Inference under superspreading: Determinants of SARS-CoV-2 transmission in Germany

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Superspreading, under-reporting, reporting delay, and confounding complicate statistical inference on determinants of disease transmission. A model that accounts for these factors within a Bayesian framework is estimated using German Covid-19 surveillance data. Compartments based on date of symptom onset, location, and age group allow to identify age-specific changes in transmission, adjusting for weather, reported prevalence, and testing and tracing. Several factors were associated with a reduction in transmission: public awareness rising, information on local prevalence, testing and tracing, high temperature, stay-at-home orders, and restaurant closures. However, substantial uncertainty remains for other interventions including school closures and mandatory face coverings. The challenge of disentangling the effects of different determinants is discussed and examined through a simulation study. On a broader perspective, the study illustrates the potential of surveillance data with demographic information and date of symptom onset to improve inference in the presence of under-reporting and reporting delay.

KEYWORDS
Covid-19, infectious diseases, instantaneous reproductive number, nonpharmaceutical interventions

1 | INTRODUCTION

In response to the Covid-19 pandemic societies around the world have responded with unprecedented policy interventions and changes in behavior. Before vaccines became available, transmission reduction was the dominant strategy to prevent direct harm from the SARS-CoV-2 virus. Yet, the impact of policy interventions remains a controversial topic in the public domain. This study aims at improving our understanding of the transmission dynamics in the first months of the Covid-19 pandemic. Additionally, the work can inform the discussion on surveillance data and inference for infectious diseases in general.

Individual variation in transmission or so-called superspreading\(^1\) complicates the collection of adequate evidence. Overdispersion in the offspring distribution (high likelihood of superspreading) is well documented for SARS-CoV-1\(^2,3\) and shown to be a dominant feature of SARS-CoV-2\(^4,6\). Under superspreading single cases convey little information as transmission kinetics are driven by few outliers. Thus, conclusions drawn from case studies with few primary cases\(^7,8\) are subject to substantial uncertainty.
In the absence of sufficiently large and detailed contact tracing data, the effectiveness of policy interventions has been studied based on surveillance data with location-specific aggregated cases, deaths, or both. However, such data provide additional challenges for inferring transmission dynamics, including a varying reporting delay, under-reporting, and a lack of established methods to account for superspreading.

Those issues are addressed with the following three points. First, by aggregating cases based on symptom onset instead of reporting date, the timing of transmission is estimated more sharply and reporting delays do not invalidate inference. Second, underreporting is accounted for by modelling infections as unobservable renewal processes. Age compartments (in addition to location) allow to identify age-specific growth factors even if reporting differs between age groups. Finally, a probabilistic infection process extends the seminal model for superspreading on the individual level. This facilitates inference on reproductive numbers and their determinants consistent with compartments with low (high) case counts providing more (less) noisy signals.

Compared to earlier studies with renewal processes considering the first wave of SARS-CoV-2, the analysis presented here provides several improvements. Instead of a deterministic transmission model with stochastic reporting, the latent infections follow a stochastic process derived from an individual-based transmission model with superspreading. In doing so, this is the first study that estimates the dispersion of the offspring distribution without contact tracing data or outbreak specific information. Further, additional day- and location-specific covariates besides policy interventions are considered to reduce the risk of confounding with seasonality, voluntary behavior changes, and testing and tracing. Finally, disaggregation by age groups allows to estimate differential impacts of interventions on subpopulations, which is crucial to inform policy.

The following section introduces the model and discusses the identification of reproductive numbers, determinants of transmission, and superspreading. It concludes by describing the estimation procedure and discussing the assumptions. Afterward, the data is described in Section 3. Section 4 presents the main study’s results and robustness checks. Section 5 investigates the main challenges of inference via simulations. Finally, a discussion is provided in Section 6, before the conclusion in Section 7. Technical details are delegated to the Appendix Section A and the Appendix S1 provides additional details in Sections S1 through S5.

2 | METHOD

This section introduces the model, followed by a discussion on the identification of reproductive numbers, superspreading, and transmission determinants. The model’s estimation procedure and assumptions are subsequently described.

2.1 | Model

The model consists of three components: The transmission model outlines the latent process of infection counts within each compartment, defined by location and age group, based on compartment-specific instantaneous reproductive numbers. The measurement model probabilistically links unobserved infections to reported cases. Lastly, the effect model aggregates signals across locations to describe how covariates (such as interventions, weather conditions, and information) impact the instantaneous reproductive number.

As illustrated in Figure 1, the model distinguishes between infections $i_t$, which are contracted at time $t$, and reported cases $c_t$ with symptom onset at time $t$. For ease of notation, compartment superscripts for age and location have been omitted.

2.1.1 | Transmission

The transmission model has three key features: Firstly, the instantaneous reproductive number $R_t$ denoting the average number of secondary infections at time $t$ caused by one primary infection. Secondly, the generation time distribution $D_t$ denotes the distribution of new infections over time as standard in the literature. Thirdly, the model allows for dispersion $\Psi$ of the offspring distribution following the seminal model of superspreading. To model the uncertainty in the number of infections, the seminal transmission model with superspreading is generalized to accommodate changing reproductive numbers and multiple time intervals. In this model the number of
FIGURE 1  Model illustration. All nodes directly connected to new infections \( i_t \) are shown. Each infection \( i_t \) with \( t' < t \) transmits on average to \( D_i(t-t')R_i \) new cases, where \( D_i \) denotes the probability mass function of the generation time. Infections at time \( t \) develop symptoms at time \( t' > t \) with probability \( D_s(t'-t) \) and are reported with probability \( r \), where \( D_s \) denotes the probability mass function of the incubation period.

secondary infections from a single primary infection follows a negative binomial distribution with mean \( R_t \) and dispersion parameter \( \Psi > 0 \), that is, \( \text{NB}(R_t, \Psi) \). The variance of this negative binomial distribution is \( R_t + \frac{R_t^2}{\Psi} \). The smaller the dispersion parameter \( \Psi \) the larger is the variance-mean ratio \( 1 + \frac{R_t}{\Psi} \) of individual transmission.

The reproductive number \( R_t \) is determined by the conditions that transmissions at time \( t \) are subject to. Given those shared conditions, the number of secondary infections caused by a primary infection is modeled as independent across individuals and days. Under this assumption the aggregated number of new infections at time \( t \) is given by

\[
i_t \sim \text{NB}(R_tP_t, \Psi P_t), \tag{1}
\]

where \( P_t = \sum_{t'} D_i(t-t')i_{t'} \) denotes the transmission pressure at time \( t \). The distribution is derived in Appendix Section A.

The model can account for superspreading quantified through the dispersion parameter \( \Psi \). If the reproductive number is constant, that is, \( R_t = R \), a single infection induces \( \text{NB}(R, \Psi) \) secondary infections, coinciding with the aforementioned seminal model of dispersion by Lloyd et al.\(^1\) Thus, priors on the dispersion \( \Psi \) can be informed by studies working in the standard framework and posterior results can be compared conveniently. The model consistently translates the information in infection numbers to the reproductive number \( R_t \). Additional details on the dispersion are given in Section 2.4.

2.1.2 | Measurement

As illustrated in Figure 1, it is assumed that an infection at time \( t \) leads to symptom onset being reported at time \( t' \) with probability \( D_s(t'-t)r \), where \( D_s(t'-t) \) denotes the probability mass function of the incubation period and \( r \) the probability of developing symptoms and being reported as a case. The aggregation of all cases \( c_t \) constitutes a sum of Bernoulli trials, following a Poisson binomial distribution, which is approximated by a Poisson distribution for computational convenience:

\[
c_t \sim \text{Poisson} \left( r \sum_{t' < t} i_{t'} D_i(t-t') \right). \tag{2}
\]

The study assumes a constant reporting rate \( r \). Expanding the model to include covariate-dependent reporting rates or additional observable case counts such as hospitalizations or deaths is possible, but outside the scope of this paper.

2.1.3 | Effects

To aggregate information across locations, the reproductive number is modeled as a function of covariates. Each location \( l \) and age group \( a \) features a basic reproductive number \( R_0^{la} \) in the absence of all interventions, under average weather conditions, and in a completely susceptible population. The reproductive number \( R_t^{la} \) is then modeled as a function of input covariates \( x_1^{la}, \ldots, x_j^{la} \), where the effect is assumed to be multiplicative such that

\[
R_t^{la} = R_0^{la} \prod_{j=1}^{J} (1 + \beta_j^{la} x_j^{la}). \tag{3}
\]
The association of covariate $x_{j,a}$ with the instantaneous reproductive number of age group $a$ is denoted by $\beta_{j,a}$. A coefficient of .5 would signify that an increase from the 0 to 1 in $x_{j,a}$ coincides with an increase in the instantaneous reproductive number by 50%. A coefficient of $-0.5$ would signify that the same change in $x_{j,a}$ is associated with a 50% reduction in transmission. Covariates are usually standardized or dummies.

Compared to alternative models where $R_{0}^{j,a} = R_{0}^{j,a} \prod_{j=1}^{J} \exp(-\beta_{j,a} x_{j,a})$, Equation (3) facilitates immediate interpretation of effect estimates $\beta_{j,a}$, but requires $1 + \beta_{j,a} x_{j,a}$ to be constrained to be non-negative. Reassuringly, this constraint was non-binding in all sampled posterior draws.

### 2.2 Identification of reproductive numbers

The model simultaneously estimates infections, reproductive numbers, and determinants of transmission. Estimating the reproductive numbers is an important step and of a separate interest in its own right. Reproductive numbers are identified even if only a fraction of infections is ascertained as cases. Importantly, the reporting rate has to be constant over time. As this assumption is more credible for symptomatic infections than for asymptomatic infections, the model targets symptomatic cases as observable fraction of all infections. As the likelihood of developing symptoms changes with age (Figure S1), the average reporting rate changes with the age composition of infected individuals. To address this, age-specific reproductive numbers are estimated, such that identification does not rely on constant reporting rates across age groups.

It is standard to aggregate cases by reporting date. By aggregating cases by the date of symptom onset instead, reporting delays are eliminated, resulting in sharper information on the timing of infections. The difference is crucial for the first weeks of the Covid pandemic when reporting behavior changed dramatically. It would be unreasonable to assume that the delay between transmission and reporting was constant. Instead, the changes in public awareness, testing technology, and administrative environments arguably strongly impacted the time between infection and reporting. As a result, case counts (by reporting date) underestimated the rate of outbreak growth initially. If reporting catches up later, estimates of the reproductive number are temporarily biased upwards. Aggregating cases by symptom onset date avoids this bias. Additionally, it reduces noise. The interval between the occurrence of infection and its report is determined by the sum of the duration from infection to the onset of symptoms and from symptom onset to the reporting of the infection. Consequently, when cases are aggregated based on their reporting date, the dispersion of the distribution $D_{s}$ in Equation (2) increases, leading to decreased precision in inference.

Previous studies argued that deaths are more reliable than case data. One limitation of death data is that identification of growth rates relies on the assumption of a constant fatality rate, which is violated if age groups are not taken into account. As shown in Figure 2, about 30% of symptomatic cases over 80 years died, while only 0.03% of cases under 35 years. If age groups are affected differently by interventions, relying on death data could induce strong biases. Effects on younger age groups are essentially undetectable.

To choose an appropriate reporting rate for the model, case fatality rates can provide some evidence. If the infection fatality rate is constant over time, the case fatality rate identifies changes in the reporting rate. The observed case fatality rate in Figure 2 does not suggest major changes over time. A comparison to age-specific infection fatality rates indicates a reporting rate close to 25%. Similar reporting rates arise based on first evidence of unpublished serological studies in Germany. Accordingly, the main specification uses a reporting rate of 25%. Robustness checks in Section 4.5 show that alternative reporting rates do not influence effect estimates. However, if age or location specific testing data would be available, it is preferable to model a variable reporting rate. Importantly, the identification of the reproductive number does not rely on the value of the reporting rate, but on the assumption that symptomatic infections were equally likely to be reported over time within a specific age group and location.

### 2.3 Identification of transmission determinants

Our primary objective is to estimate determinants of transmission, as expressed by the coefficients $\beta$ in Equation (3). In the model, cases are used to estimate infections, which in turn imply a reproductive number. Equation (3) describes the relationship between the independent variables and the mean number of new infections resulting from a single primary case.
The identification of transmission determinants depends on the degree of variability exhibited by the independent variables. If interventions were implemented in concurrently, only the combined effect would be identified. While several interventions were implemented with limited variability, with only a few administrative units deviating or varying in the timing of interventions, most interventions in Germany were executed at the state and county level, resulting in substantial heterogeneity (see Section 3 for details).

2.4 Identification of dispersion

The connection between individual superspreading and dispersion in aggregated infection numbers merits some discussion. It is illustrative to look at the special case that emerges after assuming that all secondary infections occur in the next period, that is, $D_t(1) = 1$, a common assumption for weekly case counts. In this case, Equation (1) simplifies to

$$i_t \sim \text{NB}(i_{t-1}R_t, i_{t-1}\Psi).$$

The dispersion parameter of aggregated infections equals $i_{t-1}\Psi$ and depends on the infection count $i_{t-1}$. The growth factor $\frac{i_{t-1}}{i_{t-1}}$ constitutes a random variable with mean $R_t$ and variance $\frac{R_t(\Psi+R_t)}{i_{t-1}\Psi}$ that vanishes for large infection counts $i_{t-1}$. Variance in the growth factor is caused by variation in the mean $R_t$ and noise influenced by individual dispersion $\Psi$. We can separate the two factors, as the former influences growth factors irrespective of the current infection count $i_{t-1}$, while the latter has less impact for high baseline infections $i_{t-1}$. See the Section S1.3 for empirical support of this argument, which shows that empirical location-specific growth factors in Germany fit this model, but not the standard model, and that aggregated cases can be used to estimate the dispersion parameter $\Psi$.

The presented model is based on overdispersion in individual transmission and deviates from the literature, where overdispersion is often ignored\cite{11,32-36} or assumed to be constant for aggregated infections,\cite{14,37} that is, $i_t \sim \text{NB}(i_{t-1}R_t, \Psi)$.
This alternative assumption of a constant dispersion is inherent, but often unappreciated, in inference based on standard negative binomial regression, the endemic/epidemic model,\textsuperscript{38,39} and epidemiological models with random effects.\textsuperscript{40} Additional details and comparisons can be found in Appendix Section A.

2.5 | Estimation

The model is estimated in a fully Bayesian framework, which brings several advantages. First, uncertainty statements are exact (cf, asymptotic inference methods or multi-step procedures). Second, weak and partial identification does not invalidate inference and can be analyzed with the posterior distribution. Third, following recommended practices,\textsuperscript{41} weakly informative priors can be used for the transmission characteristics. See Section S2.1 for a detailed list of all priors.

A Markov chain Monte Carlo (MCMC) sampler was constructed with JAGS 4.3.\textsuperscript{42} Note that Hamiltonian Monte Carlo\textsuperscript{43} samplers like Stan\textsuperscript{44} are not directly applicable as the infection counts constitute latent discrete variables. Convergence tests were successful. Replication files are available online. For additional details see Section S2.2.

The main disadvantage of the Bayesian approach is of computational nature. The MCMC chains may require an infeasibly long time to converge for complex models. The model presented here extends seminal studies in several directions listed above and estimates the model on more compartments than previously considered. It runs for 3.5 days on a state-of-the-art server (AMD EPYC 7742 processor with 192 GB system memory). Additional generalizations (or additional compartments or extended time frames) would require the simplification of other aspects of the model.

2.6 | Assumptions

This section summarizes the main assumption that the model shares with the seminal transmission studies.\textsuperscript{14,15}

2.6.1 | Reporting rate and timing

A correctly modeled reporting process is the key assumption to identify the reproductive number from case data. Reporting can be separated into the reporting rate $r$ (also referred to as ascertainment rate) and the timing of reporting relative to the transmission event. As this study relies on the date of symptom onset, the latter is simply the incubation period. In the main specification, the reporting rate is assumed to be constant over time following previous transmission studies.\textsuperscript{14,15}

2.6.2 | Absence of importation

The model proposed here ignores importation. Naturally, transmission between locations and age groups occur. Arguably, the obtained instantaneous reproductive number $R_{l,a}$ should only be read as reduced form summary of the current growth factor.

Extension of the model incorporating importation across compartments are straightforward but increase the computational burden and require strong additional assumptions for the identification of reproductive numbers. Consider the transmission model

$$i_{t,a} \sim NB \left( \sum_{a'} p_{l,a}^{l,a} R_{l,a,a'} \frac{1}{\sum_{a'} p_{l,a}^{l,a}} \right),$$

where $R_{l,a,a'}$ denotes the number of new infections in age group $a'$ induced by one infected individual in age group $a$. Identification of $R_{l,a,a'}$ requires that the ratio of detection rates between age groups is known. The implementation of such approaches would require reliable prevalence data that allow to identify detection rates of the German reporting system for PCR-positive test stratified by age and location.

Distortions due to omitting importation are more substantial if incidences deviate stronger between age groups and transmission between age groups is more asymmetric. The main analysis omits the age group of children under 15 years
as only 2.7% of cases, and a single death was observed in this group in the study period until May 2020. Later studies confirmed that the transmission activity in children was particularly low in the first wave in Germany: Seroprevalence surveys found children 1 to 10 years old had particularly low levels of antibodies in measures taken in May 2020, and a transmission study using age-specific contacts found children to have little contribution in the first wave in Germany.

Recently, contact matrices for Germany during the first wave were used to model transmission. A simulation study in Section 5 uses those contact matrices to investigate the model’s performance in the presence of age importation.

2.6.3 Homogeneity

Under the assumption of random mixing, that is, each infected is equally likely to infect any other member of the population, the instantaneous reproductive number $R_t^{(r)}$ can be interpreted as a random draw from the current transmission situation in the population. In a more realistic setting, transmission is heterogeneous. For example, a contact tracing study from Hong Kong finds that infections in social settings were associated with more secondary cases compared to household infections. As transmissions occur more likely within a cluster (household, workplace, location, ethnicity, social class) $R_t^{(r)}$ can be expected to exhibit auto-correlation in its error to depict an accurate description of the current average transmission dynamic in the entire population. For the same reason, local immunity acquired within a cluster of infections (e.g., within a household) may temporarily underestimate the expected transmission dynamic in the entire population, which will govern the process when infections are more equally distributed. The usage of a high number of subregional compartments can only partly control for this.

Such heterogeneity in transmission, as modeled for example via a spatial or a network structure, can lead to underestimating the effect of interventions that have a stronger effect on intra-cluster/long-distance transmission. The reduced transmissions by the second generation of infections occur later and would not be attributed correctly to the initial intervention.

Similarly, interventions might be more/less effective over time. For example the weather variables, which are identified based on daily variation in weather, are subject to the critique that long-term effects might differ substantially from short-term effects.

2.6.4 Unobservables

Ultimately any transmission dynamics can be attributed to individual behavior (potentially in interaction with external factors). While the covariates considered here to explain the instantaneous reproductive number include information that was previously not used, the analysis may still omit some shared drivers of transmission. For example, extensions to later waves would require to control for the prevalence of new variants of the virus.

2.6.5 Interaction and nonlinear effects

It is assumed that each covariate increases/decreases a share of the secondary transmissions at a particular day. This ignores interaction effects, which are likely to be of high importance for many determinants. For interpretation, estimates should be understood as measured transmission changes for an intervention under the average circumstances it was implemented. For real-valued covariates the model imposes linearity. While additional transformed terms can easily relax this assumption, this adds computational costs. Consequently, the generalizability of the findings beyond the support of the data remains uncertain.

2.6.6 Constant characteristics

Throughout, the model presented here assumes that properties of the transmission process are time-independent, in an effort to recover time dependent dynamics of the instantaneous reproductive number. This is a simplification. There is for example evidence, that the generation time distribution may be shortened by policy interventions. Further, most interventions can be argued to reduce the risk of superspreading events, thereby reducing dispersion.
Estimates of parameters like the dispersion and generation time should be understood as averages in the considered time period.

3 | DATA

The German Covid-19 surveillance data contains date of symptom onset, date of reporting, age groups (below 5, 5-10, 15-34, 35-59, 60-79, and above 80), and geographical units (county or city). Over 170,000 cases were recorded until 15 of May 2020, with 73% reporting a date of symptom onset. The first case was reported in January, and major outbreaks started at the end of February. Germany had relatively large testing capacities in the early phase of the pandemic. This is also supported by excess death data. Estimation is based on cases until mid May 2020 in the 111 most impacted counties and the four age groups above 14 years, encompassing over 60,000 symptomatic cases. Additional details are provided in Section S1.2.

For this study, interventions in 10 German states were classified from February until May 2020. Daily location-specific covariates comprise 21 policy interventions, average temperature, relative humidity, the ratio of traced infectious, local incidence, local cumulative incidence, and weekday fixed effects.

A description of the covariates can be found in Table 1. The model accounts for public health interventions with dummy variables, while real-valued covariates capture other key determinants of transmission. In particular, temperature and relative humidity are used to proxy for the impact of weather. Local incidence is included to adjust for voluntary behavioral response to risk of infection and cumulative incidence is included to adjust for the potential effect of immunity. The model also accounts for the potential impact of testing and tracing. To measure the intensity of testing and tracing at each point in time for each location a novel proxy is generated. Based on symptom onset date and reporting date (when health departments were informed about positive test), one can infer for each case the days of potential infectiousness and when test results arrived and tracing was potentially initiated (for details see Section S1.6). This allows to construct a daily location-specific proxy for the ratio of traced infectious.

The choice of coding intervention dummies should be noted. In the study period, almost no intervention was rolled back fully. Instead, they were followed by some reopening strategy designed to reduced transmission risk (eg, schools were closed and subsequently reopened under new rules). In this case, the first intervention was coded as staying active throughout such that the coefficient of the second intervention is identified by the difference between the first and second intervention (eg, between schools closed and schools open under new rules) and not the difference between no intervention and the second intervention (eg, between schools open and schools reopen with new rules). This coding applies to schools, daycares, shops, and churches (that were closed with other gatherings but reopened earlier). This coding is mathematically identical to one where the first intervention is coded as inactive when the second intervention starts. However, the chosen coding allows putting priors on the changes between subsequent intervention regimes. The only exception are the stay-at-home orders, that in some states were imposed on top of the distancing rules and rolled back before the end of the study period, and holidays. Thus, their effect is identified by the change in reproductive numbers at the beginning and the end of the intervention.

A short summary of the timeline of interventions in Germany is as follows (see Figure 3 for an illustration of the timing of interventions). On March 12, 2020, the German Health minister advised to change behavior to reduce transmission risk, which reversed previous official messaging. In the following five days, schools and daycares closed throughout Germany. It took additional five days until all states had limiting rules on sports and another five days until all states ordered restaurants closed. Non-essential shops had to close in some states starting March 17 and it took about 11 days until this was the case in all states. Public gatherings were limited starting March 17 in some states. Distancing rules in public followed March 21 in some states. Both interventions were implemented throughout Germany later. In March 25, state-funded testing was restricted to the narrow group of people with symptoms and risk contacts to preserve testing capacity for groups at risk. End of March incidence rates started to decline in most counties. April 6, public masking became mandatory in the first county. Later the policy was implemented nation-wide. Starting April 20, the first counties opened schools or daycares under new rules. Four days later, the first states allowed churches to hold mass again as an exemption from the still active distancing and gathering rules.

As argued in Section 2.3, identification of the determinants of transmission depends on heterogeneity in exposure to different intervention regimes. Here, this heterogeneity in the data is summarized. Table 2 describes the first date of implementation across all locations. Many interventions were implemented the first time (almost) in parallel and (at some point in time) in all locations, however, the last three columns reveal that there remains substantial heterogeneity.
| Label                          | Description                                                                                                                                 |
|-------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|
| Average temperature (r)       | Average daily temperature as measured in 50 km radius around geographical center of county.                                                 |
| Relative humidity (r)         | Daily relative humidity as measured in 50 km radius around geographical center of county.                                                    |
| Incidence (logarithm) (r)     | Logarithm of local incidence (in 100 000) as reported at that time.                                                                          |
| Cumulative incidence (%) (r)  | Cumulative incidence (in percentage points) by symptom onset 2 weeks before.                                                                |
| Ratio of traced infectious (r)| Ratio of reported cases among all cases that are potentially infectious (1 day before to six days after symptom onset)                     |
| Holidays                      | Public holidays                                                                                                                                 |
| Events limited                | Events above a certain size (e.g., 1000 participants) were not allowed. Size of allowed events differed.                                      |
| Public awareness rising       | First major public speeches of German President and health minister encouraging changes in behaviour.                                           |
| Sports limited                | Public sport facilities closed. Denoted as active if only individual sport is allowed.                                                         |
| Schools or daycares closed    | Either daycares or schools are closed. Partly open for key workers or vulnerable groups is also denoted as closed. Closing of individual schools if not enforced by regulations is ignored. |
| Restaurants closed            | Closing of restaurants. Limited capacity is not denoted as closed. Take-away only is denoted as closed.                                       |
| bars cl.                     | Bars were closed.                                                                                                                             |
| events cl.                    | All events were forbidden.                                                                                                                   |
| Shops closed                  | Closing of nonessential shops. Deviations in details (e.g., hardware stores) are ignored and all such restrictions are denoted as closed.       |
| Gatherings limited            | Any limitations on gatherings in public space. Changes in number of people are ignored. Common categories were one household only, two households only, or a limitation in group size to 5 or 10. |
| Speech chancellor             | The German chancellor (Angela Merkel) gave the first major speech addressing the pandemic and transmission reduction as mitigation strategy.   |
| Stay-at-home order            | Regulations that mandated to stay at home unless exceptions arise. Exceptions always included work and individual sport.                      |
| Public distancing             | Mandated minimum distance in public space between individuals. Exceptions include often the own household or family. Common distance was 1.5 meters. |
| Narrow testing                | Testing guidelines stated that testing is limited to symptomatic cases that additionally had either exposure to another case or were traveling in high risk areas as denoted by the RKI. Later testing was available for any symptomatic person. |
| Masks recommended             | Masks were recommended in public spaces.                                                                                                    |
| Masks in public               | Community masks obligatory for supermarkets and public transport.                                                                            |
| Shops changed                 | Small (<800 sqm) nonessential shops could reopen.                                                                                           |
| Schools reopen                | Schools reopen for all classes. Often under limited capacity and with new safety concept. If only particular classes were allowed, school is denoted as closed. |
| Daycares reopen               | Daycares reopen again under limited capacity and with new safety concept.                                                                 |
| Symptomatic testing           | Testing guidelines stated that all symptoms make you eligible for free testing. No known exposure was necessary anymore.                      |
| Churches reopen               | Religious public gatherings were allowed again, while other gatherings were still forbidden. Often under limited group size and safety concept.   |

Notes: First five rows describe real-valued (r) covariates. The remaining covariates are ordered by first implementation.
FIGURE 3 Implementation of interventions over the study period. The plot illustrates the activation of dummy variables at each date. Covariates are sorted by first activation. If an intervention is active in no county, it is denoted as “nowhere.” If an intervention is active in all counties, it is denoted as “everywhere.” Otherwise, it is denoted as “partly.” For the intervention timing of each location separately see Figures S25 and S26.

Time dummies explain all of the variation for nationwide interventions like public awareness rising and testing rules only. Thus, the identification of the remaining interventions does not rely solely on changes between time points, but also between locations. Additionally, the table reveals that there is no strict overlap between any two interventions. The last column shows that each intervention differs in at least 105 location-day observations from any other intervention.

Table S1 shows similar statistics for the real-valued covariates. Here, identification never depends solely on variation in time. For the correlation matrix between all important covariates see Figure S23.

4 | RESULTS

The following subsections list the estimation results of the main model. Afterwards, robustness and out-of-sample results are shown.

4.1 | Transmission dynamics

Estimation results are informative about transmission in the context of this study. The average incubation period was 5.30 days (95%-confidence interval [CI]: [5.16, 5.45]). The average generation time was slightly longer with 5.84 days (95%-CI: [5.68, 6.01]). Assuming independence this corresponds to 42% of secondary infections occurring before symptom onset.

The basic reproductive number denotes the average number of secondary infections in the absence of interventions, under average weather conditions, and in a completely susceptible population. There is no evidence for an age-dependent basic reproductive number (Table 3). Population density was positively correlated with the basic reproductive number (Table S3).

For the age groups 15 to 34 and 35 to 59 we observe high dispersion, with more than half of all cases infecting nobody and 20% of primary cases initiating 70% to 80% of secondary cases. Older age groups show less tendency for superspreading, consistent with a higher ratio of primary infections actually infecting, and less transmissions from the most infectious primary infections. For comparison to previous studies that considered dispersion abstracting from age differences, the marginal distribution of secondary infections can be simulated, which is a mixture negative binomial distribution.54
**TABLE 2** Summary of interventions.

| Label                        | First active | Days active | Locations active | $R^2$ (time) | $R^2$ (location) | Observations different |
|------------------------------|--------------|-------------|------------------|--------------|------------------|------------------------|
| Holidays                     | March 2, 2020| 38          | 111              | 0.85         | 0.00             | 2143                   |
| Events limited               | March 11, 2020| 66          | 111              | 0.93         | 0.00             | 194                    |
| Public awareness rising      | March 13, 2020| 64          | 111              | 1.00         | 0.00             | 308                    |
| Bars closed                  | March 14, 2020| 63          | 111              | 0.98         | 0.00             | 115                    |
| Schools or daycare closed    | March 14, 2020| 63          | 111              | 0.98         | 0.00             | 115                    |
| Restaurants closed           | March 14, 2020| 63          | 111              | 0.95         | 0.00             | 105                    |
| Sports limited               | March 14, 2020| 63          | 111              | 0.95         | 0.00             | 133                    |
| Events closed                | March 16, 2020| 61          | 111              | 0.74         | 0.11             | 783                    |
| Gatherings limited           | March 17, 2020| 60          | 111              | 0.79         | 0.08             | 561                    |
| Shops closed                 | March 17, 2020| 60          | 111              | 0.93         | 0.00             | 133                    |
| Second speech                | March 19, 2020| 58          | 111              | 1.00         | 0.00             | 222                    |
| Stay-at-home order           | March 20, 2020| 50          | 39               | 0.18         | 0.25             | 1986                   |
| Public distancing            | March 21, 2020| 56          | 111              | 0.97         | 0.00             | 105                    |
| Narrow testing               | March 25, 2020| 52          | 111              | 1.00         | 0.00             | 286                    |
| Masks recommended            | March 30, 2020| 47          | 111              | 0.99         | 0.00             | 609                    |
| Masks in public              | April 6, 2020 | 40          | 111              | 0.96         | 0.00             | 329                    |
| Daycares reopen              | April 20, 2020| 26          | 111              | 0.64         | 0.06             | 562                    |
| Schools reopen               | April 20, 2020| 26          | 104              | 0.59         | 0.07             | 757                    |
| Shops changed                | April 20, 2020| 26          | 111              | 0.98         | 0.00             | 406                    |
| Churches reopen              | April 24, 2020| 22          | 111              | 0.85         | 0.01             | 562                    |
| Symptomatic testing          | April 24, 2020| 22          | 111              | 1.00         | 0.00             | 329                    |

Notes: Table denotes the first implementation, total number of days intervention was active at any location, total number of locations that implemented intervention at some point, the proportion of the variance ($R^2$) that is predictable by time and location, respectively, and the minimal number of county-day observations that the intervention is different from any other intervention.

**TABLE 3** Mean and SD of posterior draws for the basic reproductive number $R_0$, dispersion $\Psi$, respective ratio of primary infections actually infecting, and ratio of transmission expected from the most infectious 20% of primary infections.

| Age    | $R_0$ Mean | $R_0$ SD | Dispersion $\Psi$ Mean | Dispersion $\Psi$ SD | Ratio infecting Mean | Ratio infecting SD | Ratio from 20% Mean | Ratio from 20% SD |
|--------|------------|----------|-------------------------|----------------------|----------------------|--------------------|---------------------|-------------------|
| 15-34  | 2.61       | 0.24     | 0.75                    | 0.16                 | 0.47                 | 0.04               | 0.69                | 0.03              |
| 35-59  | 2.61       | 0.23     | 0.36                    | 0.05                 | 0.38                 | 0.04               | 0.80                | 0.03              |
| 60-79  | 2.57       | 0.22     | 5.53                    | 2.61                 | 0.59                 | 0.04               | 0.54                | 0.02              |
| 80+    | 2.52       | 0.28     | 3.98                    | 2.05                 | 0.58                 | 0.04               | 0.56                | 0.03              |

Note: The ratios were computed assuming a constant reproductive number of 1.

Assuming equally distributed infections across age groups, the mean variance ratio of the resulting secondary infection distribution is 0.378 (95%-CI: [0.33, 0.44]), equivalent to a dispersion parameter of 0.61 (95%-CI: [0.49, 0.77]).

**4.2 Policy interventions**

Figure 4 shows the estimated changes in transmission associated with each covariate (age-specific estimates are available in Figure S11). The posterior distributions indicate a heterogeneous picture, where some covariates are sharply identified.
FIGURE 4 Change in transmission associated with covariates. The plot depicts the mean estimate and 95%-CI intervals for the change in transmission $\beta$ in Equation (3) affecting the reproductive number $R_t$. To marginalize across age, age-specific estimates are weighted by their population share. The 95%-CI of the prior is given as shaded area. Real-valued covariates ($r$) and standardized covariates ($s$) are marked.

as either decreasing, not affecting, or increasing transmission, whereas other covariates are only weakly identified with wide posterior confidence intervals.

The strongest decrease was associated with public awareness rising. Transmission reduced by 58% (95%-CI: [53%, 62%]) when government officials gave their first speeches asking for behavioral changes from the public.

The closure of restaurants was associated with additional reductions in transmission of 15% (95%-CI: [5%, 23%]). The estimate was strongest for the age group 15 to 59. School and daycare closures were associated with a 12% (95%-CI: [−5%, 28%]) reduction in transmission, but the large confidence interval does not reject a zero effect. Limiting sports was associated with additional reductions in transmission. In some states a mild stay-at-home order was imposed, which was associated with an additional 9% (95%-CI: [4%, 13%]) reduction in transmission.

Masks (mouth and nose cover including cloth masks) became mandatory in supermarkets and public transport. Compliance was found to be high.55 A small reduction of 6% (95%-CI: [−17%, 7%]) was associated with this policy. The limitation of gatherings in public spaces, the closing of events, the closing of bars, the speech of chancellor Merkel, and mandatory public distancing showed no conclusive evidence for reducing transmission. Note, however, that for most interventions moderate reductions cannot be ruled out by the posterior distribution.

The reopening of daycare and churches with precautionary measures and when shops changed rules (to allow small shops to open again) had no significant impact. Some evidence for increased transmissions was associated with school reopenings. Further, transmission increased during official holidays. The narrow testing regime was associated with 16% (95%-CI: [7%, 26%]) higher transmission. This result is driven by younger cohorts, whereas transmission in the age group 80+ was reduced.

Contrary to intuition, public distancing rules, a recommendation of mask wearing, shops closures, and limiting of event sizes was associated with increases in transmission. This will be discussed in Section 6.
4.3 Real-valued covariates

The ratio of traced infectious was associated with a reduction of transmission by 33% (95%-CI: [22%, 43%]). The actual change attributed to real-valued covariates depends on the current value of the variables across locations. Figure 5 illustrates the average estimated impact across locations over time for several covariates. Panel A of Figure 5 illustrates that testing and tracing was attributed a transmission reduction of 15% (95%-CI: [9%, 20%]) in May 2020. For the age group over 80 years, the impact is larger with a reduction of 28% (95%-CI: [17%, 37%]).

Publicly reported incidence was associated with reduced transmission. This information effect was highest in April (Panel B in Figure 5) when estimates indicate a reduction of 44% (95%-CI: [40%, 48%]). Cumulative incidence (of cases in percentage points) was associated with a 17% (95%-CI: [3%, 29%]) reduction in transmission. Assuming random mixing, full immunity after infection, and a reporting rate of 25%, theory would predict a reduction of 4%. The confidence intervals suggest that the data does not allow a sharp identification of this parameter.

Low temperature was associated with higher transmission. Relative humidity was associated with a small increase in transmission. The latter effect is mostly driven by the age group 60 to 79. The combined estimated effect of the two weather variables over time is illustrated in Panel C of Figure 5.

4.4 Differentiation between determinants

Many covariates are strongly correlated (Figure S23), which complicates inference as changes in transmission cannot be clearly associated with one specific covariate. The correlation matrix of the posterior draws in Figure S12 reveals the degree to which this applies to specific determinants of transmission. The first observation is that there remains some uncertainty in disentangling different determinants of transmission, yet most coefficients in the model are clearly separated by the data.

Among the most difficult to separate are the closing of shops and limiting of sports, which exhibit a correlation coefficient of −0.66. This indicates that their joint effect is better identified as their individual effects (as one would expect for interventions that were often implemented in parallel). As was observed in Figure 4, both interventions’ posteriors lie on different sides of the null effect, such that their joint effect is sharply identified as close to zero, while both individual coefficients have large confidence intervals.

Another example is the pair narrow testing regime and public distancing, which exhibit a correlation coefficient of −0.63. Both interventions have a posterior mean of about −17%, which results in a joint effect of reducing transmission by 34%. The contribution of the two interventions, however, is harder to estimate such that substantial uncertainty remains for public distancing that has a large 95%-CIs of [−1%, 28%] that includes the null effect.
Public awareness rising, as the most influential determinant, could be partly confounded with closures of schools and daycares. The important real-valued covariates (ratio of traced infectious, temperature, and incidence) are clearly identified and exhibit no strong posterior correlations.

While there remains substantial uncertainty about some determinants of transmission, the overall reduction associated with the combination of all interventions designed to reduce transmission (not including the ratio of traced infectious) is sharply identified by the posterior distribution with a reduction in transmission of 0.46% (95%-CI: [36%, 53%]).

4.5 | Robustness checks

This section summarizes the empirical evidence on the robustness of the results. Section S4 provides the details. The main model is estimated on data of the first wave until May 2020. The covariates for weather, information, and testing and tracing are available beyond the first wave. A robustness check considers data from May to August 2020 including the age group 5 to 14 and with the same model specifications, but substituting policy interventions with week fixed effects. This study covers another 30,000 cases in 141 counties. See Section S4.1 for details. The estimation results are consistent for information on incidence, temperature, and testing and tracing. The association with weather was less strong. School children below 15 years exhibited higher transmission during school holidays.

Additionally, the estimated main model was applied to forecast cases in 28 counties that were not part of the estimation sample. The out-of-sample results in Section S4.2 are accurate and well-calibrated. Another robustness analysis considers the main model under different reporting rates in Section S4.3. Section S4.4 establishes robustness to grouping early interventions and Section S4.5 to prior precision.

Next to the robustness checks, Section S4.6 considers alternative specifications, each lacking one of the proposed innovations of the main study. Here deviations from the main results indicate that the innovations can provide new insights. The results show that using reporting date as aggregation date and ignoring real-valued covariates (incidence, testing and tracing, and weather variables) delivers substantially different results. Estimation results are closer to the main model if age compartments are ignored. A semi-mechanistic model that incorporates superspreading with a constant dispersion in case reports\textsuperscript{14,15} also showed only slightly different results, but less efficient mixing under the considered sampling scheme.

5 | SIMULATIONS

A major concern is weather the model can reliably quantify the individual contribution of interventions given the data.\textsuperscript{16} Here, this issue is investigated with simulations.

5.1 | Artificial intervention data

In a first setting, a single intervention is considered and age groups are ignored. The intervention is active in a varying number of locations (5, 50, 100). The infection counts are initialized for 10 days with different numbers of daily infections (1, 10, 100). Five days after the end of the initialization, an intervention is active for a varying number of days (2, 4, 8). The simulated data ends 25 days after the end of the initialization. As additional factors, the simulation considers effect size (0, −0.1, −0.3) and the dispersion parameter (0.1, 0.5, 2.5). A basic reproductive number of 1 was chosen such that the expected number of infections subject to the intervention is given by the product of the number of locations, days, and daily infections. The remaining parameters (reporting rate, generation time distribution, incubation period distribution) are set to the posterior means of the application. For each scenario 50 data sets are simulated and the model is estimated.

Figure 6 illustrates the rejection rate of a null effect for the 95% CI of the posterior draws. The x-axis is the expected number of infections subject to the intervention, which can be seen to be a clear indicator of power. (Similarly, estimation error depends on the expected number of infections subject to the intervention as shown in Figure S27.) The first two rows illustrate power for a large (30%) and small (10%) reduction in transmission. Strongly over-dispersed infection processes (left column) have less power. For a small number of infections (≤100) there is no power. For a large number of infections (≥10,000) there is considerable power for all scenarios.
The last row shows size calibration. For low number of infections, the weakly informative prior centered at zero leads to conservative rejection rates. For larger number of infections, the model seems well-calibrated.

Figure 6 shows that the number of infections that occur in the identifying days and locations is a crucial predictor of power. Next, we investigate which range of values would be consistent for the different interventions in the application. The distribution of daily cases per location has 0.25- and 0.75-quantiles of 5 and 15. With a reporting rate of 25% this is consistent with 20 to 60 infections. The number of location-days that each intervention differs from any other intervention is between 100 and 2000 (compare Table 2). Combined this leads to a range of 2000 to 120 000 infections for identifying a single intervention. This range is illustrated as shaded area in Figure 6.

Considering the second column with a dispersion close to the estimated value, the shaded area indicates full power against large effects. For small effects, however, the simulation suggests full power only for the interventions with a high amount of variation, whereas interventions with low variability exhibit low power (<0.5). Reassuringly, null effects are correctly classified and Figure S27 shows that for all scenarios the mean absolute estimation error is relatively small (< 0.1).

5.2 Real intervention data

Another simulation uses the intervention data from the application, also considering age groups. All parameters were set to the main model’s posterior mean estimates, except for the latent infection process and the reported cases that were simulated. Ten data sets were simulated and estimated. The results in Panel A from Figure 7 suggest that the heterogeneity in exposure to the covariates is indeed sufficient to estimate most effects sharply under the postulated data generating process. Note that this simulation exercise cannot provide any evidence for the reliability of effect estimates under miscalibration.

The model at hand extends seminal work on transmission coefficients to include age groups. While this is arguably preferable to ignoring age groups, a major concern remains that age-specific estimates are unreliable as importations across age groups are ignored. The main model cannot be extended to include importation across age groups without reducing the complexity of other parts of the model (or innovating on the inference procedure to make more complex
(models computationally feasible). Instead, an additional simulation study was implemented to investigate the model’s performance if importation between age groups exists. Again, 10 data sets were simulated based on the posterior mean effect estimates of the main model. This time the simulation includes importation across age groups, where contact patterns between age groups where simulated based on the COVIMOD survey data on contacts for Germany during the first wave. The standardized contact matrix is given in Table S6. The more complex model cannot be estimated reliably on the data at hand, but it is straightforward to simulate from. The simulated data is then used to estimate the main model to investigate the error due to ignoring importation. The results can be seen in Panel B from Figure 7. Reassuringly, for most determinants the method recovers the average association with transmission even in the misspecified model. The simulation does, however, reveal that some coefficients are more prone to be impacted. In particular, the early interventions with strong overlap are most affected. That includes the closing of shops, bars, schools and daycare, restaurants, the limiting of sports and public distancing rules. One of the ten simulation runs confounded the effects of limiting sports and the closure of bars. The changes in transmission described by the real-valued variables are most sharply estimated, which lends some credibility to the sharp posterior intervals in the main analysis.

6 | DISCUSSION

Previous work studied dispersion, abstracting from age differences and based on contact tracing studies. Broadly, their results are similar to the marginal dispersion estimate of 0.61 (95%-CI: [0.49, 0.77]). A study4 from Hong Kong estimated a dispersion parameter of 0.33 (95%-CI: [0.14, 0.98]) or 0.19 (95%-CI: [0.13, 0.26]) when assuming a single primary case for an unresolved large cluster. A study5 from Shenzhen (China) reported 0.58 (95%-CI: [0.35, 1.18]) and a study57 in two Indian states 0.51 (95%-CI: [0.49, 0.52]). Global data-sets of outbreaks5 suggested a higher potential for superspreading with a dispersion parameter of 0.10 (95%-CI: [0.05, 0.20]). Noteworthy, the aforementioned studies do not account for changing reproductive numbers and are prone to overestimate the prominence of superspreading. Further, clusters might be more likely to be traced, while diffuse community spread is harder to identify. Other limitations apply to the
approach presented here. The model does not allow for overdispersion in reporting and is therefore prone to overestimate the dispersion in transmission. Moreover, changes in the reproductive number could be inadequately modeled. If the reproductive number is overfitted, individual variation is under-estimated (and vice versa). Finally, the estimation of age-specific dispersion might be biased due to transmission across age groups.

The effects of early interventions (including limited size events and sports, public awareness rising, and closing events, schools, and daycare, restaurants, and shops) are among the hardest to estimate. This is reflected in large confidence intervals and strong correlations between posterior draws (Section 4.4). Simultaneously occurring events that are not modeled, like the staggered declaration of international risk areas, can result in an upward bias. Additionally, early case counts are affected more strongly by importation from outside the county which also results in an upward bias.

The first major local intervention was the limiting of event sizes, which was associated with an increase in transmission. Many large events were canceled irrespective of local regulations. In fact, regulations to limit event sizes (eg, above 1000 participants as implemented in Berlin) might have communicated that such events were safe and increased the likelihood of risk contacts. The prominence of importation, as opposed to local transmission, in the early phase could explain the high magnitude of this effect, whereas an increase of local transmission due to the actual canceling of events is unlikely.

The model associates the largest single decrease in transmission with public awareness rising. A large part of this change arguably would have occurred irrespective of politicians and state institutions messaging. The assumption of time-invariant effects seems particularly challenging here, such that a waning of this effect may hide the effectiveness of subsequently implemented interventions.

There was weak evidence of public distancing and the closure of shops to have been associated with an increase in transmission. This might explain why stay-at-home orders and business closure showed no significant effect in the United States. The pattern was strongest for the age group 15 to 34 years, where the increase with public distancing was estimated to be 25% (95%-CI: [−1%, 54%]). The regulation could substitute public contacts with private contacts under higher transmission risk. However, strong posterior correlations with limiting sports and narrow testing regime indicate the potential of confounding for those estimates.

Closing schools and daycare was associated with similar reduction for all age groups, indicating that the reduction stems from behavioral changes, instead of the absence of transmission in the educational setting, which would affect other age groups one generation time later.

That narrow testing guidelines were associated with an increase in transmission is consistent with the view that testing, tracing, and isolation had an important impact. The intervention was implemented to reserve testing for risk groups. The associated decrease in transmission in the oldest age bracket indicates that this might have indeed worked as intended.

Transmission reduced by 6% with the mask mandate. As a comparison, mandatory masks for employees were associated with a reduction in transmission by 10% in the United States. With the synthetic control method a statistically significant effect of the mask mandate was estimated for specific counties in Germany. Note that mask recommendations in public spaces, as opposed to mandates, were associated with a slight increase in transmission, suggesting an increase in risk contacts.

To sum up, for some interventions there remains substantial uncertainty and the separation between interventions implemented mostly in parallel is difficult without considering additional data or expert priors. However, joint associations are often sharply identified, as illustrated by the set of all interventions designed to reduce transmission that was associated with a reduction of 0.46% (95%-CI: [36%, 53%]). A major concern for the interpretation of such estimates as causal is omitted variable bias. Without additional experimental evidence, the estimated associations provide only limited support for specific interventions. To reduce the risk of bias, a large set of covariates was included. Previous studies found stronger effects of policy interventions in the first wave without controlling for information, testing, or seasonality. For example, the shut-down in France was attributed a 77% reduction in transmission based on hospitalization and death data. An international comparison of death data estimated an effect of 81%. A reduced form approach on case growth found heterogeneous effects of policy interventions in China, South Korea, Italy, Iran, France, and the United States. As noted in other studies, growth factors substantially reduced before major policy interventions were put in place. If not controlled for, adaptation to local risk of infection can be wrongly attributed to policy interventions.

The changes in transmission associated with the real-valued covariates are of interest in their own right. Testing and tracing has been argued to be crucial to control the spread of SARS-CoV-2. The ratio of traced infectious is meant to proxy for testing, tracing, and isolation. As the data reveals only the ratio of infectious and symptomatic individuals that received a positive test result, the analysis can neither detect effects of asymptomatic screening nor is it possible to disentangle the effects of voluntary behavioral changes from official tracing, quarantine, and isolation measures. As the
effect of those components should be directly proportional to the ratio of infectious individuals that are subject to them, the estimate of the applied proxy of ratio of traced infectious encompasses all those components jointly.

Modeling studies for Germany concluded that 30% to 50% of transmission can be reduced by testing and tracing. The measured total effect in May 2020 with 15% on average and 28% for the age group over 80 years is highly relevant, but falls short of this benchmark. The large impact of testing and tracing stands in contrast to previous studies, that model testing and tracing with a dummy variable and find it among the least effective interventions. The dummy approach, however, fails to account for changes in intensity per infectious case, which is arguably the crucial measure. In Germany, the ratio of traced infectious increased steadily from the initialization of testing and tracing to the end of the study period with substantial heterogeneity across locations.

Another potential factor for transmission is voluntary behavioral response to risk of infection. Individual risk of infection depends on local incidence. In line with this argument, publicly reported incidence was associated with reduced transmission. This explains the common observation that incidence rarely exhibits prolonged exponential growth. Spread is unmitigated as long as it is undetected. In Germany during the first months of the pandemic, the reduction in transmission was driven mainly by behavioral adaptations to reported incidence instead of immunity by infection. As transmission decreases with higher incidence, there exists an equilibrium steady state prevalence. If information or behavioral adaptation is delayed, incidence moves in waves around this equilibrium value. As behavior was found to change with local incidence, indirect social and economic consequences of disease spread can be expected even in the absence of policy interventions.

Seasonal effects have been discussed to play a role in SARS-CoV-2 spread. It is important to note that the effect estimate for weather conflates the interaction of the virus with environmental circumstances and behavioral changes due to weather. The measured association with the weather variables can be extrapolated to seasonal patterns for comparison with other studies. The extrapolated change in transmission due to seasonality is 53% (95%-CI: [43%, 64%]) (based on average temperature and relative humidity in January and July). This is consistent with a reduction in transmission of 42% (95%-CI: [25%, 53%]) estimated with European data from 2020 and 2021, and an analysis of meteorological factors with Australian data ranging from July 2020 to May 2021. It is noteworthy that the model presented here allowed to predict the same seasonal patterns much earlier with data from the first wave only.

7 | CONCLUSION

Empirical evidence is paramount to inform modeling studies and policy decisions. The work presented here relies on features of the German surveillance data to improve upon early empirical studies analyzing SARS-CoV-2 transmission. Symptom onset data, age-specific compartments, a transmission process consistent with superspreading, and additional covariates can improve estimation and significantly changed inference for the data at hand.

One goal of this paper is to improve uncertainty quantification for the estimation of transmission changes. The posterior distribution revealed substantial heterogeneity for the estimation precision between interventions. For many interventions the case data is only weakly informative such that neither size nor direction of the transmission change can be confidently stated. For precisely estimated changes in transmission, the limitations of observational data apply and the results do not allow the identification of causal effects without additional context.

As the fully Bayesian approach with MCMC sampling imposes computation constraints, several simplifying assumptions were necessary. This includes the lack of importation between compartments, omission of the children until 14 years of age, and a limitation to the time frame of the first wave. Fortunately, the Bayesian framework allows to communicate some of the uncertainty and could integrate additional aspects in future work. While the recovery of age-specific growth dynamics is preferable to marginal effects, a more complex model with importation across age and locations would improve inference if compartments differ strongly in incidence. Future work may consider computational improvements or substituting the fully Bayesian approach with approximate inference methods to facilitate more complex models and simultaneous estimation across more locations and a longer time frame.

The estimation results are consistent with indirect effects (e.g., public awareness, information effects, testing intensity, etc.) playing a large role for transmission dynamics. Behavioral adaptations and second-order effects should be further investigated, as they determine the efficiency of policy interventions. Ultimately, the usefulness of health interventions depends on their ability to allocate costs of prevention effectively.

On a broader perspective, the study illustrated the potential of surveillance data with date of symptom onset. First, it can improve inference in the presence of under-reporting and reporting delay, especially if the latter is changing over time.
Second, the symptom onset data allowed the creation of a proxy for testing and tracing, which can be more adequate than modeling this aspect with a dummy variable.

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**DATA AVAILABILITY STATEMENT**
The data that support the findings of this study are openly available in https://github.com/Schmidtpk/CovidGer. Replication code is available in https://github.com/Schmidtpk/InfSup.

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**REFERENCES**
1. Lloyd-Smith JO, Schreiber SJ, Kopp PE, Getz WM. Superspreading and the effect of individual variation on disease emergence. Nature. 2005;438(7066):355-359.
2. Riley S, Fraser C, Donnelly CA, et al. Transmission dynamics of the etiological agent of SARS in Hong Kong: impact of public health interventions. *Science*. 2003;300(5627):1961-1966.
3. Lipsitch M, Cohen T, Cooper B, et al. Transmission dynamics and control of severe acute respiratory syndrome. *Science*. 2003;300(5627):1966-1970.
4. Adam DC, Wu P, Wong JY, et al. Clustering and superspreading potential of SARS-CoV-2 infections in Hong Kong. *Nat Med*. 2020;26(11):1714-1719. doi:10.1038/s41591-020-1092-0
5. Bi Q, Wu Y, Mei S, et al. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study. *Lancet Infect Dis*. 2020;20(8):911-919.
6. Endo A, Abbott S, Kucharski AJ, Funk S, et al. Estimating the overdispersion in COVID-19 transmission using outbreak sizes outside China. *Wellcome Open Res*. 2020;5(67):67.
7. Hendrix MJ. Absence of apparent transmission of SARS-CoV-2 from two stylists after exposure at a hair salon with a universal face covering policy—Springfield, Missouri. *MMWR Morb Mortal Wkly Rep*. 2020;2020:69.
8. Khanh N, Thai P, Quach H, et al. Transmission of SARS-CoV 2 during long-haul flight. *Emerg Infect Dis*. 2020;26(11):2617-2624.
9. Sehra ST, Salciccioli JD, Wiebe DJ, Fundin S, Baker JF. Maximum daily temperature, precipitation, ultra-violet light and rates of transmission of SARS-CoV-2 in the United States. *Clin Infect Dis*. 2020;71(9):2482-2487.
10. Salje H, Kiem CT, Lefrançq N, et al. Estimating the burden of SARS-CoV-2 in France. *Science*. 2020;369(6500):208-211.
11. Chernozhukov V, Kasahara H, Schrimpf P. Causal impact of masks, policies, behavior on early Covid-19 pandemic in the U.S. *J Econ*. 2020;220(1):23-62. doi:10.1016/j.jeconom.2020.09.003
12. Zhang R, Li Y, Zhang AL, Wang Y, Molina MJ. Identifying airborne transmission as the dominant route for the spread of COVID-19. *Proc Natl Acad Sci*. 2020;117(26):14857-14863. doi:10.1073/pnas.2009617117
13. Mitze T, Kosfeld R, Rode J, Wälde K. Face masks considerably reduce COVID-19 cases in Germany. *Proc Natl Acad Sci*. 2020;117(51):32293-32301. doi:10.1073/pnas.2015954117
14. Flaxman S, Mishra S, Gandy A, et al. Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe. *Nature*. 2020;584(7820):257-261.
15. Brauner JM, Mindermann S, Sharma M, et al. Inferring the effectiveness of government interventions against COVID-19. *Science*. 2021;371(6531):eab9338.
16. Soltész K, Gustafsson F, Timpka T, et al. The effect of interventions on COVID-19. *Nature*. 2020;588(7839):E26-E28. doi:10.1038/s41586-020-3025-y
17. Ng QX, De Deyn MLZQ, Yeo WS. Do face masks help? Is not the question. *Proc Natl Acad Sci*. 2020;117(44):27078-27079. doi:10.1073/pnas.202241117
18. Bhatt S, Ferguson N, Flaxman S, Gandy A, Mishra S, Scott JA. Semi-mechanistic Bayesian modeling of COVID-19 with renewal processes. *arXiv preprint arXiv:2012.00394*. 2020.
19. Olney AM, Smith J, Sen S, Thomas F, Unwin HJT. Estimating the effect of social distancing interventions on COVID-19 in the United States. *Am J Epidemiol*. 2021;190(8):1504-1509.
20. Wood SN, Inferring UK. COVID-19 fatal infection trajectories from daily mortality data: were infections already in decline before the UK lockdowns? *Biometrics*. 2021;78(3):1127-1140.
21. Monod M, Blenkinsop A, Xi X, et al. Age groups that sustain resurging COVID-19 epidemics in the United States. *Science*. 2021;371(6536):eabe8372. doi:10.1126/science.abe8372
22. Cori A, Ferguson NM, Fraser C, Cauchemez S. A new framework and software to estimate time-varying reproduction numbers during epidemics. *Am J Epidemiol.* 2013;178(9):1505-1512.
23. White LF, Moser CB, Thompson RN, Pagano M. Statistical estimation of the reproductive number from case notification data. *Am J Epidemiol.* 2021;190(4):611-620.
24. Vegvari C, Abbott S, Ball F, et al. Commentary on the use of the reproduction number R during the COVID-19 pandemic. *Stat Methods Med Res.* 2022;31(9):1675-1685.
25. Mishra S, Scott JA, Laydon DJ, et al. A COVID-19 model for local authorities of the United Kingdom. *J R Stat Soc Ser A Stat Soc.* 2022;185(Supplement_1):S86-S95.
26. Wallinger J, Teunis P. Different epidemic curves for severe acute respiratory syndrome reveal similar impacts of control measures. *Am J Epidemiol.* 2004;160(6):509-516.
27. Dehning J, Zierenberg J, Spitzner FP, et al. Inferring changepoints in the spread of COVID-19 reveals the effectiveness of interventions. *Science.* 2020;369(6500):eabb9789.
28. Russell TW, Golding N, Hellewell J, et al. Reconstructing the early global dynamics of under-ascertained COVID-19 cases and infections. *BMC Med.* 2020;18(1):1-9.
29. 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):1123-1138.
30. Robert Koch Institute. Corona-monitoring lokal. 2020. https://www.rki.de/DE/Content/Gesundheitsmonitoring/Studien/cml-studie/cml-studie_node.html. Accessed October 10, 2020.
31. Pitzer VE, Chitwood M, Havumaki J, et al. The impact of changes in diagnostic testing practices on estimates of COVID-19 transmission in the United States. *Am J Epidemiol.* 2021;190(9):1908-1917.
32. Hsiang S, Allen D, Annan-Phan S, et al. The effect of large-scale anti-contagion policies on the COVID-19 pandemic. *Nature.* 2020;584(7820):262-267.
33. Davies NG, Kucharski AJ, Eggo RM, et al. Effects of non-pharmaceutical interventions on COVID-19 cases, deaths, and demand for hospital services in the UK: a modelling study. *Lancet Public Health.* 2020;5(7):e375-e385.
34. Parker D, Planykh O. Mobility-guided estimation of Covid-19 transmission rates. *Am J Epidemiol.* 2021;190(6):1081-1087.
35. Xie S, Wang W, Wang Q, Wang Y, Zeng D. Evaluating effectiveness of public health intervention strategies for mitigating COVID-19 pandemic. *Stat Med.* 2022;41(19):3820-3836.
36. Agosto A, Campmas A, Giudici P, Renda A. Monitoring COVID-19 contagion growth. *Stat Med.* 2021;40(18):4150-4160.
37. Keller JP, Zhou T, Kaplan A, Anderson GB, Zhou W. Tracking the transmission dynamics of COVID-19 with a time-varying coefficient state-space model. *Stat Med.* 2022;41(15):2745-2767.
38. Held L, Höhle M, Hofmann M. A statistical framework for the analysis of multivariate infectious disease surveillance counts. *Stat Model.* 2005;5(3):187-199.
39. Meyer S, Held L. Incorporating social contact data in spatio-temporal models for infectious disease spread. *Biostatistics.* 2016;18(2):338-351.
40. Fisher LH, Wakefield J. Ecological inference for infectious disease data, with application to vaccination strategies. *Stat Med.* 2020;39(3):220-238.
41. Abbott S, Hellewell J, Thompson RN, et al. Estimating the time-varying reproduction number of SARS-CoV-2 using national and subnational case counts. *Wellcome Open Res.* 2020;5(112):112.
42. Plummer M. rjags: Bayesian Graphical Models using MCMC. R package version 4-10. 2019.
43. Hoffman MD, Gelman A. The no-U-turn sampler: adaptively setting path lengths in Hamiltonian Monte Carlo. *J Mach Learn Res.* 2014;15(1):1593-1623.
44. Grinsztajn L, Semenova E, Margossian CC, Riou J. Bayesian workflow for disease transmission modeling in Stan. *Stat Med.* 2021;40(27):6209-6234.
45. Tönshoff B, Müller B, Elling R, et al. Prevalence of SARS-CoV-2 infection in children and their parents in Southwest Germany. *Pediatr.* 2021;40(27):6209-6234.
46. Rodiah I, Vanella P, Kuhlmann A, et al. Age-specific contribution of contacts to transmission of SARS-CoV-2 in Germany. *Eur J Epidemiol.* 2022;38(1):39-58.
47. Keeling MJ. The effects of local spatial structure on epidemiological invasions. *Proc R Soc Lond Ser B Biol Sci.* 1999;266(1421):859-867.
48. Davis S, Trapman P, Leirs H, Begon M, Heesterbeek J. The abundance threshold for plague as a critical percolation phenomenon. *Nature.* 2008;454(7204):634-637.
49. Ali ST, Wang L, Lau EHY, et al. Serial interval of SARS-CoV-2 was shortened over time by nonpharmaceutical interventions. *Science.* 2020;369(6507):1106-1109. doi:10.1126/science.abc9004
50. Wieler L, Rexroth U, Gottschalk R. Emerging COVID-19 success story: Germany’s strong enabling environment. 2020. https://www .exemplars.health/emerging-topics/epidemic-preparedness-and-response/covid-19/germany. Accessed November 7, 2020.
51. Stang A, Standl F, Kowall B, et al. Excess mortality due to COVID-19 in Germany. *J Infect.* 2020;81:797-801.
52. Contreiras S, Dehning J, Loidolt M, et al. The challenges of containing SARS-CoV-2 via test-trace-and-isolate. *Nat Commun.* 2021;12(1):1-13.
53. Furman E. On the convolution of the negative binomial random variables. *Stat Prob Lett.* 2007;77(2):169-172.
55. Betsch C, Korn L, Sprengholz P, et al. Social and behavioral consequences of mask policies during the COVID-19 pandemic. Proc Natl Acad Sci. 2020;117(36):21851-21853.

56. Tomori DV, Rübsamen N, Berger T, et al. Individual social contact data and population mobility data as early markers of SARS-CoV-2 transmission dynamics during the first wave in Germany—an analysis based on the COVIMOD study. BMC Med. 2021;19:1-13.

57. Laxminarayan R, Wahl B, Dudala SR, et al. Epidemiology and transmission dynamics of COVID-19 in two Indian states. Science. 2020;370(6517):691-697. doi:10.1126/science.abb7672

58. Küchenhoff H, Günther F, Höhle M, Bender A. Analysis of the early COVID-19 epidemic curve in Germany by regression models with change points. Epidemiol Infect. 2021;149:e68. doi:10.1017/S0950268821000558

59. Ferretti L, Wymant C, Kendall M, et al. Quantifying SARS-CoV-2 transmission suggests epidemic control with digital contact tracing. Science. 2020;368(6491):eabb6936.

60. Gurdasani D, Ziauddeen H. On the fallibility of simulation models in informing pandemic responses. Lancet Glob Health. 2020;8(6):e776-e777. doi:10.1016/S2214-109X(20)30219-9

61. Haug N, Geyrhofer L, Londei A, et al. Ranking the effectiveness of worldwide COVID-19 government interventions. Nat Hum Behav. 2020;4(12):1303-1312.

62. Toxvaerd F. Rational disinhibition and externalities in prevention. Int Econ Rev. 2019;60(4):1737-1755.

63. Toxvaerd F. Equilibriumsocialdistancing. Covid. Economics. 2020;(15):110-133.

64. Baker RE, Yang W, Vecchi GA, Metcalf CJE, Grenfell BT. SusceptiblesupplylimitstheroleofclimateintheearlySARS-CoV-2pandemic. Science. 2020;369(6501):315-319.

65. Carlson CJ, Gomez AC, Bansal S, Ryan SJ. Misconceptions about weather and seasonality must not misguide COVID-19 response. Nat Commun. 2020;11(1):1-4.

66. Gavenčiak T, Monrad JT, Leech G, et al. Seasonal variation in SARS-CoV-2 transmission in temperate climates: a Bayesian modelling study in 143 European regions. PLoS Comput Biol. 2022;18(8):e1010435.

67. Ledebur K, Kaleta M, Chen J, et al. Meteorological factors and non-pharmaceutical interventions explain local differences in the spread of SARS-CoV-2 in Austria. PLoS Comput Biol. 2022;18(4):e1009973.

68. Pei S, Yamana TK, Kandula S, Galanti M, Shaman J. Burden and characteristicsofCOVID-19intheUnitedStatesduring2020. Nature. 2021;598(7880):338-341.

69. Weidemann F, Dehnert M, Koch J, Wichmann O, Höhle M. Bayesian parameter inference for dynamic infectious disease modelling: rotavirus in Germany. Stat Med. 2014;33(9):1580-1599.

70. Bjørnstad ON, Finkenstädt BF, Grenfell BT. Dynamics of measles epidemics: estimating scaling of transmission rates using a time series SIR model. Ecological Monographs. 2002;72(2):169-184.

71. Wakefield J, Dong TQ, Minin VN. Spatio-temporal analysis of surveillance data. In: Held L, Hens N, O’Neill P, Wallinga J, eds. Handbook of Infectious Disease Data Analysis. London, UK: Chapman and Hall/CRC; 2019:455-476.

72. Finkenstädt BF, Grenfell BT. Time series modelling of childhood diseases: a dynamical systems approach. J R Stat Soc Ser C Appl Stat. 2000;49(2):187-205.

SUPPORTING INFORMATION
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APPENDIX A. TRANSMISSION MODEL

This appendix derives Equation (1) from the assumption of independent offspring distributions consistent with the seminal work on overdispersed offspring distributions.1

Let \( i_{t,t'} \) denote the number of infections at time \( t \) caused by primary cases infected at time \( t' \), where we omit location and age for notational convenience. We have \( i_t = \sum_{t'} i_{t,t'} \). Let \( i_{j,t,t'} \) for \( j = 1, \ldots, i_t \) denote the offspring at time \( t \) of individual \( j \) infected at time \( t' \). Let \( i_{t,t'} = \sum_j i_{j,t,t'} \) denote the sum of secondary cases of individual \( j \). All distributional statements for random variables realizing at time \( t \) are meant given \( R_t \) and previous infections \( i_{t-1}, i_{t-2}, \ldots \). Let \( D_t \) denote the probability mass function of the generation time distribution with positive support.22

The following assumptions are employed:

A₁ The offspring \( i_{j,t,t'} \) has a negative binomial distribution with mean \( R_t D_t(t - t') \) and dispersion \( \Psi D_t(t - t') \).
The offspring $i_{j, t, t'}$ with $t' < t$ and $j \in \{1, \ldots, i_r\}$ are pairwise independent given $R_t$.

It follows that $i_t \sim \text{NB}(R_t P_t, \Psi P_t)$, where $P_t = \sum_{t'} D_t(t - t')i_{t'}$ denotes the transmission pressure at time $t$. The argument is as follows: As $i_{j, t, t'}$ for $j = 1, \ldots, i_r$ are independent and identically distributed, it follows that

$$i_{t, t'} = \sum_{j=1}^{i_r} i_{j, t, t'} \sim \text{NB}(R_t D_t(t - t')i_{t'}, \Psi D_t(t - t')i_{t'}).$$

As $i_{t', t}$ for $t' < t$ are independent and have a negative binomial distribution with identical parameter

$$P_{t', t} = \frac{\Psi D_t(t - t')i_{t'}}{R_tD_t(t - t')i_{t'} + \Psi D_t(t - t')i_{t'}} = \frac{\Psi}{R_t + \Psi},$$

the distribution of the sum of all transmissions at day $t$ is denoted by

$$i_t = \sum_{t' < t} i_{t', t} \sim \text{NB}(R_t P_t, \Psi P_t).$$

Note the connection to the widely used parameterization of individual dispersion,$^1$ that is, $\text{NB}(R, \Psi)$, which models the dispersion of the amount of secondary infections without generation time. If the reproductive number is constant, that is, $R_t = R$, a single infection induces $\sum t' i_{j, t, t'} \sim \text{NB}(R, \Psi)$ secondary infections, coinciding with the aforementioned seminal model. Notably, if the instantaneous reproductive number is varying over time, the number of secondary infections constitutes a mixture negative binomial distribution instead.$^{54}$

If $D_t(1) = 1$ (a common assumption for weekly case counts), the arguments presented here simplify. Specifically, the transmission pressure is $P_t = i_{t-1}$ and the assumption reduces to $i_{j, t, t-1} \sim \text{NB}(R_t, \Psi)$ and independent given $R_t$. We note the similarity to models$^{70,71}$ for the time series SIR model first introduced from a linear birth process,$^{72}$ considering only a single time step, in which case the model presented here would reduce to $i_t \sim \text{NB}(R_t i_{t-1}, i_{t-1} \Psi)$, which recovers the time series SIR model for $\Psi = 1$. Thus, the model presented here can be seen as a generalization of the time series SIR model with flexible dispersion $\Psi$ and accounting for a generation distribution $D_t$.

For comparison, consider the standard assumption of inference based on negative binomial regression, the endemic/epidemic model,$^38$ or epidemiological models with random effects,$^40$ that is, $i_t \sim \text{NB}(R_t i_{t-1}, \Psi)$. This model is not consistent with the perspective that individual transmission counts are independent given $R_t$. As we model the reproductive number $R_t$, the assumption of independent offspring distributions is more suitable (for empirical evidence see Section S1.3). A similar point applies to the study by Flaxman et al.$^{14}$ where dispersion is independent of the total count in the death reports.