

## **Rapid Review der Wirksamkeit nicht-pharmazeutischer Interventionen bei der Kontrolle der COVID-19-Pandemie**

Francisco Pozo-Martin, Florin Cristea, Charbel El Bcheraoui

Robert Koch-Institut, Zentrum für Internationalen Gesundheitsschutz (ZIG), ZIG 2: Evidenzbasierte Public Health

***NB: Dieses Papier ist eine erste Zusammenfassung der Evidenz, die von den Autoren erstellt wurde. Eine weitere Ausarbeitung findet statt.***

### **Zusammenfassung:**

EMBASE und Google Scholar wurden nach veröffentlichten Studien durchsucht, die sich auf die Wirksamkeit von nicht-pharmazeutischen Interventionen (NPIs) bei der Kontrolle der COVID-19-Pandemie beziehen.

Aus einer Gesamtzahl von >4900 Titeln/Abstracts konnten wir 27 Studien identifizieren, die für unsere Suche relevante Evidenz präsentierten. Davon basierten 16 auf statistischen Analysen von Daten aus der realen Welt, und 11 waren eine Extrapolation/Simulation zur Vorhersage der Wirksamkeit von NPIs unter verschiedenen Szenarien.

In Tabelle 1 stellen wir die 16 Studien vor, die auf statistischen Analysen von Daten aus der realen Welt basieren. Die Daten zeigen Folgendes:

- Messungen der Wirksamkeit von NPIs sind immer noch spärlich und basieren selten auf subnationalen Daten in großem Maßstab. Beispielsweise haben wir keine Analyse auf Distriktebene (oder PSU-Ebene) für die gesamte Anzahl der Distrikte (Landkreise o.ä.) in einem Land gefunden.
- Die Definition derselben NPI-Ebenen variiert von Studie zu Studie stark. Dies könnte darauf zurückzuführen sein, dass der Modus einer NPI von Land zu Land unterschiedlich definiert ist.
- Die am häufigsten untersuchten NPIs, und zwar in absteigender Reihenfolge, sind internationale Reisekontrollen, Anforderungen an das Tragen von Masken, Quarantäne, Schließung von Schulen, Testrichtlinien, Richtlinien zur Ermittlung von Kontaktpersonen, Schließung von Arbeitsplätzen, Anforderungen an den Aufenthalt zu Hause, Absage von öffentlichen Veranstaltungen, Sperren, Beschränkungen für Versammlungen, Beschränkungen des öffentlichen Verkehrs, Beschränkungen für interne Reisen und öffentliche Informationskampagnen.
- Wirksamkeit von Maßnahmen in diesen Studien wird wie folgt dargestellt: von der Verringerung von R, über das Auftreten von Krankheiten bis hin zu Erkrankungs- und Todesraten.
- Studien, die mehrere Länder mit klareren statistischen Modellierungsstrategien und -ergebnissen umfassen (in Tabelle 1), zeigen, dass die Beschränkung von Versammlungen, die Schließung von Arbeitsplätzen, die Schließung von Schulen und das Tragen von Masken im Hinblick auf die betrachteten relativen Ergebnisse bei der Kontrolle der Epidemie wirksam sind.

In unserer Analyse (Pozo-Martin et al.), die als einzige eine Längsschnittanalyse nachahmt, 37 Länder abdeckt, die größte Anzahl von NPIs umfasst, die jeweils in einer Ordinalskala analysiert wurden, und

die durchschnittliche tägliche Wachstumsrate der Fallzahlen als Maß für das Ergebnis verwendet, finden wir einen starken Dosis-Wirkungs-Effekt von Einschränkungen von Versammlungen, Anforderungen an das Tragen von Masken sowie Schließungen von Arbeitsplätzen und Schulen auf das Wachstum der COVID-19-Pandemie.

In Tabelle 2 stellen wir 11 Simulationsstudien vor, die ihren Schwerpunkt hauptsächlich auf Tests, Kontaktverfolgung, "soziale" Distanzierung und Schulschließung legen. Angesichts des spekulativen Charakters dieser Studien, ihrer unterschiedlichen Qualität und des unterschiedlichen Schwerpunkts gegenüber den auf Daten basierenden Studien halten wir jedoch die in Tabelle 1 dargestellten Studien für aussagekräftiger.

Es ist wesentlich darauf hinzuweisen, dass diese Form statistischer Analyse nicht erschließen kann, inwieweit einzelne Maßnahmen oder Richtlinien implementiert beziehungsweise befolgt wurden. Dies bedeutet, dass bestimmte Maßnahmen oder Richtlinien ggf. in einzelnen Ländern nicht wirken, weil sie nicht, oder nicht genügend, umgesetzt wurden. Es ist auch möglich, dass kleinere subnationale Variationen hier nicht erkannt werden.

**Table 1. Evidence from statistical studies of the impact of policies on the COVID epidemic.**

| Study title / Setting                                      | Policies analysed   | Outcome(s) of interest  | Data and data analysis  | RESULTS   |   | Recommendations  |
|--|---|---|---|---|---|--|
|  |   |   |   | Variables   | Parameters  |  |
| <p>Pozo-Martin et al. (1)</p> <p>37 OECD member states</p> | <ol style="list-style-type: none"> <li>1. School closing</li> <li>2. Workplace closing</li> <li>3. Cancelling public events</li> <li>4. Restrictions on gatherings</li> <li>5. Public transport restrictions</li> <li>6. Stay-at-home requirements</li> <li>7. Restrictions on internal travel</li> <li>8. International travel controls</li> <li>9. Public information campaigns</li> <li>10. Mask wearing requirements</li> <li>11. Testing policy</li> <li>12. Contact tracing policy</li> </ol> | <p>Average daily growth in the weekly number of cases diagnosed</p> | <p>Epi data: ECDC and Johns Hopkins</p> <p>Policy data: Oxford COVID policy tracker, WHO tracker, peer-reviewed literature</p> <p>Analysis: Longitudinal analysis with repeated measures (12 weeks) with data from 37 countries.</p>                                      | <p>Statistically significant parameters:</p> <ul style="list-style-type: none"> <li>- Restrictions on gatherings: gatherings of more than 100 people not permitted (</li> <li>- Restrictions on gatherings: gatherings of between 11 and 100 people not permitted</li> <li>- Restrictions on gatherings: gatherings of fewer than 10 people not permitted</li> <li>- School closing: require closing of only some levels or categories, e.g. just high school, or just public schools</li> <li>- School closing: require closing of all levels</li> <li>- Workplace closing: require closing (or work from home) for some sectors or categories of workers</li> <li>- Workplace closing: require closing (or work from home) of all-but-essential workplaces (e.g. grocery stores, doctors)</li> <li>- Mask-wearing: recommended</li> <li>- Mask-wearing: required in some public places or in some geographical areas</li> <li>- Mask-wearing: required in all public places in all geographical areas</li> <li>- Total number of tests performed per thousand population</li> </ul> | <ul style="list-style-type: none"> <li>-0.370 (0.088) ***</li> <li>-0.531 (0.086) ***</li> <li>-0.494 (0.083) ***</li> <li>-0.167 (0.064) ***</li> <li>-0.270 (0.073) ***</li> <li>-0.146 (0.044) ***</li> <li>-0.201 (0.049) ***</li> <li>-0.050 (0.052)</li> <li>-0.090 (0.044) *</li> <li>-0.285 (0.060) ***</li> <li>-0.004 (0.002) **</li> </ul> | <p>There is evidence that restrictions on gatherings, mask-wearing requirements, school closing requirements, workplace closing requirements and volume of testing per unit of population are effective policies to control the epidemic. There is a dose-response effect whereby higher intensity of policies tends to have a higher impact</p> |
| <p>Brauner et al. (2)</p> <p>41 countries</p>              | <ol style="list-style-type: none"> <li>1. Mask wearing mandatory in (some) public spaces</li> <li>2-4. Gatherings limited to 1000/100/10 people or less</li> <li>5-6. Some/ All but essential shops closed</li> <li>7-8. School closed / Universities closed</li> <li>9. Stay at home orders with exemptions</li> </ol>   | <p>Mean % reduction in R</p>  | <p>Bayesian mechanistic model linking infection cycle to observed deaths (same model as Flaxman)</p> <p>Data on deaths: retrospective, country-specific (?)</p> <p>Data on policies: Oxford COVID policy response tracker / ACAPS / Epidemic forecasting NPI database</p> | <p>Mean % reduction in R</p> <ol style="list-style-type: none"> <li>1. mandating mask-wearing in (some) public spaces: 2% (-14%–16%),</li> <li>2. limiting gatherings to 1000 people or less: 2% (-20%–22%),</li> <li>3. limiting gatherings to 100 people or less: 21% (1%–39%),</li> <li>4. limiting gatherings to 10 people or less: 36% (16%–53%),</li> <li>5. closing some high-risk businesses: 31% (13%–46%),</li> <li>6. closing most nonessential businesses: 40% (22%–55%),</li> <li>7. closing schools and universities: 39% (21%–55%),</li> <li>8. issuing stay-at-home orders: 18% (4%–31%).</li> </ol>  | <p>Gathering restrictions, workplace closing and school/ university closing, as well as stay-at home orders are effective.</p> <p>Note: the authors excluded testing policy, contact tracing and quarantining from the analysis</p>   |  |

| Study title / Setting   | Policies analysed  | Outcome(s) of interest   | Data and data analysis   | RESULTS   |   | Recommendations  |
|---|--|--|--|---|---|--|
| Lyu et al. (3)<br><br>Iowa (no stay at home order)/ Illinois (stay at home order) (USA)   | Stay at home (SAH) orders  | Reduce rate of infections  | Cross-sectional study, difference-in-differences regression (8 counties in Iowa, 7 counties in Illinois)<br><br>Data: daily state-level testing data   | Diff in cases per 10,000 pop (Illinois vs Iowa)   | 10 days after SAH: - 0.51 (SE=0.09)<br>20 days after SAH: - 1.15 (SE=0.49)<br>30 days after SAH: - 4.71 (SE=1.99) | Stay at home order is effective  |
| Vicentini et al. (4)<br><br>Italy   | 1. Containment and travel restrictions<br>2. Lockdown of epicentre of outbreak<br>3. School closure and nationwide lockdowns | Changes in the growth curve for the number of patients hospitalised in ICU | Statistical analysis, exact type unclear from paper. It does not seem to be multilevel.<br><br>They fit growth curves to each period where the policies were implemented and extend them into the future to see impact of policies | Graphical presentation of results   |   | Only with a national lockdown could the growth curve be flattened  |
| Viner et al. (5)<br><br><b>Review</b> of school closure and management activities (note, was published very early – end of April) | School closure in coronavirus outbreaks (not only COVID)   | Multiple   | Rapid systematic review. 16 studies included:<br>-Six papers looked at school actions in SARS outbreak (Taiwan, Singapore, Beijing). Only one report modelled the impact of school closures on COVID-19 transmission (UK)          | Observational studies<br><br>Cowling et al noted that the social distancing measures implemented during the COVID-19 outbreak in Hong Kong reduced community transmission by 44%, which was much greater than the estimated 10–15% reduction in influenza transmission conferred by school closures implemented alone during the 2009 pandemic in Hong Kong<br><br>China: One study <sup>36</sup> concluded that school closures made very little difference to the prevention of SARS in Beijing, given the very low attack rate in schools before closures<br><br>Seattle: routine viral surveillance to evaluate impact of 5-day closure of all schools due to extreme weather – they found 5.6% reduction in transmission of coronavirus infections<br><br>Modelling studies. By April, only Ferguson et al (Imperial College study) modelled school closing. They concluded that school closure as an isolated measure was predicted to reduce total deaths by around 2–4% during a COVID-19 outbreak in the UK, whereas single measures such as case isolation would be more effective, and a combination of measures would be the most effective |   | Little evidence in April 2020 about impact of school closures. Contradictory results from past modelling studies of SARS, best available evidence from Ferguson’s model is that the impact of school closing is relatively low.<br><br>Based on past studies of flu, there is considerable heterogeneity in the impact of school closures on transmission depending on characteristics of influenza serotype transmission<br><br>Analyses using UK clinical data from the 1957 Asian influenza pandemic suggest that school closures would reduce the epidemic size by less than 10% when the R was similar to that of COVID-19 (ie, 2 · 5–3 · 5). |

| Study title / Setting  | Policies analysed  | Outcome(s) of interest   | Data and data analysis  | RESULTS  | Recommendations   |
|--|--|--|---|--|---|
| <p>Flaxman et al. (6)</p> <p>Europe (11 countries)</p>   | <ol style="list-style-type: none"> <li>1. Lockdown</li> <li>2. Cancel public events</li> <li>3. School closures</li> <li>4. Self-isolation</li> <li>5. Social distancing encouraged</li> </ol>                     | <p>Relative reduction in R, Attack rate, deaths averted by interventions</p> | <p>Bayesian mechanistic model linking infection cycle to observed deaths</p> <p>Data on deaths: retrospective, based on ECDC data</p> <p>Infection to death distribution: based on assumptions regarding the time from infection to onset of symptoms and assumptions regarding the time from onset of symptoms to death</p> <p>Infection-fatality ratio also based on assumptions and age structure and contact patterns in each country</p> | <p>Results for relative reduction in R presented graphically.</p> <p>Deaths averted by joint implementation until May 14 / Attack rate (credible intervals not provided)</p> <p>Austria – 65000 / 0.76%<br/>                     Belgium – 110000 / 8%<br/>                     Denmark – 34000 / 1%<br/>                     France – 690000 / 3.4%<br/>                     Germany – 560000 / 0.85%<br/>                     Italy – 630000 / 4.6%<br/>                     Norway – 12000 / 0.46%<br/>                     Spain – 450000 / 5.5%<br/>                     Sweden – 26000 / 3.7%<br/>                     Switzerland – 52000 / 1.9%<br/>                     UK – 470000 / 5.1%</p> <p>The impact of lockdown is significantly different from that of any other intervention, other interventions are not significant (they were implemented at the same time)</p> | <p>Lockdown is effective, cannot say anything about other interventions (this is a limitation of the study)</p>                     |
| <p>Chen et al. (7)</p> <p>Italy, Spain, Germany, France, UK, Singapore, South Korea, China, US</p> | <ol style="list-style-type: none"> <li>1. Travel restrictions</li> <li>2. Mask-wearing</li> <li>3. Lockdown</li> <li>4. Social distancing</li> <li>5. School closure</li> <li>6. Centralised quarantine</li> </ol> | <p>Rates of disease transmission and recovery</p>                            | <p>*MIXED STUDY:</p> <p>Regression with delayed effect / dynamic transmission model</p> <p>Data on infections, recoveries and deaths from the CSSE Johns Hopkins database</p> <p>Data on policies: local government websites, official public health authorities, and major newspapers</p>  | <p>Modelled rates with confidence intervals</p> <ol style="list-style-type: none"> <li>1. Travel restrictions: -0.343 [-0.786, 0.100]</li> <li>2. Mask wearing (MW) 0.651 [0.009, 1.294]</li> <li>3. Lockdown (LD) 1.063 [0.427, 1.699]</li> <li>4. Social distancing (SD) -0.279 [-0.986, 0.427]</li> <li>5. School closure (SC) 0.972 [0.339, 1.604]</li> <li>6. centralized quarantine 2.042 [1.493-2.592]</li> </ol>   | <p>Mask wearing, Lockdown, School closure and centralised quarantine are statistically significant</p>                              |
| <p>Banholzer et al. (8)</p> <p>U.S., Canada,</p>   | <ol style="list-style-type: none"> <li>1. School closure</li> <li>2. Border closure</li> <li>3. Event ban</li> <li>4. Gathering ban</li> </ol>   | <p>Relative reduction in disease incidence</p>                               | <p>Semi-mechanistic Bayesian hierarchical model.</p>  | <p>Modelled reduction in disease incidence with credible intervals</p> <ol style="list-style-type: none"> <li>1. School closure: 8% (0-23%)</li> <li>2. Border closure: 31% (19-42%)</li> </ol>  | <p>Highest impact is from venue closures, followed by gathering bans, followed by border closures and work ban on non-essential</p> |

| Study title / Setting   | Policies analysed  | Outcome(s) of interest    | Data and data analysis  | RESULTS  | Recommendations                               |
|---|--|---------------------------|---|--|---|
| Australia, Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, the Netherlands, Portugal, Spain, Sweden, UK, Norway, Switzerland | 5. Venue closure<br>6. Lockdown<br>7. Work ban on non-essential businesses                     |                           | Data on cases from the CSSE Johns Hopkins database<br><br>Data on policies: local government websites, official public health authorities, and major newspapers   | 3. Event ban: 23% (8-35%)<br>4. Gathering ban: 34% (21-34%)<br>5. Venue closure: 36% (20-48%)<br>6. Lockdown: 5% (0-14%)<br>7. Work ban on non-essential businesses: 31% (16-44%)  | businesses                                    |
| Hsiang et al (9)<br><br>China, South Korea, Italy, Iran, France, US   | 1. Restricting travel<br>2. Distancing<br>3. Quarantine and lockdown<br>4. Additional policies | Growth rate in infections | Linear regression on estimated growth rates.<br><br>Epidemiological and policy data comes from a variety of in-country sources including government public health websites, regional newspaper articles and crowd-sourced information on Wikipedia. Note they use sub-national data | China.<br>Emergency declaration (weeks 1/2/3/4/5): -0.01/-0.17*/-0.23*/-0.25*/-0.25*<br>Travel ban (weeks 1/2/3/4/5): -0.02/-0.01/-0.03/-0.05/-0.08<br>Home isolation (weeks 1/2/3/4/5): -0.01/-0.03/-0.04*/-0.05*/-0.04*<br><br>South Korea.<br>Emergency declaration: -0.13*<br>Quarantine inbound travellers: -0.02<br>WFH, no gathering, other social distancing: -0.08*<br>Quarantine positive cases: -0.08<br><br>Italy.<br>School closures: -0.11<br>Quarantine positive cases:-0.08<br>WFH, no gathering, other social distancing:-0.14*<br>Travel ban, transit suspension:-0.33<br>Business closure:-0.12 | Variable impact of policies across countries. |

| Study title / Setting                               | Policies analysed                 | Outcome(s) of interest                   | Data and data analysis  | RESULTS  | Recommendations   |
|---|-----------------------------------|--|---|--|---|
|   |                                   |  |   | <p>Home isolation:0.03</p> <p>Iran.<br/>Travel ban, WHF, school closure: -0.33*<br/>Home isolation: -0.15*</p> <p>France:<br/>School closure:-0.01<br/>Cancel events, no gathering, other social distancing:-0.24*<br/>Business closures, home isolation: -0.16*</p> <p>United States.<br/>Slow the spread guidelines:-0.05<br/>Other social distancing:-0.25<br/>Paid sick leave:-0.03<br/>Quarantine positive cases:-0.06<br/>Travel ban, transit suspension:-0.01<br/>School closure:-0.03<br/>Religious closure:-0.01<br/>WFH:-0.05*<br/>No gathering:-0.01<br/>Business closure:-0.06*<br/>Home isolation:-0.12*</p> <p>*statistical significance</p> |   |
| <p>Aravindakshan et al (10)</p> <p>24 countries</p> | <p>1. Mask wearing (reported)</p> | <p>Daily growth rate in active cases</p> | <p>Cross-sectional analysis. The model incorporated as independent variables reported mask wearing from a survey, social mobility other non-pharmaceutical interventions and testing (as control variables). The model includes country- and time-fixed effects.</p> <p>Data on cases came from Johns Hopkins School of Public Health</p> | <p>Graphical presentation of results.</p> <p>The model finds that reported mask wearing of 100% is associated with 7% (95% CI: 3.94%-9.99%) drop in daily COVID-19 cases. The authors report that this would lead to 88.5% (95% CI: 68.7%-89.2%) decline in active cases when compared with 0% of people reporting wearing masks</p>   | <p>Mask wearing can potentially play a significant role in mitigating the spread of the disease</p> |

| Study title / Setting            | Policies analysed   | Outcome(s) of interest  | Data and data analysis   | RESULTS  | Recommendations  |
|----------------------------------|---|---|--|--|--|
|                                  |   |   | Data on policies came from the COVID Government Response dataset. Data on mobility came from Google  |  |  |
| Liu et al. (11)<br>131 countries | 1. Internal containment and closure policies<br>2. International travel restrictions<br>3. Economic policies<br>4. Health systems policies<br><br>131 countries | Reproduction number (R)   | Panel regression.<br><br>Data on epidemiological variables was sourced from EpiForecast<br><br>Data on policies was sourced from Oxford COVID-19 Policy Tracker  | Graphical presentation of results.<br><br>The authors found strong evidence for the association between school closure and internal movement restrictions. They also found strong evidence of the association with the initiation of workplace closure, income support and debt/ contract relief policies. Finally, they found that cancellation of public events and restrictions on gatherings were significant predictors of R when they were established with high intensity         | School and work closures, restrictions on gatherings and cancellation of public events, economic policies such as income support and contract relief had an impact on controlling the epidemic |
| Chernozhukov et al. (12)<br>USA  | 1. Mandatory face masks for employees in public businesses<br>2. Stay at home orders<br>3. Closure of K-12 schools<br>4. Closure of non-essential businesses    | Weekly growth rate in infections  | Econometric structural outcomes model.<br><br>Data on cases and mortality are from the New York Times, Johns Hopkins University and the Covid Tracking Project<br><br>Data on policies is from the COVID-19 US policy database | Graphical presentation of results.<br><br>The authors state:<br><br>Mandating masks for employees on Mach 14 could have led to 21% (95% CI: 9.32-19.47) fewer cumulative cases and 34% fewer deaths by the end of May.<br><br>Without business closures in the US, cases and deaths would have been 40% (note: wide confidence intervals) higher than they were at the end of May<br><br>Without stay-at-home orders, there would have been 37% more cases per week by the start of June | Mask wearing mandate, business closing and stay-at home orders had an impact on the growth of infections in the USA  |
| Aggarwal et al. (13)             | Facemask use in community settings  | Clinically diagnosed or self-reported influenza-like illness (ILI)                                    | Pooled effect size was estimated by random-effects model<br><br>9 studies were included in qualitative synthesis and 8 studies in quantitative synthesis.  | There was no significant reduction in ILI either with facemask alone (n = 5, pooled effect size -0.17; 95% confidence interval [CI] -0.43-0.10; P = 0.23; I2 = 10.9%) or facemask with handwash (n = 6, pooled effect size (n=6, pooled effect size -0.09; 95% CI -0.58 to 0.40; P = 0.71, I2 = 69.4%).  | Existing data pooled from randomized controlled trials do not reveal a reduction in occurrence of ILI with the use of facemask alone in community settings                                     |
| <b>Travel related policies</b>   |   |   |  |  |  |
| Shi et al (14)<br>28 countries   | Travel restrictions   | Risk of importation of cases, median time of importation of cases as a function of effective distance | Data: Automatic Dependent Surveillance Broadcast exchange data (flight network) + publicly available databases<br><br>Analysis: Hazard-based   | H1: No travel restrictions<br>H2: Travel restrictions, 25%-50% of flights cancelled<br>H3: H2 + travel restrictions in 10 highest volume passenger hubs.<br><br>Results shown graphically<br>NA  | Travel restrictions based on reductions in passenger volume would only make a minor contribution to the prevention of virus importation among countries.                                       |



| Study title / Setting   | Policies analysed                                    | Outcome(s) of interest             | Data and data analysis  | RESULTS   | Recommendations   |
|---|--|------------------------------------|---|---|---|
| Wells et al. (15)<br><br>Worldwide                                | Travel restrictions                                  | Daily rate of exportation of cases | model<br><br>Estimate country-level risk of exporting cases based on daily COVID-19 incidence data and airport network connectivity. Used Monte Carlo simulations. Model calibrated to data | Graphical presentation of results<br><br>Travel lockdowns in China reduced by Feb15 daily case exports by 83%. Estimated that 64% of cases are pre-symptomatic upon arrival to destination. Estimated that self-identification of where traveller has been before (at arrival, questionnaire) can catch 95% of cases  | Travel lockdowns in China averted 71% of case exports. Additional info on incubation period and self-identification at airport increases impact of airport screening                        |
| Burns et al. (16)<br><br><b>Review</b> of travel control policies | Travel-control measures during the COVID-19 epidemic | Multiple                           | Cochrane rapid review with 25 COVID-related studies:<br>-17 modelling studies<br>-7 observational screening studies<br>-1 ecological study  | <p>1. Travel restrictions reducing cross-border travel. 11 modelling studies in this category, one observational ecological study. Very low-certainty evidence suggests that when implemented at the beginning of the outbreak, these measures may lead to a reduction in the number of new cases of between 26% to 90% (4 studies), in the number of deaths (1 study), in the time to outbreak of between 2 and 26 days (2 studies), in the risk of outbreak of between 1% to 37% (2 studies), and in the effective reproduction number (2 studies). Low-certainty evidence suggests a reduction in the number of imported or exported cases of between 70% to 81% (5 studies), and in the growth acceleration of the epidemic progression (1 study).</p> <p>2. Entry and exit screening at the border. 12 studies on entry or exit screening with or without quarantine. Screening approaches included various combinations of symptom-based screening, single (and rarely repeated) PCR testing and observation during quarantine. Very low-certainty evidence suggests delays in outbreak of between 1 to 183 days (3 modelling studies); low-certainty evidence was found for a detection rate of infected travellers of between 10% to 53% (3 modelling studies). Very low-certainty evidence suggests that the proportion of cases detected ranged from 0% to 75% and that the positive predictive value ranged from 0% to 100% (6 observational studies). These outcomes should be interpreted in relation to both the screening approach used and the prevalence of infection among the travellers screened; for example, symptom-based screening alone tended to perform worse than a combination of symptom-based and PCR screening with subsequent observation during quarantine.</p> <p>3. Quarantine of travellers crossing borders. One modelling study identified in this category reporting on a reduction in the number of cases seeded by imported cases. Quality of the evidence was rated as “very low”.</p> | The evidence on travel restrictions suggests an impact of travel restrictions, screening at the border and quarantine on controlling the epidemic, but the quality of this evidence is low. |

**Table 2. Evidence from simulation studies of the impact of policies on the COVID epidemic**

| Study title / Setting | Policies analysed   | Outcome(s) of interest                               | Data and data analysis   | RESULTS   | Recommendations   |
|-----------------------|---|--|--|---|---|
| Min et al. (17)       | <ol style="list-style-type: none"> <li>1. Social distancing in adults</li> <li>2. Spring semester postponing</li> <li>3. Diagnostic testing</li> <li>4. Contact tracing</li> </ol>          | Epidemic size with each policy compared to no policy | <p>Dynamic transmission model. No sampling, parameters from the literature. Some model parameters calibrated to existing data on cases.</p> <p>Four parameters are included in the model:</p> <ul style="list-style-type: none"> <li>-rate at which exposed become infectious</li> <li>-detection rate</li> <li>-quarantine probability</li> <li>-effective contact rate (calibrated to real data)</li> </ul> <p>To simulate effect of policies the authors make informed assumptions about changes in the effective contact rate</p>  | <p>Severely reduced social distancing vs status quo (estimated relative number of cumulative cases = x 27) :</p> <p>Mildly reduced social distancing vs status quo (estimated relative number of cumulative cases = x 4.5) :</p> <p>School opening severe scenario vs status quo (estimated relative number of cumulative cases = x 1.05)</p> <p>School opening mild scenario vs status quo (estimated relative number of cumulative cases = x 1.03)</p> <p>Non-extensive diagnostic testing and contact tracing (estimated relative number of cumulative cases = x 1.4)</p>  | Social distancing is more effective policy than delayed school opening or massive diagnostic testing and contact tracing  |
| Ng et al. (18)        | <ol style="list-style-type: none"> <li>1. Case detection and isolation</li> <li>2. Contact tracing and quarantine</li> <li>3. Physical distancing</li> <li>4. community closures</li> </ol> | Range of outcomes, e.g. total attack rate            | <p>Agent-based transmission model. No sample of data. Efficacy of interventions compared to no intervention. Simulations for the model done until 2022.</p> <p>Parameters in model:</p> <ul style="list-style-type: none"> <li>-rate of infectiousness</li> <li>-detection rate</li> <li>-effective contact rate (calibrated)</li> </ul> <p>Scenarios modelled are:</p> <ol style="list-style-type: none"> <li>1. Minimal control (no further restrictions once closures are lifted)</li> <li>2. Maintained physical distancing</li> <li>3. Enhanced case detection and contact tracing</li> <li>4. Combined interventions</li> </ol> <p>Policies modelled</p> | <p>Minimal control vs no intervention (Total attack rate is 56 rather than 64)</p> <p>Maintained physical distancing vs no intervention (Total attack rate is 41.6 rather than 64)</p> <p>Enhanced case detection and contact tracing vs no intervention (Total attack rate is 0.36 versus 64)</p> <p>Combined interventions vs no intervention (Total attack rate is 0.25 versus 64)</p> <p>Addition of extended school closures to the minimal control or maintained physical distancing scenarios reduced the total attack rate minimally compared with these scenarios alone</p> <p>Extended closures of workplace and mixed-age venues tended to result in much lower total attack rates under</p> | <p>enhancing case detection and isolation to capture 50% of all cases, while enhancing contact tracing to capture and quarantine all contacts of these cases, was most effective, especially when combined with maintaining physical distancing to reduce the contact rate among individuals in the population by 20%</p> <p>Partial community closure was the only intervention explored that was capable of driving the epidemic to extinction on its own</p> |

| Study title / Setting                                      | Policies analysed   | Outcome(s) of interest  | Data and data analysis   | RESULTS   | Recommendations   |
|--|---|---|--|---|---|
|  |   |   |  | minimal control and maintained physical distancing  |   |
| Renardy et al. (19)<br><br>Washtenaw County, Michigan (US) | 1. Workplace closures<br>2. School closures<br>3. Social distancing | Range of outcomes, e.g. current/ cumulative cases, current/ cumulative hospitalisations, deaths | Discrete, stochastic, network-based model. No sample of data, parameters taken from the literature. Model is calibrated to match COVID-19 cases, hospitalisation and deaths in Washtenaw county at a specific period of time<br><br>Parameters:<br>Basic reproduction number, incubation period, infectious period, mortality fraction, time from symptom onset to death, fraction who are asymptomatic, fraction of symptomatic who will seek care, fraction of symptomatic who will be hospitalised, time to seek care, duration of hospital stay, initial proportion of population latent, initial proportion of population infectious<br><br>Efficacy of interventions compared to reopening scenarios:<br><br>1) Increase both non-essential workplace and casual contact weights from stay-at-home levels to 50% of normal, occurring over a period of either one, two, or three months<br>2) Increase non-essential contact weight to 50% of normal over a period of 1,2,3 months (normal = pre-epidemic contact weight)<br><br>Parameters: | Shown graphically:<br><br>1. Varied speed of lifting stay-at home restrictions (1,2,3 months) – Delayed timing affects timing of the epidemic peak, but not size<br>2. Varied saturation levels for casual contacts, representing no, 25% or 50% increase in contacts by lifting stay at home restrictions – lower level of casual contacts decreases both the peak and its magnitude (to about half) | Delaying reopening only buys time, maintaining lower levels of casual contacts (social distancing) is effective |
| Son et al. (20)<br>Daegu (South Korea)                     | School opening  | Cumulative cases of COVID-19  | Individual-based transmission model. No sample of data.<br><br>Parameters: infection probability (requires probability of encountering individual who is infected in the household, average period between symptom onset to confirmation, average period to recovery)  | Between Feb 1 and March 31 2020:<br><br>School closed (6677 hospitalisation)<br>School opening after Apr 6 (6716 hospitalisations)<br>School opening after Apr 6 and mean period from symptom onset to hospitalisation increases to 4.3 days  | Delaying school opening saves hospitalisations  |

| Study title / Setting   | Policies analysed  | Outcome(s) of interest                                    | Data and data analysis   | RESULTS   | Recommendations   |
|---|--|---|--|---|---|
| Tsay et al. (21)<br>USA<br><br>For parameter estimation:<br>Italy<br>Spain<br>Germany | 1. Social distancing<br>2. Quarantine  | Optimal policies to minimise number of infected cases     | Dynamic transmission model with optimal control (dynamic optimisation strategy with objective minimise growth curve of epidemic). Parameter estimation solved using regression analysis based on Johns Hopkins data. Some parameters taken from the literature<br><br>Parameters include: rate of testing, initial exposed, recovery rate, death rate  | Graphical presentation of results   | US: To keep peak at 700,000 cases, quarantining of infected is more important than social distancing<br>To keep peak at 1,400,000 cases, recommendation is establishing periodic suppression measures when a threshold of cases has been reached<br><br>Overall quarantining of infected individuals is the most important measure, on-off social distancing is important to flatten the curve, screening and testing are key in periods immediately preceding periods of social distancing |
| Tuite et al. (22)<br><br>Canada   | 1. Testing (+ enhanced testing and contact tracing)<br>2. Isolation of cases<br>3. Physical distancing measures (+ restrictive physical distancing measures) | Prevalent cases requiring ICU care, % population infected | Dynamic transmission model (SEIR). No sample. Parameters expressing the natural history and clinical course of infection taken from the literature. Parameters fitted using MCMC<br><br>Parameters: latent period, infectious period, reproductive number, relative risk of transmission for cases in isolation, average length of stay in hospital, probability of severe infection<br><br>Analysis based on two scenarios: fixed duration of policies, on-off policies depending on a threshold of ICU capacity. Base case = limited testing, isolation and quarantine | Graphical presentation of results   | Scenario 1: fixed duration of policies – effectiveness depends on intervention duration (6 months or less, no appreciable difference in final attack rate)<br><br>Scenario2: on-off. Interventions projected to be effective for reducing the % pop infected with shorter duration of physical distancing than the fixed duration approach  |
| Wan et al. (23)<br><br>China  | Different levels of lifting of restrictions modelled by changing the contact rate  | Cumulative cases  | Dynamic transmission model. Initial conditions data taken from COVID-19 databases + national bureau of statistics  | Graphical presentation of results   | Contact rate has to be below 0.3 to guarantee that the reproduction number is under 1 and the epidemic is put out   |
| Zamir et al. (24)   | 1. Stay at home<br>2. Face masks<br>3. Hand washing<br>4. Quick case detection   | Epidemic curves for infected/ susceptible                 | Dynamic transmission model with optimal control incorporating transmission from foodstuff to humans. Parameters all based on the literature and assumptions.<br><br>Parameters: latent period, infectious period, recovery rate, disease transmission from source, quarantine period, shedding coefficient, death rate etc   | Graphical presentation of results   | The study does not compare the relative impact of the different interventions<br><br>Putting them all in place would have a big impact on the epidemic after 50 days (=1/3 of cases)  |
| Dehning et al. (25)<br><br>Germany  | 1. Mild social distancing<br>2. Strong social distancing<br>3. Contact ban   | Spreading rate of the infection                           | Bayesian inference of transmission rate + dynamic transmission model. The authors modelled the effects of the interventions as change points in the effective spreading rate of the infection at the date when the interventions   | Graphical presentation of results. The authors concluded that models with two or three change points fit the data better than other models, essentially providing | This is evidence that cancelling of large events, closing of schools/childcare facilities/ contact ban are effective  |

| Study title / Setting                              | Policies analysed   | Outcome(s) of interest                               | Data and data analysis   | RESULTS   | Recommendations  |
|--|---|--|--|---|--|
|  |   |  | <p>were established.</p> <p>Change points modelled:</p> <ol style="list-style-type: none"> <li>1. Mild social distancing – based on cancelling of large events (9 March)</li> <li>2. Strong social distancing – based on closing of schools, childcare facilities and most stores (16 March)</li> <li>3. Contact ban – based on contact ban and closing of all non-essential stores (23 March)</li> </ol>  | <p>evidence that the interventions were effective</p>   | <p>interventions</p>   |
| <p>Lorch et al. (26)</p> <p>Tübingen (Germany)</p> | <p>Several policies within:</p> <ol style="list-style-type: none"> <li>1. Mobility restrictions</li> <li>2. Testing and tracing</li> <li>3. Social distancing and business restrictions</li> </ol>  | <p>Epidemiological parameters</p>                    | <p>Spatiotemporal model with stochastic differential equations (incorporates a variation of a dynamic transmission model).</p> <p>Epidemiological parameters: rate of exposure at locations, proportion of asymptomatic infections, relative infectiousness of asymptomatic infected.</p> <p>Demographic data comes from Facebook, COVID-19 data comes from the national health authorities.</p> <p>Policy data from Tübingen authorities.</p> <p>The model simulates several approaches to implementing the policies, e.g. alternating curfews for random groups, social distancing of the elderly population, basic or advanced contact tracing,</p> | <p>Graphical presentation of results. The model shows that:</p> <p>Social distancing of elderly population is very effective at avoiding hospitalisations. Random curfew of 3 or 4 population groups significantly reduces exposure to the virus. Basic and Advanced contact tracing significantly reduces the number of infections.</p>  | <p>The measures described in the results can be effective at stopping exposure and infection</p>   |
| <p>Keeling et al. (27)</p> <p>England</p>          | <p>Strategies for school opening from June 1:</p> <ol style="list-style-type: none"> <li>1. Open year 0, year 1, year 6 (full class sizes)</li> <li>2. Open year 0, year 1 and year 6 (half-class sizes)</li> <li>3. Open all primary schools</li> <li>4. Open year 0, years 1,6,10 and 12 (full class sizes)</li> <li>5. Open year 0, years 1,6,10 and 12 (half class sizes)</li> <li>6. Open primary</li> </ol> | <p>Clinical case impact, Reproduction number (R)</p> | <p>Dynamic transmission model. The model was calibrated to hospitalisations, ICU occupancy and deaths.</p> <p>Data on epidemiological parameters was for the most part fitted from an earlier model using Markov Chain Monte Carlo processes</p> <p>Data on policies was modelled based on assumptions</p>   | <p>Graphical presentation of results.</p> <p>The authors consistently found that school reopening had a larger clinical case impact when R in the community was high. However, the authors also found that the largest increase in cases, ICU admissions and deaths was due to relaxations other than reopening of schools.</p> <p>In all strategies, the simulations did not lead to an increase in the reproduction number above R=1 (compared to when schools were closed). Selecting subsets of age groups to return to school led to the smallest increase in R notably in the</p> | <p>Reopening of schools leads to more mixing and more transmission of the disease. Choosing a subset of year-groups to return to school can be an effective strategy</p> |

| Study title / Setting | Policies analysed   | Outcome(s) of interest | Data and data analysis | RESULTS     | Recommendations |
|-----------------------|---|------------------------|------------------------|-------------|-----------------|
|                       | schools + year 10 + year 12<br>7. Open all secondary schools<br>8. Open all schools |                        |                        | simulations |                 |

## References.

1. Pozo-Martin F, Weishaar H, Cristea F, Hanefeld J, Schaade L, El Bcheraoui C. Impact of type and timeliness of public health policies on COVID-19 epidemic growth: Organization for Economic Cooperation and Development (OECD) member states, January – July 2020. 2020.
2. Brauner JM, Mindermann S, Sharma M, Stephenson AB, Gavenčiak T, Johnston D, et al. The effectiveness of eight nonpharmaceutical interventions against COVID-19 in 41 countries. medRxiv. 2020:2020.05.28.20116129.
3. Lyu W, Wehby GL. Shelter-In-Place Orders Reduced COVID-19 Mortality And Reduced The Rate Of Growth In Hospitalizations. Health affairs (Project Hope). 2020;39(9):1615-23.
4. Vicentini C, Bordino V, Gardois P, Zotti CM. Early assessment of the impact of mitigation measures on the COVID-19 outbreak in Italy. Public Health. 2020;185:99-101.
5. Viner RM, Russell SJ, Croker H, Packer J, Ward J, Stansfield C, et al. School closure and management practices during coronavirus outbreaks including COVID-19: a rapid systematic review. The Lancet Child and Adolescent Health. 2020;4(5):397-404.
6. Flaxman S, Mishra S, Gandy A, Unwin HJT, Mellan TA, Coupland H, et al. Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe. Nature. 2020;584(7820):257-61.
7. Chen X, Qiu Z. Scenario analysis of non-pharmaceutical interventions on global COVID-19 transmissions. arXiv preprint arXiv:200404529. 2020.
8. Banholzer N, van Weenen E, Kratzwald B, Seeliger A, Tschernutter D, Bottrighi P, et al. Impact of non-pharmaceutical interventions on documented cases of COVID-19. medRxiv. 2020:2020.04.16.20062141.
9. Hsiang S, Allen D, Annan-Phan S, Bell K, Bolliger I, Chong T, et al. The effect of large-scale anti-contagion policies on the COVID-19 pandemic. Nature. 2020;584(7820):262-7.
10. Aravindakshan A, Boehnke J, Gholami E, Nayak A. Mask-Wearing During the COVID-19 Pandemic. medRxiv. 2020:2020.09.11.20192971.
11. Liu Y, Morgenstern C, Kelly J, Lowe R, Jit M. The impact of non-pharmaceutical interventions on SARS-CoV-2 transmission across 130 countries and territories. medRxiv. 2020:2020.08.11.20172643.
12. Chernozhukov V, Kasahara H, Schrimpf P. Causal Impact of Masks, Policies, Behavior on Early Covid-19 Pandemic in the U.S. medRxiv. 2020:2020.05.27.20115139.
13. Aggarwal N, Dwarakanathan V, Gautam N, Ray A. Facemasks for prevention of viral respiratory infections in community settings: A systematic review and meta-analysis. Indian journal of public health. 2020;64:S192-S200.

14. Shi S, Tanaka S, Ueno R, Gilmour S, Tanoue Y, Kawashima T, et al. Travel restrictions and sars-cov-2 transmission: An effective distance approach to estimate impact. *Bulletin of the World Health Organization*. 2020;98(8):518-29.
15. Wells CR, Sah P, Moghadas SM, Pandey A, Shoukat A, Wang Y, et al. Impact of international travel and border control measures on the global spread of the novel 2019 coronavirus outbreak. *Proc Natl Acad Sci U S A*. 2020;117(13):7504-9.
16. Burns J, Movsisyan A, Stratil JM, Coenen M, Emmert-Fees KMF, Geffert K, et al. Travel-related control measures to contain the COVID-19 pandemic: a rapid review. *Cochrane Database of Systematic Reviews*. 2020(9).
17. Min KD, Kang H, Lee JY, Jeon S, Cho SI. Estimating the Effectiveness of Non-Pharmaceutical Interventions on COVID-19 Control in Korea. *Journal of Korean medical science*. 2020;35(35):e321.
18. Ng V, Fazil A, Waddell LA, Bancej C, Turgeon P, Otten A, et al. Projected effects of nonpharmaceutical public health interventions to prevent resurgence of SARS-CoV-2 transmission in Canada. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne*. 2020.
19. Renardy M, Eisenberg M, Kirschner D. Predicting the second wave of COVID-19 in Washtenaw County, MI. *Journal of Theoretical Biology*. 2020;507.
20. Son WS. Individual-based simulation model for COVID-19 transmission in Daegu, Korea. *Epidemiology and health*. 2020;42:e2020042.
21. Tsay C, Lejarza F, Stadtherr MA, Baldea M. Modeling, state estimation, and optimal control for the US COVID-19 outbreak. *Scientific reports*. 2020;10(1):10711.
22. Tuite AR, Fisman DN, Greer AL. Mathematical modelling of COVID-19 transmission and mitigation strategies in the population of Ontario, Canada. *CMAJ*. 2020;192(19):E497-E505.
23. Wan H, Cui JA, Yang GJ. Risk estimation and prediction of the transmission of coronavirus disease-2019 (COVID-19) in the mainland of China excluding Hubei province. *Infectious Diseases of Poverty*. 2020;9(1).
24. Zamir M, Shah Z, Nadeem F, Memood A, Alrabaiah H, Kumam P. Non Pharmaceutical Interventions for Optimal Control of COVID-19. *Computer Methods and Programs in Biomedicine*. 2020;196.
25. Dehning J, Zierenberg J, Spitzner FP, Wibral M, Neto JP, Wilczek M, et al. Inferring change points in the spread of COVID-19 reveals the effectiveness of interventions. *Science*. 2020;369(6500):eabb9789.
26. Lorch L, Trouleau W, Tsirtsis S, Szanto A, Schölkopf B, Gomez-Rodriguez M. A spatiotemporal epidemic model to quantify the effects of contact tracing, testing, and containment. *arXiv preprint arXiv:200407641*. 2020.



27. Keeling MJ, Tildesley MJ, Atkins BD, Penman B, Southall E, Guyver-Fletcher G, et al. The impact of school reopening on the spread of COVID-19 in England. medRxiv. 2020:2020.06.04.20121434.