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REVIEW ARTICLE

Impact of COVID-19 Nonpharmaceutical Interventions on *Bordetella pertussis*, Human Respiratory Syncytial Virus, Influenza Virus, and Seasonal Coronavirus Antibody Levels: A Systematic Review

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During the COVID-19 pandemic, nonpharmaceutical interventions (NPIs) were introduced to reduce the spread of SARS-CoV-2. This also resulted in a reduction of notifications of other acute respiratory infections and an altered seasonality when NPIs were lifted. Without circulation of pathogens, waning of antibodies is expected, which is a first indicator of decreased immunity. Here, by performing a systematic literature review, we investigated whether reduced antibody levels due to waning immunity contributed to the altered seasonality after NPIs were lifted. Thirteen articles met the inclusion criteria and reported antibody levels or seroprevalence of human respiratory syncytial virus, seasonal human coronavirus, *Bordetella pertussis*, and influenza virus. We show that the COVID-19 pandemic most likely led to waning of pathogen-specific antibodies, with the strongest evidence for human respiratory syncytial virus and seasonal human coronavirus and with a larger decrease in children vs adults. Waning antibodies might have resulted in out-of-season activity for these pathogens.

Keywords. antibody waning; seroprevalence; respiratory pathogens; COVID-19 pandemic; seasonality of infection.

The burden of disease caused by respiratory tract infections is high, and the majority of these infections occur in young children and the elderly [1]. The European Center for Disease Prevention and Control defines acute respiratory infections (ARIs) as a sudden onset of symptoms, at least 1 of 4 symptoms (cough, sore throat, shortness of breath, and coryza), and a clinician's judgment that the illness is due to an infection [2]. Viruses that are associated with ARIs are influenza, human respiratory syncytial virus (HRSV), seasonal human coronavirus (hCoV), human metapneumovirus, rhinoviruses, enteroviruses, adenoviruses, and human bocavirus [3]. Besides these viruses, the bacterial pathogens *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Moraxella catarrhalis*, *Mycoplasma pneumonia*, and *Chlamydophila pneumonia* cause ARI [4, 5]. In many regions, infections with respiratory viruses such as HRSV and influenza virus are increasingly reported in the winter season, while infections with human metapneumovirus and rhinovirus can be detected throughout the year [3]. Less clear seasonal circulation patterns have been found in tropical and subtropical regions of the world. Changes in environmental factors—notably, the combination of temperature, humidity, and human behavior—are acknowledged as major contributing factors underlying the seasonal patterns [3]. Viruses such as influenza, HRSV, and coronaviruses spread via short- and long-range aerosols but also via droplets, while pathogens such as rhinoviruses are more likely to transmit via fomites and direct contact [6]. The efficiency of transmission is additionally affected by seasonal environmental factors that affect the stability of the respiratory viruses, as well as host factors and viral factors.

Since the start of the COVID-19 pandemic, nonpharmaceutical interventions (NPIs) such as physical distancing, wearing face masks, closing schools and sport centers, and working from home were introduced to reduce the spread of SARS-CoV-2. Strikingly, this resulted in a major decrease of notifications for other airborne respiratory pathogens in the 2020 and 2021 seasons [7–13]. It is largely unknown how the prolonged absence of circulation resulted in an altered seasonality of some respiratory pathogens. The absence of reinfections due to the NPIs reduced boosting of humoral immunity could result in a decline of antibody levels, which is expected to increase vulnerability to infection.

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Considering the out-of-season relapse of several infectious diseases, investigating how antibody levels develop during lockdowns can help us understand the impact of humoral immunity on seasonal fluctuations.

Infections with pathogens that are circulating at a high level in the population will boost antibody levels population-wide. Such reinfections apparently sustain immunity on the individual level as well as the population level. In the absence of reexposure to endemic pathogens, antibody levels decline, as shown for hCoV, which is a first indicator that the level of immunity is decreasing [14]. We expect antibody waning to be a contributing factor to seasonality. Previously, we showed a decrease of HRSV antibodies during the pandemic in a preliminary analysis [15]. The antibody half-life could be different for each pathogen but differ per age. Infants are dependent on sufficient levels of maternal immunoglobulin G (IgG) antibody levels for protection against infectious diseases in the first months of life [16, 17].

To investigate whether reduced levels of antibodies as a result of waning immunity in the population may explain the altered seasonality of infection after the lifting of NPIs, we performed a systematic literature review. To this end, we selected literature that studied the prevalence and levels of serum antibodies for the most common respiratory infections other than SARS-CoV-2 during the COVID-19 period.

METHODS

Design

A systematic review of seroprevalence studies was performed according to the PRISMA guideline (Preferred Reporting Items for Systematic Reviews and Meta-analyses) [18, 19]. Duplicates were excluded by EndNote.

A primary search strategy in PubMed, Embase, and Scopus was designed to identify relevant scientific articles, including preprints. Inclusion criteria were articles published between 1 January 2020 and 20 October 2023, in which antibody levels (IgG, immunoglobulin A [IgA], or immunoglobulin M) were measured or seroprevalence was determined of respiratory pathogens in individuals of any age. The most commonly reported respiratory viruses involved in ARI were included (influenza virus, HRSV, human metapneumovirus, hCoV, enterovirus, rhinovirus, bocavirus, adenovirus), as well as 5 bacteria that are frequently associated with ARI (*M pneumonia*, *C pneumonia*, *S pneumoniae*, *H influenzae*, *M catarrhalis*) [4, 5]. Although not primarily presenting with typical ARI, 3 additional airborne transmissible pathogens were included in the survey (measles virus, *Bordetella pertussis*, and *Neisseria meningitidis*; all vaccine preventable), as some evidence suggested that their circulation may have been affected [9, 20]. Exclusion criteria were zoonoses, SARS-CoV-2 infections, nonhuman studies, studies with >24 months between time points, studies with the first measurement in the second half of 2020, antibodies not measured in serum, and review articles. The complete search term for the different databases can be found in Supplementary Methods 1.

Two authors (C. M. G. and M. V.) independently performed the selection process. All articles were first screened on title and abstract, and remaining articles were read in depth.

Data Extraction and Risk of Bias

A datasheet was generated listing the different studies, designs, population characteristics, results of antibody measurements or seroprevalence, and levels of quality. The quality of the studies was evaluated by C. M. G. and M. V. using a modified Newcastle-Ottawa scale for cohort studies (Supplementary Methods 2) [21]. According to these guidelines, studies were rated with stars in 3 categories: selection of cohorts, comparability of cohorts, and outcome of study. Guided by the qualification items, studies were rated for their quality with a maximum of 9 stars. The overall quality of the study was rated high (7 or 8 stars), intermediate (6 stars), or low (≤5 stars).

Data

Stringency indices from 1 January 2020 to 30 June 2022 for the Netherlands, Germany, France, Canada, and China were downloaded from Our World in Data (https://ourworldindata.org/COVID-stringency-index; accessed 9 February 2024) [22]. The stringency index is a measure based on 9 response indicators, including school closures, workspace closures, and travel bans. The value is a scale from 0 to 100, where 100 is the strictest. For Canada and China, policy differs per region; therefore, stringency indices per region were used. For the Netherlands, Germany, and France, nationwide stringency indices were used.

RESULTS

Study Selection and Characteristics

Our search resulted in 3675 unique articles that were subsequently screened by title and abstract (Figure 1). Sixteen articles were assessed by full text. One study was first excluded by title but later included per the abstract. Ten articles met all inclusion criteria and reported antibody levels or seroprevalence estimates against respiratory pathogens during the COVID-19 period.

Three articles documented >1 study population, which resulted in 13 evaluated studies [23–25]. In some studies, >1 target pathogen was evaluated, giving rise to 18 independent pathogen investigations, organized in Table 1 according to pathogen. All studies had a period of NPIs between the antibody sampling points (Figure 2). For all studies, the first antibody measurement was in 2019 or at the start of the COVID-19 pandemic (before June 2020). Three studies had their last measurements at the end of 2020 [26, 27]. The other

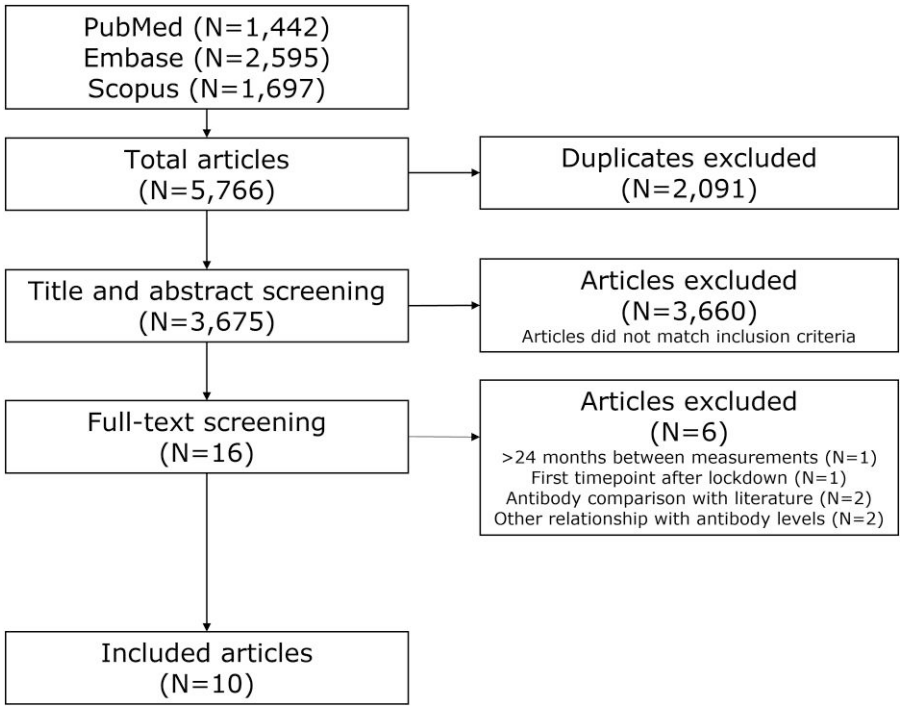

Figure 1. PRISMA flow diagram of study selection.

10 studies had their last measurements in 2021 or 2022. The time between the measurements ranged from 6 to 24 months.

Six studies were conducted in the Netherlands, 3 in Canada, 2 in China, 1 in Germany, and 1 in France. Six studies reported antibody levels to HRSV, 5 to influenza virus, 4 to hCoV, and 3 to *B pertussis*. Three studies were population based [15, 28, 29]; 3 were performed in female health care workers (HCWs) [25, 26, 30]; 2 used serum from annual health examinations [27, 31]; 1 was in lactating women [23]; 1 was in a cohort of men who have sex with men [24]; 1 was in adult patients with COVID-19 [24]; and 1 used leftover plasma samples from clinical chemistry analysis [32]. Twelve studies reported antibody levels and 2 reported seroprevalence. The main characteristics are described in Table 1.

All countries applied different strategies and timing to control COVID-19. The NPIs between January 2020 and August 2022 in each study are shown in Figure 2 [33]. In the Netherlands and Germany, schools were completely closed at all levels multiple times during the pandemic, while in France this occurred only during the first lockdown. However, France mandated a stricter face-covering policy during the pandemic, as did Jiangsu, China. China and Canada had a stricter travel control policy as compared with most European countries.

Risk-of-Bias Assessment

For the 13 studies, risk-of-bias assessment qualified 4 as low risk of bias, 6 as medium risk, and 3 as high risk (Supplementary Table 1). Most studies scored high on the selection process, while more differences were seen on the comparability measure; this was mostly due to the difference in type of study. Cross-sectional studies had lower scores due to less comparable cohorts. Common reasons for studies with a high risk of bias were a select group of individuals, a limited sample size, and a cross-sectional study survey.

B pertussis

In a study in Canada with a medium risk of bias, 18 female HCWs were followed during the first year of the COVID-19 pandemic (May–June 2020 to February–May 2021) [30]. There was no change in the proportion of individuals with anti–pertussis toxin antibody levels >40 IU/mL (1 individual in 2020 as well as 2021, 5.6%). However, the proportion with undetectable antibody levels (≤5 IU/mL) increased from 10 of 18 (55.5%) in 2020 to 12 of 18 (66.6%) in 2021.

B pertussis seroprevalence was reported in 2 studies of medium risk of bias in Beijing, China [27], and high risk of bias in Jiangsu, China [31]. Both used leftover serum from patients who attended annual health examinations. In both studies, antibody levels were divided into categories, in which those ≥100 IU/mL were regarded as evidence for recent infection (within the last year) and levels between 40 and 100 IU/mL were considered to reflect infections >1 year ago. In the study in Beijing (N = 1518), the investigators compared 2 consecutive time points and found that the median concentrations of anti–

Table 1. Characteristics of Studies Describing HRSV, Influenza Virus, hCoV, and *Bordetella pertussis*

Study	Country	Design	Sample Size	Sampling Population	Age	Sex	Time Points of Analysis	Antibody Parameter (Assay)	Antigen	Risk of Bias[a]	Change in Antibody Levels or Seroprevalence
HRSV											
Pletz (2022) [28]	Thuringia, Germany	Longitudinal	189	Population	40.8–70 y (IQR)	54% female	May 2020, Oct 2020, Apr 2021	IgG (ELISA)	Anti-HRSV	+	Decrease of HRSV antibodies
Grobben (2022) [26]											
Study 1	Netherlands	Longitudinal	84	Health care workers	Unknown	Unknown	Apr-May 2020, Oct-Nov 2020	IgG, IgA (Luminex assay)	Prefusion HRSV	+/–	No change for HRSV
Study 2	Netherlands	Cross-sectional	Apr-May 2020, 38; Oct-Nov 2020, 38	Lactating women who encountered SARS-CoV-2	31 y (mean)	100% female	Apr-May 2020, Oct-Nov 2020	IgG, IgA (Luminex assay)	Prefusion HRSV	–	Increase for HRSV IgG and IgA
Reicherz (2022) [25]											
Study 1	BC, Canada	Longitudinal	18	Health care workers	28–41 y	100% female	Feb-May 2020, May-Jun 2021	IgG (multiplex serology assay), neutralization	Prefusion HRSV	+/–	Decrease of HRSV antibodies and neutralizing capacity
Study 2	BC, Canada	Cross-sectional	2020, 20; 2021, 65	Participants in immunoprophylaxis program; population	4–11 mo (IQR)	Unknown	Feb-May 2020, May-Jun 2021	IgG (multiplex serology assay), neutralization	Prefusion HRSV	–	Decrease of HRSV antibodies and neutralizing capacity
den Hartog (2023) [15]	Netherlands	Longitudinal	558	Population	1–89 y	57.7% female	Jun 2020, Feb 2021, Jun 2021	IgG (multiplex immunoassay)	Postfusion HRSV	+	Decrease of HRSV antibodies
Influenza											
Pletz (2022) [28]	Thuringia, Germany	Longitudinal	153	Population	40.8–70 y (IQR)	54% female	May 2020, Oct 2020, Apr 2021	HI assay	A/H3N2, A/H1N1, B/Yamagata, B/Victoria	+	No change for influenza
Grobben (2022) [26]											
Study 1	Netherlands	Longitudinal	84	Health care workers	Unknown	Unknown	Apr-May 2020, Oct-Nov 2020	IgG, IgA (Luminex assay)	H1N1 influenza hemagglutinin	+/–	No change for influenza
Study 2	Netherlands	Cross-sectional	Apr-May 2020, 38; Oct-Nov 2020, 38	Lactating women who encountered SARS-CoV-2	31 y (mean)	100% female	Apr-May 2020, Oct-Nov 2020	IgG, IgA (Luminex assay)	H1N1 influenza hemagglutinin	–	Increase for influenza IgA
de Jong (2023) [24]											
Study 1	Netherlands	Longitudinal	100	Amsterdam Cohort Studies on HIV infection and AIDS	22–70 y	100% male	Summer 2019, summer 2020, summer 2021	HI assay	A/H3N2, A/H1N1pdm09, B/Yamagata, B/Victoria	+	No change for influenza
Study 2	Netherlands	Longitudinal	65	Adult patients with COVID-19	16–85 y	Unknown	Summer 2020, summer 2021	HI assay	A/H3N2, A/H1N1pdm09, B/Yamagata, B/Victoria	+/–	No change for influenza

Table 1. Continued

Study	Country	Design	Sample Size	Sampling Population	Age	Sex	Time Points of Analysis	Antibody Parameter (Assay)	Antigen	Risk of Bias[a]	Change in Antibody Levels or Seroprevalence
hCoV											
Grobben (2022) [26]											
Study 1	Netherlands	Longitudinal	84	Health care workers	Unknown	Unknown	Apr-May 2020, Oct-Nov 2020	IgG, IgA (Luminex assay)	4 spike HCoV	+/–	Decrease of OC43 IgG levels
Study 2	Netherlands	Cross-sectional	Apr-May 2020, 38; Oct-Nov 2020, 38	Lactating women who encountered SARS-CoV-2	31 y (mean)	100% female	Apr-May 2020, Oct-Nov 2020	IgG, IgA (Luminex assay)	4 spike HCoV	–	Increase for NL63 and 229E IgG and OC43, HKU1, 229E IgA
Sikkema (2023) [32]	Netherlands	Cross-sectional	2020, 613; 2021, 284	Leftover hospital serum	6 mo–18 y	Unknown	Mar-Apr 2020, Jan-Mar 2021	IgG (protein microarray)	4 spike S1 and 4 nucleocapsid hCoV proteins	+/–	Decrease of antibodies to all hCoVs
De Thoisy (2023) [29]	Crépy-en-Valois, France	Longitudinal	2520	Population	≥5 y	36.5% female	Apr 2020, Nov 2020, Apr 2021, Nov 2021	IgG, IgA (multiplex assay)	4 spike S1 and 4 nucleocapsid hCoV proteins	+	Decrease of anti-S hCoV
B pertussis											
Chen (2022) [27]	Beijing, China	Cross-sectional	2019, 735; 2020, 783	Leftover hospital serum	20–39 y	47.2% female	Jan-Dec 2019, Aug-Nov 2020	IgG (ELISA)	Anti-PT	+/–	Lower median concentration for *B pertussis* in 2020
Chen (2022) [31]	Jiangsu, China	Cross-sectional	2019, 348; 2020, 217; 2021, 223	Leftover hospital serum	≥15 y	58.9% female	2019, 2020, 2021	IgG (ELISA)	Anti-PT, anti-FHA	–	Decrease in detectable *B pertussis* antibody levels but higher GMC
Reicherz (2022) [25]	BC, Canada	Longitudinal	18	Health care workers	28–41 y (IQR)	100% female	May-Jun 2020, Feb-May 2021	IgG (ELISA)	Anti-PT, anti-FHA, anti-PRN	+/–	Significant decrease of *B pertussis* antibody levels

Abbreviations: ELISA, enzyme-linked immunosorbent assay; FHA, filamentous hemagglutinin; GMC, geometric mean concentration; hCoV, human coronavirus (seasonal); HI, hemagglutination inhibition; HRSV, human respiratory syncytial virus; IgA, immunoglobulin A; IgG, immunoglobulin G; PRN, pertactin; PT, pertussis toxin.

[a]Risk-of-bias analysis based on Newcastle-Ottawa scale: +, low risk of bias; +/–, medium risk of bias; –, high risk of bias. Complete risk-of-bias assessment can be found in Supplementary Table 1.

pertussis toxin IgG antibodies had decreased between 2019 and 2020. The percentage of individuals with antibody levels ≥40 IU/mL did not change (2.04% vs 1.66%) [31]. For the study in Jiangsu (N = 788), more individuals had antibody levels >40 IU/mL in 2020 vs 2019 (5.5% vs 21.2%), and this decreased in 2021 (17.0%) [27].

Human Respiratory Syncytial Virus

Two longitudinal studies with a low risk of bias applied anti-HRSV antibody testing in 2020 and 2021. The first study was a prospective cohort in the Netherlands (N = 558; age, 1–89 years), which demonstrated a significant decrease of anti-HRSV IgG antibodies for most age groups between June 2020 and June 2021 [15]. The other study concerns the inhabitants of a small rural town in Germany [28]. For 189 of the 883 inhabitants of this community, anti-HRSV antibodies were measured in May 2020 and April 2021. A small monthly decrease of −0.6 relative units/mL was detected.

Antibody levels against HRSV were studied by Reicherz et al. In this study with a medium risk of bias, paired serum samples from 18 female HCWs were analyzed for HRSV IgG antibody levels in February to May 2020 and May to June 2021 [25]. In addition, antibody levels were studied in infants in 2020 (n = 20) and 2021 (n = 65) yet on a cross-sectional basis (high risk of bias). For female HCWs and infants, anti-HRSV antibody levels had significantly declined in 2021 vs 2020. For infants, this decrease was ∼15-fold. Besides a decrease in antibody levels, the neutralization capacity decreased 12-fold in women and 3.4-fold in infants in 2021 vs 2020.

In a study in the Netherlands with a medium risk of bias, anti-HRSV IgG and IgA antibodies were measured in the serum of lactating women in spring (n = 38) and fall (n = 38) 2020 [26]. Antibody levels in lactating women with previous SARS-CoV-2 infection increased 1.7-fold for anti-HRSV IgG and 3.5-fold for anti-HRSV IgA. Antibody levels were also measured in 84 HCWs without past SARS-CoV-2 infection. This high–risk of bias study showed no differences in anti-HRSV IgG antibodies in serum over time.

Influenza

The study in Germany investigating anti-HRSV antibodies measured anti-influenza antibodies in 153 unvaccinated inhabitants (low risk of bias) [28]. Neither strain-specific influenza titers as measured by hemagglutination inhibition (HI) nor seroprevalence showed significant changes over time.

Likewise, in a study based on 2 cohorts in the Netherlands, no significant change in HI titers against influenza was detected [24]. In men who have sex with men (N = 100; low risk of bias) and a prospective cohort study on the longterm outcomes of a SARS-CoV-2 infection (N = 65; medium risk of bias), influenza antibodies were compared between 2019 and 2021. No significant waning of HI titers in both cohorts was noted [24].

In the study measuring anti-HRSV antibodies (medium risk of bias) in 76 lactating women, antibodies against influenza were measured [26]. In lactating women with previous SARS-CoV-2 infection, no difference was detected for influenza IgG antibodies, whereas IgA antibodies against influenza showed a 2-fold increase. In HCWs without past SARS-CoV-2 infection (high risk of bias), there was no difference in influenza IgG antibody levels in serum over time as well.

Seasonal Human Coronavirus

A longitudinal cohort in northern France included 2520 samples from 898 individuals and measured nucleocapsid and S1 antibody levels of all 4 hCoVs (NL63, OC43, 229E, and HKU1) [29]. In this low–risk of bias study, a decline in anti-S IgG levels for all 4 hCoVs was detected between April 2020 and November 2021. After exclusion of probable infections based on a >8-fold increase for ≥2 biomarkers, antibody waning seems to occur more rapid in children compared to adults.

In a cross-sectional study with a medium risk of bias based on a cohort of Dutch children (N = 613), nucleocapsid and S1 antibody levels of all 4 hCoVs were measured in leftover serum samples. For all 4 hCoVs, IgG antibodies decreased in children from 6 months until 18 years between early 2020 and early 2021 [32]. The decrease was largest for children from 6 to 12 months.

Four hCoVs were measured in 76 lactating women who experienced a SARS-CoV-2 infection [26]. In this medium–risk of bias study, hCoV-NL63 and hCoV-229E IgG antibody levels increased 2- and 1.5-fold over time, respectively. An increase in IgA antibody levels was also noted for hCoV-OC43 (3.2-fold), hCoV-HKU1 (3.2-fold), and hCoV-229E (2.2-fold). In the group of HCWs without previous SARS-CoV-2 infection (high risk of bias), only hCOV-OC43 IgG antibody levels significantly decreased.

DISCUSSION

In this systematic review, we detected a decay in antibody levels of different respiratory pathogens during the COVID-19 pandemic, with strongest evidence for hCoV and HRSV but no evidence for decay of antibodies to influenza virus. This type of research will increase our understanding whether antibody waning could contribute to seasonality and determine groups at risk for an infection after a period of reduced circulation.

In 10 of the 13 studies, a decrease of antibody levels to HRSV, hCoV, and/or *B pertussis* was detected. The observed antibody decrease for HRSV and hCoV seemed to be larger in children than adults, and more infants who did not have their first infection were present [25, 29, 32]. Interestingly, no significant decrease of antibody levels for influenza was observed in 4 studies conducted in the Netherlands and Germany. In 2 *B pertussis* studies in China, besides a reduction in median antibody levels, more individuals with high antibody levels were detected [27, 31],

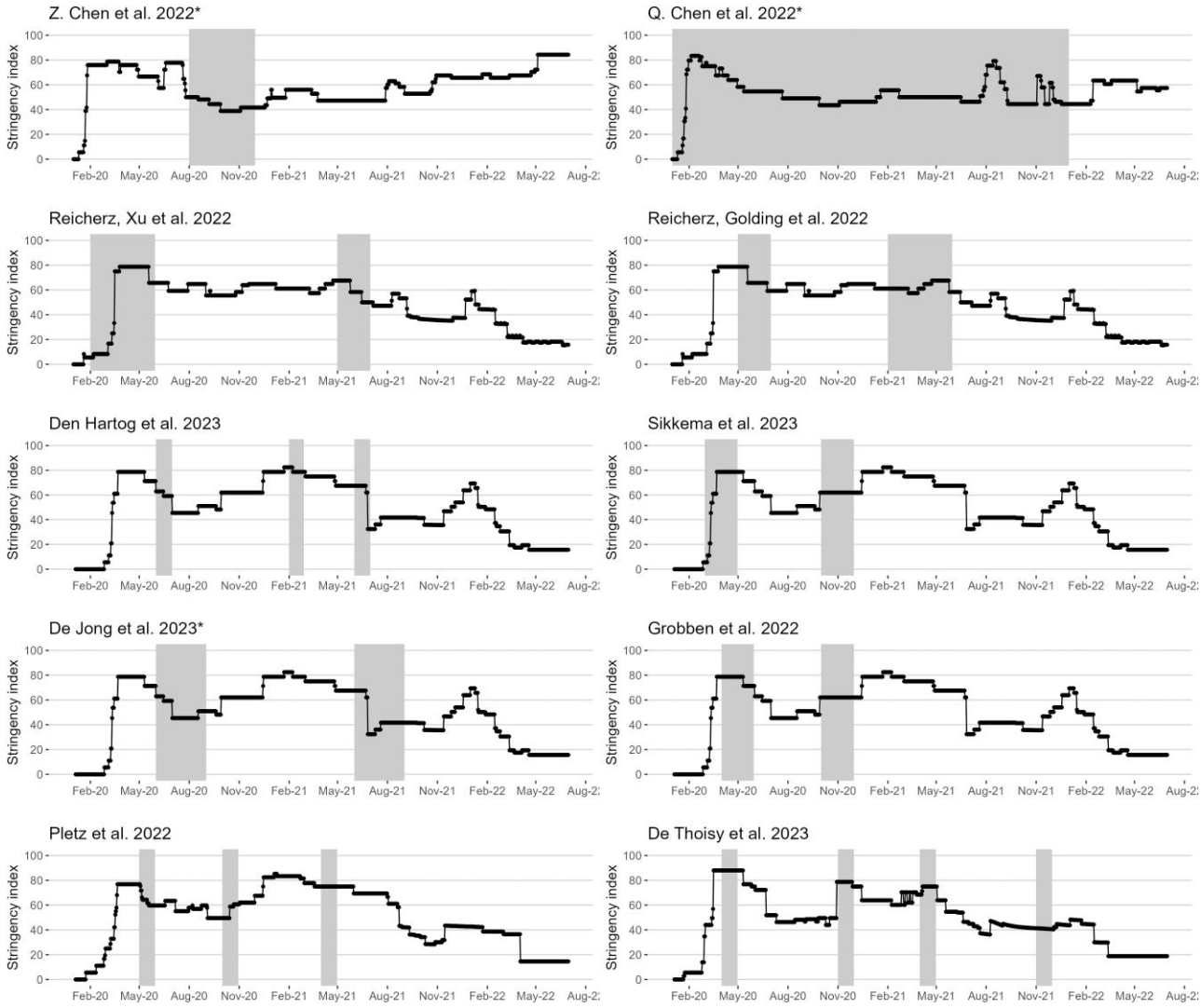

Figure 2. Stringency index per study. The relative stringency index of nonpharmaceutical interventions per country between January 2020 and June 2022. Vertical gray bars show the sampling periods per study. *Studies also having a sampling period in 2019.

suggesting that *B pertussis* circulation was not completely absent in the Chinese population during the study period. Samples were collected when the lockdown in Beijing and Jiangsu had ended. This might explain increasing *B pertussis* antibody levels in the population. All other countries had a period with NPIs between the consecutive time points.

Annual incidence rates of HRSV, *B pertussis*, and influenza infection are high, substantially higher than what is usually reported during an infection season on clinical terms [4–6]. Annual infection rates of mostly asymptomatic HRSV and influenza have been reported to reach 40% to 50% or higher, depending on age and even including repeated infections during 1 season [5, 6]. As a consequence, population-level immunity is expected to be boosted, thereby reducing the number of susceptible individuals, which leads to interruption of widespread virus transmission. After this period of infections, antibody levels wane. Depending on the amount of waning, this inevitably leads to a more susceptible population again but may vary per pathogen. The period with NPIs led to a longer period of reduced pathogen circulation, which forms a likely explanation for a more significant decay in antibody levels for the various pathogens evaluated. After NPIs were lifted, unusual numbers of out-of-season notifications were reported for several pathogens.

For HRSV, unusual out-of-season activity in the summer of 2021 was observed [9, 34, 35]. Although this can be in part explained by an increase in testing [36], there was a high peak in hospitalizations of children with HRSV reported in several countries, indicating a true increase in infections [37–39]. The incidence of hCoV infections returned after NPIs were released, with a delayed peak in spring and summer

2021 [9]. For HRSV and hCoV, waning of antibody levels was detected, which suggests that this might have resulted in an out-of-season onset of infections after release of NPIs. Influenza and *B pertussis* notifications remained absent after relaxation of NPIs in the regular season of 2020 to 2021 [9, 11, 12, 40]. Influenza notifications returned with an uncommon late onset during the 2021–2022 season and an earlier onset in the 2022–2023 season [41]. However, influenza B/Yamagata has been sporadically reported since the start of the COVID-19 pandemic and may have gone extinct [42]. For influenza, antibody levels remain unchanged over time. Waning might occur over a longer period, and other factors might be contributing to influenza seasonality as compared with HRSV and hCoV infections. *B pertussis* notifications remained absent for 3 years until 2023. Periods with lower levels of notifications are not uncommon for *B pertussis*, as it is known to peak every 3 to 5 years [43]. Although a reduction in antibody levels was detected in 2 studies, this does not directly associate with an increase in infections, and other factors might be involved in the seasonality of *B pertussis* infections.

In 2 studies [25, 32], infants showed the highest decrease in antibody levels. These infants possibly had not yet been infected with HRSV and hCoV and therefore showed mostly a decrease of maternally derived antibodies. The half-life of antibodies after the first infection was found to be as fast as 2 months for HRSV antibodies [44]. Yet, after a second infection, neutralizing titers showed a slower decrease [44]. So, multiple exposures to diverse pathogens contribute to the development of robust immunologic memory. Not surprising, our study showed a larger decrease of antibody levels in children vs adults, which might be explained by the less frequent exposure to these pathogens. This would also suggest that children and especially infants without primary infection were more susceptible to infections after a period of reduced circulation and might contribute to the seasonality of HRSV and hCoV. Although other immune mechanisms contribute to the protection against infection, changes in antibody levels likely provided a good indicator of adaptive immunity and for the impact of the introduction and lifting of NPIs.

Our review highlights that there is limited information on the seroprevalence of respiratory infections during the pandemic and points at several limitations. First, our review is a descriptive study, and no causal inference can be made upon these data. The interpretation of the findings of the presence or absence of antibodies decay during the pandemic depends on the quality and design of the studies. The studies varied in risk of bias. Most studies (7 of 13) used demographic subgroups of individuals, not representative for the general population, or they had limited sample sizes. Second, the number of studies was low, and articles were found for only 4 of the previously named pathogens involved in ARI. For all other pathogens involved in ARI, decay levels are unknown. Studies were conducted in 5 countries in 3 continents. Antibody kinetics might be different in other countries; therefore, whether our findings apply globally needs to be determined. Furthermore, the studies used different antibody detection methods and had different time spans between the sampling points, which made it difficult to directly compare results. It is also not clear what normal year-to-year changes in antibody levels are and whether a decline was caused only by NPIs. Studies with longitudinal data of antibody levels before the COVID-19 pandemic are scarce. Further research should analyze data from prepandemic seasons or examine antibody levels after the return of a normal seasonality pattern.

Nonetheless, this systematic review shows that the COVID-19 pandemic most likely led to the waning of antibodies for 3 of the 4 included respiratory infections, with the highest evidence of waning for HRSV and hCoV. Degree of waning varied per pathogen, with a larger effect in children and with a larger group of infants who had not yet been infected. Waning of antibodies seemed to contribute to seasonality for HRSV and hCoV but less for *B pertussis* infections. How this waning of antibodies relates to susceptibility to infection remains to be determined. The COVID-19 pandemic provides a unique opportunity to investigate these questions.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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