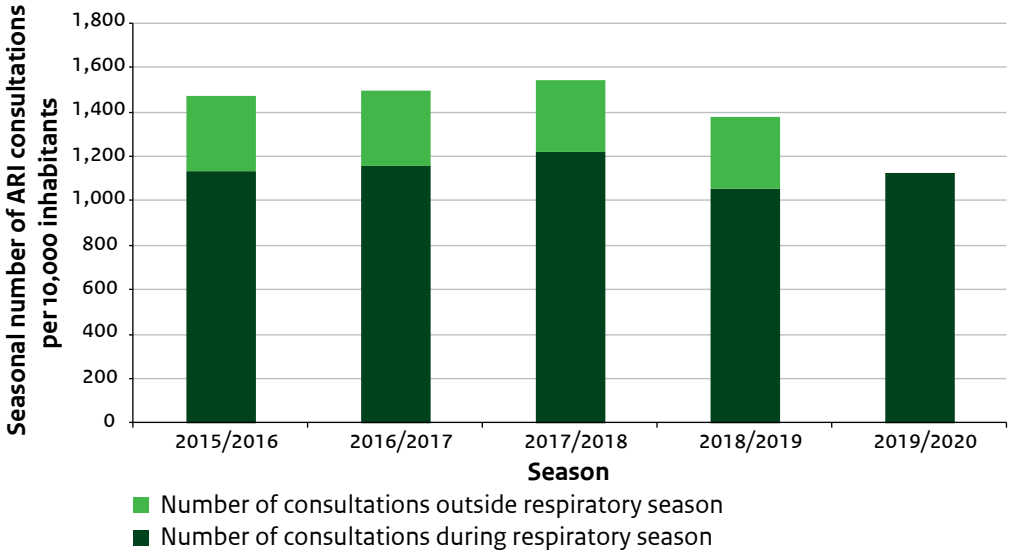
ARI surveillance is a complementary syndromic surveillance system, using data from electronic medical records of GPs participating in the Nivel Primary Care Database. However, it covers a broader respiratory case definition: acute upper respiratory infection, acute/chronic sinusitis, acute laryngitis/tracheitis, acute bronchitis/bronchiolitis or influenza (and therefore includes the ILI case definition). Besides, a larger number of GPs participate in the ARI surveillance and no specimens are taken.

SNIV is a third system for respiratory surveillance of ILI in nursing homes (SNIV). Nursing home residents are a vulnerable group for influenza virus-related complications, but are not captured in the GP surveillance because they receive primary care from elderly care physicians.

2.1.3 Figures

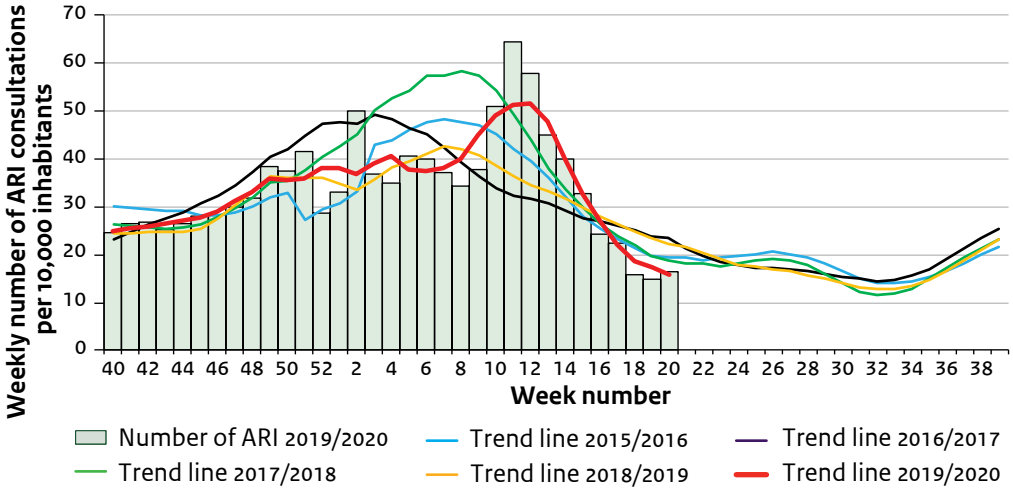
GP consultations for ARI

Figure 2.1 Seasonal cumulative number of ARI consultations in primary care within the respiratory season (week 40 through week 20) and outside the respiratory season (week 21 through week 39) of 2015/2016 - 2019/2020 (Source: Nivel Primary Care Database).



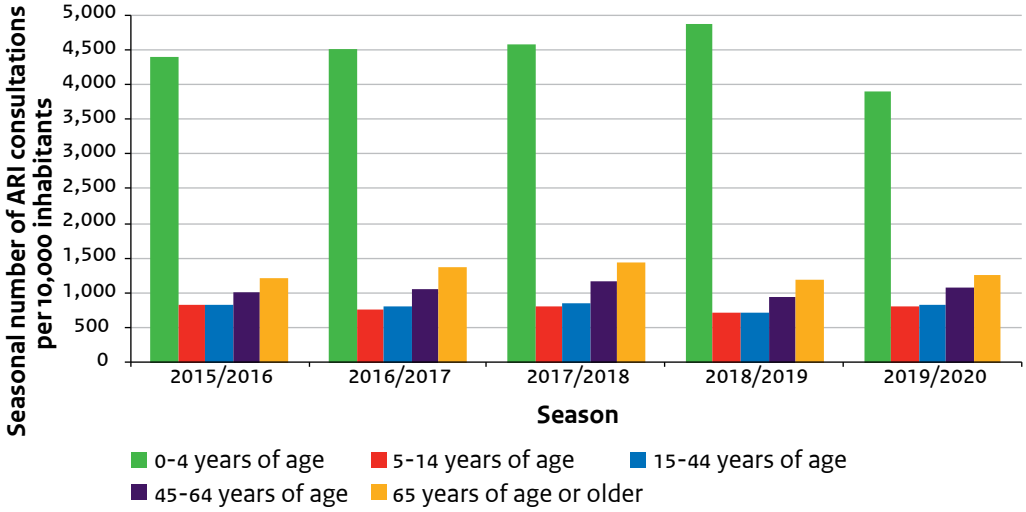
Footnote: ARI = acute respiratory infections (including influenza-like illness); GP = general practitioner.
For the 2019/2020 season, numbers for outside the respiratory season (week 20 through 39 2020) are not yet available.

Figure 2.2 Weekly number of ARI consultations in primary care per 10,000 inhabitants in the respiratory season (week 40 through week 20) of 2019/2020 and trend lines for seasons 2015/2016 - 2019/2020 (Source: Nivel Primary Care Database).



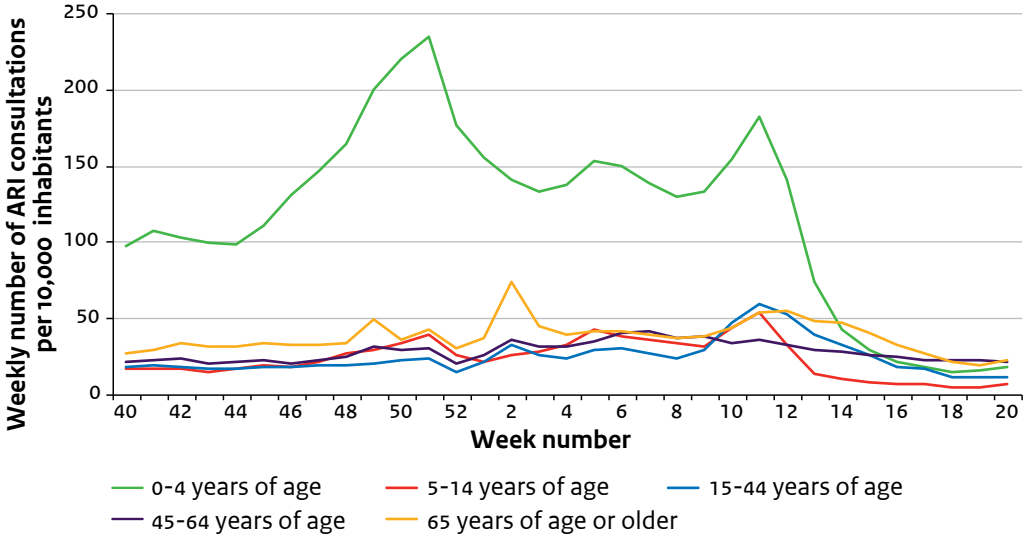
Footnote: Trend lines indicate a 5-weeks moving average. ARI = acute respiratory infection, including influenza-like illness; GP = general practitioner.

Figure 2.3 Seasonal cumulative number of ARI consultations in primary care in the respiratory seasons (weeks 40 through 20) of 2015/2016 through 2019/2020 per 10,000 inhabitants by age group (Source: Nivel Primary Care Database).



Footnote: ARI = acute respiratory infection, including influenza-like illness; GP = general practitioner.

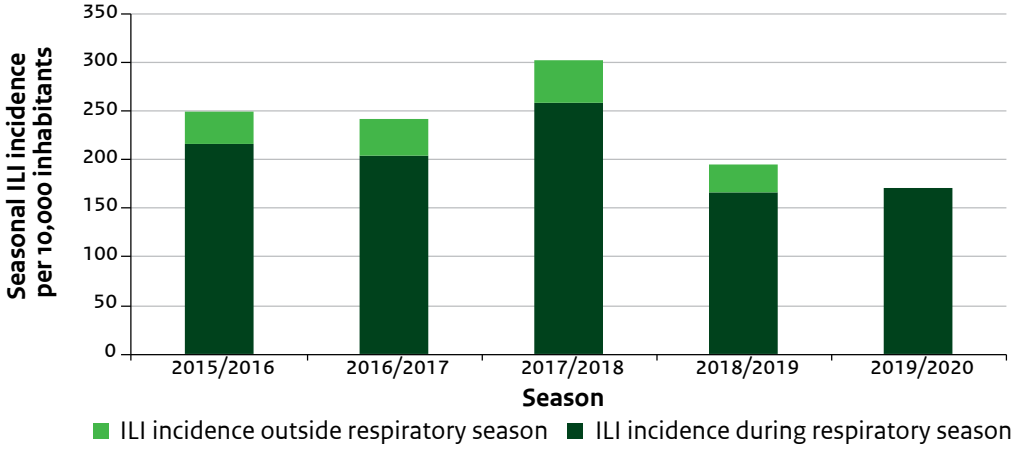
Figure 2.4 Weekly number of ARI consultations in primary care per 10,000 inhabitants in 2019/2020 (weeks 40 through week 20 of 2020) by age group (Source: Nivel Primary Care Database).



Footnote: ARI = acute respiratory infection, including influenza-like illness; GP = general practitioner.

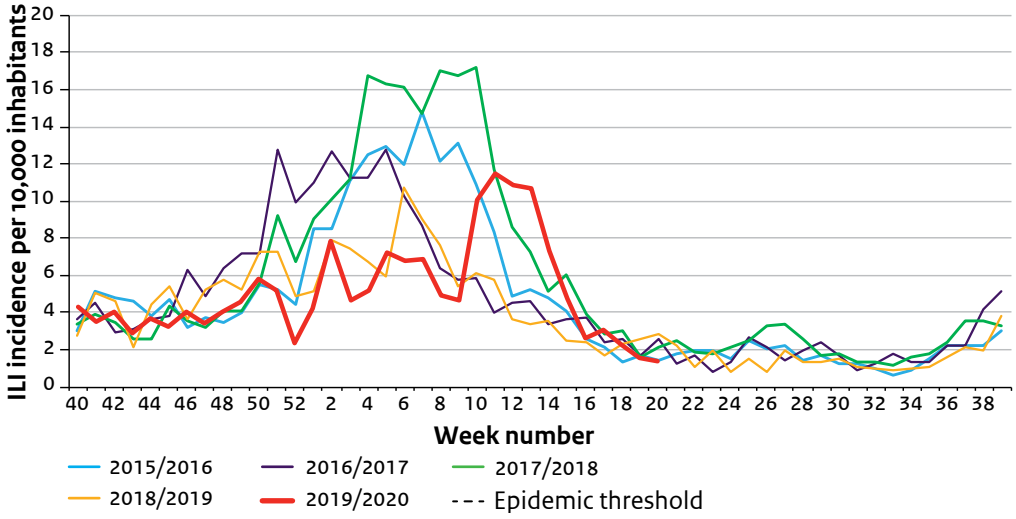
ILI incidence: sentinel GP practices

Figure 2.5 Seasonal ILI incidence in primary care within the respiratory season (week 40 through week 20) and outside the respiratory season (week 21 through week 39) of 2015/2016 - 2019/2020 (Source: Nivel Primary Care Database).



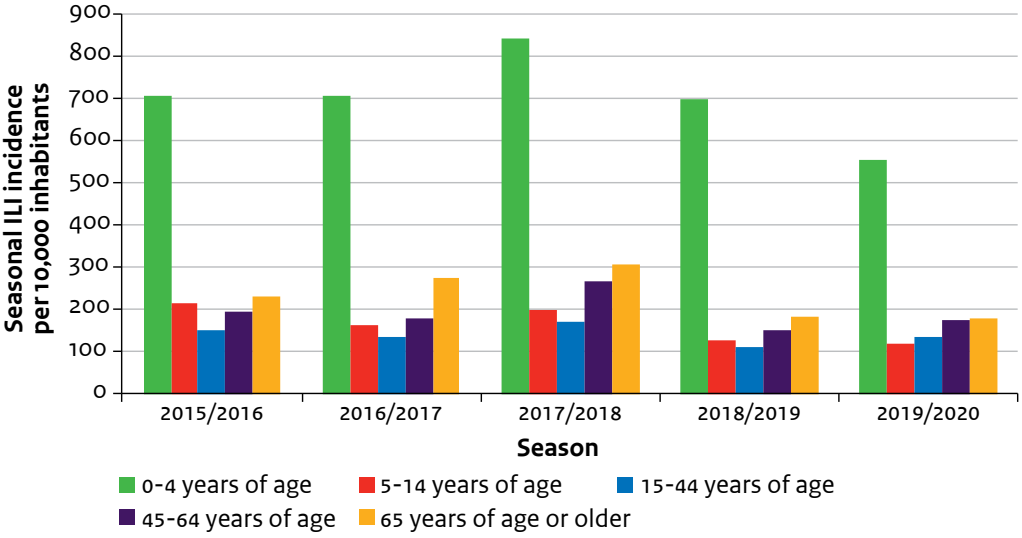
Footnote: ILI = influenza-like illness.
For the 2019/2020 season, numbers for outside the respiratory season (week 20 through 39 2020) are not yet available.

Figure 2.6 Weekly ILI incidence in primary care during the seasons 2015/2016 - 2019/2020 (through week 20 of 2019) (Source: Nivel Primary Care Database).



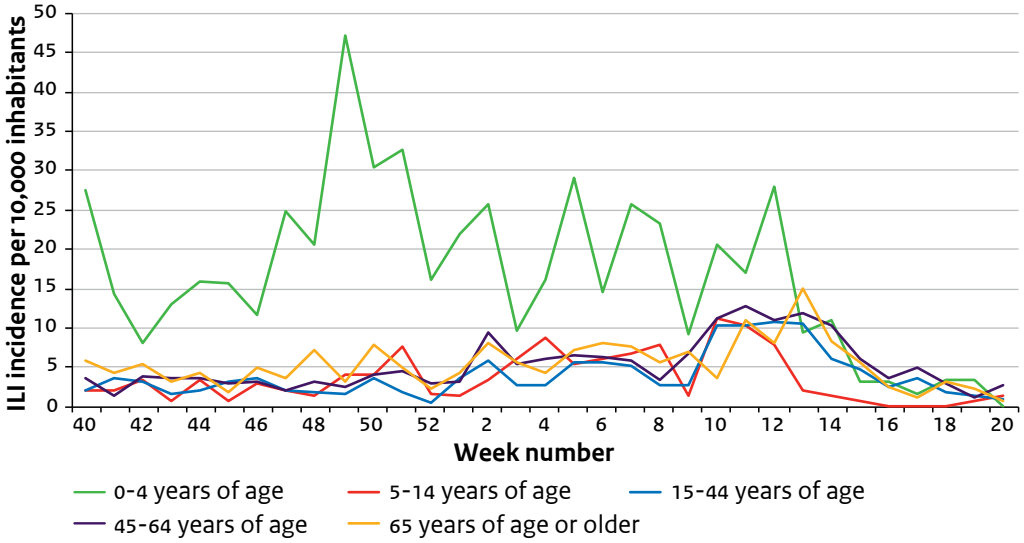
Footnote: ILI = influenza-like illness.
Epidemic threshold was set at 5.1 per 10,000 inhabitants for the seasons 2015/2016 through 2018/2019, and at 5.8 per 10,000 inhabitants for the 2019/2020 season.

Figure 2.7 Seasonal ILI incidence in primary care in the respiratory seasons 2015/2016 - 2019/2020 per 10,000 inhabitants by age group (Source: Nivel Primary Care Database).



Footnote: ILI = influenza-like illness.

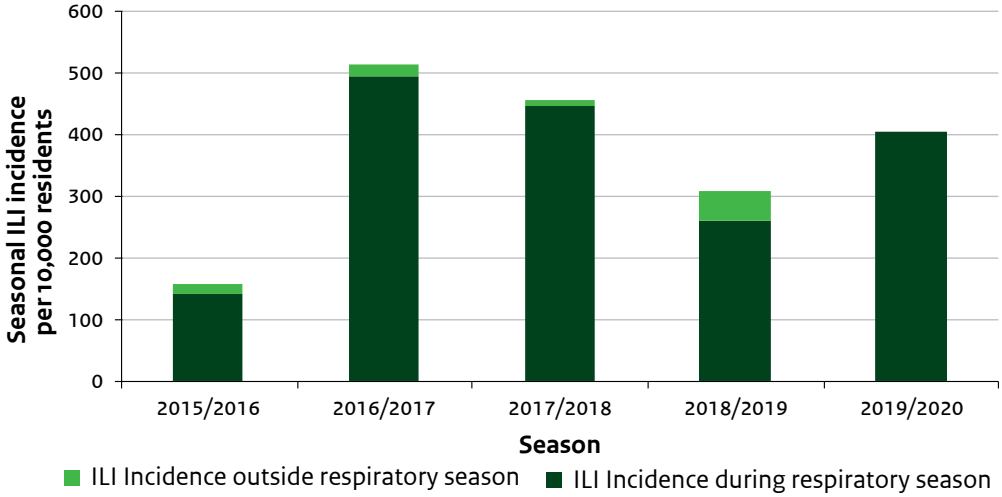
Figure 2.8 Weekly ILI incidence in primary care per 10,000 inhabitants in respiratory season 2019/2020 by age group (Source: Nivel Primary Care Database).



Footnote: ILI = influenza-like illness.

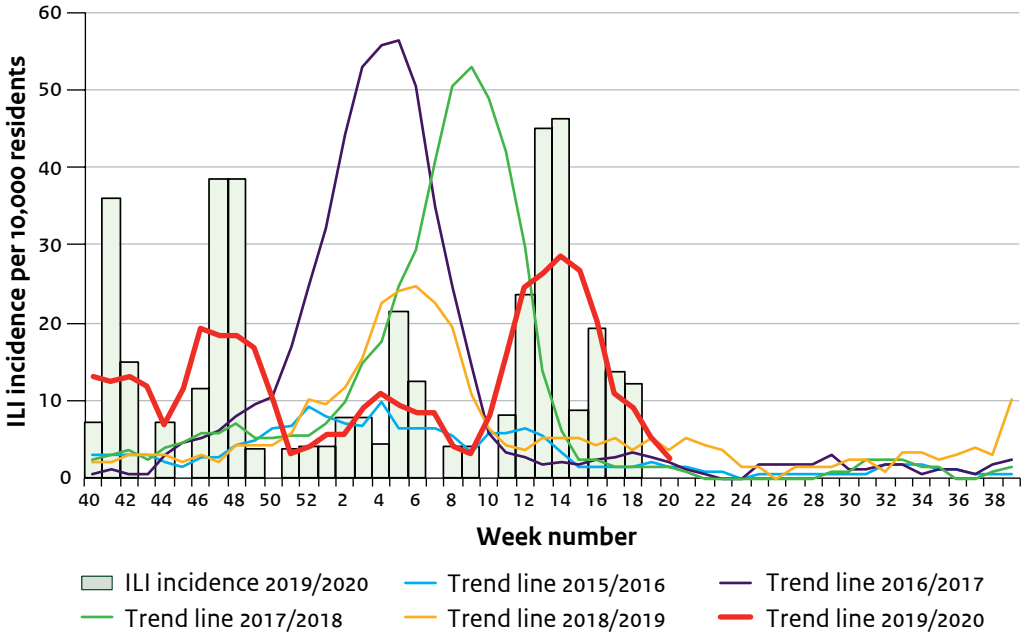
ILI incidence: in nursing homes

Figure 2.9 Seasonal ILI incidence in SNIV nursing homes per 10,000 residents within the respiratory season (week 40 through week 20) and outside the respiratory season (week 21 through week 39) of 2015/2016 - 2019/2020 (Source: SNIV, RIVM).



Footnote: ILI = influenza-like illness.
For the 2019/2020 season, numbers for outside the respiratory season (week 20 through 39 2020) are not yet available.

Figure 2.10 Weekly ILI incidence in SNIV nursing homes per 10,000 residents in the 2019/2020 respiratory season (week 40 of 2019 through week 20 of 2020) and trend lines for the seasons 2015/2016-2019/2020 (Source: SNIV, RIVM).



Footnote: Trend lines are based on 5-week moving averages. No epidemic threshold for this data has been calculated. ILI = influenza-like illness; SNIV = national sentinel surveillance network for infectious diseases in nursing homes.

2.2 Community-acquired pneumonia (CAP) in primary care

Authors: Daphne Reukers, Mariëtte Hooiveld
Contributors: Marit de Lange, Marjolein Korndewal, Rianne van Gageldonk-Lafeber, Annabel Niessen

2.2.1 Key points

- The seasonal number of GP consultations for pneumonia (week 40 2019 through week 20 2020) in 2019/2020 was 187 per 10,000 inhabitants, which was lower than the previous four seasons.
- The peak in weekly pneumonia GP consultations (9 per 10,000 inhabitants) was observed in week 2 of 2020.
- The seasonal number of GP consultations for pneumonia in 2019/2020 (week 40 2019 through week 20 2020) for the age groups 0-4 years, 45-64 years and 65 years or older (200, 163 and 494 per 10,000 inhabitants, respectively) was lower than the previous four seasons.
- The seasonal number of GP consultations for persons 5-14 years and 15-44 years (82 and 72 per 10,000 inhabitants, respectively) was comparable to the previous four seasons.
- The seasonal incidence (week 40 2019 through week 20 2020) of pneumonia in nursing homes was 1,263 per 10,000 residents. Which was comparable to the previous four seasons.
- The peak in the weekly incidence for pneumonia (71 patients per 10,000 residents) reported by nursing homes was observed in week 7 of 2020. The peak in the trend line (week 13) coincided with the first peak in the weekly notifications of SARS-CoV-2 (week 15).
- In conclusion, fewer cases of pneumonia were registered during the 2019/2020 season in general practices compared to the previous four seasons. However, the incidence of pneumonia in nursing homes was average compared to previous seasons.

2.2.2 Background

Pneumonia is an infection of the lower respiratory tract with high morbidity and mortality, especially in the elderly. Typical symptoms include cough, chest pain, fever and difficulty breathing.

Many studies in the Netherlands and other countries show that *Streptococcus pneumoniae* is the predominant aetiological agent of community-acquired pneumonia (CAP), but CAP can be caused by many other microorganisms, mainly bacteria and viruses (van Gageldonk-Lafeber, Wever et al. 2013). In daily clinical care, a general practitioner (GP) diagnosis of CAP is based on clinical criteria, often without confirming the presence of a new infiltrate on a chest x-ray and without laboratory-confirmed diagnosis (Verheij, Hopstaken et al. 2011). Also in hospital settings, there is a lack of guidelines on diagnostic testing in CAP patients. Therefore, the causative pathogens remain unknown in the majority of CAP patients, since microbiological tests are not systematically used and are usually limited to blood and sputum cultures for bacterial causes. Developing hospital or national guidelines could lead to a more systematic diagnostic testing policy in CAP patients and minimize the amount of testing bias.

The pneumonia surveillance in this report includes both the registration of pneumonia by GPs (Nivel Primary Care Database) and the registration of incidence of pneumonia in nursing homes (SNIV).

2.2.3 Discussion

The influenza epidemic in 2019/2020 was mild compared to the previous four seasons, which resulted in relatively low numbers of patients consulting their GP with pneumonia. However, the number of pneumonia consultations did show, to some extent, a plateau and only significantly decreased after week 12, which is likely due to the start of the SARS-CoV-2 epidemic. The peak in weekly pneumonia GP consultations in 2019/2020 (week 2 2020) was earlier than the influenza epidemic, which started in week 5, and also earlier than the peak of influenza-like illness in week 11, 2020 (Chapter 2.1).

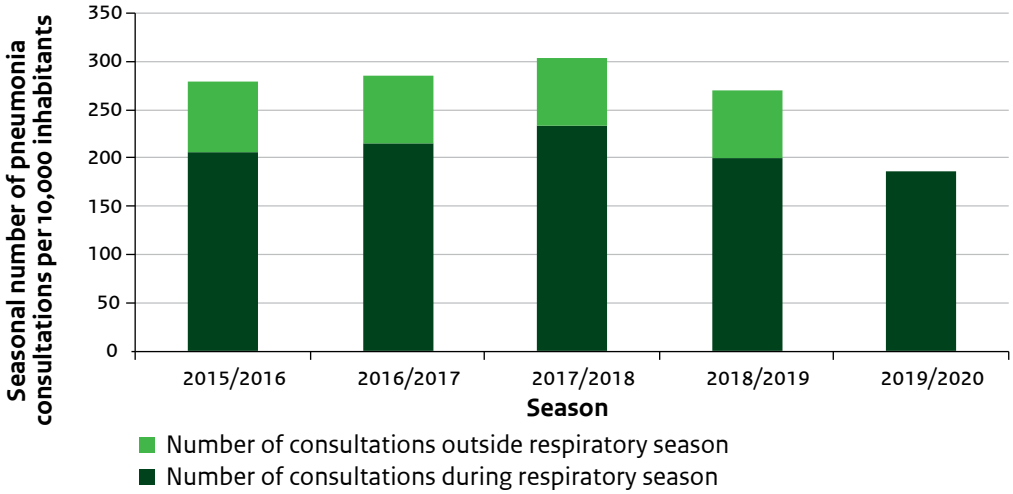
The number of pneumonia consultations was low or average in all age groups. In children younger than five years, the number of pneumonia consultations peaked in week 51 2019. This relatively early peak coincided approximately with the peak in the number of RSV diagnoses (week 1 2020, Chapter 4). Nevertheless, because laboratory diagnostics are not included in the pneumonia surveillance, it is unclear to what extent pneumonia is associated with the circulation of RSV, influenza virus and other pathogens.

The peak in the weekly incidence for pneumonia in SNIV nursing homes in week 7 coincided with the influenza epidemic and was within the range of the peak incidences in the four previous seasons. In week 7, mainly influenza virus was circulating, as 42% of the specimens taken from ILI patients by sentinel GPs were positive for influenza virus (Chapter 3). However, there were also several peaks in week 11-15, which coincided with the peak in the COVID-19 epidemic in week 15 (Chapter 5.7). The seasonal incidence (week 40 2019 through week 20 2020) of pneumonia in SNIV nursing home residents was also average compared to the previous four seasons.

2.2.4 Figures

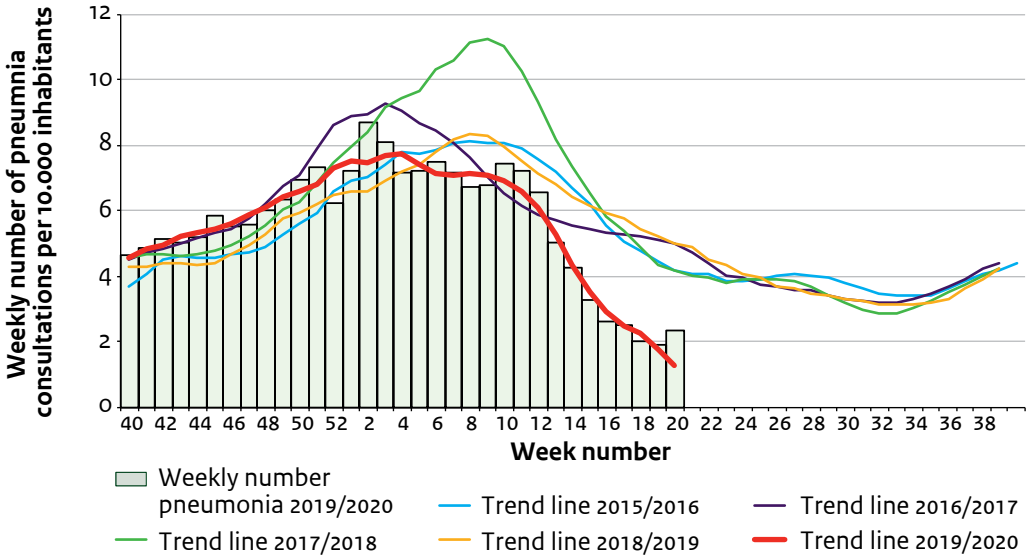
GP consultations for pneumonia

Figure 2.11 Seasonal cumulative numbers of patients consulting their GP for pneumonia per 10,000 inhabitants within the respiratory season (week 40 through week 20) and outside the respiratory season (week 21 through week 39) of 2015/2016 - 2019/2020 (Source: Nivel Primary Care Database).



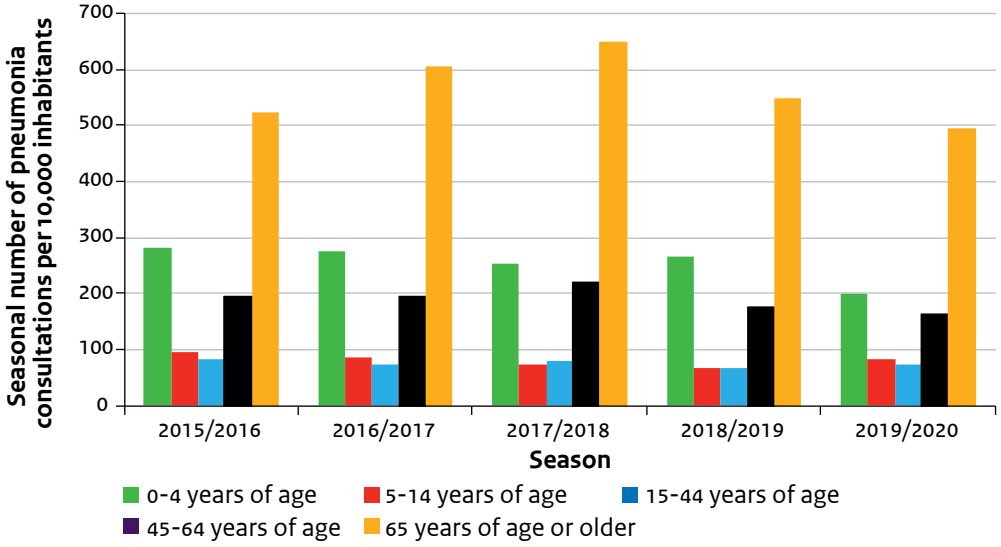
Footnote: GP = general practitioner.

Figure 2.12 Weekly numbers of patients consulting their GP for pneumonia per 10,000 inhabitants in 2019/2020 (week 40 2019 through week 20 2020) and the trend lines for 2015/2016 - 2019/2020 (2019/2020: through week 20). (Source: Nivel Primary Care Database).



Footnote: GP = general practitioner. Trend lines are based on a 5-week moving average.

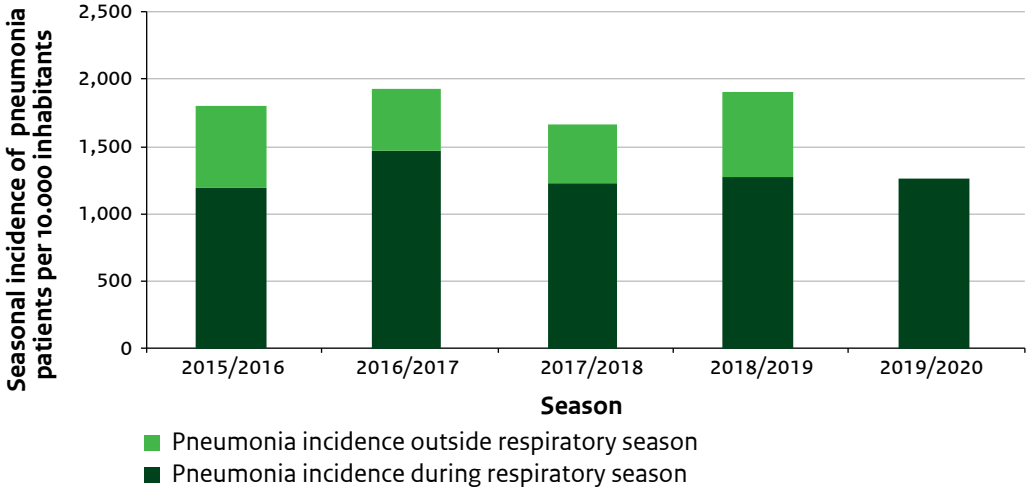
Figure 2.13 Seasonal cumulative number of GP consultations for pneumonia per 10,000 inhabitants by age group in the respiratory seasons 2015/2016 – 2019/2020 (week 40 through week 20) (Source: Nivel Primary Care Database).



Footnote: GP = general practitioner.

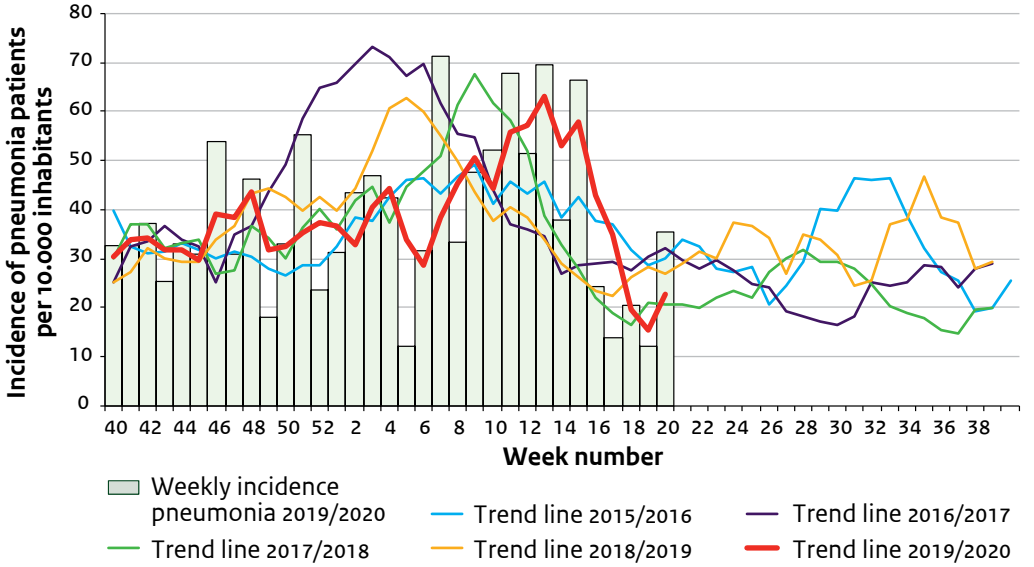
Incidence of pneumonia (nursing homes)

Figure 2.14 Seasonal incidence of pneumonia in SNIV nursing homes per 10,000 residents within the respiratory season (week 40 trough week 20) and outside the respiratory season (week 21 through week 39) of 2015/2016 - 2019/2020 (Source: SNIV, RIVM).



Footnote: SNIV = national sentinel surveillance network for infectious diseases in nursing homes.

Figure 2.15 Weekly incidence of pneumonia patients in SNIV nursing homes per 10,000 residents in 2019/2020 and trend lines for the seasons 2015/2016 – 2019/2020 (through week 20). (Source: SNIV, RIVM).



Footnote: SNIV = national sentinel surveillance network for infectious diseases in nursing homes. Trend lines are based on a 5-week moving average.

2.3 Severe acute respiratory infections (SARI)

Authors: Annabel Niessen, Anne Teirlinck
Contributors: Inge Roof, Peter Wever, Rianne van Gageldonk-Lafeber

2.3.1 Key points

- The seasonal cumulative SARI incidence was 29 per 10,000 inhabitants in the 2019/2020 season (week 40 2019 through week 20 2020). This is similar to the previous season 2018/2019 (28 per 10,000 persons), lower than in season 2017/2018 (33 per 10,000) and higher than in season 2016/2017 (16 per 10,000).
- The peak in weekly SARI incidence was reached in week 13 of 2020, during the first wave of the COVID-19 outbreak with an incidence of 2 per 10,000 inhabitants.
- The current SARI-surveillance proved not suitable for detecting COVID-19 cases since many COVID-19 have been classified under non-SARI specific financial codes. Therefore, the SARI-incidence has likely been underestimated and criteria for SARI will be reconsidered for future surveillance.

2.3.2 Background

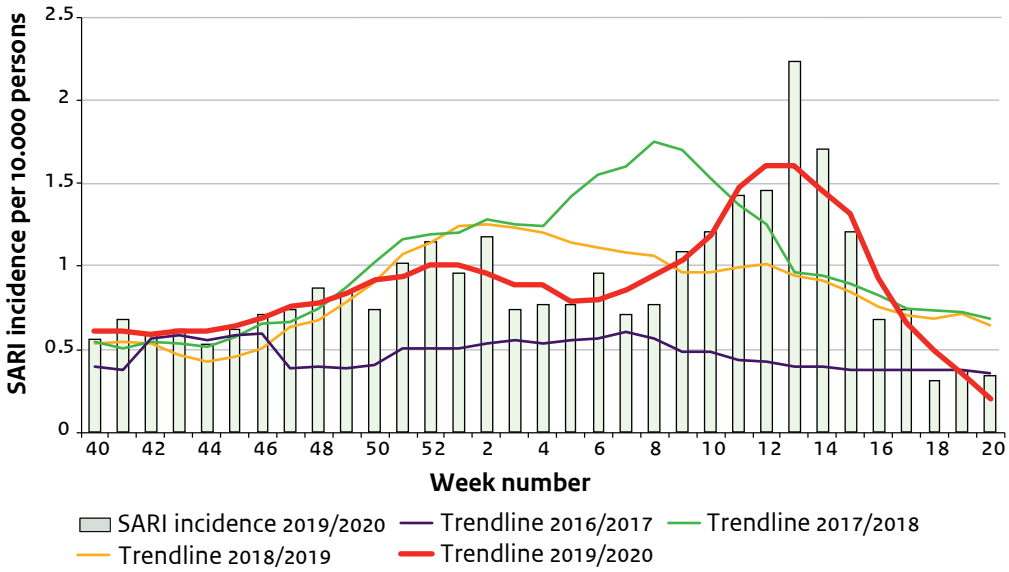
Severe acute respiratory infections requiring hospitalisation (SARI) are an important cause of morbidity and mortality worldwide. After the 2009 influenza A(H1N1) pandemic, the World Health Organization (WHO) and European Centre of Disease Prevention and Control (ECDC) recommended every country to implement a SARI surveillance system for pandemic preparedness. The ongoing COVID-19 pandemic underlines the need for SARI surveillance. A pilot study was started in 2015 in Leiden University Medical Center (LUMC) and Jeroen Bosch Hospital (JBZ) in the Netherlands with the main objective to set up a sentinel surveillance system for SARI. In LUMC, a passive syndromic SARI surveillance was in effect until October 2018, after which the collaboration with the ICT provider ended. During the 2019/2020 season, an active SARI surveillance based on DBC-codes was only operational in JBZ. A more extensive surveillance system based on data of four hospitals, with the aim of including more hospitals once established, is currently being prepared and expected to be in place at the end of 2020.

2.3.3 Discussion

Based on the current SARI-surveillance in the JBZ, the cumulative SARI incidence this season (2019/2020) was comparable with 2018/2019. However the peak in weekly SARI incidence in 2019/2020 was reached considerably later than previous three seasons, and coincided with the COVID-19 epidemic. In the weeks before the COVID-19 outbreak, weekly SARI incidence was lower than in the previous two seasons, but higher than in 2016/2017. The peak in SARI incidence during the COVID-19 outbreak was not considerable higher than the peak in previous seasons, suggesting an incomplete coverage of COVID-19 patients in the SARI surveillance, given the high number of COVID-19 patients admitted in the JBZ at that time. Indeed, COVID-19 patients that have been classified under non-SARI specific financial codes, were not registered. For future SARI surveillance, these additional codes will be considered for inclusion for a more complete picture of SARI patients that were admitted to the hospital.

2.3.4 Figure

Figure 2.16 SARI incidence at the Jeroen Bosch Hospital during influenza seasons 2016/2017 through 2019/2020 based on DBC/DOT codes (financial codes).



Footnote: SARI = severe acute respiratory infection. Trend lines are based on a 5-week moving average.

2.4 Weekly mortality monitoring

Author: Liselotte van Asten
Contributors: Marit de Lange, Anne Teirlinck, Ursula de Bruijn- van Leijden, Felicia Minnaard, Lenny Stoeldraijer, Carel Harmsen

2.4.1 Key Points

- An average of 2,883 deaths occurred weekly in the Netherlands over the past 5 years, 2015-2019.
- Cumulated excess mortality during the short 5-week influenza epidemic (weeks 5-7 and 10-11 of 2020) was 617, which is lower than average in the past 5 years (6,443 excess deaths).
- After the first COVID-19 case was reported (on February 27th, the end of calendar week 9, 2020) excess mortality was observed from week 12 through 19 (Thursday March 12 to Wednesday May 6, 2020), totalling at 9,554 cumulated excess deaths in those 8 weeks.
- The first two weeks of the COVID-19 pandemic overlapped with the final two weeks of the influenza epidemic. In those two weeks (week 10 and 11 2020), excess mortality was estimated at 213.
- Both in the 2019/2020 influenza epidemic and in the first wave of the COVID-19 epidemic excess mortality was mostly observed in persons aged 75 years and older.
- Mortality peaked in week 15 (April 2-8 of 2020, in the COVID-19 epidemic) with a record-high of 5,143 deaths (2,240 above expected baseline level).

2.4.2 Background

The Dutch weekly mortality monitoring system was initiated in August 2009, during the influenza A(H1N1)pdm09 pandemic. It is a collaboration between the RIVM Centre for Infectious Disease Control (RIVM CIb) and Statistics Netherlands (CBS). The system monitors the number of deaths reported nationwide (population size of 17.3 million in 2019) from all causes, as information on cause of death is not available in real-time.
Each week, the death notification data is checked for the presence of any excess mortality (i.e. mortality levels above a pre-defined threshold) in deaths reported within 1, 2, and 3 weeks (coverage 45%, 97% and 99% respectively). Excess mortality gives an indication of the impact of any expected and unexpected events that potentially affect population health. Examples of such events are heat waves, cold snaps, or seasonal influenza epidemics for which the morbidity and mortality burden varies due to variations in the circulation of influenza (sub) types.

2.4.3 Discussion

The 2019/2020 season was characterised by low excess mortality during the short influenza epidemic and high excess mortality during the ensuing first wave of the COVID-19 epidemic. In April 2020, weekly deaths peaked at a record-high level since the monitoring was initiated in 2009. While total excess mortality during the first COVID-19 wave (9,554) seemed similar in number to the excess mortality during the severe 2017/2018 influenza epidemic, the excess deaths occurred in a shorter time period (8 weeks vs 18) and were mitigated by social distancing measures.

2.4.4 Figures

Figure 2.17 Weekly number of deaths from 2011 to 2020 (through week 20 of 2020) by date of death (notified within three weeks from date of death). (Source: Statistics Netherlands).

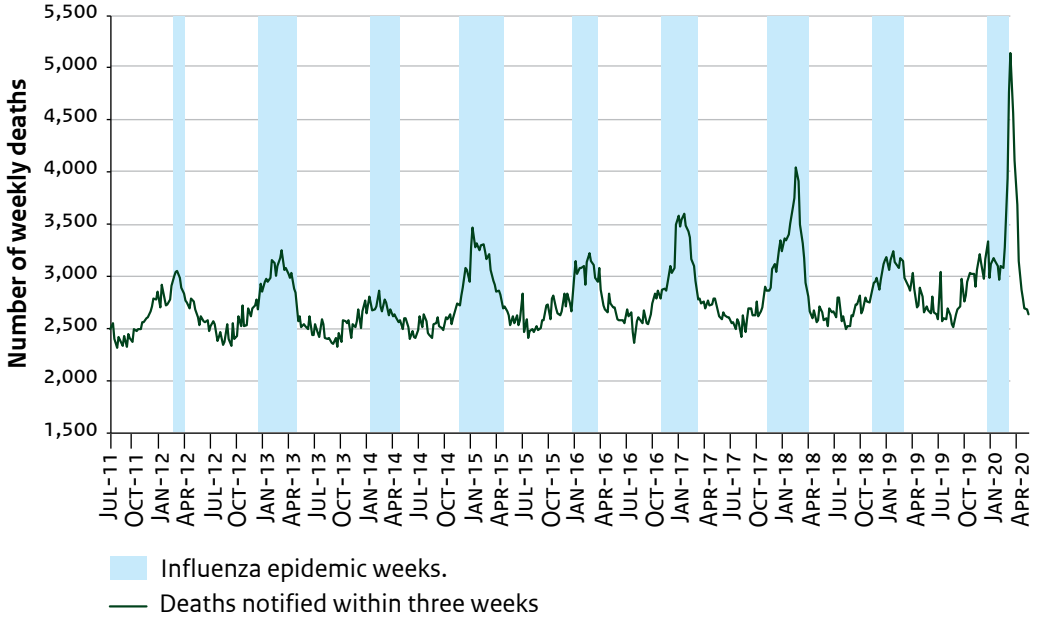
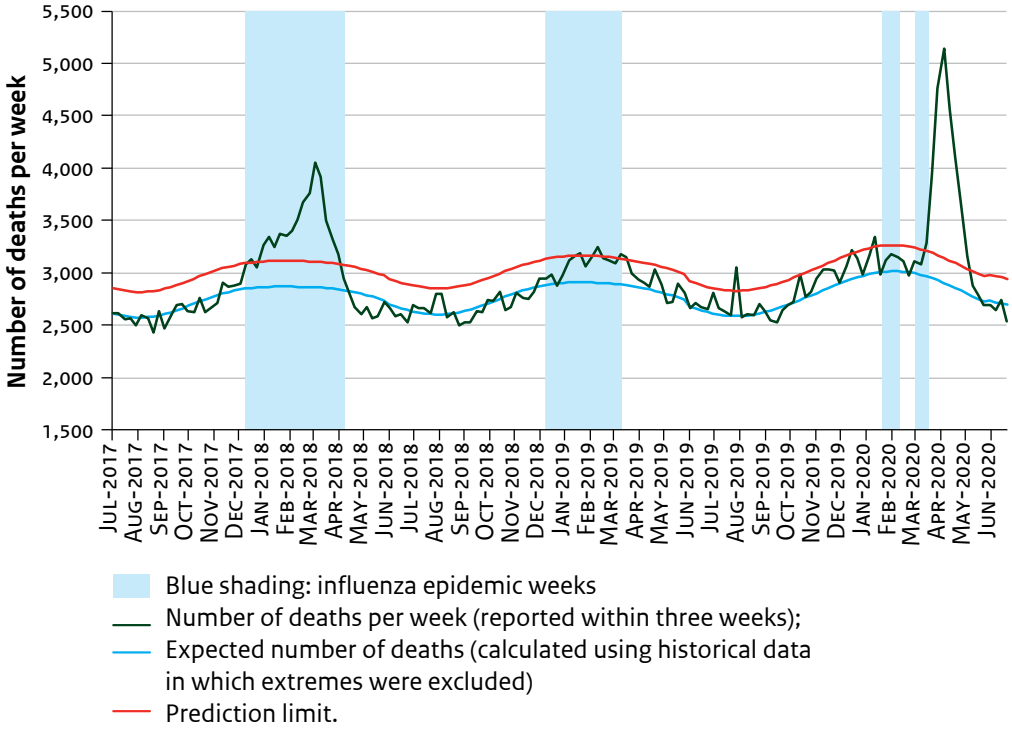


Figure 2.18 Observed and expected ('baseline') weekly number of deaths, July 2017 to June 2020. (Source: Statistics Netherlands).



Chapter 3
Influenza

Authors: Marit de Lange, Scott McDonald, Frederika Dijkstra, Adam Meijer
Contributors: Anne Teirlinck, Daphne Reukers, Mariëtte Hooiveld, Ron Fouchier

3.1 Key points

- In the 2019/2020 winter season, the influenza epidemic lasted for 5 weeks (week 5 through week 7 and week 10 and 11 of 2020), which is shorter than the average duration of 10 weeks in the last 25 years.
- Throughout the epidemic, mainly influenza virus type A was detected, with A(H1N1)pdm09 and A(H3N2) detected in approximately equal proportions in ILI patients visiting the GP.
- In the second part of the epidemic, a declining proportion ILI patients visiting the GP presented with influenza virus. In week 12 through week 14 of 2020, the ILI incidence was still above the epidemic threshold, but in those weeks almost no influenza virus was detected, while SARS-CoV-2 was more frequently detected in the ILI specimens, in accordance with the increasing number of COVID-19 patients that were reported during that period in the Netherlands.
- Almost all circulating A(H1N1)pdm09 viruses belonged to clade 6B.1A-5-183P, but these were separated in at least two larger groups. The group with most viruses had few common amino-acid substitutions in the HA antigenic site Sb. These amino acid substitutions had a moderate effect on the loss of antigenic similarity with the vaccine strain. Most A(H3N2) viruses belonged to clade 3C.3a, the clade to which the vaccine strain belongs. Furthermore, viruses from several subclades of 3C.2a1b were circulating, which were antigenically different from the vaccine strain. The circulating B/Victoria viruses were antigenically similar to the vaccine strain.
- All viruses tested for antiviral susceptibility were sensitive to neuraminidase inhibitors and for Baloxavir marboxil.
- In the 2019/2020 respiratory season 231 (95% uncertainty interval (UI): 197 – 270) persons per 10,000 inhabitants had symptoms of an influenza virus infection, which was lower than in the four previous seasons. This corresponds to an estimated 400,000 symptomatic cases.

Symptomatic influenza incidence in respiratory season 2019/2020 was highest for the age group 0-4 years.

- Preliminary end-of-season analysis of the European I-MOVE study, in which the Netherlands participates, estimated an influenza vaccine effectiveness of 48% (95% CI: 38% – 57%) for patients at the primary care level against any influenza, 45% (95% CI: 29% – 57%) against influenza virus type A(H1N1)pdm09, 49% (95% CI: 30% - 62%) against influenza virus type A(H3N2), and 57% (95% CI: 39% – 70%) against influenza virus type B.
- The influenza vaccination programme of 2019 was estimated to have averted 1,624 (95%CI: -2,142 – 6,135) GP ILI consultations caused by an influenza virus in the age group 65 years and older in the 2019/2020 season.

3.2 Background

Influenza is an acute respiratory infection caused by influenza viruses. Most patients recover quickly, although an influenza virus infection can cause severe illness especially in elderly and in patients with an underlying medical condition.
Human influenza viruses cause yearly epidemics, mostly in winter. Most influenza virus 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). Different combinations of HA and NA proteins result in various subtypes, for example H1N1 and H3N2, the subtypes currently causing seasonal epidemics. Influenza type B viruses are divided into genetic lineages based on their gene coding for the HA. Currently, circulating influenza B viruses belong to the lineage B/Yamagata/16/88 or B/Victoria/2/87. Both type A and B influenza viruses are constantly mutating, possibly resulting in small phenotypic changes that may result in escape from existing natural or vaccine induced immunity, a process known as antigenic drift.

3.3 Epidemiological situation, season 2019/2020

In the 2019/2020 season, there was a 5 week influenza epidemic divided in two short periods, one from week 5 of 2019 through week 7 and one in week 10 and 11 of 2020. Data on the influenza-like illness (ILI) incidence, obtained through sentinel general practitioner (GP) surveillance, can be found in Chapter 2.1. In the first part of the epidemic (week 5 through 7), mainly influenza virus type A was detected, with A(H1N1)pdm09 and A(H3N2) detected in approximately equal proportions in ILI patients visiting the GP. Of the detected influenza B viruses, the Victoria lineage was predominant. The second part of the epidemic paralleled the start of the COVID-19 outbreak in the Netherlands. In weeks 10 and 11, influenza virus was still detected in ILI patients visiting the GP, although with declining percentage in week 11. For the influenza viruses that were detected, influenza A was still predominant, with A(H1N1)pdm09 and A(H3N2) detected in approximately equal proportions. In week 12 through week 14, the ILI incidence was still above the epidemic threshold, but almost no influenza virus was detected.

SARS-CoV-2 was more frequently detected in the ILI specimens in those last three weeks (see chapter 5.7).

A selection of influenza virus positive specimens of patients from the sentinel surveillance and from patients submitted from hospital and peripheral laboratories were subjected to direct sequencing of the hemagglutinin (HA) genome segment from the clinical specimen. 221 A(H3N2), 146 A(H1N1)pdm09 and 17 B/Victoria influenza viruses were successfully sequenced. Except for one A(H1N1)pdm09 virus belonging to clade 6B.1A-7-183P, the A(H1N1)pdm09 viruses belonged to clade 6B.1A-5-183P but separated in at least two larger groups. The smaller cluster of sequences (subclade 5B; 6B.1A-5B) has a high number of common amino-acid substitutions. The group with most viruses (subclade 5A; 6B.1A-5A) has few common amino-acid substitutions, but notably D187A and Q189E in the HA antigenic site Sb. Nevertheless, these amino acid substitutions had moderate effect on loss of antigenic similarity with vaccine strain A/Brisbane/02/2018 (H1N1)pdm09-like virus. Most A(H3N2) viruses belonged to clade 3C.3a (n=150), the clade to which the vaccine strain A/Kansas/14/2017 (H3N2)-like virus belongs. The next most prominent clade was 3C.2a1b/197R (n=54) and the remaining A(H3N2) viruses belonged to subclades 3C.2a1b/135K (n=8), 3C.2A1b/94N (n=6), 3C.2a1b/137F (n=2) and 3C.2a1b/131K (n=1). Viruses belonging to clade 3C.2a1b are antigenically different from the vaccine strain. The 17 B/Victoria viruses belonged to clade 1A.3, viruses with a 3 amino-acid deletion in the HA1. These viruses are antigenically similar to the vaccine strain B/Colorado/06/2017-like virus, that is a 2 amino-acid deletion variant, in human serology studies.

All 409 viruses tested for antiviral susceptibility were sensitive for neuraminidase inhibitors and all 154 tested viruses were sensitive for Baloxavir marboxil.

Preliminary end-of-season analysis of the European I-MOVE study, in which the Netherlands participates, estimated an influenza vaccine effectiveness (VE) of 48% (95% CI: 38% – 57%) for patients at the primary care level against any influenza, 45% (95% CI: 29% – 57%) against influenza virus type A(H1N1)pdm09, 49% (95% CI: 30% - 62%) against influenza virus type A(H3N2), and 57% (95% CI: 39% – 70%) against influenza virus type B. The VE was lowest for people aged 65 years or older.

To compare the intensity of symptomatic influenza virus infection in the total population between seasons, the influenza incidence was estimated using statistical modelling. These estimated incidences combine medically-attended ILI incidence, estimated non-medically attended ILI incidence, and the percentage specimens positive for influenza virus (McDonald, Presanis et al. 2014, Teirlinck, de Gier et al. 2018). During the 2019/2020 season, an estimated 231 (95% uncertainty interval (UI): 197 – 270) persons per 10,000 inhabitants had ILI symptoms caused by an influenza virus infection, which was lower than the estimated incidences in 2015/2016, 2016/2017, and 2017/2018 seasons and comparable to season 2018/2019.
The estimated incidence of the 2019/2020 season corresponded to an estimated 400,000 symptomatic persons. The estimated symptomatic influenza incidence in the 2019/2020 respiratory season was highest in children in the age group 0-4 years (710 per 10,000

inhabitants of 0-4 years; 95% UI: 427 – 1140). The estimated symptomatic influenza incidence was comparable for influenza virus type A(H3N2) and type A(H1N1)pdm09 (109 (95% UI: 88 – 134), and 94 (95% UI: 74 – 117) respectively). The type B specific symptomatic influenza incidence in respiratory season 2019/2020 was low for both the Yamagata and the Victoria lineage, which was 1 per 10,000 inhabitants (95% UI 0-5), and 18 per 10,000 inhabitants (95% UI 10-28) respectively.

The influenza vaccination programme of 2019 was estimated to have averted 1,624 (95%CI: 1,624 (-2,142 – 6,135) GP ILI consultations caused by an influenza virus in the age group 65 years and older in the 2019/2020 season. This estimate is based on a vaccination coverage of 61.3 (95% CI: 54.8 – 67.4), a VE of 17.1 (95%CI: -16.9 – 51.0) and an estimated incidence of GP ILI consultations caused by an influenza virus of 14,048 (95%CI: 9,089 – 20,221). The estimated number of averted GP ILI consultations caused by an influenza virus was much lower than in the four previous seasons. This is not only due to low VE in persons 65 years, but also due to the lower incidence of medical attended ILI in the 2019/2020 season. In the population aged 65 years and older, the influenza vaccination programme was estimated to have prevented 10.4% (95% CI: (-17.2 – 28.8) of the total number of these consultations that would have been expected without the vaccination programme. With these estimates, 1,251 (95% CI: -11,756 – 11,594) persons aged 65 years and older have to be vaccinated in order to prevent one GP consult for ILI caused by an influenza virus.

3.4 Discussion

During the first part of the epidemic in the 2019/2020 season, mainly influenza virus type A was detected in specimens taken from ILI patients. During the second part of the epidemic, influenza type A virus was also the predominant influenza virus type detected, but the influenza positivity rate was declining. On the other hand, the SARS-CoV-2 positivity rate was rising in those weeks. The elevated ILI incidence from week 10-14 can therefore, at least partially, be ascribed to the increasing number of SARS-CoV-2 infections.

The WHO recommended an update for three of the four Northern Hemisphere for 2020/2021 vaccine components (WHO 2020). The component of the B/Yamagata lineage remains unchanged as hardly any new variants were observed worldwide. The component of the B/Victoria lineage was changed to a B/Washington/02/2019-like virus, as this virus has a three amino acid deletion in hemagglutinin, as do the vast majority of the circulating B/Victoria lineage viruses, which is crucial for its antigenic properties. As A(H1N1)pdm09 component, an A/Guangdong-Maonan/SWL1536/2019-like virus was recommended which, like most of the subclade 5A viruses, has some amino acid substitutions in haemagglutinin. In the Netherlands, 67 percent of the H3N2 strains was of clade 3C.3a, which means that the vaccine choice for A/Kansas/14/2017 (clade 3C.3a) worked out well for the Netherlands in the 2019/2020 season. Due to the worldwide increase in circulation of clade 3C.2a1b viruses with T135K, it has been decided to recommend an A/Hong Kong/2671/2019-like virus with this substitution for the 2020/2021 vaccine for the Northern Hemisphere.

Because EMA approval for Baloxavir marboxil (Xofluza®) (BXM), a cap-dependent acidic endonuclease inhibitor, is anticipated in 2021, monitoring of reduced susceptibility amino acid substitutions in the polymerase acidic protein (PA) genome segment has been added for the 2019/2020 season. All tested viruses in the 2019/2020 season were inferred to be sensitive for Baloxivir marboxil.
Preliminary I-MOVE estimates indicate that the 2019/2020 influenza vaccine has provided substantial protection against medically-attended influenza. This is especially remarkable for the influenza virus type A(H3N2), of which the estimate is usually lower, due to adaptations in the virus during the passage of the virus in eggs to produce the vaccine. Similar A(H3N2) high VE estimates were obtained in Canada (Skowronski, Zou et al. 2020). Clade-specific end-of-season estimates of the I-MOVE consortium might give more conclusive insight in the A(H3N2) influenza VE estimates. In spite of the very low VE in persons 65 years and older, the influenza vaccination programme was estimated to have prevented 10% of the otherwise expected total number of GP ILI consultations caused by an influenza virus in the population aged 65 years and older that would have been expected without the vaccination programme (i.e. 1,624 consultations). Due to the wide confidence intervals of the I-MOVE VE estimates, the confidence intervals for the impact estimates were also very wide, with even the lower bound of number of averted events below zero.

3.5 Tables and figures

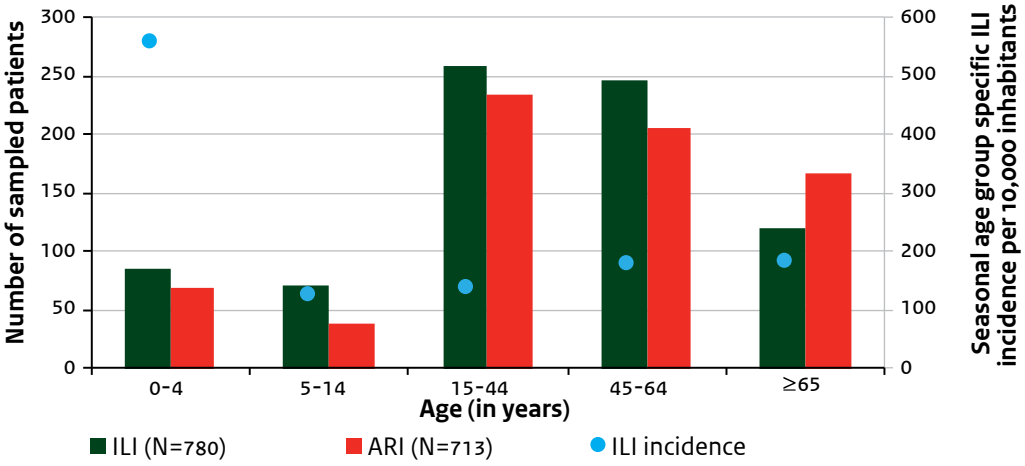
Virus surveillance

Table 3.1 Characteristics of influenza-like illness (ILI) and other acute respiratory infection (ARI) patients, who were sampled in the Nivel GP sentinel surveillance in the 2019/2020 season (through week 20 of 2020) (Source: NIC location RIVM).

Characteristics	ILI patients n/N (%)	Other ARI patients n/N (%)
Vaccinated against influenza	162/777 (21)	192/710 (27)
If yes, brand was Influvac If yes, brand was Vaxigrip	87/132 (64) 45/132 (34)	115/176 (65) 61/176 (35)
Belongs to target group for vaccination	271/778 (35)	321/712 (45)
Lung disease (e.g. asthma, COPD)	108/271 (40)	122/321 (38)
Immune deficiency due to treatment (e.g. chemotherapy and radiotherapy)	13/271 (5)	19/321 (6)
Immune deficiency due to disease (e.g. HIV)	15/271 (5)	13/321 (4)
Cardiac disease (myocardial infarction, angina pectoris, arrhythmias, valvular heart disease, heart failure)	56/271 (21)	70/321 (22)
Diabetes mellitus	40/271 (15)	51/321 (16)
Obese (BMI > 30)	83/767 (11)	88/709 (12)
Smoking: Yes or stopped less than one year ago No, stopped more than one year ago Never	 113/744 (15) 85/744 (11) 546/744 (73)	 97/668 (14) 106/668 (16) 465/668 (70)
Women: Pregnant	 5/476 (1)	 9/402 (2)
Delay in sampling, in days[a]	4 (3-7)	5 (3-10)

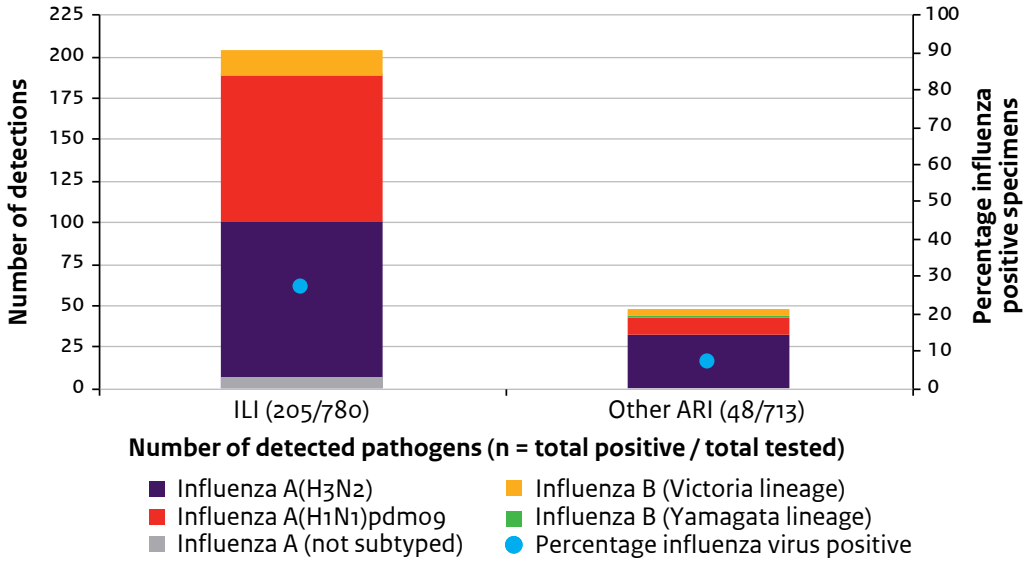
[a] Number of days between the symptom onset and the day of sampling (median, 1st, and 3rd quartile)
Footnote: ILI =influenza-like illness; ARI = acute respiratory tract infection; GP = general practitioner; n = the number in the corresponding group; N = total number of patients, for whom the information was available. Please note that the 'other ARI' patients do not include the ILI patients.

Figure 3.1 Age distribution of ILI and other ARI patients, sampled by Nivel sentinel GPs, and the ILI cumulative seasonal incidence per age category in the 2019/2020 respiratory season (week 40 of 2019 through week 20 of 2020) (Source: Nivel Primary Care Database, NIC location RIVM).



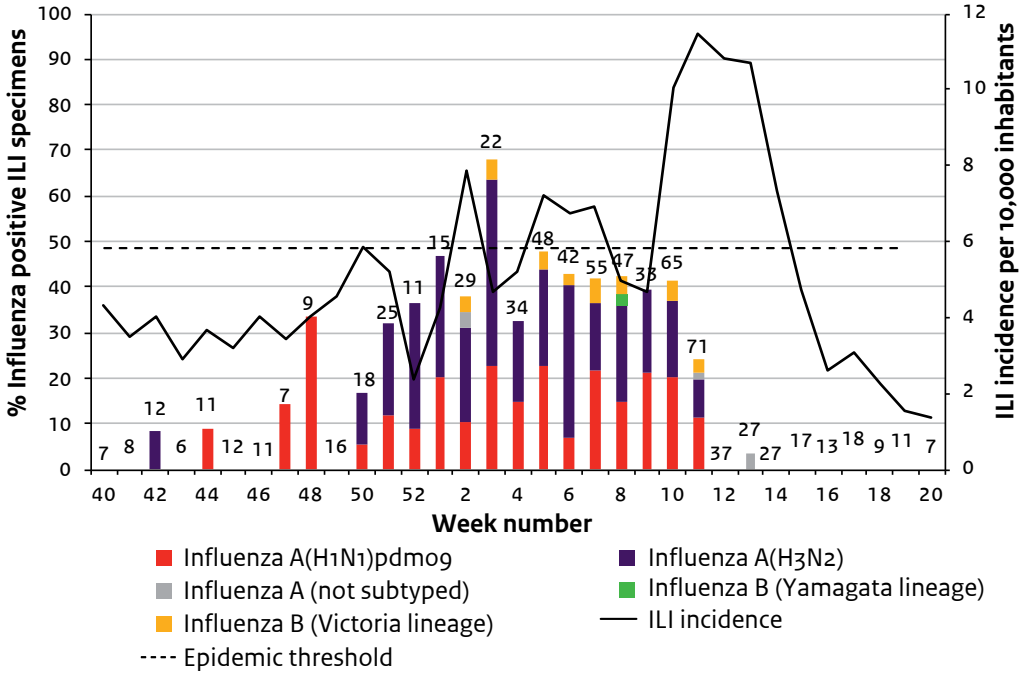
Footnote: ILI = influenza-like illness; ARI = acute respiratory tract infections, GP = general practitioner. Please note that the 'other ARI' patients do not include the ILI patients.

Figure 3.2 Number and proportion of influenza viruses detected in specimens taken from ILI and other ARI patients, who were sampled in the Nivel GP sentinel surveillance during the 2019/2020 respiratory season (through week 20 of 2020) (Source: NIC location RIVM).



Footnote: ILI = influenza-like illness; ARI = acute respiratory tract infection.
Please note that the 'other ARI' patients do not include the ILI patients.

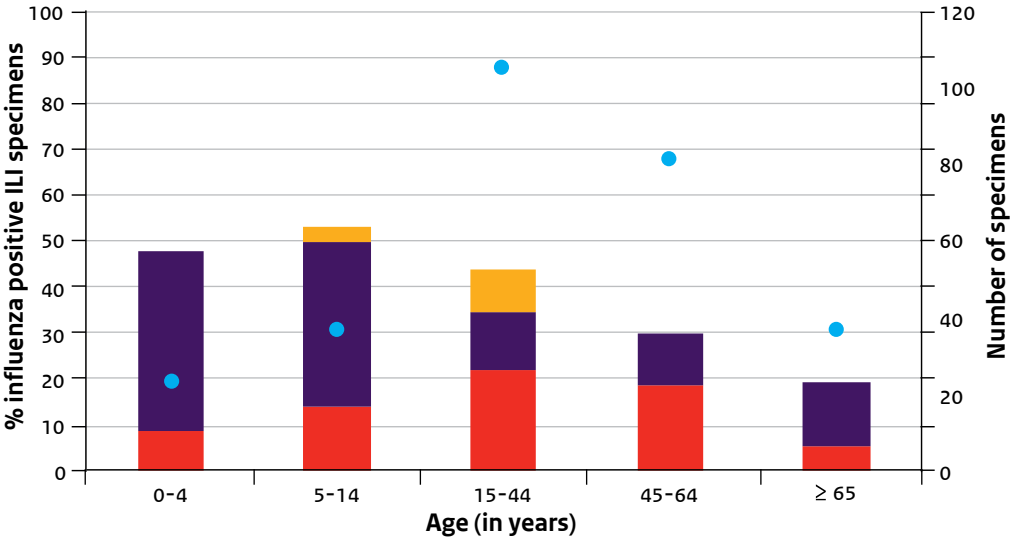
Figure 3.3 Percentage of specimens taken from ILI patients by sentinel GPs positive for influenza virus and ILI incidence with the epidemic threshold during the 2019/2020 respiratory season (week 40 of 2019 through week 20 of 2020), displayed by week of sampling (Source: Nivel Primary Care Database, NIC location RIVM).



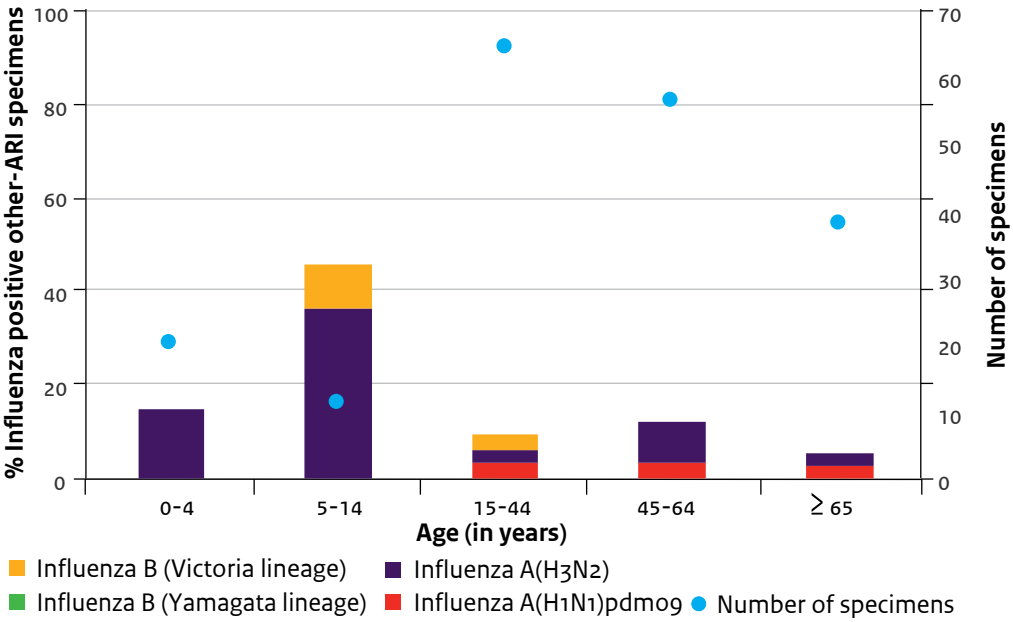
Footnote: ILI = influenza-like illness; GP = general practitioner.
The numbers above the bars are the total number of tested specimens.

Figure 3.4 Percentage of influenza virus positive specimens taken from ILI (graph A) and other ARI (graph B) patients per age group, taken by sentinel GPs, during the first epidemic period (week 5 through 7, and week 10 and 11 of 2020) of the 2019/2020 season (Source: NIC location RIVM).

A: ILI

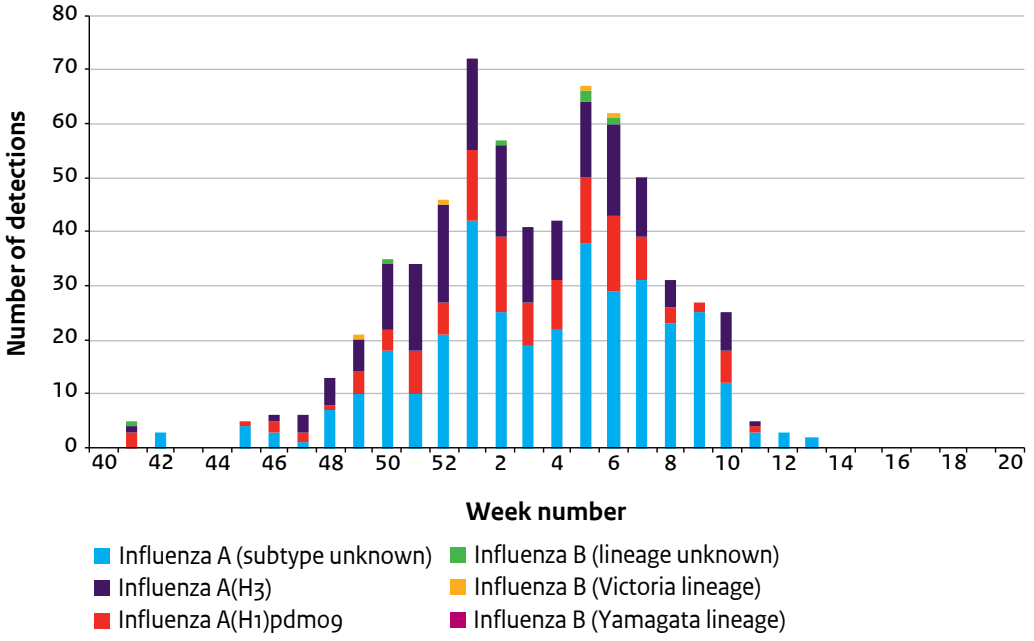


B: Other ARI



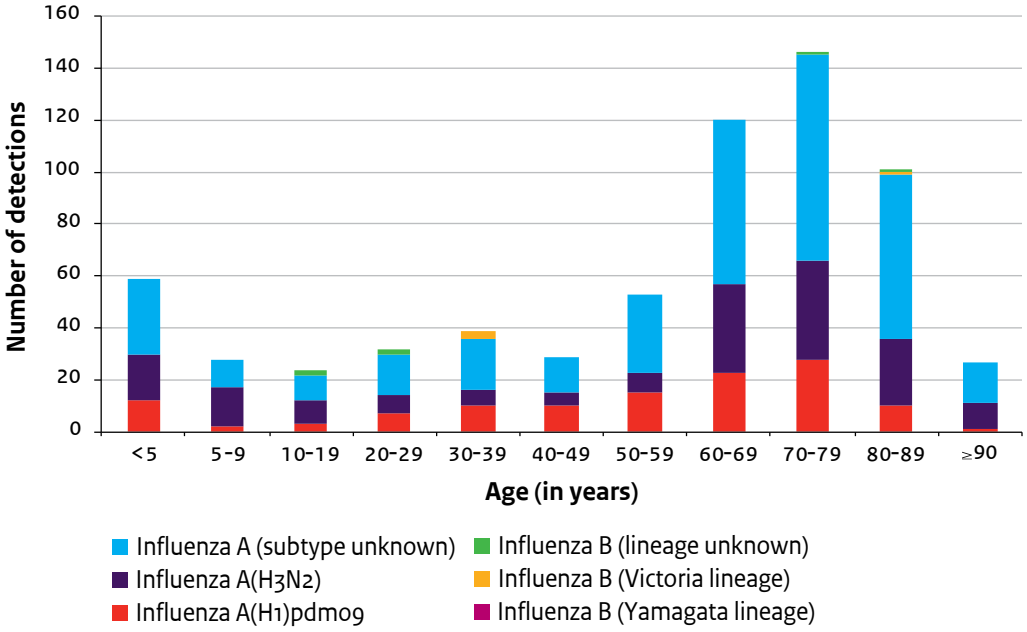
Footnote: ARI = acute respiratory tract infection, ILI = influenza-like illness.
Please note that the 'other ARI' patients do not include the ILI patients.

Figure 3.5 Subtyping of influenza viruses submitted by Dutch laboratories to the NIC location Erasmus MC during the 2019/2020 season, displayed by week of specimen collection, excluding specimens taken for sentinel GP surveillance and submitted to NIC location Erasmus MC for antigenic characterisation (Source: NIC location Erasmus MC).



Footnote: NIC= national influenza centre, GP = general practitioner.
Note: Since the beginning of 2018, the laboratories are requested to send only a representative set of influenza virus positive samples per week (5-6 specimens) to the Erasmus MC. Therefore, the trend in the samples received by Erasmus MC is not a reflection of the course of the epidemic. The graph only shows what viruses were submitted to the Erasmus MC for further characterization. In addition, for laboratories that continue to submit all influenza virus positive specimens, 5-6 viruses per week are selected for subtyping. The influenza viruses that were not subtyped are displayed in the figure as subtype or lineage unknown, these also include specimens that had a too low viral load for subtype/lineage determination by MinION sequencing.

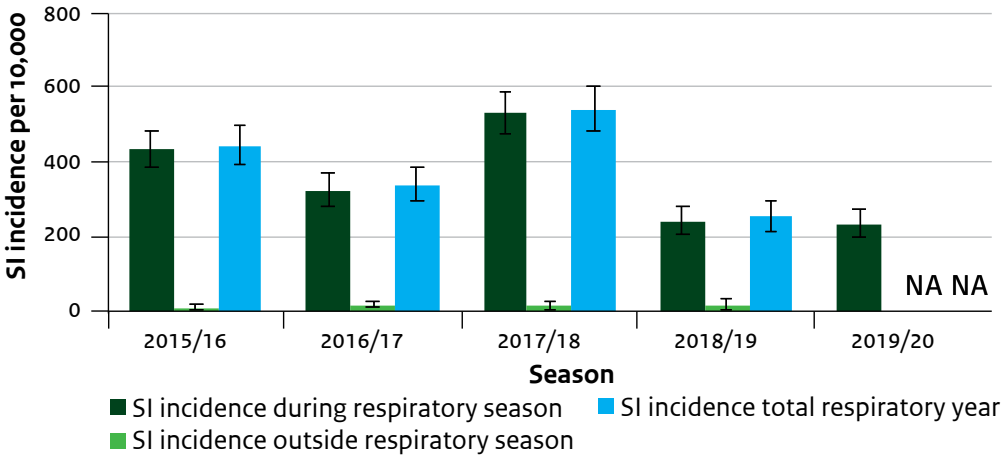
Figure 3.6 Subtyping of influenza viruses submitted by Dutch laboratories to the NIC location Erasmus MC during the 2019/2020 season, displayed by age group, excluding specimens taken for sentinel GP surveillance and submitted to NIC location Erasmus MC for antigenic characterisation (Source: NIC location Erasmus MC).



Footnote: NIC = national influenza centre, GP = general practitioner.
Note: Since the beginning of 2018, the laboratories were requested to send only a representative set of influenza virus positive samples per week (5-6 specimens) to the Erasmus MC. Therefore, the trend in the samples received by Erasmus MC is not a reflection of the course of the epidemic. The graph only shows what viruses were submitted to the Erasmus MC for further characterization. In addition, for laboratories that continue to submit all influenza virus positive specimens, 5-6 viruses per week are selected for subtyping. The influenza viruses that were not subtyped are displayed in the figure as subtype or lineage unknown, these also include specimens that had a too low viral load for subtype/lineage determination by MinION sequencing.

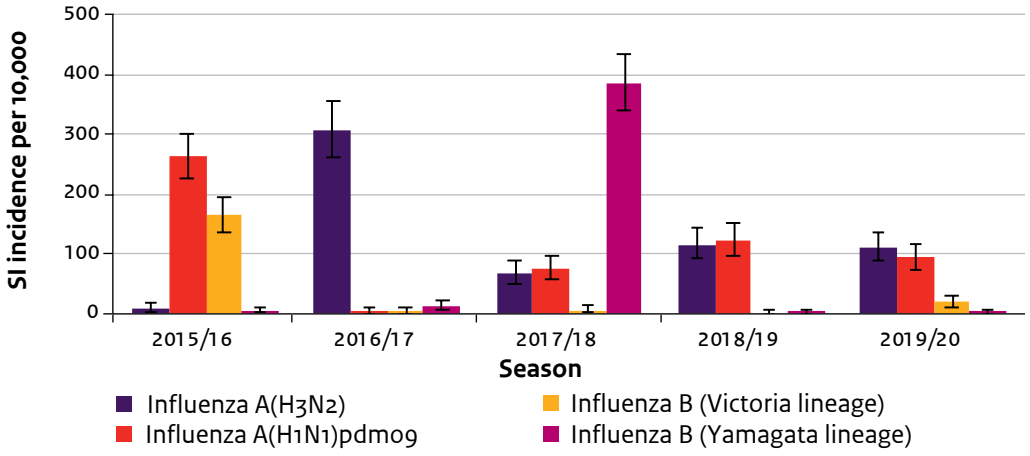
Symptomatic influenza incidence estimation

Figure 3.7 Estimated symptomatic influenza (SI) incidence per 10,000 inhabitants during the respiratory season (week 40 through week 20 the next year), outside the respiratory season (week 21 through week 39) and for the total respiratory year (week 40 through week 39 the next year), for the seasons 2015/2016 through 2019/2020 (Source: Nivel Primary Care Database, NIC location RIVM, Influenzanet).



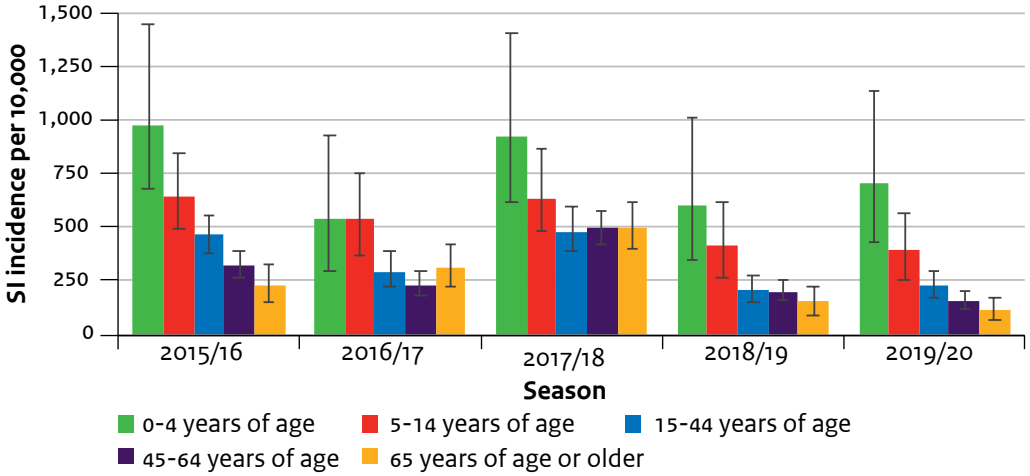
Footnote: NA= not yet available.
Error bars represent 95% uncertainty intervals (UI). For the 2019/2020 season, no numbers for outside the respiratory season were yet available.

Figure 3.8 Estimated symptomatic influenza (SI) incidence per 10,000 inhabitants by subtype for the respiratory seasons (week 40 through week 20) 2015/2016 through 2019/2020 (Source: Nivel Primary Care Database, NIC location RIVM, Influenzanet).



Footnote: Error bars represent 95% uncertainty intervals (UI).

Figure 3.9 Estimated symptomatic influenza (SI) incidence per 10,000 inhabitants by age group for the respiratory seasons (week 40 through week 20) 2015/2016 through 2019/2020 (Source: Nivel Primary Care Database, NIC location RIVM, Influenzanet).



Footnote: Error bars represent 95% uncertainty intervals (UI).

Influenza diagnostics in virological laboratories

Figure 3.10 Weekly number of influenza virus type A and B diagnoses, reported by the virological laboratory surveillance in the period week 1 of 2010 through week 20 of 2020 (Source: Virological laboratory surveillance, RIVM).

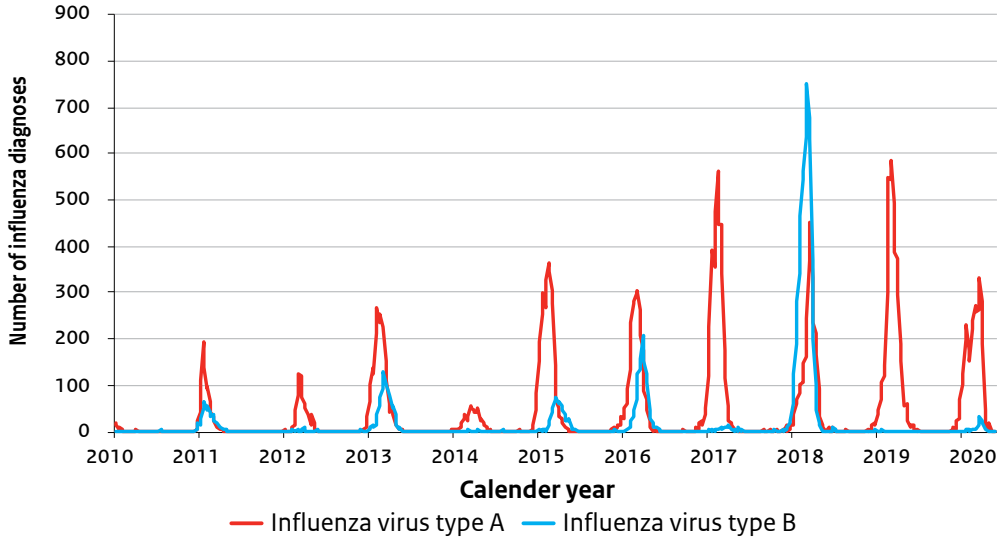
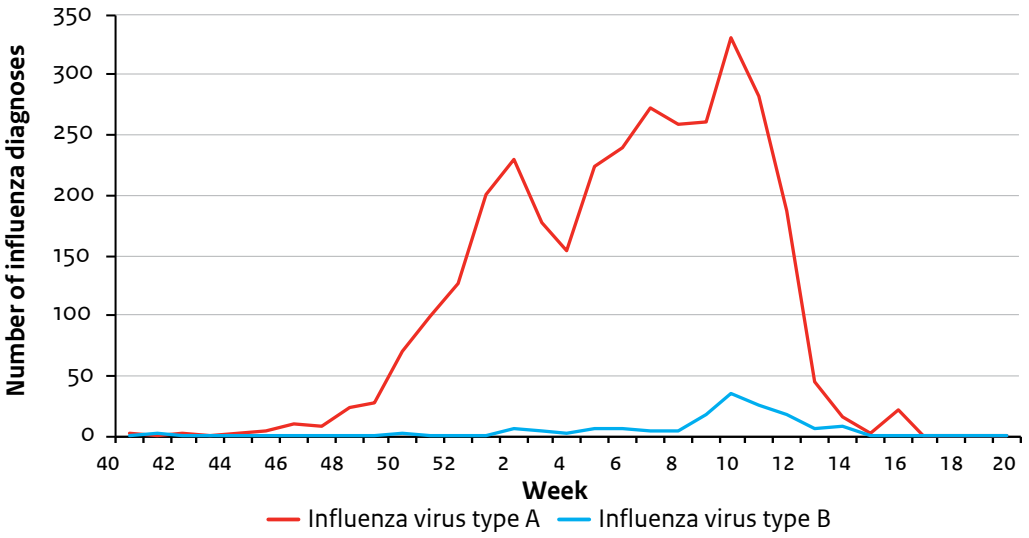


Figure 3.11 Weekly number of influenza virus type A and B diagnoses reported in the virological laboratory surveillance, for the period week 40 of 2019 through week 20 of 2020 (Source: Virological laboratory surveillance, RIVM).



Antiviral susceptibility

Table 3.2 Reduced inhibition of influenza viruses by neuraminidase inhibitors and Baloxavir marboxil, 2017/2018 – 2019/2020 (Source: NIC location RIVM, NIC location Erasmus MC)[a]

Antiviral Influenza virus (sub)type	**Viruses with reduced inhibition by season**		
	2017/2018 n/N (%)	**2018/2019 n/N (%)**	**2019/2020 n/N (%)**
Neuraminidase inhibitor			
A(H1N1)pdm09	1/233 (1)[b]	3/331(1)[c]	0/151 (0)
A(H3N2)	0/355 (0)	0/421 (0)	0/242 (0)
B	0/156 (0)	0/4 (0)	0/16 (0)
Baloxavir marboxil[d]			
A(H1N1)pdm09	None tested	None tested	0/39 (0)
A(H3N2)	None tested	None tested	0/114 (0)
B	None tested	None tested	0/1 (0)

[a] 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.

[b] One virus with highly reduced inhibition by oseltamivir due to mixture 275H/Y amino acid substitution in the neuraminidase. No patient characteristics or antiviral exposure data available.

[c] Three viruses with highly reduced inhibition by oseltamivir due to H275Y (n=1) or mixture 275H/Y (n=2) amino acid substitution. Two patients were admitted to ICU of which one was treated with oseltamivir prior to specimen collection and the other had an unknown treatment status. One community patient had no prior treatment with oseltamivir.

[d] Because EMA approval for Baloxavir marboxil (Xofluza®) (BXM), a cap-dependent acidic endonuclease inhibitor, is anticipated in 2020, monitoring of reduced susceptibility amino acid substitutions in the polymerase acidic protein (PA) genome segment has been added for the 2019/2020 season.

Influenza vaccine effectiveness

Table 3.3 Preliminary Influenza vaccine effectiveness in the 2019/2020 season in Europe, estimated in the I-MOVE multicentre case control study, against laboratory confirmed influenza virus, per age group (Source: I-MOVE study).

		Cases			Controls				
	Age group	All	Vaccinated	%	All	Vaccinated	%	Adjusted VE	95% CI
Any influenza	All ages	3480	239	7	4516	629	14	48	38-57
	0-14 years	1427	45	3	1531	68	4	50	23-68
	15-64 years	1854	104	6	2498	310	12	54	41-64
	≥ 65 years	199	90	45	487	251	52	28	-5-51
	Target group	645	163	25	1233	439	36	41	24-54
A(H1N1) pdm09	All ages	1447	113	8	4316	601	14	45	29-57
	0-14 years	449	15	3	1482	68	5	57	17-78
	15-64 years	912	55	6	2371	293	12	50	30-64
	≥ 65 years[a]	86	43	50	463	240	52	5	-55-42
	Target group	295	75	25	1182	423	36	38	14-55
A(H3N2)	All ages	810	75	9	4047	539	13	49	30-62
	0-14 years	340	7	2	1437	67	5	60	7-82
	15-64 years	390	29	7	2203	272	12	59	37-74
	≥ 65 years[a]	80	39	49	407	200	49	22	-33-54
	Target group	199	60	30	1053	369	35	32	2-53
B	All ages	1181	46	4	3971	595	15	57	39-70
	0-14 years	619	22	4	1288	62	5	43	-3-69
	15-64 years	532	17	3	2224	295	13	63	37-79
	≥ 65 years[b]	30	7	23	459	238	52	-	-
	Target group	144	25	17	1092	413	38	59	30-76

[a] Due to low sample size, crude VE estimate only.
[b] Due to low sample size, VE estimation not attempted.

Impact of the influenza vaccination programme

Table 3.4 Impact estimations for ILI GP consultations caused by influenza virus for the 2019/20 season. Number between brackets are 95% CIs. (Sources: Nivel Primary Care Database, I-MOVE/I-MOVE+ study and NIC location RIVM).

Input parameters:	
Vaccine coverage	61.3 (54.8 – 67.4)
Vaccine effectiveness[a]	16.9 (-16.9 – 51.0)
Incidence	14,048 (9,089 – 20,221)
Estimated impact:	
Number of adverted events	1,624 (-2,142 – 6,135)
Number of averted events per 100,000 population	49 (-65 – 185)
NNV	1,251 (-11,756 – 11,594)
Prevented fraction	0.10 (-0.17 – 0.29)

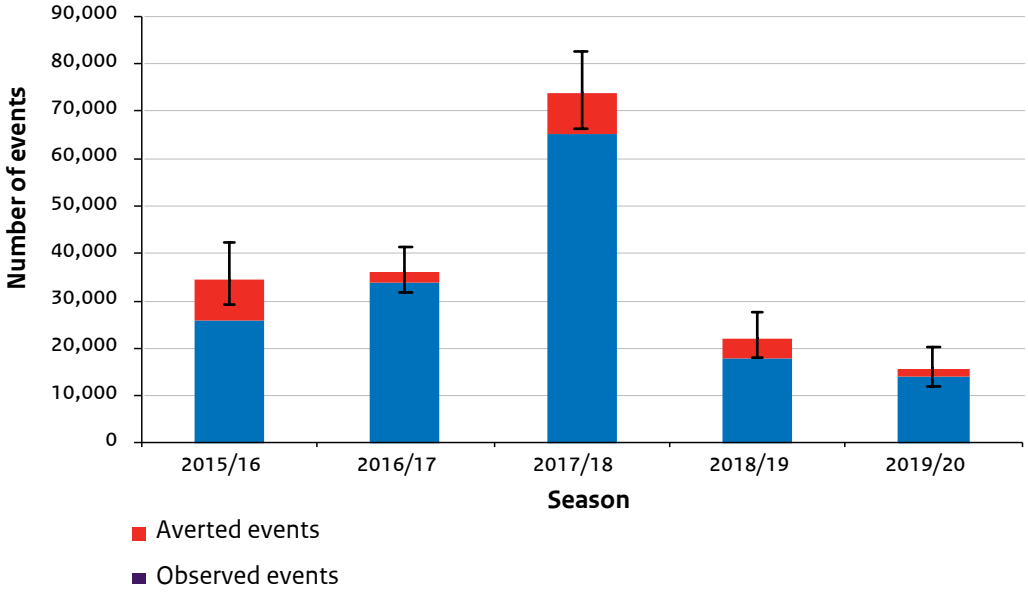
Footnote: ILI = influenza-like illness, GP = general practitioner, CI = confidence interval, NNV = number of vaccinated persons needed to avoid one influenza-associated event.
[a] See table 3.5.

Table 3.5 Weighted overall vaccine effectiveness (VE) against influenza confirmed ILI for the population of 65 years and older in the Netherlands as used for the impact estimations. Number between brackets are 95% CIs. (Sources: I-MOVE/I-MOVE+ study and NIC location RIVM).

Input parameters	
I-MOVE+ pooled VE against H1N1	5 (-55 – 42)
I-MOVE+ pooled VE against H3N2	22 (-33 – 54)
I-MOVE+ pooled VE against B[a]	n.a.
Proportion H1N1/H3N2/B in NL (sentinel)	0.29/0.71/ 0
Weighted overall VE against influenza confirmed ILI for NL	17.1 (-16.9 – 51.0)

Footnote: VE = vaccine effectiveness, ILI = influenza-like illness, CI = confidence interval, n.a. = not available
[a] Due to low sample size, VE estimation not calculated.

Figure 3.12 Impact estimations for ILI GP consultations caused by influenza virus, 2015/16 – 2019/20. Blue bars represent the estimated number of observed cases. Red bars represent the estimated number of cases averted by the influenza vaccination campaign of the concerning season, with 95% CIs. (Sources: Nivel Primary Care Database, I-MOVE/I-MOVE+ study and NIC location RIVM).



Footnote: ILI = influenza-like illness, GP = general practitioner, CI = confidence interval.
Estimates for the seasons 2015/16 through 2018/19 are as reported in the RIVM Annual report Surveillance of influenza and other respiratory infections 2018/2019.

Chapter 4
RS-Virus

Authors: Anne Teirlinck, Mariëtte Hooiveld, Wim van der Hoek, Adam Meijer
Contributors: Marit de Lange, Daphne Reukers, Sofie Mooij

4.1 Keypoints

- The RSV season started in week 46 of 2019 and lasted 19 weeks. The average length of RSV seasons from 2010/2011 – 2018/2019 was 18 weeks (range 16 – 20 weeks).
- During the respiratory season, the number of RSV diagnoses in the virological laboratory surveillance peaked in week 2 of 2020 (n=170). The number of diagnoses exceeded the medium intensity threshold of 155 detection in that same week.
- In the 2019/2020 respiratory season, in 93 of the 1493 (6.2%) patients with an acute respiratory infection (ARI), RS-viruses were detected in nose swabs and throat swabs, collected by sentinel GPs. The peak percentage of RSV positive patients in week 52 2019 was 40%, both timing and height of the peak was within the range of previous four seasons.
- The overall percentage of RSV positive specimens taken by the GPs was highest in children in the age group 0-1 years (34%) and was much lower in the other age groups (range 3-7%).

4.2 Background

Respiratory Syncytial Virus (RSV) causes respiratory infection and is commonly contracted by children, in temperate countries mostly in the winter season. During their first two years of life, most children are infected with this virus and re-infections later in life are very common. Especially in risk groups, such as new-borns and preterm infants, infection can lead to severe illness, hospitalisation and even death. Studies suggest that RSV is also a common cause for respiratory infections in the elderly causing outbreaks in elderly care facilities (Meijer, Overduin et al. 2013). RSV is subdivided in RSV-A and RSV-B, based on the different antigenic properties of their attachment glycoprotein G. These two types may circulate simultaneously in the population. Currently, no vaccine for RSV is available, but many vaccine candidates are in the pipeline. Most vaccine and monoclonal antibody candidates that are currently in phase 2 and

phase 3 clinical trials are based on the fusion protein (F-protein) [https://www.path.org/resources/rsv-vaccine-and-mab-snapshot/].

4.3 Epidemiological situation, season 2019/2020

The RSV season (defined using virological laboratory surveillance data) lasted 19 weeks from week 46 of 2019 through week 12 of 2020 and exceeded the medium intensity threshold of 155 detections for one week (week 2 of 2020). The total number of positive RSV diagnoses reported by the 19 Dutch virological laboratories participating in the virological laboratory surveillance in 2019/2020 was within the range of the last ten seasons (n=1731; through week 20 of 2020). The number of RSV-diagnoses peaked in week 2 of 2020 (n=170). In the 2019/2020 respiratory season (week 40 through week 20), 93 of 1493 (6.2%) total ARI (ILI plus other ARI) patients that were sampled in the GP sentinel surveillance tested RSV positive, of which two patients had an infection with both RSV-A and B. Among the 95 RS-viruses detected, 61 were RSV-A (64%) and 34 were RSV-B (36%). The peak percentage of RSV positive patients in week 52 2019 was 40%, both timing and height of the peak is within the range of previous four seasons.

4.4 Discussion

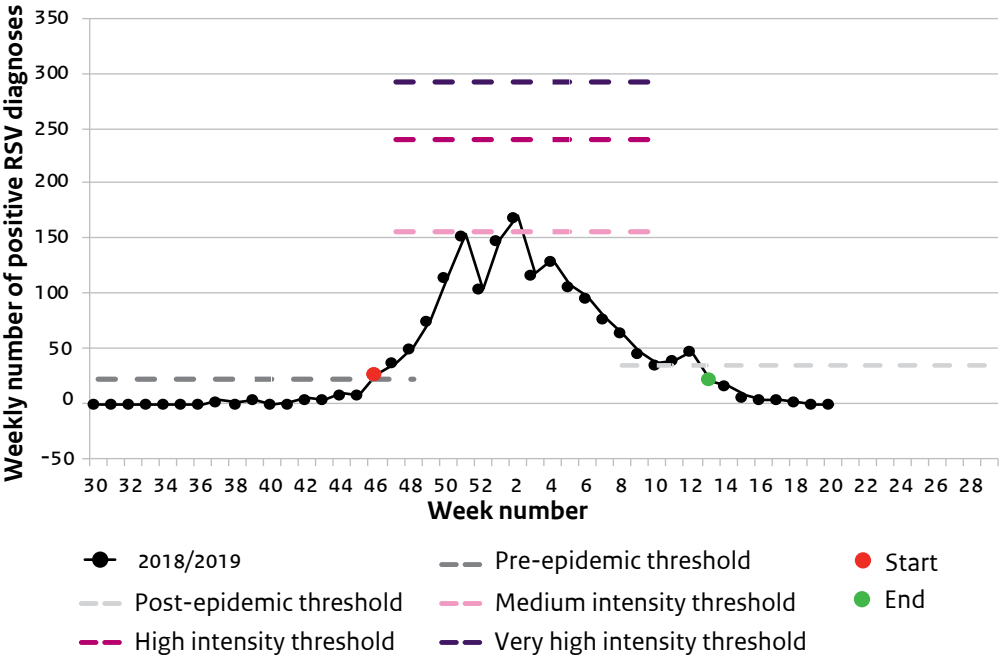
The virological laboratory surveillance provides real-time data on absolute number of RSV diagnoses, but a denominator, age distribution, clinical background information, information on testing strategies by laboratories and RSV typing information is lacking. Such background information is available for influenza-like illness (ILI) and other acute respiratory infection (ARI) patients that are swabbed by sentinel GPs. Since the sentinel surveillance is primarily aiming to detect influenza, patients with ILI are oversampled in the group of total ARI patients that are sampled.

The percentage of positive specimens from the GP sentinel surveillance was lower in this season compared to the previous seasons 2018/2019 (12%) and 2016/2017 (12%), and similar to 2017/2018 (6%). This season, more samples were collected with a different age distribution than previous seasons in weeks 10-20 (total 622 samples, compared to about 100-300 in other seasons during these weeks). This higher number of samples due to the COVID-19 pandemic possibly partly explains the relatively low RSV percentage. Nevertheless, the overall percentage RSV positive specimen from week 40 trough week 9 was still somewhat lower in season 2019/2020 (10%) compared to three out of four previous seasons (respectively 10%, 13%, 7% and 14% in seasons 15/16, 16/17, 17/18 and 18/19). The height and timing of the RSV curve, that peaked well before the start of the COVID-19 outbreak, was within the range of previous seasons. In the virological laboratory surveillance, the peak number and cumulative numbers are somewhat, but not much lower than previous three seasons. Compared to influenza, the seasonal RSV epidemics show a very consistent pattern over the years in timing and intensity.

A reliable RSV surveillance, both at national and European scale, is important for monitoring RSV trends and, given the current developments in vaccine and monoclonal antibodies, for establishing a platform for future estimation of immunization impact. Therefore, RIVM works closely together with ECDC and other public health institutes, specifically SSI (Denmark) in order to strengthen international collaboration on RSV surveillance. Furthermore, RIVM is partner in the RESCEU project [http://resc-eu.org], which aims to explore the burden (clinical, economic and social) from RSV. The aim is to create a sound epidemiological and virological baseline, before the introduction of a vaccine, to identify appropriate target groups for vaccination. RESCEU has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement 116019. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and the European Federation of Pharmaceutical Industries and Associations.

4.5 Tables and figures

Figure 4.1 Number of weekly reported RSV diagnoses in respiratory season 2019/2020, and epidemic thresholds and intensity levels, based on the number of RSV diagnosis in the period 2009/2010-2018/2019 (Source: virological laboratory surveillance and MEM web application (Lozano 2018)).



Footnote: The MEM epidemic and intensity thresholds were as follow: pre-epidemic threshold: 22; post-epidemic threshold: 35; medium intensity: 155, high intensity: 240; very high intensity; 291.

Figure 4.2 Number of weekly reported RSV diagnoses (black line) and total number of RSV diagnoses in the respiratory season (blue dot) in the virological laboratory surveillance for the period 2015/2016-2019/2020 (until week 20) (Source: virological laboratory surveillance).

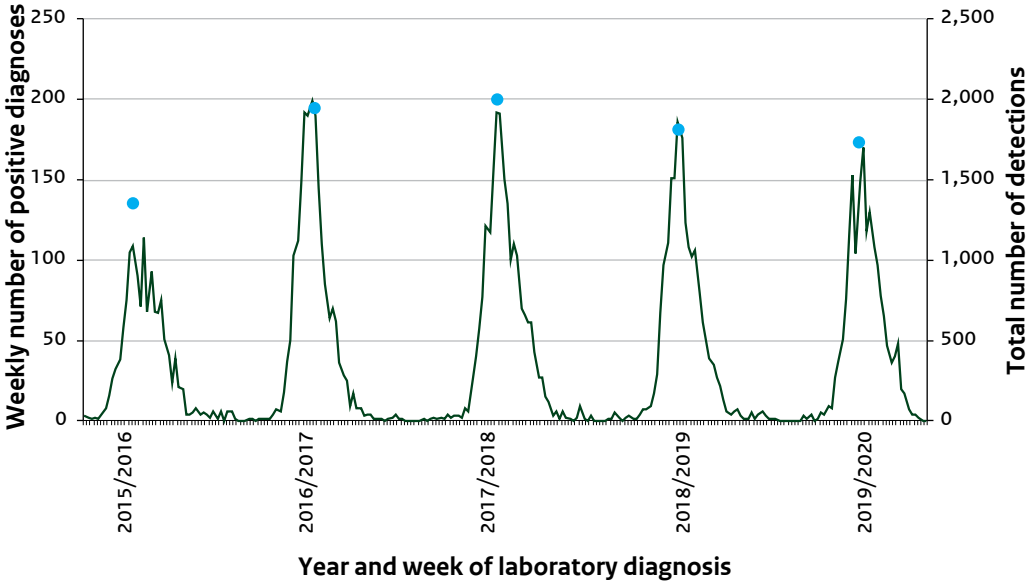


Table 4.1 Number of reported respiratory syncytial virus (RSV) diagnoses in the virological laboratory surveillance for the period 2010/2011-2019/2020 (through week 20).

RSV diagnoses	weeks 40-20 (N)	weeks 21-39 (N)	weeks 40-39 (N)
2010/2011	2702	27	2729
2011/2012	1838	51	1889
2012/2013	2199	12	2211
2013/2014	1629	16	1645
2014/2015	1670	32	1702
2015/2016	1348	42	1390
2016/2017	1938	21	1959
2017/2018	1996	32	2028
2018/2019	1807	31	1838
2019/2020	1731[a]	-[b]	-[b]

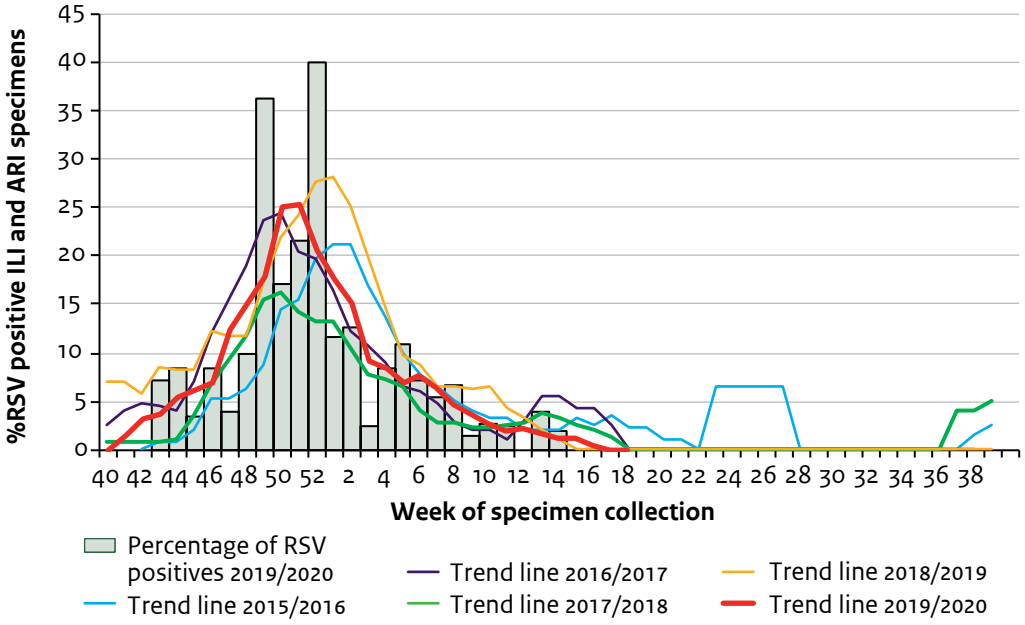
[a] Data for weeks 40 of 2019 through week 20 of 2020 are preliminary.
[b] Data for weeks 21-39 of 2020 are not yet available.

Table 4.2 RSV seasonal trends in the virological laboratory surveillance for the period 2010/2011-2019/2020 (through week 20): season onset and duration, epidemic intensity, and peak. Week is week of laboratory diagnosis report. Thresholds for the epidemic period and intensity are defined by MEM.

	Onset week (week number)	Season duration (N weeks)	Above medium intensity level (N weeks)	Above high intensity level (N weeks)	Peak	
					Timing (week number-year)	RSV diagnoses (N)
2010/2011	46	20	6	0	3-2011	264
2011/2012	47	18	0	0	51-2011	125
2012/2013	46	20	4	0	2-2013	182
2013/2014	48	17	0	0	1-2014	134
2014/2015	49	18	0	0	8-2015	162
2015/2016	48	19	0	0	4-2016	114
2016/2017	45	16	4	0	52-2016	199
2017/2018	46	19	2	0	1-2018	192
2018/2019	47	16	2	0	1-2019	186
2019/2020	46	19	1	0	2-2020	170

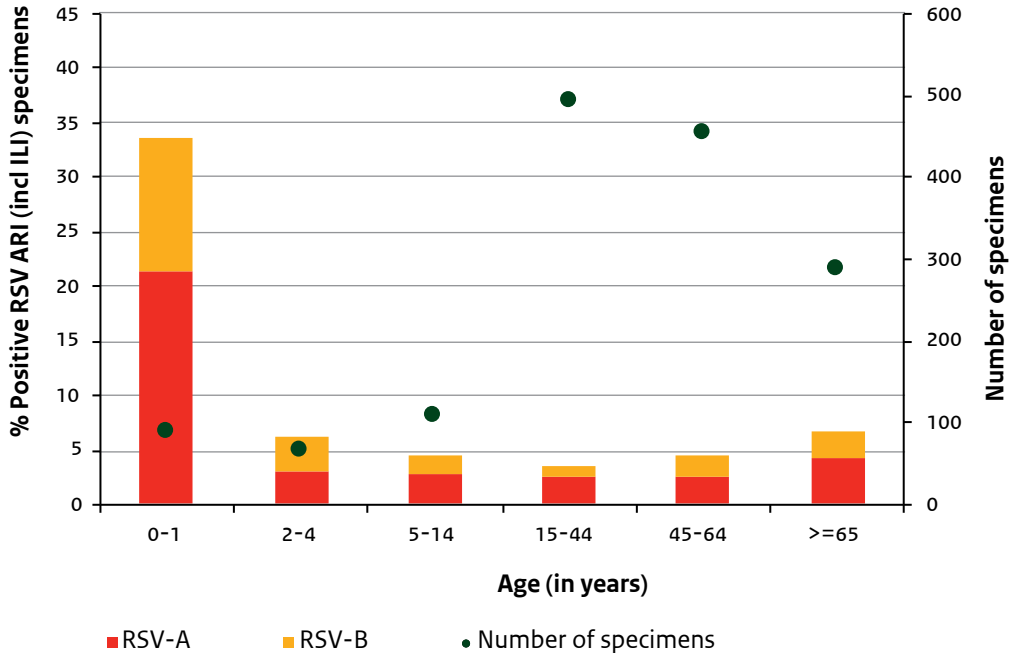
Note: The epidemic thresholds for seasons up to and including 2016/2017 were calculated based on data of seasons 2005/2006 up to and including 2016/2017 (Vos, Teirlinck et al. 2019). The thresholds of the seasons from 2017/2018 onward were calculated separately per season, based on data of the previous ten seasons.

Figure 4.3 Percentage of RSV-positive specimens from ILI and other ARI patients, sentinel influenza surveillance during the seasons 2015/2016 – 2019/2020 (week 40 2019 through week 20 of 2020) (Source: Nivel Primary Care Database, RIVM).



Footnote: Trend lines indicate a 5-weeks moving average. ILI= influenza-like illness; ARI = acute respiratory infection

Figure 4.4 Percentage of RSV-A and RSV-B positive specimens from patients with ILI and other ARI, and the number of tested specimens, sentinel influenza surveillance during the respiratory season of 2019/2020 (week 40 of 2019 through week 20 of 2020), displayed for six age groups. (Source: Nivel Primary Care Database, RIVM).



Footnote: Please note that for the virological surveillance, the other ARI patients do not include the ILI patients.

Chapter 5
Notifiable Respiratory Diseases

5.1 Legionnaires' disease

Author: Petra Brandsema
Contributor: Sjoerd Euser

5.1.1 Key points

- The increasing trend of Legionnaires' disease (LD) observed from 2012 to 2017 did not continue in 2019. With 566 LD cases notified in 2019, the number of patients was similar to 2017 and 2018. The incidence was 3.3 cases per 100,000 inhabitants.
- Most cases (70%) have acquired the infection in the Netherlands, of which the majority (352 cases) is community acquired.
- Most notified patients (97%) were admitted to hospital. The proportion of Intensive Care Unit (ICU) admission was fairly constant at 25% in the age groups from 30 to 70 years and increased in the age group 70 to 79 years.
- The case fatality was 3.9%, and was similar in domestic cases (4%) and in cases with travel abroad (3.6%).
- In August 2019, a particularly high number of LD cases was notified (n=120). This increase appeared to be weather associated, as cases were geographically dispersed and the rise followed after a warm and dry July and showery weather in August.
- 30% Of LD patients had travelled abroad in the 10 days before onset and 16% of these patients were part of a cluster in a travel accommodation. Italy, France and Germany were the most frequently reported countries of travel.
- In summer 2019, 11 people at a French campsite became ill due to *Legionella*. In total eight Dutch cases were involved in this travel associated cluster of legionellosis, of which five cases were children, who had all used the same jacuzzi at the holiday home. The children and three of their parents had a positive urine antigen test for *Legionella*, but did not require hospitalisation. Pneumonia was reported in 4 Dutch cases, of which one adult were

hospitalised. The high attack rate and simultaneous onset of symptoms fits with a mixed outbreak of Pontiac fever and Legionnaires' disease.
- A cluster of seven cases across 2018 and 2019 was linked to a Dutch wellness resort. Sampling results suggested a high pressure cleaner was the most likely source of infection.
- A waste water treatment plant (WWTP) was found as most likely source of a cluster of four patients in the east of the Netherlands. A legionella strain detected in this WWTP (genotype ST47) matched with the clinical strain of one of these patients. This specific genotype is found in one third domestic (non-imported) LD patients in the Netherlands, but is rarely found in sampling of sources. Before 2019 this genotype had only been found in outdoor spa-pools and in soil.
- For the first time since the start of environmental sampling of LD patients in the Netherlands, a patient with a ST47 clinical strain, was matched to a drinking water installation at home.
- In a town with an increased LD incidence, *Legionella pneumophila* was found in three wet cooling towers and in a WWTP. There were no clinical isolates from patients available for comparison, but the serotyping of environmental strains suggested a cooling tower as probable source of infection.
- A cluster of two patients was linked to a private rental holiday home. *Legionella pneumophila* serogroup 1 was detected in the shower of the rental home. Since no clinical isolates from patients were available, comparison with the legionella strain from the rental home was not possible.
- Other genotypical matches identified a cooling reservoir of an injection moulding machine (n=1), one wet cooling tower (n=1) and a shower hose at home (n=1), as source of infection.
- Six percent of clinical isolates from patients (seven patients) was *Legionella longbeachae*. This *Legionella* species is usually related to gardening and potting soil, but it has also been found in waste water treatments plants.

5.1.2 Background

Legionellosis is an infection caused by inhalation of *Legionella* bacteria. Symptoms may range from mild to severe disease, but most diagnosed patients have a severe pneumonia (Legionnaires' disease (LD)). The incubation period of LD is usually 2-10 days and rarely exceeds 14 days. LD affects mostly the middle aged and elderly population, and men are more at risk than women. Furthermore, smoking, impaired health status and travel are risk factors for severe LD. Legionellosis without pneumonia is called pontiac fever (PF), but this syndrome is rarely diagnosed outside a cluster setting. PF is excluded from the European case definition for LD used in this report.

Legionella bacteria are common in the natural environment, usually in low numbers. At present 61 different species of *Legionella* have been described and 28 species have been associated with human disease. Most LD outbreaks are associated with manmade water systems, such as wet cooling towers, whirlpools, water distribution systems and waste water treatment plants. For the majority of non-outbreak cases (sporadic cases) however, the source of infection remains unknown. The common seasonal pattern of LD shows an increase during summer, especially after warm weather with heavy rainfall. These wet weather conditions are favourable for the survival of aerosolized *Legionella* bacteria, and this may lead to increased transmission.

However, it remains unclear which environmental sources are driving the weather related increase of Legionnaires' disease.

Most LD patients are diagnosed with an urine antigen test for *Legionella pneumophila* serogroup 1, which is the causative agent in most LD patients. Other serogroups or *Legionella* species can be diagnosed using culture or PCR on sputum or bronchial lavage. *Legionella pneumophila* of *Legionella* species PCR using specimens from the upper respiratory tract have very low sensitivity and are of limited diagnostic value. The culture method is important for obtaining a clinical isolate for typing. This is especially relevant for identification of sources through comparison of clinical strains to *Legionella* strains found in environmental sources. However, a clinical isolate is available for only one out of five Dutch patients, which is a limitation for source finding.

5.1.3 Tables and figures

Figure 5.1 Annual numbers of notified Legionnaires' disease, 2009 through 2019, by infection acquired abroad or domestic (acquired within the Netherlands) (Source: Osiris).

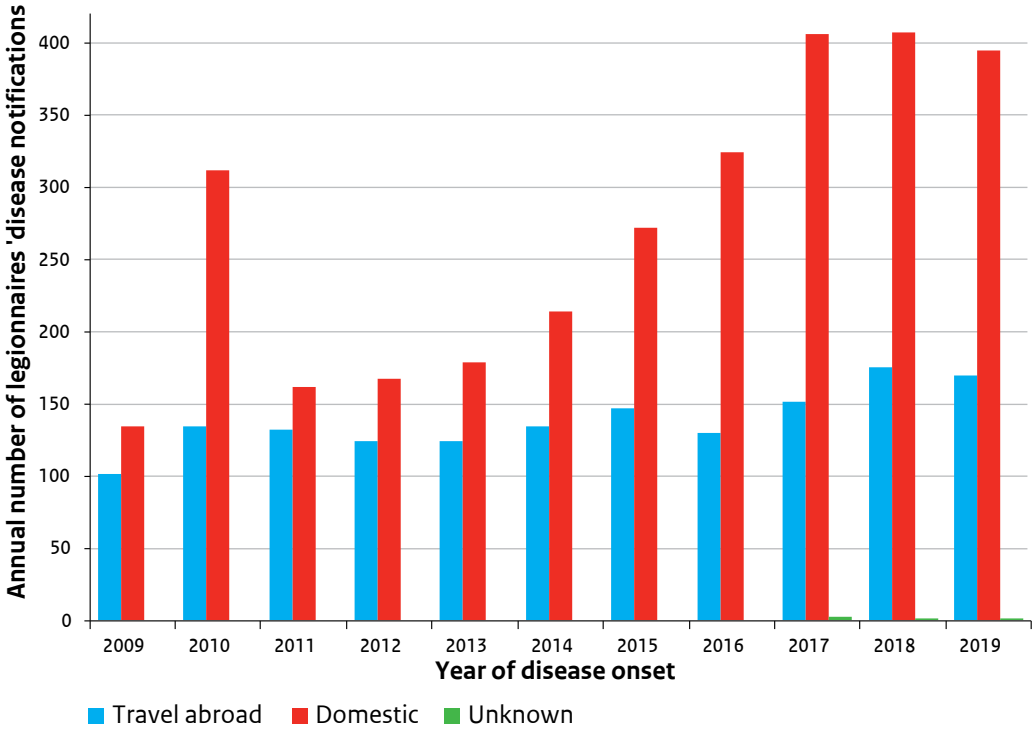


Figure 5.2 Notifications of Legionnaires' disease acquired abroad or acquired in the Netherlands (domestic), by month of disease onset in 2019 and the monthly average over 2014-2018. (Source: Osiris).

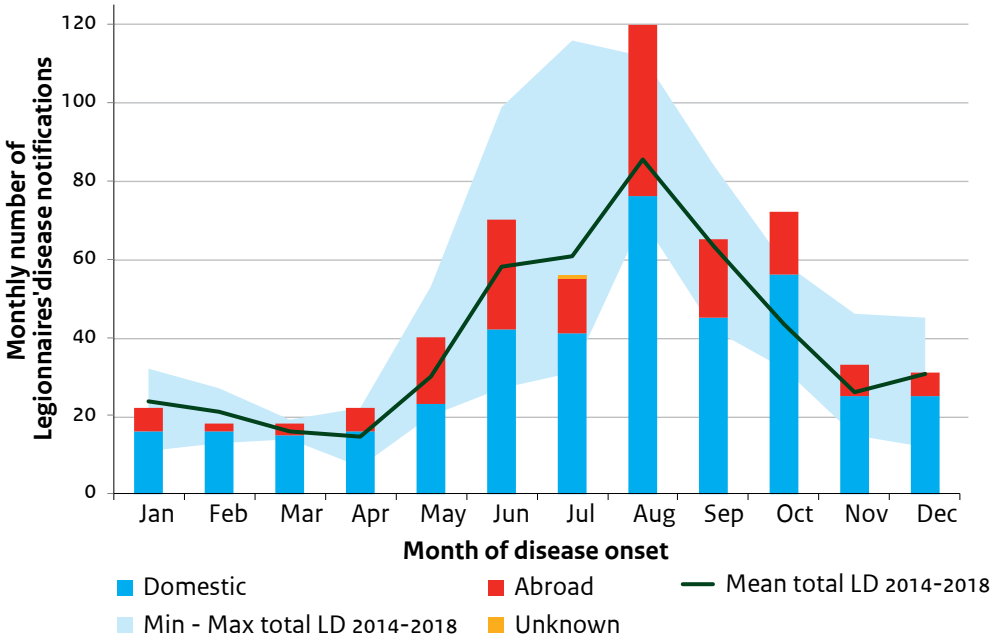


Table 5.1 Number of legionellosis notifications in 2015 – 2019, incidence, clinical and epidemiological background, mortality and diagnostics (Source: Osiris).

Year of onset disease[a]	2015	2016	2017	2018	2019
Number of Legionellosis notifications[b]	438	468	575	594	587
Non-residents	5	6	7	10	8
Not fulfilling EU case definition:[b]	14	8	7	-	13
Pontiac fever or extrapulmonal	10	2	2	-	4
LD	13	6	5	-	1
Single high titre[c]	-	-	-	-	8
PCR nose or throat swab sample	19	14	14	10	21
Total excluded from analysis					
Total included:	**n(%)**	**n(%)**	**n(%)**	**n(%)**	**n(%)**
Legionnaires'disease (LD) (=100%)[b]	**419 (100)**	**454 (100)**	**561 (100)**	**584 (100)**	**566 (100)**
% difference to year before	+20%	+8%	+24%	+4%	-3%
Confirmed Legionnaires' disease[b]	393 (94)	422 (93)	519 (93)	536 (92)	524 (93)
Probable Legionnaires' disease[b]	26(6)	32 (7)	42 (7)	48 (8)	42 (7)
LD Incidence (per 100,000 residents)	2.5	2.7	3.3	3.4	3.3
Male gender	293 (70)	327 (72)	401 (71)	420 (72)	407 (72)
Median age (Q1-Q3)	62 (53-69)	63 (55-72)	64 (54-73)	64 (57-74)	65 (55-73)
Hospital admission[d]	410 (98)	449 (99)	543 (97)	571 (98)	551 (97)
ICU admission[d]	unk	unk	unk	unk	99/353 (28%)
X-thorax confirmed pneumonia[d]	401 (96)	436 (96)	540 (99)	546 (98)	549 (99)
Deaths[d]	13 (3)	20 (4)	31 (6)	29 (5)	22 (4)
Acquired abroad of domestic:					
Imported[e]	145 (35)	130 (29)	152 (27)	177(30)	170 (30)
% Difference to year before	+8%	-10%	+17%	+17%	-4%
Not imported	273 (65)	324 (71)	406 (72)	405 (69)	395 (70)
% Difference to year before	+28%	+19%	+25%	-0.5%	-3%
Country unknown	1 (<1)	-	3 (<1)	2(1)	1 (<1)

Year of onset disease[a]	2015	2016	2017	2018	2019
Setting of infection:					
Travel abroad[f]	145 (35)	130 (29)	152 (27)	177(30)	169 (30)
Domestic travel[e,f]	24 (6)	17 (4)	45 (8)	35(6)	38 (7)
Nosocomial (hospital acquired)	2 (<1)	-	1 (<1)	-	2 (<1)
Other healthcare facilities	3 (<1)	7(2)	5 (<1)	5(<1)	4 (<1)
Community acquired	244 (58)	300 (66)	355 (63)	361(62)	352 (62)
Setting unknown	1(<1)	-	3 (<1)	6 (1)	1 (<1)
Diagnostics					
Legionella cultured performed (=yes)	181 (43)	209 (46)	229 (41)	263 (45)	271 (48)
Positive culture	79 (19)	84 (19)	92 (16)	111 (19)	113(20)
Proportion *L.pneumophila* sg1 in culture (or PCR) positives[g]	87%	85%	82%	85%	85%
Positive urine antigen test	381 (91)	404 (89)	501 (89)	515 (88)	503 (89)
Positive PCR	65 (16)	88 (19)	103 (18)	102(17)	115 (20)
of which PCR only[h]	21 (5)	26 (6)	39 (7)	46 (8)	39 (7)
Significant titer rise	6 (1)	6 (1)	6 (1)	2(<1)	4 (<1)
Direct immunofluorescence	1(<1)	-	-	-	-

Analysis based on data as available on March 2020, including all authorized notifications.

[a] If date of onset disease was unknown, date of diagnosis minus median diagnostic delay was used to estimate onset.

[b] 2012 EU/EEA case definition for confirmed cases or probable cases of Legionnaires' disease. The numbers do not add up to the total excluded as categories for exclusion may overlap. PCR on upper respiratory samples such as swabs are reported in osiris from 2019 onward. Depending on the type of PCR used, these may be clinical valid diagnosis, but it does not fulfill the EU case definition for surveillance. Pontiac Fever cases are clinical cases without pneumonia with an epidemiological link. Extra pulmonal LD can for example be endocarditis or wound infection.

[c] Diagnosis based on a single high titer not specific for *L. pneumophila* serogroup1 or single high titer without information on type of serology.

[d] Percentage based on the number of patients for which this specific information was available. Admission at Intensive Care Unit (ICU) was registered from July 2019 onwards.

[e] An imported case is a case with travel abroad in the 2-10 days before onset or a community acquired case with probable or confirmed source abroad but without overnight stay, or a nosocomial case in a hospital abroad.

[f] Travel Associated Legionnaires Disease (TALD) is defined as travel (including at least 1 overnight stay) in the period of 2-14 days before disease onset (2015) or 2-10 days before disease onset (from 2016 onward), unless source finding suggests a non-travel associated source. A case with travel in the 11-14

days before onset will also be classified as travel associated if the case is part of a travel associated cluster or when environmental sampling confirms the travel site as source.

[g] Proportion of clinical specimens (culture or PCR) available for typing at the reference lab.

[h] No other diagnostic method reported in Osiris.

Figure 5.3 Age and gender distribution of cases with Legionnaires' disease with onset of disease in 2019 and age and gender specific incidence (LD notifications per 100,000 inhabitants). (source: Osiris and CBS statline).

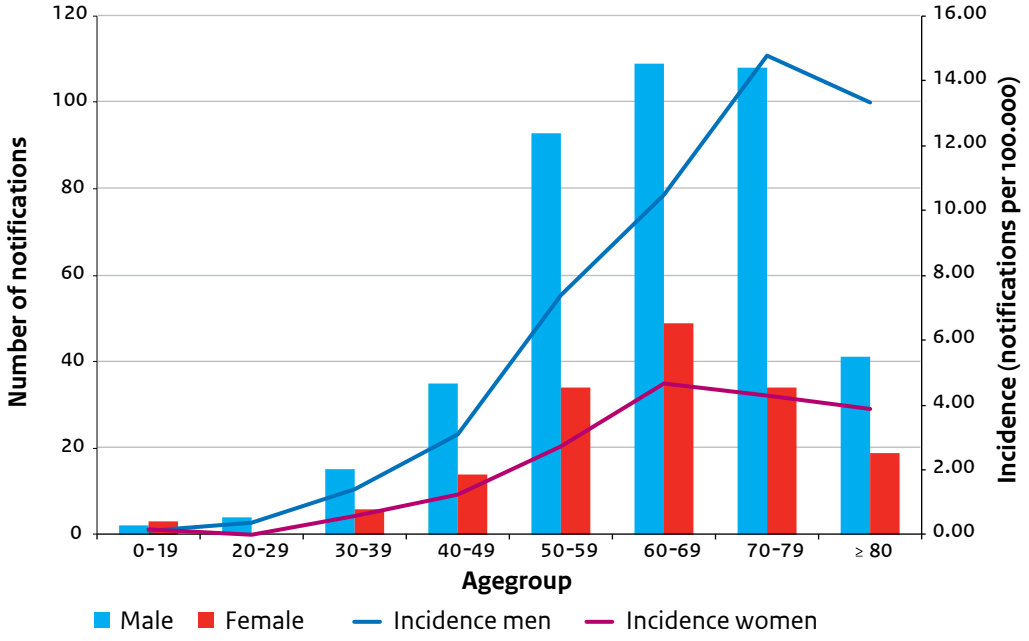


Figure 5.4 Distribution of the risk factors smoking and relevant underlying illness per age group reported in cases with Legionnaires' disease with onset disease in 2019. (source: Osiris).

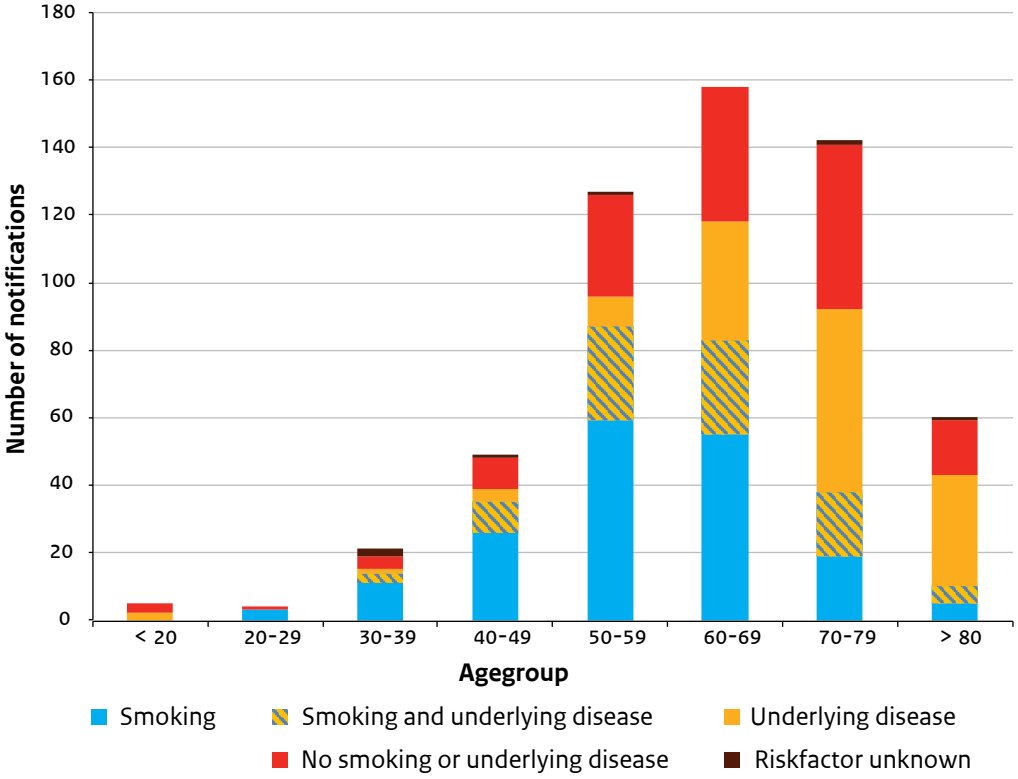


Table 5.2 Number of deaths and case fatality (CF) reported in cases of Legionnaires' disease with onset of disease in 2017-2019 by setting of infection and by age group and gender. (Source Osiris).

Setting of infection	2017			2018			2019		
	Deaths n	Total n	CF %	Deaths n	Total n	CF %	Deaths n	Total n	CF %
Travel abroad	2	152	1.3	1	177	0.5	6	169	3.6
Domestic	28	406	6.9	28	405	6.9	16	396	4.0
Country unknown	1	3	33	0	3	0	0	1	0
Domestic categories									
Domestic travel	3	45	6.7	2	35	5.7	3	38	7.9
Community acquired	24	355	6.8	24	361	6.6	13	352	3.7
Nosocomial	0	1	-	-	-	-	0	2	0
Healthcare associated	1	5	20	0	5	0	0	4	0
Setting unknown	1	3	33	2	6	33	0	1	0
Age group									
0-39	1	27	3.7	0	12	0	0	30	0
40-49	1	59	1.7	1	50	2.0	0	49	0
50-59	4	120	3.3	3	139	2.2	2	127	1.6
60-69	9	160	5.6	7	165	4.2	5	158	3.2
70-79	9	132	6.8	11	136	8.1	7	142	4.9
>= 80	7	63	11.1	7	82	8.5	8	60	13.3
Gender									
Male	20	401	5.0	15	420	3.6	15	407	3.7
Female	11	160	6.9	14	164	8.5	7	159	4.4
Total	**31**	**561**	**5.5**	**29**	**584**	**5.0**	**22**	**566**	**3.9**

Figure 5.5 Total number and proportion of patients admitted at Intensive Care in 2019 per age group. (Source Osiris, registration only from July-December 2019).

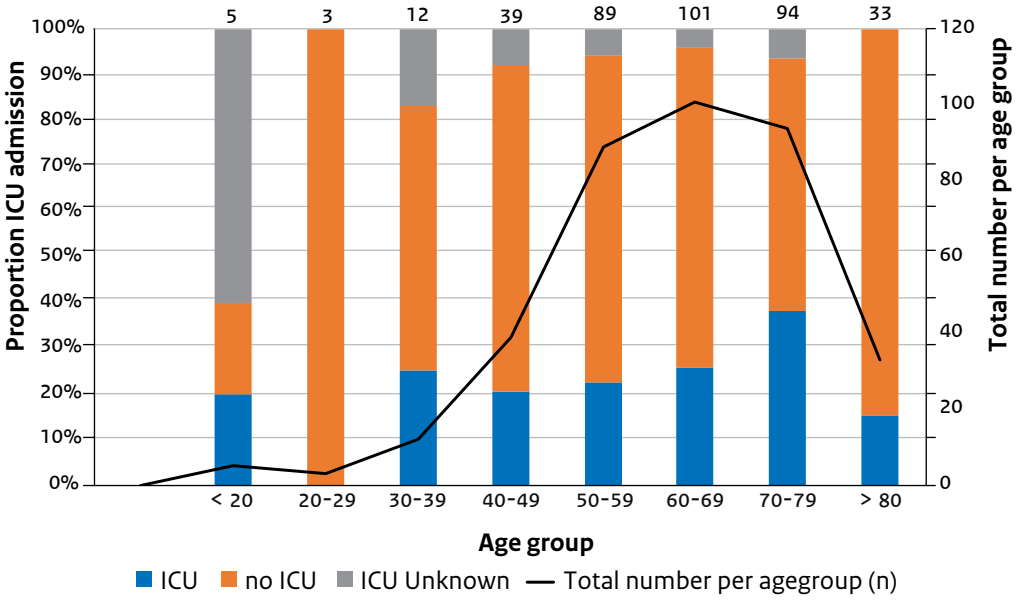


Figure 5.6 Regional incidence of domestic Legionnaires' disease per 100,000 inhabitants in 2019 by two-digit postcode area.

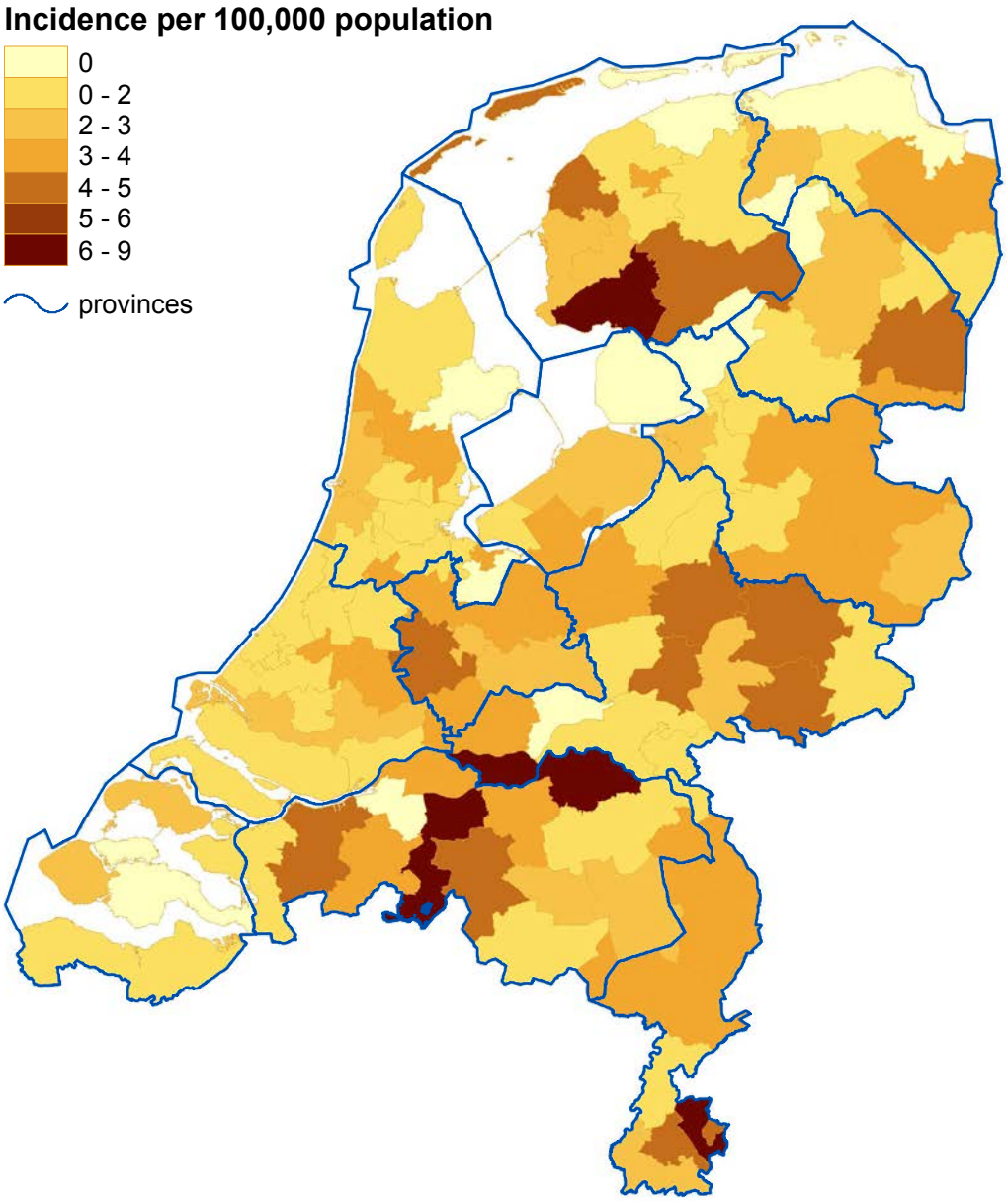


Table 5.3 Number and percentage of *Legionella* species, serogroup and Sequence Based typing (ST-type) of patients with Legionnaires'disease with onset in 2019, compared to 2011-2014 and 2015-2018. (source: BEL, Osiris). The table includes both LD patients with disease acquired in the Netherlands (domestic cases) and patients with disease acquired abroad (imported cases).

Type *Legionella*[a] isolates available for typing at reference lab[a]	**2011- 2014 n = 235**	**2015-2018 n = 339**	**2019 N=104[a]**
L. pneumophila (total)[a]	226 (96%)	316 (93%)	98 (94%)
L. pneumophila serogroup 1	211 (90%)	291 (86%)	88 (85%)
L. pneumophila serogroup 2	2 (<1%)	5 (1%)	1 (1%)
L. pneumophila serogroup 3	6 (3%)	6 (2%)	3 (3%)
L. pneumophila serogroup 4	-	2 (<1%)	1 (1%)
L. pneumophila serogroup 5	-	1 (<1%)	2 (2%)
L. pneumophila serogroup 6	3 (1%)	7 (2%)	2 (2%)
L. pneumophila serogroup 7-14	4 (2%)	6 (2%)	-
L. pneumophila serogroup unknown	3 (1%)	1 (<1%)	1 (1%)
Legionella nonpneumophila (total)[a]	6 (3%)	20 (6%)	6 (6%)
L. longbeachae	4 (1%)	15 (4%)	5 (5%)
L. bozemanii	-	2 (<1%)	-
L. anisa	-	1 (<1%)	1 (<1%)
L. other species	-	1 (1%)	-
Isolates reported, but not available at reference lab[b]	n=11	n=27	n=9
L. pneumophila	11	24	7
L. longbeachae	0	3	2
Most frequent ST-types[a]	n=224	n=301	n=100
ST 47	49 (22%)	92 (31%)	23 (23%)
ST82	2 (1%)	15 (5%)	7 (7%)
ST62	14 (6%)	17 (6%)	4 (4%)
ST42	17 (8%)	8 (3%)	5 (5%)
ST1646	4 (2%)	13 (4%)	-
ST1	9 (4%)	11 (4%)	2 (2%)
ST23	10 (4%)	10 (3%)	1 (1%)
ST46	11 (5%)	9 (3%)	4 (4%)
ST37	12 (5%)	8 (3%)	3 (3%)
ST224	-	4 (1%)	4 (4%)
ST48	4 (2%)	5 (2%)	3 (3%)
Total number different ST- types	69	86	36

[a] Based on the number of patients for whom clinical specimens were available at the reference lab for typing (mostly cultures, sporadically PCR with typing).

[b] Patients with positive culture, *Legionella* species based on information reported in Osiris without confirmation reference lab.

5.2 Psittacosis

Author: Frederika Dijkstra
Contributors: Ingrid Keur en Edou Heddema

5.2.1 Key points

- In 2019, 91 patients with psittacosis were notified. This is a vast increase compared to previous years (on average 53 in previous 5 years).
- The higher number of notifications this year is mainly due to an increase in the autumn and winter of 2019/2020, which started in the east of the country, and expanding to the middle and south of the country. For detailed description see Chapter 3 'Uitgelicht' of the report 'Staat van Zoonosen 2019' (Vlaanderen, Cuperus et al. 2020)
- The median age of the patients was 65 years, similar to 2018.
- Most of the notified patients were admitted to the hospital (94%), which was similar to previous years.
- Almost all patients were diagnosed by PCR (98%).
- 75 samples from notified patients were sent for genotyping.
- Similar to previous years, genotype A (mainly, but not exclusively associated with parrots) and genotype B (associated with pigeons) were most prevalent (respectively 48% and 25%).
- in five patients a quite recently described *C. psittaci* genotype was detected with characteristics of genotype B and E. In two patients an previously unknown *C. psittaci* genotype was found (one SNP difference with type A), and in two patients genotype C was found.
- With the typing method used, also other closely related Chlamydia species can be detected. This resulted in the detection of *C. caviae* in two patients.
- In consultation between the public health service and the Netherlands Food and Consumer Product Safety Authority (NVWA), it is decided whether sampling of a possible source location is useful for tracing the source of a human case. Data from the Source Tracing Tool showed that for 32 patients at least one possible source location was sampled by the NVWA. Out of these in total 36 possible source locations, 11 possible source locations tested positive (31%). On ten locations genotyping of *C. psittaci* positive material was performed. Eight positive locations had a genotypical match with material of the related patient(s). On three locations this concerned genotype A and on five location genotype B. On one location there was a genotypical mismatch with the material of the related patient (genotype A was detected on the location and genotype B was found in the patient). Furthermore, on one location no genotypical comparison was possible, because ZuyerlandMC did not receive any material from the patient.
- In addition to the human notifications that the NVWA received for human source tracing, NVWA also receives notifications of clinical ill birds or positive laboratory test results of birds. In 2019, 26 of such veterinary notifications were received. 24 times a location was visited and birds were sampled (cloaca and/or faecal swabs). In six ill birds, *C. psittaci* DNA was not detected by the NVWA. In one case the suspected bird had already died at the time of notification. This location was visited to sample contact birds, but no *C. psittaci* DNA could be detected. In three other cases *C. psittaci* DNA was detected. Fourteen times a location was visited by the NVWA after the birds were given an antibiotic treatment, in two cases *C. psittaci*

DNA was still detected and in the other 12 cases the bacteria were eliminated after the antibiotic treatment. In the five positive samples genotype A was found in three of these cases, genotype B in one case and for one sample the genotype could not be determined.

- In addition, the NVWA was able to back trace in four of these cases to the previous location of the animals. Several animals were sampled at these locations. In one of these cases, the animals tested positive (genotype A). In the three other cases negative.

5.2.2 Tables and figures

Figure 5.7 Number of notifications of human psittacosis by year and laboratory confirmation method, 2010 through 2019 (Source: Osiris).

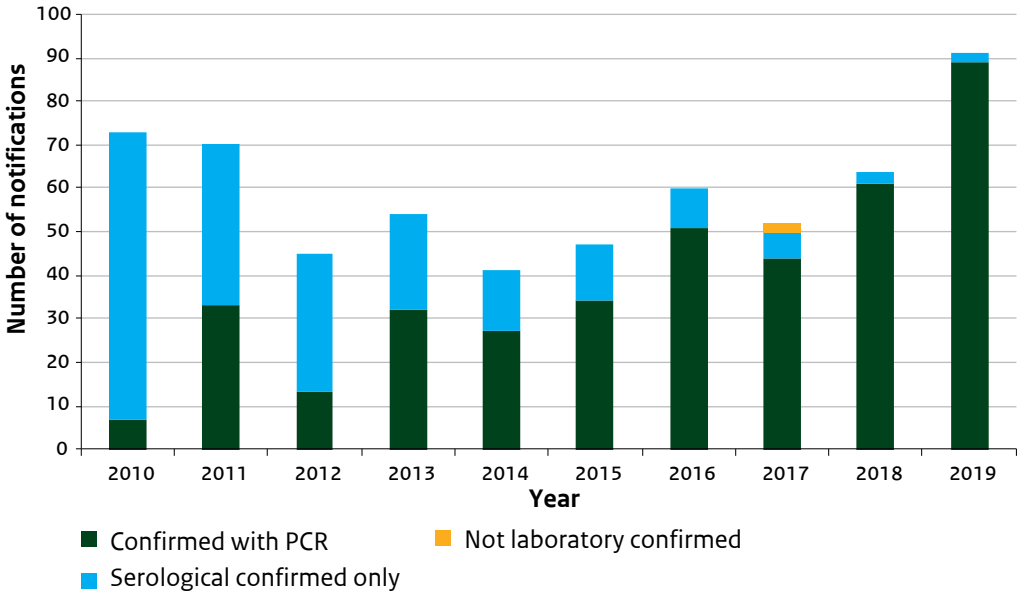


Table 5.4 Demographic, clinical and diagnostic characteristics of notified patients with psittacosis and positive diagnoses in the virological laboratory surveillance, in 2015-2019 (Source: Osiris and virological laboratory surveillance, NWKV). Numbers between brackets are percentages, unless otherwise specified.

N (%), unless otherwise specified	2015	2016	2017	2018	2019
Notifications					
Number of notifications[a]	47 (100)	60 (100)	52 (100)	64 (100)	91 (100)
Incidence per 100,000 inhabitants	0.28	0.35	0.30	0.37	0.53
Median age in years (Q1-Q3)	57 (41 – 68)	58 (45 – 71)	55 (39 – 69)	65 (56 – 72)	65 (50 – 74)
Male gender[b]	32 (68)	48 (80)	27 (52)	50 (78)	71 (78)
Hospitalised[b]	37 (79)	49 (82)	44 (85)	58 (91)	86 (94)
Deaths[b]	1 (2)	1 (2)	0	0	0
Infected abroad[b]	0	4 (7)	0	1 (2)	3 (3)
Diagnostics used for notifications					
Median diagnostic delay in days (Q1-Q3)[d]	10 (8 – 14)	9 (6 – 14)	11 (7 – 27)	11 (17 – 19)	10 (7 – 14)
Mode of confirmation of laboratory diagnosis					
PCR[e]	33 (70)	50 (83)	44 (85)	62 (97)	89 (98)
Serological only	14 (30)	10 (17)	6 (12)	2 (3)	2 (2)
None	0	0	2 (4)	0	0
Number of patients eligible for genotyping[f]	36	50	44	62	89
Notified patients for whom diagnostic material for genotyping was received by Zuyderland MC[g]	30 (83)	37 (74)	36 (82)	55 (89)	75 (82)
Typing outcomes					
C. psittaci genotype A	11 (37)	12 (32)	11 (31)	19 (35)	36 (48)
C. psittaci genotype B	9 (30)	13 (35)	13 (36)	13 (24)	19 (25)
C. psittaci genotype C	2 (7)	1 (3)	0	1 (2)	2 (3)
C. psittaci genotype E/B	2 (7)	0	0	0	0
C. psittaci genotype most similar to A (1 SNP difference)	0	0	0	0	2 (3)

N (%), unless otherwise specified	2015	2016	2017	2018	2019
C. psittaci genotype most similar to C (93% homology)	0	0	2 (6)	0	0
C. psittaci genotype with characteristics of B and E	1 (3)	2 (5)	0	3 (5)	5 (7)
Negative for any *C. psittaci* genotype	2 (7)	7 (19)	8 (22)	3 (5)	2 (3)
Negative for any *C. psittaci* genotype	1 (4)	2 (7)	7 (19)	0	3 (5)
Of which further diagnostics revealed					
C. caviae	1 (3)	0	2 (6)	2 (4)	2 (3)
C. felis	0	0	1 (3)	0	0
No assessement possible	3 (10)	2 (5)	2 (6)	16 (29)	9 (12)
Virological laboratory surveillance[g]					
Number of positive diagnoses	18	30	15	26	30

[a] 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 yet definite) are included.

[b] Percentage based on the number of patient for whom this specific information was available.

[c] Notification delay = number of days between date of laboratory confirmation and date of notification at the Public Health Service. Negative delays and delays of more than a year are excluded.

[d] 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.

[e] PCR= 'PCR only' or 'combination of PCR and serological confirmation'.

[f] Genotyping of notified patients was started on 27 Augustus 2012. *C. psittaci* strains of notified psittacosis patients are genotyped at the Zuyderland MC in Sittard-Geleen/Heerlen using ompA genotyping. This method distinguishes at least nine avian genotypes of *C. psittaci* (A – F, E/B, M56, and WC). Each genotype is more or less bird type specific. This method can furthermore identify *C. abortus*. Genotyping is only possible if diagnosis is based on PCR.

[g] Percentage based on the number of patients eligible for genotyping

Footnote: NWKV = Dutch Working Group for Clinical Virology of the Dutch Society for Medical Microbiology (in Dutch: NVMM).

5.3 Q-fever

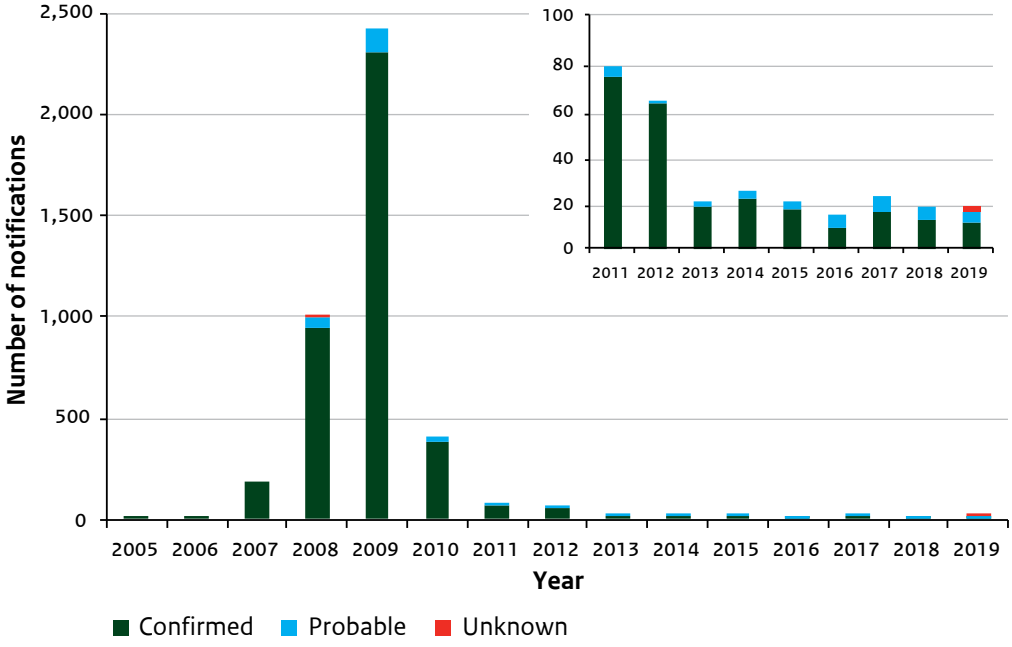
Author: Frederika Dijkstra
Contributor: Ingrid Keur

5.3.1 Key points

- In 2019, 18 patients with acute Q fever were notified. This is in line with the notifications in the years 2013-2018, in which the annual numbers varied from 14 to 26.
- Similar to previous years, the number of notifications (18) was lower than in the virological laboratory surveillance (69 positive diagnoses).
- As in previous years, most patients were male (83%). The median age was 62 years, which is higher than in the previous 4 years.
- The median diagnostic delay has increased to 43 days. Since 2008, the diagnostic delay has not been that long. In the years 2008 – 2018 the median diagnostic delay varied between 16 and 33 days. In 2005 and 2006, the 2 years just before the epidemic, similar diagnostic delays were seen (46 days).
- In spring, there was a cluster of three confirmed and one probable patients in the south of the country. All four patients were admitted to the hospital. The dates of onset of disease were between the end of March and the end of May. One patient travelled abroad during the incubation period and two patients mentioned the same petting farm as a possible source. Since 2010, mandatory vaccination of dairy sheep and goats on farms with more than 50 animals and on farms with a public function is in place. Therefore, the NVWA checked whether the animals on this petting farm as well as the concerning animals on goat and sheep farms in a radius of five kilometres were vaccinated against Q fever. All these farms were vaccinated. Source tracing by the Public Health Service in close collaboration with the NVWA did not reveal any concrete source.
- Possible animal sources of infection can be sampled in the following situations:
  - *Bulk milk monitoring:* In 2019, the NVWA received two notifications of a positive sample in the bulk milk monitoring from the GD Animal Health (GD). NVWA took official samples on both farms, but *C. burnetii* could not be demonstrated.
  - *Investigation of veterinary abortion waves:* In 2019, the NVWA received two notifications of abortion among small ruminants at two different farms. The NVWA visited both locations. At one farm the NVWA took samples of the animals, but in none of the samples *C. burnetii* could be demonstrated. At the other farm samples could not be taken because the sheep that had aborted recently, were already slaughtered. At this farm also other health problems in the animals were present and in samples of an aborted foetus *Chlamydia spp.* was detected by the GD.
  - *Source finding following human cases:* In 2019, public health services reported seven human cases to the NVWA for source finding. For these seven human cases no likely/possible source could be identified.

5.3.2 Tables and figures

Figure 5.8 Number of notifications of acute Q fever by case classification[a] and year, 2005-2019 (Source: Osiris). The insert zooms in on the years 2011 through 2019.



[a] The distinction between confirmed and probable notifications has been made since 1 July 2008.

Table 5.5 Demographic, clinical and diagnostic characteristics of notified acute Q fever patients and positive diagnoses in the laboratory surveillance, 2015-2019 (Source: Osiris and virological laboratory surveillance, NWKV).

N (%), unless otherwise specified	2015	2016	2017	2018	2019
Notifications					
Number of notifications[a]	20 (100)	14 (100)	22 (100)	18 (100)	18 (100)
Confirmed[b]	17 (85)	9 (64)	16 (73)	12 (67)	11 (61)
Probable[c]	3 (15)	5 (36)	6 (27)	6 (33)	5 (28)
Unknown	0	0	0	0	2 (11)
Incidence per 100,000 inhabitants	0.12	0.08	0.13	0.10	0.10
Median age in years (Q1-Q3)	58 (39 – 70)	49 (30 – 66)	53 (28 – 64)	50 (40 – 71)	62 (49 - 68)
Male gender[d]	9 (45)	11 (79)	16 (73)	15 (83)	15 (83)
Hospitalised[d]	12 (60)	7 (50)	13 (59)	15 (83)	12 (71)
Deaths notified in Osiris[d]	1 (5)	0	0	0	0
Infected abroad[d]	2 (10)	3 (21)	8 (36)	3 (17)	4 (27)
Median notification delay in days (Q1-Q3)[e]	1 (0 – 3)	1 (0 – 3)	0 (0 – 5)	0 (0 – 2)	1 (0 – 7)
Median diagnostic delay in days (Q1-Q3)[f]	27 (12 – 44)	14 (11 – 31)	29 (15 – 43)	16 (7 – 32)	43 (17 – 57)
Virological laboratory surveillance[g]					
Number of positive diagnoses	125	89	65	44	69

[a] 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.

[b] Confirmed case = a patient with clinical and laboratory diagnostic confirmation (seroconversion or a fourfold increases in IgG titre or PCR or isolation).

[c] Probable case = a clinical confirmed case with IgM antibodies against phase 2 of *C. burnetii*.

[d] Percentage based on the number of patients for whom this specific information was available.

[e] Notification delay = number of days between date of laboratory confirmation and date of notification at the Public Health Service. Negative delays and delays of more than a year are excluded.

[f] 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.

Footnote: NWKV = Dutch Working Group for Clinical Virology of the Dutch Society for Medical Microbiology (NVMM).

5.4 Tuberculosis

Authors: Erika Slump
Contributors: Henrieke Schimmel, Karlijn van Beurden, Gerard de Vries

5.4.1 Key points

- In 2019, 759 tuberculosis (TB) patients were notified, a decrease of 5% compared to 2018 (797 notifications). TB in the Netherlands has been steadily declining since 1998, with an increase in some years (2009, 2015 and 2016) related to immigration.
- The incidence rate of TB in 2019 was 4.4 per 100,000 population.
- Most patients were foreign born (75%), mainly from Eritrea (n=88), followed by Morocco (n=58), India (n=41), Indonesia (n=38) and Somalia (n=30), and 76 other countries (n=312).
- 273 (48%) of the foreign-born patients resided less than 5 years in the country.
- 445 patients (59%) had pulmonary TB, 193 with smear-positive sputum, the most infectious form of TB. The other 314 patients (41%) had extrapulmonary TB.
- 18% of all TB patients were detected by active case-finding: 12% by screening of risk groups such as immigrants and asylum seekers and 6% by contact investigation. The majority (82%) was found by symptoms.
- Nine patients had rifampicin-resistant TB, including six patients with multidrug-resistant (MDR) TB and one with extensively drug-resistant (XDR) TB. All these patients were foreign born.
- 576 TB patients (76%) were tested for HIV in 2019, of whom 21 were HIV positive (2.8% of all TB patients and 3.6% of TB patients tested for HIV).
- In 2018, 89% of TB patients with rifampicin-sensitive TB completed treatment successfully (90% over the years 2013-2017[1]).
- 29 of 41 patients (71%) with rifampicin-resistant TB diagnosed in 2015-2017 completed treatment successfully.

[1] Treatment takes at least 6 months for drug-sensitive TB and often 20 months for rifampicin-resistant TB. Treatment outcome of drug-sensitive TB patients of 2019 and rifampicin-resistant TB patients of 2018 is not yet known.

5.4.2 Tables and figures

Figure 5.9 Tuberculosis incidence (per 100,000 population) in 2019 by two digit postal code area.

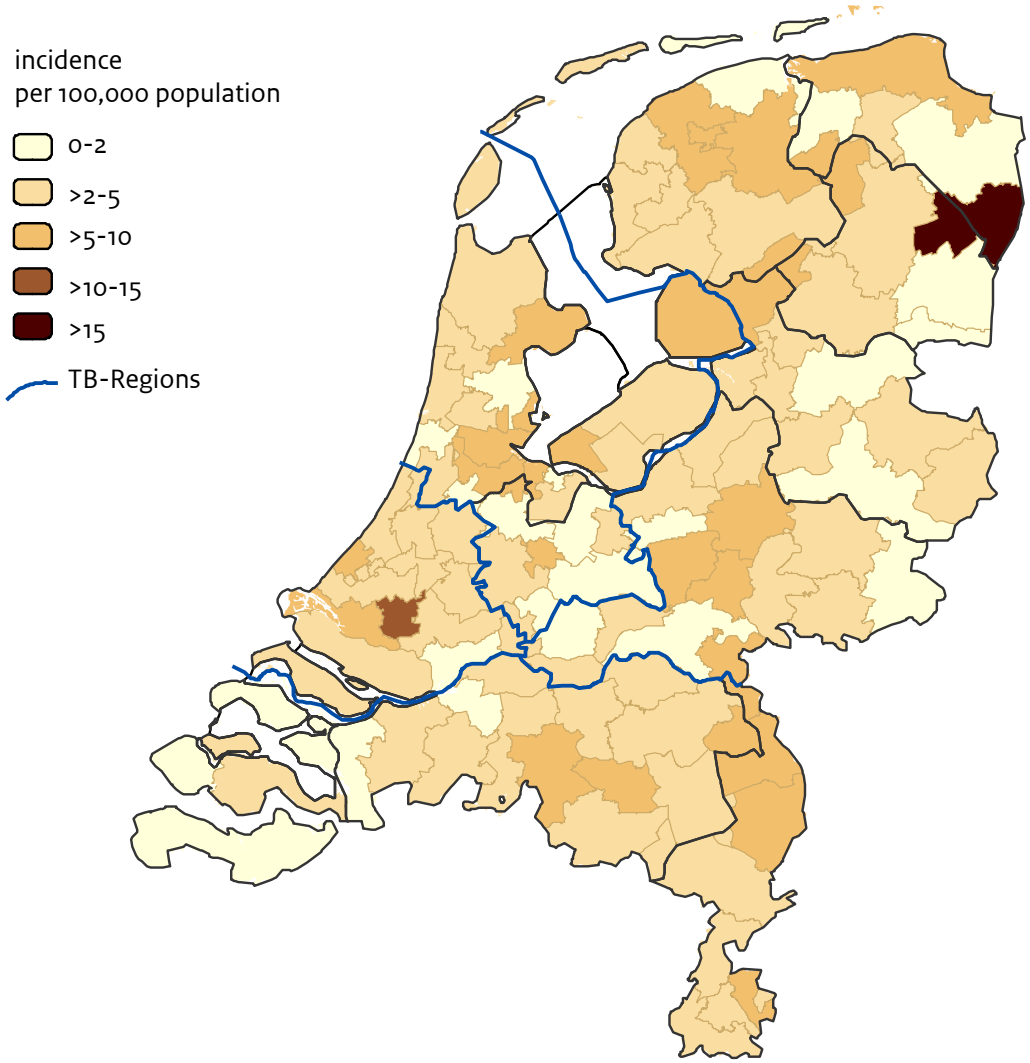


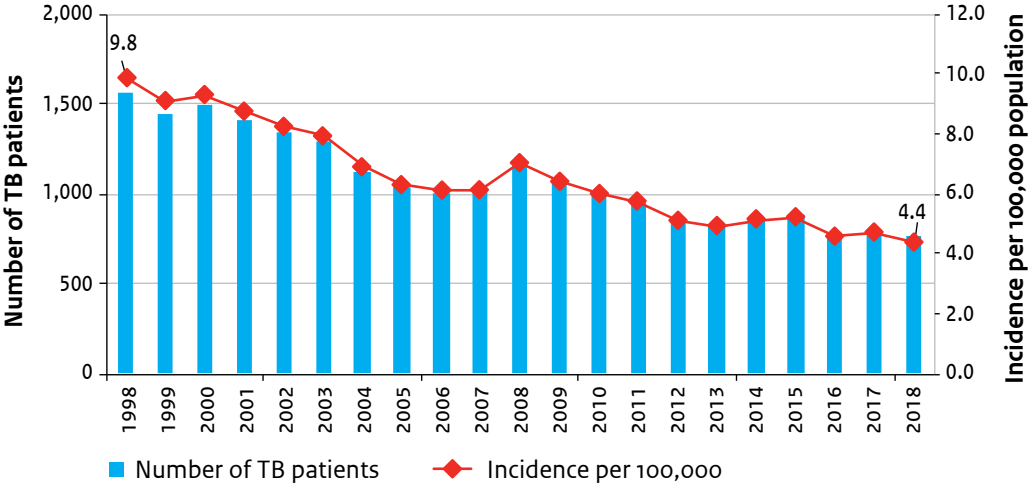
Table 5.6 Summary tuberculosis data the Netherlands, 2017, 2018 and 2019.

	2017	2018	2019
	N(%)	N(%)	N(%)
Number of notifications	783	797	759
Incidence per 100,000 population	4.6	4.7	4.4
Mean age (years)	39	39	41
Age <15 years	34 (4.3)	20 (2.5)	47 (6.2)
Age ≥65 years	102 (13)	113 (14)	112 (15)
Male to female ratio	1.6	1.7	1.4
Foreign born	586 (75)	617 (77)	569 (75)
5 years in the Netherlands	294 (50)	317 (51)	273 (48)
Residence in 1 of 4 largest cities[a]	212 (27)	217 (27)	206 (27)
Previous episode of TB (treatment)	28 (3.6)	41 (5.1)	30 (4.0)
HIV status known	602 (77)	623 (78)	576 (76)
HIV positive [c]	23 (3.8)	21 (3.3)	21 (3.6)
TNF-alpha inhibitors	11 (1.4)	12 (1.5)	10 (1.3)
Found by active case finding	148 (19)	162 (20)	133 (18)
Pulmonary tuberculosis (PTB & EPTB)	461 (59)	461 (58)	445 (59)
Sputum-smear positive PTB	205 (26)	210 (26)	193 (25)
Culture-confirmed TB	544 (70)	557 (70)	503 (66)
Rifampicin resistant TB (incl. MDR TB/XDR TB)[b]	11 (2.0)	6 (1.1)	9 (1.8)
Isoniazid resistance[b]	34 (6.3)	35 (6.3)	17 (3.4)
TB patients in risk groups:			
-Immigrants <2.5 years in the Netherlands	54 (7)	74 (9)	61 (8)
-Asylum seekers <2.5 years in the Netherlands	134 (17)	129 (16)	107 (14)
Latent tuberculosis Infection	1,889	1,522	1,236

TB=tuberculosis, PTB= pulmonary TB, EPTB= combination of pulmonary and extrapulmonary TB
HIV= Human Immunodeficiency Virus, TNF = Tumor Necrosis Factor, MDR = Multidrug-resistant, XDR = extensively drug-resistant.

[a] Amsterdam, Rotterdam, The Hague and Utrecht
[b] percentage of culture-confirmed TB
[c] percentage of cases with known HIV status

Figure 5.10 Number of tuberculosis (TB) patients and incidence per 100.000 population, 1999-2019.



More detailed information about the TB surveillance in the Netherlands and the latest surveillance report 'Tuberculose in Nederland, 2019' is available through the tuberculosis webpage of the RIVM, only available in Dutch).

The web-based application TBC-online (http://www.tbc-online.nl) provides information about TB in the Netherlands. TBC-online offers the opportunity to make tables and graphs of selected variables in the National Tuberculosis Register.

5.5 Animal influenza viruses

Authors: Marit de Lange, Adam Meijer

5.5.1 Key points

In 2019, no humans were tested for animal influenza viruses in the Netherlands. However, Belgian authorities notified one Eurasian avian-like H1N1 swine influenza virus infection in a pig farmer just across the border in the Dutch province of Noord-Brabant.

5.5.2 Background

Many different animals, including ducks, chickens and pigs, can host influenza A viruses. Humans can be infected with avian, swine and other zoonotic influenza viruses, such as avian influenza virus subtypes A(H5N1), A(H7N9), and A(H9N2) and swine influenza virus subtypes A(H1N1), A(H1N2) and A(H3N2), sometimes with high morbidity and mortality. The WHO provides a monthly overview of animal influenza virus infections in humans worldwide (WHO 2020). In the Netherlands, human infection with an animal influenza virus is a notifiable disease group B1, meaning that the attending physician and the laboratory are obliged to report a suspected patient to the Public Health Service within 24 hours. This allows timely implementation of legal measures if necessary, such as mandatory hospitalisation or isolation, mandatory investigation and prohibition of profession as possible options for containment. In case of suspicion of human infection, because of exposure to an infected farm or because of possible infected bird exposure during foreign travel, diagnostics are performed by the RIVM (CIb/IDS).

5.5.3 Epidemiological situation

In 2019, there were no commercial poultry holdings infected with avian influenza virus. On pig farms there is no surveillance system for influenza virus infections in the Netherlands. Therefore, no people were tested with influenza-like illness that was associated with an infected farm in the Netherlands. Furthermore, no returning travellers with possible animal influenza virus exposure were tested within the same time period. However, in 2020, the Dutch authorities received a notification from the Veterinary faculty of the Ghent University, Belgium, of an Eurasian avian-like H1N1 swine influenza virus infected pig farmer just across the in the Dutch province of Noord-Brabant. On the 23rd of September 2019, the animal care taker presented with influenza-like illness. Additionally, on the 25th of September 2019, the pig farmer also became ill with influenza-like illness, and the pigs also showed symptoms. The pigs were sampled by a Belgian veterinarian, who also instructed the animal care taker and pig farmer to take a nasal self-swab. The samples were sent to the lab of the veterinary faculty in Ghent via the veterinarian for swine influenza surveillance. No influenza virus was detected in the sample of the animal care taker. Influenza type A was detected in the samples from the pig farmer and the pigs. Further research on the basis of antigenic characterization and whole genome sequencing indicated an Eurasian avian-like H1N1 swine influenza virus. The pig farmer was diagnosed with pneumonia by the general practitioner based on clinical symptoms and was treated with amoxicillin, after which he recovered. The farmer had no travel history, had not visited trade fairs and had not bought new animals. (source: GGD West-Brabant).

5.6 MERS-CoV

Authors: Daphne Reukers, Adam Meijer

5.6.1 Background

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, although a large outbreak of nosocomial transmission starting with one imported case occurred in South-Korea. Dromedary camels are a major reservoir host for MERS-CoV and an source of MERS-infections in humans, although the route of transmission from animals to humans is not fully understood. 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 Public Health Service [http://www.rivm.nl/en/Topics/M/MERS_Coronavirus]. This enables the Public 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 ErasmusMC. In May 2014, Middle East respiratory syndrome coronavirus (MERS-CoV) infection, with closely related viral genomes, was diagnosed in two Dutch residents, returning from a pilgrimage to Medina and Mecca, Kingdom of Saudi Arabia (Fanoy, van der Sande et al. 2014, Kraaij-Dirkzwager, Timen et al. 2014).

5.6.2 Epidemiological situation

In 2019, a total of 8 patients with (severe) acute respiratory illness, returning from countries where exposure to MERS-CoV is possible, were tested for MERS-CoV as well as 6 patients in 2020 (until May 2020). None of them had an infection with MERS-CoV.

5.7 COVID-19

Author: Wim van der Hoek, Daphne Reukers
Contributor: Anne Teirlinck, Liselotte van Asten, Rianne van Gageldonk-Lafeber

5.7.1 Key points

- In 2020, since the first notified patient on February 27 through May 17 (week 20), a total of 44,000 cases with COVID-19 were notified in the Netherlands, resulting in a cumulative incidence of 253 per 100,000 population.
- The number of notifications reached a peak of 7,794 notifications in the second week of April (week 15).
- From week 9 through week 20, a total of 11,095 COVID-19 patients were hospitalised with a peak in week 13 when 3,284 hospitalisations were notified.
- Up to week 20, 5,803 notified COVID-19 patients were reported as deceased, predominantly in the age group of 65 years or older, resulting in a case fatality of 13%. The infection fatality rate was estimated at 1%.
- An unprecedented peak was observed in overall mortality in the total Dutch population in the week of April 2-8 (Thursday through Wednesday), with a record-height of 5,143 deaths, which was 2,240 deaths above expected baseline level. Excess mortality in the population was observed from week 12 through 19 (Thursday March 12 through Wednesday May 6), totalling 9,554 cumulative excess deaths within these 8 weeks. Excess mortality was mostly observed in persons aged 75 years and older. By week 20, deaths were not significantly elevated beyond expected levels, but reports of lab-confirmed COVID-19 deaths continued at low levels.

5.7.2 Background

At the end of December 2019, public health authorities in Wuhan, China reported a cluster of patients with unexplained pneumonia. On January 9th 2020 the causative pathogen was isolated and later named 'severe acute respiratory syndrome coronavirus 2' (SARS-CoV-2). SARS-CoV-2 spread more rapidly to other countries compared to previous severe outbreaks caused by coronaviruses (SARS-CoV in 2003 and MERS-CoV in 2012). On January 30, 2020 the WHO declared it a public health emergency of international concern (PHEIC).

5.7.3 Epidemiological situation 2020 (up to May 17th)

Laboratory-confirmed COVID-19, the disease caused by SARS-CoV-2, became a group A notifiable disease in the Netherlands on January 28, 2020. The first case of COVID-19 in the Netherlands was reported on February 27, 2020 in the province of Noord Brabant. By mid-March 2020 it became clear that there had been unnoticed community transmission in the provinces of Noord Brabant and Limburg, most likely initiated by multiple introductions by Dutch tourists returning from northern Italy and Austria (Reusken, Buiting et al. 2020). This was amplified by the yearly carnival celebrations lasting for three days, mostly in the south of the Netherlands, characterised by large social gatherings. In response, the national Outbreak Management Team (OMT) recommended a range of mitigation measures.

The epidemiological data that were available in Osiris are strongly biased by the prevailing testing policies, which were influenced by global scarcity of testing materials. Initially, only health care workers, people from risk groups (the elderly and people with certain chronic medical conditions), and people returning from high-incidence countries, were tested for SARS-CoV-2 when symptomatic (according to changing case definitions). Most hospitals also tested patients admitted for severe acute respiratory infections (SARI). From June 1, 2020 onwards (week 23), universal testing, even with mild symptoms, was actively promoted. Therefore, the epidemic curve of notifications before this week must be interpreted with caution.

In 2020, the epidemic showed a biphasic pattern. In the first wave, notifications primarily included elderly, with large numbers of complications. The high number of hospital admissions overwhelmed hospital wards and intensive care units, particularly in the southern provinces. This lead to downscaled and halted regular hospital care and weekly scaling up of Intensive Care units barely keeping up with the increasing admissions. The number of notifications peaked at 7,794 in week 15, hospital admissions peaked at 3,284 in week 13 and notified COVID-19 deaths peaked at 1,173 in week 14. An unprecedented peak was observed in overall mortality in the total Dutch population in week 15 (April 2-8, Thursday through Wednesday) with a record-high of 5,143 deaths, which was 2,240 deaths above expected baseline level. Excess mortality in the population was observed from week 12 through 19 (Thursday March 12 through Wednesday May 6), totalling at 9,554 cumulative excess deaths within those 8 weeks. Excess mortality was mostly observed in persons aged 75 years and older. By week 20, deaths were not significantly elevated beyond expected levels, but reports of laboratory-confirmed COVID-19 deaths continued at low levels. Until week 20, 5,803 notified COVID-19 patients were reported as deceased, resulting in a case fatality of 13%. Using results from national seroprevalence surveys, the infection fatality rate was estimated at 1% (van Asten, Harmsen et al. 2021).

5.7.4 Discussion

The COVID-19 pandemic is still affecting many countries globally, including the Netherlands. In response, a range of new surveillance tools have been rapidly developed. The present report only provides selected basic data from the routine respiratory surveillance tools: the national infectious diseases register 'Osiris'; the virological laboratory surveillance; and the primary care sentinel GPs. The unprecedented spike of excess mortality due to COVID-19 is shown in chapter 2.4. A weekly comprehensive situation report is published on the RIVM website (https://www.rivm.nl/en/novel-coronavirus-covid-19/current-information). Detailed future descriptions of the epidemic will reflect on the surveillance results in relation to the major changes that took place over time in case definitions, testing policies, and the hygiene and social distancing control measures that were implemented.

5.7.3 Tables and figures

Figure 5.11 Weekly Notifications of COVID-19 in the Netherlands in 2020, week 9 through week 20. **A** Number of COVID-19 patients notified by the Public Health Service by week of notification. **B** Number of hospitalisations notified by the Public Health Service. **C** Number of deceased COVID-19 patients notified by the Public Health Service. (Source: Osiris, last update on November 4, 2020).

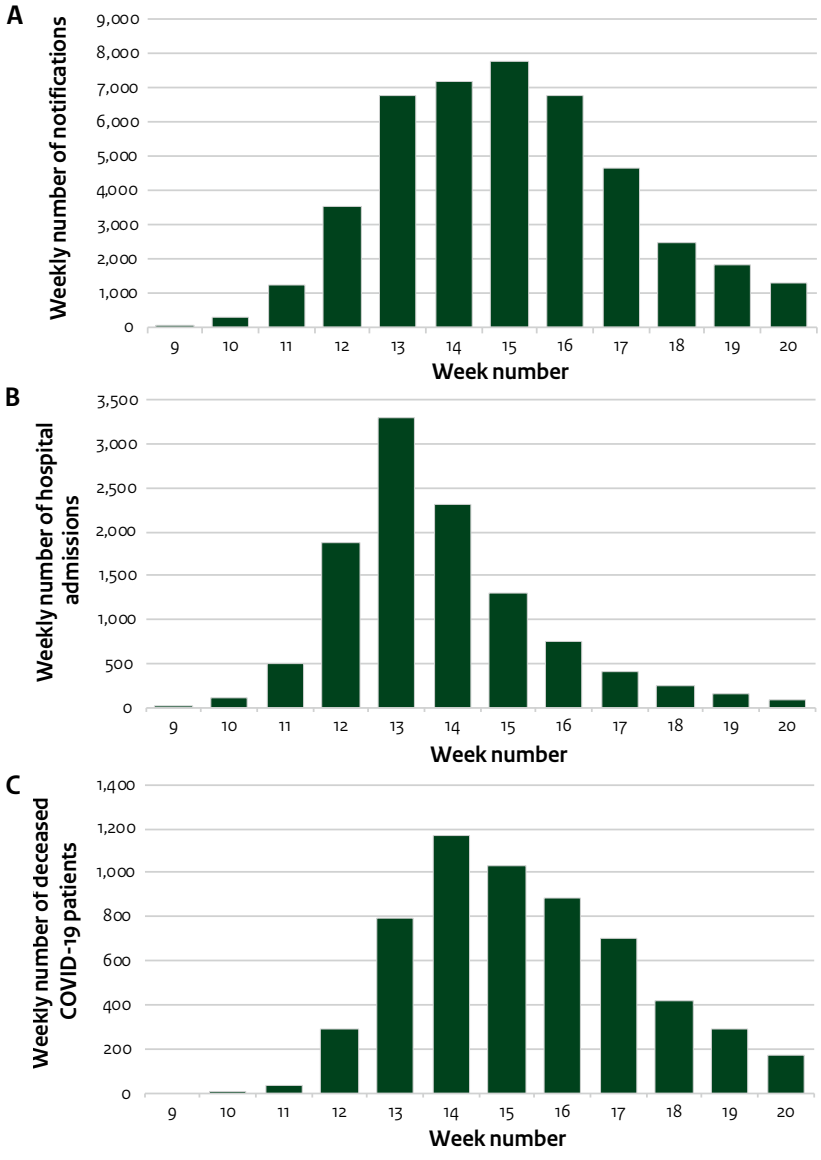


Table 5.7 Demographic, clinical and diagnostic characteristics of notified COVID-19 patients and positive diagnoses in the virological laboratory surveillance, week 9 through week 20 2020 (Source: Osiris and virological laboratory surveillance, NWKV, last updated on November 4, 2020).

N (%), unless otherwise specified	2020
Notifications (Osiris)	**week 9 - 20**
Number of notifications	43,993
Incidence per 100,000 inhabitants	253
Age groups[a]	
0-4 years of age	80 (0.2)
5-14 years of age	85 (0.2)
15-44 years of age	10,363 (24)
45-64 years of age	14,483 (33)
65 years or older	18,928 (43)
Male gender[a]	16,149 (37)
Hospitalised	11,095 (25)
Deaths notified in Osiris	5,806 (13)
Virological Laboratory Surveillance	**week 11 - 20**
Number of persons tested	300,365
Number of SARS-CoV-2 positive persons	47,272 (16)

[a] 57 missing age or gender.

Figure 5.12 Age distribution of A notifications, B hospitalisations and C deceased patients with COVID-19 with onset of disease in 2020 from week 9 through week 20. (source: Osiris, last updated on November 4, 2020).

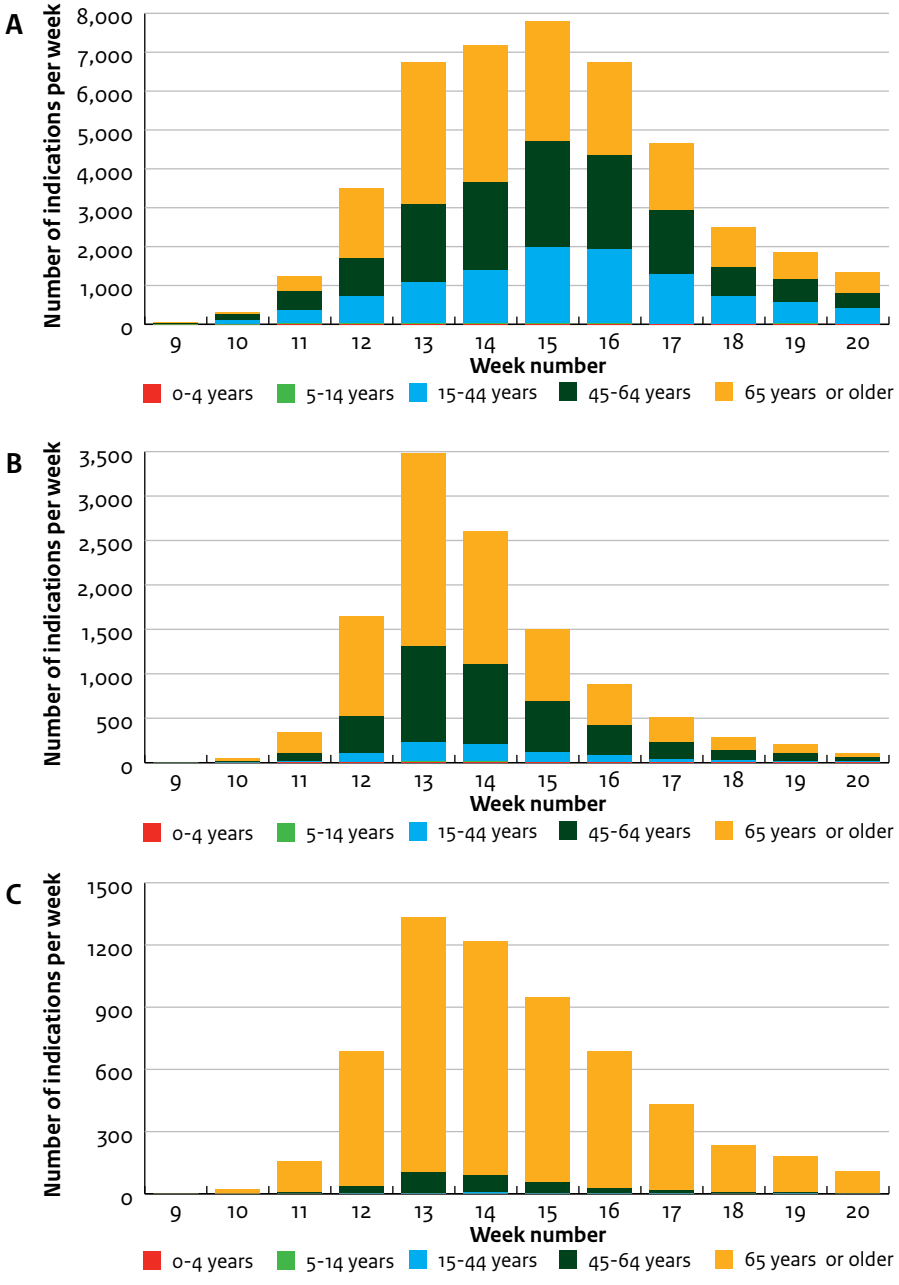


Figure 5.13 Regional incidence of COVID-19 per 100,000 inhabitants in 2020 week 9 through week 20 by two-digit postcode area. (source: Osiris, last updated on November 4, 2020).

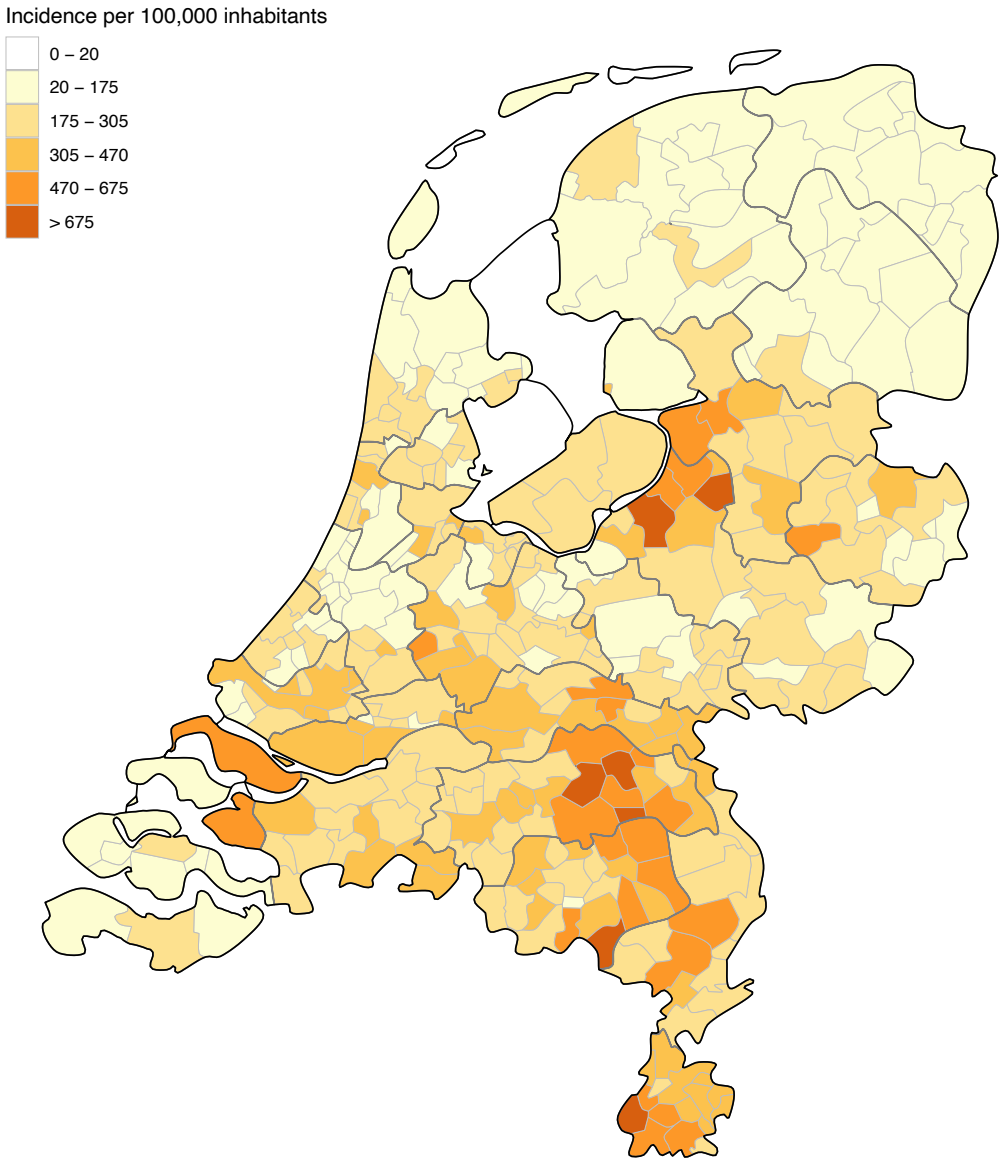
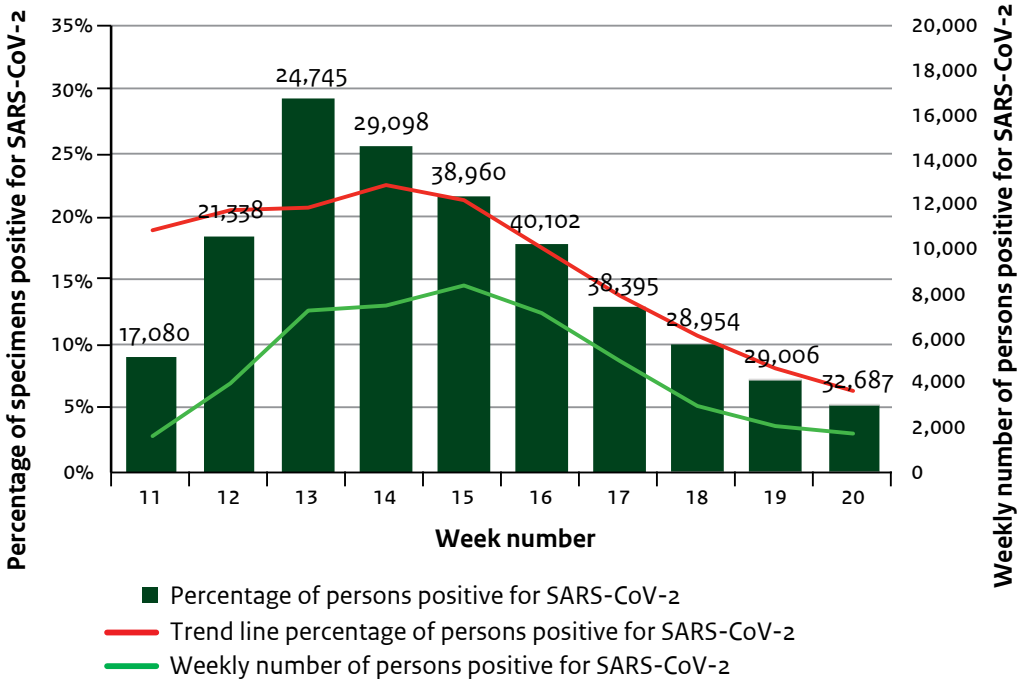
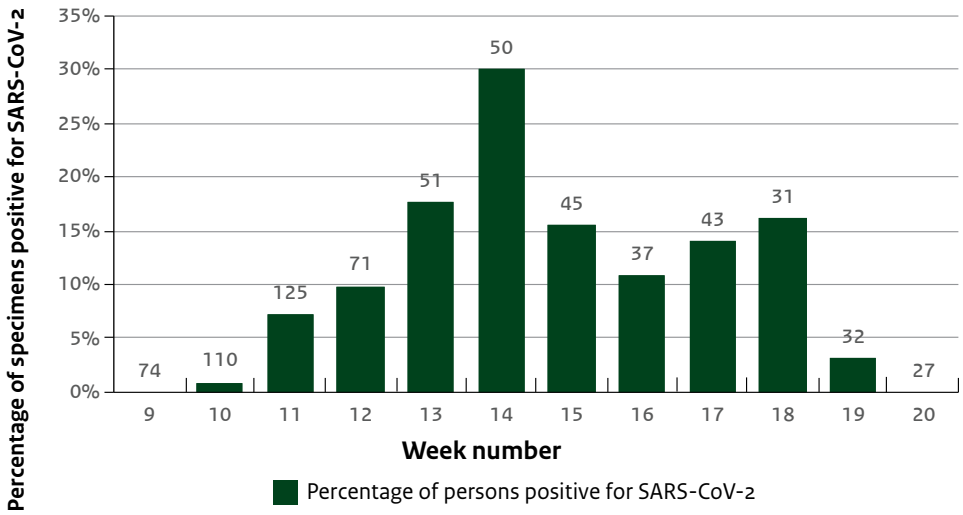


Figure 5.14 Number and percentage of persons testing positive for SARS-CoV-2 as reported by the virological laboratory surveillance in 2020 (week 11 through week 20) and a 5-week moving average of percentage of persons positive for SARS-CoV-2. (Source: Virological Laboratory Surveillance, NWKV. Last updated on October 27, 2020).



Footnote: The numbers above the bars are the total number of persons tested for SARS-CoV-2.

Figure 5.15 Percentage of SARS-CoV-2 positive specimens from ILI and other ARI patients, taken by sentinel GPs during 2020 (week 9 through week 20). (Source: Nivel Primary Care Database, RIVM. Last updated on November 4, 2020).



Footnote: The numbers above the bars are the total number of tested specimens.

Chapter 6
Other respiratory infections reported in the weekly virological surveillance

Authors: Daphne Reukers, Frederika Dijkstra
Contributors: Adam Meijer, Sofie Mooij

6.1 Key points

- In the first weeks of 2019, influenza virus A, RSV and rhinovirus were most often detected. In spring and summer, rhinovirus and adenovirus were the primary detections and towards the end of the year 2019 RSV and rhinovirus were most detected.
- The total number of positive rhinovirus (N=3,313 in 2019) steadily increased since 2015, when 2,410 positive test results were reported. Although the peak of reports was higher in 2017 than in 2019 (120 reports in week 39 2017 vs 113 reports in week 50 2019), the total number of reports was higher in 2019 than in 2017 (2,755 vs 3,313).
- The total number of positive hMPV (N=806) test results in 2019 has slightly decreased compared to 2018 (N=846). However, the total number was still relatively high compared to three years before (range 2015-2017: N=542-652).
- The total number of parainfluenza virus type 1 detections in 2019 was the highest reported in 5 years (range 2015-2018: N=55-208), especially because of high numbers of positive test results at the end of the year with a peak of N=31 in week 46 of 2019 (range 2015-2018: N=8-23). Parainfluenza virus type 2 was lower than 2018 and within the range of the years before (N=102, range 2015-2018: 70-150). As in previous years, the total number of positive parainfluenza virus test results was highest for type 3. The total number of positive tests for this type in 2019 was also the highest reported since 5 years (N=610, range 2015-2018: 344-585), as was the peak in detections in week 20 2019 (N=47, range 2015-2018: 19-39).

The detections of parainfluenza virus type 4 were also the highest reported since 5 years (N=190, range 2015-2018: 65-145).

- The total number of positive adenovirus (N=1,664) test results in 2019 was the highest reported since five years (range 2015-2018: N=1322-1623).
- The total number of positive bocavirus (N=207) test results in 2019 was also the highest reported since five years (range 2015-2018: N=114-177).
- The numbers of positive diagnoses for *Mycoplasma pneumoniae*, coronavirus (excluding SARS-CoV-2) and *Chlamydia pneumoniae* were within the range of the four previous years.

6.2 Discussion

The virological laboratory surveillance includes weekly data on the number of positive test results for respiratory pathogens originating 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 data from primary care and hospitals (Bijkerk, de Gier et al. 2016). It is likely that patient population and disease severity differs between primary care and hospitals. In the last three years, generally higher numbers of positive test results were found than the years before. Changes in the number of positive test results 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 and testing procedures by the physicians and/or microbiological laboratories. One such change in testing might be the increased application of respiratory panels, which can be used for detection of the causative agent of disease in patients displaying a respiratory disease syndrome. In these panels, molecular detection of the most common viruses is performed in one test. However, which viruses are included in the respiratory panels and the extent to which the panels are used, differs between laboratories and between years.

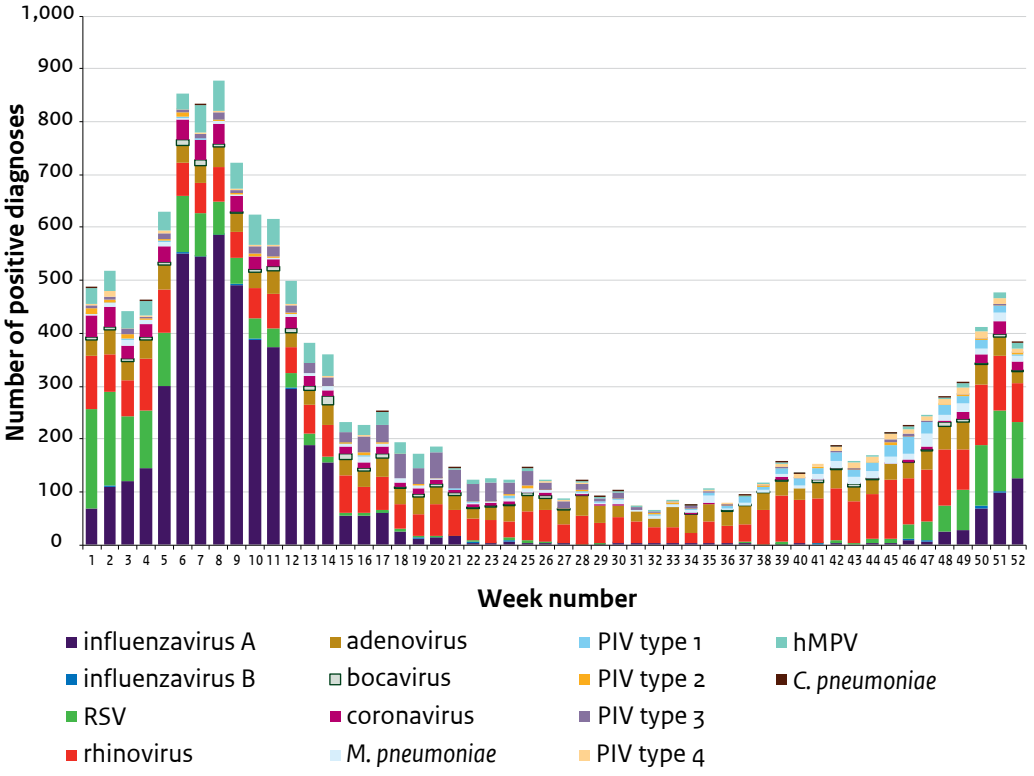
6.3 Tables and figures

Table 6.1 Number of reported positive tests of rhinovirus, *Mycoplasma pneumoniae,* human metapneumovirus, coronavirus (excluding SARS-CoV-2), parainfluenza virus type 1-4, *Chlamydia pneumoniae*, adenovirus and bocavirus in the virological laboratory surveillance for the period 2015-2019. (Source: Virological laboratory surveillance, NWKV).

Number of positive diagnoses											
Year	Rhinovirus	*M. pneumoniae*	hMPV	Coronavirus (excl. SARS-CoV-2)	PIV type 1	PIV type 2	PIV type 3	PIV type 4	*C. pneumoniae*	Adenovirus	Bocavirus
2015	2410	525	652	575	149	72	344	122	31	1322	114
2016	2589	608	542	712	55	108	411	65	19	1612	159
2017	2706	400	629	708	208	70	585	145	17	1379	177
2018	2755	328	846	682	94	150	476	112	17	1623	150
2019	3313	360	806	600	291	102	610	190	21	1664	207

M. pneumoniae = *Mycoplasma pneumoniae.*
hMPV= human metapneumovirus.
PIV= parainfluenza virus.
C. pneumoniae = *Chlamydia pneumonia.*
NWKV = Dutch Working Group for Clinical Virology of the Dutch Society for Medical Microbiology (NVMM).

Figure 6.1 Number of reported positive tests of influenza virus type A and B, respiratory syncytial virus , rhinovirus, *Mycoplasma pneumoniae*, human metapneumovirus , coronavirus (excluding SARS-CoV-2), parainfluenza virus type 1-4, *Chlamydia pneumoniae*, adenovirus and bocavirus in the virological laboratory surveillance for the year 2019. (Source: Virological laboratory surveillance, NWKV).



Footnote: *M. pneumoniae* = *Mycoplasma pneumoniae;* hMPV= human metapneumovirus; PIV= parainfluenza virus; *C. pneumoniae* = *Chlamydia pneumonia*; RSV= Respiratory Syncytial Virus; NWKV = Dutch Working Group for Clinical Virology of the Dutch Society for Medical Microbiology (NVMM).

Figure 6.2 Number of weekly reported positive test results of rhinovirus in the virological laboratory surveillance for the calendar year 2019 and the trend lines* for the calendar years 2015 – 2019.

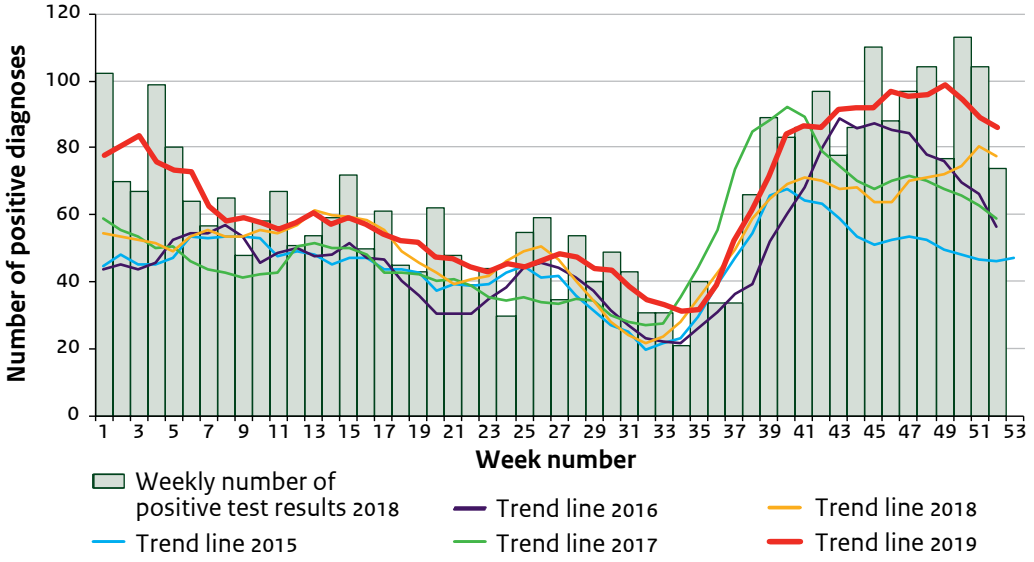
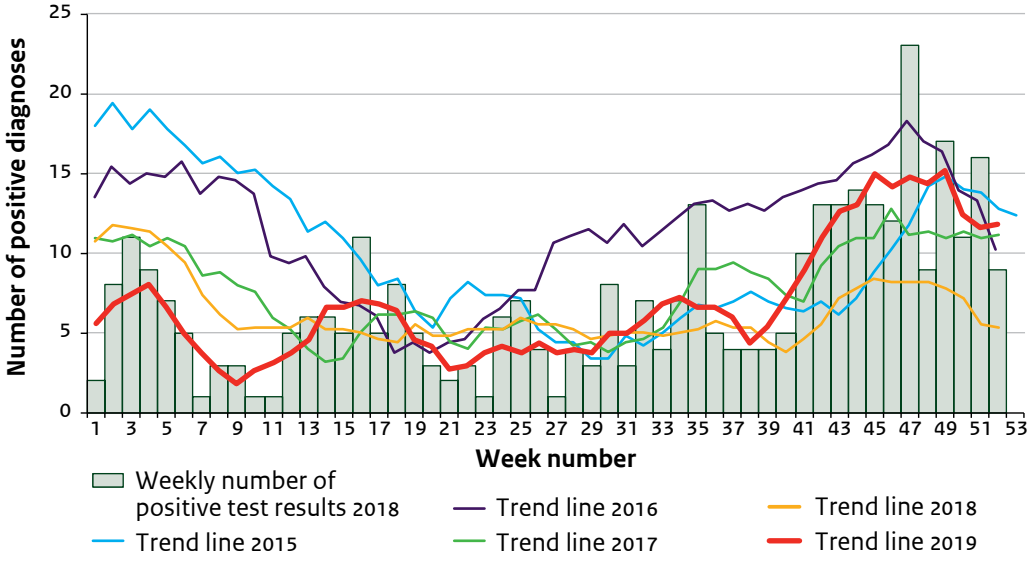


Figure 6.3 Number of weekly reported positive test results of *Mycoplasma pneumoniae* in the virological laboratory surveillance for the calendar year 2019 and the trend lines* for the calendar years 2015 – 2019.



* 5-week moving average.

Figure 6.4 Number of weekly reported positive test results of human metapneumovirus in the virological laboratory surveillance for the calendar year 2019 and the trend lines* for the calendar years 2015 – 2019.

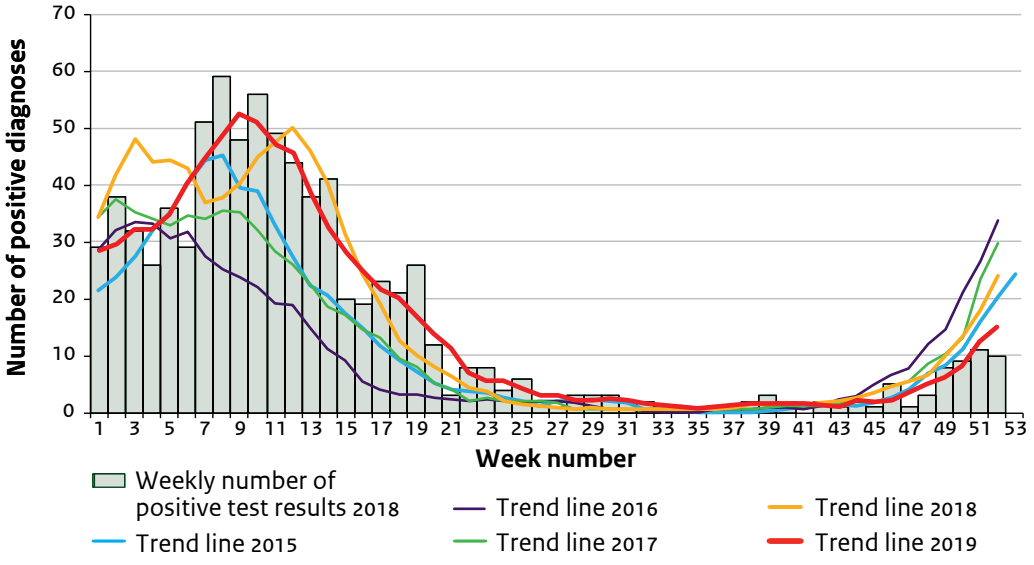
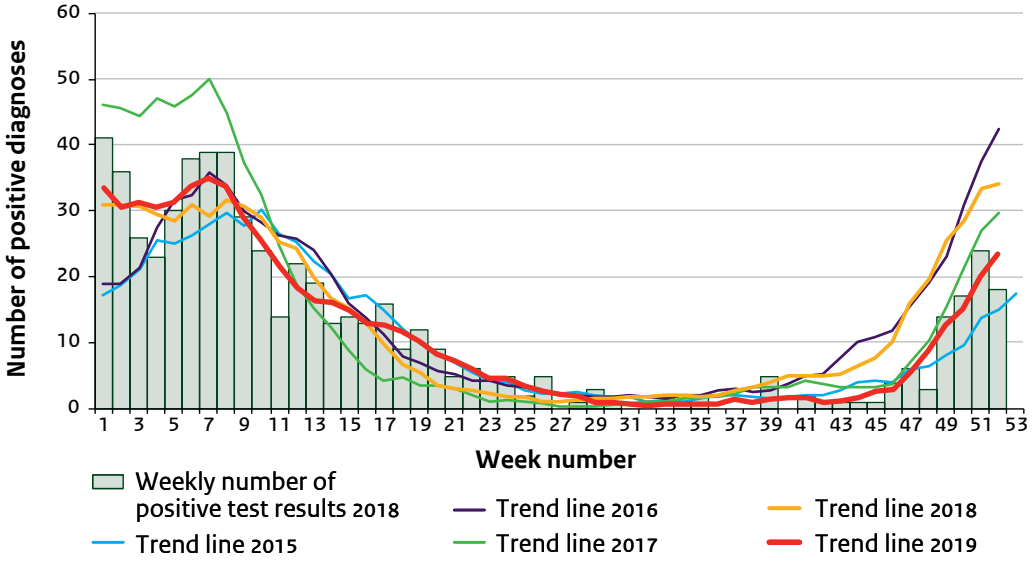


Figure 6.5 Number of weekly reported positive test results of coronavirus (excluding SARS-CoV-2) in the virological laboratory surveillance for the calendar year 2019 and the trend lines* for the calendar years 2015 – 2019.



* 5-week moving average.

Figure 6.6 Number of weekly reported positive test results of parainfluenza virus type 1 in the virological laboratory surveillance for the calendar year 2019 and the trend lines* for the calendar years 2015 – 2019.

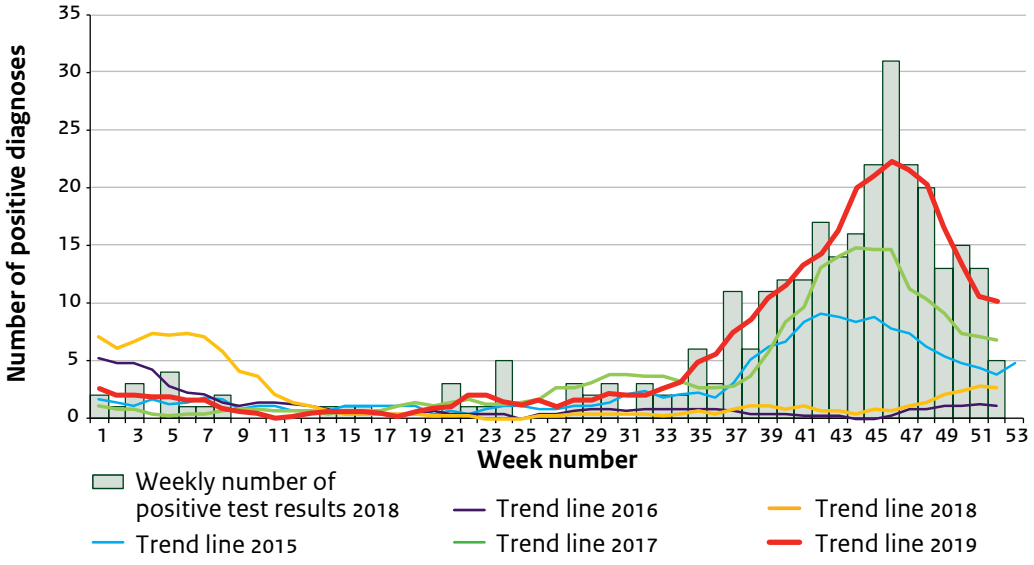
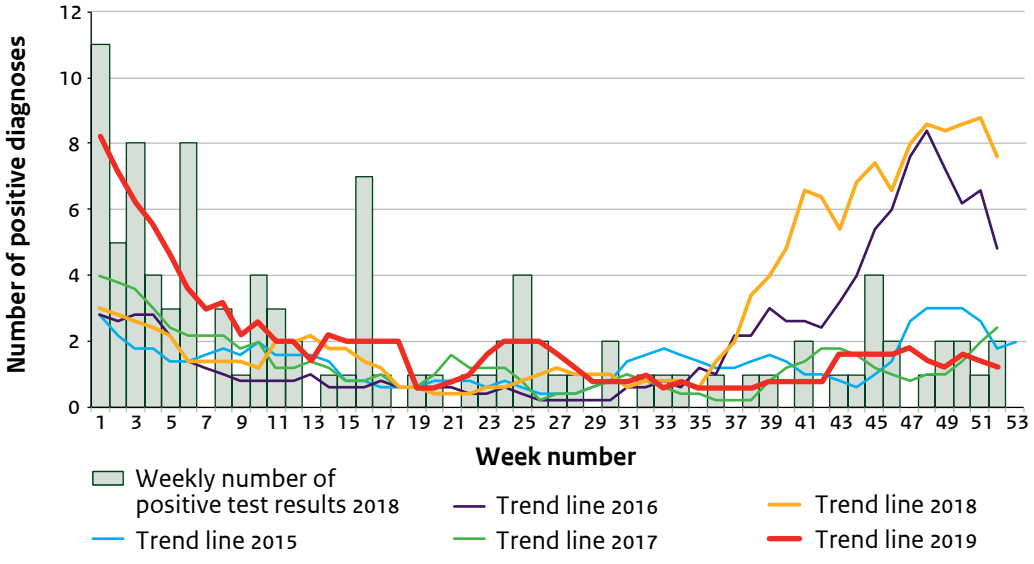


Figure 6.7 Number of weekly reported positive test results of parainfluenza virus type 2 in the virological laboratory surveillance for the calendar year 2019 and the trend lines* for the calendar years 2015 – 2019.



* 5-week moving average.

Figure 6.8 Number of weekly reported positive test results of parainfluenza virus type 3 in the virological laboratory surveillance for the calendar year 2019 and the trend lines* for the calendar years 2015 – 2019.

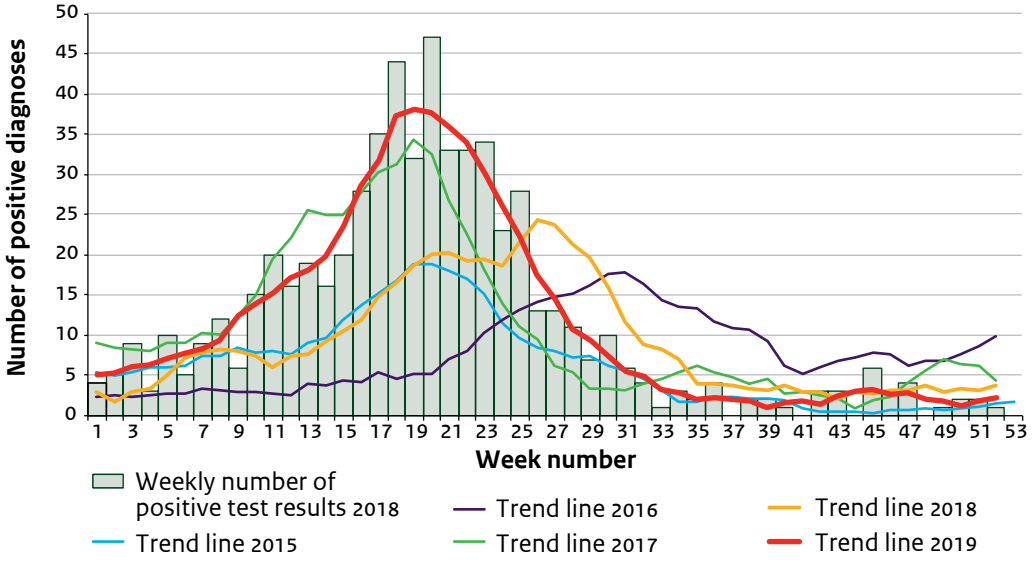
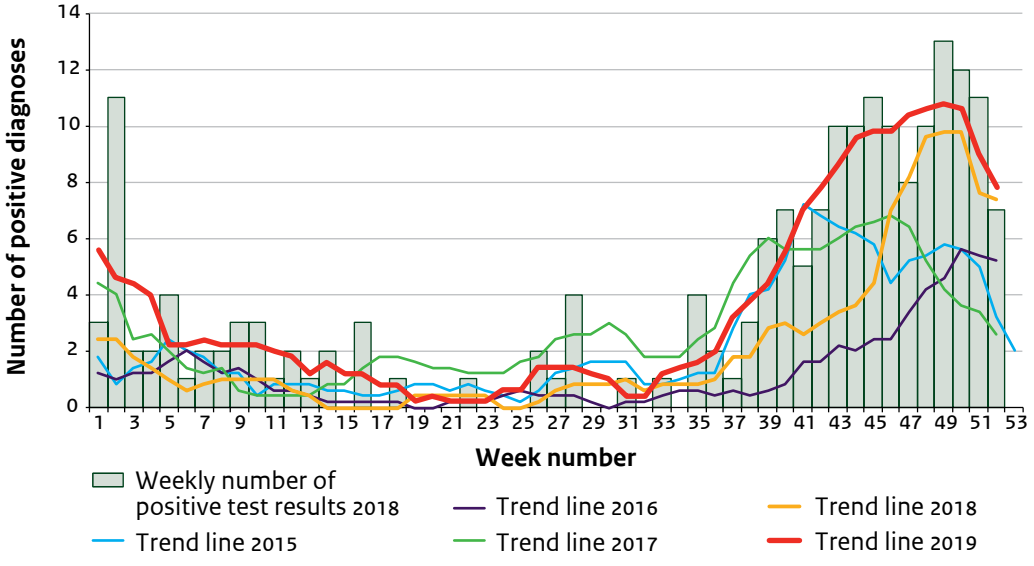


Figure 6.9 Number of weekly reported positive test results of parainfluenza virus type 4 in the virological laboratory surveillance for the calendar year 2019 and the trend lines* for the calendar years 2015 – 2019.



* 5-week moving average.

Figure 6.10 Number of weekly reported positive test results of *Chlamydia pneumoniae* in the virological laboratory surveillance for the calendar year 2019 and the trend lines* for the calendar years 2015 – 2019.

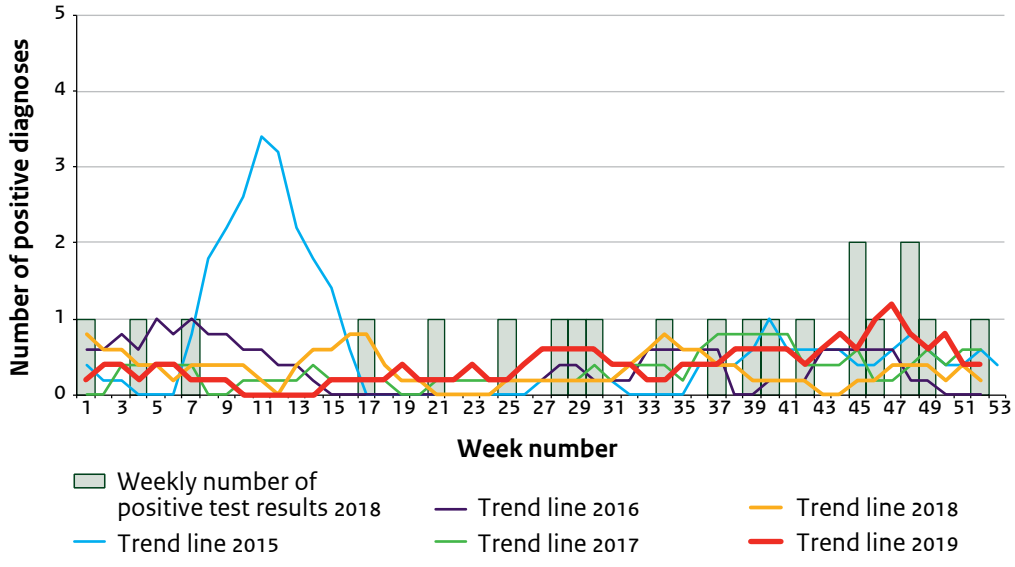
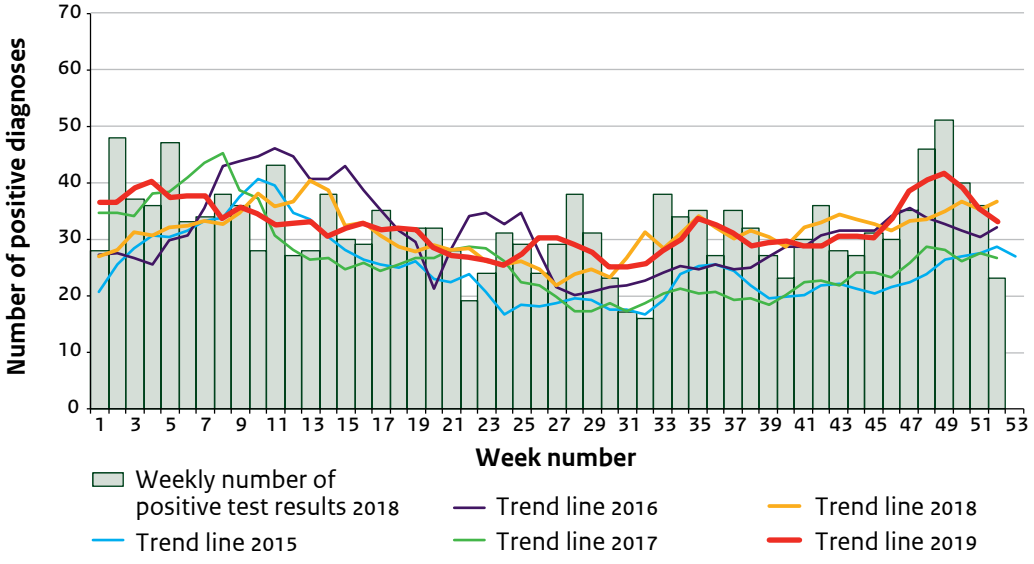
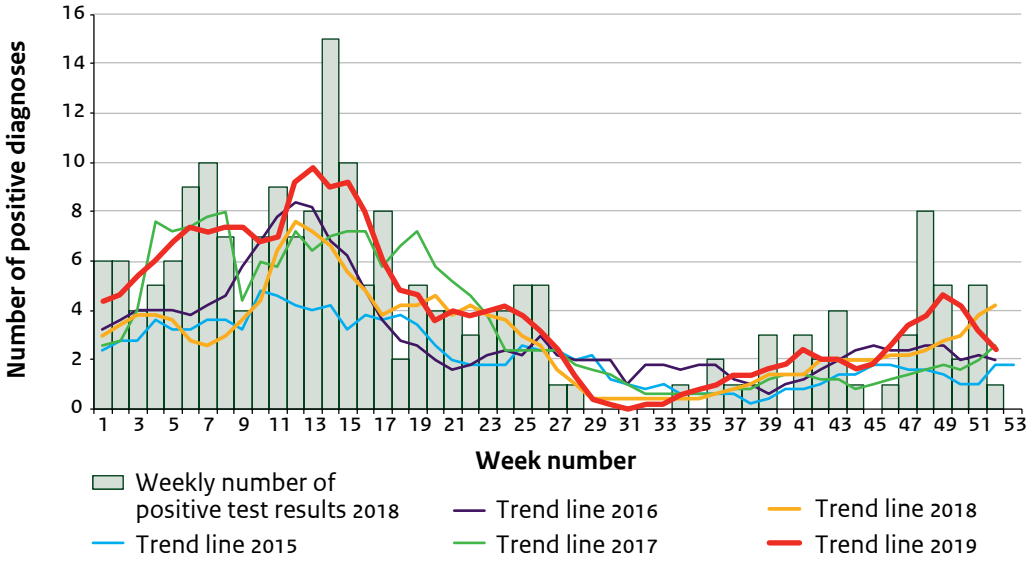


Figure 6.11 Number of weekly reported positive test results of adenovirus in the virological laboratory surveillance for the calendar year 2019 and the trend lines* for the calendar years 2015 – 2019.



* 5-week moving average.

Figure 6.12 Number of weekly reported positive test results of bocavirus in the virological laboratory surveillance for the calendar year 2019 and the trend lines* for the calendar years 2015 – 2019.



* 5-week moving average.

Chapter 7
Burden of respiratory infectious diseases in the Netherlands

Authors: Brechje de Gier, Daphne Reukers
Contributors: Scott McDonald, Gerard de Vries, Erika Slump, Petra Brandsema, Frederika Dijkstra, Marit de Lange, Adam Meijer, Anne Teirlinck

7.1 Key points

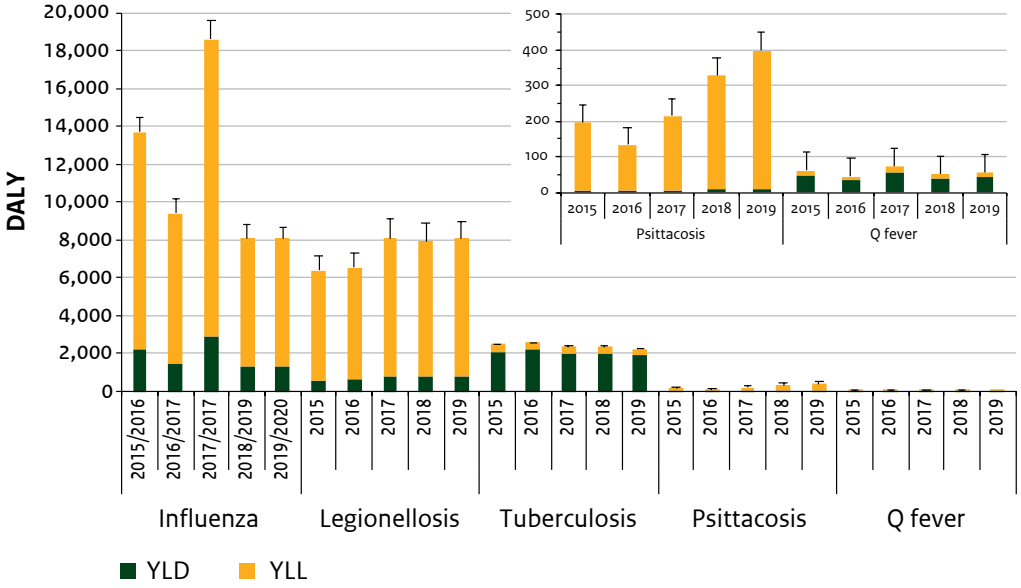
- The respiratory infectious diseases with the highest disease burden in 2019 were influenza, with an estimated 8100 DALY (95% CI 7600-8700) for season 2019/2020, and legionellosis, with an estimated 7900 DALY (7100-8900) for 2019. Disease burden in 2019 was estimated at 2300 DALY (2300-2400) for tuberculosis; 330 DALY (250-430) for psittacosis, and 52 DALY (44-61) for Q fever.
- The influenza burden of season 2018/2019 was similar to the previous season of 2018/2019, but low compared to the three seasons before that.
- For psittacosis, the burden estimate for 2019 has increased and is the highest reported since 2015. The burden of legionellosis has steadily increased during the past five years, but stabilized in 2019 compared to 2018.
- The burden of tuberculosis and Q-fever remained relatively stable during the last five years.
- When assessing the average burden per individual case, the burden is highest for tuberculosis and lowest for influenza. This burden per individual case is a characteristic of the disease and is independent of time.

7.2 Background

Estimates of the burden of infectious diseases are used to compare health impact between different infectious diseases in the Dutch population and to follow trends in time. The burden of a disease is a combination of incidence and severity. Disease burden is expressed here in disability-adjusted life years (DALY), which indicates the number of healthy life years lost due to a disease. DALY is the sum of years of life lost due to mortality (YLL) and years lived with disability due to morbidity (YLD) (Mangen, Plass et al. 2013). The burden of infectious diseases in the Netherlands was estimated using the Burden of Communicable Diseases in Europe (BCoDE) methodology, which entails a pathogen- and incidence-based approach (Mangen, Plass et al. 2013). This means that all health loss due to an infection is attributed to the event of infection and (future) long-term sequelae of infection are included in the burden assigned to the year of infection. The DALY estimates presented in this chapter can be interpreted as the disease burden that is and will be suffered due to the average annual respiratory infections that occurred in the years 2015 to 2019, or the disease burden that theoretically could have been avoided by preventing infections in those years.

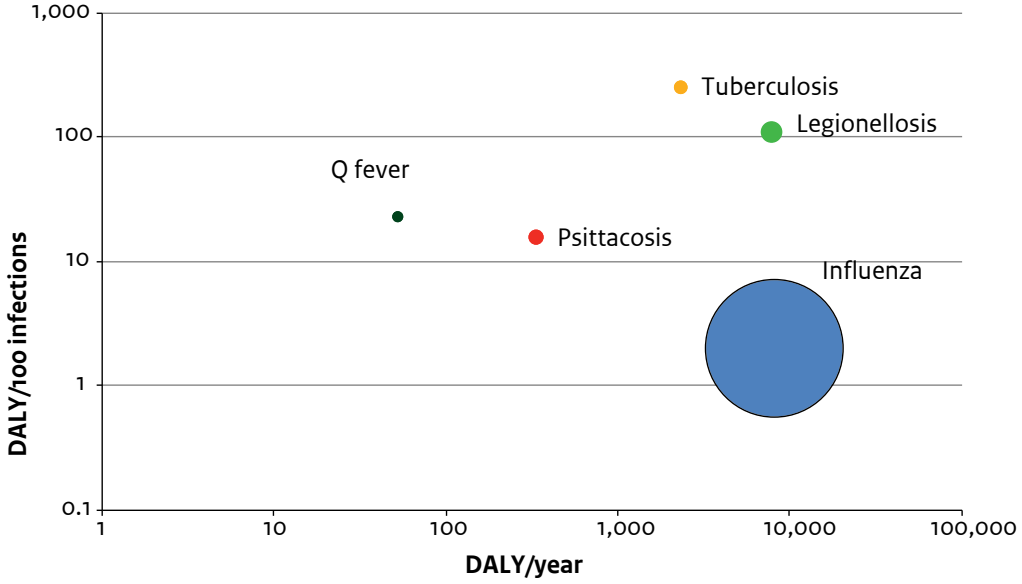
7.3 Tables and figures

Figure 7.1 Average annual DALY, caused by respiratory infectious diseases in the Netherlands, split by YLL (years of life lost due to mortality) and YLD (years lived with disability), ranked by the average disease burden caused by the annual incident cases in 2015-2019 (seasons 2015/2016 through 2019/2020 for influenza).



Footnote: Error bars indicate 95% confidence intervals. The insert zooms in for psittacosis and Q fever.

Figure 7.2 Ranking of respiratory diseases by estimated burden at population (DALYs/year) and individual level (DALYs/100 infections) in 2019 (for influenza respiratory season 2019/2020). The area of each bubble is proportional to the estimated incidence of the disease.



Footnote: both axes are on a logarithmic scale.

Table 7.1 Estimated annual disease burden in YLD per year, YLL per year, DALY per year, DALY per 100 cases (with 95% confidence intervals) and estimated annual number of acute infections in the years 2015 to 2019 (season 2015/2016 to 2019/2020 for influenza) in the Netherlands in order of highest to lowest average DALY/year in 2019.

Disease	YLD/ year	YLL/ year	DALY/ year	DALY/ 100 cases[ab]	Annual acute infections[c]
Influenza					
2015/ 2016	2200 (2000-2300)	11500 (10800-12200)	13700 (12800-14500)		682000
2016/ 2017	1500 (1300-1600)	7900 (7300-8600)	9400 (8600-10200)		471000
2017/ 2018	2900 (2700-3100)	15700 (14800-16600)	18600 (17500-19600)		933000
2018/ 2019	1300 (1200-1400)	6800 (6300-7300)	8000 (7400-8700)		402000
2019/ 2020	1300 (1200-1400)	6800 (6300-7300)	8100 (7600-8700)	2 (2 -2)	405000
Legionellosis					
2015	590 (540-650)	5800 (5100-6500)	6400 (5700-7200)		5500
2016	640 (580-700)	5900 (5200-6600)	6500 (5800-7300)		5900
2017	790 (720-870)	7300 (6500-8100)	8000 (7200-9000)		7300
2018	820 (750-900)	7100 (6300-8000)	7900 (7100-8900)		7600
2019	790 (730-870)	7300 (6500-8100)	8100 (7300-9000)	110 (100-120)	7400
Tuberculosis					
2015	2100 (2100-2100)	390 (350-430)	2500 (2400-2500)		970
2016	2200 (2200-2200)	400 (360-440)	2600 (2500-2600)		990
2017	2000 (1900-2000)	350 (320-390)	2300 (2300-2400)		880

Disease	YLD/ year	YLL/ year	DALY/ year	DALY/ 100 cases[ab]	Annual acute infections[c]
2018	2000 (2000-2010)	340 (310-380)	2300 (2300-2400)		890
2019	1900 (1800-1900)	350 (320-390)	2200 (2200-2200)	260 (250-260)	850
Psittacosis					
2015	5 (4-6)	190 (140-250)	190 (150-260)		1300
2016	4 (3-4)	120 (90-170)	130 (100-170)		950
2017	5 (5-6)	210 (160-270)	220 (170-280)		1500
2018	7 (5-8)	320 (240-420)	330 (250-430)		1800
2019	9 (8-11)	390 (290-500)	400 (300-510)	16 (13-19)	2500
Q fever					
2015	48 (41-56)	14 (12-17)	62 (52-72)		280
2016	34 (27-43)	11 (9-14)	46 (36-56)		190
2017	54 (45-64)	18 (15-22)	72 (60-86)		300
2018	40 (33-46)	12 (10-15)	52 (43-61)		250
2019	44 (37-53)	11 (9-14)	56 (46-66)	23 (19-27)	250

[a] for Q fever, asymptomatic acute infections can lead to disease burden from sequelae, the estimated annual DALY were therefore divided by the sum of both symptomatic and asymptomatic acute infections per year.

[b] DALY/ 100 cases is only shown for 2019 since this measure is a characteristic of the disease and is independent of time.

[c] this number includes asymptomatic acute infections for Q fever.

Chapter 8
General discussion and conclusion

Authors: Rianne van Gageldonk-Lafeber, Anne Teirlinck, Daphne Reukers

Influenza surveillance

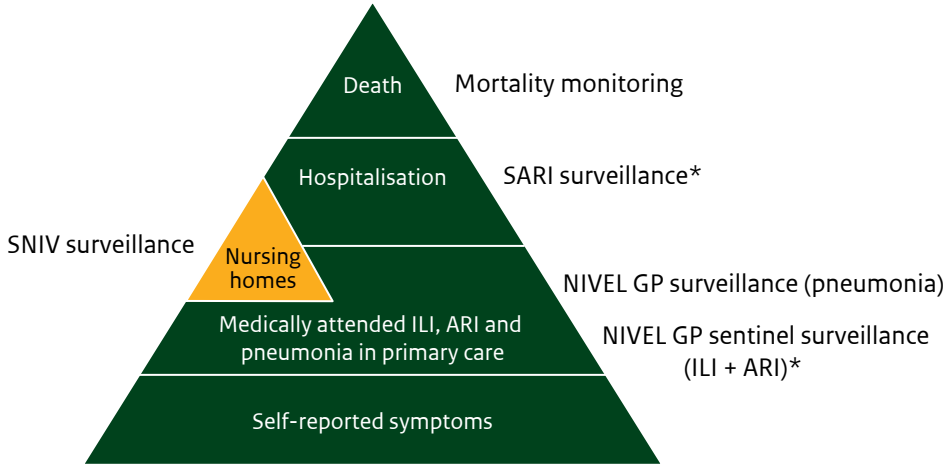
The influenza epidemic in the 2019/2020 season lasted for five weeks, which is shorter than the average ten weeks duration over the past 25 years. Seasonal ILI incidence reported by GPs was low compared with the previous four seasons, as well as the seasonal number of GP consultations for pneumonia. The seasonal number of patients with ILI in nursing homes was within the range of the four previous seasons. The epidemic was divided in two parts: week 5 through 7 and week 10 and 11. In the first part of this epidemic, mainly influenza virus type A was detected with equal proportions of influenza type A(H1N1)pdm09 and A(H3N2). The ILI incidence reported by GPs peaked in the second part of the epidemic, which coincided with the start of the COVID-19 pandemic. In this part of the influenza epidemic, the ILI incidence was still above the epidemic threshold, while a declining percentage of influenza virus and an increasing percentage of SARS-CoV-2 was detected. In week 12 through week 14 2020, the ILI incidence was still above the epidemic threshold, but almost no influenza virus was detected. Therefore, while week 10 and 11 still formally fitted the definition for influenza epidemic, the elevated ILI incidence in these weeks can, at least partially, be attributed to the increasing number of SARS-CoV-2 infections. The ILI incidence in nursing homes peaked in week 14. No sampling is performed in this surveillance system, therefore the etiology cannot be confirmed. However, this is also most probably and at least partially due to the COVID-19 outbreak.

The current COVID-19 epidemic once again emphasizes the importance of surveillance of severe acute respiratory infections (SARI), which is still the missing link in the Dutch respiratory surveillance system (figure 8.1). As described in the previous edition of this annual report we are planning to set up a SARI surveillance system making use of the Dutch financial 'DBC' codes. A pilot study showed that these financial codes are currently the only routinely collected data suitable for an automated SARI-surveillance generating near real-time (weekly) data on the number of hospitalised patients with an acute respiratory infection. These data will be

combined with patient demographics and microbiological test results (Groeneveld, Dalhuijsen et al. 2017, Marbus, van der Hoek et al. 2020). Unfortunately the SARI surveillance system is not in place yet, because of shifting priorities due to the COVID-19 epidemic.

Since 2017, we have no information available on the base of the surveillance pyramid: the self-reported ILI incidence in the general population, which was formerly assessed via Influenzanet/'*Grote Griep Meeting*'. Accelerated by the COVID-19 outbreak, a new platform Infectieradar has recently started by RIVM. This platform is again based on Influenzanet, an existing European partnership between different universities and governments. The aim of this collaboration is to monitor and map symptoms of viral infections, such as influenza, in humans in the Netherlands. Participants complete an online application form, which contains various medical, geographical and behavioural questions. Subsequently, participants are reminded weekly to report any symptoms they have experienced in the past week. The incidence of ILI is determined on the basis of a uniform case definition, so it can also be compared between countries participating in Influenzanet. Influenzanet has also been adapted to collect additional information on trends and symptoms related to COVID-19 in order to provide useful insights to limit the spread of this virus. Infectieradar is operational since November 2020 and the first results are expected by the end of 2020. These results will be added to the next annual report in 2021.

Figure 8.1. The respiratory infections surveillance pyramid in the Netherlands.



Footnote: Systems with * also include virological surveillance.

Influenza vaccination

For the estimation of influenza vaccine effectiveness (VE), RIVM participates in the European I-MOVE consortium. This enables to pool data from different European countries and provide robust estimates of VE early in the influenza season, for each circulating virus and for different age groups. The estimates of the influenza VE over the years are, on average, only moderate. However, because of the high burden of disease from influenza, vaccination with a moderately effective vaccine can still prevent many influenza virus infections, complications such as pneumonia, and deaths. For the 2019/2020 season, the I-MOVE estimates, including Dutch data, indicate that the influenza vaccine has provided substantial protection against medically-attended influenza. The Dutch influenza vaccination programme was estimated to have averted around 10% of the otherwise expected GP consultation for ILI caused by influenza virus among those aged 65 years and above during this season. This is lower than last season, when 20% GP consultation for ILI were prevented in this age group, due to a relatively low VE in this older age groups this year. Since the 2019/2020 season, inactivated quadrivalent influenza vaccines (QIV) are used in the National Influenza Prevention Program in the Netherlands (Blokhuis 2018). In the QIV, both commonly circulating influenza B lineages (Victoria lineage and Yamagata lineage) are included in the vaccine, instead of selecting one of those lineages.

Notifiable respiratory diseases

In the virological laboratory surveillance 69 diagnoses of *C. burnetii* were reported and 18 acute Q fever cases were notified in Osiris. As in previous years the number of notified cases are less than the number of cases in the virological surveillance, as a positive laboratory result can also indicate a past infection and these do not fulfil the national notification criteria for acute Q fever. The number of notified cases is in line with the number of notifications from 2014-2018 (varying from 14 to 26), which is comparable to the levels before the large 2007-2010 Q fever epidemic.

The number of notified tuberculosis cases show a steady decline since 1998, although increases related to immigration are seen in some years. In 2019, the number of notified tuberculosis cases decreased with 5% to 759. Therefore, the number of notified tuberculosis cases was below 800 patients for the second year since registration started in 1950. Most TB patients notified in 2019 were foreign born (75%).

The increasing trend in incidence of Legionnaires' disease (LD) did not continue in 2019. The number of 566 notified patients in 2019 was similar to 2017 and 2018 and remained high compared to the number of notifications before 2015. Although there were several smaller clusters, most notifications were sporadic cases. For the first time since the start of environmental sampling of LD patients in the Netherlands, a patient with a ST47 clinical strain was matched to a drinking water installation at home while another patient with a ST47 strain was matched to a waste water treatment plant. Studies on the risk of Legionnaires' disease linked to biological wastewater treatment plants are ongoing.

In 2019, the notified number of patients with psittacosis was considerably higher than in previous years. The increase in notifications started in autumn in the east of the Netherlands

and later expanded to the middle and south (Vlaanderen, Cuperus et al. 2020). The outbreak investigation showed that beside petting birds, also wild (garden) birds played a role in this increase.

The above mentioned notifiable infectious diseases presenting as pneumonia are often underreported because most cases of community acquired pneumonia are diagnosed on clinical criteria without laboratory diagnostics. This does not apply to COVID-19 which was added to the list of notifiable diseases in January 2020. Since the first notified case in February, a steep increase in the number of cases was observed. The first wave of the Dutch COVID-19 epidemic lasted until June. The high number of hospital admissions overwhelmed wards and intensive care units and caused an unprecedent peak in overall mortality of the Dutch population. This report describes the COVID-19 situation up to week 20 of 2020. At the time of writing, we are in a second wave of the epidemic. The most up-to date information on the COVID-19 situation can be found on the RIVM website (https://www.rivm.nl/coronavirus-covid-19/actueel). The outbreak of COVID-19 majorly impacts both the circulation and the surveillance of other (respiratory) infectious diseases. The impact in the current report is still minor, since the outbreak in the Netherlands started when circulation of most seasonal infections was already declining. For the reporting of the year 2020 however, the surveillance data should be interpreted with more caution.

This annual report provides an update on the burden of respiratory infectious diseases expressed in disability-adjusted life years (DALY). Influenza remains the infectious disease with the highest burden in the Netherlands (van Lier, McDonald et al. 2016, de Gier, Schimmer et al. 2019). This is also the case for the European (EU) region, with influenza responsible for 30% of the total burden from infectious diseases (Cassini, Colzani et al. 2018). The burden of psittacosis in 2019 was the highest estimated since 2015. The annual report 'Staat van Infectieziekten' (report in preparation) has information on the burden of COVID-19, which will be added to this report next year for the reporting of the year 2020.

An overall objective of RIVM is to make surveillance information available to the public as quickly as possible. A weekly comprehensive situation report on COVID-19 is published on the RIVM website (see above). Furthermore, the RIVM website provides weekly updated information on influenza and RSV 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 outbreaks. Up-to-date information on the incidence of legionellosis, psittacosis and Q fever is also available at https://www.atlasinfectieziekten.nl/.

Chapter 9
Methods for respiratory surveillance

9.1 Respiratory season, respiratory year and calendar year

The aim of this annual report is to describe the surveillance of influenza and other respiratory infections in the Netherlands. Since respiratory illnesses mainly occur in winter, the data is usually presented for the respiratory season or the respiratory year. A respiratory season is defined as the period from week 40 through week 20 of the next year and the 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 2019/2020 is limited to the respiratory season to allow a timely reporting. Respiratory infections may occur outside the respiratory season to a limited extend. Because the notifiable diseases legionellosis, tuberculosis, Q fever and psittacosis as well as the majority of pathogens monitored in the virological laboratory surveillance occur without typical winter seasonality, the results of these diseases refer to the 2019 calendar year (weeks 1-52).

9.2 Data sources

Nivel Primary Care Database

Nivel (Netherlands institute for health services research) holds the integral monitoring and information services for primary care, called 'Nivel Primary Care Database' (Verheij and Koppes 2019). The Nivel Primary Care Database holds longitudinal data recorded in electronic medical files by general practitioners (GPs) 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 about 350 participating general practices spread over the country [https://nivel.nl/nl/zorgregistraties-eerste-lijn/surveillance].

- In the 2019/2020 respiratory season, the coverage was about 1.3 million persons (8% of the Dutch population, representative for age). The participating GPs do not actively report patients and do not take laboratory specimens for surveillance purposes but make their electronic patient information systems available for automatic, anonymised, data extraction (de Gier, Nijsten et al. 2017).
- A proportion of the GPs participating in Nivel Primary Care Database take part in sentinel influenza surveillance. These GPs actively report on the number of patients who consult them for ILI. From a subset of patients with ILI or other ARI, they collect a throat swab and nose swab and send it to RIVM for virological laboratory diagnostics (influenza virus, RSV, rhinovirus, enterovirus and, since February 2020, SARS-CoV-2). The population of these 40 sentinel practices covers approximately 0.8% of the Dutch population and is representative for age, sex, regional distribution and population density (Donker 2018).

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. In the 2018/2019 respiratory year, 26 locations from 13 different institutions participated. The participating nursing homes weekly report the number of residents with ILI and lower respiratory tract infections (LRTI) 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 season are not yet complete and should be considered preliminary data. The annual total bed capacity is reported once a 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.

Death notification data, Statistics Netherlands (CBS)

In the Netherlands, deaths are notified to municipalities and then reported to 'Statistics Netherlands' (In Dutch: Centraal Bureau voor de Statistiek: CBS), which collects and monitors all Dutch vital statistics. Weekly, RIVM receives data and analyses updated 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. Of all death notifications, 44% (median) is received by CBS within 1 week after the date of death, 97% within 2 weeks after date of death and 99% within 3 weeks of date of death.

Virological laboratory surveillance

On a weekly basis, about 19 virological 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 specimens 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 is useful as an additional source. It can be used to follow

trends of respiratory infections over a prolonged period, because of their relative robust reporting history.
In order to monitor the total number of people tested and the number of people tested positive for SARS-CoV-2 virus in the Netherlands, all laboratories in the Netherlands that perform diagnostics for SARS-CoV-2 were asked to report these data from March 9th onwards. These data also contain no background information concerning patient status, clinical data or origin of specimen (primary or hospital care). The laboratories report daily numbers of the previous week every Monday before noon. The number of people with a positive result differs from the number of COVID-19 patients reported by the Public Health Services, because people may be tested more than once and positive laboratory results are reported more rapidly than disease notifications.

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. In January 2020, COVID-19 was added to the list of notifiable diseases. Medical doctors and medical-microbiological laboratories notify cases to the Public 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 Public Health Services and registered in Osiris-NTR. Osiris is a dynamic system and due to corrections and additions of the Public Health Services, small differences may exist between the data reported in this report and earlier or elsewhere reported data. Osiris notifications consist of anonymous patient data, date of disease onset, diagnostic information (dates, diagnostic methods and outcome) and information on source finding and contact tracing. For tuberculosis, Osiris also registers information regarding treatment and treatment outcome.

New respiratory virus infections

In case of a suspected human infection with animal influenza virus, such as influenza A(H5N1) virus or influenza A(H7N9) virus, diagnostics are performed by the RIVM (CIb/IDS). For suspected infection with the Middle East Respiratory Syndrome Coronavirus (MERS-CoV), diagnostics are performed by the ErasmusMC. Both human infection with animal influenza and MERS-CoV are notifiable in the Netherlands.

9.3 Data analysis

Influenza-like-illness (ILI)
ILI incidence is estimated using two data sources: 1) Nivel Primary Care Database - sentinel GP practices and 2) SNIV nursing homes. These two data sources 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)
- 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 2018).
For chapter 2.1 and 3, the preliminary weekly numbers as reported during the season are used. The influenza epidemic threshold during the 2019/2020 season is set at an ILI incidence of 5.8 per 10,000 persons per week, based on historical data (Vega Alonso, Lozano Alonso et al. 2004, Hooiveld, Donker et al. 2019). 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 numerator, 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

Acute respiratory infections (ARI)

Weekly numbers on patients consulting for an acute respiratory infection (ICPC code R74), including acute/chronic sinusitis (ICPC code R75), acute laryngitis/tracheitis (ICPC code R77), acute bronchitis/bronchiolitis (ICPC code R78) or influenza (ICPC code R80) are obtained from Nivel Primary Care Database. Please note that the ILI syndrome is a subset of, and included in the ARI syndrome. Although ARI is less specific for an influenza virus infection than ILI, seasonal estimates are highly correlated. Weekly ARI consultation rates are calculated as the number of patients consulting their GP in a given week, divided by the total number of enlisted patients. Cumulation of this weekly surveillance data over the season (separated for week 40 through 20 and week 21 through 39) is reported as the seasonal number of consultations.

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, reported as lower respiratory tract infections (LRTI), data are also obtained from nursing homes (SNIV), in which the incidence of LRTI is based on the weekly number of residents with new clinical diagnosis LRTI, registered by the SNIV nursing homes. The denominator is the number of observed resident weeks.

Severe acute respiratory infections (SARI)

An active surveillance system is implemented at Jeroen Bosch Hospital (JBZ). This SARI surveillance pilot study makes a distinction between syndromic surveillance and surveillance based on laboratory confirmed outcomes. Laboratory outcomes are essential for pathogen detection and vaccine effectiveness calculations.
The SARI case definition as defined as:
a hospitalised person with:

- at least one systemic symptom or sign: fever or feverishness, malaise, headache or myalgia or deterioration of general condition (asthenia or loss of weight or anorexia or confusion or dizziness)

And

- at least one respiratory symptom or sign (cough, sore throat or shortness of breath)

And

- the symptoms should not have started (or clearly worsened, if chronic) more than 7 days ago

Jeroen Bosch Hospital

Since October 2015, an active SARI surveillance is implemented at JBZ. On-site inclusion of any patient fulfilling the SARI case definition take place by research nurses. In February 2017, the SARI surveillance pilot study changed from research to a quality-of-care management strategy. The quality-of-care of SARI patients is now evaluated based on quality indicators, such as diagnostics, infection control measures, and treatment. A short web-based questionnaire was completed by the research nurse about symptoms, influenza and pneumococcal vaccination status, comorbidities and several risk factors of every included SARI patient. In addition,

routinely collected respiratory specimens were used for influenza virus detection. If influenza virus diagnostics were not requested by the treating physician, influenza detection, influenza virus type A subtyping and type B lineage determination were performed in research setting at NIC, location RIVM, Centre for Infectious Disease Research, Diagnostics and laboratory Surveillance (IDS). SARI patients of all ages are included in the SARI surveillance pilot study at JBZ. No outpatients are included in the SARI surveillance at the JBZ. Retrospectively, the weekly total number of SARI patients is based on a selection of DBC/DOT codes related to SARI and provided with a lag of one week.

Determining excess mortality

Every Thursday the number of reported deaths, as provided by Statistics Netherlands (CBS), is evaluated for the presence of significant excess deaths above the expected levels of death (the baseline), at 2 different time-lags: deaths reported within 1 week (45% of all deaths) and deaths reported within 2 weeks after date of death (97% of all deaths). The baselines and prediction limits are calculated using a Serfling type algorithm on historical mortality data from the 5 previous years. In the historical data, any weeks with extreme underreporting were removed (the 7.5% most underreported values, often coinciding with public holidays). Also periods with high excess mortality in winter and summer were removed so as not to influence the calculated baseline with time-periods with previous excess mortality. When the observed number of deaths exceeds the upper limit of the prediction interval mortality is considered to be significantly increased (excess deaths calculated as the number of deaths above the baseline).

Influenza virus, RS-virus and other respiratory viruses

Surveillance of circulating viruses

At the National Influenza Centre (NIC) location RIVM the respiratory specimens are analysed that are taken for the influenza virus surveillance at the GP sentinel practices. Additionally, a selection of Dutch virology laboratories submit a representative set of influenza virus positive specimens (5-6 specimens per week is the request) to the Erasmus MC. For laboratories that continued to send all influenza virus positive specimen this selection of 5-6 specimens per week for further characterisation is done by Erasmus MC. Therefore, the trend in the specimens received by Erasmus MC is not a reflection of the course of the epidemic since 2018 when this procedure was installed.

The GP sentinel practices from Nivel Primary Care Database were requested to take specimens (combined throat swabs and nose swabs) of ILI or other ARI patients. The criteria for specimen collection have changed over de years to comply with standards in international influenza vaccine effectiveness studies (see previous reports for more details, (Reukers, van Asten et al. 2019)). Since the 2018/2019 season, after the I-MOVE+ study stopped but I-MOVE continued, the GPs were instructed to swab

- at least two ILI patients on Monday through Wednesday;
- when on those days no ILI patients attended the GP or no ILI patients were willing to participate, on Thursday through Sunday, GPs were instructed to swab at least the first two ILI patients or patients with an acute respiratory infection other than ILI (ARI);
- at least one child below the age of 10 with ILI or other ARI throughout the week.

The GP specimens are analysed by NIC location RIVM for influenza viruses, RSV, rhinoviruses, enteroviruses and, since February 2020, SARS-CoV-2. 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. At the start of the influenza epidemic, the proportion of influenza virus in specimens collected from ILI patients is often low. Although RSV explains a large proportion of these cases especially in very young children, a relatively large proportion of specimens remains negative for the pathogens tested. Therefore, a retrospective analysis was performed on specimens negative in our routinely used assays. We used a commercial multiplex PCR assay (Fast Track Diagnostics FTD Respiratory pathogens 21) diagnosing 21 pathogens: influenza A virus, influenza A(H1N1)pdm09 virus, influenza B virus, human rhinovirus, human coronavirus NL63, 229E, OC43 and HKU1, human parainfluenza 1, 2, 3 and 4, human metapneumoviruses A/B, human bocavirus, human respiratory syncytial viruses A/B, human adenovirus, enterovirus, human parechovirus, *Mycoplasma pneumoniae*.

Virus isolation
Influenza viruses are isolated from influenza virus PCR positive clinical specimens in cell culture on MDCK-SIAT or MDCK or hCK mono culture cell lines at Erasmus MC or on mixed MDCK-SIAT and MDCK-I cell lines at RIVM. Successfully grown viruses are used for antigenic characterisation and phenotypic determination of antiviral susceptibility.

Influenza virus antigenic and genetic characterization
Whereas subtyping and lineage determination at RIVM are performed using RT-PCR assays, Erasmus MC changed since the 2018/2019 season to MinION next generation sequencing of the HA and NA and PA genes for simultaneous subtyping/lineage determination and genetic characterisation of influenza viruses.
Antigenic characterization is performed by NIC location Erasmus MC in Rotterdam for a subset of influenza viruses and influenza virus positive clinical specimens submitted by peripheral laboratories and the sentinel GP surveillance after successful virus isolation at RIVM. This provides an indication of the degree of antigenic match between the circulating influenza viruses and the vaccine virus. Because new ferret sera have to be generated at Erasmus MC, the results of this thorough antigenic characterisation takes some time and is completed after this report has been published.
A subset of influenza viruses are characterized genetically by sequence analysis of the haemagglutinin genome segment at RIVM. This is done on a systematic sample of most prevalent influenza virus types, lineage and subtypes if the number of detections is high and on all if the number of detections is moderate and variation is low, and on all sporadically detected types, lineages and subtypes from the GP sentinel surveillance. At Erasmus MC this is done using MinION sequencing of all received specimens with high virus load, as described above. Sequences from both locations are combined for detailed phylogenetic and amino acid substitution analysis giving 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 has been the case for increasing numbers of A(H3N2) viruses since 2013.

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 from the Nivel sentinel influenza surveillance, the phenotypic antiviral susceptibility for neuraminidase inhibitors (oseltamivir and zanamivir) is determined by NIC location RIVM. For a subset of 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. In addition, the virus in the clinical specimen is sequenced to exclude that the resistance substitution emerged during the virus isolation procedure. 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 NIC location RIVM. Of all viruses tested at Erasmus MC and a subset of viruses tested at RIVM as described above, the neuraminidase gene is sequenced and analysed for any markers previously associated with reduced neuraminidase inhibitor susceptibility. From a systematic sample of influenza virus positive clinical specimens the whole genome is sequenced at the NIC location RIVM in order to screen for other and new molecular markers for reduced susceptibility for antivirals and markers for virulence. 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. 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 by sequencing at NIC location RIVM. Molecular markers indidicative for resistance to the polymerase inhibitor baloxavir are assessed in a subset of influenza virus positive clinical specimens by sequencing at NIC location Erasmus MC and RIVM. 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.

Estimating symptomatic influenza incidence in the general population

We estimated the incidence of symptomatic infection with influenza virus by combining all relevant data sources via Bayesian evidence synthesis (Teirlinck, de Gier et al. 2018). This estimation procedure can be viewed as similar to the 'multiplier method' or 'direct method', but with correct propagation of the uncertainty inherent in each data source to the final estimate. The relevant data sources are: (i) ILI: number of ILI patients per season and per age-group, with catchment population size (<5, 5-14, 15-44, 45-64, 65+ years) (data from Nivel Primary Care Database was used); (ii) under ascertainment: age-group specific number of respondents reporting ILI and number of respondents reporting ILI and who contacted their GP (extracted from the InfluenzaNet, 2016/2017 data was used for that season and the

following seasons, as Influenzanet stopped in 2016/2017; (Friesema, Koppeschaar et al. 2009, Koppeschaar, Colizza et al. 2017), (iii) influenza positivity rate: number of positive tests and number tested, per age-group (from virological surveillance; see chapter 3); and (iv) sensitivity of virological testing: estimated at 95-100%. As an improvement over previous work (McDonald, Presanis et al. 2014), analysis was restricted to the winter season (week 40 through week 20 of the next year).
To show variation in symptomatic influenza incidence by virus subtype/lineage across seasons, we also fitted a model in which data were stratified by subtype A(H1N1)pdm09 and A(H3N2) and lineage (B/Victoria, B/Yamagata) rather than age-group.

Impact of the influenza vaccination programme

We estimated number of GP visits averted by the influenza vaccination programme in the Netherlands among those aged 65 years or older. First, the observed number of cases was estimated for GP visits based on incidence of ILI from sentinel GP surveillance, influenza virus positivity rate, and sensitivity of virological testing (i.e. the same method as described in the paragraph 'Estimating symptomatic influenza incidence in the general population', but without the correction for underascertainment based on data of InfluenzaNet). Secondly, the number of averted cases was calculated from the estimated observed cases, national vaccination coverage and VE. Vaccination coverage of the age group 65 years and older was sourced from pseudo-anonymized data from electronic medical files of general practices participating in Nivel Primary care Database (Heins, Hooiveld et al. 2020). These vaccination coverages were estimated with multilevel logistic regression analysis, in which the clustering of patients in GP practices is taken into account.
VE was based on subtype specific I-MOVE primary care study VEs, corrected for the proportion of influenza virus (sub)types circulating in the Netherlands among patient with ILI or ARI of 65 years and older who were sampled in the sentinel GP practices of Nivel.
The impact measures calculated were:

- Number of GP visits averted. This was calculated as:

$$NAE = N - n = \frac{n}{1-(VC*VE)} - n = n * (\frac{VC*VE}{1-(VC*VE)})$$

where NAE = number of averted events,
N = Expected number of events without the vaccination programme
n = Observed number of events
VC = vaccination coverage
VE = Vaccine effectiveness

- Prevented fraction (PF), which was calculated as: PF = NAE/N
- Number needed to vaccinate to prevent one event, which was calculated as: NVN = 1/(VE*N/population size).

95% CIs were derived through Monte Carlo simulation.

Virological laboratory surveillance

To describe trends over time in adenovirus, bocavirus, coronavirus, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, para-influenza virus, rhinovirus and human metapneumovirus (hMPV), we use the weekly number of positive diagnoses reported in the virological laboratory surveillance. Trends are reported for the 2019 calendar year. Number of diagnoses of psittacosis, Q fever, influenza and RSV as reported in virological laboratory surveillance, as well as the number of persons tested positive for SARS-CoV-2 in the daily virological laboratory surveillance are given in their respective chapters.

Moving Epidemic Method (MEM) for RSV seasonality

Previously, we defined the RSV season as the period with at least 20 RSV-diagnoses per week reported by the virological laboratory surveillance. We now used the Moving Epidemic Method (MEM), that was originally developed to assess influenza seasonality (Vega, Lozano et al. 2013), to establish the epidemic thresholds for RSV, using the virological laboratory surveillance data of the previous 12 seasons (Vos, Teirlinck et al. 2019). MEM was applied with the Moving Epidemic Method Web Application (Lozano 2018) and absolute detection numbers per week for all 12 seasons in the fixed criterium model and a manually optimised slope parameter of 1.4 that had been established previously (Vos, Teirlinck et al. 2019). We calculated the mean length, timing and coverage of the epidemic period by calculating pre-and post-epidemic thresholds using the arithmetic mean and its one-sided 95% point confidence interval (CI). The start of the RSV season is defined as the first week when the number of RSV-diagnoses is above the pre-epidemic threshold, lasting for at least two consecutive weeks. The end of the RSV season is defined as the first week when the number of diagnosis is below the post-epidemic threshold, lasting for at least two consecutive weeks. We also calculated epidemic intensity levels using the geometric mean and its one sided 40% (medium), 90% (high) and 97.5% (very high) point CI. For the MEM calculations, a season was defined from week 30 through week 29 of the next year to be able to include enough data points to calculate a precise pre-epidemic threshold as RSV circulation might start as early as week 40. The epidemic thresholds for seasons up to and including 2016/2017 were calculated based on data of seasons 2005/2006 up to and including 2016/2017 (Vos, Teirlinck et al. 2019). The thresholds of the seasons from 2017/2018 onward were calculated separately per season, based on data of the previous ten seasons. For displaying results in this annual report, the respiratory season as defined for influenza (week 40- week 39) is used.

Burden of disease

To estimate disease burden in DALY, an incidence- and pathogen-based approach was applied to quantify the burden due to illness, disability and premature mortality associated with all short and long-term consequences of infection. The underlying outcome trees, disease progression probabilities, and other parameters have been previously described (Reukers, Van Asten et al. 2018). DALY estimates incorporate both years of life lost (YLL) due to premature mortality and years lived with disability (YLD) (Murray and Lopez 2013). YLD were calculated by multiplying the number of acute cases, duration of a health state and the disability weight of the health state. The disability weight is a value between 0 (perfect health) and 1 (death). We used the European disability weights collected by Haagsma et al. (Haagsma, Maertens de

Noordhout et al. 2015). To estimate YLL, remaining life expectancy tables were taken from the GBD 2010 study (WHO 2013).

The incidence of symptomatic infection with influenza was estimated as described in the method of estimating influenza incidence in the general population. We estimated the disease burden associated with tuberculosis, legionellosis, psittacosis and Q fever incident in 2014, 2015, 2016, 2017 and 2018 separately. We estimated the burden of influenza for respiratory seasons (week 40 to week 20) for the seasons 2014-2015 through 2018-2019. No time discounting was applied.

Acknowledgements

Many people have contributed to the present report. We especially thank the following persons for their contributions to respective chapters:

Guus Rimmelzwaan, **Ruud van Beek, Ron Fouchier, Mark Pronk** and **Pascal Lexmond** (NIC location Erasmus MC) for data on influenza viruses submitted by Dutch virology laboratories.

Paul Bergervoet, Marjolein Korndewal, Jeroen Alblas and **Anja Haenen** (CIb/EPI) for provision and analysis of pneumonia and ILI data in SNIV.

Inge Roof (CIb/EPI), **Peter Schneeberger**, **Peter Wever** and **Eric Hazenberg** (JBZ) for their cooperation in the SARI project.

Carel Harmsen, **Lenny Stoeldraijer**, **Ursula de Bruijn- van Leijden** and **Felicia Hofstede-Minnaard** (Statistics Netherlands, department demography) for their cooperation and provision of weekly data in the mortality monitoring.

Ben Bom (RIVM/SSC Campus) for compiling the map for Legionnaires' disease, tuberculosis and SARS-CoV-2.

Julika Vermolen (CIb/Corporate Communication) for editing the 'Publiekssamenvatting'.

Willem Verdouw (CIb/Corporate Communication) for managing the production of this report.

In addition, we want to thank the following people or authorities for their contribution and/or cooperation for delivering data we used in this report:

- **Nivel Primary Care Database team**, participating general practitioners and their patients
- **Pieter Overduin (sequencing), Mariam Bagheri, John Sluimer** and **Gabriel Goderski (virus isolation** and **phenotypic antiviral susceptibility testing)** and **Sharon van den Brink (sequencing** and **molecular diagnostics group)** and **Lisa Wijsman, Anne-Marie van den Brandt, Bas van der Veer** and **Jeroen Cremer (molecular diagnostics group),** technicians of the department respiratory and enteritic viruses (REV) respiratory viruses group and of the molecular diagnostics group of discipline Virology (CIb/IDS)
- The medical microbiological laboratories and the laboratories which participated to the virological laboratory surveillance of the **Working Group for Clinical Virology**
- Medical doctors and nurses of the **Public Health Services** who took care of the Osiris and the Osiris-NTR notifications
- **Inger Bregman**, **Lieke Blijboom, Sofie Mooij** and **Giske Lagerweij** (CIb/EPI)
- **Priscila de Oliveira Bressane Lima, Stijn Andeweg, Janneke Heijne** and **Sara Wijburg** (CIb/EPI)
- **Miranda Kamst** and **Dick van Soolingen** (CIb/IDS, Bacterial and Parasitological Diagnostics)
- **SNIV** team and participating nursing homes.

- **Jeroen den Boer, Jacqueline de Vries, Wim Houtenbos, Arjen Veen, Ruud Jansen, Paul Badoux, Bjorn Herpers, Liane Kosten, Jan Willem Meester** and **Awatef Hamdan** (Regional Public Health Laboratory Kennemerland) of the *Legionella* Source Identification Unit (BEL) for their contribution to source investigation and environmental sampling for legionellosis.
- **Helma Ruijs, Alvin Bartels, Marijke van Cooten-Boot, Felix ter Schegget** and **Laura van Vossen** (CIb/LCI) and **Willemijn Lodder** and **Harrold van den Berg** (CIb/Z&O).

References

Bijkerk P, de Gier B, Nijsten DRE, Duijster JW, Soetens LW and Hahné SJM. (2016). "State of Infectious Diseases in the Netherlands, 2015." RIVM Retrieved November 2020, from https://www.rivm.nl/bibliotheek/rapporten/2016-0069.pdf.

Blokhuis P (2018). Kamerbrief over Maatregelen griep. Ministerie van Volksgezondheid Welzijn en Sport. https://www.rijksoverheid.nl/documenten/kamerstukken/2018/10/10/kamerbrief-over-maatregelen-griep.

Cassini A, Colzani E, Pini A, Mangen MJ, Plass D, McDonald SA, Maringhini G, van Lier A, Haagsma JA, Havelaar AH, Kramarz P, Kretzschmar ME and on behalf of the BCoDE Consortium (2018). "Impact of infectious diseases on population health using incidence-based disability-adjusted life years (DALYs): results from the Burden of Communicable Diseases in Europe study, European Union and European Economic Area countries, 2009 to 2013." Euro Surveill **23**(16).

de Gier B, Nijsten DRE, Duijster JW and Hahné SJM. (2017). "State of Infectious Diseases in the Netherlands, 2016." RIVM Retrieved November 2020, from https://www.rivm.nl/bibliotheek/rapporten/2017-0029.pdf.

de Gier B, Schimmer B, Mooij SH, Raven CFH, Leenstra T and Hahné SJM. (2019). "State of Infectious Diseases in the Netherlands, 2018." RIVM Retrieved November 2020, from https://www.rivm.nl/bibliotheek/rapporten/2019-0069.pdf.

Donker G. (2018). "Nivel Zorgregistraties eerste lijn - Peilstations 2016." Nivel Retrieved November 2020, from https://www.nivel.nl/sites/default/files/bestanden/Nivel_zorgregistraties_Peilstations_2016.pdf.

Fanoy EB, van der Sande MA, Kraaij-Dirkzwager M, Dirksen K, Jonges M, van der Hoek W, Koopmans MP, van der Werf D, Sonder G, van der Weijden C, van der Heuvel J, Gelinck L, Bouwhuis JW and van Gageldonk-Lafeber AB (2014). "Travel-related MERS-CoV cases: an assessment of exposures and risk factors in a group of Dutch travellers returning from the Kingdom of Saudi Arabia, May 2014." Emerg Themes Epidemiol **11**: 16.

Friesema IH, Koppeschaar CE, Donker GA, Dijkstra F, van Noort SP, Smallenburg R, van der Hoek W and van der Sande MA (2009). "Internet-based monitoring of influenza-like illness in the general population: experience of five influenza seasons in The Netherlands." Vaccine **27**(45): 6353-6357.

Groeneveld GH, Dalhuijsen A, Kara-Zaitri C, Hamilton B, de Waal MW, van Dissel JT and van Steenbergen JE (2017). "ICARES: a real-time automated detection tool for clusters of infectious diseases in the Netherlands." BMC Infect Dis **17**(1): 201.

Haagsma JA, Maertens de Noordhout C, Polinder S, Vos T, Havelaar AH, Cassini A, Devleesschauwer B, Kretzschmar ME, Speybroeck N and Salomon JA (2015). "Assessing disability weights based on the responses of 30,660 people from four European countries." Popul Health Metr **13**: 10.

Heins M, Hooiveld M and Korevaar J. (2020). "Monitor Vaccinatiegraad Nationaal Programma Griepppreventie 2019." Retrieved November 2020, from https://www.nivel.nl/sites/default/files/bestanden/1003843.pdf.

Hooiveld M, Donker G, Fouchier R, van der Hoek W, Koopmans M, Korevaar J, de Lange M, Teirlinck A and Meijer A (2019). "Grenswaarde griepepidemie in winter 2019-2020. Utrecht: Nivel, 2019."

Koppeschaar CE, Colizza V, Guerrisi C, Turbelin C, Duggan J, Edmunds WJ, Kjelso C, Mexia R, Moreno Y, Meloni S, Paolotti D, Perrotta D, van Straten E and Franco AO (2017). "Influenzanet: Citizens Among 10 Countries Collaborating to Monitor Influenza in Europe." JMIR Public Health Surveill **3**(3): e66.

Kraaij-Dirkzwager M, Timen A, Dirksen K, Gelinck L, Leyten E, Groeneveld P, Jansen C, Jonges M, Raj S, Thurkow I, van Gageldonk-Lafeber R, van der Eijk A, Koopmans M and Netherlands ME-Coitot (2014). "Middle East respiratory syndrome coronavirus (MERS-CoV) infections in two returning travellers in the Netherlands, May 2014." Euro Surveill **19**(21).

Lozano JE. (2018). "Second release of the MEM Shiny Web Application R package.", from http://memapp.iecscyl.com:8080/memapp/.

Mangen MJ, Plass D, Havelaar AH, Gibbons CL, Cassini A, Muhlberger N, van Lier A, Haagsma JA, Brooke RJ, Lai T, de Waure C, Kramarz P, Kretzschmar ME and consortium BC (2013). "The pathogen- and incidence-based DALY approach: an appropriate [corrected] methodology for estimating the burden of infectious diseases." PLoS One **8**(11): e79740.

Marbus SD, van der Hoek W, van Dissel JT and van Gageldonk-Lafeber AB (2020). "Experience of establishing severe acute respiratory surveillance in the Netherlands: Evaluation and challenges." Public Health in Practice **1**: 100014.

McDonald SA, Presanis AM, De Angelis D, van der Hoek W, Hooiveld M, Donker G and Kretzschmar ME (2014). "An evidence synthesis approach to estimating the incidence of seasonal influenza in the Netherlands." Influenza Other Respir Viruses **8**(1): 33-41.

Meijer A, Overduin P, Hommel D, van Rijnsoever-Greven Y, Haenen A and Veldman-Ariesen MJ (2013). "Outbreak of respiratory syncytial virus infections in a nursing home and possible sources of introduction: the Netherlands, winter 2012/2013." J Am Geriatr Soc **61**(12): 2230-2231.

Murray CJL and Lopez AD (2013). "Measuring the Global Burden of Disease." New England Journal of Medicine **369**(5): 448-457.

Pel J (1965). "Proefonderzoek naar de frequentie en de aetiologie van griepachtige ziekten in de winter 1963-1964." Huisarts en Wetenschap **86**: 321.

Reukers DFM, Van Asten L, Brandsema P, Dijkstra F, Donker G, van Gageldonk AB, Hooiveld M, de Lange MMA, Marbus SD, Teirlinck AC, Meijer A and van der Hoek W. (2018). "Annual report Surveillance of influenza and other respiratory infections in the Netherlands: winter 2017/2018." RIVM Retrieved November 2020, from www.rivm.nl/bibliotheek/rapporten/2018-0049.pdf.

Reukers DFM, van Asten L, Brandsema PS, Dijkstra F, Donker GA, van Gageldonk-Lafeber AB, Hooiveld M, de Lange MMA, Marbus S, Teirlinck AC, Meijer A and van der Hoek W. (2019). "Annual report Surveillance of influenza and other respiratory infections in the Netherlands: winter 2018/2019." RIVM Retrieved November 2020, from www.rivm.nl/bibliotheek/rapporten/2019-0079.pdf.

Reusken CB, Buiting A, Bleeker-Rovers C, Diederen B, Hooiveld M, Friesema I, Koopmans M, Kortbeek T, Lutgens SP, Meijer A, Murk JL, Overdevest I, Trienekens T, Timen A, Van den Bijllaardt W, Van Dissel J, Van Gageldonk-Lafeber A, Van der Vegt D, Wever PC, Van der Hoek W and Kluytmans J (2020). "Rapid assessment of regional SARS-CoV-2 community transmission through a convenience sample of healthcare workers, the Netherlands, March 2020." Euro Surveill **25**(12).

Skowronski DM, Zou M, Sabaiduc S, Murti M, Olsha R, Dickinson JA, Gubbay JB, Croxen MA, Charest H, Jassem A, Krajden M, Bastien N, Li Y and De Serres G (2020). "Interim estimates of 2019/20 vaccine effectiveness during early-season co-circulation of influenza A and B viruses, Canada, February 2020." Euro Surveill **25**(7).

Slump E, van Beurden KM, Erkens CGM, Schimmel HJ, van Soolingen D and **de Vries G (2020).** "Tuberculose in Nederland 2019 Surveillancerapport inclusief rapportage monitoring van interventies." RIVM Retrieved December 2020, from https://www.rivm.nl/bibliotheek/rapporten/ 2020-0159.pdf.

Teirlinck AC, de Gier B, Meijer A, Donker G, de Lange M, Koppeschaar C, van der Hoek W, Kretzschmar ME and McDonald SA (2018). "The incidence of symptomatic infection with influenza virus in the Netherlands 2011/2012 through 2016/2017, estimated using Bayesian evidence synthesis." Epidemiol Infect: 1-6.

van Asten L, Harmsen C, Stoeldraijer L, Klinkenberg D, Teirlinck A, de Lange M, Meijer A, van de Kassteele J, van Gageldonk-Lafeber A, van den Hof S and van der Hoek W (2021). "Excess Deaths during Influenza and Coronavirus Disease and Infection-Fatality Rate for

Severe Acute Respiratory Syndrome Coronavirus 2, the Netherlands." Emerging Infectious Disease journal **27**(2).

van Gageldonk-Lafeber AB, Wever PC, van der Lubben IM, de Jager CP, Meijer A, de Vries MC, Elberse K, van der Sande MA and van der Hoek W (2013). "The aetiology of community-acquired pneumonia and implications for patient management." Neth J Med **71**(8): 418-425.

van Lier A, McDonald SA, Bouwknegt M, group EPI, Kretzschmar ME, Havelaar AH, Mangen MJ, Wallinga J and de Melker HE (2016). "Disease Burden of 32 Infectious Diseases in the Netherlands, 2007-2011." PLoS One **11**(4): e0153106.

Vega Alonso T, Lozano Alonso JE, Ortiz de Lejarazu R and Gutierrez Perez M (2004). "Modelling influenza epidemic—can we detect the beginning and predict the intensity and duration?" International Congress Series **1263**: 281– 283.

Vega T, Lozano JE, Meerhoff T, Snacken R, Mott J, Ortiz de Lejarazu R and Nunes B (2013). "Influenza surveillance in Europe: establishing epidemic thresholds by the moving epidemic method." Influenza Other Respir Viruses **7**(4): 546-558.

Verheij TJM, Hopstaken RM, Prins JM, Salomé PL, Bindels PJ, Ponsioen BP, Sachs APE, Thiadens HA and Verlee E (2011). "NHG-Standaard Acuut hoesten (Eerste herziening) " Huisarts Wet 2011:54(2):68-92.

Vlaanderen F, Cuperus T, Keur I, De Rosa M, Rozendaal H, Friesema I, van der Poel W, Franz E and Maassen K. (2020). "State of Zoonotic Diseases in the Netherlands, 2019." RIVM Retrieved November 2020, from https://www.rivm.nl/bibliotheek/rapporten/2020-0130.pdf.

Vos LM, Teirlinck AC, Lozano JE, Vega T, Donker GA, Hoepelman AI, Bont LJ, Oosterheert JJ and Meijer A (2019). "Use of the moving epidemic method (MEM) to assess national surveillance data for respiratory syncytial virus (RSV) in the Netherlands, 2005 to 2017." Euro Surveill **24**(20).

WHO (2013). WHO methods and data sources for global burden of disease estimates 2000-2011. Geneva, World Health Organisation.

WHO (2020). "Avian and other zoonotic influenza - Monthly Risk Assessment Summary." Retrieved November 2020, from https://www.who.int/influenza/human_animal_interface/HAI_Risk_Assessment/en/.

WHO (2020). "Recommended composition of influenza virus vaccines for use in the 2020-2021 northern hemisphere influenza season." Retrieved November 2020, from https://www.who.int/influenza/vaccines/virus/recommendations/202002_recommendation.pdf?ua=1.

Abbreviations

ARDS	Acute Respiratory Distress Syndrome
ARI	acute respiratory infection
BCoDE	burden of communicable diseases in Europe
BEL	*Legionella* Source Identification Unit (NL: Bronopsporingseenheid legionellapneumonie)
BWTP	biological wastewater treatment plant
CAP	community-acquired pneumonia
CBS	Statistics Netherlands (NL: Centraal Bureau voor de Statistiek)
CFR	case fatality rate
CIb	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 CIb (NL: Centrum Infectieziekteonderzoek, Diagnostiek en Screening)
CIb/LCI	National Coordination Centre for Communicable Disease Control of CIb (NL: Landelijke Coördinatie Infectieziektebestrijding)
COVID-19	coronavirus disease 2019
DALY	disability-adjusted life years
DBC/DOT	NL: Diagnose Behandel Combinatie Op weg naar Transparantie
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
EuroMOMO	European monitoring of excess mortality
GGD	Public Health Services (NL: Gemeentelijke Gezondheidsdienst)
GP	general practitioner
HIV	Human Immunodeficiency Virus
hMPV	human metapneumovirus
ICARES	Integrated Crisis Alert and Response System
ICU	intensive care unit
ILI	influenza-like illness
I-MOVE	influenza monitoring vaccine effectiveness
JBZ	Jeroen Bosch Hospital
LD	Legionnaires' Disease
LTBI	latent tuberculosis infection
LUMC	Leiden University Medical Centre
MDR-TB	Multi Drug Resistant tuberculosis
MERS-CoV	Middle East Respiratory Syndrome Coronavirus

NVWA	the Netherlands Food and Consumer Product Safety Authority (NL: Nederlandse Voedsel- en Waren Autoriteit)
NIC	National Influenza Centre
Nivel	Netherlands institute for health services research (NL: Nederlands instituut voor onderzoek van de gezondheidszorg)
NTR	Dutch Tuberculosis Registry (NL: Nederlands Tuberculose Register)
NVMM	Dutch Society for Medical Microbiology (NL: Nederlandse Vereniging voor Medische Microbiologie)
NZa	Dutch Healthcare Authority (NL: Nederlandse Zorgautoriteit)
PCR	Polymerase Chain Reaction
PIV	parainfluenza virus
POCT	point-of-care test
PTB	pulmonary tuberculosis
QIV	quadrivalent influenza vaccine
RIVM	National Institute for Public Health and the Environment
RSV	respiratory syncytial virus
SARI	severe acute respiratory infections
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SNIV	national sentinel surveillance network for infectious diseases in nursing homes
TALD	Travel Associated Legionnaires' disease
UMCU	University Medical Centre Utrecht
VE	vaccine effectiveness
WHO	World Health Organization
YLD	years lived with disability due to morbidity
YLL	years of life lost due to mortality

Journal publications by the department for respiratory infections in 2019

Adlhoch C, Gomes Dias J, Bonmarin I, Hubert B, Larrauri A, Oliva Domínguez JA, Delgado-Sanz C, Brytting M, Carnahan A, Popovici O, Lupulescu E, O'Donnell J, Domegan L, Van Gageldonk-Lafeber AB, Meijer A, Kynčl J, Slezák P, Guiomar R, Orta Gomes CM, Popow-Kraupp T, Mikas J, Staroňová E, Melillo JM, Melillo T, Ikonen N, Lyytikäinen O, Snacken R and Penttinen P (2019). "Determinants of Fatal Outcome in Patients Admitted to Intensive Care Units With Influenza, European Union 2009–2017." Open Forum Infectious Diseases **6**(11).

Backer JA, van Boven M, van der Hoek W and Wallinga J (2019). "Vaccinating children against influenza increases variability in epidemic size." Epidemics **26**: 95-103.

Backer JA, Wallinga J, Meijer A, Donker GA, van der Hoek W and van Boven M (2019). "The impact of influenza vaccination on infection, hospitalisation and mortality in the Netherlands between 2003 and 2015." Epidemics **26**: 77-85.

de Boer PT, de Lange MMA, Wielders CCH, Dijkstra F, van Roeden SE, Bleeker-Rovers CP, Oosterheert JJ, Schneeberger PM and van der Hoek W (2020). "Cost-effectiveness of Screening Program for Chronic Q Fever, the Netherlands." Emerg Infect Dis **26**(2): 238-246.

de Gier B, Vlaminckx BJM, Woudt SHS, van Sorge NM and van Asten L (2019). "Associations between common respiratory viruses and invasive group A streptococcal infection: A time-series analysis." Influenza Other Respir Viruses **13**(5): 453-458.

de Lange MMA, Gijsen LEV, Wielders CCH, van der Hoek W, Scheepmaker A and Schneeberger PM (2019). "Reply to Million and Raoult." Clin Infect Dis **68**(1): 170-171.

de Lange MMA, Scheepmaker A, van der Hoek W, Leclercq M and Schneeberger PM (2019). "Risk of chronic Q fever in patients with cardiac valvulopathy, seven years after a large epidemic in the Netherlands." PLoS One **14**(8): e0221247.

Duijster JW, Doreleijers SDA, Pilot E, van der Hoek W, Kommer GJ, van der Sande MAB, Krafft T and van Asten L (2020). "Utility of emergency call centre, dispatch and ambulance data for syndromic surveillance of infectious diseases: a scoping review." Eur J Public Health **30**(4): 639-647.

Fouchier R, Meijer A, Donker G, van der Hoek W, de Lange M and Koopmans M (2019). "Influenzaseizoen 2017/2018 in Nederland." Ned Tijdsch Med Microbiol **27**(nr1).

Hanssen DAT, Morroy G, de Lange MMA, Wielders CCH, van der Hoek W, Dijkstra F and Schneeberger PM (2019). "Notification data and criteria during a large Q-fever epidemic reassessed." Epidemiol Infect **147**: e191.

Jajou R, Kohl TA, Walker T, Norman A, Cirillo DM, Tagliani E, Niemann S, de Neeling A, Lillebaek T, Anthony RM and van Soolingen D (2019). "Towards standardisation: comparison of five whole genome sequencing (WGS) analysis pipelines for detection of epidemiologically linked tuberculosis cases." Euro Surveill **24**(50).

Jajou R, van der Laan T, de Zwaan R, Kamst M, Mulder A, de Neeling A, Anthony R and van Soolingen D (2019). "WGS more accurately predicts susceptibility of *Mycobacterium tuberculosis* to first-line drugs than phenotypic testing." J Antimicrob Chemother **74**(9): 2605-2616.

Kissling E, Pozo F, Buda S, Vilcu AM, Rizzo C, Gherasim A, Horváth JK, Brytting M, Domegan L, Meijer A, Paradowska-Stankiewicz I, Machado A, Vučina VV, Lazar M, Johansen K, Dürrwald R, van der Werf S, Bella A, Larrauri A, Ferenczi A, Zakikhany K, O'Donnell J, Dijkstra F, Bogusz J, Guiomar R, Filipović SK, Pitigoi D, Penttinen P and Valenciano M (2019). "Effectiveness of influenza vaccine against influenza A in Europe in seasons of different A(H1N1) pdm09 and the same A(H3N2) vaccine components (2016-17 and 2017-18)." Vaccine X **3**: 100042.

Kissling E, Rose A, Emborg HD, Gherasim A, Pebody R, Pozo F, Trebbien R, Mazagatos C, Whitaker H and Valenciano M (2019). "Interim 2018/19 influenza vaccine effectiveness: six European studies, October 2018 to January 2019." Euro Surveill **24**(8).

Lankelma JM, Hermans MHA, Hazenberg E, Macken T, Dautzenberg PLJ, Koeijvoets K, Jaspers JWH, van Gageldonk-Lafeber AB and Lutgens SPM (2019). "Implementation of point-of-care testing and a temporary influenza ward in a Dutch hospital." Neth J Med **77**(3): 109-115.

Lipworth S, Jajou R, de Neeling A, Bradley P, van der Hoek W, Maphalala G, Bonnet M, Sanchez-Padilla E, Diel R, Niemann S, Iqbal Z, Smith G, Peto T, Crook D, Walker T and van Soolingen D (2019). "SNP-IT Tool for Identifying Subspecies and Associated Lineages of *Mycobacterium tuberculosis* Complex." Emerg Infect Dis **25**(3): 482-488.

Machado A, Mazagatos C, Dijkstra F, Kislaya I, Gherasim A, McDonald SA, Kissling E, Valenciano M, Meijer A, Hooiveld M, Nunes B and Larrauri A (2019). "Impact of influenza vaccination programmes among the elderly population on primary care, Portugal, Spain and the Netherlands: 2015/16 to 2017/18 influenza seasons." Euro Surveill **24**(45).

Mackenzie GA, Vilane A, Salaudeen R, Hogerwerf L, van den Brink S, Wijsman LA, Overduin P, Janssens TKS, de Silva TI, van der Sande MAB, Kampmann B and Meijer A (2019). "Respiratory syncytial, parainfluenza and influenza virus infection in young children with acute lower respiratory infection in rural Gambia." Sci Rep **9**(1): 17965.

Mollers M, Barnadas C, Broberg EK, Penttinen P, Teirlinck AC and Fischer TK (2019). "Current practices for respiratory syncytial virus surveillance across the EU/EEA Member States, 2017." Euro Surveill **24**(40).

Monge S, Duijster J, Kommer GJ, van de Kassteele J, Donker GA, Krafft T, Engelen P, Valk JP, de Waard J, de Nooij J, van der Hoek W and van Asten L (2020). "Use of Ambulance Dispatch Calls for Surveillance of Severe Acute Respiratory Infections." Emerg Infect Dis **26**(1): 148-150.

Nielsen J, Vestergaard LS, Richter L, Schmid D, Bustos N, Asikainen T, Trebbien R, Denissov G, Innos K, Virtanen MJ, Fouillet A, Lytras T, Gkolfinopoulou K, Heiden MA, Grabenhenrich L, Uphoff H, Paldy A, Bobvos J, Domegan L, O'Donnell J, Scortichini M, de Martino A, Mossong J, England K, Melillo J, van Asten L, de Lange MM, Tønnessen R, White RA, da Silva SP, Rodrigues AP, Larrauri A, Mazagatos C, Farah A, Carnahan AD, Junker C, Sinnathamby M, Pebody RG, Andrews N, Reynolds A, McMenamin J, Brown CS, Adlhoch C, Penttinen P, Mølbak K and Krause TG (2019). "European all-cause excess and influenza-attributable mortality in the 2017/18 season: should the burden of influenza B be reconsidered?" Clin Microbiol Infect **25**(10): 1266-1276.

Othoniel B, Rugani B, Heijungs R, Beyer M, Machwitz M and Post P (2019). "An improved life cycle impact assessment principle for assessing the impact of land use on ecosystem services." Sci Total Environ **693**: 133374.

Post PM, Hogerwerf L, Huss A, Petie R, Boender GJ, Baliatsas C, Lebret E, Heederik D, Hagenaars TJ, CJ IJ and Smit LAM (2019). "Risk of pneumonia among residents living near goat and poultry farms during 2014-2016." PLoS One **14**(10): e0223601.

Reukers DFM, Marbus SD, Smit H, Schneeberger P, Donker G, van der Hoek W and van Gageldonk-Lafeber AB (2020). "Media Reports as a Source for Monitoring Impact of Influenza on Hospital Care: Qualitative Content Analysis." JMIR Public Health Surveill **6**(1): e14627.

Reukers DFM, van Jaarsveld CHM, Knoop H, Bleeker-Rovers CP, Akkermans R, de Grauw W, van der Velden K, van Loenhout JAF and Hautvast JLA (2019). "Explaining the long-term impact of chronic Q fever and Q fever fatigue syndrome on psychosocial functioning: A comparison with diabetes and the general population." J Psychosom Res **121**: 37-45.

van den Boogaard J, Slump E, Schimmel HJ, van der Hoek W, van den Hof S and de Vries G (2020). "High Incidence of Active Tuberculosis in Asylum Seekers from Eritrea and Somalia in the First 5 Years after Arrival in the Netherlands." Emerg Infect Dis **26**(4): 675-681.

van Roeden SE, Wever PC, Kampschreur LM, Gruteke P, van der Hoek W, Hoepelman AIM, Bleeker-Rovers CP and Oosterheert JJ (2019). "Chronic Q fever-related complications and mortality: data from a nationwide cohort." Clin Microbiol Infect **25**(11): 1390-1398.

Vos LM, Teirlinck AC, Lozano JE, Vega T, Donker GA, Hoepelman AI, Bont LJ, Oosterheert JJ and Meijer A (2019). "Use of the moving epidemic method (MEM) to assess national surveillance data for respiratory syncytial virus (RSV) in the Netherlands, 2005 to 2017." Euro Surveill **24**(20).

Zhang L, van der Hoek W, Krafft T, Pilot E, Asten LV, Lin G, Wu S, Duan W, Yang P and Wang Q (2020). "Influenza vaccine effectiveness estimates against influenza A(H3N2) and A(H1N1) pdm09 among children during school-based outbreaks in the 2016-2017 season in Beijing, China." Hum Vaccin Immunother **16**(4): 816-822.

D.F.M. Reukers[1], L. van Asten[1], P.S. Brandsema[1], F. Dijkstra[1], J.M.T. Hendriksen[2], W. van der Hoek[1], M. Hooiveld[1,2], M.M.A. de Lange[1], F.A. Niessen[1], A.C. Teirlinck[1], A. Meijer[3], A.B. van Gageldonk-Lafeber[1]

1 Infectious Diseases, Epidemiology and Surveillance, Centre for Infectious Disease Control, National Institute for Public Health and the Environment (RIVM), Bilthoven
2 Nivel (Netherlands institute for health services research), Utrecht
3 Infectious Disease Research, Diagnostics and Laboratory Surveillance, Centre for Infectious Disease Control, National Institute for Public Health and the Environment (RIVM), Bilthoven

RIVM report 2020-0177

Published by:

National Institute for Public Health and the Environment
PO Box 1 | 3720 BA Bilthoven
The Netherlands
www.rivm.nl/en

January 2021

Committed to *health and sustainability*

012488