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Annual report

Surveillance of acute respiratory infections in the Netherlands: winter 2022/2023

SARS-CoV-2, influenza virus, RSV and other respiratory viruses

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Colophon

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Synopsis

Surveillance of acute respiratory infections in the Netherlands: winter 2022/2023

Each year, RIVM presents an overview of how many persons in the Netherlands got the flu and other respiratory infections. Since 2020, this report has also included an overview of how many people contracted the coronavirus SARS-CoV-2. Many respiratory infections showed reduced circulation during the first COVID-19 epidemic years. However, during the 2022/2023 winter season, many pathogens showed pre-epidemic numbers of detections again or even exceeded the numbers in previous seasons.

Coronavirus
Between May 2022 and May 2023, there were 4 waves in the SARS-CoV-2 epidemic in the Netherlands, all caused by the Omicron variant. This variant caused less severe illness than previous variants, resulting in fewer hospital admissions. In this period, 28,633 persons with a positive SARS-CoV-2 test were admitted to the hospital of which 1,812 persons were admitted to intensive care. From May 2022 to May 2023, 5,349 persons died as a result of COVID-19.

Flu epidemic
The flu epidemic in the winter of 2022/2023 started in week 50 and lasted 14 weeks. About 169,000 people went to their GP with flu-like illness. This was higher than previous season, but still lower than the seasons before the COVID-19 epidemic. An estimated 837,000 persons have had the flu between October 2022 and May 2023. Most people became ill from the type A(H1N1)pdm09 and B (Victoria lineage) influenza virus, but influenza virus type A(H3N2) was also frequently detected. People who got the flu shot were 52 percent less likely to get the flu. That is comparable to the seasons before the COVID-19 epidemic.

RSV
At the end of the summer of 2022, the number of RSV detections started to decrease, after more than a year of increased circulation in the Netherlands. The number of detections and the number of hospital admissions of children below 2 years of age started to increase again in the autumn and reached a peak in the last weeks of 2022. The total number of RSV detections in the winter of 2022/2023 was much higher than previous seasons. It is not clear whether there were actually more patients or whether infections were reported more often. Hospitals often combine the test for SARS-CoV-2 with RSV, so RSV infections could also be observed more often.

Keywords: respiratory infections, flu, influenza, RS virus, pneumonia, SARS-CoV-2, COVID-19, coronavirus

Publiekssamenvatting

Surveillance van acute luchtweginfecties in Nederland: winter 2022/2023

Het RIVM brengt elk jaar in kaart hoeveel mensen in Nederland de griep en andere luchtweginfecties hebben gehad. Sinds 2020 gebeurt dat ook voor het aantal mensen met het coronavirus SARS-CoV-2. In de eerste jaren van de corona-epidemie zijn veel andere acute luchtweginfecties minder vaak gemeld. In het winterseizoen van 2022/2023 was het aantal gemelde infecties weer ongeveer hetzelfde of soms zelfs hoger dan voor de corona-epidemie.

Coronavirus
Tussen mei 2022 en mei 2023 waren er vier golven in de corona-epidemie in Nederland, allemaal veroorzaakt door de Omikron-variant. Van deze variant werden mensen minder ernstig ziek dan van de vorige, waardoor er minder ziekenhuisopnames waren. In deze periode zijn 28.633 mensen met een positieve corona testuitslag opgenomen in het ziekenhuis, waarvan 1.812 op de intensive care. Van mei 2022 tot en met mei 2023 is van 5.349 mensen bekend dat ze zijn overleden aan corona.

Griepepidemie
De griepepidemie in de winter van 2022/2023 begon in week 50 en duurde 14 weken. Ongeveer 169.000 mensen gingen naar de huisarts met griepachtige klachten. Dit waren er meer dan in het winterseizoen ervoor, maar nog steeds minder dan voor de corona-epidemie. Naar schatting hebben tussen oktober 2022 en mei 2023 ongeveer 873.000 mensen de griep gehad. Mensen zijn vooral ziek geworden van het type A(H1N1)pdm09 en B (Victoria-lijn). Ook is het type A(H3N2) griepvirus vaak gevonden. Mensen die de griepprik hebben gehaald, hadden 52 procent minder kans om griep te krijgen. Dat is ongeveer hetzelfde als voor de corona-epidemie.

RS-virus
Aan het eind van de zomer in 2022 begon het aantal RS-virus infecties te dalen, nadat deze infecties ruim een jaar lang veel vaker waren gemeld. In het najaar steeg het aantal infecties en het aantal ziekenhuisopnames van kinderen onder de 2 jaar weer, met een piek in de laatste weken van 2022. Ook in de winter van 2022/2023 was het aantal gemelde infecties veel hoger dan in eerdere winters. Het is niet duidelijk of er echt meer infecties waren of dat ze vaker zijn gemeld. Ziekenhuizen combineren de test op SARS-CoV-2 vaak met de test op RSV, waardoor RSV infecties mogelijk vaker worden opgemerkt.

Kernwoorden: luchtweginfecties, griep, influenza, RS-virus, longontsteking, pneumonie, SARS-CoV-2, COVID-19, coronavirus

Contents

Introduction

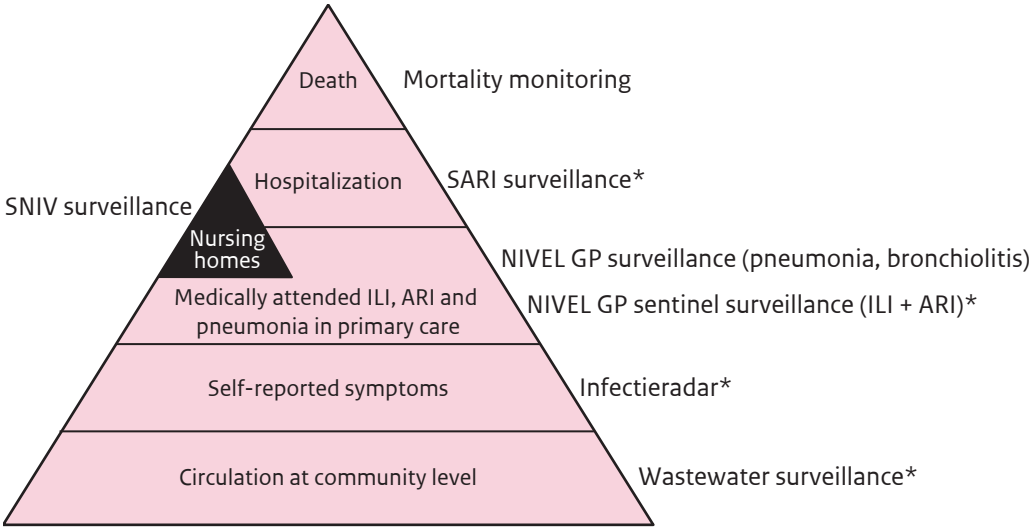
Aim and focus of this report

This report describes the trends and epidemiology of acute respiratory infections, including COVID-19, influenza, Respiratory Syncytial Virus (RSV) and other infections, in the winter of 2022/2023 in the Netherlands. This annual report is meant for policymakers, 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 partners within and outside the RIVM.

This report starts with an overview and interpretation of the 2022/2023 respiratory season. The different components of surveillance of respiratory infections can be visualised as a pyramid, based on the severity of symptoms, as displayed in Figure 1. Several surveillance systems are in place that provide data on different layers of the respiratory surveillance pyramid. Chapter 1 describes the syndromic surveillance from the second and third layer of the surveillance pyramid in the Netherlands (participatory surveillance (Infectieradar), general practice (GP) sentinel surveillance (Nivel) and nursing home surveillance (SNIV)). Chapter 1 presents the data from these systems for different syndromes: acute respiratory infections (ARI), influenza-like illness (ILI), COVID-like illness, bronchiolitis and community-acquired pneumonia (CAP). Chapters 2-4 focus on the epidemiology of COVID-19, influenza and RSV, respectively, and presents the virological surveillance of all systems in which virological data or pathogen specific data is collected (Figure 1). Wastewater surveillance provides information on the bottom of the surveillance pyramid (circulation at community level). Currently only SARS-CoV-2 is monitored in wastewater, this is therefore included in Chapter 2. In Chapter 5, the data for several respiratory pathogens from the weekly virological laboratory surveillance is presented of which the majority of samples originate from hospitalised patients.
Lastly, Chapter 6 shows the mortality and burden associated with influenza epidemics and COVID-19 waves.

More information on the background of the syndromes and pathogens, and the methods used in the surveillance systems, is given in Chapter 8. The notifiable respiratory diseases legionellosis, Q-fever, psittacosis and tuberculosis are not included in this report. The last three will be reported in the Staat van Zoönosen and the TiN rapport, respectively. The trends of legionellosis will be reported in a separate report. All three reports are scheduled for publication at the end of 2023 or beginning of 2024.

Figure 1 The respiratory infections surveillance pyramid in the Netherlands



Footnote: *Systems with * (also) include virological surveillance. Wastewater surveillance currently only detects SARS-CoV-2.*

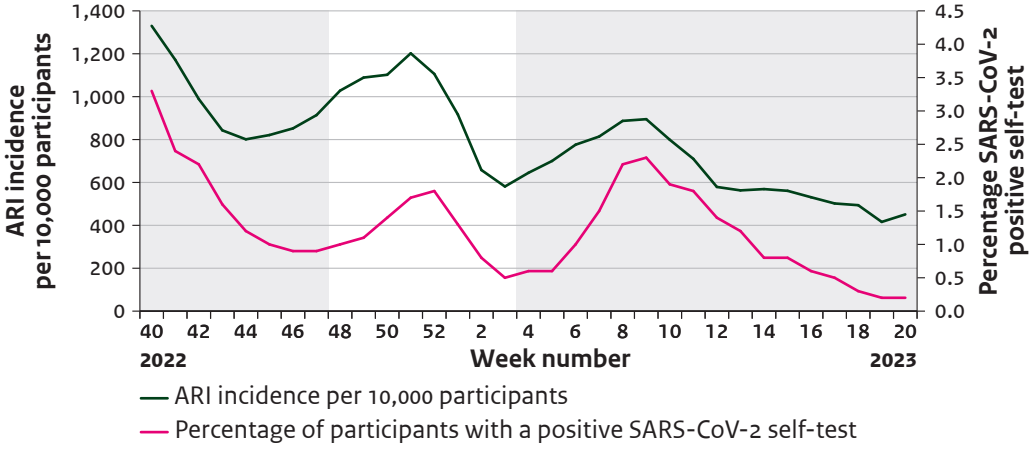
Collaborations: national and international

For the surveillance of respiratory infectious diseases, the CIb collaborates with many partners: Netherlands institute for health services research (Nivel), including the network of sentinel general practices; the surveillance network in nursing homes (SNIV); the National Influenza Centre (NIC), location Erasmus MC and Statistics Netherlands (CBS). The National Intensive Care Evaluation (in Dutch: stichting NICE) provides data on COVID-19 hospital and intensive care admissions. 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).
A part of the data in this report is also reported internationally. COVID-19 is reported weekly to the European Centre for Disease Prevention and Control (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/World Health Organisation (WHO) regional office for Europe FluNews Europe Bulletin, and in FluNet and FluID of the WHO 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 influenza vaccine effectiveness at a European level, RIVM and Nivel participate in the European Vaccine Effectiveness, Burden and Impact Studies (VEBIS) network. For enhancing RSV surveillance on a European level, RIVM is partner in the PROMISE consortium, that is funded by the Innovative Medicines Initiative (IMI). Within this context, RIVM is also establishing a Network of RSV Laboratories in Europe (RSVLabNet).

Summary and interpretation of the 2022/2023 respiratory season

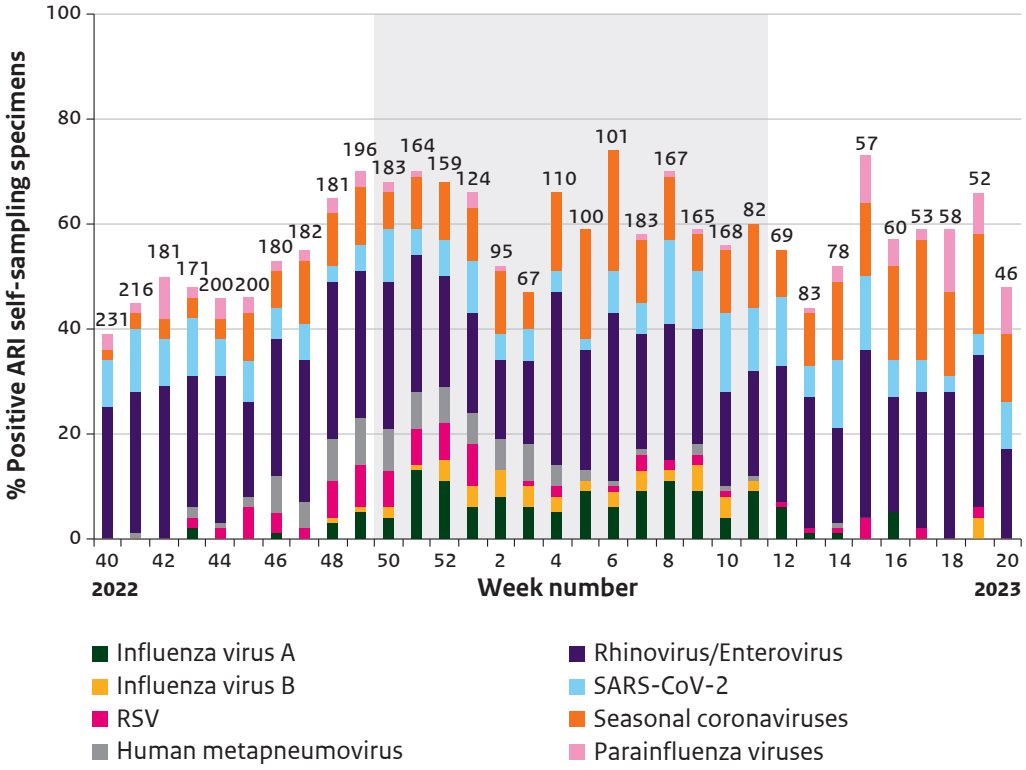
The acute respiratory infection (ARI) (including influenza-like-illness (ILI)) incidence as reported in the Infectieradar study and the weekly number of ARI consultations and the ILI incidence reported by general practitioners (GPs) and among nursing home residents all peaked at the end of 2022. This peak coincided with peaks in SARS-CoV-2, influenza virus and RSV circulation (see Chapter 2, 3 and 4). The ARI (including ILI) incidence as reported in the Infectieradar study also showed two other peaks in the 2022/2023 winter season (week 41 2022 and week 9 2023). These peaks coincided with peaks in the percentage of participants with a positive SARS-CoV-2 self-test (Figure 2). In the participants with a negative SARS-CoV-2 self-test who sent in a self-sampling specimen to the RIVM, rhinovirus was most often detected during the winter season (Figure 3). In the weeks before the second peak in the ARI incidence as reported in the Infectieradar study (week 52 2022), the percentage of self-sampling specimens positive for influenza virus and RSV did increase, but rhinovirus was still detected more often (Figure 3).

Figure 2 Weekly self-reported ARI (including ILI) incidence per 10,000 participants and the weekly percentage of participants reporting a SARS-CoV-2 positive (self)test in the general population as reported in the Infectieradar study during the respiratory season (week 40 through week 20) of 2022/2023 (Source: Infectieradar, RIVM).



Footnote: *The grey shading marks the COVID-19 periods during the 2022/2023 respiratory season; 6d, 6e and 6f until week 20 2023 (see Chapter 2). ARI = acute respiratory infections; ILI = influenza-like illness; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.*

Figure 3 Percentage of self-sampling specimens from participants in the Infectieradar study with ARI (including ILI) and a negative SARS-CoV-2 self-test result positive for influenza virus type A and B, RSV, hMPV, rhinovirus/enterovirus, SARS-CoV-2, human seasonal coronaviruses or parainfluenza viruses during the 2022/2023 respiratory season (week 40 of 2022 through week 20 of 2023) (Source: RIVM).

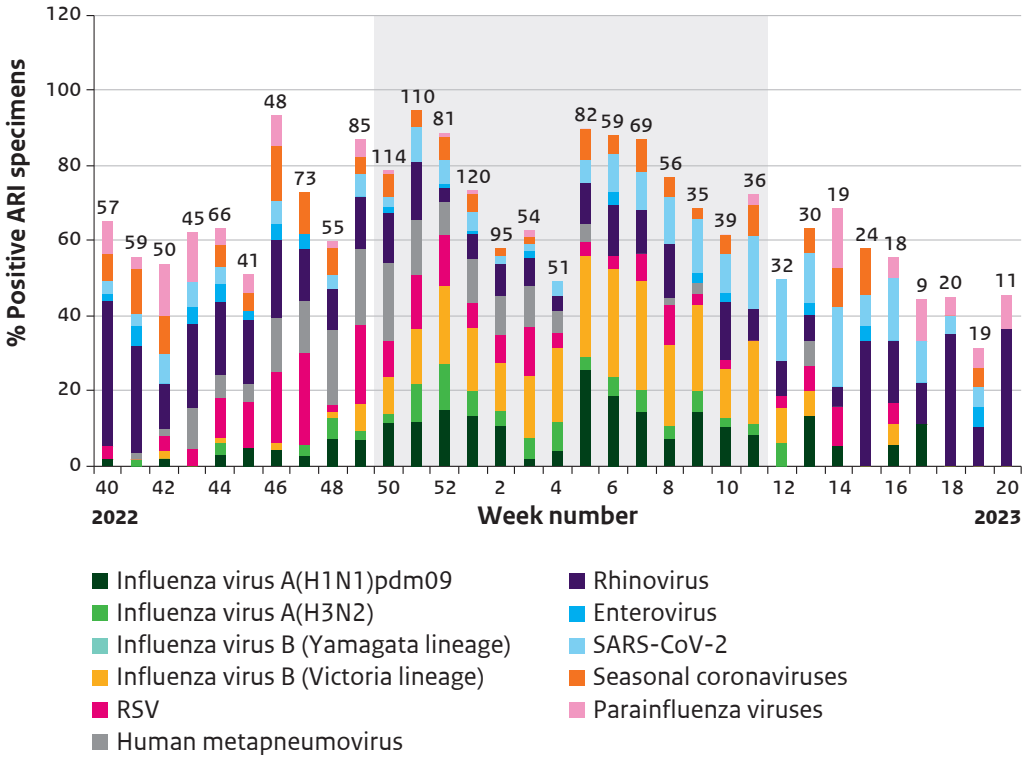


Footnote: *The numbers above the bars are the total number of tested specimens.*
The grey shading marks the influenza epidemic weeks, from week 50 2022 through week 11 2023 (see Chapter 3).
ARI = acute respiratory infections; ILI = influenza-like illness; RSV = respiratory syncytial virus; hMPV = human metapneumovirus; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

The number of GP consultations because of ILI and other ARI in 2022/2023 was relatively low compared to the pre-COVID-19 seasons. Several factors related to the COVID-19 pandemic might have influenced this rate, such as possible changes in healthcare-seeking behaviour and the availability of SARS-CoV-2 self-tests, therefore the comparison of the GP consultation rate with previous seasons should be interpreted with caution. Furthermore, the consultation rate could be underestimated, as COVID-19 related consultations are excluded from the ARI numbers. On the contrary, the seasonal number of patients with ILI in nursing homes was higher than the four previous seasons including the two seasons before the COVID-19 pandemic. In the specimens taken from patients with ARI in the GP sentinel surveillance, influenza virus A(H1N1)pdm09, influenza virus B (Victoria lineage), RSV and rhinovirus were the most detected pathogens. The percentage of specimens positive for RSV started to increase from week 44 2022 and for influenza virus started to increase in week 48 2022 (Figure 4). Influenza virus and RSV are more frequently detected in the GP specimens compared to the self-sampling specimens from the Infectieradar study (Figure 3), but the trends in occurence of these pathogens do coincide. Furthermore, these trends also coincide with the trends in the number of positive tests for these pathogens in the virological laboratory surveillance (Figure 5). However, the number of samples positive for influenza virus and RSV compared to other respiratory pathogens is even higher than in the sentinel GP specimens, likely because the majority of samples in the virological laboratory surveillance originate from hospitalised patients. The specimens from the sentinel GPs are from medically attended ARI patients and in the Infectieradar study ARI is defined based on self-reported symptoms (not necessarily medically attended). The proportion of the detected respiratory pathogens seems to differ between these three systems, likely caused by a difference in severity of symptoms. It should be noted that the virological laboratory surveillance is based on positive test results without information on the total number of tests performed. Not all clinical samples are necessarily tested on all viruses displayed in Figure 5. Besides, SARS-CoV-2 is not (yet) included in this surveillance system.

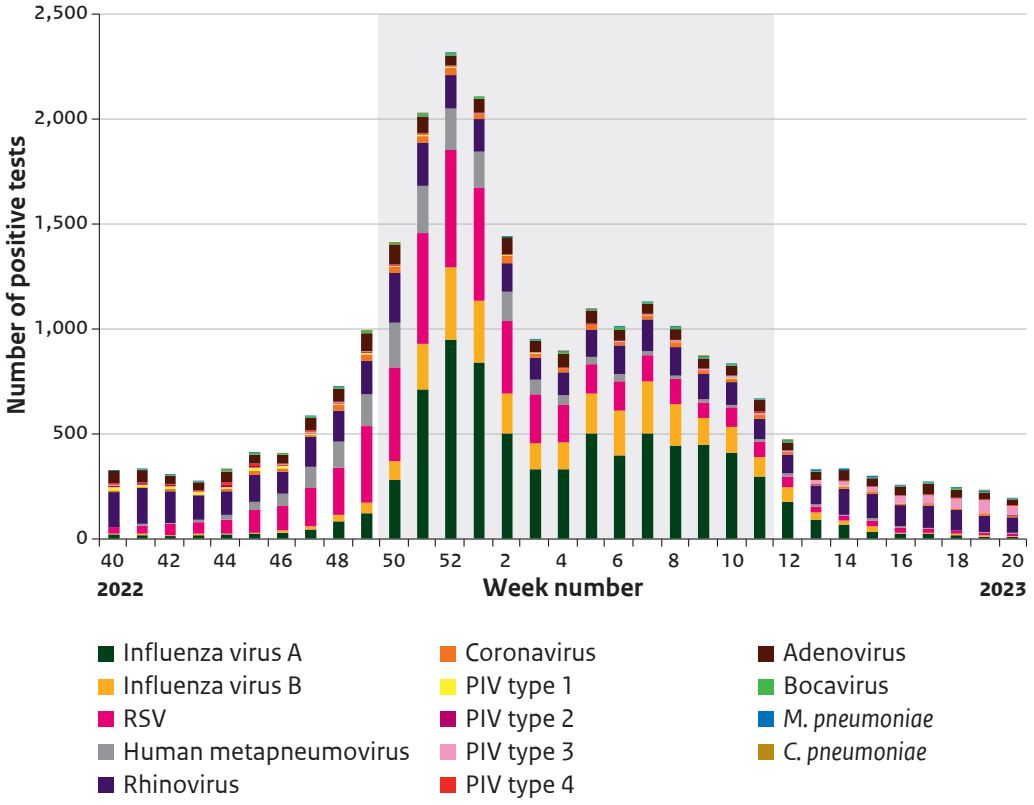
The weekly number of bronchitis/bronchiolitis GP-consultations in children below the age of 5 years followed the same trend as the RSV virological laboratory detections and RSV-bronchiolitis admissions in children below the age of 2 years, with a peak at the end of 2022. The peak in GP consultations was higher than during the COVID-19-pandemic winter seasons, similar to the 2021 summer-peak and lower than in the two pre-pandemic seasons of 2018/2019 and 2019/2020. The number of GP consultations and nursing home patients for pneumonia increased steadily throughout the beginning of the 2022/2023 winter season, and reached a peak in week 1 of 2023, also closely coinciding with the aforementioned peaks in SARS-CoV-2, influenza virus and RSV circulation.

Figure 4 Percentage of specimens from patients with ARI (including ILI) taken by sentinel GPs and positive for influenza viruses type A and B, RSV, hMPV, rhinovirus, enterovirus, SARS-CoV-2, human seasonal coronaviruses or parainfluenza viruses during the 2022/2023 respiratory season (week 40 of 2022 through week 20 of 2023) (Source: RIVM; Nivel Primary Care Database).



Footnote: *The numbers above the bars are the total number of tested specimens.*
The grey shading marks the influenza epidemic weeks, from week 50 2022 through week 11 2023 (see Chapter 3).
ARI = acute respiratory infections; ILI = influenza-like illness; GP = general practitioner; RSV = respiratory syncytial virus; hMPV = human metapneumovirus; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Figure 5 Number of reported positive tests in the virological laboratory surveillance for influenza virus type A and B, RSV, hMPV, rhinovirus, human seasonal coronaviruses (excluding SARS-CoV-2), parainfluenza virus types 1-4, adenovirus, bocavirus, *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* for the 2022/2023 respiratory season (week 40 of 2022 through week 20 of 2023) (Source: Virological laboratory surveillance, NWKV).



Footnote: *The detections in the virological laboratory surveillance are test results of clinical samples that were not necessarily tested on all viruses displayed in this figure. Number of performed tests are unknown.*
The grey shading marks the influenza epidemic weeks, from week 50 2022 through week 11 2023 (see Chapter 3).
RSV= Respiratory Syncytial Virus; hMPV= human metapneumovirus; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; PIV= parainfluenza virus; M. pneumoniae = Mycoplasma pneumoniae; C. pneumoniae = Chlamydia pneumoniae; NWKV = Dutch Working Group for Clinical Virology of the Dutch Society for Medical Microbiology (NVMM).

COVID-19

Since the beginning of the COVID-19 pandemic up to week 20 of 2023, there have been six different periods and several subperiods (in period 2 and 6) of the COVID-19 epidemic in the Netherlands. These periods are based on different indicators showing increased virus circulation. Vaccination against COVID-19 was first rolled out in January 2021. In September 2022 (week 38) a new COVID-19 vaccination round started. The results from the Pienter corona serosurveillance study show that in summer 2022, more than 95% of the population had antibodies against SARS-CoV-2 and around 75% had evidence of a previous infection in their blood. In the 2022/2023 winter season, no COVID-19 measures were in place, only the advice to use a self-test in case of symptoms and self-isolate after a positive test result. At the end of February 2023, the Outbreak Management Team (OMT) concluded the Netherlands had reached an endemic phase for the Omicron variant (OMT advice 146). Since March 10th 2023, only general recommendations to prevent the spread of respiratory viruses remained, such as stay home if you are ill, cough and sneeze into the elbow and ensure good ventilation. As of March 17th 2023, the national testing facilities of the Public Health Service (PHS) were closed. On May 5th 2023, the WHO declared COVID-19 officially not a Public Health Emergency of International Concern (PHEIC) anymore.

This report describes the period from week 21 of 2022 to week 20 of 2023, and focuses on the last four waves; subperiod 6c (week 23–34 2022), 6d (week 35–47 2022), 6e (week 48 2022 – week 3 2023) and 6f (week 4–20 2023). During these subperiods, the Variant of Concern (VOC) Omicron had different subtypes of which BA.5 (period 6c and 6d), BQ.1 (period 6e) and XBB.1.5 (period 6f) were the dominant variants. Peaks in the number of SARS-CoV-2 virus particles in wastewater, self-reported positive tests by Infectieradar participants, COVID-19 hospital admissions and mortality were seen in June/July 2022 (week 25-29), October 2022 (week 40-42), December 2022 (week 51-52), and February/March 2023 (week 9-10). Since the start of period 6 in 2022, when the Omicron variant became dominant, there was more virus circulation compared to previous periods (1-5) with different, more pathogenic dominant variants such as Alpha and Delta, but also more measures in certain periods. In period 6, the peaks in average number of SARS-CoV-2 virus particles in wastewater ranged between 1,700 and 2,400 (times 100 billion per 100,000 inhabitants), compared to 500-1,100 (times 100 billion per 100,000 inhabitants) during peaks in periods 1-5. The percentage of Infectieradar participants reporting a positive test ranged between 1.8% and 4.2% in the last four waves, and shows a declining trend since the highest percentage of 6.0% reporting a positive test at the peak of the second Omicron wave (period 6b). Even though there was more virus circulation, the peaks in hospital and ICU-admissions due to SARS-CoV-2 infections, and in COVID-19 mortality became less high over time. In the last four waves the peaks in hospital admissions per week varied from 5-6 per 100,000, which was lower compared to the peaks of 11-12 per 100,000 in periods 2,3 and 5, and much lower than the peak of 19 per 100,000 in March 2020. The highest weekly COVID-19 mortality in the last four waves was 1.3 per 100,000, while this was 6.2 per 100,000 at the peak of period 5. A trend is observed that COVID-19 became less severe over time, due to Omicron variants and immunity in the population as a result of vaccination and/or previous infection.

Influenza

Based on expert opinion, taking into consideration all available influenza surveillance systems, such as ILI GP consultations and virological results of the Nivel/RIVM sentinel practice, it was established that the influenza epidemic started from week 50 of 2022 and lasted until week 11 of 2023. Influenza virus type A and B were detected in equal proportions during the season in the sentinel GP-surveillance. In the other surveillance systems (virological laboratory surveillance, NIC surveillance and Infectieradar), the majority of the influenza viruses were type A.

Among the subtyped A viruses, subtype A(H1N1)pdm09 was detected in higher proportions, compared to the A(H3N2) subtype. These (sub)types were detected in all age groups. The characterised B viruses were all from the Victoria lineage. This type was most frequently detected in age groups under 50 years. Like previous season, no B/Yamagata lineage was detected this season (Paget, Caini et al. 2022). The percentage of specimens positive for influenza virus was much higher among patients visiting a sentinel GP (24% of all sampled ARI-patients in the 2022/2023 season), than in persons from the general population who participated in the Infectieradar self-sampling study (6% of all sampled patients in the 2022/2023 season).

The vast majority of the A(H1N1)pdm09 viruses with sequence data belong to clade 6B.1A.5a.2, except for some viruses which belong to clade 6B.1A.5a.1. The A(H1N1)pdm09 strain included in the 2022/2023 influenza vaccine belonged to clade 6B.1A.5a.2. All sequenced A(H3N2) viruses belong to clade 3C.2a1b.2a, which has also recently been further subdivided into several subclades, namely 2a.1, 2a.1b, 2a.3a, 2a.3a.1, 2a.3b and 2b. Antigenic differences were small between selected viruses from each subclade. The A(H3N2) strain included in the 2022/2023 influenza vaccine belonged to clade 3C.2a1b.2a.2a. The influenza B viruses with sequence data all belong to clade V1A.3a.2 of the Victoria lineage, as does the vaccine strain. For the 2023/2024 vaccine, an update of the A(H3N2) component was not considered necessary as most viruses reacted well with human antisera raised against the current vaccine strain. For the same reason, an update of the B/Victoria vaccine component was also not considered necessary. On the other hand, the A(H1N1)pdm09 vaccine component, is changed because human antisera against the current vaccine did not optimally recognize the viruses belonging to the new 5a.2a.1 clade.

Results from the VEBIS European pooled analysis, using data from week 40 2022 through week 20 2023, showed that the influenza vaccine effectiveness against any influenza virus infection was 52% (95% CI: 46%-57%), 37% (95% CI: 26-46%) against influenza type A(H3N2) infection, 45% (95% CI: 33%-55%) against influenza virus type A(H1N1)pdm09, and 74% (95% CI: 67%-80%) against influenza B/Victoria lineage infection for all ages.

The influenza vaccination programme of 2022/2023 is estimated to have averted 1,799 (95%CI: -94 – 4,198) GP ILI consultations caused by an influenza virus in the age group 65 years and older. During the 2022/2023 season, an estimated 470 (95% uncertainty interval (UI): 405 – 550) persons per 10,000 inhabitants had ILI symptoms caused by an influenza virus infection. This estimated incidence corresponded to an estimated 837,000 symptomatic persons in the Netherlands. The estimated symptomatic influenza incidence was highest in children in the age group younger than 5 years.

RSV

At the end of the summer of 2022, the number of RSV detections started to decrease, after more than a year of increased circulation in the Netherlands. Detections started to increase again in autumn (since week 39 2022) and reached a peak in week 52 2022. After a sharp drop in detections from week 2 to 5 of 2023 (from 344 to 137 detections), the number of detections gradually decreased further and have been on low levels since April 2023 until the end of the reporting period (May 21st, 2023). While the absolute number of RSV detections was much higher than in previous seasons (5017 in season 2022/2023 and on average 1631 in seasons 2013/2014 through 2021/2022), the timing of the peak (week 52 of 2022) was within the range of the timing in pre-pandemic seasons. Since testing practices have probably changed since the COVID-19 pandemic, the number of RSV positive tests and subsequent outcomes on onset and duration of the RSV season (based on absolute numbers, calculated with the MEM epidemic and intensity thresholds, see table 4.1) should be interpreted with caution.
The number of children below 2 years of age that were hospitalized in the winter season of 2022/2023 with RSV-bronchiolitis followed a similar trend in time as the virological detections. The peak number of hospitalizations (n=100, week 51 2022) in the 33 hospitals participating in the SPREAD-study was however lower than in the summer peak of 2021 (n=163).
The percentage of samples collected by sentinel GPs from patients with ARI that were positive for RSV peaked in week 46 of 2022 (18/73 = 25% of samples positive) and gradually declined until no RSV was detected anymore from week 17 of 2023 until the end of the reporting period. The percentage positive was highest in children aged 0-1 years, where 32% of these sampled children was positive for RSV, followed by age group 2-4 years (13%) and 65 years and older (11%). The percentage was lowest in the age groups 5-64 years (range 4 – 8%). RSV-B was dominant over the entire season of 2022/2023, in all age groups.

Other respiratory infections reported in the weekly virological surveillance

Several respiratory viruses showed a different pattern in the timing and extent of circulation during the first two respiratory seasons of the COVID-19 pandemic compared to previous seasons. However, most respiratory viruses showed a regular pattern again in season 2022/2023 corresponding to what was observed before the COVID-19 pandemic.
During the spring of 2022, from week 21 of 2022, rhinovirus and parainfluenza virus type 3 were most often detected. During the spring, there was a slight increase in the number of rhinovirus and parainfluenza virus type 3 detections, but the numbers decreased during the summer. At the start of the respiratory season, week 40 of 2022, rhinovirus was again most often detected. At the end of the year, rhinovirus (n=239, week 50) and hMPV (n=223, week 51) reached a peak in the number of detections, coinciding with the start of the influenza epidemic (Chapter 3). At the end of the respiratory season, in week 20 2023, rhinovirus and parainfluenza virus type 3 were most often detected, but overall detections were low.
Some viruses showed higher total numbers of detections and higher peaks during the 2022/2023 season (from week 21 2022 to week 20 2023) compared to previous seasons, such as rhinovirus (n=5,924), hMPV (n=1,900), parainfluenza virus type 3 (n=932) and adenovirus (n=2,560). The total number of parainfluenza virus type 1 detections (n=254) was much

higher than the seasons 2018/2019, 2020/2021 and 2021/2022 (average of 28 detections), but lower than season 2019/2020 (n=343). The peak in detections of hMPV and the first peak in detections of parainfluenza virus type 1 were earlier and the peaks were considerably higher than previous seasons (with the exception of season 2019/2020 for parainfluenza virus type 1). However, increases in numbers 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. For example, by an increased application of multiplex respiratory panels in PCR diagnostics. In these panels, molecular detection of the most common viruses is performed with one kit including several multiplex tests. However, which viruses are included in the respiratory panels and the extent to which the panels are used, differs between kits used by laboratories and between years.

Mortality and burden

The 2022/2023 season was characterised by excess mortality during COVID-19 periods 6c-6f, including the influenza epidemic which occurred within COVID-19 periods 6e and 6f in the Netherlands. The burden for COVID-19 was an estimated 93,800 DALY (91,600-96,100) and was higher than influenza with an estimated 9,400 DALY (8,600-10,200). The burden of COVID-19 is for 95% due to premature mortality. The presented burden estimate of COVID-19 represents an underestimation of the actual burden since long-term consequences of the disease are not taken into account. Furthermore, there is insufficient data about the epidemiology and long-term impact of COVID-19 at this time to properly estimate the DALY/100 cases disease burden measure.

Integrating and enhancing the surveillance of respiratory viruses in the Netherlands

In February 2023, the SARS-CoV-2 Omicron variants reached an endemic phase in the Netherlands (OMT letter 146). However, effective surveillance remains important to maintain early detection of resurgences, new variants and changes in protection against severe illness due to SARS-CoV-2 infection. Monitoring of these developments around SARS-CoV-2 will shift from a pathogen specific system to a larger integrated surveillance system for acute respiratory infections, including viruses such as influenza and RSV. Several new RSV immunisation strategies are currently entering or are planned to enter the market, therefore surveillance of RSV becomes more eminent. It will be important to monitor the seasonality, burden, potential virological changes and impact of these immunization strategies. Traditionally, the GP sentinel surveillance system in the Netherlands primarily focuses on the influenza-like illness (ILI) case definition, but in the near future more focus will be given to the broader acute respiratory infection (ARI) case definition, which is less specific for influenza but more sensitive for other respiratory viruses (Geismar, Nguyen et al. 2023). A broader case definition will allow a comprehensive monitoring of circulation of influenza, RSV, SARS-CoV-2 and other respiratory pathogens. Before the COVID-19 pandemic, the influenza epidemic was based on the GP sentinel data, both ILI incidence and presence of influenza in samples of ILI-patients. The last

two winter seasons, the start of an influenza epidemic was based on expert opinion taking into consideration all available respiratory surveillance systems, as the ILI incidence could not be directly compared to the pre-COVID-19 pandemic seasons.
The COVID-19 pandemic showed the importance of strong, reliable and sustainable surveillance systems to monitor the spread of respiratory infections. Many existing surveillance systems were enhanced during the pandemic, while some new systems were set up. An example of such a system is the community based surveillance system Infectieradar, which has proven to be of great value in the early detection of a resurgence of the SARS-CoV-2 virus based on the occurrence of COVID-19 related symptoms. Infectieradar has been operational since November 2020 and provides information on the second layer of the surveillance pyramid: the self-reported respiratory symptoms in the general population (Figure 1). In September 2022, Infectieradar was expanded with self-tests and self-swabs (in participants with a positive self-test, and in a sample of participants with a negative self-test) followed by laboratory testing (PCR and sequencing). This virological surveillance enables the monitoring of infections and virus variants of SARS-CoV-2, influenza virus and other respiratory viruses in the general population. A weekly overview of the results of Infectieradar are published on the website. Furthermore, monitoring the wastewater surveillance is an important system to determine circulation of SARS-CoV-2 at community level. It is currently only limited to the detection of SARS-CoV-2, but might be expanded to include other pathogens, such as influenza, in the future. Lastly, the COVID-19 pandemic has underscored the need for a comprehensive and sustainable Severe Acute Respiratory Infections (SARI) surveillance system. Hospital data is a crucial source of information for monitoring respiratory viruses with pandemic potential, and viruses that can cause outbreaks and have an impact on public health. A COVID-19 hospital patient register was set up early in the pandemic, but this manual system is not sustainable and should be replaced by an automated SARI surveillance system. A SARI surveillance system using the Dutch financial 'DBC' codes to monitor SARI hospital admissions and SARI aetiology, combined with laboratory test results, has recently started in a small number of hospitals and aims to expand to a larger number of hospitals. Furthermore, a SARI ICU surveillance is in development, specifically monitoring real-time ICU admissions for SARI.

An overall objective of RIVM is to make surveillance information accessible to the public. The RIVM website therefore provides weekly updated information on respiratory infections, including COVID-19, influenza and RSV trends, as well as respiratory infections in SNIV nursing homes and trends in all-cause mortality.

Chapter 1
Syndromic surveillance

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

Authors: Marit de Lange, Adam Meijer, Mariëtte Hooiveld
Contributors: Daphne Reukers, Anne Teirlinck, Liz Jenniskens, Mirthe Biesheuvel, Albert Jan van Hoek

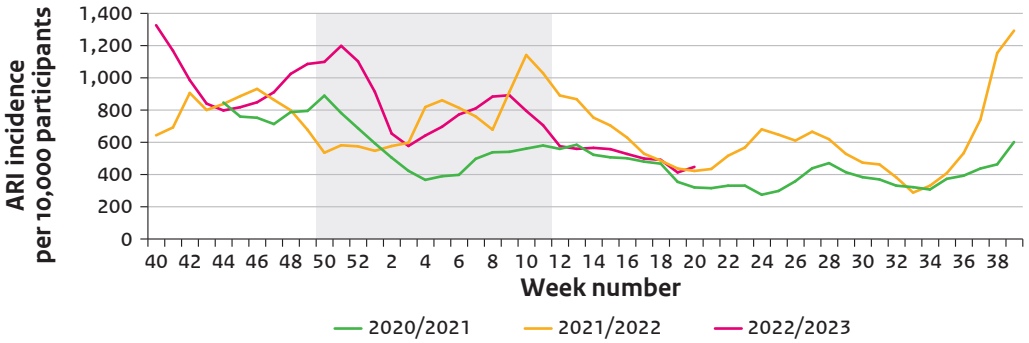
1.1.1 Key points

- The self-reported ARI (including ILI) incidence among the general population as reported in the Infectieradar study showed three peaks in the 2022/2023 winter season (week 40 2022, 51 2022, and 9 2023). The increase in incidence of the first peak, started in the previous season.
- The weekly number of ARI consultations and the ILI incidence reported by GPs and among nursing home residents peaked all at the end of 2022, coinciding with the second peak in the Infectieradar study.
- The seasonal number of consultations because of ILI and ARI in primary care in 2022/2023 was relatively low compared to the pre-COVID-19 seasons, but higher than the two previous seasons.
- The seasonal number of patients with ILI in nursing homes was higher than the four previous seasons.
- The weekly number of ARI consultations and the ILI incidence reported by GPs were highest in young children (0-4 years), which is in line with four previous seasons. The peak in weekly number of ARI consultations in 0-4 years old preceded the peak in the older age groups.

1.1.2 Figures

ARI (including ILI) incidence: self-reported in general population

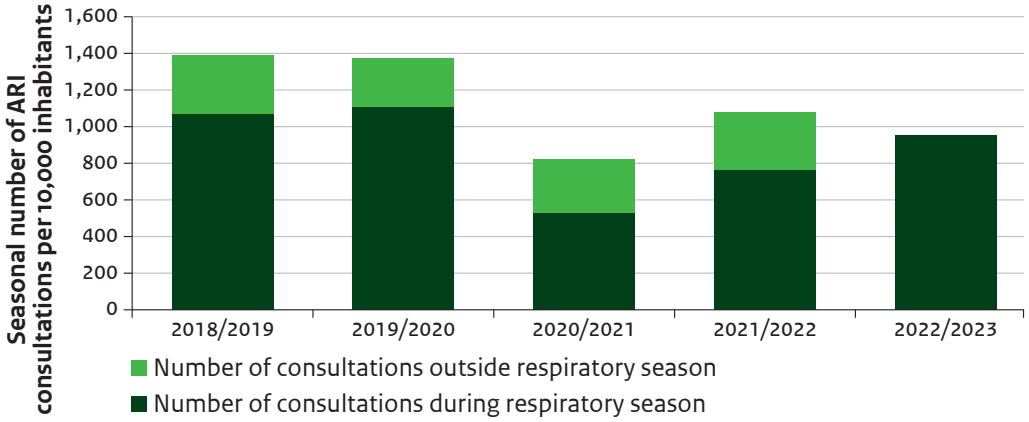
Figure 1.1 Weekly incidence of self-reported ARI (including ILI) per 10,000 participants in the general population as reported in the Infectieradar study during the respiratory season (week 40 through week 20) of 2022/2023 and for seasons 2020/2021 and 2021/2022 (Source: Infectieradar, RIVM).



Footnote: *The grey shading marks the influenza epidemic weeks, from week 50 2022 through week 11 2023 (see Chapter 3).*
ARI = acute respiratory infections (including influenza-like illness).

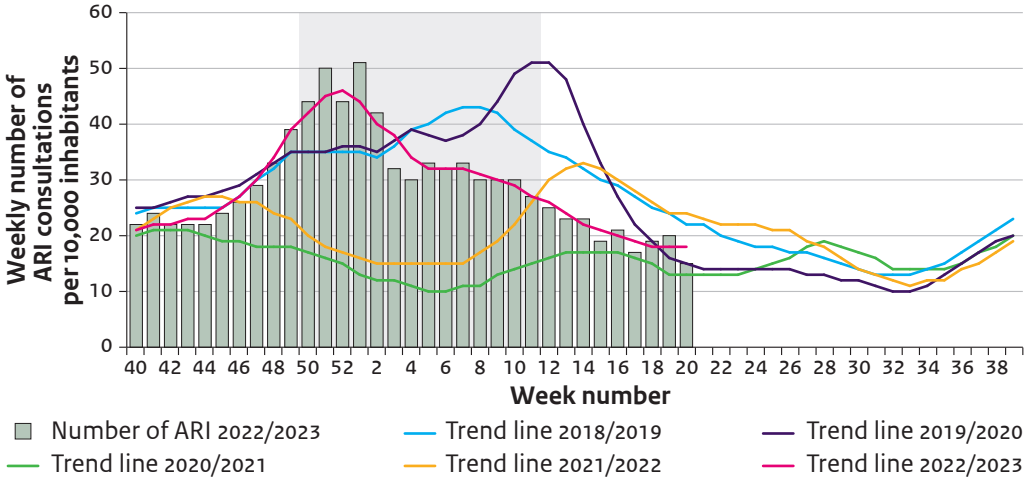
GP consultations for ARI (including ILI)

Figure 1.2 Seasonal cumulative number of ARI (including ILI) consultations in primary care within the respiratory season (week 40 through week 20) and outside the respiratory season (week 21 through week 39) of 2018/2019 - 2022/2023 (Source: Nivel Primary Care Database).



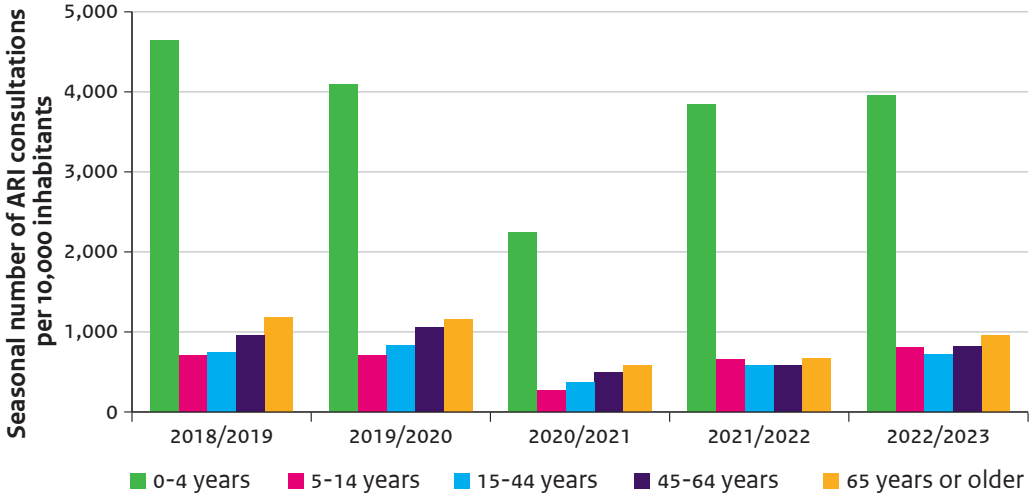
Footnote: *ARI = acute respiratory infections (including influenza-like illness); GP = general practitioner.*
For the 2022/2023 season, numbers for outside the respiratory season (week 20 through 39 2023) are not yet available.

Figure 1.3 Weekly number of ARI (including ILI) consultations in primary care per 10,000 inhabitants in the respiratory season (week 40 through week 20) of 2022/2023 and trend lines for seasons 2018/2019 - 2022/2023 (Source: Nivel Primary Care Database).



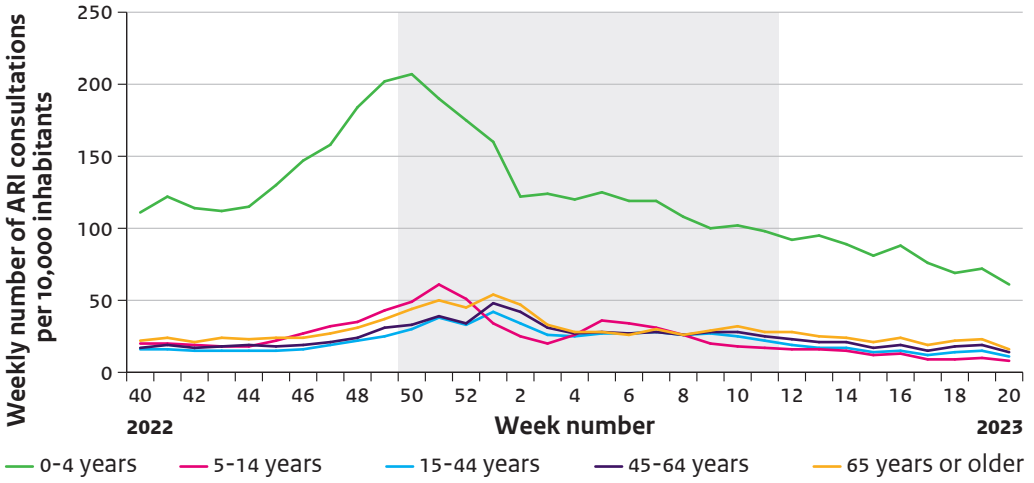
Footnote: *The grey shading marks the influenza epidemic weeks, from week 50 2022 through week 11 2023 (see Chapter 3). Trend lines indicate a 5-weeks moving average. ARI = acute respiratory infection, including influenza-like illness; GP = general practitioner.*

Figure 1.4 Seasonal cumulative number of ARI (including ILI) consultations in primary care in the respiratory seasons (weeks 40 through 20) of 2018/2019 through 2022/2023 per 10,000 inhabitants by age group (Source: Nivel Primary Care Database).



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

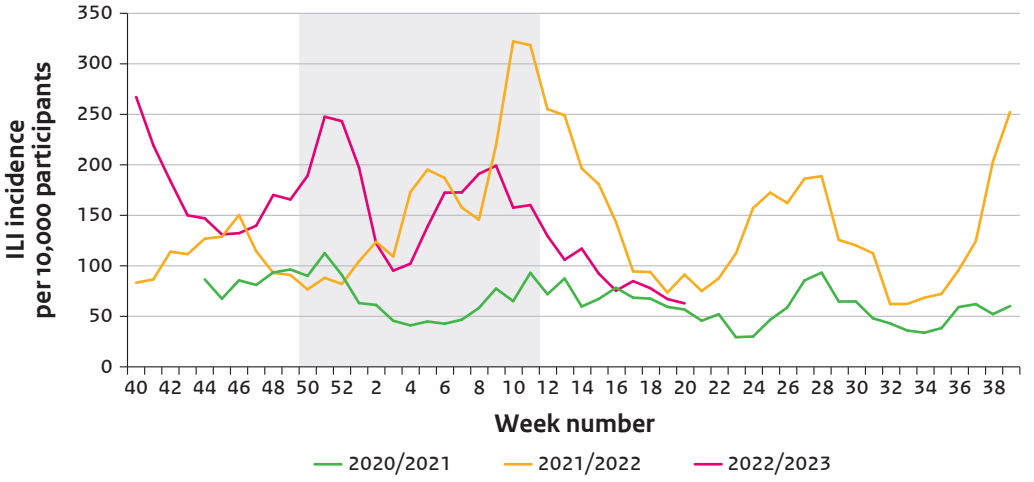
Figure 1.5 Weekly number of ARI (including ILI) consultations in primary care per 10,000 inhabitants in 2022/2023 (weeks 40 through week 20 of 2023) by age group (Source: Nivel Primary Care Database).



Footnote: *The grey shading marks the influenza epidemic weeks, from week 50 2022 through week 11 2023 (see Chapter 3). ARI = acute respiratory infection, including influenza-like illness.*

ILI incidence: self-reported in general population

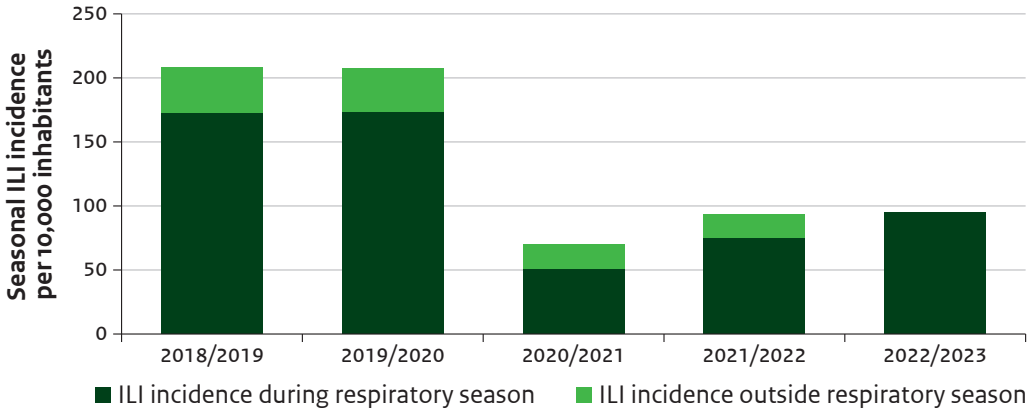
Figure 1.6 Weekly ILI incidence per 10,000 participants in the general population during the respiratory season (week 40 through week 20) of 2022/2023 and for seasons 2020/2021 and 2021/2022 (Source: Infectieradar, RIVM).



Footnote: *the grey shading marks the influenza epidemic weeks, from week 50 2022 through week 11 2023. ILI = influenza-like illness*

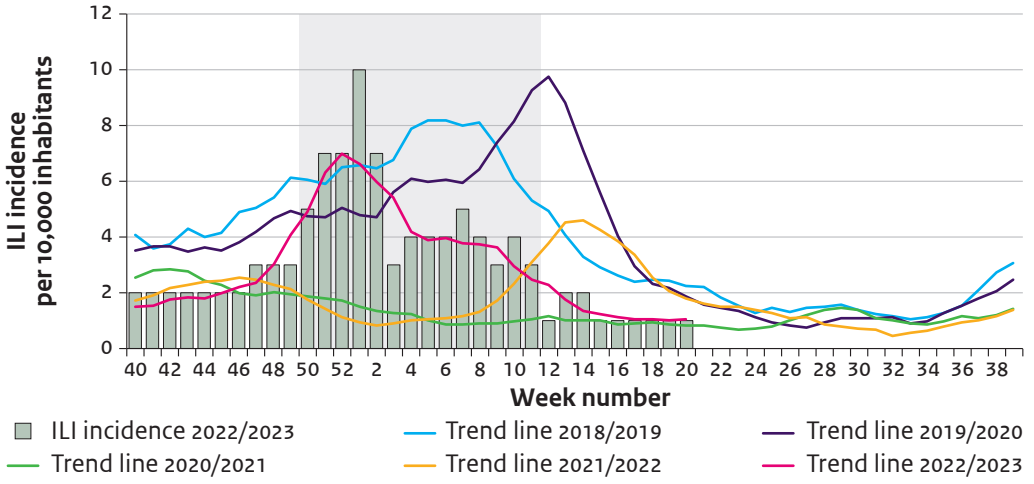
ILI incidence: sentinel GP practices

Figure 1.7 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 2018/2019 - 2022/2023 (Source: Nivel Primary Care Database).



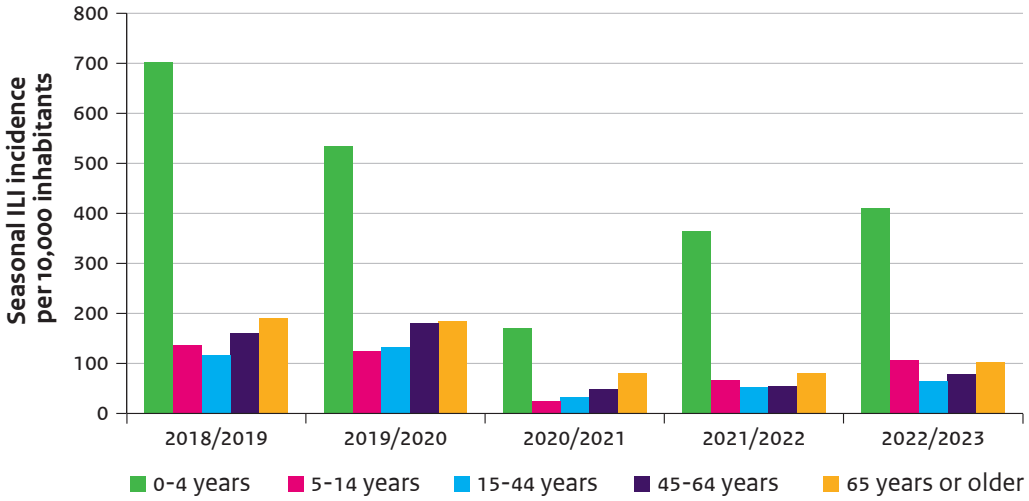
Footnote: *ILI = influenza-like illness.*
For the 2022/2023 season, numbers for outside the respiratory season (week 20 through 39 2023) are not yet available.

Figure 1.8 Weekly ILI incidence in primary care in the respiratory season (week 40 through week 20) of 2022/2023 and trend lines for seasons 2018/2019 - 2022/2023 (Source: Nivel Primary Care Database).



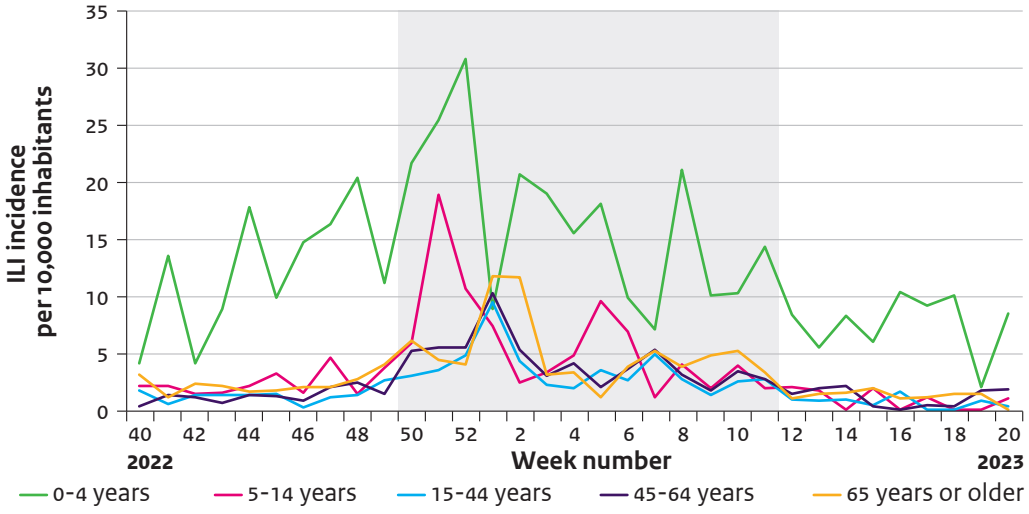
Footnote: *The grey shading marks the influenza epidemic weeks, from week 50 2022 through week 11 2023 (see Chapter 3). Trend lines indicate a 5-weeks moving average. ILI = influenza-like illness.*

Figure 1.9 Seasonal ILI incidence in primary care in the respiratory seasons 2018/2019 - 2022/2023 per 10,000 inhabitants by age group (Source: Nivel Primary Care Database).



Footnote: *ILI = influenza-like illness.*

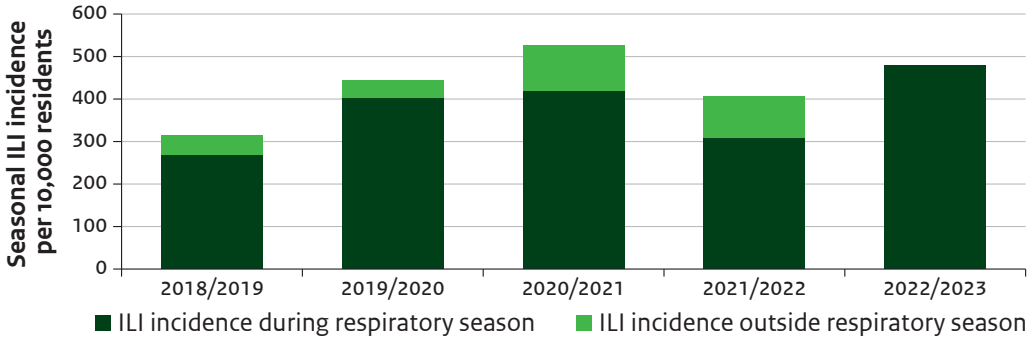
Figure 1.10 Weekly ILI incidence in primary care per 10,000 inhabitants in respiratory season 2022/2023 by age group (Source: Nivel Primary Care Database).



Footnote: *The grey shading marks the influenza epidemic weeks, from week 50 2022 through week 11 2023 (see Chapter 3). ILI = influenza-like illness.*

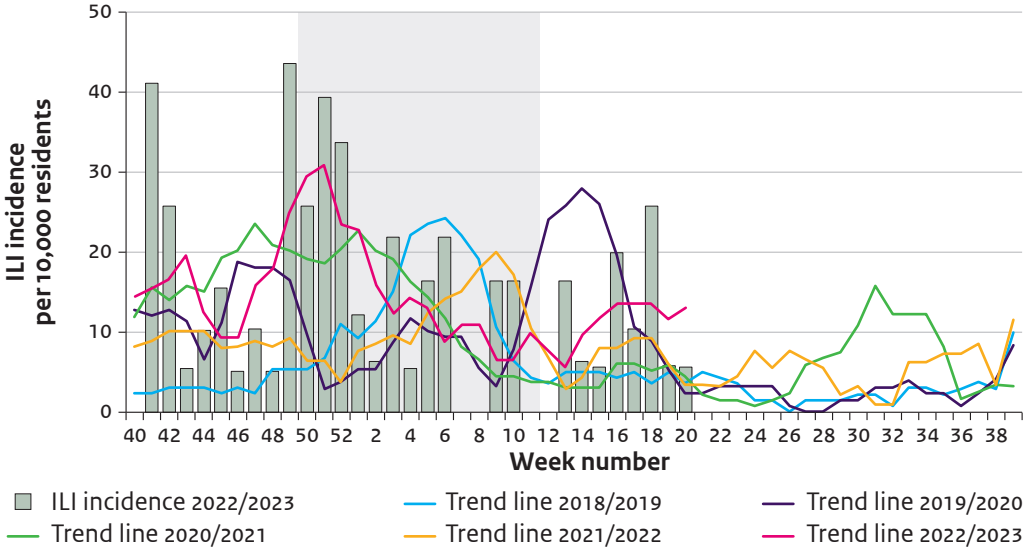
ILI incidence: in nursing homes

Figure 1.11 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 2018/2019 - 2022/2023 (Source: SNIV, RIVM).



Footnote: *ILI = influenza-like illness.*
For the 2022/2023 season, numbers for outside the respiratory season (week 20 through 39 2023) are not yet available.

Figure 1.12 Weekly ILI incidence in SNIV nursing homes per 10,000 residents in the 2022/2023 respiratory season (week 40 of 2022 through week 20 of 2023) and trend lines for the seasons 2018/2019 - 2022/2023 (Source: SNIV, RIVM).



Footnote: *The grey shading marks the influenza epidemic weeks, from week 50 2022 through week 11 2023 (see Chapter 3). Trend lines are based on 5-week moving averages. ILI = influenza-like illness; SNIV = national sentinel surveillance network for infectious diseases in nursing homes.*

1.2 COVID-19-like illness

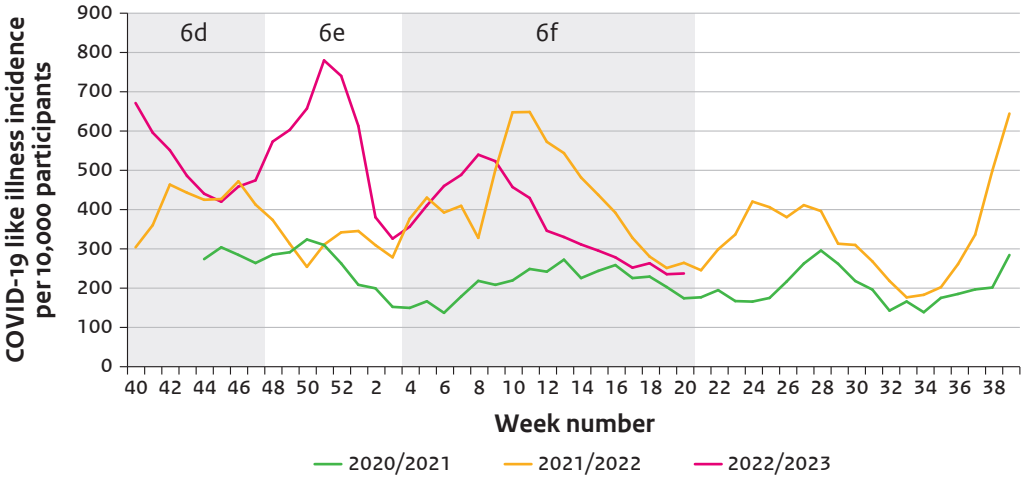
Authors: Femke Jongenotter, Albert Jan van Hoek, Irene Veldhuijzen
Contributor: Daphne Reukers

1.2.1 Key points

- From week 33 2022, self-reported COVID-19-like illness incidence per 10,000 participants in the general population started to increase.
- In the 2022/2023 season three peaks in the COVID-like illness incidence per 10,000 participants in the general population occurred: 671 per 10,000 participants in week 40 2022, 780 per 10,000 participants in week 51 2022, and 540 per 10,000 participants in week 8 2023.

1.2.2 Figure

Figure 1.13 Weekly self-reported COVID-19-like illness incidence per 10,000 participants in the general population as reported in the Infectieradar study during the respiratory season (week 40 through week 20) of 2022/2023 and for seasons 2020/2021 and 2021/2022 (Source: Infectieradar, RIVM).



Footnote: *The grey shading marks the COVID-19 periods during the 2022/2023 respiratory season; 6d, 6e and 6f until week 20 2023 (see Chapter 2).*

1.3 Bronchiolitis

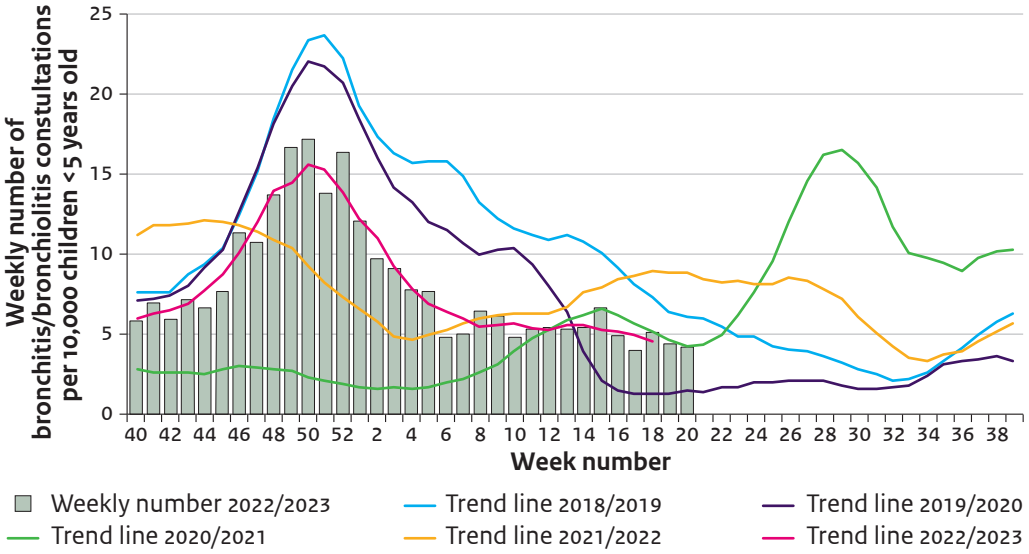
Authors: Anne Teirlinck, Mariette Hooiveld

1.3.1 Key points

- The weekly number of bronchitis/bronchiolitis GP-consultations (ICPC-code R78) in children below 5 years of age peaked at the end of 2022.
- The timing of the peak coincided with the two pre-pandemic seasons 2018/2019 and 2019/2020, but was lower than these seasons and also lower than the out-of-season peak in the season 2020/2021.

1.3.2 Figure

Figure 1.14 Weekly number of patients below 5 years of age consulting their GP for bronchitis/bronchiolitis (ICPC-code R78) per 10,000 children in 2022/2023 (week 40 2022 through week 20 2023) and the trend lines for 2018/2019 - 2022/2023 (2022/2023: through week 20) (source: Nivel Primary Care Database).



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

1.4 Community-acquired pneumonia (CAP) in primary care

Authors: Daphne Reukers, Mariëtte Hooiveld
Contributors: Marit de Lange, Mirthe Biesheuvel

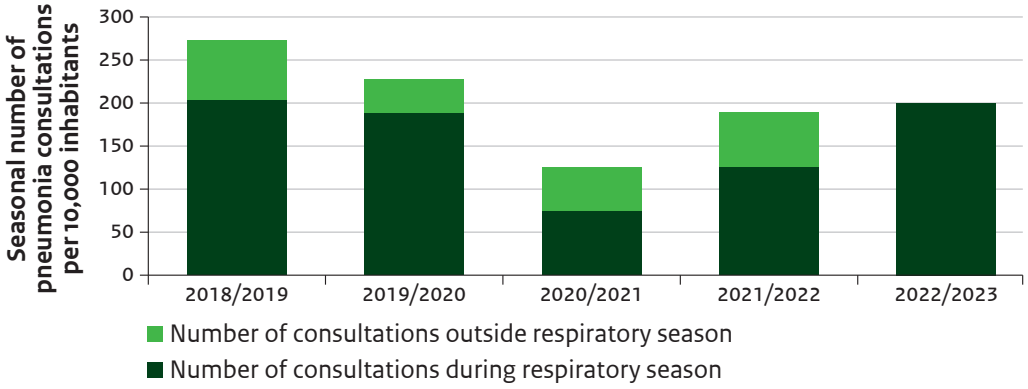
1.4.1 Key points

- The seasonal number of GP consultations for pneumonia (week 40, 2022 through week 20, 2023) was 200 per 10,000 inhabitants, which was higher than previous two season, but comparable with the two pre-pandemic seasons 2018/2019 and 2019/2020.
- The weekly number of pneumonia GP consultations increased steadily throughout the beginning of the 2022/2023 respiratory season and reached a peak in week 1 of 2023 (11 consultations per 10,000 inhabitants). Which was earlier and higher than the four previous seasons.
- The weekly number of pneumonia GP consultations were highest in patients of 65 years or older, which is in line with the four previous seasons.
- The seasonal incidence of pneumonia in nursing homes was 1482 per 10,000 residents, which was higher than previous two seasons, but lower than the two pre-pandemic seasons 2018/2019 and 2019/2020.
- The highest peak in the weekly incidence for pneumonia (103 patients per 10,000 residents) was reported in week 1 in 2023 by the SNIV nursing homes and was higher than the peaks in the previous four seasons (range: 55-74 per 10,000 residents).

1.4.2 Figures

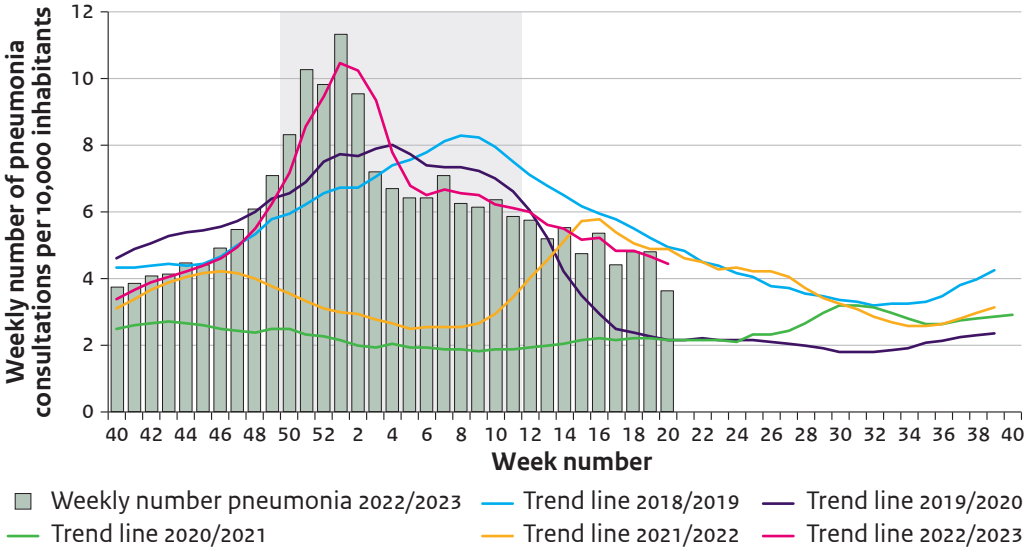
GP consultations for pneumonia

Figure 1.15 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 2018/2019 - 2022/2023 (Source: Nivel Primary Care Database).



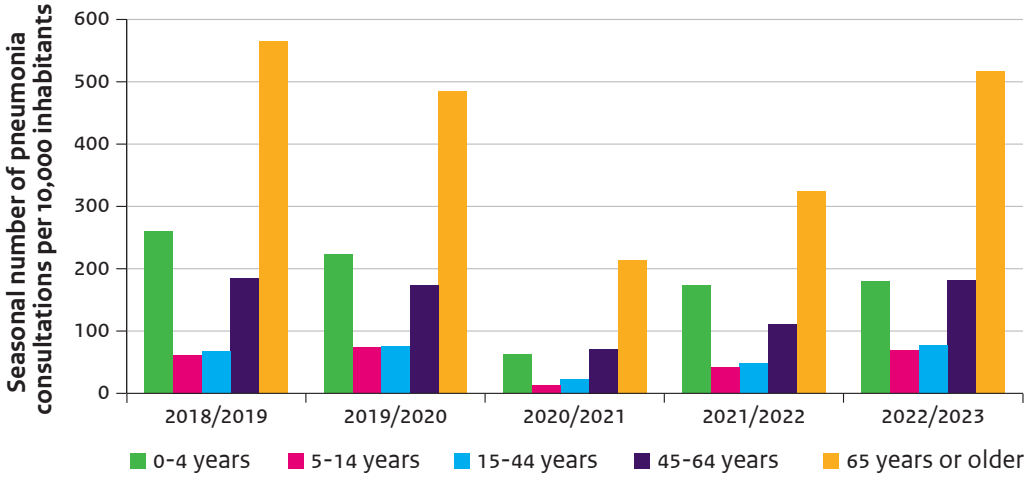
Footnote: *GP = general practitioner.*
For the 2022/2023 season, numbers for outside the respiratory season (week 20 through 39 2023) are not yet available.

Figure 1.16 Weekly numbers of patients consulting their GP for pneumonia per 10,000 inhabitants in 2022/2023 (week 40 through week 20) and the trend lines for 2018/2019 - 2022/2023 (week 40 through week 20). (Source: Nivel Primary Care Database).



Footnote: *The grey shading marks the influenza epidemic weeks, from week 50 2022 through week 11 2023 (see Chapter 3). GP = general practitioner. Trend lines are based on a 5-week moving average.*

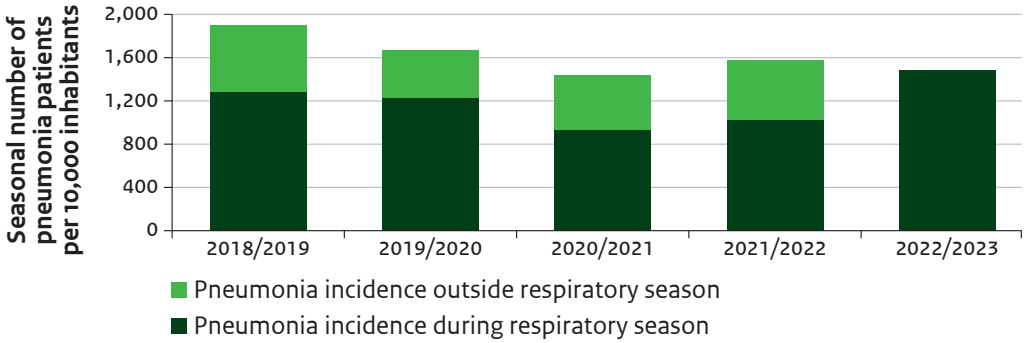
Figure 1.17 Seasonal cumulative number of GP consultations for pneumonia per 10,000 inhabitants by age group in the respiratory seasons 2018/2019 - 2022/2023 (week 40 through week 20) (Source: Nivel Primary Care Database).



Footnote: *GP = general practitioner.*

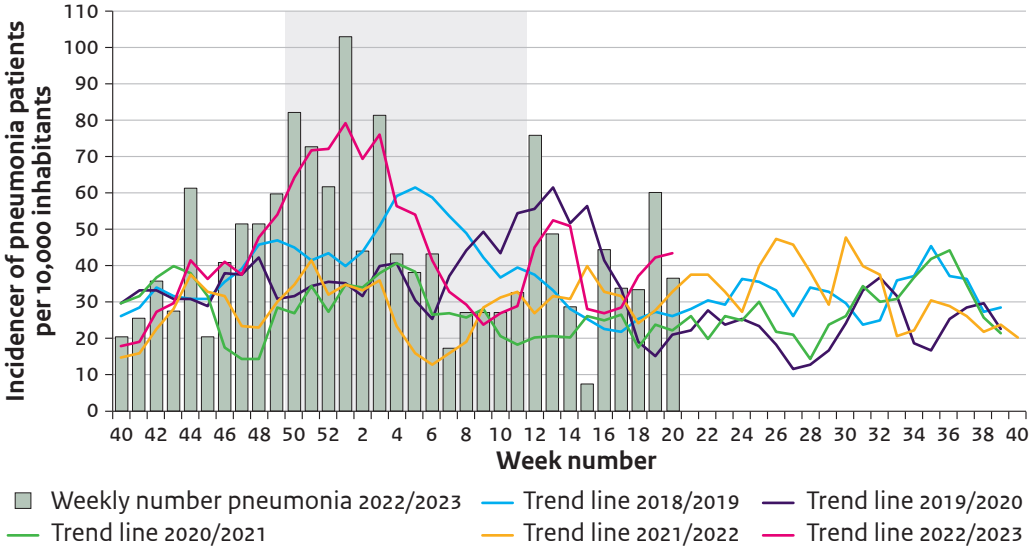
Incidence of pneumonia (nursing homes)

Figure 1.18 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 2018/2019 - 2022/2023 (Source: SNIV, RIVM).



Footnote: *SNIV = national sentinel surveillance network for infectious diseases in nursing homes.*
For the 2022/2023 season, numbers for outside the respiratory season (week 20 through 39 2023) are not yet available.

Figure 1.19 Weekly incidence of pneumonia patients in SNIV nursing homes per 10,000 residents in 2022/2023 and trend lines for the seasons 2018/2019 - 2022/2023 (through week 20). (Source: SNIV, RIVM).



Footnote: *The grey shading marks the influenza epidemic weeks, from week 50 2022 through week 11 2023 (see Chapter 3).*
SNIV = national sentinel surveillance network for infectious diseases in nursing homes. Trend lines are based on a 5-week moving average.

Chapter 2
COVID-19

Authors: Femke Jongenotter, Irene Veldhuijzen
Contributors: COVID-19 Surveillance Team (RIVM), Consortium National Sewage Surveillance (RIVM)

2.1 Key points

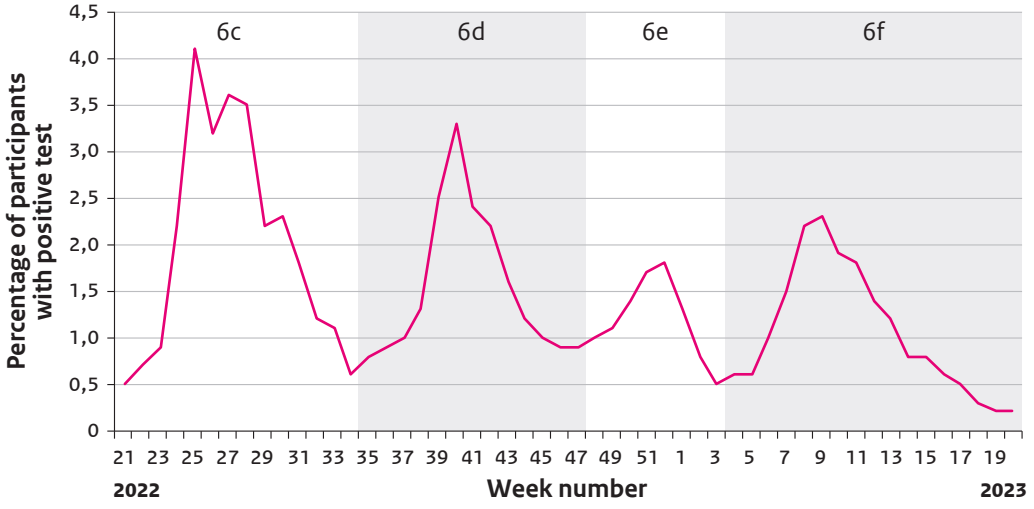
- The SARS-CoV-2 epidemic in the Netherlands is divided into 6 periods and period 2 and 6 are divided into sub-periods. Periods included in this report (from week 21 of 2022 through week 20 of 2023) are 6c to 6f of the SARS-CoV-2 epidemic in the Netherlands.
- Dominant SARS-CoV-2 Omicron subvariants were BA.5 (period 6c and 6d), BQ.1 (period 6e) and XBB.1.5 (period 6f).
- During the 2022/2023 season, from week 21 2022 up to week 20 in 2023, a total of 536,972 cases tested positive for SARS-CoV-2 by the Public Health Service (PHS) or by other health professionals, resulting in a cumulative incidence of 3,053 per 100,000 inhabitants (based on the population of 1-1-2023) including reinfections. The majority of these notifications were tests performed at the PHS. The percentage of positive tests were overall high (average around 60%) indicating that the tests performed were mostly confirmation tests of positive self-tests. The testing policy changed after the first two Omicron waves in Q1 2022 (period 6a-b), from 11 April it was no longer advised to confirm a positive self-test at the PHS. As a result a comparison of the number of cases notified by the PHS in the 2022/2023 period described in this chapter with previous periods as an indicator for the number of infections is not valid.
- During the 2022/2023 season, a total of 31,013 SARS-CoV-2 notifications were reported among nursing home residents.
- A total of 28,633 patients positive for SARS-CoV-2 were hospitalised of whom 1,812 were admitted to the Intensive Care Unit (ICU) in the 2022/2023 season. The reasons of hospital admission was not taken into account for these patients.
- The cumulative incidence of weekly new hospitalisations was 1,670 per 100,000 population, with the highest incidence in persons aged 80 years and older (1,246) and 60-79 years old (333).
- The cumulative incidence of weekly new ICU admissions was 69 per 100,000 population, with the highest incidence in persons aged 80 years and older (34) and 60-79 years old (28).
- The number of deaths attributed to COVID-19 was 5,349 for the period week 21 of 2022 through week 20 of 2023.

2.2 Tables and Figures

Table 2.1 Overview of different periods of the SARS-CoV-2 epidemic in the Netherlands.

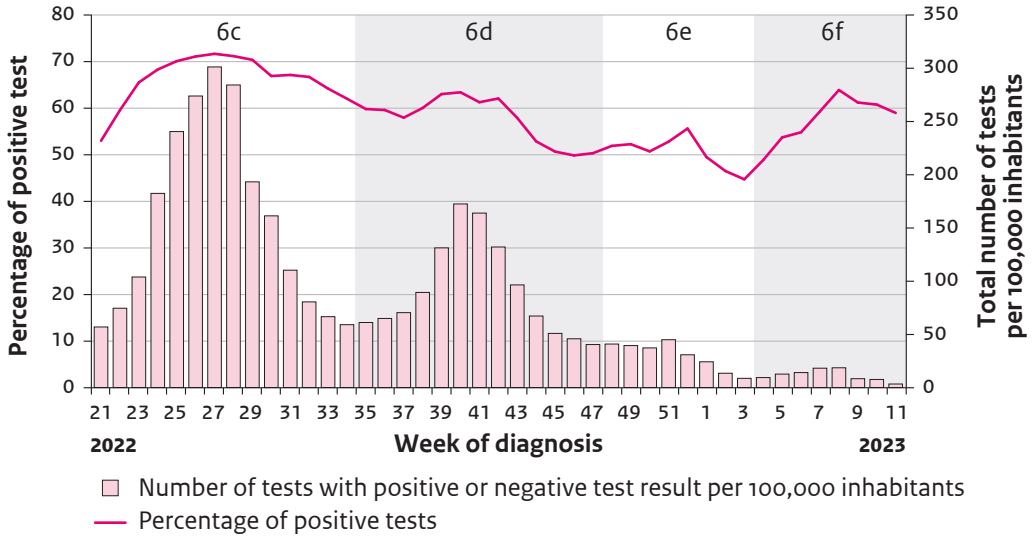
Period	sub	start	end	start year week	end year week
1		Feb-20	Jun-20	2020 W9	2020 W26
2	a	Jul-20	Nov-20	2020 W27	2020 W48
2	b	Dec-20	Jan-21	2020 W49	2021 W4
3		Feb-21	Jun-21	2021 W5	2021 W26
4		Jul-21	Sep-21	2021 W27	2021 W39
5		Oct-21	Dec-21	2021 W40	2021 W52
6	a	Jan-22	Feb-22	2022 W1	2022 W8
6	b	Mar-22	May-22	2022 W9	2022 W22
6	c	Jun-22	Aug-22	2022 W23	2022 W34
6	d	Sep-22	Nov-22	2022 W35	2022 W47
6	e	Dec-22	Jan-23	2022 W48	2023 W3
6	f	Feb-23	May-23	2023 W4	2023 W20

Figure 2.1 Weekly percentage of participants in Infectieradar reporting a SARS-CoV-2 positive (self)test from week 21 2022 through week 20 2023 (Source: Infectieradar, RIVM).



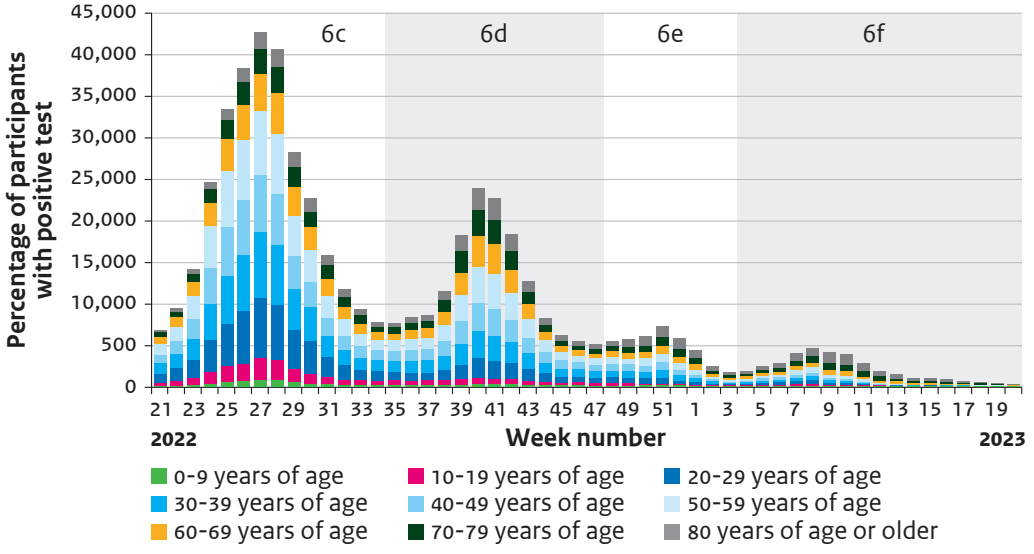
Footnote: *The grey shading marks the different sub-periods 6c to 6f.*

Figure 2.2 Total number of tests[1] performed at PHS test locations per 100,000 inhabitants, and percentage of positive tests from week 21 2022 through week 11 2023 (Source: CoronIT).



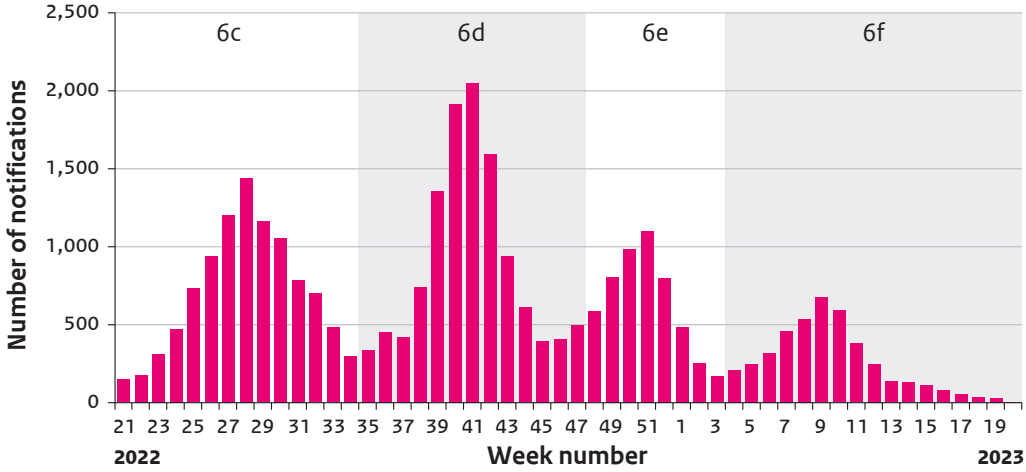
Footnote: *Number of tests with a positive or negative test result. The grey shading marks the different sub-periods 6c to 6f.*

Figure 2.3 Number of SARS-CoV-2 notifications per age group per week from week 21 2022 through week 20 2023 (Source: Osiris).



Footnote: *The grey shading marks the different sub-periods 6c to 6f.*

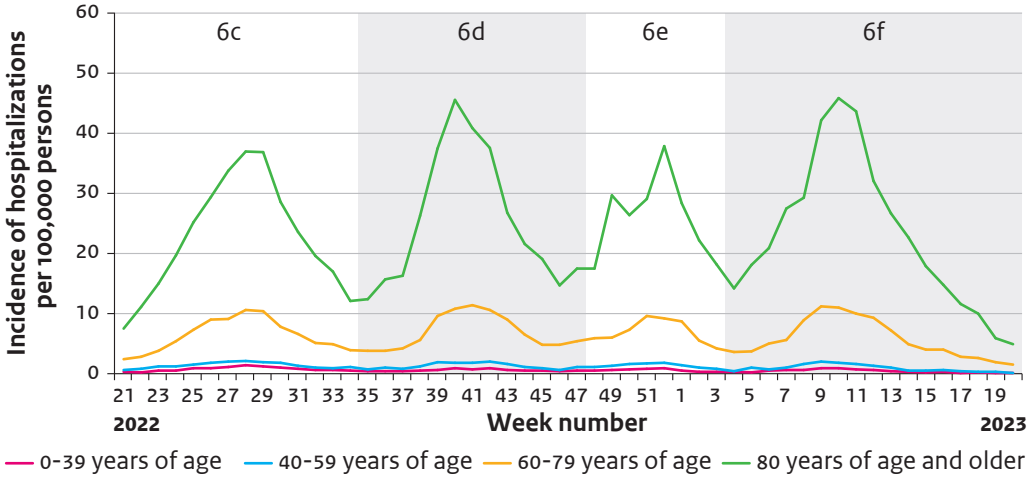
Figure 2.4 Notifications among nursing home residents from week 21 2022 through week 20 2023 (Source: Osiris).*



Footnote: ** An index was a nursing home resident if their postal code was known by the Dutch Patients Federation as a nursing home and if their age was 70 years or older. Therefore, the number of notifications among nursing home residents could be an underestimation. The grey shading marks the different sub-periods 6c to 6f.*

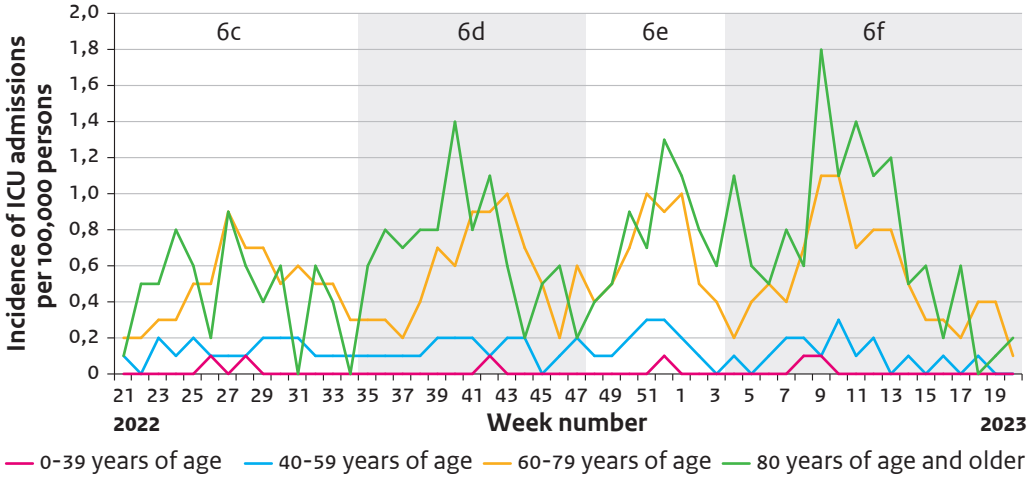
Figure 2.5 A. Weekly incidence of hospitalizations of patients with SARS-CoV-2 infections per 100,000 persons from week 21 2022 through week 20 2023 (including admissions directly to the ICU) by age group, B. Weekly incidence of admissions to ICU (directly or from hospital wards) of patients with SARS-CoV-2 infections per 100,000 persons from week 21 2022 through week 20 2023 by age group (Source: NICE).

A:



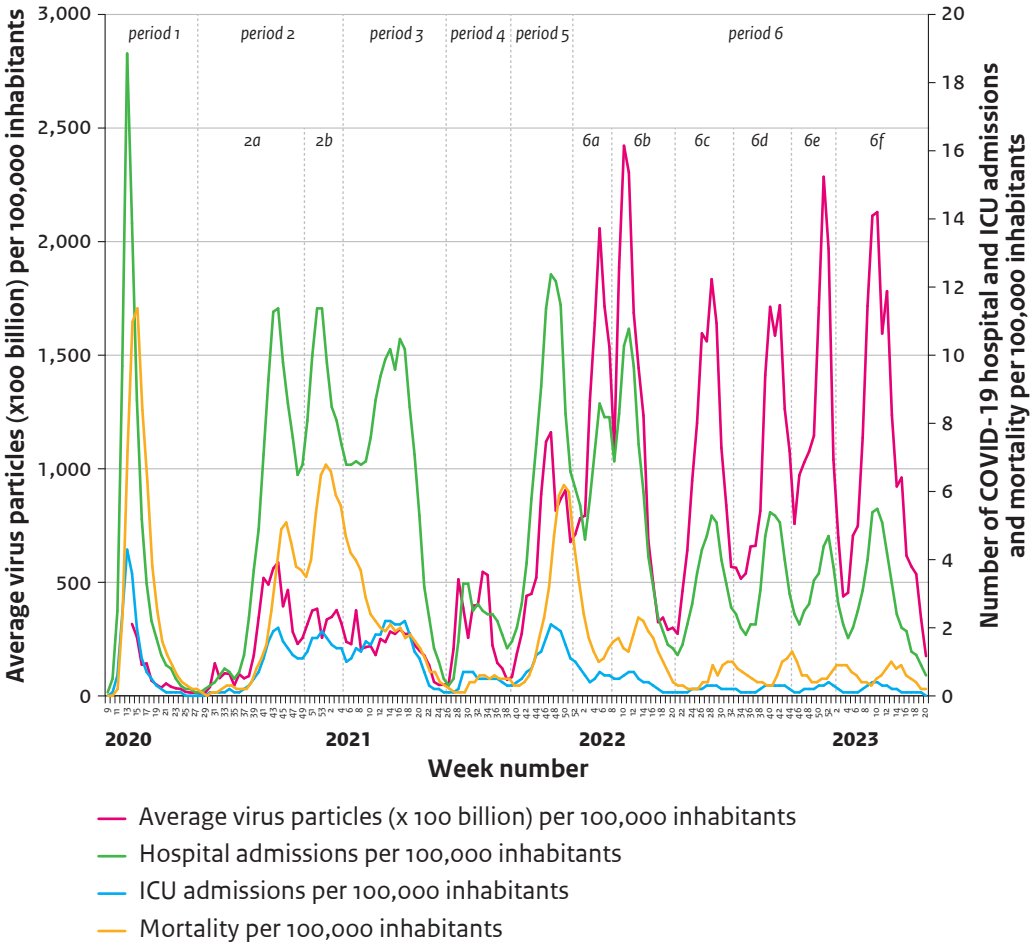
Footnote: *The grey shading marks the different sub-periods 6c to 6f.*

B:



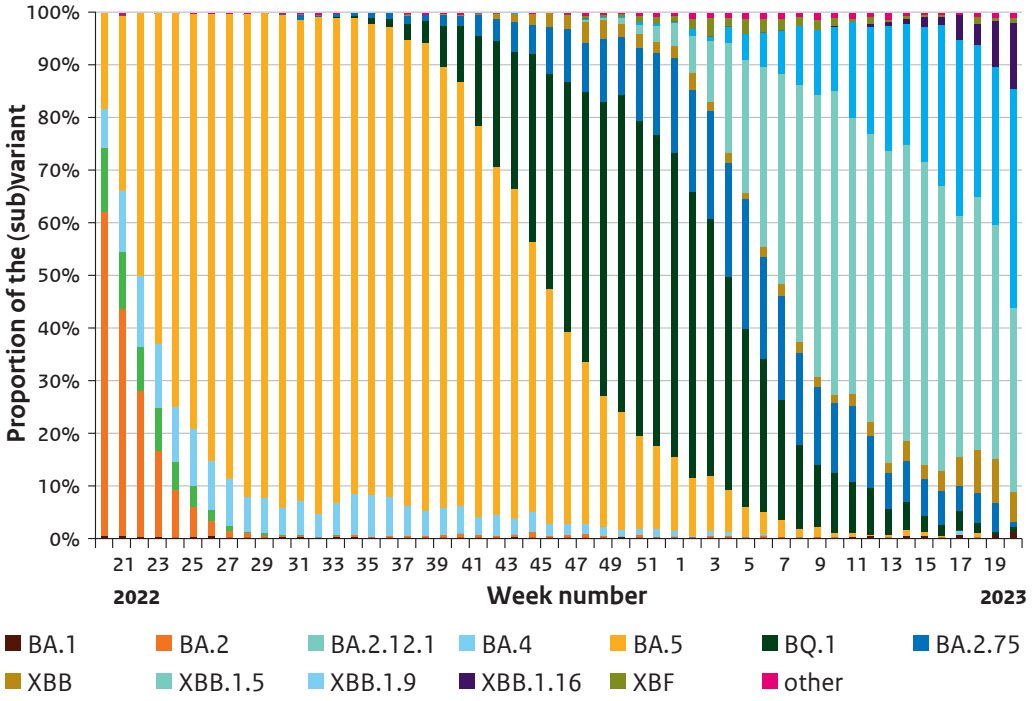
Footnote: *The grey shading marks the different sub-periods 6c to 6f.*

Figure 2.6 Average number of SARS-CoV-2 virus particles (x 100 billion) per 100,000 inhabitants, number of hospitalizations and ICU admissions of patients with SARS-CoV-2 infections per 100,000 inhabitants and COVID-19 mortality per 100,000 inhabitants from week 9 2020 (hospital and ICU admissions, mortality) and week 14 2020 (sewage water)* through week 20 2023 (Source: National Sewage surveillance, RIVM, NICE and Statistics Netherlands (CBS)).



Footnote: *Data from the National Sewage Surveillance was available from week 14 2020 and onwards.*

Figure 2.7 The estimate of the number of notifications per variant subtype per week, the calculations were constantly adjusted based on the most recent data (Source: Genomic surveillance of SARS-CoV-2).



Chapter 3
Influenza

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3.1 Key points

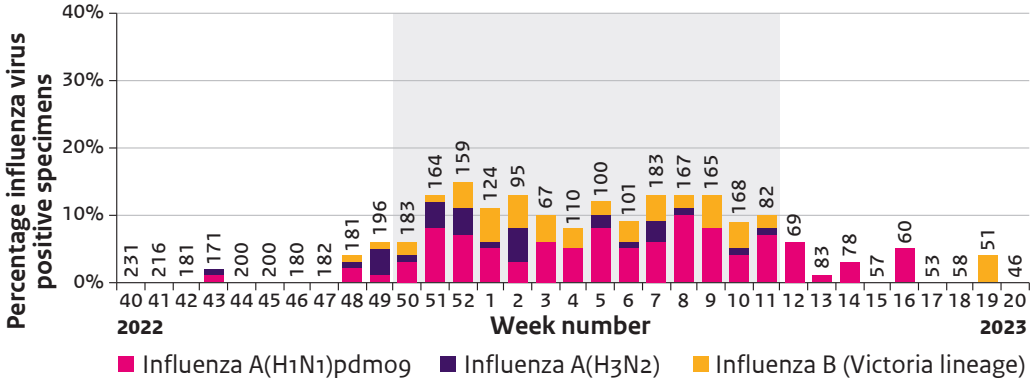
- An influenza epidemic was established from week 50 of 2022 through week 11 of 2023.
- During the 2022/2023 season, both influenza virus type A and B were detected. The influenza subtype A(H1N1)pdm09 was more frequently detected than the A(H3N2) subtype. All characterised B viruses belonged to the Victoria lineage.
- Influenza virus type A(H1N1)pdm09 and A(H3N2) were detected in all age groups, while influenza virus type B (Victoria-lineage) was mainly detected in patients <50 years of age.
- The estimated incidence of symptomatic influenza corresponds to a total of 837,000 persons with symptomatic influenza virus infections during the 2022/2023 season. The estimated symptomatic influenza incidence was highest in children in the age group <5 years and for influenza virus type B/Victoria lineage.
- Results from the VEBIS European pooled analysis showed that the influenza vaccine effectiveness (VE) against any influenza virus infection for all ages was 52% (95% CI: 46%-57%). The highest VE was found against influenza B/Victoria lineage with 74% (95% CI: 67%-80%).
- In the 2022/2023 season, two A(H1N1)pdm09 viruses were found with amino acid substitutions associated with reduced susceptibility for neuraminidase inhibitors. One virus with amino acid substitution NA-S247N was previously reported to have a 2 to 8-fold reduced inhibition by Oseltamivir and 2 to 5-fold reduced inhibition by Zanamivir. Unfortunately, virus isolation was negative for this virus and therefore no phenotypic confirmation could be obtained. Another clinical specimen contained viruses with NA-D199G/D(91%G) and NA-H275Y/H(8%Y), previously associated with 17-fold reduced and 221 to 1637-fold highly reduced inhibition by Oseltamivir, respectively. However, by likely selective growth benefit of viruses with NA-H275Y over those with NA-D199G, the virus isolate that was phenotypically tested contained NA-D199G/D(24%G) and NA-H275Y/H(75%Y) generating a 445-fold highly reduced inhibition by Oseltamivir and 1.8-fold normal inhibition by Zanamivir, mainly driven by the NA-H275Y amino acid substitution.

3.2 Tables and figures

Virological surveillance

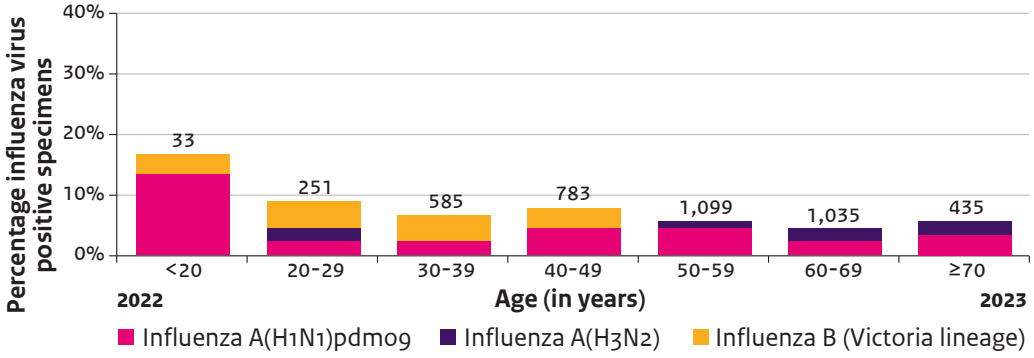
Self-sampling (Infectieradar)

Figure 3.1 Percentage of self-sampling specimens from participants in the Infectieradar study with ARI and a negative SARS-CoV-2 self-test result positive for influenza virus type A and B during the 2022/2023 respiratory season (week 40 of 2022 through week 20 of 2023) (Source: RIVM).



Footnote: *The numbers above the bars show the weekly number of tested specimens. Double infections of influenza virus type A(H1N1) pdm09 and influenza virus type B (Victoria lineage) were detected in 1% of the influenza virus positive specimens.*
ARI = acute respiratory infections; ILI = influenza-like illness; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
The grey shading marks the influenza epidemic weeks, from week 50 2022 through week 11 2023.

Figure 3.2 Percentage of self-sampling specimens from participants in the Infectieradar study with ARI and a negative SARS-CoV-2 self-test result positive for influenza virus type A and B per age group during the 2022/2023 respiratory season (week 40 of 2022 through week 20 of 2023) (Source: RIVM).



Footnote: *At the top of the bars, the received number specimens that week is displayed. Double infections of influenza virus type A(H1N1)pdm09 and influenza virus type B (Victoria lineage) were detected in 1% of the influenza virus positive specimens.*
ARI = acute respiratory infections; ILI = influenza-like illness; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

GP consultations (Nivel Primary Care Database)

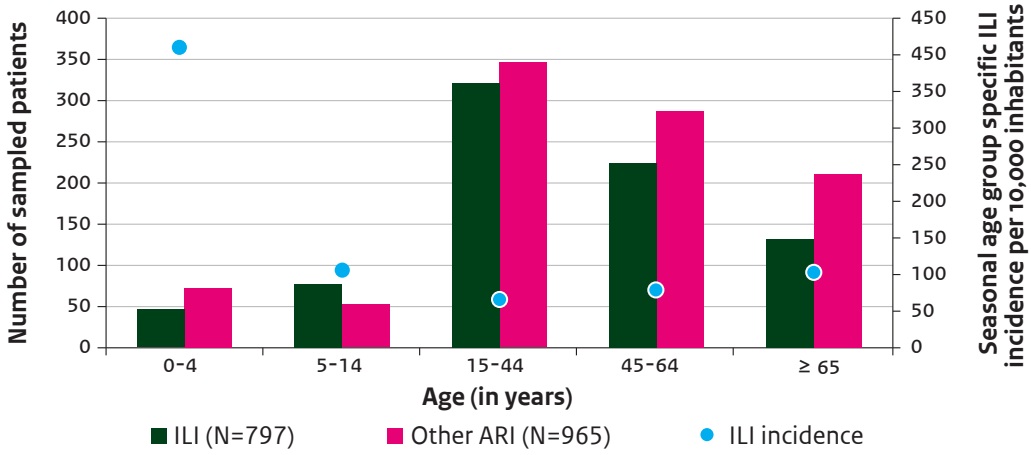
Table 3.1 Characteristics of influenza-like illness (ILI) and other acute respiratory infection (ARI) patients, who were sampled in the Nivel/RIVM GP sentinel surveillance in the 2022/2023 season (through week 20 of 2023) (Sources: NIC location RIVM and Nivel Primary Care Database).

Characteristics	ILI patients n/N (%)	Other ARI patients n/N (%)
Male gender	320/797 (40)	369/965 (38)
Vaccinated against influenza	183/795 (23)	266/961 (28)
Belongs to medical target group for vaccination	310/797 (39)	427/964 (44)
Lung disease (e.g. asthma, COPD)	121/310 (39)	166/425 (39)
Immune deficiency due to treatment (e.g. chemotherapy and radiotherapy)	8/310 (3)	13/425 (3)
Immune deficiency due to disease (e.g. HIV)	8/310 (3)	8/425 (2)
Cardiac disease (myocardial infarction, angina pectoris, arrhythmias, valvular heart disease, heart failure)	56/310 (18)	61/425 (14)
Diabetes mellitus	40/310 (13)	47/425 (11)
Obese (BMI > 30, BMI > 40 from 16 November 2022 onwards)	26/309 (7)	42/421 (10)
Age 60 years or older on 30 April 2023	194/310 (63)	297/427 (70)
Smoking:		
Yes or stopped less than one year ago	98/738 (13)	124/905 (14)
No, or stopped more than one year ago	104/738 (14)	133/905 (15)
Never	536/738 (73)	648/905 (72)
Women:		
Pregnant	5/477 (1)	12/592 (2)
Delay in sampling, in days[a]	4 (3-6)	4 (3-7)

[a] *Number of days between the symptom onset and the day of sampling (median, 1st, and 3rd quartile)*

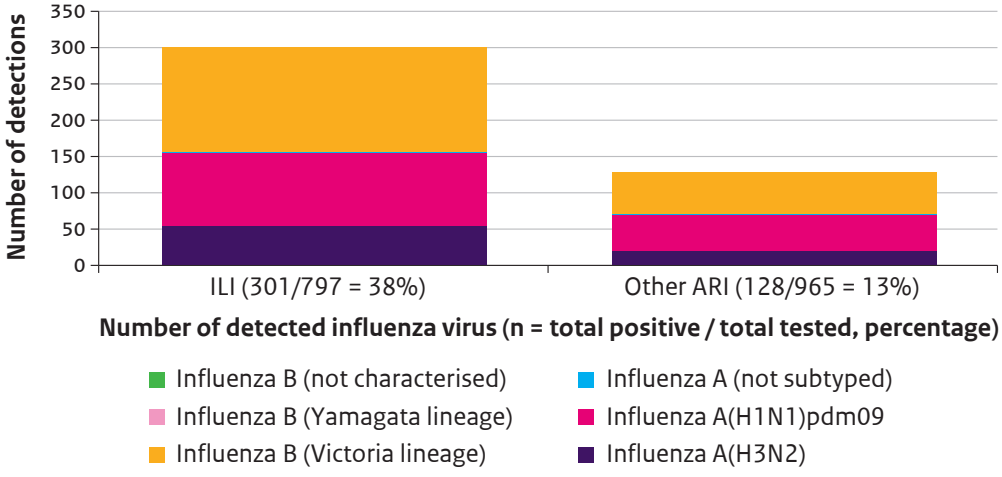
Footnote: *ILI =influenza-like illness; ARI = acute respiratory tract infection; GP = general practitioner; n = the number in the corresponding group; N = total number of patients, for whom the information was available; COPD = Chronic Obstructive Pulmonary Disease; HIV = Human Immunodeficiency Virus; BMI = Body Mass Index. Please note that the 'other ARI' patients do not include the ILI patients.*

Figure 3.3 Age distribution of ILI and other ARI patients, sampled by Nivel sentinel GPs, and the ILI cumulative seasonal incidence per age category in the 2022/2023 respiratory season (week 40 of 2022 through week 20 of 2023) (Sources: Nivel Primary Care Database and NIC location RIVM).



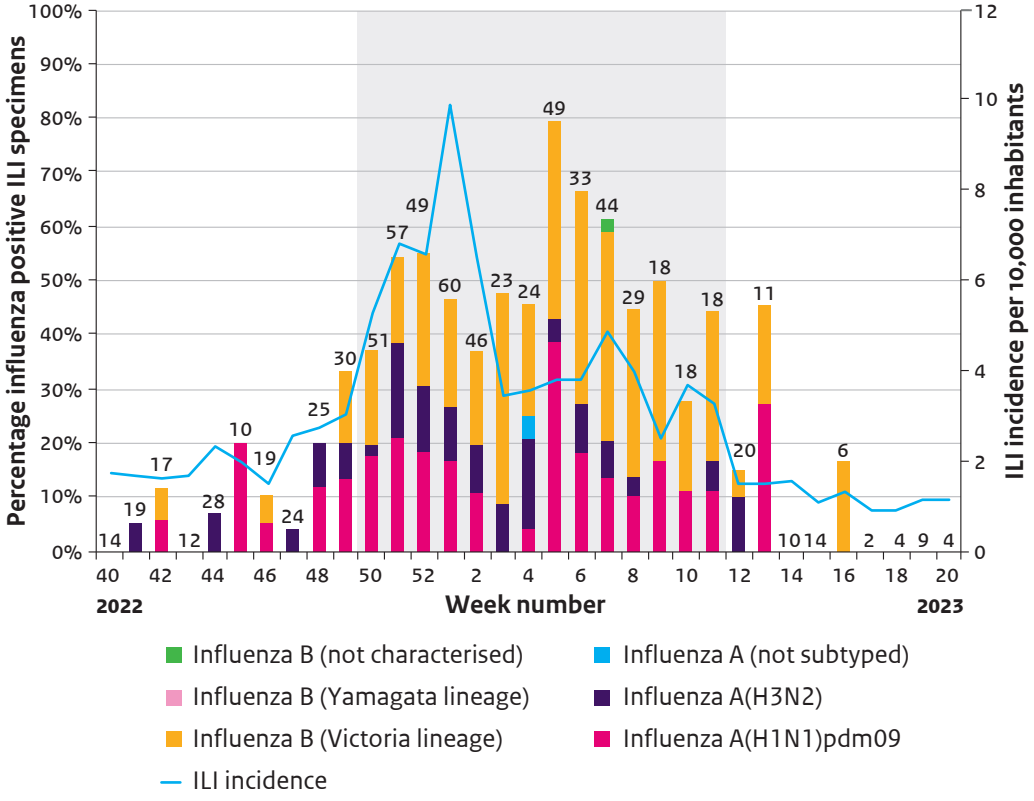
Footnote: *ILI = influenza-like illness; ARI = acute respiratory tract infections, GP = general practitioner.*
Please note that the 'other ARI' patients do not include the ILI patients.

Figure 3.4 Number and proportion of influenza viruses detected in specimens taken from ILI and other ARI patients, who were sampled in the Nivel/RIVM GP sentinel surveillance during the 2022/2023 respiratory season (through week 20 of 2023) (Sources: Nivel Primary Care Database and NIC location RIVM).



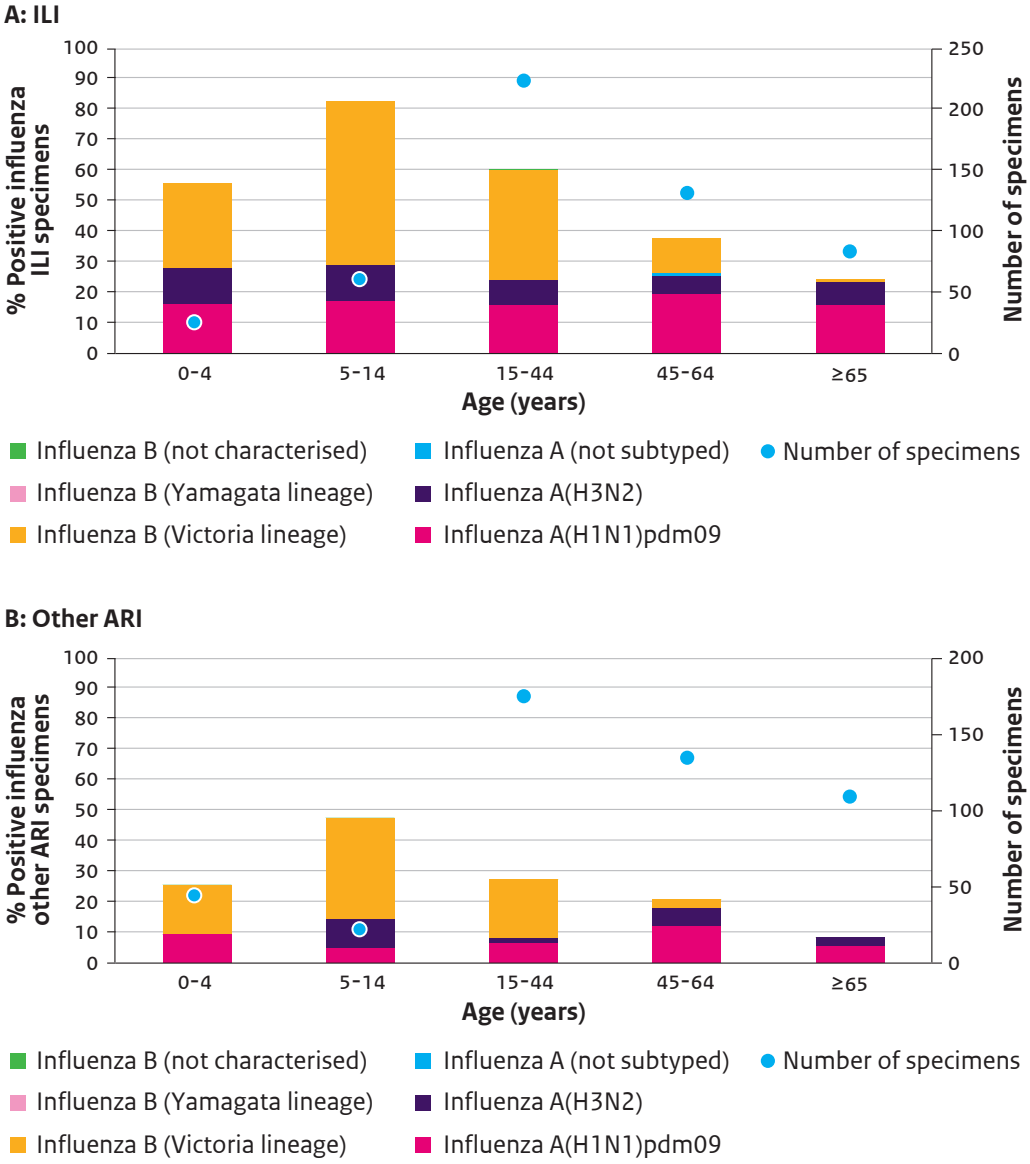
Footnote: *ILI = influenza-like illness; ARI = acute respiratory tract infection.*
Please note that the 'other ARI' patients do not include the ILI patients.

Figure 3.5 Percentage of specimens taken from ILI patients by sentinel GPs positive for influenza virus per week and weekly ILI incidence during the 2022/2023 respiratory season (week 40 of 2022 through week 20 of 2023) (Sources: Nivel Primary Care Database and NIC location RIVM).



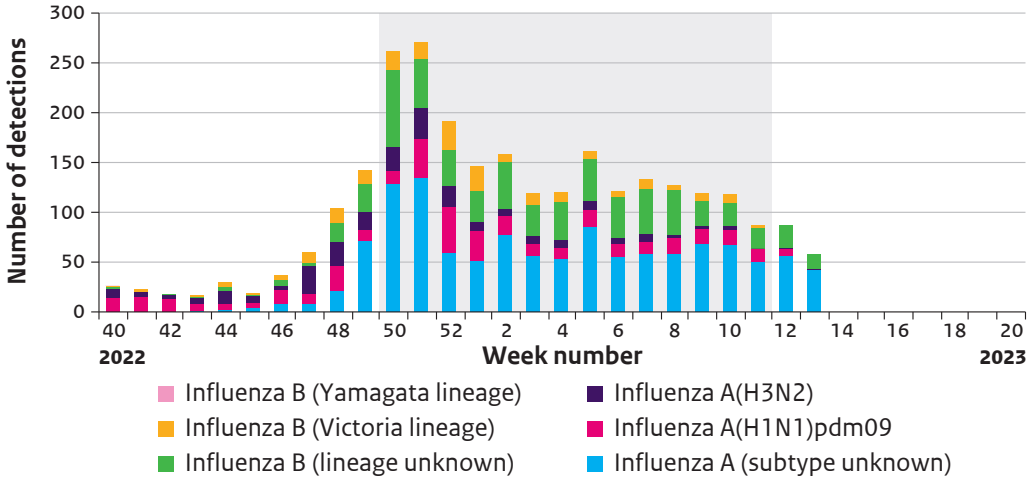
Footnote: *ILI = influenza-like illness; GP = general practitioner.*
The numbers above the bars are the total number of tested specimens.
The grey shading marks the influenza epidemic weeks, from week 50 2022 through week 11 2023.

Figure 3.6 Percentage of influenza virus positive specimens originating from ILI (graph A) and other ARI (graph B) patients per age group, taken by sentinel GPs, during the influenza epidemic period (week 50 2022 through 11 2023) of the 2022/2023 season (Sources: Nivel Primary Care Database and NIC location RIVM).



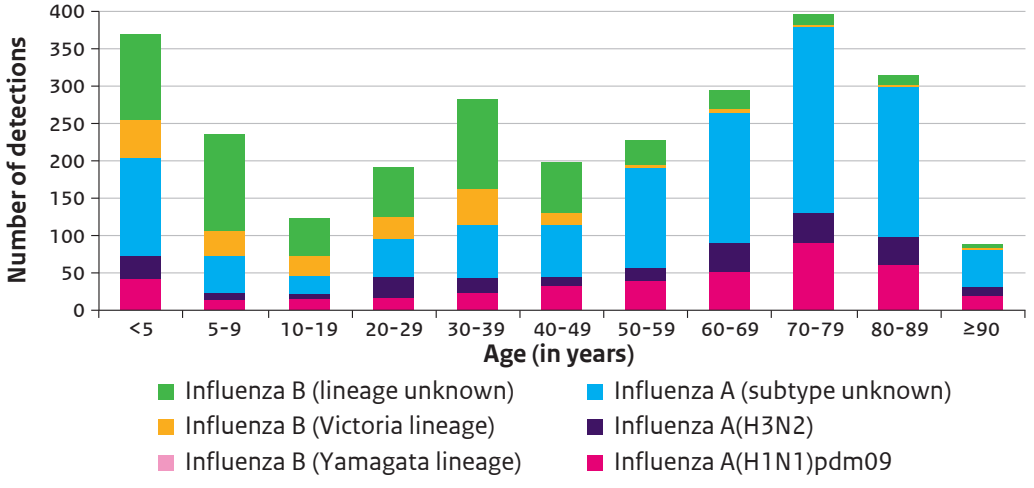
Footnote: *ARI = acute respiratory tract infection, ILI = influenza-like illness.*
Please note that the 'other ARI' patients do not include the ILI patients.

Figure 3.7 Subtyping of influenza viruses submitted by Dutch laboratories to the NIC locations Erasmus MC and RIVM during the 2022/2023 season, displayed by week of specimen collection (Sources: NIC location RIVM, NIC location Erasmus MC).



Footnote: *NIC= national influenza centre, GP = general practitioner.*
The grey shading marks the influenza epidemic weeks, from week 50 2022 through week 11 2023.

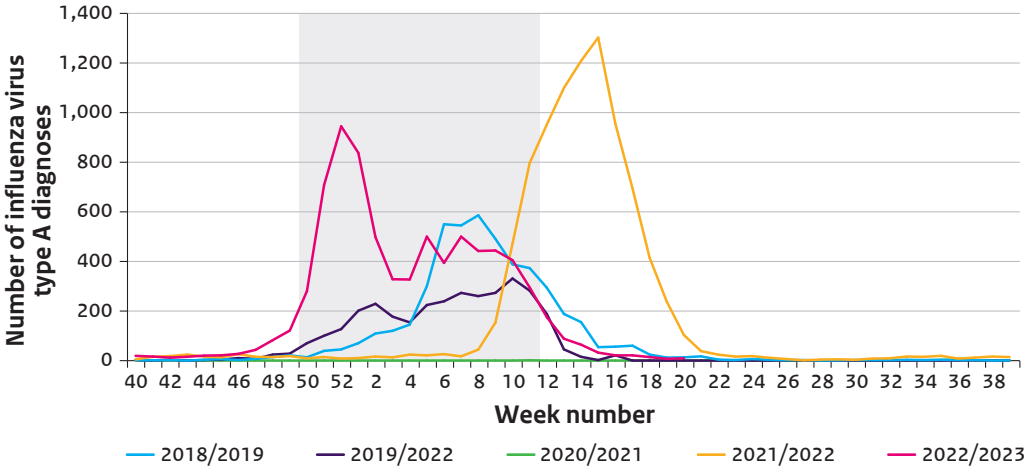
Figure 3.8 Subtyping of influenza viruses submitted by Dutch laboratories to the NIC locations Erasmus MC and RIVM during the 2022/2023 season, displayed by age group, excluding specimens taken for sentinel GP surveillance and submitted to NIC locations Erasmus MC or RIVM for antigenic characterisation (Sources: NIC location RIVM, NIC location Erasmus MC).



Footnote: *NIC = national influenza centre, GP = general practitioner.*

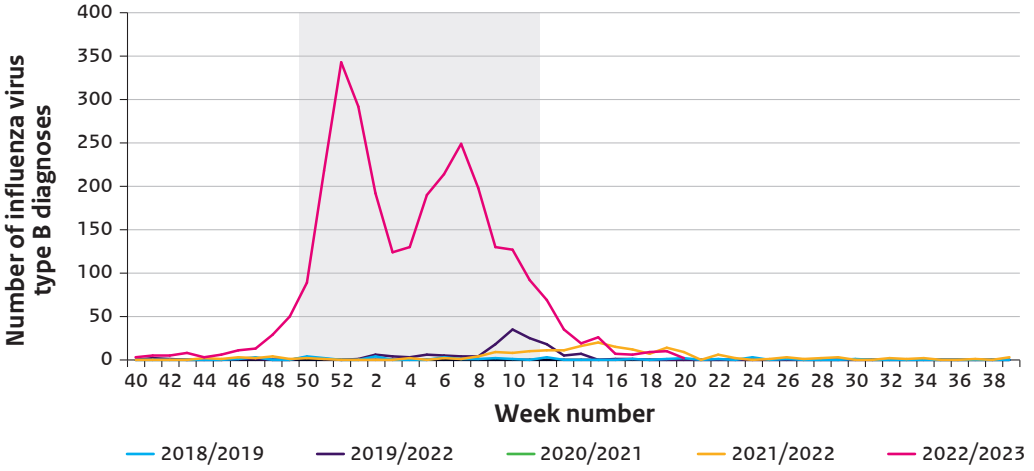
Virological laboratory surveillance

Figure 3.9 Weekly number of influenza virus type A diagnoses, reported by the virological laboratory surveillance in the seasons 2018/2019 through 2022/2023 (through week 20 2023) (Source: Virological laboratory surveillance, RIVM).



The grey shading marks the influenza epidemic weeks, from week 50 2022 through week 11 2023.

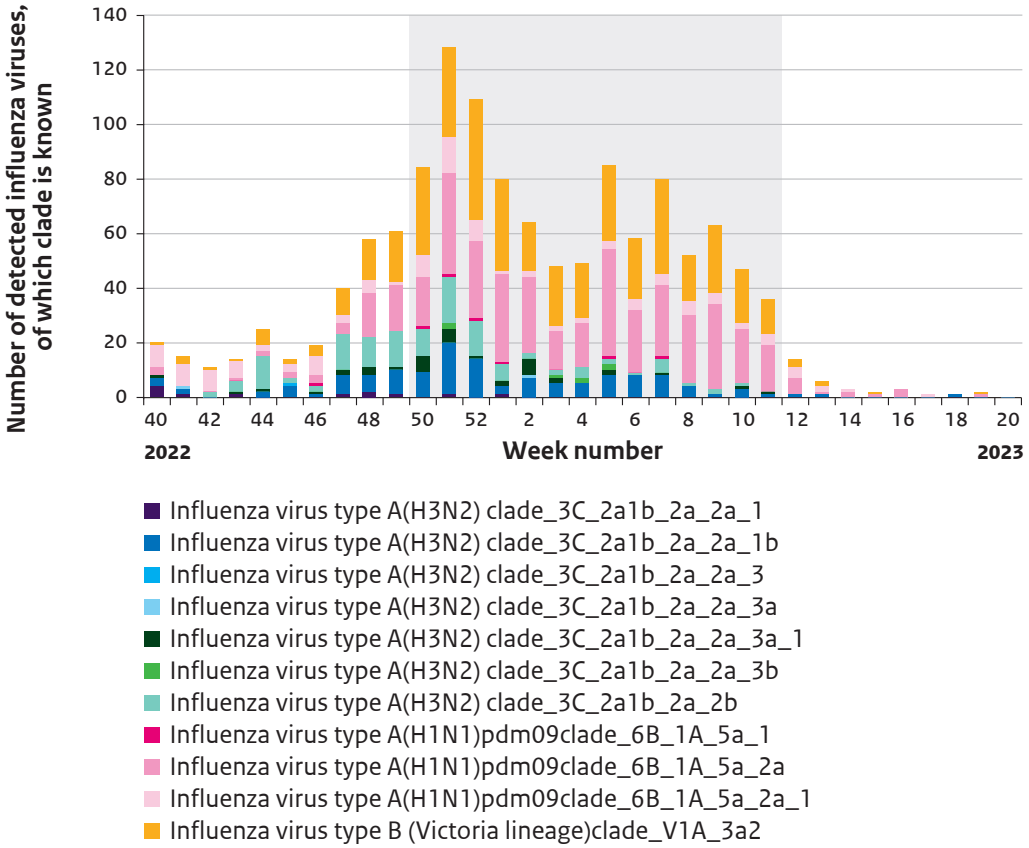
Figure 3.10 Weekly number of influenza virus type B diagnoses, reported by the virological laboratory surveillance in the seasons 2018/2019 through 2022/2023 (through week 20 2023) (Source: Virological laboratory surveillance, RIVM).



The grey shading marks the influenza epidemic weeks, from week 50 2022 through week 11 2023.

Influenza virus genetic characterisations

Figure 3.11 Weekly influenza virus genetic characterisation results of specimens taken in the Nivel/RIVM sentinel GP surveillance, NIC surveillance, and Infectieradar, 2022/2023 season (Sources: Nivel/RIVM sentinel GP surveillance, NIC surveillance, Infectieradar).



Footnote: *GP = general practitioner, NIC = national influenza Centre, PHS = Public Health Services. The grey shading marks the influenza epidemic weeks, from week 50 2022 through week 11 2023.*

Antiviral susceptibility

Table 3.2 Reduced inhibition of influenza viruses by neuraminidase inhibitors and Baloxavir marboxil, 2020/2021 – 2022/2023 (through week 13 2023) (Sources: NIC location RIVM, NIC location Erasmus MC)[a]

	Viruses with reduced inhibition by season		
	2020/2021[b] n/N (%)	2021/2022 n/N (%)	2022/2023[c] n/N (%)
Neuraminidase inhibitor			
A(H1N1)pdm09	ND	1/432 (<1%)[d]	1/555 (<1%)[e]
A(H3N2)	0/20 (0%)	3/1772 (<1%)[f]	0/339 (0%)
B	0/1 (0%)	0/62 (0%)	0/415 (0%)[g]
Baloxavir marboxil[f]			
A(H1N1)pdm09	ND	0/285 (0%)	0/443 (0%)
A(H3N2)	ND	2/1158 (<1%)[h]	0/292 (0%)
B	ND	0/41 (0%)	0/406 (0%)

Footnote: *ND = not determined.*

[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] *During the winter period 2020/2021 no influenza viruses were detected. Only very late in the season after COVID-19 measures were partly lifted in summer 2021 few influenza viruses were detected and analysed for antiviral susceptibility.*

[c] *Preliminary data up to week 13/2023.*

[d] *One virus with NA-H275Y associated with highly reduced inhibition by oseltamivir was detected; additional data on treatment status of the patient unknown.*

[e] *One virus with NA-D199G previously associated with reduced inhibition by oseltamivir that appeared highly reduced inhibited by oseltamivir and normal inhibited by zanamivir by phenotypic testing. The patient did not receive influenza antiviral treatment prior to specimen collection.*

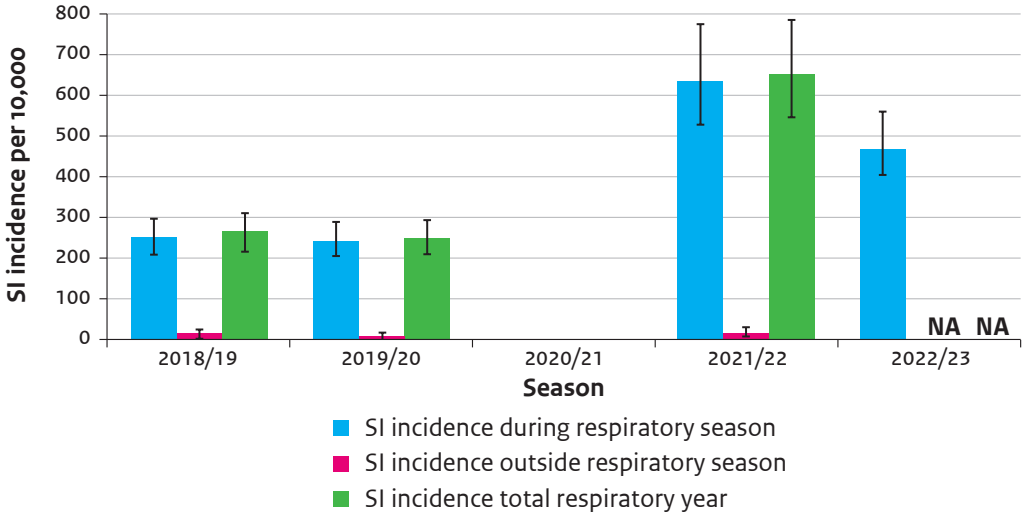
[f] *Three viruses with NA-N329R associated with reduced inibition by zanamivir; by phenotypic testing two were indeed RI by zanamvir and with fold-change around the RI threshold and one was NI by both oseltamivir and zanamivir. All three viruses came from the same submitter. Influenza antiviral treatment history of all three patients was unknown.*

[g] *A cluster of B/Victoria viruses emerged almost exclusively in The Netherlands with NA-K360E previously associated with highly reduced inhibition by peramivir. However, by phenotypic testing of 9 of these virus isolates they appeared normal inhibited by peramivir, likely due to compensating additional amino acid substitutions A395V and L396F/S in the close vicinity of the 360 position in the 3D structure of the neuraminidase.*

[h] *Two viruses showed the amino acid substitution PA-E23G, previously associated with mild reduced susceptibility to baloxavir marboxil. By phenotypic testing at the WHO CCs for influenza in Tokyo and Atlanta of one virus, the virus was clearly reduced susceptible for baloxavir marboxil. One patient was hospitalized. The status of the other patient was unknown. For both patients no antiviral exposure data available.*

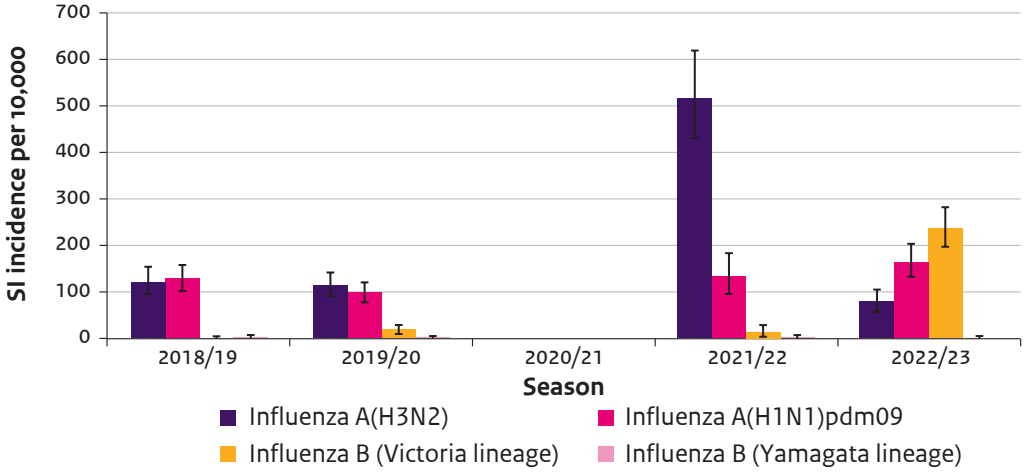
Symptomatic influenza incidence estimation

Figure 3.12 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 2018/2019 through 2022/2023 (Sources: Nivel Primary Care Database, NIC location RIVM, De Grote Griepmeting (until season 2019/20), Infectieradar (from 2021/22 onwards)).



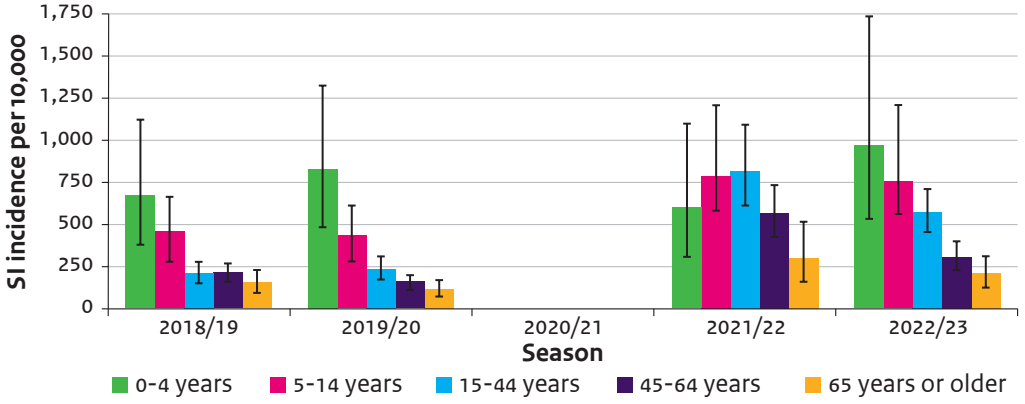
Footnote: *NA = not yet available, SI = symptomatic influenza.*
Error bars represent 95% uncertainty intervals (UI). For the 2022/2023 season, no numbers for outside the respiratory season were yet available. Incorrect estimates for the 2021/2022 season have been published in the annual report of last year. These estimates have now been corrected.
For the 2022/2023 season, SI for outside the respiratory season (week 20 through 39 2023) is not yet available.

Figure 3.13 Estimated symptomatic influenza (SI) incidence per 10,000 inhabitants by subtype for the respiratory seasons (week 40 through week 20) 2018/2019 through 2022/2023 (Sources: Nivel Primary Care Database, NIC location RIVM, De Grote Griepmeting (until season 2019/20), Infectieradar (from 2021/22 onwards)).



Footnote: *SI = symptomatic influenza.*
Error bars represent 95% uncertainty intervals (UI). Incorrect estimates for the 2021/2022 season have been published in the annual report of last year. These estimates have now been corrected.

Figure 3.14 Estimated symptomatic influenza (SI) incidence per 10,000 inhabitants by age group for the respiratory seasons (week 40 through week 20) 2018/2019 through 2020/2023 (Sources: Nivel Primary Care Database, NIC location RIVM, De Grote Griepmeting (until season 2019/20), Infectieradar (from 2021/22 onwards)).



Footnote: *SI = symptomatic influenza.*
Error bars represent 95% uncertainty intervals (UI). Incorrect estimates for the 2021/2022 season have been published in the annual report of last year. These estimates have now been corrected.

Table 3.3 Pooled adjusted seasonal vaccine effectiveness against any influenza, influenza A, A(H3N2), A(H1N1)pdm09 and B, overall, by age group and among target group. VEBIS primary care multicentre case control study, influenza season 2022/2023. (Sources: personal communication EpiConcept about VEBIS primary care study and NIC location RIVM).

		Cases			Controls				
	Age group	All	Vaccinated	%	All	Vaccinated	%	Adjusted VE	95% CI
Any influenza virus	All ages	8,001	542	8	22,952	4,414	19	52	46 - 57
	0-14 years	2,895	70	2	5,826	407	7	68	59 - 76
	15-64 years	4,681	237	5	13,065	1,454	11	52	44 - 58
	65+ years	425	235	55	4,061	2,553	63	30	12 - 44
	Target group	1,889	416	22	9,213	3,597	39	43	35 - 51
A(H3N2)	All ages	3,469	265	8	20,192	3,944	20	37	26 - 46
	0-14 years	1,323	33	2	4,949	348	7	56	34 - 71
	15-64 years	1,923	114	6	11,579	1,270	11	36	20 - 48
	65+ years	223	118	53	3,664	2,326	63	23	-5 - 44
	Target group	853	205	24	8,201	3,233	39	30	15 - 43
A(H1N1) pdm09	All ages	1,354	167	12	22,545	4,392	19	45	33 - 55
	0-14 years	286	14	5	5,681	407	7	56	26 - 76
	15-64 years	935	70	7	12,839	1,442	11	51	36 - 63
	65+ years	133	83	62	3,911	2,489	64	28	-7 - 52
	Target group	471	140	30	9,088	3,582	39	36	18 - 49
B (Victoria lineage)	All ages	2,821	79	3	21,239	4,233	20	74	67 - 80
	0-14 years	1,175	19	2	5,618	403	7	83	73 - 90
	15-64 years	1,613	43	3	11,877	1,388	12	71	60 - 79
	Target group	465	45	10	8,452	3,446	41	67	54 - 77

Table 3.4 Impact estimations for ILI GP consultations caused by influenza virus for the 2022/2023 season. Numbers between brackets are 95% CIs. (Sources: Nivel Primary Care Database personal communication EpiConcept about VEBIS primary care study, and NIC location RIVM).

Input parameters	
Vaccine coverage	72.6 (65.8 – 78.4)
Vaccine effectiveness[a]	27.8 (6.3 – 49.3)
Incidence	7,115 (4,528 – 10,442)
Estimated impact	
NAE	1,799 (94 – 4,198)
NAE (per 100,000 pop.)	51 (3 – 119)
NNV	1,423 (491 – 8,411)
PF	0.202 (0.01 – 0.34)

Footnote: *ILI = influenza-like illness, GP = general practitioner, CI = confidence interval, NAE = number of averted events, Pop.= population, NNV = number of vaccinated persons needed to avoid one influenza-associated event, PF = prevented fraction.*

[a] *See table 3.5 for the input parameters that were used for the calculation of the weighted overall vaccine effectiveness.*

Table 3.5 Input parameters used for the calculation of the 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. Numbers between brackets are 95% CIs. (Sources: VEBIS primary care study and NIC location RIVM).

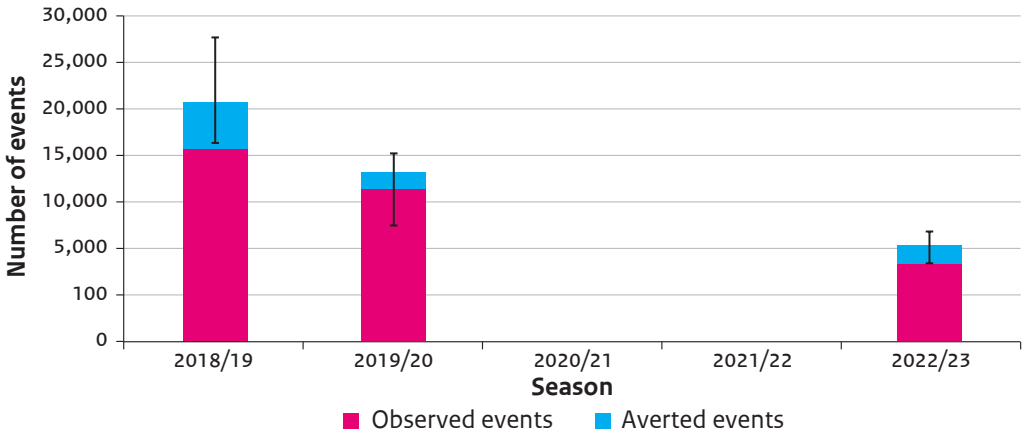
VEBIS PC pooled adjusted VE against H1N1[a]	28 (-7 – 52)
VEBIS PC pooled adjusted VE against H3N2[a]	23 (-5 – 44)
VEBIS PC pooled adjusted VE against B[a,b]	67 (54 – 77)
Proportion H1N1/H3N2/B in NL (sentinel)	0.69/0.28/ 0.03

Footnote: *PC = primary care, VE = vaccine effectiveness, ILI = influenza-like illness, CI = confidence interval.*

[a] *From table 3.3.*

[b] *Due to low number of cases in the age group 65 years and older, adjusted VE estimation was not attempted for this age group. Instead, the VEBIS PC pooled adjusted VE against B for the 'target group' is used.*

Figure 3.15 Impact estimations for ILI GP consultations caused by influenza virus, 2018/19 – 2019/20 and 2022/23. Blue bars represent the estimated number of observed cases. Orange bars represent the estimated number of cases averted by the 2022 influenza vaccination campaign, with 95% CIs. (Sources: Nivel Primary Care Database, VEBIS primary care study and NIC location RIVM).



Footnote: *Due to probable altered healthcare-seeking behaviour during the COVID-19 pandemic, the impact was not estimated for the 2020/2021 and 2021/2022 season.*

Chapter 4
RS-Virus infection

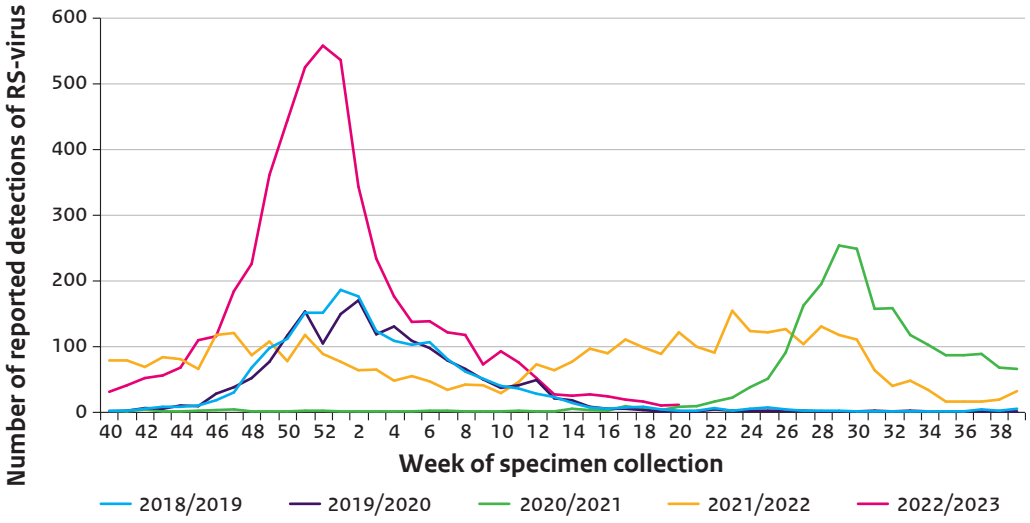
Authors: Anne Teirlinck, Femke Jongenotter, Adam Meijer
Contributors: Marit de Lange, Mariëtte Hooiveld, Daphne Reukers, Liz Jenniskens, Michiel van Boven, Puck van Kesteren

4.1 Keypoints

- The absolute number of RSV detections as reported by the virological laboratory surveillance was much higher than in previous seasons, the timing of the peak (week 52 of 2022) was within the range of the timing in pre-pandemic seasons.
- The peak number of hospitalizations of children <2 years of age (n=100) in 33 hospitals of the SPREAD study was reported in week 51 2022, and was lower than in the summer peak of 2021 (n=163).
- The percentage of samples collected by sentinel GPs from patients with acute respiratory infections (ARI), that was positive for RSV peaked in week 46 of 2022 (18/73 = 25% of samples positive).
- RSV-B was dominant over the entire season of 2022/2023, in all age groups.
- The percentage of RSV positive ARI specimens taken by the GPs was highest in children in the age 0-1 years, where 32% of the sampled children of 0-1 years was positive for RSV, followed by age group 2-4 years (13%) and >65 years (11%). The percentage was lowest in the age groups 5-64 years (range 4 – 8%).

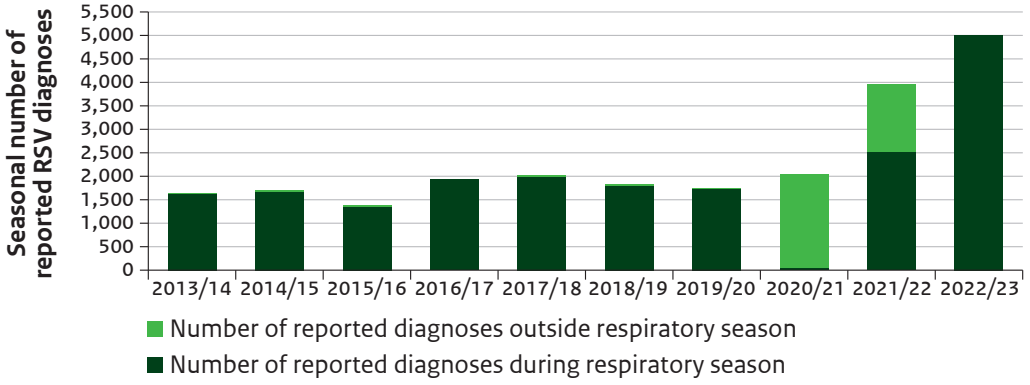
4.2 Tables and figures

Figure 4.1 Number of weekly reported RSV detections in the virological laboratory surveillance for the seasons 2018/2019 to 2022/2023 (Source: virological laboratory surveillance, NWKV).



Footnote: *NWKV = Dutch Working Group for Clinical Virology of the Dutch Society for Medical Microbiology (NVMM). Please note that since testing practices are likely changed since the COVID-19 pandemic, the number of RSV diagnoses and subsequent outcomes on onset and duration of the RSV season should be interpreted with caution.*

Figure 4.2 Seasonal number of reported RSV detections in the virological laboratory surveillance within the respiratory season (week 40 through week 20) and outside the respiratory season (week 21 through week 39) of 2013/2014 to 2022/2023 (Source: virological laboratory surveillance, NWKV).



Footnote: *RSV = respiratory syncytial virus. For the 2022/2023 season, numbers for outside the respiratory season (week 20 through 39 2023) are not yet available.*

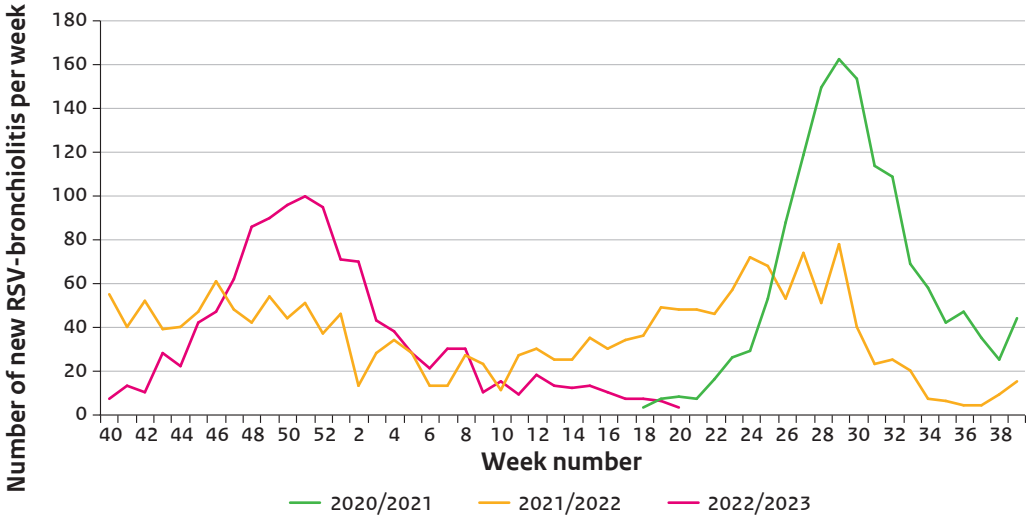
Table 4.1 RSV seasonal trends in the virological laboratory surveillance for the period 2013/2014 - 2022/2023 (through week 20): season onset and duration, epidemic intensity, and peak. Week is week of laboratory diagnosis report. Thresholds for the epidemic period and intensity are defined by MEM.

Season	Onset week (week number)	Season duration (N weeks)	Above medium intensity level (N weeks)	Above high intensity level (N weeks)	Above very high intensity level (N weeks)	Peak	
						Timing (week number-year)	RS-virus diagnoses (N)
2013/2014	48	17	0	0	0	1-2014	134
2014/2015	49	18	0	0	0	8-2015	162
2015/2016	48	19	0	0	0	4-2016	114
2016/2017	45	16	4	0	0	52-2016	199
2017/2018	46	19	2	0	0	1-2018	192
2018/2019	47	16	2	0	0	1-2019	186
2019/2020	46	19	1	0	0	2-2020	170
2020/2021	23	Continued into 2021/2022	Summerpeak: 6	2	2	29-2021	254
2021/2022	Continuing since 2020/2021	64	Winterpeak: 0	0	0	47-2021	120
			Summerpeak: 1	0	0	23-2022	154
2022/2023	39	26	10	8	6	52-2022	560

[a] *at date of final data extraction: 31-05-2022.*

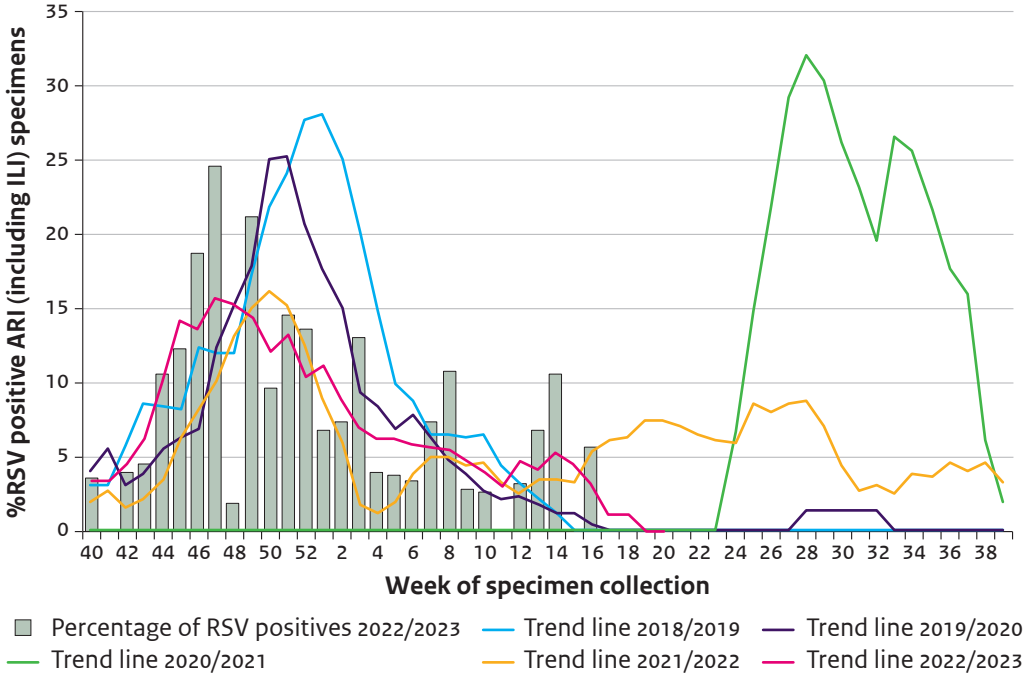
Note: *The MEM epidemic and intensity thresholds (Lozano 2018) were based on pre-pandemic data and therefore similar to the thresholds that were set for season 2020/2021 (based on data of seasons 2010/2011-2019/2020) and were as follow: pre-epidemic threshold: 21; post-epidemic threshold: 31; medium intensity: 150, high intensity: 212; very high intensity; 248. Since testing practices are likely changed since the COVID-19 pandemic, the number of RSV diagnoses and subsequent outcomes on onset and duration of the RSV season should be interpreted with caution and are therefore displayed in a grey font.*

Fig 4.3: Hospital admission for RSV bronchiolitis in children younger than 2 years old in 33 hospitals reporting to the SPREAD study. Week 18/2021 until week 20/2023 (Source: UMCU).



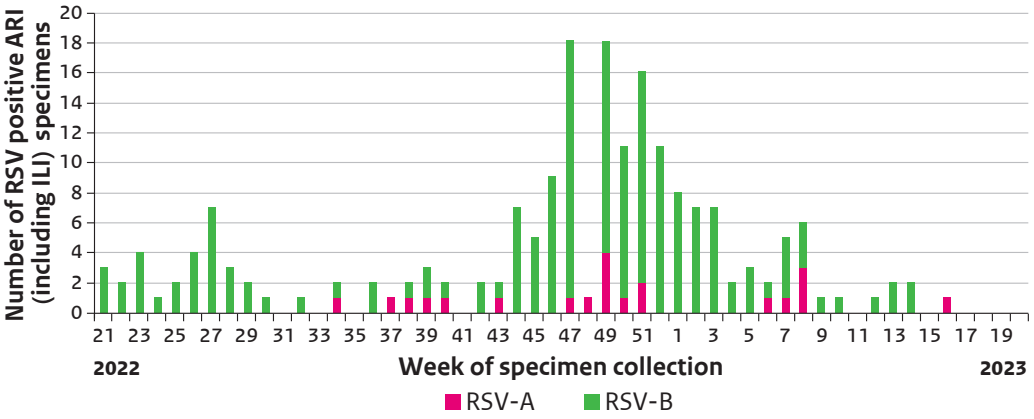
Footnote: *This figure displays the hospital admissions over the whole period since the start of this surveillance in week 18 of 2021, until the end of the reporting period (week 20/2023). This graph shows the admissions as reported by 33/42 hospitals that participated in the SPREAD study, selected for consistent data reporting over the full period to allow for visualization of the trend in time. Date of final data extraction: 21-06-2023.*

Figure 4.4 Percentage of specimens from patients with influenza-like illness (ILI) and other acute respiratory infections (ARI) positive for RSV taken by sentinel GPs during the 2022/2023 respiratory season (week 40 of 2022 through week 20 of 2023) (Source: RIVM; Nivel Primary Care Database).



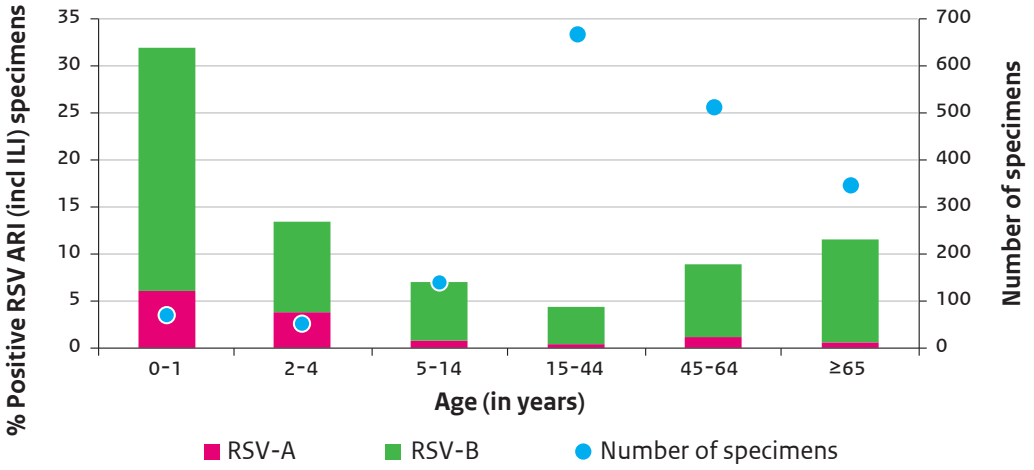
Footnote: *Trend lines indicate a 5-week moving average. ILI= influenza-like illness; ARI = acute respiratory infection; GP = general practitioner; RSV = respiratory syncytial virus.*

Figure 4.5 Number 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 2022/2023 (week 21 of 2022 through week 20 of 2023). (Source: Nivel Primary Care Database, RIVM).



Footnote: *Because of the continuing out-of-season circulation of RSV, this figure displays the characteristics from week 21 of 2022 onwards instead of the usual week 40 of 2022.*

Figure 4.6 Percentage of RSV-A and RSV-B positive specimens within the age group, from patients with ILI and other ARI, and the number of tested specimens, sentinel influenza surveillance during the respiratory season of 2022/2023 (week 40 of 2022 through week 20 of 2023), displayed for six age groups. (Source: Nivel Primary Care Database, RIVM).



Chapter 5
Other respiratory infections reported in the weekly virological surveillance

Authors: Daphne Reukers

5.1 Key points

- SARS-CoV-2 detections are not yet included in the general weekly virological surveillance (see Chapter 2 COVID-19). For the trends in the virological surveillance for influenza see Chapter 3 and for RSV see Chapter 4.
- The total number of rhinovirus (n=5,924), hMPV (n=1,900), parainfluenza virus type 3 (n=932) and adenovirus (n=2,560) detections in 2022/2023, as well as the peak in detections per week was the highest reported compared to previous seasons.
- The total number of parainfluenza virus type 1 detections (n=254) was much higher than the seasons 2018/2019, 2020/2021 and 2021/2022 (average of 28 detections), but lower than season 2019/2020 (n=343).
- The peak in detections of hMPV and the first peak in detections of parainfluenza virus type 1 was earlier and the peaks were considerably higher than previous seasons (with the exception of season 2019/2020 for parainfluenza virus type 1).
- The total number of seasonal coronaviruses (OC43, 229E, NL63 and HKU1; excluding SARS-CoV-2) (n=628), parainfluenza virus type 2 (n=126) and type 4 (n=144), *C. pneumoniae* (n=14), *M. pnuemoniae* (n=139) and bocavirus (n=263) detections and the peak in detections per week of these pathogens in 2022/2023 was within the range of the total number of detections in the last four seasons.

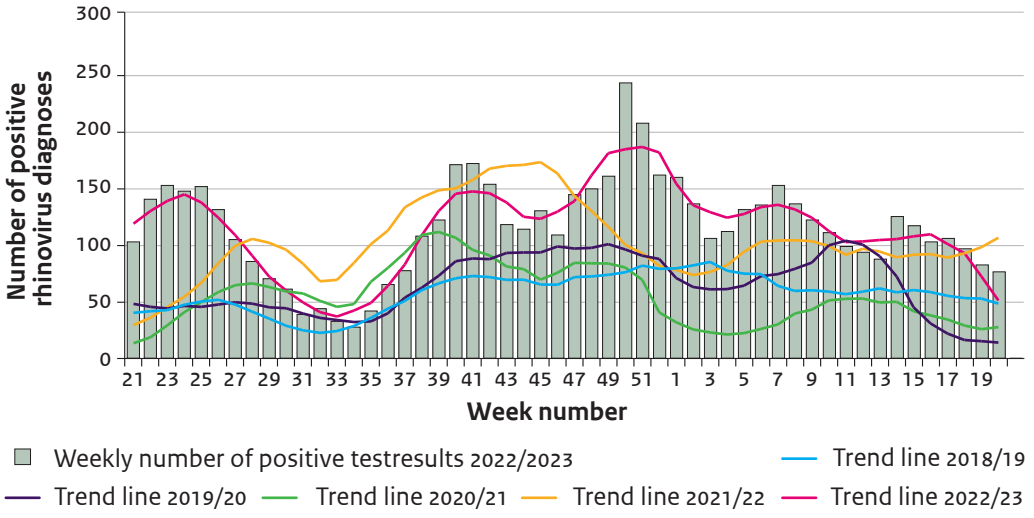
5.2 Tables and figures

Table 5.1 Number of reported positive tests for rhinovirus, *Mycoplasma pneumoniae*, human metapneumovirus, seasonal coronaviruses (excluding SARS-CoV-2), parainfluenza virus types 1-4, *Chlamydia pneumoniae*, adenovirus and bocavirus in the virological laboratory surveillance for the season 2018/2019 – 2022/2023. (Source: Virological laboratory surveillance, NWKV).

	Number of positive diagnoses										
Year	Rhinovirus	hMPV	Coronavirus (excl. SARS-CoV-2)	PIV type 1	PIV type 2	PIV type 3	PIV type 4	*C. pneumoniae*	*M. pneumoniae*	Adenovirus	Bocavirus
2018/19	2,945	819	703	42	180	654	139	12	292	1,649	196
2019/20	3,248	694	572	343	54	315	177	23	486	1,545	148
2020/21	2,874	13	243	24	20	380	19	9	158	862	147
2021/22	5,237	1,058	572	18	140	626	349	6	114	2,217	320
2022/23	5,924	1,900	628	254	126	932	144	14	139	2,560	263

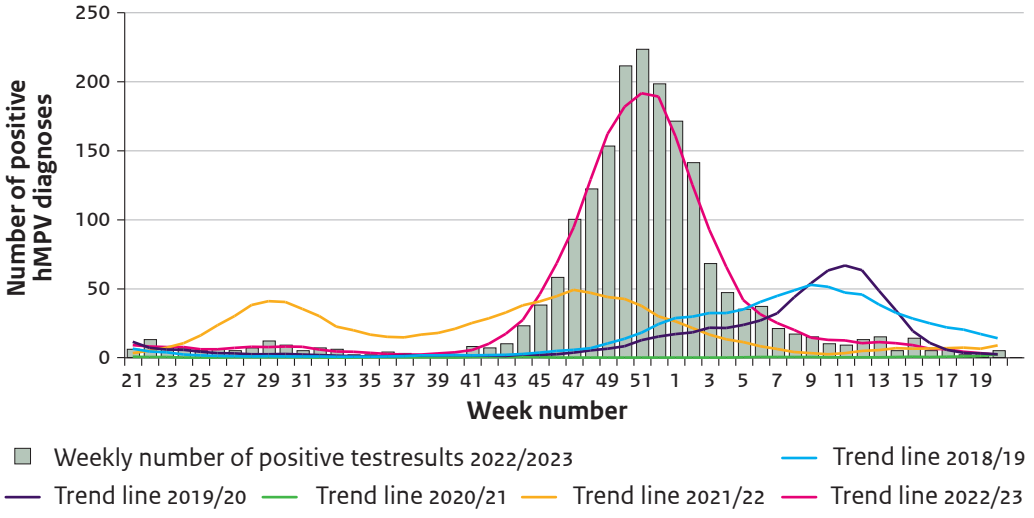
Footnote: *M. pneumoniae = Mycoplasma pneumoniae; hMPV= human metapneumovirus; PIV= parainfluenza virus; C. pneumoniae = Chlamydia pneumoniae ; NWKV = Dutch Working Group for Clinical Virology of the Dutch Society for Medical Microbiology (NVMM).*

Figure 5.1 Number of weekly reported positive test results for rhinovirus in the virological laboratory surveillance for the season 2022/2023 and the trend lines* for the season 2018/2019 – 2022/2023.



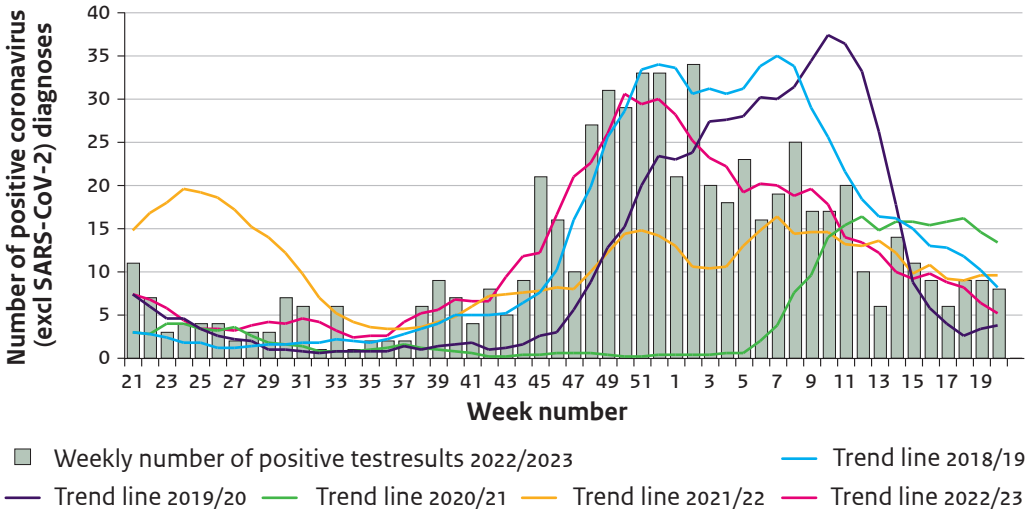
*5-week moving average

Figure 5.2 Number of weekly reported positive test results for human metapneumovirus in the virological laboratory surveillance for the season 2022/2023 and the trend lines* for the season 2018/2019 – 2022/2023.



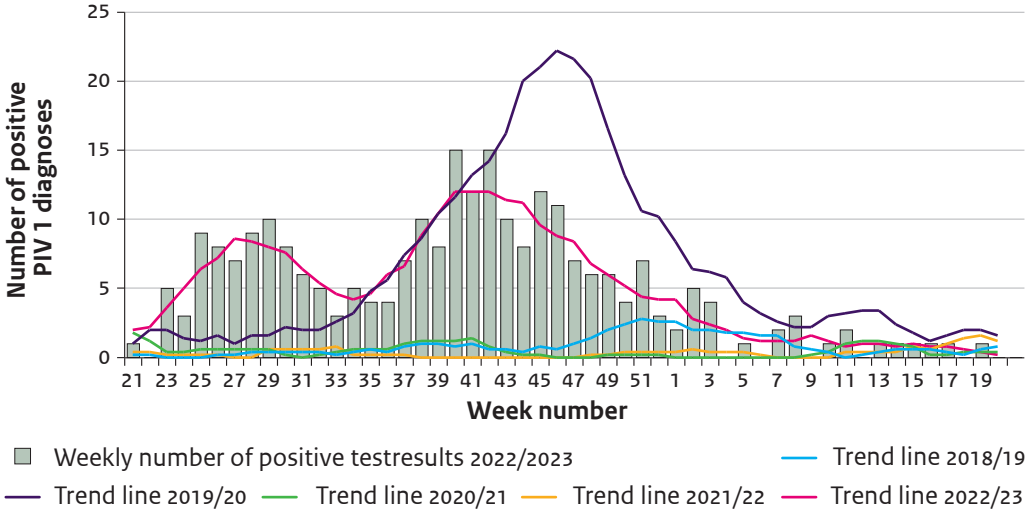
*5-week moving average

Figure 5.3 Number of weekly reported positive test results for seasonal coronaviruses (excluding SARS-CoV-2) in the virological laboratory surveillance for the season 2022/2023 and the trend lines* for the season 2018/2019 – 2022/2023.



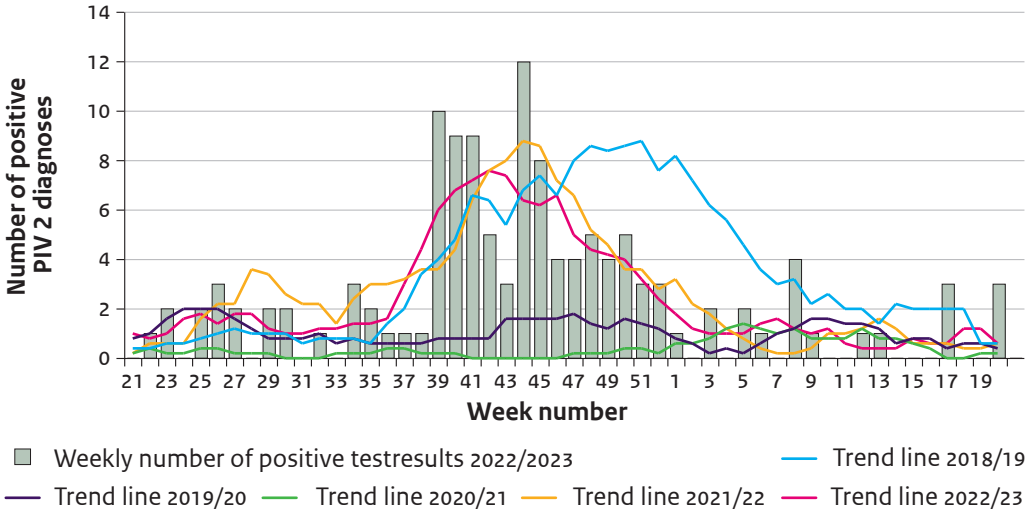
*5-week moving average

Figure 5.4 Number of weekly reported positive test results for parainfluenza virus type 1 in the virological laboratory surveillance for the season 2022/2023 and the trend lines* for the season 2018/2019 – 2022/2023.



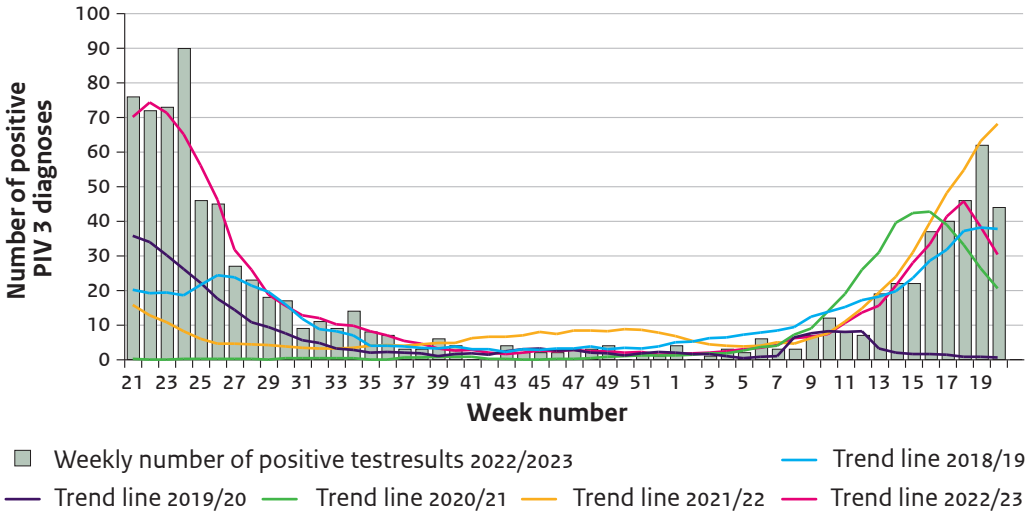
*5-week moving average

Figure 5.5 Number of weekly reported positive test results for parainfluenza virus type 2 in the virological laboratory surveillance for the season 2022/2023 and the trend lines* for the season 2018/2019 – 2022/2023.



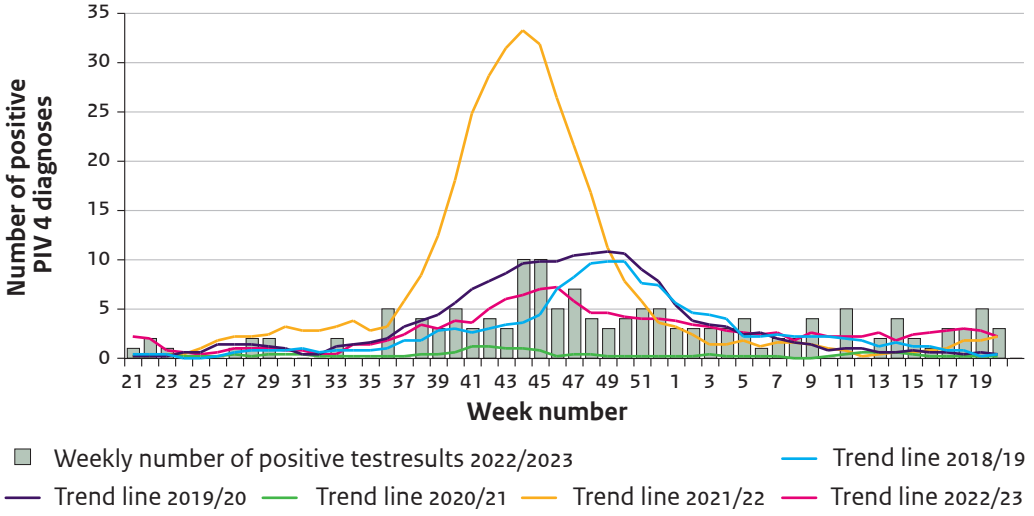
*5-week moving average

Figure 5.6 Number of weekly reported positive test results for parainfluenza virus type 3 in the virological laboratory surveillance for the season 2022/2023 and the trend lines* for the season 2018/2019 – 2022/2023.



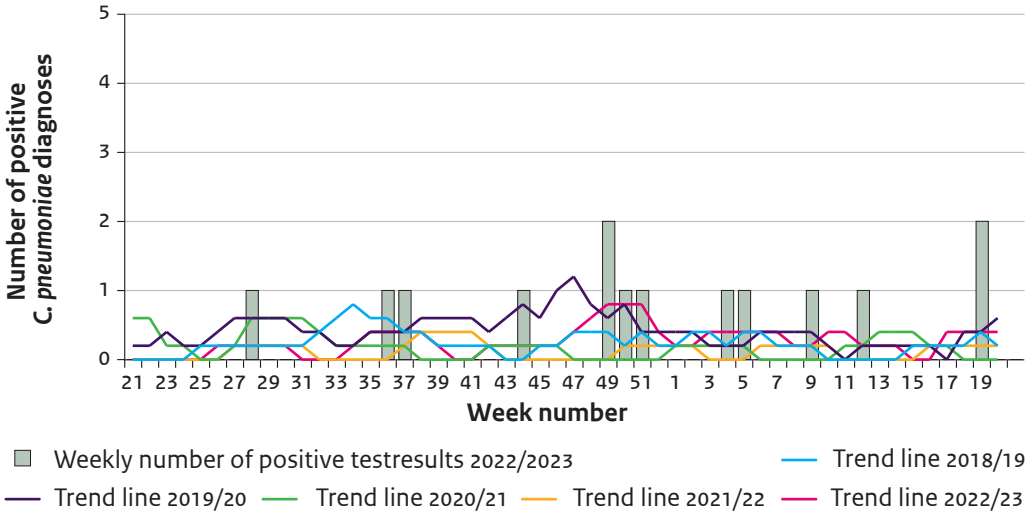
*5-week moving average

Figure 5.7 Number of weekly reported positive test results for parainfluenza virus type 4 in the virological laboratory surveillance for the season 2022/2023 and the trend lines* for the season 2018/2019 – 2022/2023.



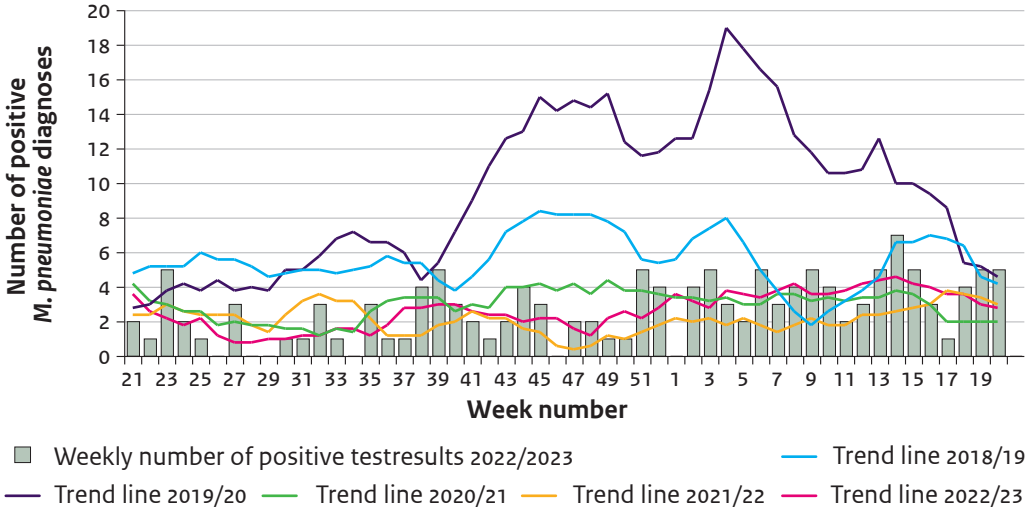
*5-week moving average

Figure 5.8 Number of weekly reported positive test results for *Chlamydia pneumoniae* in the virological laboratory surveillance for the season 2022/2023 and the trend lines* for the season 2018/2019 – 2022/2023.



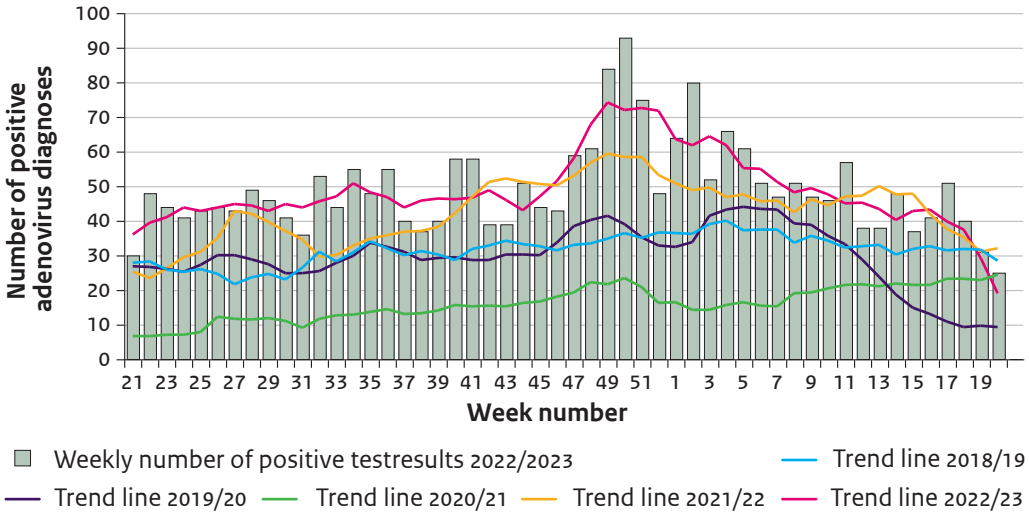
*5-week moving average

Figure 5.9 Number of weekly reported positive test results for *Mycoplasma pneumoniae* in the virological laboratory surveillance for the season 2022/2023 and the trend lines* for the season 2018/2019 – 2022/2023.



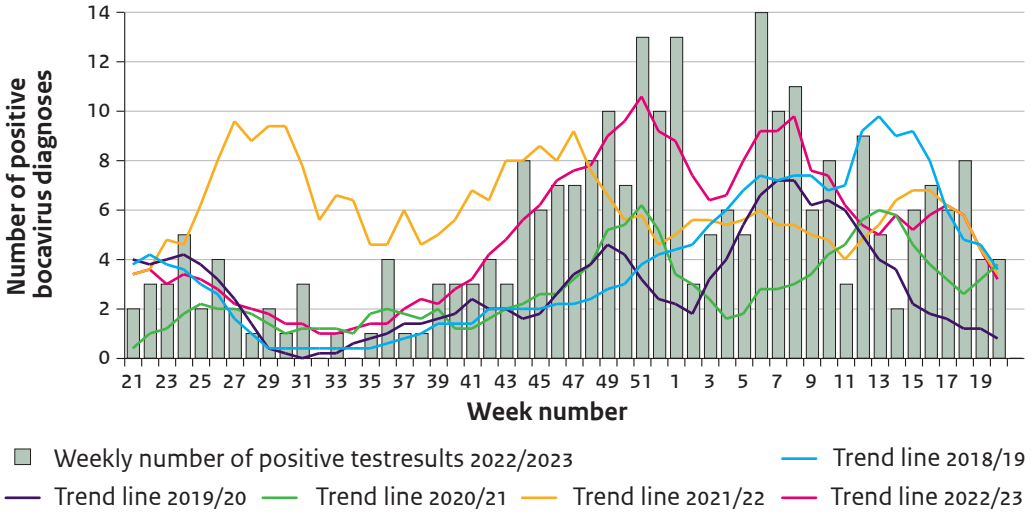
*5-week moving average

Figure 5.10 Number of weekly reported positive test results for adenovirus in the virological laboratory surveillance for the season 2022/2023 and the trend lines* for the season 2018/2019 – 2022/2023.



*5-week moving average

Figure 5.11 Number of weekly reported positive test results for bocavirus in the virological laboratory surveillance for the season 2022/2023 and the trend lines* for the season 2018/2019 – 2022/2023.



5-week moving average

Chapter 6
Mortality and burden of respiratory infectious diseases in the Netherlands

6.1 Weekly mortality monitoring

Author: Liselotte van Asten
Contributors: Marit de Lange, Ursula de Bruijn-van Leijden, Lina van der Loo, Lenny Stoeldraijer, Carel Harmsen

6.1.1 Key Points

- An average of 3,124 deaths occurred weekly in the Netherlands over the past five years, 2018-2022.
- Excess mortality was observed in 23 of the 33 weeks of the 2022/2023 respiratory season, defined as week 40 of 2022 to week 20 of 2023 (or in 29 weeks of the total 2022/2023 season from week 21 2022 to week 20 of 2023).
- There were 3 periods of excess mortality from week 21 2022 to week 20 2023 (the latter two periods of excess were mostly within the 2022/2023 respiratory season):
  - Week 25-35 2022 - mostly overlapping with omicron covid period 6c which was week 23-34.
  - week 39-44 2022 - mostly overlapping with omicron covid period 6d which was week 35-47.
  - week 47 2022 – week 13 2023 (except week 9) - in which the influenza epidemic and COVID-19 periods 6e and 6f overlapped.
- Cumulated excess mortality was 2,965 during COVID period 6c (week 23-34 2022).
- Cumulated excess mortality was 6,683 during the 14 influenza epidemic weeks (weeks 50 2022 - week 11 of 2023), within the ongoing COVID-19 epidemic (COVID-19 periods 6e and 6f). In the five influenza epidemics before the COVID-19 introduction, excess deaths averaged 6,439 per influenza epidemic (2014/2015 – 2018/2019).
- Cumulated excess mortality during the entire respiratory season (weeks 40 to 20 of 2022/2023) was 10,096. This is lower than in the 3 previous respiratory seasons (since the introduction of COVID-19) with 12,390, 14,715, and 13,903 excess deaths, but higher than in the five pre-COVID-19 respiratory seasons (7,205 on average from 2014/2015 – 2018/2019).
- Mortality peaked at 4,132 deaths in week 52, which is 920 above expected baseline level.

- This is a bit lower than the peak in the previous winter (4,312 deaths in week 48) but a bit higher than the peak one winter earlier (4,092 deaths in week 1 2021).
- Excess mortality during the 2022/2023 winter season was mostly observed in age groups 55 years and older.

6.1.2 Figures

Figure 6.1 Weekly number of deaths from 2014 to 2023 by date of death (notified within three weeks from date of death) (Source: Statistics Netherlands).

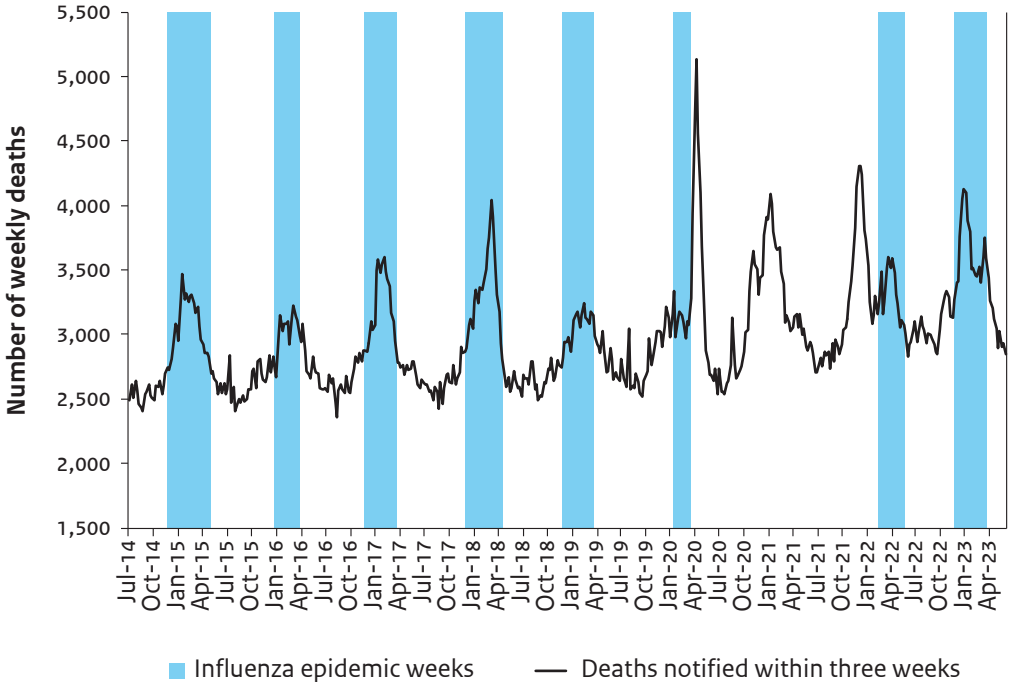
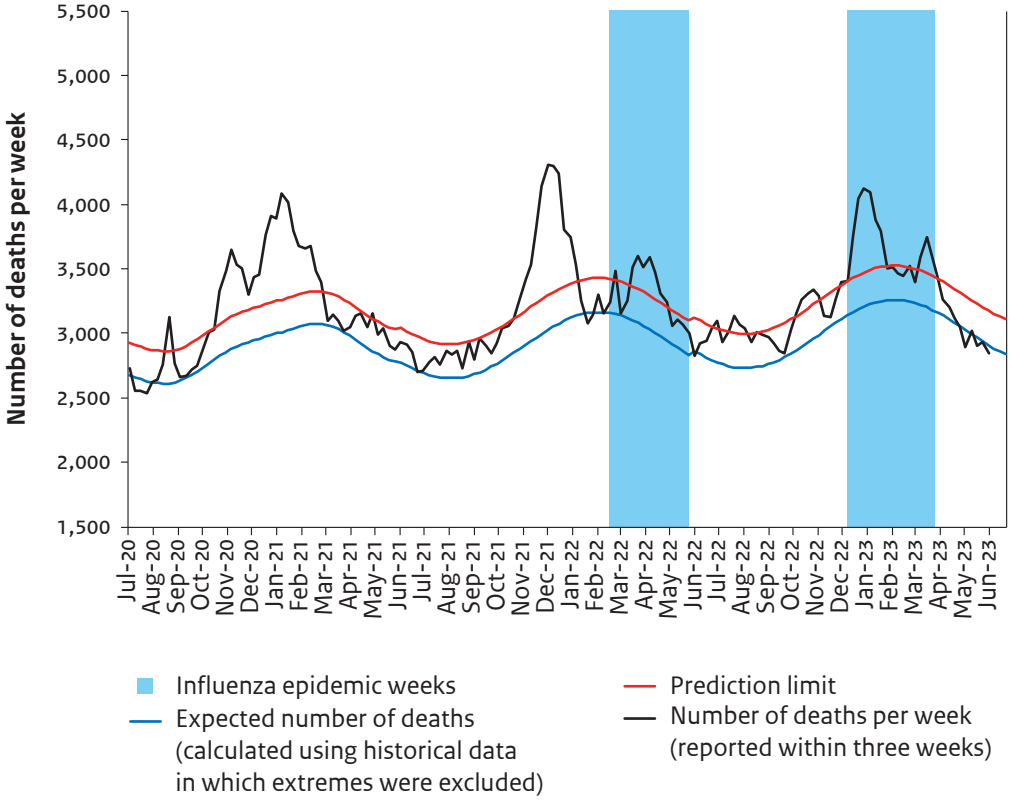


Figure 6.2 Observed and expected ('baseline') weekly number of deaths, July 2020 to June 2023 (Source: Statistics Netherlands).



6.2 Burden of COVID-19 and influenza

Authors: Scott McDonald, Pieter de Boer
Contributors: Daphne Reukers, Marit de Lange

6.2.1 Key points

- The respiratory infectious disease with the highest disease burden in 2022 was COVID-19 with an estimated 93,800 DALY (91,600-96,100), followed by influenza with an estimated 9,400 DALY (8,600-10,200)
- The burden of COVID-19 is for 93% is due to premature mortality caused by COVID-19. The presented burden estimate of COVID-19 represents an underestimation of the actual burden since long-term consequences of the disease are not taken into account. Furthermore, there is insufficient data about the epidemiology and long-term impact of COVID-19 at this time to properly estimate the DALY/100 cases disease burden measure.

6.2.2 Tables and figures

Table 6.1 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 2018 to 2022 (season 2018/2019 to 2022/2023 for influenza) in the Netherlands in order of highest to lowest average DALY/year in 2022.

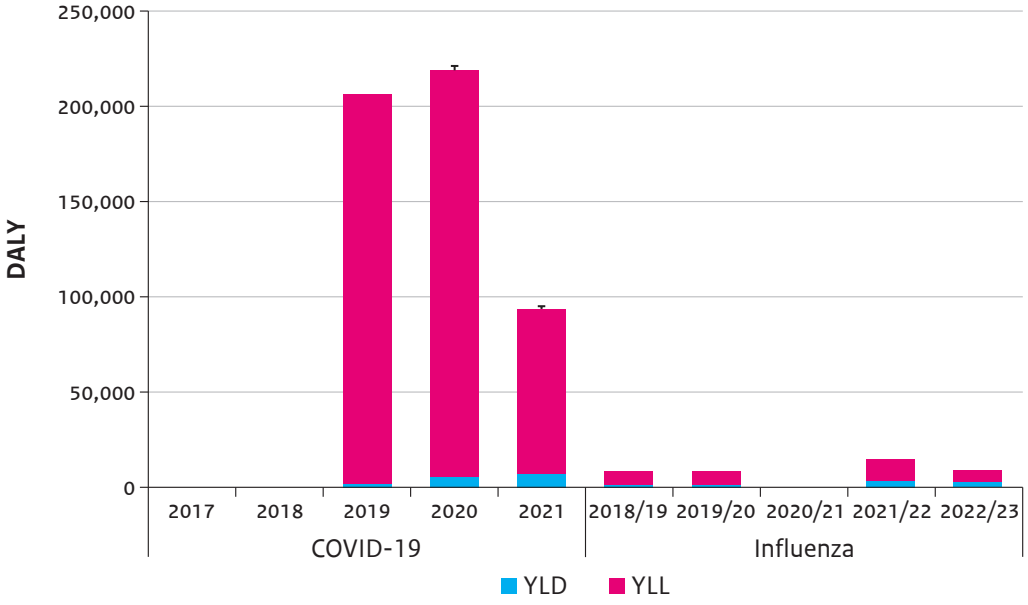
Disease	YLD/ year	YLL/ year	DALY/ year	DALY/ 100 cases [a,b]	Annual acute infections
COVID-19					
2018	-	-	-	-	-
2019	-	-	-	-	-
2020	1,600 (1,500-1,700)	205,000 (202,000-209,000)	207,000 (204,000-210,000)	-	-
2021	5,300 (5,300-5,400)	214,000 (210,000-217,000)	219,000 (215,000-223,000)	-	-
2022	7,000 (6,900-7,100)	86,800 (84,600-89,200)	93,800 (91,600-96,100)	-	-
Influenza					
2018/2019	1,400 (1,300-1,500)	4,200 (3,800-4,800)	5,600 (5,100-6,200)		429,000
2019/2020	1,400 (1,300-1,500)	3,600 (3,200-4,000)	4,900 (4,500-5,400)		412,000
2020/2021 [c]	-	-	-		-
2021/2022	3,500 (3,300-3,700)	11,500 (9,900-13,300)	15,000 (13,300-16,900)		1,114,000
2022/2023	2,600 (2,500-2,800)	6,700 (6,000-7,500)	9,400 (8,600-10,200)	1 (1-1)	822,000

[a] *DALY/ 100 cases is only shown for 2022/2023 since this measure is a characteristic of the disease and is independent of time.*

[b] *YLL estimates for all seasons have been revised using a statistical modelling approach for estimating case-fatality ratios, that takes into account the differential severity of infection per influenza (sub)type and the distribution of sub(type) circulating in the specific season (McDonald, Teirlinck et al. 2023).*

[c] *Since there were no influenza cases reported by the NIVEL sentinel GP practices during the 2020/2021 respiratory season, the influenza burden could not be calculated for this season only.*

Figure 6.3 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 2017-2022 (seasons 2017/2018 through 2022/2023 for influenza, but omitting 2020/2021).



Footnote: *Error bars indicate 95% confidence intervals.*

Chapter 7
Background and methods for respiratory surveillance

7.1 Respiratory season, respiratory year and calendar year

The aim of this annual report is to describe the surveillance of COVID-19, 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 2022/2023 is limited to the respiratory season to allow a timely reporting. Respiratory infections may occur outside the respiratory season to a limited extend.

7.2 Background on COVID-19, Influenza and RSV

COVID-19

COVID-19 is the disease caused by SARS-CoV-2 viruses. The disease can cause respiratory symptoms and fever, and in severe cases it leads to shortness of breath. SARS-CoV-2 was declared as a public health emergency of international concern (PHEIC) by the WHO on the 30th of January 2020. In February 2023, the Outbreak Management Team (OMT) of the Netherlands declared that the endemic phase for the Omicron subvariants of SARS-CoV-2 was reached. On the 5th of May 2023, the WHO declared COVID-19 officially not a PHEIC anymore. After SARS-CoV-2 Wildtype, several Variants of Concern (VoC) were declared by the WHO (Alpha, Delta and Omicron). Since January 2022, different subtypes were established for the Omicron variant that cause COVID-19. The COVID-19 surveillance in this report includes community-based surveillance (Infectieradar), notifications of SARS-CoV-2 infections, hospitalisations and COVID-19 mortality reported by CBS. Self-reported COVID-19-like complaints and positive SARS-CoV-2 test results were weekly reported by participants of Infectieradar. Notification of SARS-Cov-2 positive test results by laboratories and physicians to the Public Health Services (PHS) were mandatory until the 1st of July 2023. Hospitalisations were received through the NICE foundation which registered all positive SARS-CoV-2 infections in by hospital admissions (including ICU). For more information about COVID-19 vaccination coverage, see the annual report (van Lier, Hament et al. 2023).

Influenza

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, usually 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, which are the subtypes currently causing seasonal epidemics. Influenza type B viruses are divided into genetic lineages based on their gene coding for the HA. While two influenza B virus lineages (B/Yamagata/16/88 and B/Victoria/2/87) have co-circulated, B/Yamagata-lineage circulation has not been confirmed since March 2020 (Paget, Caini et al. 2022). 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. The influenza surveillance in this report includes virological laboratory surveillance and GP sentinel surveillance. The ILI surveillance performed by sentinel general practitioners (GPs) of the Nivel Primary Care Database 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. The National Influenza Center (NIC) is a collaboration between RIVM, Nivel and the Erasmus Medical Center (Erasmus MC). A large number of hospital laboratories in the Netherlands send in influenza virus samples for which the type, subtype or lineage and genetic characteristics are determined in order to see whether the vaccines also match the circulating viruses.

RSV

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 and causing outbreaks in elderly care facilities (Meijer, Overduin et al. 2013; Shi, Denouel et al. 2020). RSV is subdivided in RSV-A and RSV-B, based on the different antigenic properties of their attachment glycoprotein G. The RSV surveillance in this report includes virological laboratory surveillance, GP sentinel surveillance, GP primary care surveillance of bronchiolitis and hospital surveillance. Since early May 2021, the Wilhelmina Children's Hospital (WKZ) of UMC Utrecht weekly registers the number of (RSV-)bronchiolitis admissions of children below 2 years of age in 45 hospitals in Netherlands. This data is collected and analysed in the context of the SPREAD-study, which aims to compare characteristic of children being admitted during earlier winter epidemics with those being admitted since summer 2021, and is also used for modelling purposes. RIVM can use the aggregated data for RSV surveillance, to get a broader perspective on RSV circulation, both in mild and in severe patients. In recent years, efforts have been made to develop drugs and vaccines to prevent children from becoming seriously ill from an infection with RSV. The Ministry of Health, Welfare and Sport asked the Health Council of the Netherlands to issue

advice on these products. To support this advice, RIVM gathered background information for the Health Council.

7.3 Data sources

Infectieradar
The community-based surveillance system, Infectieradar, has been operational since November 2020. This platform provides information on self-reported respiratory symptoms in the general population. 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. It is 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 in humans in the Netherlands. Infectieradar has been adapted to collect additional information on trends and symptoms related to COVID-19. The ILI incidence is determined on the basis of a uniform case definition. Therefore, data can be compared between countries participating in InfluenzaNet. In the fall of 2022 (starting week 40 2022), Infectieradar was expanded with a self-test study. Participants in this study may be asked to take a nose and throat sample if they have completed a corona self-test. The RIVM investigates whether this sample contains the coronavirus SARS-CoV-2, an influenza virus or another virus causing a cold.

Nivel Primary Care Database
Nivel (the Netherlands institute for health services research) holds the integral monitoring and information services for primary care, called 'Nivel Primary Care Database' (Hasselaar, 2021). The Nivel Primary Care Database holds longitudinal data recorded in electronic medical files by 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 data in electronic medical records from about 390 participating general practices spread over the country.
- In the 2022/2023 respiratory season, the coverage was about 1.75 million persons (9% 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 (Hasselaar J 2021).
- 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 on influenza virus, RSV, rhinovirus, enterovirus, since February 2020, SARS-CoV-2 and since January 2021 parainfluenza virus types 1-4, human metapneumovirus and human seasonal coronaviruses. The number of sentinel general practices taking part in the virological respiratory surveillance has been increasing since the end of 2021, from 40 tot more than 100 practices.

National sentinel surveillance network for infectious diseases 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 health care from elderly care physicians. The nursing homes participating in this network serve as sentinels for the national surveillance of infectious diseases in nursing homes. In the 2022/2023 respiratory year, 18 locations from 9 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 thus 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.

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 are asked to report these data. These data do not always contain background information concerning patient status, clinical data or origin of specimen (primary or hospital care). The laboratories report daily or weekly 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 PHS, because people may be tested more than once and positive laboratory results are reported more rapidly than disease notifications.

Osiris
According to Dutch legislation, COVID-19 is a notifiable disease. Medical doctors and medical-microbiological laboratories notify cases to the PHS, who subsequently report these to the RIVM via the online registration program Osiris. Osiris is a dynamic system and due to corrections and additions of the PHS, 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.

CoronIT
As of the 8th of February 2022, the main data source of COVID-19 notifications and performed tests is CoronIT. This system registers the performed tests and positive tests in the PHS test streets. Afterwards, the positive test results are transferred to a second PHS system, HPZone. In HPZone patient information is registered which is communicated to the RIVM through Osiris. Due to the high number of notifications, positive test results were directly communicated to the RIVM from CoronIT. Notifications that are part of the sample of source- and contact-tracing and notifications of healthcare institutions are still reported through HPZone and Osiris.

NICE
The National Intensive Care Evaluation (NICE) foundation provides the continued and complete registration of all available data of participating ICU departments, with the aim to monitor and optimize the quality of ICU care. During the COVID-19 pandemic, they registered the numbers of new SARS-CoV-2 hospital admissions (including ICU admissions). As of week 4 of 2022 NICE started to differentiate between the reasons of hospital admission among patients with a positive test for SARS-CoV-2. There were four categories: 1) Hospital admission due to COVID-19, 2) Hospital admission is a combination of COVID-19 and another (underlying) condition, 3) Hospital admission is not due to COVID-19 and 4) Reason of hospital admission is (still) unknown.

SPREAD-Study (UMCU)
Paediatricians or research nurses of 45 participating hospitals, distributed over all regions in the Netherlands, are asked to weekly share the following data with UMCU:
- Weekly number of new bronchiolitis-related admissions in the patient population
- Weekly number of bronchiolitis-related admissions tested for RSV in the patient population
- Weekly number of RSV-positive admissions in the patient population.

The patient population is defined as children younger than 2 years old. In this report, the data from 33 out of these 45 hospitals are reported, selected on the basis of consistent data reporting over the full period of week 18/2021 until week 20/2023, to enable a description of the trend over this period.

Death notification data, Statistics Netherlands (CBS)
The Dutch weekly mortality monitoring system monitors the number of deaths reported nationwide (population size of 17.8 million on January 2023) from all causes, as information on cause of death is not available in real-time. In the Netherlands, deaths are notified to municipalities and then reported to CBS, which collects and monitors all vital statistics for the Netherlands. 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. The death notification data is checked for the presence of any excess all-cause mortality (i.e. mortality

levels above a pre-defined threshold). Excess mortality gives an indication of the impact of any expected and unexpected events that potentially affect population health. Examples of such events are heat waves, cold snaps, COVID-19, or seasonal influenza epidemics for which the morbidity and mortality burden varies due to variations in the circulation of influenza (sub)types.

7.4 Data analysis

Influenza-like-illness (ILI)
Acute respiratory infections (ARI) and the subgroup of influenza-like illness (ILI) are clinical syndromes caused by a range of viruses and bacteria. However, the case definition for ILI is more specific for influenza virus infection. ILI incidence is estimated using three data sources: 1) Infectieradar, 2) Nivel Primary Care Database - sentinel GP practices and 3) SNIV nursing homes. These three data sources use different ILI case definitions.

For the first time, we also present the ILI incidence from the community-based surveillance system Infectieradar in this annual report. The case definition of ILI used by infectieradar is in accordance with 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

In the Nivel Primary Care Database - sentinel GP practices, ILI is defined in accordance with 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 (Jansen, Hendriksen et al. 2022). For chapter 2.1 and 3, the preliminary weekly numbers as reported during the season are used. Before the COVID-19 pandemic, an influenza epidemic was declared based

on the influenza-like illness (ILI) incidence in primary care in combination with the virological results obtained from the Nivel/RIVM sentinel practice surveillance system. However, in the 2022/2023 respiratory season, people with respiratory symptoms may have performed a COVID-19 self-test, which could have caused a reduction in GP consultations. Therefore, because the ILI GP consultation rate was lower than before the COVID-19 pandemic and – due to changes in healthcare-seeking behaviour – not directly comparable with previous seasons, a combination of several surveillance systems were taken into account to monitor the influenza epidemic this season.

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. As for Infectieradar, the ILI ECDC case definition was used to monitor the ILI incidence in this system.

Acute respiratory infections (ARI)
We also present the ARI (including ILI) incidence from the community-based surveillance system Infectieradar in this annual report. Any participant who coughs, has a runny nose, has shortness of breath or has a sore throat is considered an ARI case.
Weekly numbers on GP-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 the Nivel Primary Care Database. The weekly ARI numbers therefore exclude pneumoniae and COVID-19 consultations. 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.
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.

COVID-19-like illness
We only present the COVID-19-like illness incidence from the community-based surveillance system Infectieradar in this annual report. Any participant who has a fever, cough, shortness of breath or loss of smell and/or taste is considered an COVID-19-like case.

Bronchiolitis
Bronchiolitis mostly affects young children below 2 years of age and symptoms are similar to a common cold (mild fever, cough and runny nose), but can also worsen to wheezing and shortness of breath. Bronchiolitis is commonly caused by respiratory syncytial virus (RSV) among other viruses, such as human metapneumovirus (hMPV), rhinovirus and parainfluenza virus. Acute bronchitis and bronchiolitis is included in the registration by GPs (Nivel Primary Care Database). Weekly numbers of patients below 5 years old consulting their GP for bronchitis/bronchiolitis (ICPC code R78) are obtained from Nivel Primary Care Database. Weekly bronchitis/bronchiolitis consultation rates are calculated as the number of patients below 5 years old consulting their GP in a given week, divided by the total number of enlisted patients below 5 years old.

Pneumonia
Pneumonia is an infection of the lower respiratory tract with relatively 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). CAP is included in the registration by GPs (Nivel Primary Care Database) and in the SNIV nursing homes. Pneumonia data are obtained from the Nivel Primary Care Database, similar to acute respiratory infections described above and is defined as the weekly number of patients consulting their GP for pneumonia (ICPC code R81), regardless of being a new or already existing pneumonia episode. The total practice population of participating GP practices serves as the denominator. Pneumonia data are reported as lower respiratory tract infections (LRTI) and 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.

Influenza virus, RSV 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 and the self-sampled nose and throat samples from participants in Infectieradar. 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 the 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 are requested to take specimens (combined throat swabs and nose swabs) of ILI or other ARI patients. Since the 2021/2022 season, the GPs were instructed to swab at least the first two persons in the week with an acute respiratory infection (ARI), including at least:
- one ILI patient (according to the Pel-criteria)
- one child below the age of 10 with ILI or other ARI throughout the week.

With a maximum of five samples per GP per week.

The GP and Infectieradar specimens are analysed by NIC location RIVM for influenza viruses, RSV, rhinoviruses, enteroviruses, since February 2020, SARS-CoV-2, and since January 2021 parainfluenza virus types 1-4, human metapneumovirus and human seasonal coronaviruses. 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. Parainfluenza virus types 1-4, human metapneumovirus and human seasonal coronaviruses were added due to signals of increased circulation within and outside of The Netherlands despite the COVID-19 measures. 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.

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 characterisation
Whereas subtyping and lineage determination at RIVM are performed using RT-PCR assays, in the 2018/2019 season Erasmus MC changed 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 characterisation 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 will be completed after this report has been published.
A subset of influenza viruses are characterised genetically by sequence analysis of the haemagglutinin genome segment at RIVM. The genetic characterisation 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, genetic characterisation 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 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. The test 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 indicative of resistance to the polymerase inhibitor baloxavir are assessed in a subset of influenza virus positive clinical specimens by sequencing at NIC locations 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.

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. Number of diagnoses of 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.

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 appropriate 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 (InfluenzaNet data for 2016/2017 was used for seasons 2018/2019 through 2019/2020, as InfluenzaNet stopped in 2016/2017; (Friesema, Koppeschaar et al. 2009, Koppeschaar,

Colizza et al. 2017) for season 2021/2022 and 2022/2023, comparable data were extracted from Infectieradar), (iii) influenza positivity rate: number of positive tests and number tested, per age-group (from virological surveillance; see Chapter 4); and (iv) sensitivity of virological testing: estimated at 95-100%. 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/Infectieradar). Secondly, the number of averted cases was calculated from the estimated number of 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, Korevaar et al. 2022). 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 VEBIS 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.

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). The MEM 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 diagnoses 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. The MEM epidemic and intensity thresholds for seasons 2021/2022 and 2022/2023 were based on pre-pandemic data and therefore similar to the thresholds that were set for season 2020/2021 (based on data of seasons 2010/2011-2019/2020). Since testing practices are likely changed since the COVID-19 pandemic, the number of RSV diagnoses and subsequent outcomes on onset and duration of the RSV season should be interpreted with caution.

Determining excess mortality

Every Thursday the number of reported deaths, as provided by 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).

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).

We estimated the burden of influenza for respiratory seasons (week 40 to week 20) for the seasons 2017/2018 through 2021/2022. No time discounting was applied.

Because we had direct data on the incidence of severe and critical health outcomes and mortality due to COVID-19, we did not need to rely on estimated progression (or transitional) probabilities between health outcomes, as is the case for most of the other infectious diseases for which disease burden is routinely computed and reported in the Netherlands. The notified and reported cases of COVID-19 are directly used as input to estimate the burden of COVID-19. In short, the cumulative number of mild/moderate (symptomatic) infections is estimated by using OSIRIS data on positive tests adjusted for case ascertainment using behavioural data on the proportion of people who get tested, available per age-group and over time, given COVID-19 related symptoms. The number of severe and critical cases, which are defined by the number of non-ICU and ICU hospital admissions, is based on NICE data. The cumulative number of fatal cases in 2021 is published by CBS. However, there is insufficient information about the epidemiology and long-term impact of COVID-19 to estimate the disease burden in DALY/100 cases and compare this with the disease burden of other respiratory infections. In addition, it is still unclear what the long-term effects are of people with mild/moderate COVID-19 as well as for people with a more severe disease course. Since there is insufficient data to accurately calculate the long-term sequelae for COVID-19, the burden estimate of COVID-19 is based on the acute phase of the disease. For details on the parameter values to estimate the YLD, see the State of Infectious Disease 2019 (Lagerweij, Schimmer et al. 2021). To estimate YLL, remaining life expectancy tables were adopted from the GBD 2010 study (WHO 2013), to allow burden to be compared with that for the other respiratory infections.

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References

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.

Geismar C, Nguyen V, Fragaszy E, Shrotri M, Navaratnam AMD, Beale S, Byrne TE, Fong WLE, Yavlinsky A, Kovar J, Hoskins S, Braithwaite I, Aldridge RW, Hayward AC (2023). "Symptom profiles of community cases infected by influenza, RSV, rhinovirus, seasonal coronavirus, and SARS-CoV-2 variants of concern." *Sci Rep* **13**(1):12511.

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.

Hasselaar J. (2021). "Nivel Primary Care Database." Retrieved July 2022, from https://www.nivel.nl/en/nivel-zorgregistraties-eerste-lijn/nivel-primary-care-database.

Heins M, Korevaar J, Knottnerus B, Hooiveld M (2022). "Monitor Vaccinatiegraad Nationaal Programma Griepppreventie (NPG) 2021." Utrecht: Nivel.

Jansen T, Hendriksen J, Hooiveld M, Haitsma I, Wentink E, Baarda E, van der Burgh R and Korevaar J. (2022). "Peilstations jaarrapport 2019 en 2020. Nivel Zorgregistraties Eerste Lijn. Utrecht: Nivel, 2022." Retrieved July 2022, from https://www.nivel.nl/nl/publicatie/peilstations-jaarrapport-2019-en-2020-nivel-zorgregistraties-eerste-lijn.

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.

Lagerweij G, Schimmer B, Mooij S, Raven S, Schoffelen AF, de Gier B and Hahné S (2021). Staat van Infectieziekten in Nederland, 2019. State of Infectious Diseases in the Netherlands, 2019, Rijksinstituut voor Volksgezondheid en Milieu RIVM, 10.21945/rivm-2020-0048.

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

McDonald SA, Teirlinck AC, Hooiveld M, van Asten L, Meijer A, de Lange M, van Gageldonk-Lafeber AB and Wallinga J (2023). "Inference of age-dependent case-fatality ratios for seasonal influenza virus subtypes A(H3N2) and A(H1N1)pdm09 and B lineages using data from the Netherlands." *Influenza Other Respir Viruses* **17**(6): e13146.

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 CJ and Lopez AD (2013). "Measuring the global burden of disease." *N Engl J Med* **369**(5): 448-457.

Paget J, Caini S, Del Riccio M, van Waarden W and Meijer A (2022). "Has influenza B/Yamagata become extinct and what implications might this have for quadrivalent influenza vaccines?" *Euro Surveill* **27**(39).

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

Reukers DMF, van Asten L, Brandsema PS, Dijkstra F, Donker GA, van Gageldonk-Lafeber AB, Hooiveld M, de Lange MMA, Marbus S, van den broek I, Meijer A and van der Hoek W (2018). Annual report Surveillance of influenza and other respiratory infections: Winter 2017/2018. Surveillance van griep en andere luchtweginfecties: winter 2017/2018, Rijksinstituut voor Volksgezondheid en Milieu RIVM, 10.21945/rivm-2018-0049.

Shi T, Denouel A, Tietjen AK, Campbell I, Moran E, Li X, Campbell H, Demont C, Nyawanda BO, Chu HY, Stoszek SK, Krishnan A, Openshaw P, Falsey AR, Nair H and RESCEU Investigators (2020). "Global Disease Burden Estimates of Respiratory Syncytial Virus-Associated Acute Respiratory Infection in Older Adults in 2015: A Systematic Review and Meta-Analysis. " *J Infect Dis.* **7**;222(Suppl 7):S577-S583.

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* **147**: e30.

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 EA, Hament J-M, Knijff M, Westra M, Ernst A, Giesbers H, Drijfhout IH, Dorn T, van Vliet JA and de Melker HE (2023). Vaccinatiegraad en jaarverslag Rijksvaccinatieprogramma Nederland 2022. Vaccination coverage and annual report of the National Immunisation Programme in the Netherlands, 2022, Rijksinstituut voor Volksgezondheid en Milieu RIVM.

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).

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

Abbreviations

ARI	acute respiratory infection
BCoDE	burden of communicable diseases in Europe
CAP	community-acquired pneumonia
CBS	Statistics Netherlands (NL: Centraal Bureau voor de Statistiek)
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
ECDC	European Centre for Disease Prevention and Control
EISN	European Influenza Surveillance Network
EuroMOMO	European monitoring of excess mortality
GGD	Public Health Service (NL: Gemeentelijke Gezondheidsdienst)
GP	general practitioner
hMPV	human metapneumovirus
ICU	intensive care unit
ILI	influenza-like illness
I-MOVE	influenza monitoring vaccine effectiveness
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)
NVMM	Dutch Society for Medical Microbiology (NL: Nederlandse Vereniging voor Medische Microbiologie)
NZa	Dutch Healthcare Authority (NL: Nederlandse Zorgautoriteit)
PCR	Polymerase Chain Reaction
PHS	Public Health Service (NL: Gemeentelijke Gezondheidsdienst)
PIV	parainfluenza virus
POCT	point-of-care test

QIV	quadrivalent influenza vaccine
RIVM	National Institute for Public Health and the Environment
RSV	respiratory syncytial virus
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SNIV	national sentinel surveillance network for infectious diseases in nursing homes
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 2022

Ainslie KEC, Backer JA, de Boer PT, van Hoek AJ, Klinkenberg D, Korthals Altes H, Leung KY, de Melker H, Miura F and Wallinga J (2022). "A scenario modelling analysis to anticipate the impact of COVID-19 vaccination in adolescents and children on disease outcomes in the Netherlands, summer 2021." *Euro Surveill* **27**(44).

Andeweg SP, Vennema H, Veldhuijzen I, Smorenburg N, Schmitz D, Zwagemaker F, van Gageldonk-Lafeber AB, Hahne SJM, Reusken C, Knol MJ, Eggink D, SeqNeth Molecular surveillance group and RIVM COVID Molecular Epidemiology group (2023). "Elevated risk of infection with SARS-CoV-2 Beta, Gamma, and Delta variants compared with Alpha variant in vaccinated individuals." *Sci Transl Med* **15**(684): eabn4338.

Bagaria J, Jansen T, Marques DF, Hooiveld M, McMenamin J, de Lusignan S, Vilcu AM, Meijer A, Rodrigues AP, Brytting M, Mazagatos C, Cogdale J, van der Werf S, Dijkstra F, Guiomar R, Enkirch T, Valenciano M and I-MOVE-COVID study team (2022). "Rapidly adapting primary care sentinel surveillance across seven countries in Europe for COVID-19 in the first half of 2020: strengths, challenges, and lessons learned." *Euro Surveill* **27**(26).

den Boogert EM, de Lange MMA, Wielders CCH, Rietveld A, Surveillance RC-, Epidemiology T, Knol MJ and van Gageldonk-Lafeber AB (2022). "Incidence and severity of SARS-CoV-2 infection in former Q fever patients as compared to the Dutch population, 2020-2021." *Epidemiol Infect* **150**: e116.

Eggink D, Andeweg SP, Vennema H, van Maarseveen N, Vermaas K, Vlaemynck B, Schepers R, van Gageldonk-Lafeber AB, van den Hof S, Reusken CB and Knol MJ (2022). "Increased risk of infection with SARS-CoV-2 Omicron BA.1 compared with Delta in vaccinated and previously infected individuals, the Netherlands, 22 November 2021 to 19 January 2022." *Euro Surveill* **27**(4).

Erkens C, Tekeli B, van Soolingen D, Schimmel H and Verver S (2022). "Recurrent tuberculosis in the Netherlands - a 24-year follow-up study, 1993 to 2016." *Euro Surveill* **27**(12).

Ferland L, Carvalho C, Gomes Dias J, Lamb F, Adlhoch C, Suetens C, Beaute J, Kinross P, Plachouras D, Hannila-Handelberg T, Fabiani M, Riccardo F, van Gageldonk-Lafeber AB, Teirlinck AC, Mossong J, Vergison A, Melillo J, Melillo T, Mook P, Pebody R, Coutinho

Rehse AP and Monnet DL (2022). "Risk of hospitalization and death for healthcare workers with COVID-19 in nine European countries, January 2020-January 2021." *J Hosp Infect* **119**: 170-174.

Han WGH, Swart A, Bonacic Marinovic A, Eggink D, Reimerink J, Wijsman LA, van der Veer B, van den Brink S, van den Brandt AM, van Tol S, Godeke GJ, Brouwer F, Hoogerwerf M, Dutch FFXC-RG, Reukers DFM, Rots N, Reusken C and Meijer A (2022). "SARS-CoV-2 RNA and antibody dynamics in a Dutch household study with dense sampling frame." *Sci Rep* **12**(1): 7937.

Heijmink L, Tonis J, Gilhuis N, Gerkema M, Hart L, Raven S, van den Boogaard J, Hofhuis A, van den Hof S and Visser O (2022). "Epidemiological evaluation of mass testing in a small municipality in the Netherlands during the SARS-CoV-2 epidemic." *Epidemiol Infect* **150**: e193.

Helfferich J, de Lange MM, Benschop KS, Jacobs BC, Van Leer-Buter CC, Meijer A, Bakker DP, de Bie E, Braakman HM, Brandsma R, Neuteboom RF, Niks EH, Niermeijer JM, Roelfsema V, Schoenmaker N, Sie LT, Niesters HG, Brouwer OF and te Wierik MJ (2022). "Epidemiology of acute flaccid myelitis in children in the Netherlands, 2014 to 2019." *Euro Surveill* **27**(42).

Hogerwerf L, Post PM, Bom B, van der Hoek W, van de Kassteele J, Stemerding AM, de Vries W and Houthuijs D (2022). "Proximity to livestock farms and COVID-19 in the Netherlands, 2020-2021." *Int J Hyg Environ Health* **245**: 114022.

Huiberts A, van Cleef B, Tjon ATA, Dijkstra F, Schreuder I, Fanoy E, van Gageldonk A, van der Hoek W and van Asten L (2022). "Influenza vaccination of school teachers: A scoping review and an impact estimation." *PLoS One* **17**(8): e0272332.

Kaaijk P, Olivo Pimentel V, Emmelot ME, Poelen MCM, Cevirgel A, Schepp RM, den Hartog G, Reukers DFM, Beckers L, van Beek J, van Els C, Meijer A, Rots NY and de Wit J (2022). "Corrigendum: Children and Adults With Mild COVID-19: Dynamics of the Memory T Cell Response Up to 10 Months." *Front Immunol* **13**: 893720.

Kaaijk P, Pimentel VO, Emmelot ME, Poelen MCM, Cevirgel A, Schepp RM, den Hartog G, Reukers DFM, Beckers L, van Beek J, van Els C, Meijer A, Rots NY and de Wit J (2022). "Children and Adults With Mild COVID-19: Dynamics of the Memory T Cell Response up to 10 Months." *Front Immunol* **13**: 817876.

Kaaijk P, Swaans N, Nicolaie AM, Bruin JP, van Boxtel RAJ, de Lange MMA, Meijer A, Sanders EAM, van Houten MA, Rots NY, Luytjes W and van Beek J (2022). "Contribution of Influenza Viruses, Other Respiratory Viruses and Viral Co-Infections to Influenza-like Illness in Older Adults." *Viruses* **14**(4).

Kiss P, de Rooij MMT, Koppelman GH, Boer J, Vonk JM, Vermeulen R, Hogerwerf L, Sterk HAM, Huss A, Smit LAM and Gehring U (2023). "Residential exposure to livestock farms and lung function in adolescence - The PIAMA birth cohort study." *Environ Res* **219**: 115134.

Kissling E, Hooiveld M, Martinez-Baz I, Mazagatos C, William N, Vilcu AM, Kooijman MN, Ilic M, Domegan L, Machado A, de Lusignan S, Lazar M, Meijer A, Brytting M, Casado I, Larrauri A, Murray JK, Behillil S, de Gier B, Mlinaric I, O'Donnell J, Rodrigues AP, Tsang R, Timnea O, de Lange M, Riess M, Castilla J, Pozo F, Hamilton M, Falchi A, Knol MJ, Kurecic Filipovic S, Dunford L, Guiomar R, Cogdale J, Cherciu C, Jansen T, Enkirch T, Basile L, Connell J, Gomez V, Sandonis Martin V, Bacci S, Rose AM, Pastore Celentano L, Valenciano M and I-MOVE-COVID ECDC primary care study teams (2022). "Effectiveness of complete primary vaccination against COVID-19 at primary care and community level during predominant Delta circulation in Europe: multicentre analysis, I-MOVE-COVID-19 and ECDC networks, July to August 2021." *Euro Surveill* **27**(21).

Linssen RS, Teirlinck AC, van Boven M, Biarent D, Stona L, Amigoni A, Comoretto RI, Leteurtre S, Bruandet A, Bentsen GK, Drage IM, Wang X, Campbell H, van Woensel JBM, Bont L and Bem RA (2022). "Increasing burden of viral bronchiolitis in the pediatric intensive care unit; an observational study." *J Crit Care* **68**: 165-168.

McDonald SA, Lagerweij GR, de Boer P, de Melker HE, Pijnacker R, Mughini Gras L, Kretzschmar ME, den Hartog G, van Gageldonk-Lafeber AB, Rivm Covid-19 surveillance et, van den FS and Wallinga J (2022). "The estimated disease burden of acute COVID-19 in the Netherlands in 2020, in disability-adjusted life-years." *Eur J Epidemiol* **37**(10): 1035-1047.

Mutubuki EN, van der Maaden T, Leung KY, Wong A, Tulen AD, de Bruijn S, Haverman L, Knoop H, Franz E, van Hoek AJ and van den Wijngaard CC (2022). "Prevalence and determinants of persistent symptoms after infection with SARS-CoV-2: protocol for an observational cohort study (LongCOVID-study)." *BMJ Open* **12**(7): e062439.

Niessen A, Teirlinck AC, McDonald SA, van der Hoek W, van Gageldonk-Lafeber R, RIVM COVID-19 Epidemiology Surveillance group and Knol MJ (2022). "Sex differences in COVID-19 mortality in the Netherlands." *Infection* **50**(3): 709-717.

Onstwedder C, Lock-Wah-Hoon J, van Dorp S, Braks M, van Asten L, Zheng Y, Krafft T, Tong Y, van der Hoek W, Liu QY, Pilot E, Wang Q and Fanoy E (2022). "Comparing Vector-Borne Disease Surveillance and Response in Beijing and the Netherlands." *Ann Glob Health* **88**(1): 59.

Reukers DFM, de Boer PT, Loohuis AO, Wever PC, Bleeker-Rovers CP, van Gageldonk-Lafeber AB, van der Hoek W and Timen A (2022). "Targeted Screening for Chronic Q Fever, the Netherlands." *Emerg Infect Dis* **28**(7): 1403-1409.

Reukers DFM, van Boven M, Meijer A, Rots N, Reusken C, Roof I, van Gageldonk-Lafeber AB, van der Hoek W and van den Hof S (2022). "High Infection Secondary Attack Rates of Severe Acute Respiratory Syndrome Coronavirus 2 in Dutch Households Revealed by Dense Sampling." *Clin Infect Dis* **74**(1): 52-58.

Reukers DFM, van Jaarsveld CHM, Akkermans RP, Keijmel SP, Morroy G, van Dam ASG, Wever PC, Wielders CCH, van der Velden K, van Loenhout JAF and Hautvast JLA (2022). "Impact of Q-fever on physical and psychosocial functioning until 8 years after Coxiella burnetii infection: An integrative data analysis." *PLoS One* **17**(2): e0263239.

Schuit E, Venekamp RP, Veldhuijzen IK, van den Bijllaardt W, Pas SD, Stohr J, Lodder EB, Hellwich M, Molenkamp R, Igloi Z, Wijers C, Vroom IH, Nagel-Imming CRS, Han WGH, Kluytmans J, van den Hof S, van de Wijgert J and Moons KGM (2022). "Head-to-head comparison of the accuracy of saliva and nasal rapid antigen SARS-CoV-2 self-testing: cross-sectional study." *BMC Med* **20**(1): 406.

Spruijt I, Joren C, Schimmel H, Procee F, Alam Y, van den Hof S and Erkens C (2022). "The identification of prevalent tuberculosis disease through infection screening among high-risk migrants in the Netherlands." *Eur Respir J* **59**(5).

van den Hoogen LL, Smits G, van Hagen CCE, Wong D, Vos ERA, van Boven M, de Melker HE, van Vliet J, Kuijer M, Woudstra L, Wijmenga-Monsuur AJ, GeurtsvanKessel CH, Stoof SP, Reukers D, Wijsman LA, Meijer A, Reusken C, Rots NY, van der Klis FRM, van Binnendijk RS and den Hartog G (2022). "Seropositivity to Nucleoprotein to detect mild and asymptomatic SARS-CoV-2 infections: A complementary tool to detect breakthrough infections after COVID-19 vaccination?" *Vaccine* **40**(15): 2251-2257.

van der Maaden T, Mutubuki EN, de Bruijn S, Leung KY, Knoop H, Slootweg J, Tulen AD, Wong A, van Hoek AJ, Franz E and van den Wijngaard CC (2023). "Prevalence and Severity of Symptoms 3 Months After Infection With SARS-CoV-2 Compared to Test-Negative and Population Controls in the Netherlands." *J Infect Dis* **227**(9): 1059-1067.

Wang X, Li Y, Vazquez Fernandez L, Teirlinck AC, Lehtonen T, van Wijhe M, Stona L, Bangert M, Reeves RM, Boas H, van Boven M, Heikkinen T, Klint Johannesen C, Baraldi E, Dona D, Tong S, Campbell H and Respiratory Syncytial Virus Consortium in Europe I (2022). "Respiratory Syncytial Virus-Associated Hospital Admissions and Bed Days in Children <5 Years of Age in 7 European Countries." *J Infect Dis* **226**(Suppl 1): S22-S28.

Weehuizen JM, van Roeden SE, Hogewoning SJ, van der Hoek W, Bonten MJM, Hoepelman AIM, Bleeker-Rovers CP, Wever PC and Oosterheert JJ (2022). "No increased risk of mature B-cell non-Hodgkin lymphoma after Q fever detected: results from a 16-year ecological analysis of the Dutch population incorporating the 2007-2010 Q fever outbreak." *Int J Epidemiol* **51**(5): 1481-1488.

Willemstein IJM, de Vries G, Essink DR, Slump E, van Gageldonk-Lafeber AB, van den Hof S and van den Boogaard J (2022). "TB in migrants residing in the Netherlands for at least 5 years at diagnosis, 2003-2018." *Int J Tuberc Lung Dis* **26**(11): 1050-1057.

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