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Natural experiments to assess the effectiveness of Covid-19 containment measures

Methodological principles, implementation in NPI studies and a case study

Almost every country in the world has taken measures to contain infections (non-pharmaceutical interventions, NPI) during the coronavirus pandemic. Comprehensive packages of measures (lockdowns) have been implemented in many countries. As most of these measures also have negative effects (e.g. learning deficits due to school closures, restrictions on individual freedoms, economic losses), assessing their actual effectiveness - i.e. their influence on the overall incidence of infection - is of great importance. However, the question of a causal conclusion is by no means trivial here. In medicine, the randomised controlled trial (RCT) is often regarded as the ‚gold standard' of evidence. The (statistical) inference of causal influences of interventions is ensured by the existence of a control group (control conditions) that is comparable to the intervention group (structural equality), as well as randomisation and, in many cases, blinding (Kabisch et al. 2011: 663 ff.). Irrespective of the fact that it is already challenging to fulfil all of these quality criteria in ‚real' experiments, it quickly becomes apparent that this principle of evidence generation cannot be directly transferred to the assessment of the effectiveness of pandemic containment measures. However, the effectiveness of NPIs - which are political interventions - can be tested with the help of so-called natural experiments, which are analysed using econometric methods. This article first outlines the methodological principle behind this and then, in a first step, discusses the problems in the implementation of existing NPI studies. Of particular importance here are, on the one hand, the necessary control conditions in order to be able to draw causal conclusions with regard to the effectiveness of measures and, on the other hand, the specification of the analysis models in these studies. In the second step, the results of a natural experiment are presented with regard to five NPIs that were implemented in Germany during the second wave of coronavirus; Switzerland serves as a control group, where these measures - including school and daycare centre closures - were dispensed with.

Methodological problems of model-based studies to assess the effectiveness of NPIs

Natural experimentsand their statistical analysis in assessing the effectiveness of NPIs

>> NPIs are policy interventions, such as the introduction of a minimum wage, a temporary VAT reduction for an industry or the banning of a particular herbicide. There is no randomisation in such interventions, as a specific measure is not introduced in randomly selected sub-areas. Blinding is also not possible, as the members of the intervention group know whether the measure exists or not. Provided that a certain intervention is carried out in one area and not in another, there is, as in a ‚real' experiment, an intervention group and a control group; in such a case, one speaks of a natural experiment (or quasi-experiment). It is also a before-and-after study with a control group that allows a causal conclusion to be drawn about the effectiveness of an intervention (Kugler et al. 2014: 114 ff.; Wooldridge 2012: 457). However, there are no laboratory conditions, but real-world conditions. Unlike in a ‚real' experiment, the variance of the independent variables is not controlled by the researchers, so that it cannot be referred to as a field experiment, but rather as a field study (Eifler/Leitgöb 2019: 210 ff.).

Provided that data on the outcome is available for the same units of analysis for at least two points in time - i.e. panel data - econometrics offers various methods for statistically analysing the intervention effect (Kugler et al. 2014: 114 ff.). The difference-in-differences approach (DiD), which is based on a linear regression model, is particularly prominent. In addition to the fact that control conditions exist, the causality of results is derived from the fact that the study units are assigned to the intervention or control group via the specification of the independent variables. It is not necessary for both groups to have the same initial level; in fact, the DiD approach is specifically designed for the case that the intervention and control groups have different levels of the outcome of interest before the intervention begins. The approach compares how the outcome would have developed in the treatment group without the intervention (counterfactual) with the development of their actual outcome with the intervention. The development of all study units before the start of the intervention and the development of the control group from the time of the intervention serve as reference points for this. The basic assumption is that the intervention group and the control group would have developed in the same way (or not statistically significantly differently) without the intervention (Kugler et al. 2014: 120 ff.; Wooldridge 2012: 454 ff.). The DiD approach can be extended by fixed effects for the study units and/or the points in time, which allows the approach to be generalised (Goodman-Bacon 2021: 255 ff.).

With regard to the numerous studies on the effectiveness of corona NPIs, it can first be noted that no causal modelling approach in the above sense is usually used (exceptions e.g. de Haas et al. 2022; Kosfeld et al. 2021; von Bismarck-Osten et al. 2022). This is less problematic, as this circumstance could be compensated for by a different specification of the respective analysis models. Much more serious, however, is the fact that the above-mentioned initial conditions for a natural experiment - namely the existence of an intervention and a control group - are often not present.

The majority of NPI studies refer to the first coronavirus wave (e.g. Banholzer et al. 2021; Brauner et al. 2021; Flaxman et al. 2020; Haug et al. 2020), which poses a problem in terms of their validity: In spring 2020, the containment measures were very similar internationally, meaning that there was only a slight variance between the countries compared. Greater differentiation only took place from the second coronavirus wave (autumn/winter 2020/2021), of which Germany and its neighbouring countries are a good example (e.g. school closures in Germany and Austria, but not in France and Switzerland). The problem of low variance between the study units also applies if only the sub-regions of a single country are included in the analysis and there were only minor differences in the implementation of measures within the country. This case is found both in peer-reviewed scientific studies, which are otherwise certainly not objectionable (e.g. Kosfeld et al. 2021; Khazaei et al. 2023), as well as in publicly funded NPI studies such as the Swiss evaluation of measures (Funk et al. 2022) and the Robert Koch Institute's ‚StopptCOVID' study on the German measures (an der Heiden et al. 2023). It is not possible to derive causal effects of measures if there are no control conditions due to a lack of variance between the study units, i.e. if the same measures were implemented (almost) simultaneously in the entire study area.

The control conditions are also weakened by the fact that many studies aggregate individual measures that actually vary between the countries or regions analysed. For example, the closure of primary and secondary schools and universities is often combined into an NPI and an effect is then estimated for this aggregate (e.g. Brauner et al. 2021; Gavenciak et al. 2022; Haug et al. 2020; Sharma et al. 2021). The problem here is that different types of schools and universities were by no means treated equally; in many countries, universities were switched to distance learning from the second wave of coronavirus, but schools were left open (e.g. France, Switzerland). Other studies even aggregate the closures of schools, universities and daycare centres into one NPI (e.g. Kosfeld et al. 2021), which means that another dimension of comparison is lost. In the cases mentioned, for example, a (possible) effect of the closure of a single type of school can no longer be separated from a (possible) effect of the closure of other types of schools or universities.

The control conditions are further influenced by the choice of the spatial level of analysis and the study period: A large-scale level of analysis is often chosen, especially entire countries (e.g. Banholzer et al. 2021; Brauner et al. 2021; Flaxman et al. 2020; Haug et al. 2020; Gavenciak et al. 2022), which masks regional differences in the incidence of infection and the design of pandemic measures. For example, some NPIs in Germany were implemented at district level (e.g. curfews); the later ‚federal emergency brake' was also district-specific. Two studies, which otherwise have control conditions, limit their data to the year 2020 and thus end their analysis in the middle of the second coronavirus wave (Levelu/Sandkamp 2023; Sharma et al. 2021). It is difficult to derive effects here because only a (relatively small) part of the entire intervention period is included in the analysis.

Problems in the model specification for NPI studies

Almost all empirical NPI studies are based on regression analyses with measures as independent variables. The dependent variable in the regression model is usually the effective reproduction number (e.g. an der Heiden et al. 2023; Brauner et al. 2021; Flaxman et al. 2020; Gavenciak et al. 2022; Khazaei et al. 2023; Levelu/Sandkamp 2023; Li et al. 2021; Sharma et al. 2021). In such a model, the effect of a single explanatory variable is considered in isolation, i.e. under otherwise constant conditions (ceteris paribus). The empirically estimated influence of a variable is therefore, mutatis mutandis, only ‚valid' in combination with the other explanatory variables in the model. In order to estimate it without bias, other variables must therefore also be included in the model that are not of interest but may influence the dependent variable. This is the principle of control variables, which are included in such models in order to ‚factor out' their influence (Hilmert 2019: 4 ff.; Wooldridge 2012: 97). This aspect of model specification can be generalised: a regression model in which variables that actually influence the dependent variable are missing is underspecified. As a result, the influences of the explanatory variables included in the model may also be over- or underestimated; this is referred to as omitted variable bias (Greene 2012: 96 ff.; Wooldridge 2012: 88 ff.).

A look at the analysis methodology of previous NPI literature shows that many of the studies with the effective reproduction number as the dependent variable only integrate NPI as independent variables in their regression models (e.g. Brauner et al. 2021; Flaxman et al. 2020; Li et al. 2021; Sharma et al. 2021). For example, Gavenciak et al. (2022: 4) with reference to the work of Brauner et al. (2021) and Sharma et al. (2021): ‚Both models assume the time-varying reproduction number R(t) to be a product of R0, the ‚natural' reproduction number when no NPIs are in place, multiple terms representing the effects of interventions, and noise terms modelling the influence of other, unobserved, factors on R(t).' In such a model, there are therefore no other independent variables that could have an influence on the time course of Rt. It is therefore implicitly assumed that the effective reproduction number is constant as long as no corona measures are in force.

However, as sufficiently documented in the epidemiological literature, the time course of Rt depends not only on containment measures, but also on the following aspects, among others:

- Decrease in susceptible population: An affected person is immunised after their own infection - at least for a certain period of time - and can therefore (temporarily) neither become newly infected themselves nor infect another person; the same applies to vaccination (Mercer et al. 2011: 984 f.; Nishiura/Chowell 2009: 104)
- Population heterogeneity: Not every individual has the same probability of infecting themselves or others, partly due to very different contact patterns (Müller 2021: 70 f.; Viboud et al. 2016: 31 ff.)
- Voluntary changes in behaviour: Individual reduction of infection risks independent of measures (Mercer et al. 2011: 984 f.; Nishiura/Chowell 2009: 104; Viboud et al. 2016: 31 ff.), which has also been demonstrated in the coronavirus pandemic, e.g. with regard to mobility behaviour (e.g. Goolsbee/Syverson 2021; Jacobsen/Jacobsen 2020).
- Seasonality: SARS-CoV-2, like other respiratory viral diseases (e.g.

influenza, RSV, other coronaviruses), follows a seasonal cycle in temperate climates with a focus on autumn and winter (Dbouk/ Drikakis 2021; Moriyama et al. 2020: 84 ff.) .

Of course, it is impossible to take all real explanatory factors into account in a statistical model. However, the models of the above-mentioned studies cannot be fully specified, which makes it difficult to interpret the results with regard to the NPI variables (omitted variable bias, see above). This is because if only measures are provided as explanatory variables in the model, any change in the R value is necessarily attributed to the effect of these measures, even if it occurred for other reasons. Individual later NPI studies have expanded their analysis models to include certain aspects mentioned above, e.g. model terms for seasonal fluctuations (an der Heiden et al. 2023; Gavenciak et al. 2022), the effect of Covid-19 vaccinations on the R-value (an der Heiden et al. 2023) or (possible) voluntary behavioural changes (Levelu/ Sandkamp 2023); however, these models also do not include any variables that, apart from these partial aspects, could bring about a change in the effective reproduction number. Only the work by Khazaei et al. (2023), published in November 2023, takes voluntary behavioural changes into account as a kind of ‚own measure' and also the decreasing probability of (re)infection due to previous infections and vaccinations in the model equation.

Another aspect with regard to the consideration of control variables is that many studies only include part of the implemented coronavirus measures in the regression models. For example, the above-mentioned studies, which summarise the closure of schools and universities into an NPI, do not even consider the closure of childcare facilities or at least do not indicate whether this measure is included in the above-mentioned aggregate (Brauner et al. 2021; Gavenciak et al. 2022; Sharma et al. 2021). Khazaei et al. (2023), on the other hand, make a deliberate selection of eight NPIs (including school closures, curfews, restrictions on people attending events). Regardless of whether these omissions are due to a deliberate selection or a lack of data, there is a similar problem here as with other conceivable control variables: The effect of a specific measure found in the model may be over- or underestimated because not all other measures are included in the model. It is possible, for example, that an effect found is actually due to other measures that do not appear in the model.

Case study: Baden-Württemberg and Switzerland in the second coronavirus wave

In the second coronavirus wave, the intensity of government containment measures had already differentiated significantly between the countries, so that effectiveness analyses based on natural experiments are possible in many places. This can be seen, for example, in a direct comparison between Germany and neighbouring Switzerland: although measures of varying intensity were established in both countries (with a time lag), Switzerland, unlike Germany, refrained from closing childcare facilities, primary and secondary schools, hotels and body-related services (e.g. hairdressers). This difference provides a good basis for a natural experiment, as no-treatment control conditions prevail in relation to these interventions. Therefore, the influence of these five NPIs is analysed here with regard to Switzerland and neighbouring Baden-Württemberg. The spatial level of analysis is the NUTS3 level, i.e. urban and rural districts (Baden-Württemberg) and cantons (Switzerland).

The empirical analysis is based on the previous NPI studies (see above): A regression model is constructed with the effective reproduction number as the dependent variable and the corona measures as independent variables (in the form of dummy variables) (see Fig. 1). However, the model specification is modified in two respects: Firstly, the intervention effect is analysed according to the difference-in-differences approach (DiD). Following the formalisation in Wooldridge (2012: 457 f.), the intervention group for a specific measure (e.g. closure of primary schools) and the intervention period (e.g. days on which the primary schools in the intervention group were not closed due to holidays but as a corona measure) are each marked with a dummy variable and the interaction of these two variables is also included in the model. The coefficient of this interaction term is the DiD estimator and indicates the intervention effect of the specific measure (percentage change in the R-value).

Secondly, control variables are added to the model that can influence the course of Rt independently of pandemic measures. Analogous to the model by Levelu/Sandkamp (2023: 9 f.), the R value is included in the model ten days in advance, as it is assumed that people may react to increased infection numbers and engage in individual risk avoidance. Furthermore, cumulative numbers of infections and vaccinated people as well as their interaction with time are included in the model in order to take into account the (possible) deceleration of the infection wave due to (temporary) immunity (see above). A model was estimated for each of the five NPIs. All other corona measures are also included in the model as control variables in order to isolate the actual effect of the intervention of interest (Fig. 1.)

Table 1 shows the model estimates and the associated model goodness statistics. Figure 2 shows the DiD estimators from the five models and the associated confidence intervals based on robust standard errors. A significant DiD estimator below zero signals the effectiveness of a measure in the form of an average reduction in the effective reproduction number. This shows that the closure of body-related services causes an average reduction in the effective reproduction number of approx. 1.7%. This measure, which was taken in Baden-Württemberg (and throughout Germany) in the second coronavirus wave but not in Switzerland, can therefore be considered effective. No such effect can be found for the other four NPIs analysed. The DiD estimators for the closure of schools, day-care centres and hotels are even positive, suggesting a counterproductive effect. This cannot be due to the fact that the model design makes it difficult to reject the null hypothesis in terms of statistical significance, because on the one hand these point estimates are also significant (just with a different sign than expected), and on the other hand the theoretically expected effect has been proven for another NPI analysed - the closure of services close to the body (Fig. 1, Tab. 1).

A look at the control variables shows that theyhave a statistically significant influence on the dependent variable in mostcases. It can be seen, for example, that the R-value decreases significantly with increasing numbers of both infected and vaccinated people, which corresponds to the epidemiological basis in relation to the effective reproduction number (see e.g. Mercer et al. 2011: 984 f.; Nishiura/Chowell 2009: 104). The fact that the R value ten days earlier also has a significantly lowering influence may indicate that there were voluntary changes in behaviour in the sense that people reacted to increased infection numbers and avoided infection risks. However, the extent to which this actually happened and what impact these behavioural changes had on the infection wave cannot be determined on the basis of this statistical result. In general, the content of the control variables should not be overinterpreted. However, it should be noted that they must necessarily be integrated into such a model to analyse the effectiveness of NPIs; without them, the model would be underspecified.

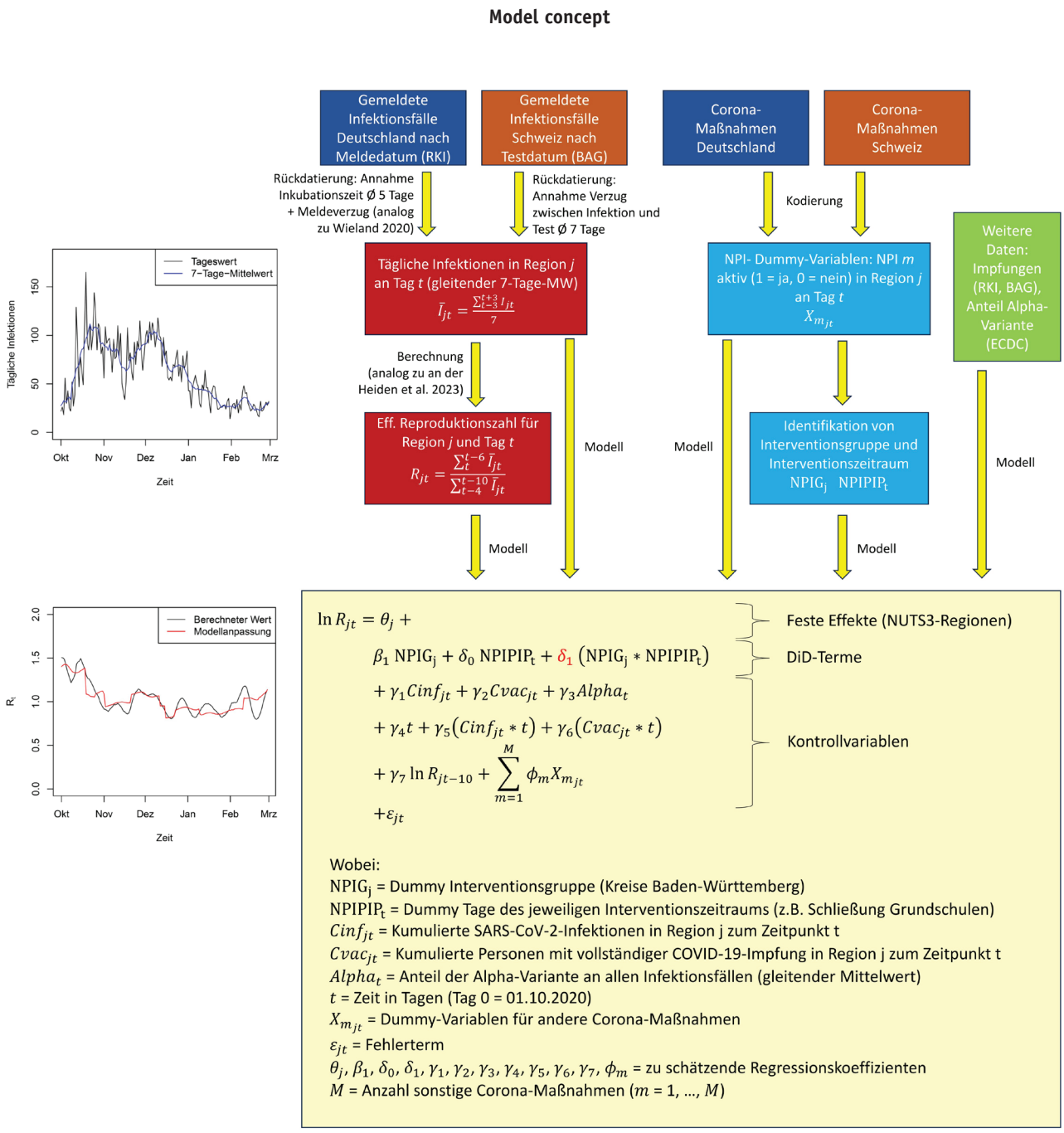


Fig 1: Model concept.

Conclusion

The assessment of the effectiveness of pandemic measures, unlike the effect of a drug or therapy, is not a medical issue. NPIs are political interventions whose effectiveness can be tested in the same way as other state interventions. The prerequisite for this is that the initial conditions of a natural experiment exist, i.e. that there is an intervention group and a control group that can be compared, and that panel data is available for the study units. If these conditions are met, econometrics offers an established method of analysis with the difference-in-differences approach, which can map any initial differences between the study units of the two groups and at the same time take other influences into account in the form of control variables.

The literature on corona measures - whereby only representative examples can be given here and no complete literature list can be presented - shows that many studies do not fully fulfil these requirements and that their results must be interpreted taking these limitations into account. Under no circumstances can the causal effect of a measure be inferred if the studies that found this effect have no control conditions, i.e. no comparison region(s) without this measure were included in the analysis. The effect size of measures must also at least be questioned if studies only consider NPI as explanatory variables or if important control variables are missing. This problem does not concern the researchers involved, as they have documented their methodology and its limitations, but above all the reception of such studies in the media and poli-

Model results					
	Koeffizienten (Standardfehler)				
Unabhängige Variablen	**Modell 1: Schließung Kitas/ Kindergärten**	**Modell 2: Schließung Grundschulen**	**Modell 3: Schließung Weiterführende Schulen**	**Modell 4: Schließung Hotels**	**Modell 5: Schließung körpernahe Dienstleistungen**
DiD-Terme:					
Interventionsgruppe	0,568*** (0,034)	0,568*** (0,034)	0,557*** (0,034)	0,585*** (0,033)	0,554*** (0,032)
Interventionszeitraum	-0,048*** (0,008)	-0,080*** (0,007)	-0,110*** (0,008)	-0,053 (0,038)	-0,078*** (0,006)
Interventionsgruppe x Interventionszeitraum	0,038* (0,017)	0,072*** (0,010)	0,089*** (0,010)	0,081** (0,030)	-0,017* (0,008)
Kontrollvariablen:					
Infizierte kumuliert	-0,00001*** (0,00000)	-0,00001*** (0,00000)	-0,00001*** (0,00000)	-0,00000*** (0,00000)	-0,00001*** (0,00000)
Geimpfte kumuliert	-0,00001*** (0,00000)	-0,00001*** (0,00000)	-0,00002*** (0,00000)	-0,00002*** (0,00000)	-0,00002*** (0,00000)
Anteil Alpha-Variante	-0,001** (0,0003)	-0,001** (0,0003)	-0,0004 (0,0003)	-0,0004 (0,0003)	0,001** (0,0003)
Zeit [Tage]	0,002*** (0,0002)	0,003*** (0,0002)	0,003*** (0,0002)	0,002*** (0,0002)	0,002*** (0,0002)
Infizierte kumuliert x Zeit [Tage]	0,00000*** (0,000)	0,00000*** (0,000)	0,00000*** (0,000)	0,00000*** (0,000)	0,00000*** (0,000)
Geimpfte kumuliert x Zeit [Tage]	0,00000*** (0,000)	0,00000*** (0,00000)	0,00000*** (0,000)	0,00000*** (0,00000)	0,00000*** (0,000)
ln R_{jt-10}	-0,180*** (0,010)	-0,183*** (0,010)	-0,173*** (0,011)	-0,180*** (0,011)	-0,174*** (0,010)
Andere NPI (Anzahl)	35	35	36	35	35
Feste Effekte (Region)	ja	ja	ja	ja	ja
Beobachtungen	10.570	10.570	10.570	10.570	10.570
R^2	0,626	0,630	0,631	0,625	0,633
Adj. R^2	0,622	0,626	0,627	0,621	0,630
Resid.-Std.-fehler	0,124 (df = 10459)	0,123 (df = 10459)	0,123 (df = 10458)	0,124 (df = 10459)	0,123 (df = 10459)
F-Statistik	157,708*** (df = 111; 10459)	160,284*** (df = 111; 10459)	159,628*** (df = 112; 10458)	157,133*** (df = 111; 10459)	162,849*** (df = 111; 10459)
Legende: *p < 0,05, **p < 0,01, ***p < 0,001; Robuste Standardfehler; Interventionsgruppe = Kreise Baden-Württemberg. Abhängige Variable: ln R_{jt}					

Tab. 1: Model results.

tics. In any case, the methodology of an NPI study must be critically scrutinised with regard to control conditions and model specification in order to be able to answer the following question beyond doubt: Can the study make a causal statement about the effect of a measure? Another aspect that is not dealt with here is the efficiency or proportionality of a measure, which should be the subject of political or social debate.

The case study shows that the closures of schools, childcare facilities and hotels have no dampening effect on the effective reproduction number in a direct comparison of two neighbouring regions with a ‚real' control group, i.e. they are ineffective in terms of the methodology of previous NPI studies.

On the one hand, this reveals the importance of natural experiments and their adequate statistical analysis and, on the other hand, the necessity of control variables in the model, as these have a demonstrable influence on the incidence of infection. Without them, the model would be misspecified and the effects of the analysed measures would possibly be misjudged. The findings tend to be similar to those in the (few) studies that have investigated coronavirus measures with ‚real' control conditions and a DiD approach; for example, no effect was found for night-time curfews (de Haas et al. 2022) and school closures (von Bismarck-Osten et al. 2022).

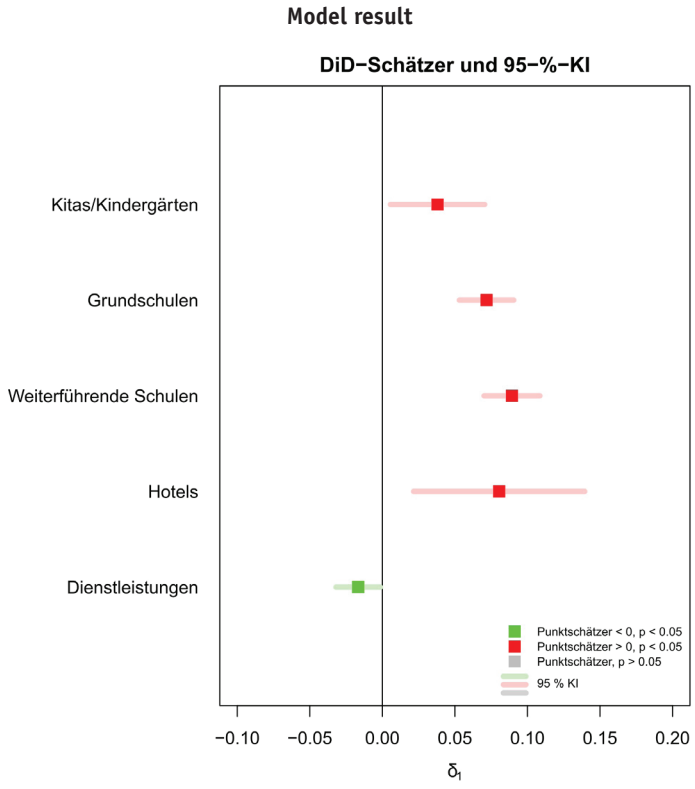


Fig 2: Model result

Limits of the method

Of course, the limitations of the method are also evident here: it was only possible to carry out a causal analysis in the sense of a natural experiment for five measures, as only here were ‚real' control conditions available. A statement on other NPIs cannot be made on this basis.

Furthermore, it must be pointed out that a natural experimentsuch as this one can only ever make statements with regard to an average intervention effect, i.e. an effect at population level. The results do not reflect any individual risk. The fact that school closures, for example, do not show an infection-reducing effect in society does not, of course, mean that a person cannot become infected with SARS-CoV-2 in a school or that no infections have taken place in schools. It is just that the infections that were (possibly) prevented by school closures are so few that their aggregate effect is not reflected in the incidence of infection in society as a whole. Evasion effects are also conceivable, i.e. that infections that were (possibly) prevented by school closures were even overcompensated by the fact that pupils and teachers were instead in another location where the risk of infection is (possibly) much higher. <<

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Author's declaration

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