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Estimating the incidence of SARS-CoV-2 infections by jointly modelling seroprevalence, hospitalization and mortality data, February 2020 – January 2021, Belgium

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Abstract

Background Belgium experienced two SARS-CoV-2 epidemic waves in 2020, in spring and autumn. Due to limited testing capacity, restrictive case definitions, asymptomatic infections, and incomplete testing compliance, case counts represent only a lower bound of SARS-CoV-2 infection incidence. We estimated this incidence from February 2020 to January 2021 by jointly modelling seroprevalence and surveillance data.

Methods We developed a hierarchical Bayesian model that jointly fits seroprevalence, hospitalization, and mortality data to a shared latent incidence curve, represented by a spline. The model accounts for time-varying serological test sensitivity (reflecting seroconversion and seroreversion) using informative priors, and simultaneously estimates test specificity, infection-to-event distributions, and time-varying infection hospitalization rates (IHR) and infection fatality rates (IFR). Seroprevalence data comprised 37,235 samples from two repeated cross-sectional studies: residual laboratory samples tested with the EuroImmun IgG ELISA and blood donor samples tested with the Wantai Ab ELISA. Hospitalization and mortality counts were obtained from national COVID-19 surveillance.

Results By early 2021, an estimated 19.0% (95% Credible Interval (CrI) 17.4–20.7), 13.6% (CrI 11.5–15.8) and 10.8% (CrI 8.7–13.2) of the Belgian 18–49, 50–64 and 65–74 year-olds had been infected with SARS-CoV-2. The first wave mostly affected the younger age group, with a peak weekly incidence of 2.0% (CrI 1.7–2.3) late March 2020. The second wave peaked late October 2020 with weekly incidences of 1.6% (CrI 1.2–2.1) among 65–74 year-olds and 2.8% (CrI 2.4–3.3) among 18–49 year-olds. IHR and IFR were considerably higher in older age groups and declined over time. Among 65–74 year-olds IHR declined from 9.9% (CrI 7.3–14.2) to 5.0% (CrI 3.5–7.1) and IFR from 2.8% (CrI 2.0–4.0) to 1.2% (CrI 0.9–1.7).

Conclusion An estimated 16.3% (CrI 15.1–17.4) of the Belgian adult population had been infected with SARS-CoV-2 by early 2021. Joint modelling of seroprevalence and surveillance data provides a framework for estimating infection burden.

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Keywords Seroprevalence, Incidence, SARS-CoV-2, COVID-19, Statistical modelling, Surveillance data, Seroconversion, Seroreversion, Bayesian hierarchical model

Text box 1. Contributions to literature

- Combines multiple data sources: This study uniquely integrates two different blood testing studies with hospital and death records using advanced statistical methods, providing more reliable estimates of COVID-19 infections than single-source studies.
- Accounts for test limitations: Unlike previous studies, this research properly adjusts for the fact that antibody tests become less accurate over time and may miss infections, leading to more precise infection estimates.
- Shows declining severity over time: Demonstrates that the chances of hospitalization and death from COVID-19 decreased throughout 2020, even before vaccines were available, providing important insights for pandemic preparedness.
- Reveals true infection burden: Found that by early 2021, one in six Belgian adults had been infected with COVID-19 - much higher than confirmed case counts suggested due to limited testing capacity early in the pandemic.
- Provides methodological framework: Establishes a statistical approach that other countries can adapt to better estimate infection rates during health emergencies when testing is incomplete.

Background

In Belgium, the first infections with SARS-CoV-2 were reported by the end of February 2020. A rapid increase in cases resulted in a strict lockdown on 18 March 2020 and a first peak in cases was reached at the beginning of April [1]. During this first lockdown no social interactions were allowed outside of the household and non-essential travel was forbidden. The gradual easing of restrictions started in May 2020, but many measures remained in place during the summer of 2020. Because of a resurgence of cases by the end of September, a new partial lockdown was implemented 16 October 2020. The second lockdown involved less restrictions, allowing, for example, a single contact outside of the household [2]. While case counts, COVID-19 related hospitalizations and deaths during 2020 have been well documented [3], the actual number of infections remains unknown. The case count can only be considered a lower bound since limited testing capacity and a restrictive initial case definition defined the testing policy in the first half of 2020 [4]. Testing capacity increased and case ascertainment was higher in the second half of 2020. During the surge of infections in October, however, the testing strategy changed again and the testing of asymptomatic high-risk contacts was no longer mandated. In addition to a changing testing strategy, a proportion of SARS-CoV-2 infections are asymptomatic and adherence to testing policy is incomplete further impacting and limiting the detection of infections.

Since the majority of infected individuals produce antibodies to SARS-CoV-2 that persist for at least several months [5–8], serological screening can be used to estimate the proportion of the population previously infected with SARS-CoV-2 [9, 10]. While seroprevalence studies were very common during the COVID-19 pandemic, especially in the pre-vaccination era, there is no consensus on how best to interpret their results [11]. Qualitative serological tests classify samples as seropositive or seronegative based on whether antibody titers exceed a detection threshold. Titers however require time to build-up after infection and will typically decline over longer time periods. Serological tests also have imperfect sensitivity and specificity. Various approaches have been used to address this: selecting assays with stable longitudinal performance, combining multiple immunoassays [12, 13], or applying Rogan-Gladen estimators to correct for misclassification [14]. In addition, published sensitivity and specificity estimates for a given assay often vary considerably. Results are sensitive to which estimates are used — leading to discrepancies in reported IFR estimates [12, 15]. In Belgium, the two prospective cross-sectional seroprevalence studies set up to estimate past exposure to SARS-CoV-2 used qualitative serological tests with different reported characteristics. The Euro-Immun test's sensitivity estimates vary as widely as from 64.1% to 94.4% [16], declining over time since infection [12, 17, 18]. The Wantai test has a reported 94.2–98.0% sensitivity which remains stable for at least 13 to 15 months after infection [19–23]. We previously developed a framework that allows for the harmonization of these sensitivity estimates [24]. The suggested sensitivity distribution over time since infection captured the process of antibody build-up to detectable levels, seroconversion, and subsequent waning of antibodies, seroreversion, using a Weibull-bi-exponential distribution.

Seroprevalence data combined with sensitivity and specificity data can be used to back-estimate incidence with or without additional data sources. Surveillance data offers indirect evidence through the monitoring of events following infection. Without additional information on transition rates (e.g. IHR and IFR), however, they only serve as proxies for incidence's trends. Previous studies have suggested frameworks to combine incidences estimated from seroprevalence data with surveillance data, either using a stepwise [25, 26] or a joint approach [15, 27]. None of these frameworks, however, allowed for the inclusion of all data available in Belgium: two cross-sectional seroprevalence studies and mortality and hospital surveillance data. We aim to jointly estimate the incidence of SARS-CoV-2 infections and the associated IFR and IHR for the Belgian general population aged 18 to 74

years old within a Bayesian hierarchical framework that propagates uncertainty from each data source.

Methods

Study population and period

Our study population included 18 to 74 year-olds within the general population in Belgium. Our study period ran from February 2020 to January 2021. The seroprevalence studies followed a repeated cross-sectional design. Both studies collected the first samples on 30 March 2020. The last collection round for the RLS ended on 17 October 2020. The last collection round considered here for the BDS ended on 31 January 2021. Seroprevalence within the general population was only minimally affected by vaccination at the end of January 2021 since nursing homes were prioritized during the mass rollout of vaccination which started in January 2021. Seroprevalence is a delayed indicator. To build up to the seroprevalence observed at the end of March 2020 we needed to start estimating incidences earlier. We therefore allowed the model to start estimating incidences from 16 February onwards. This is the week during which the first hospitalizations were recorded. The first COVID-19 deaths were recorded in the week starting 1 March 2020.

Data sources

Seroprevalence

The RLS was coordinated by the Centre for the Evaluation of Vaccination, Vaccine & Infectious Disease Institute, at the University of Antwerp. A total of 16,547 serum samples were included from 7 collection rounds with approximately one-month intervals between consecutive rounds. Samples were collected from ambulatory patients through 10 private diagnostic laboratories and analyzed using the Anti-SARS-CoV-2 IgG ELISA from EuroImmun (cat n° EI 2606-9601G; Medizinische Labordiagnostika AG, Germany). This semi-quantitative test detects IgG antibodies against the SARS-CoV-2 S1 protein. Details and results from this study have been published in Herzog et al. [28].

The BDS was coordinated by Sciensano [29], Belgium's institute for public health, in cooperation with the Red Cross. A total of 20,688 plasma samples were included from 23 collection rounds with 14-day intervals. The Wantai SARS-CoV-2 Ab ELISA (cat n° WS-1096; Beijing Wantai Biological Pharmacy Enterprise Co. Ltd., China) was used for the qualitative detection of total antibodies directed to the Receptor-Binding Domain (RBD). This ELISA detects anti-RBD IgG, IgA and IgM concomitantly.

For both studies, data on age (in years), sex and region of residence were collected alongside sample data: 'date of sampling' and 'qualitative test result'. Exclusion criteria can be found in the supporting information. To account for non-representative sampling with respect to sex and region, we applied post-stratification weights within each age group. For each stratum str, sex and region combination within age group a, we calculated weights as:

$$w_{a,str} = \frac{\pi_{a,str}}{\widehat{p}_{a,str}}$$

Where $\pi_{a,str}$ is the population proportion of stratum str within age group a (from national demographic data) and $\widehat{p}_{a,str}$ is the corresponding proportion in the sample. Weighted sample sizes were obtained by multiplying observed counts by these weights. The weighted counts were then summed across sex and region strata within each age group for inclusion in the binomial likelihood.

Data on COVID-19 mortality and hospitalization

Belgian COVID-19 mortality surveillance has been described elsewhere [30]. In short, the surveillance aimed to be exhaustive by including data from multiple sources and by including both laboratory-confirmed and clinically suspect deaths of COVID-19. The number of deaths within the surveillance data compare closely to all-cause excess mortality [1] and 'cause-of-death'-certificates [31]. We excluded deaths in nursing homes as these occurred outside the general population.

A Clinical Hospital Survey (CHS) collected data on all COVID-19 cases within the hospital [32]. As we only wanted to include hospitalizations because of COVID-19, we excluded asymptomatic cases found during screening within the hospital. There is no formal assessment of the coverage of the survey in 2020, but in comparison to an exhaustive survey on hospital intakes and capacity [32] it appears to be close to 100% (S1 Fig).

The model

We estimated weekly incidences of SARS-CoV-2 infections at week t ($incidence_t$) by age group. Incidence was multiplied by population size to obtain estimated numbers of infections. These numbers were jointly fitted to seroprevalence, hospital and mortality data. The hierarchical Bayesian model included three likelihoods:

(1) A beta-binomial for the number of positive tests out of the total number of serological tests by calendar week given the estimated number of infections and sensitivity (test- (Wantai or EuroImmun), severity- and 'time-since-infection'-specific) and specificity (test-specific).
(2) A binomial for the number of COVID-19 hospitalizations by calendar week given the estimated number of infections and the estimated

infection hospitalization rate (IHR) ('calendar time'-specific).

(3) A binomial for the number of COVID-19 deaths by calendar week given the estimated number of infections and the estimated infection fatality rate (IFR) ('calendar time'- specific).

The model was fitted independently for each age group (18–49, 50–64, 65–74 years). Except for the test specificity all input data and estimated coefficients were age-specific. The latent spline representing incidence was modelled as a function of time using a cubic B-spline without penalization with 10 internal knots. The spline coefficients were given weakly informative normal priors with mean 0 and standard deviation 100. We explore the model structure in more detail below. A glossary with details on the variables included in the model can be found in the supporting information.

Seroprevalence

Likelihood We selected a beta-binomial likelihood to account for the expected additional variance associated with seroprevalence's samples of convenience [33]. Specifically, we modeled the probability of detectable antibodies (coined seropositivity) $Pobs_{test,t}$ as informing a beta-distributed random probability $Psample_{test,t}$, which was then used as the parameter in the binomial likelihood for the observed positive samples.

$$N.pos_{test,\,t} \sim$$

$$Binomial(\,Psample_{test,t}\,,\; N_{test,\,t})$$

$$Psample_{test,t} \sim Beta(Pobs_{test,t} * r,\; (1 - Pobs_{test,t}) * r)$$

The overdispersion parameter r was given an informative gamma prior (shape = 5, scale = 1000) so by default the overdispersion should be limited. The prior however has sufficient variance to include overdispersion if necessary. We defined the cumulative incidence ($cumulative.incidence_t$) as the cumulative proportion of individuals that were infected with SARS-CoV-2 in the population at week t. We obtained it by summing weekly incidences. To obtain the seroprevalence from the cumulative incidence by week and test ($Pobs_{test,t}$) for the incidence up to week t, we used a Rogan-Gladen type estimator [14, 34].

$$\begin{aligned} Pobs_{test,t} &= sensitivity_{\,test,t} \bullet incidence_t \\ &+ (1 - cumulative.incidence_t) \\ &* (1 - specificity_{test}) \end{aligned}$$

$sensitivity_{\,test,t} \bullet incidence_t$ represents a convolution: for samples collected at week t, we sum over all prior infections weeks s, multiplying each week's incidence by the sensitivity corresponding to the elapsed time ($t - s$) since infection. This accounts for the fact that someone infected in week s and sampled in week t has a detection probability that depends on how many weeks have passed since their infection.

Sensitivity Informative priors for the sensitivity were based on accompanying work [24]. Normal approximations of the posterior distributions of the shape, scale and exponential parameters of the scale Weibull-bi-exponential distribution served as informative priors in the current model. In addition to age, we estimated severity-specific test sensitivity, distinguishing asymptomatic, symptomatic, and hospitalized infections. Since both BDS and RLS excluded hospitalized cases, we applied sensitivity estimates for non-hospitalized infections only, assuming a 30%/70% mixture of asymptomatic and symptomatic infections [35, 36]. Distributions for the test sensitivity formed by these informative priors are presented in S2 Fig and the priors themselves are presented in S1 Table.

We included a sensitivity analysis (SA) to investigate our decisions to include test sensitivity as a time-varying process with assumed severity mixture. In the SA, we included constant test-specific sensitivity estimates. They can be regarded as partially accounting for antibody decay as they were derived from data obtained at different time points [37]. Test sensitivity of the EuroImmun-assay is included as in Herzog et al. [28] (154 true positive and 27 false negative, approximately 85% sensitivity). For the Wantai-assay, test sensitivity is included based on Harritshøj et al. [38] (145 true positive and 5 false negative, approximately 97% sensitivity).

Specificity The specificity included in the Rogan-Gladen estimator was estimated from published research on samples collected prior To 2020. The specificity was assumed equal over age-groups as validation studies rarely report age-stratified results. We included five studies for Euro-Immun [38–42] (1834 true negative and 22 false positives, approximately 98.8% specificity) and five for Wantai [38, 40–43] (2066 true negatives and 20 false positives, approximately 99% specificity). A breakdown of the data used per study is presented in S2 Table. Specificity represents the probability for obtaining negative samples from non-infected individuals and it was included as a binomial likelihood function in the model. A beta-prior (shape = 20, scale = 0.1) was chosen for the specificity parameter.

Mortality and hospitalization

The binomial likelihoods for hospitalization and mortality:

$$Hospitalizations_t \sim binom\left(IHR_{period},\ incidence.hosp_t\right)$$

$$Deaths_t \sim binom\left(IFR_{period},\ incidence.death_t\right)$$

Discrete delay distributions were used to estimate the number of infections relevant for the number of hospitalizations ($incidence.hosp_t$) or deaths ($incidence.death_t$) at week t. For both hospitalizations and deaths, delays could amount to a maximum of eight weeks. Delays beyond three weeks share the same proportion parameter.

$$\begin{aligned} incidence.hosp_t = & \ prop1_{hosp} * incidence_t \\ & + prop2_{hosp} * incidence_{t-1} \\ & + prop3_{hosp} * incidence_{t-2} \\ & + prop4_{hosp} * incidence_{t-3:t-7} \end{aligned}$$

Given the Dirichlet prior distribution for the proportions ($prop$) in week $t-1:8$, proportions over the delay period summed to one. We allowed the IHR and IFR to vary across six pre-defined periods to accommodate potential temporal changes in hospital admission thresholds, treatment effectiveness or healthcare capacity. The periods were chosen based on major policy transitions (lockdowns, easing of restrictions) rather than assumed changes in clinical outcomes: pre-lockdown and first lockdown (16 February – 9 May), first inter-wave period (10 May – 18 July), summer (19 July – 22 August), second inter-wave period (23 August – 3 October), second lockdown (4 October – 12 December), and third inter-wave period (13 December 2020–31 January 2021). Both IHR and IFR had uniform priors on (0,1).

Software and code

Hierarchical Bayesian models were fitted using the Nimble package in R [44]. Code is provided in the supporting information. This package uses Markov Chain Monte Carlo (MCMC) sampling to sample from posterior distributions. We used three MCMC chains with 50,000 iterations each and a burn-in of 20,000 iterations. Thinning was set to 20. 95% Credible Intervals are included as CrI. Convergence of the different chains was checked using the Gelman-Rubin statistic, effective sample size and trace plots (Supporting Information).

Results

Data description

The number of samples collected by each of the seroprevalence studies by month is presented in Table 1 and Table 2 For those months during which both the BDS and RLS collected samples, around 4,100 samples were collected each month. For March 2020, the BDS only sampled the Flemish region, leading to a lower total number of samples for March (N = 3,349). For the summer period and after October only the BDS collected samples (N = 1,799-3,035 per collection round). The combined unweighted seroprevalence increased over time to reach 19% in the youngest age group (18–49 years) and 13% in the oldest age group (65–74 years) by the end of January 2021. After post-stratification weighting, the seroprevalence for the youngest age group decreased to 17%, while it remained at 13% for the oldest age group (Table1 and 2).

Observed Seroprevalence and the cumulative proportion infected

On 5 July 2020, the cumulative incidence (expressed as a percentage) was estimated at 5.5% (CrI 4.9–6.1), 4.0% (CrI 3.3–4.7) and 2.4% (CrI 1.7–3.2) for the 18–49, 50–64 and 65–74 year-olds, respectively. On 31 January 2021,

Table 1 Number of samples and the Seroprevalence (weighted and unweighted) by collection month per age group (A) and per study (BDS = Blood Donor Samples, RLS = Residual Laboratory Samples Laboratory Samples) (B), March 2020-January 2021, Belgium. (A) Numbers and Seroprevalence per age group

Age Group	2020-03	2020-04	2020-05	2020-06	2020-07	2020-08	2020-09	2020-10	2020-11	2020-12	2021-01
Number of samples											
18–49	1,861	2,420	2,506	3,679	1,096	1,622	2,416	2,386	1,085	1,093	1,777
50–64	904	1,100	1,024	1,655	395	581	1,076	1,016	394	410	811
65–74	584	686	625	926	309	464	625	637	320	305	447
Total	3,349	4,206	4,155	6,260	1,800	2,667	4,117	4,039	1,799	1,808	3,035
Seroprevalence - Unweighted (%)											
18–49	2.4	5.4	6.6	5.8	6.2	5.7	4.7	7.1	18	18.7	18.5
50–64	2.5	5.7	5.5	4.5	5.1	5.3	3.7	4.8	9.4	18.3	14.1
65–74	2.9	3.5	3.7	3.6	3.6	3.7	3.5	3	7.8	12.1	12.5
Seroprevalence - Weighted (%)											
18–49	2.6	5.5	6.6	5.9	6.1	5.7	4.8	7.2	16.8	17.4	17.4
50–64	3.1	5.5	5.3	4.4	4.3	5.2	3.6	4.5	8.1	17.8	13.8
65–74	3.4	4.2	3.4	3.2	3.6	4.1	3.7	3.1	7.2	10.8	12.8

Table 2 Number of samples and the Seroprevalence (weighted and unweighted) by collection month per age group (A) and per study (BDS = Blood Donor Samples, RLS = Residual Laboratory Samples) (B), March 2020-January 2021, Belgium. (B) Numbers and seroprevalence per study

Study	2020-03	2020-04	2020-05	2020-06	2020-07	2020-08	2020-09	2020-10	2020-11	2020-12	2021-01
Number of samples											
RLS	2,765	2,406	2,356	4,460	—	—	2,320	2,240	—	—	—
BDS	584	1,800	1,799	1,800	1,800	2,667	1,797	1,799	1,799	1,808	3,035
Total	3,349	4,206	4,155	6,260	1,800	2,667	4,117	4,039	1,799	1,808	3,035
Seroprevalence - Unweighted (%)											
RLS	2.7	5.3	6.3	5	—	—	4	4.8	—	—	—
BDS	1.9	4.9	5.3	5.3	5.5	5.3	4.6	7.3	14.3	17.5	16.4
Seroprevalence - Weighted (%)											
RLS	3	5.7	6.5	5.1	—	—	4.2	5	—	—	—
BDS	2.1	4.8	4.9	5.2	5.3	5.3	4.5	7	13.2	16.4	15.7

the cumulative incidence was estimated at 19.0% (CrI 17.4–20.7), 13.6% (CrI 11.5–15.8) and 10.8% (CrI 8.7–13.2) for the 18–49, 50–64 and 65–74 year-olds, respectively (Fig. 1). Over the general Belgian population aged 18 to 74 years the cumulative incidence was 16.3% (CrI 15.1–17.4).

Overlaid curves of the cumulative incidence by age group are presented in the S3 Fig. The posterior estimates for the Weibull-Bi-exponential distribution representing the sensitivity of the serological tests by age group, clinical severity and time since infection are presented in Fig. 2.

Infections, IHR and IFR

Infections were mainly acquired during the two 'waves' (surges of SARS-CoV-2 infections) peaking in March and October 2020, with few infections in between. While the younger age group was most affected during the first wave, the impact during the second wave was more evenly distributed across all age groups. The proportion infected among 65–74 year-olds however remained smaller than among the younger age groups. During the week with the highest incidence of the first wave, starting on 22 March 2020, the percentage infected was 2.0% (CrI 1.7–2.3), 1.4% (CrI 1.1–1.7) and 0.7% (CrI 0.5-1.0) in 18–49, 50–64 and 65–74 year-olds, respectively. During the week with the highest incidence of the second wave, starting 25 October 2020, the weekly proportion infected was 2.8% (CrI 2.4–3.3), 2.1% (CrI 1.6–2.7) and 1.6% (CrI 1.2–2.1) in 18–49, 50–64 and 65–74 year-olds, respectively (Fig. 3).

The IHR declined over the study period. During the first lockdown (February - May 2020) the percentage hospitalized after infection was estimated at 9.9% (CrI 7.3–14.2). It was estimated at 5.0% (CrI 3.5–7.1) in the period following the second lockdown (October - December 2020) in the oldest age group. For 50–64 year-olds the IHR went from 4.2% (CrI 3.5–5.1) to 2.3% (CrI 1.7–3.1) and in the youngest age group, the percentage declined from 1.0% (CrI 0.8–1.1) to 0.4% (CrI 0.3–0.6). A similar trend in which the rates were significantly reduced over 2020 was observed for the IFR. For 65–74 year-olds, the IFR decreased from 2.8% (CrI 2.0–4.0) to 1.2% (CrI 0.9–1.7), for 50–64 year-olds, it decreased from 0.5% (CrI 0.4–0.6) to 0.3% (CrI 0.2–0.4). For 18–49 year-olds, the IFR remained low at 0.03% (CrI 0.02–0.04) throughout the study period. During the period from mid-July to end of August, both the IHR and IFR transiently increased.

Time to event

The discrete delay distribution for hospitalizations peaked in the first week. Of those infections that result in hospitalization, 67% (CrI 58–76, 18-49y), 75% (CrI 63–88, 50-64y) and 89% (CrI 76–97, 65-74y) did so within the week of infection. In comparison, only few infections resulted in death within the same week, between 9 and 13%. For the youngest age group, deaths mostly occurred two weeks after infection. While for the older age groups deaths were spread over the weeks following the first week after infection (S3 Table).

Sensitivity analysis

Our sensitivity analysis (SA) to assess robustness to the distribution and informative priors used for the tests' sensitivity resulted in the following two main observations. The SA-sensitivity was higher for younger age groups resulting in a decrease in estimated incidence compared to the main analysis (17.4% compared to 19%). Second, the fit to the seroprevalence data was worse in the SA, illustrated by a smaller estimate for the overdispersion parameter, compared to the main analysis. SA results are presented in the S4 Fig.

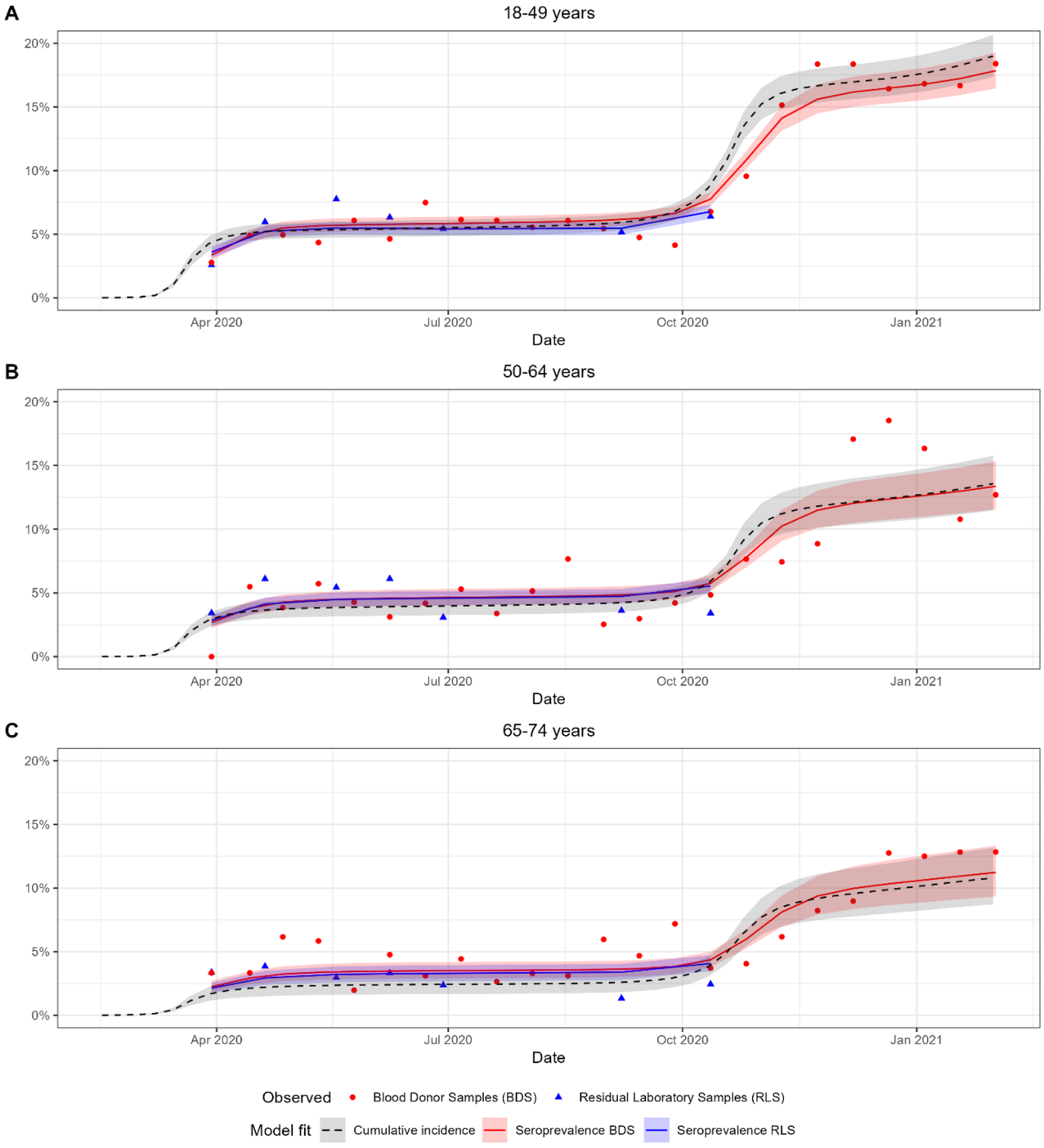

Fig. 1 The observed, weighted seroprevalence (points) and posterior model fit for seroprevalence (colored lines) by study, date of collection round and age group. In addition the cumulative incidence (grey line) and 95% Credible intervals (transparant ribbons) are presented. **A** 18-49 years, (**B**) 50-64 years and (**C**) 65-74 years. February 2020 - January 2021, Belgium

Model goodness of fit

The model provided acceptable posterior predictive intervals for the fitted data: seroprevalence results of RLS and BDS, the age-specific hospitalizations and deaths (S5 Fig). Graphical overviews by age group of the time series of infections, cases, hospital intakes and deaths are provided in S6 Fig.

Discussion

Our work contributes to an ongoing effort to estimate the incidence of SARS-CoV-2 infections during the initial year of the pandemic. We combined data from two different repeated cross-sectional seroprevalence studies, including informative priors for the characteristics of

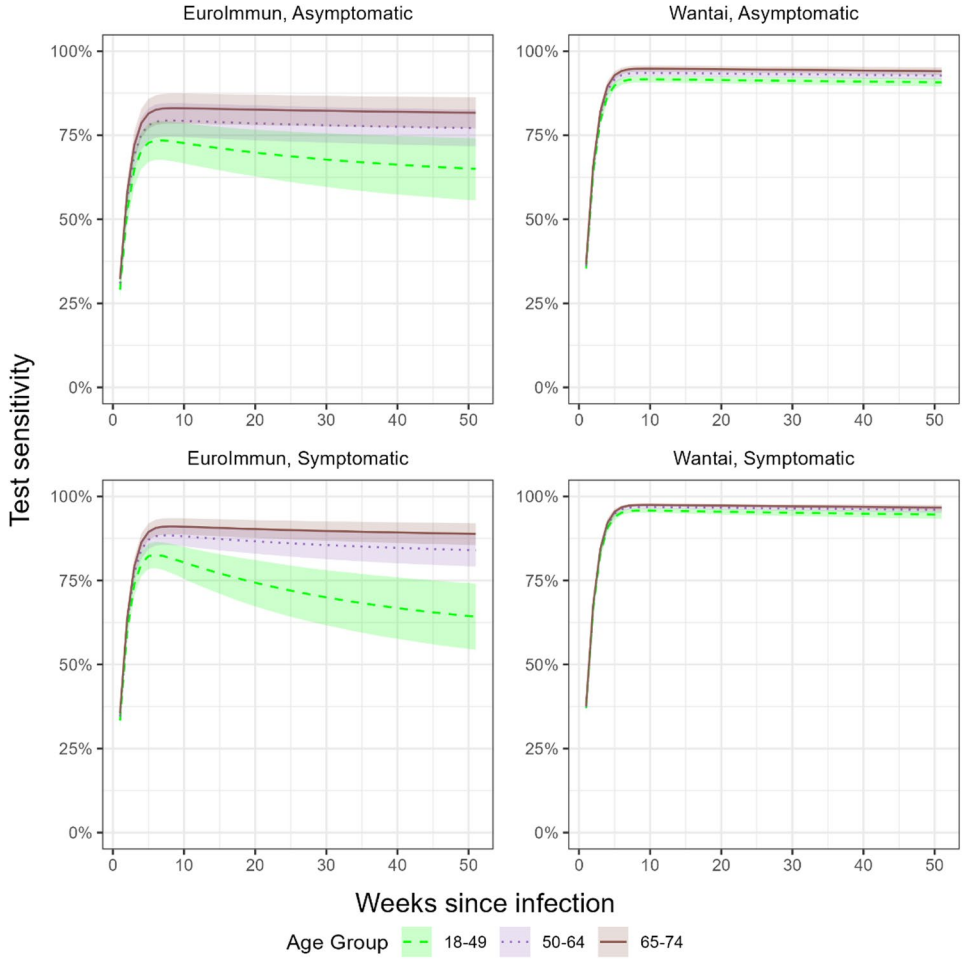

Fig. 2 Posterior 'time-since-infection'-varying estimates for the test sensitivity of the EuroImmun (left) and Wantai (right) test. For asymptomatic infection (upper) and symptomatic infection (lower) by age group (18–49 years, 50–64 years and 65–74 years). 95% Credible intervals are presented as transparent ribbons

the serological tests, with surveillance data on COVID-19 hospitalizations and deaths. Posterior incidence estimates showed two waves in 2020, with little transmission in between. We estimated that 16.3% of the general Belgian population aged 18 to 74 years old had been infected by the start of 2021. The first wave mainly affected those under 50 years old. The second wave affected age groups more equally and was associated with lower IHR and IFR.

Seroprevalence results

With seroprevalence estimates around 16% for the general adult population, Belgium ranked high among countries affected by COVID-19 in the initial year. A systematic review of sero-epidemiological studies estimated the worldwide seroprevalence at 4.5% by December 2020 [11]. Among European countries, Germany (1.7%, November [37]), Norway (0.9%, December [45]), Denmark (2.2%, October [46]) and Iceland (0.9% June [47]) can be classified as having low seroprevalence. European countries reporting higher seroprevalence included Spain, the Netherlands and England with 9.8% (November 2020 [48]), 12.2% (February 2021 [49]) and 12.1% (December 2020 [50]), respectively. A direct comparison, however, is not possible given the limitations of seroprevalence studies presented earlier.

While we did report age group-specific estimates, we did not explore incidences within specific settings. Other Belgian seroprevalence studies have examined healthcare workers (~ 7% after the first wave [13, 51]), nursing home residents and staff (17–21% [52]), and children (6 months to 16 years, comparable or lower than adults [53–55]), with detailed findings presented in the supporting information.

IHR and IFR

Our IHR and IFR and their evolution over time are in accordance with results from meta-analyses which likewise reported a decrease over 2020 [26, 56, 57]. These findings have been linked to improvements in treatment [58]. Discussion remains about the exact trend over 2020

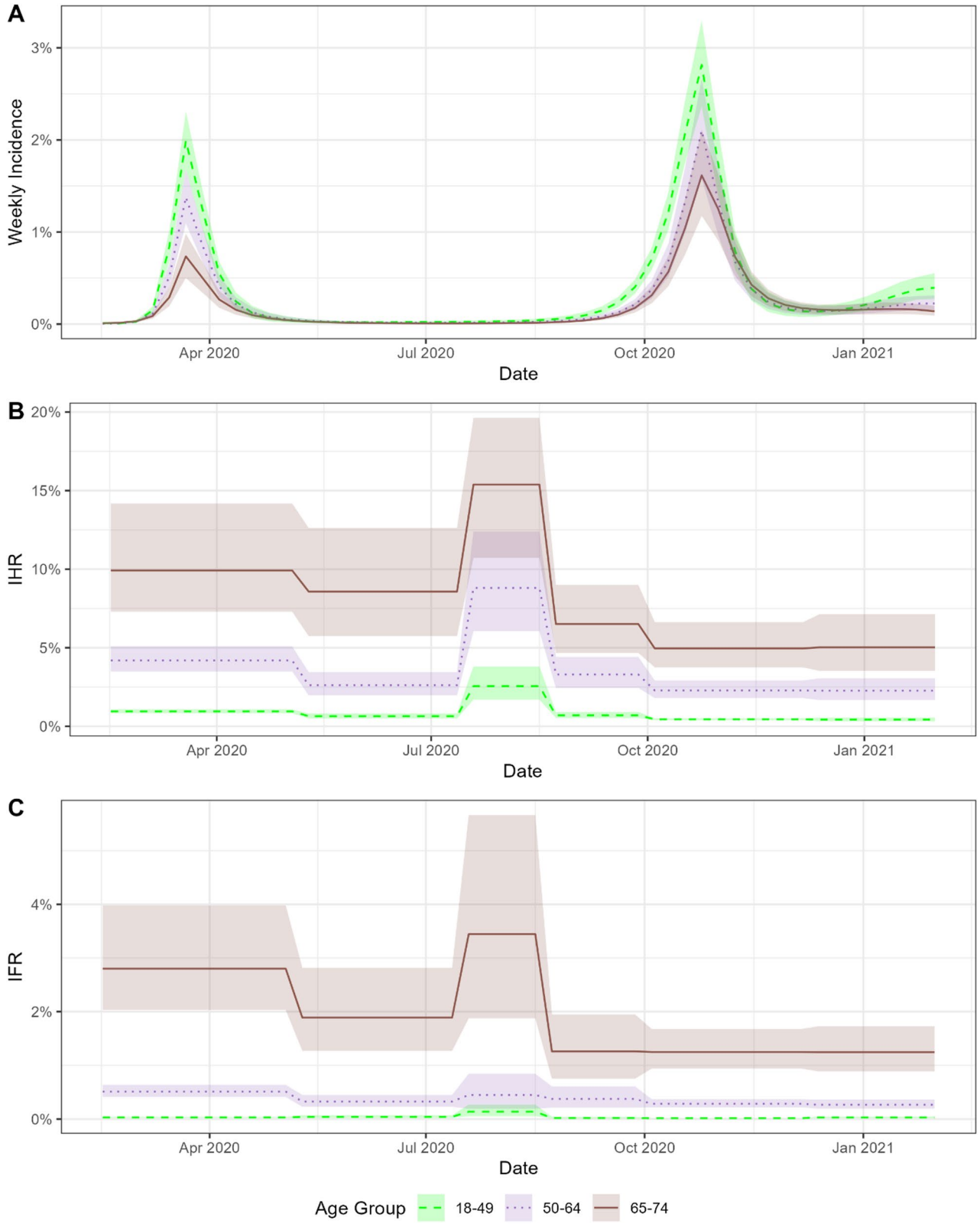

Fig. 3 **A** Weekly incidence of SARS-CoV-2 infections and 95% Credible Interval (CrI), **B** infection hospitalization rate (IHR) and CrI and **C** the infection fatality rate (IFR) and CrI. February 2020 – January 2021, Belgium

[59]. Because of temporal changes in hospital occupancy and admission protocols [60], short-term trends might deviate from the long-term trend. We observed elevated IHR and IFR estimates in August 2020, coinciding with a prolonged heatwave associated with considerable excess mortality [61]. A heatwave could directly increase IHR and IFR through heightened patient vulnerability. However, it is also likely that COVID-19 mortality surveillance captured some heat-related deaths, and that the low infection incidence during this period amplified this effect—even minor numerator misclassification disproportionately affects ratios when the denominator is small. The subsequent apparent decrease in IHR and IFR from August to November thus more plausibly reflects the resolution of this artifact than a true change in IFR, with autumn estimates rejoining the overall declining trend observed throughout 2020.

Molenberghs et al. [62] estimated lower IFR for the first wave using the same mortality data but derived incidence from a stochastic compartmental model [63] that assumed perfect serological test specificity. This yielded higher cumulative incidence estimates (6.9% by 4 May 2020) and consequently lower IFR. Our explicit modeling of imperfect specificity produces more conservative incidence estimates.

Methods

Several approaches exist for combining seroprevalence and surveillance data to estimate incidence. Unlike stepwise methods that first estimate IFR from seroprevalence before deriving incidence (e.g., REMEDID [64], IHME [26], Shioda et al. [25]), an approach that requires temporal homogeneity of IFR [27], we directly incorporated all data within a unified Bayesian framework. A key distinction is our treatment of test sensitivity: we included age- and severity-specific estimates using a Weibull-Bi-exponential distribution with informative priors derived from longitudinal serological data, capturing both seroconversion and seroreversion. This contrasts with approaches that ignore severity of infection [65], estimate sensitivity parameters directly from serosurvey data [25], assume fixed seroconversion delays [66] or average over assays [66]. Like Shioda et al. [25], we used a Weibull distribution for the seroconversion. For the seroreversion, we used a mixture of two exponential distributions. Others included single Weibull distributions [25, 67, 68] or constant exponential rates [69–71]. Similar to Takahashi et al. [27], Kadelka et al. [15] and others [66, 72], we estimated the parameters of these distributions from longitudinal data on serological testing [24]. Kadelka et al. demonstrated the importance of this choice, revising Buss et al.'s cumulative incidence estimate for Manaus from 76% [69] to 47.6% [15] after incorporating longitudinal antibody data. Our framework also estimated delay distributions from the data rather than requiring them a priori [25, 64], and explicitly modeled test specificity—important when prevalence is low and false positives can substantially inflate estimates.

Barber et al. [26] pursued similar objectives with comparable Belgian data, though they included seroprevalence indirectly, ignored specificity, and assumed more aggressive EuroImmun sensitivity decay. Despite these differences, their results align with ours: approximately 18% of Belgians infected by early 2021, accumulated over two waves, with comparable IFR estimates and trends.

Limitations

We observed overdispersion in the seroprevalence data. While priors initially favored minimal overdispersion, the data supported substantial excess variability beyond that expected from modelled infection rates and sample sizes alone. This likely reflects limitations inherent to these convenience samples: unmeasured cohort heterogeneity, spatial effects, differing protocols between BDS and RLS, and selection biases. For example, Herzog et al. [28] noted that self-confinement behavior among typical healthcare-seeking individuals may have affected participation in earlier RLS rounds differently than later ones. With only broad age stratification and limited participant information available, we could not fully characterize or adjust for these sources of variability. Robust inference from seroprevalence studies requires designs that better control for such biases [73].

This study uses a spline to model the underlying incidence of infections. This incidence is constrained by the spline's structure. We explored different possible splines by fitting them to advanced mortality and hospitalization time series. Other possibilities have not been explored in this paper. Case data is presented alongside the model outputs (S6 Fig), but it was not used in the model fit or for deciding on possible knot placement. Case ascertainment was not investigated in this paper. In addition, the estimation of IHR and IFR might be sensitive to the periods over which they are estimated.

PCR-confirmed infection is used in this paper as a proxy for SARS-CoV-2 infection. Much of the work on test sensitivity and specificity, but also work on IFR and IHR is based on PCR-confirmed infections. Translating modelled infection timing to potential PCR-confirmation timing would require an additional step incorporating delays, test sensitivity, and specificity associated with PCR testing itself.

In conclusion: by early 2021, one in six Belgian adults had been infected with SARS-CoV-2—substantially higher than confirmed case counts. We observed declining IHR and IFR throughout 2020 suggesting improvements in clinical management. Our integrated modelling approach, which jointly fits multiple data sources while

accounting for time-varying test sensitivity, provides a template for estimating infection burden when surveillance is incomplete.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13690-026-01860-z.

Supplementary Material 1.

Supplementary Material 2.

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Authors' contributions
TB designed the study, conducted analysis, and wrote the initial draft. RDP and LG conducted the BDS and performed initial analysis. SA, ID, NiHe, NaHa, and MH supervised methodology and writing. AM coordinated seroprevalence studies. SAH coordinated the RLS study and analysis. All authors approved the final manuscript.

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Data availability
The datasets supporting the conclusions of this article are available online or can be obtained after request. The RLS data is available on Zenodo (http://doi.org/10.5281/zenodo.4664403). Other datasets (Belgian surveillance data on cases, hospitalizations and deaths) can be obtained from https://epidata.sciensano.be/epistat/dashboard/#covid. The BDS dataset analyzed during the current study is available from the corresponding author on reasonable request.

Declarations

Ethics and consent to participate
The BDS protocol was approved by the ethical committee of UZ Leuven (ethical approval S63932-UZ Leuven). Donors were excluded from the study if no consent was given for the use of residual blood for scientific research. The RLS protocol was approved by the Ethics Committee of the University Hospital Antwerp-University of Antwerp on 30 March 2020 (ref 20/13/158; Belgian Number B3002020000047). The committee agreed with inclusion without informed consent, on the condition of the samples being collected anonymously.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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References

1. Sierra NB, Bossuyt N, Braeye T, Leroy M, Moyersoen I, Peeters I, et al. All-cause mortality supports the COVID-19 mortality in Belgium and comparison with major fatal events of the last century. Arch Public Health. 2020;78(1):1–8.
2. Luyten J, Schokkaert E. Belgium's response to the COVID-19 pandemic. Health Econ Policy Law. 2022;17(1):37–47.
3. Sciensano. Epistat - Belgian COVID-19 opendata. Available from: https://epistat.wiv-isp.be/covid/ Cited 2020 Sep 12.
4. Meurisse M, Lajot A, Dupont Y, Lesenfants M, Klamer S, Rebolledo J, et al. One year of laboratory-based COVID-19 surveillance system in belgium: main indicators and performance of the laboratories (March 2020-21). Arch Public Health Arch Belg Sante Publique. 2021;79(1):188.
5. Duysburgh E, Mortgat L, Barbezange C, Dierick K, Fischer N, Heyndrickx L, et al. Persistence of IgG response to SARS-CoV-2. Lancet Infect Dis. 2021;21(2):163–4.
6. To KKW, Tsang OTY, Leung WS, Tam AR, Wu TC, Lung DC, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. Lancet Infect Dis. 2020;20(5):565–74.
7. Xu X, Sun J, Nie S, Li H, Kong Y, Liang M, et al. Seroprevalence of Immunoglobulin M and G antibodies against SARS-CoV-2 in China. Nat Med. 2020;26(8):1193–5.
8. Wajnberg A, Amanat F, Firpo A, Altman DR, Bailey MJ, Mansour M, et al. Robust neutralizing antibodies to SARS-CoV-2 infection persist for months. Science. 2020;370(6521):1227–30.
9. Rostami A, Sepidarkish M, Leeflang MMG, Riahi SM, Nourollahpour Shiadeh M, Esfandyari S, et al. SARS-CoV-2 Seroprevalence worldwide: a systematic review and meta-analysis. Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis. 2021;27(3):331–40.
10. Hanson KE, Caliendo AM, Arias CA, Englund JA, Hayden MK, Lee MJ, et al. Infectious diseases society of America guidelines on the diagnosis of COVID-19:Serologic testing. Clin Infect Dis Off Publ Infect Dis Soc Am; 2020.
11. Bergeri I, Whelan MG, Ware H, Subissi L, Nardone A, Lewis HC, et al. Global SARS-CoV-2 Seroprevalence from January 2020 to April 2022: A systematic review and meta-analysis of standardized population-based studies. PLOS Med. 2022;19(11):e1004107.
12. Lohse S, Sternjakob-Marthaler A, Lagemann P, Schöpe J, Rissland J, Seiwert N, et al. German federal-state-wide Seroprevalence study of 1st SARS-CoV-2 pandemic wave shows importance of long-term antibody test performance. Commun Med. 2022;2(1):1–12.

13. Mortgat L, Verdonck K, Hutse V, Thomas I, Barbezange C, Heyndrickx L, et al. Prevalence and incidence of anti-SARS-CoV-2 antibodies among healthcare workers in Belgian hospitals before vaccination: a prospective cohort study. BMJ Open. 2021;11(6):e050824.
14. Rogan WJ, Gladen B. Estimating prevalence from the results of a screening test. Am J Epidemiol. 1978;107(1):71–6.
15. Kadelka S, Bouman JA, Ashcroft P, Regoes RR. Correcting for antibody waning in cumulative incidence Estimation from sequential serosurveys. Am J Epidemiol. 2024;193(5):777–86.
16. Gededzha MP, Mampeule N, Jugwanth S, Zwane N, David A, Burgers WA, et al. Performance of the EUROIMMUN Anti-SARS-CoV-2 ELISA assay for detection of IgA and IgG antibodies in South Africa. PLoS ONE. 2021;16(6):e0252317.
17. Bailie CR, Tseng YY, Carolan L, Kirk MD, Nicholson S, Fox A, et al. Trend in sensitivity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) serology one year after mild and asymptomatic coronavirus disease 2019 (COVID-19): unpacking potential bias in Seroprevalence studies. Clin Infect Dis Off Publ Infect Dis Soc Am. 2022;75(1):e357–60.
18. Perez-Saez J, Zaballa ME, Yerly S, Andrey DO, Meyer B, Eckerle I et al. Persistence of anti-SARS-CoV-2 antibodies: immunoassay heterogeneity and implications for serosurveillance. Clin Microbiol Infect. 2021;27(11):1695.e7-1695.e12.
19. Dehgani-Mobaraki P, Zaidi AK, Yadav N, Floridi A, Floridi E. Longitudinal observation of antibody responses for 14 months after SARS-CoV-2 infection. Clin Immunol. 2021;230:108814.
20. Gallais F, Gantner P, Bruel T, Velay A, Planas D, Wendling MJ, et al. Evolution of antibody responses up to 13 months after SARS-CoV-2 infection and risk of reinfection. EBioMedicine. 2021;71:103561.
21. Petersen MS, Pérez-Alós L, Armenteros JJA, Hansen CB, Fjallsbak JP, Larsen S, et al. Factors influencing the immune response over 15 months after SARS-CoV-2 infection: A longitudinal population-wide study in the Faroe Islands. J Intern Med. 2023;293(1):63–81.
22. Hønge BL, Hindhede L, Kaspersen KA, Harritshøj LH, Mikkelsen S, Holm DK, et al. Long-term detection of SARS-CoV-2 antibodies after infection and risk of re-infection. Int J Infect Dis IJID Off Publ Int Soc Infect Dis. 2022;116:289–92.
23. Barrios MH, Nicholson S, Bull RA, Martinello M, Rawlinson W, Mina M, et al. Comparative longitudinal serological study of Anti-SARS-CoV-2 antibody profiles in people with COVID-19. Microorganisms. 2023;11(8):1985.
24. Braeye T, Abrams S, Hens N. Factors influencing SARS-CoV-2 IgG test sensitivity: A bayesian analysis of seroconversion and seroreversion by time since infection, test, age and disease severity. PLoS ONE. 2026;21(2):e0328144.
25. Shioda K, Lau MSY, Kraay ANM, Nelson KN, Siegler AJ, Sullivan PS, et al. Estimating the cumulative incidence of SARS-CoV-2 infection and the infection fatality ratio in light of waning antibodies. Epidemiology. 2021;32(4):518.
26. Barber RM, Sorensen RJD, Pigott DM, Bisignano C, Carter A, Amlag JO, et al. Estimating global, regional, and National daily and cumulative infections with SARS-CoV-2 through Nov 14, 2021: a statistical analysis. Lancet. 2022;399(10344):2351–80.
27. Takahashi S, Peluso MJ, Hakim J, Turcios K, Janson O, Routledge I, et al. SARS-CoV-2 serology across scales: A framework for unbiased Estimation of cumulative incidence incorporating antibody kinetics and epidemic recency. Am J Epidemiol. 2023;192(9):1562–75.
28. Herzog SA, Bie JD, Abrams S, Wouters I, Ekinci E, Patteet L, et al. Seroprevalence of IgG antibodies against SARS-CoV-2 – a serial prospective cross-sectional nationwide study of residual samples, Belgium, March to October 2020. Eurosurveillance. 2022;27(9):2100419.
29. Aantal bloeddonoren en. gezondheidswerkers met antistoffen tegen coronavirus stijgt. sciensano.be. Available from: https://www.sciensano.be/nl/pershoek/aantal-bloeddonoren-en-gezondheidswerkers-met-antistoffen-tegen-coronavirus-stijgt Cited 2025 Mar 21.
30. Renard F, Scohy A, Van der Heyden J, Peeters I, Dequeker S, Vandael E, et al. Establishing an ad hoc COVID-19 mortality surveillance during the first epidemic wave in Belgium, 1 March to 21 June 2020. Euro Surveill Bull Eur Sur Mal Transm Eur Commun Dis Bull. 2021;26(48):2001402.
31. Vernemmen C, Ekelson R, Jurčević J, Nganda S, Scohy A, Dequeker S, et al. COVID-19 mortality statistics: A comparative study of epidemiological surveillance data and death certificates in 2020 in Belgium. Quetelet J. 2023;11(1):1–39.
32. Van Goethem N, Vilain A, Wyndham-Thomas C, Deblonde J, Bossuyt N, Lernout T, et al. Rapid establishment of a National surveillance of COVID-19 hospitalizations in Belgium. Arch Public Health Arch Belg Sante Publique. 2020;78(1):121.
33. Abrams S, Aerts M, Molenberghs G, Hens N. Parametric overdispersed frailty models for current status data. Biometrics. 2017;73(4):1388–400.
34. Meyer MJ, Yan S, Schlageter S, Kraemer JD, Rosenberg ES, Stoto MA. Adjusting COVID-19 Seroprevalence survey results to account for test sensitivity and specificity. Am J Epidemiol. 2022;191(4):681–8.
35. Buitrago-Garcia D, Ipekci AM, Heron L, Imeri H, Araujo-Chaveron L, Arevalo-Rodriguez I, et al. Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: update of a living systematic review and meta-analysis. PLOS Med. 2022;19(5):e1003987.
36. Sah P, Fitzpatrick MC, Zimmer CF, Abdollahi E, Juden-Kelly L, Moghadas SM, et al. Asymptomatic SARS-CoV-2 infection: A systematic review and meta-analysis. Proc Natl Acad Sci U S A. 2021;118(34):e2109229118.
37. Neuhauser H, Rosario AS, Butschalowsky H, Haller S, Hoebel J, Michel J, et al. Nationally representative results on SARS-CoV-2 Seroprevalence and testing in Germany at the end of 2020. Sci Rep. 2022;12:19492.
38. Harritshøj LH, Gybel-Brask M, Afzal S, Kamstrup PR, Jørgensen CS, Thomsen MK, et al. Comparison of 16 serological SARS-CoV-2 immunoassays in 16 clinical laboratories. J Clin Microbiol. 2021;59(5). https://doi.org/10.1128/jcm.02596-20.
39. Meyer B, Torriani G, Yerly S, Mazza L, Calame A, Arm-Vernez I, et al. Validation of a commercially available SARS-CoV-2 serological immunoassay. Clin Microbiol Infect. 2020;26(10):1386–94.
40. Scheiblauer H, Nübling CM, Wolf T, Khodamoradi Y, Bellinghausen C, Sonntagbauer M, et al. Antibody response to SARS-CoV-2 for more than one year – kinetics and persistence of detection are predominantly determined by avidity progression and test design. J Clin Virol. 2022;146:105052.
41. Lassaunière R, Frische A, Harboe ZB, Nielsen ACY, Fomsgaard A, Krogfelt KA et al. Evaluation of nine commercial SARS-CoV-2 immunoassays. medRxiv; 2020. p. 2020.04.09.20056325. Available from: https://www.medrxiv.org/content/https://doi.org/10.1101/2020.04.09.20056325v1. Cited 2024 Mar 4.
42. GeurtsvanKessel CH, Okba NMA, Igloi Z, Bogers S, Embregts CWE, Laksono BM, et al. An evaluation of COVID-19 serological assays informs future diagnostics and exposure assessment. Nat Commun. 2020;11(1):3436.
43. Nyagwange J, Kutima B, Mwai K, Karanja HK, Gitonga JN, Mugo D, et al. Comparative performance of WANTAI ELISA for total Immunoglobulin to receptor binding protein and an ELISA for IgG to Spike protein in detecting SARS-CoV-2 antibodies in Kenyan populations. J Clin Virol. 2022;146:105061.
44. License. and Citation – NIMBLE. Available from: https://r-nimble.org/license-and-citation Cited 2021 Jun 18.
45. Anda EE, Braaten T, Borch KB, Nøst TH, Chen SLF, Lukic M, et al. Seroprevalence of antibodies against SARS-CoV-2 in the adult population during the pre-vaccination period, Norway, winter 2020/21. Euro surveill bull Eur Sur Mal transm. Eur Commun Dis Bull. 2022;27(13):2100376.
46. Espenhain L, Tribler S, Sværke Jørgensen C, Holm Hansen C, Wolff Sönksen U, Ethelberg S. Prevalence of SARS-CoV-2 antibodies in denmark: nationwide, population-based seroepidemiological study. Eur J Epidemiol. 2021;36(7):715–25.
47. Gudbjartsson DF, Norddahl GL, Melsted P, Gunnarsdottir K, Holm H, Eythorsson E, et al. Humoral immune response to SARS-CoV-2 in Iceland. N Engl J Med. 2020;383(18):1724–34.
48. Pérez-Gómez B, Pastor-Barriuso R, Fernández-de-Larrea N, Hernán MA, Pérez-Olmeda M, Oteo-Iglesias J, et al. SARS-CoV-2 infection during the first and second pandemic waves in spain: the ENE–COVID study. Am J Public Health. 2023;113(5):533–44.
49. Vos ERA, van Hagen CCE, Wong D, Smits G, Kuijer M, Wijmenga-Monsuur AJ, et al. SARS-CoV-2 Seroprevalence trends in the Netherlands in the variant of concern era: input for future response. Influenza Other Respir Viruses. 2024;18(6):e13312.
50. Coronavirus (COVID-19). Infection Survey - Office for National Statistics. . Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/coronaviruscovid19infectionsinthecommunityinengland/antibodydatafortheukjanuary2021 Cited 2024 Sep 17.
51. Naesens R, Mertes H, Clukers J, Herzog S, Brands C, Vets P, et al. SARS-CoV-2 Seroprevalence survey among health care providers in a Belgian public multiple-site hospital. Epidemiol Infect. 2021;149:e172.
52. De Rop L, Vercruysse H, Alenus U, Brusselmans J, Callens S, Claeys M, et al. SARS-CoV-2 seropositivity in nursing home staff and residents during the first SARS-CoV-2 wave in Flanders, Belgium. Viruses. 2024;16(9):1461.
53. Boey L, Roelants M, Merckx J, Hens N, Desombere I, Duysburgh E, et al. Age-dependent Seroprevalence of SARS-CoV-2 antibodies in school-aged

children from areas with low and high community transmission. Eur J Pediatr. 2022;181(2):571–8.
54. Cremer K, Frère J, Chatzis O, Mendonca RD, Kabamba B, Renard F, et al. SARS-CoV-2 antibody Seroprevalence in children and workers from Belgian French-Speaking primary schools. Health (N Y). 2023;15(9):917–37.
55. Dethioux L, Dauby N, Montesinos I, Rebuffat E, Hainaut M. SARS-CoV-2 Seroprevalence in children and their family members, July–October 2020, Brussels. Eur J Pediatr. 2022;181(3):1009–16.
56. Levin AT, Hanage WP, Owusu-Boaitey N, Cochran KB, Walsh SP, Meyerowitz-Katz G. Assessing the age specificity of infection fatality rates for COVID-19: systematic review, meta-analysis, and public policy implications. Eur J Epidemiol. 2020;35(12):1123–38.
57. COVID-19 Forecasting Team. Variation in the COVID-19 infection-fatality ratio by age, time, and geography during the pre-vaccine era: a systematic analysis. Lancet Lond Engl. 2022;399(10334):1469–88.
58. Cheng C, Zhou H, Weiss JC, Lipton ZC. Unpacking the Drop in COVID-19 Case Fatality Rates: A Study of National and Florida Line-Level Data. AMIA Annu Symp Proc. 2022;2021:285.
59. de Boer PT, van de Kassteele J, Vos ERA, van Asten L, Dongelmans DA, van Gageldonk-Lafeber AB, et al. Age-specific severity of severe acute respiratory syndrome coronavirus 2 in February 2020 to June 2021 in the Netherlands. Influenza Other Respir Viruses. 2023;17(8):e13174.
60. Taccone FS, Goethem NV, Pauw RD, Wittebole X, Blot K, Oyen HV et al. The role of organizational characteristics on the outcome of COVID-19 patients admitted to the ICU in Belgium. Lancet Reg Health – Eur [Internet]. 2021 Mar 1 [cited 2021 May 11];2. Available from: https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(20)30019-3/abstract
61. Aanzienlijke oversterfte tijdens de hittegolf van. augustus 2020. sciensano.be. Available from: https://www.sciensano.be/nl/pershoek/aanzienlijke-oversterfte-tijdens-de-hittegolf-van-augustus-2020 Cited 2025 Mar 21.
62. Molenberghs G, Faes C, Verbeeck J, Deboosere P, Abrams S, Willem L, et al. COVID-19 mortality, excess mortality, deaths per million and infection fatality ratio, Belgium, 9 March 2020 to 28 June 2020. Eurosurveillance. 2022;27(7):2002060.
63. Abrams S, Wambua J, Santermans E, Willem L, Kuylen E, Coletti P, et al. Modelling the early phase of the Belgian COVID-19 epidemic using a stochastic compartmental model and studying its implied future trajectories. Epidemics. 2021;35:100449.
64. García-García D, Vigo MI, Fonfría ES, Herrador Z, Navarro M, Bordehore C. Retrospective methodology to estimate daily infections from deaths (REMEDID) in COVID-19: the Spain case study. Sci Rep. 2021;11(1):11274.
65. Fox T, Geppert J, Dinnes J, Scandrett K, Bigio J, Sulis G et al. Antibody tests for identification of current and past infection with SARS-CoV-2. Cochrane Database Syst Rev. 2022;(11). Available from: https://www.cochranelibrary.com/cdsr/doi/ https://doi.org/10.1002/14651858.CD013652.pub2/full. Cited 2024 Jun 2.
66. Brazeau NF, Verity R, Jenks S, Fu H, Whittaker C, Winskill P, et al. Estimating the COVID-19 infection fatality ratio accounting for seroreversion using statistical modelling. Commun Med. 2022;2(1):1–13.
67. Sullivan PS, Siegler AJ, Shioda K, Hall EW, Bradley H, Sanchez T, et al. Severe acute respiratory syndrome coronavirus 2 cumulative Incidence, united States, August 2020–December 2020. Clin Infect Dis. 2022;74(7):1141–50.
68. Lamba K, Bradley H, Shioda K, Sullivan PS, Luisi N, Hall EW, et al. SARS-CoV-2 cumulative incidence and period seroprevalence: results from a statewide Population-Based serosurvey in California. Open Forum Infect Dis. 2021;8(8):ofab379.
69. Buss LF, Prete CA, Abrahim CMM, Mendrone A, Salomon T, de Almeida-Neto C, et al. Three-quarters attack rate of SARS-CoV-2 in the Brazilian Amazon during a largely unmitigated epidemic. Science. 2021;371(6526):288–92.
70. Chen S, Flegg JA, White LJ, Aguas R. Levels of SARS-CoV-2 population exposure are considerably higher than suggested by Seroprevalence surveys. PLOS Comput Biol. 2021;17(9):e1009436.
71. Duong S, Burtniak J, Gretchen A, Mai A, Klassen P, Wei Y, et al. Riding high: Seroprevalence of SARS-CoV-2 after 4 pandemic waves in Manitoba, Canada, April 2020–February 2022. BMC Public Health. 2023;23(1):2420.
72. Petrie JG, Eisenberg MC, Lauring AS, Gilbert J, Harrison SM, DeJonge PM, et al. The variant-specific burden of SARS-CoV-2 in michigan: March 2020 through November 2021. J Med Virol. 2022;94(11):5251–9.
73. Blaizot S, Herzog SA, Abrams S, Theeten H, Litzroth A, Hens N. Sample size calculation for estimating key epidemiological parameters using serological data and mathematical modelling. BMC Med Res Methodol. 2019;19(1):51.

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