

The Impact of COVID-19 Restrictions on Childhood Vaccination Uptake: A Rapid Review

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COLLATERAL GLOBAL

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Abstract

Background

Vaccines are highly effective for preventing a range of childhood infections. However, there have been concerns about an alarming decline in vaccinations in 2020 due to the COVID-19 pandemic.

Methods

We performed a rapid review for studies that assessed childhood vaccination uptake during restrictive phases of the COVID-19 pandemic.

Results

We found 35 published studies that compared changes in the pattern of childhood vaccinations before and during the pandemic. Thirteen were surveys; two mixed-methods surveys and interviews, three modelling studies and 17 retrospective cohort studies with historical controls. We also included ten reports by national or international agencies that had original data on vaccination uptake. Significant global disruptions to vaccine services were reported in Africa, Asia, America (including Latin America and the Caribbean) and Europe. We also found evidence of significant disruption to vaccine uptake for diphtheria tetanus pertussis, BCG, measles and polio. Countries where vaccination rates were already suboptimal had greater drops in uptake and there was evidence of smaller declines in younger children compared to older children. Children born to women who could not read and write were more likely to be incompletely immunized. Various initiatives were used to drive up vaccination rates post restrictions.

Conclusions

Obstacles to the delivery of vaccination services during the Covid-19 pandemic drove down immunisation rates, especially in disadvantaged people and poorer countries.

Introduction

Vaccines have proven to be highly effective at preventing disease and deaths associated with a range of childhood infections. Many childhood diseases that used to be common, including diphtheria, measles, mumps, rubella, pertussis, polio and tetanus, can be prevented by vaccination. The distribution and uptake of vaccines has improved across the globe. In 2019, 86% of infants worldwide received three doses of diphtheria, tetanus, pertussis (DTP3) vaccines, and childhood immunisation is estimated to prevent 2 to 3 million annual deaths from infectious diseases.^[1]

Despite their effectiveness, the WHO and UNICEF warned of an 'alarming decline' in vaccinations in 2020 due to the COVID-19 pandemic. Data from the first four months highlighted a substantial drop in the number of children completing three doses of the DTP3 vaccine - the first time in 28 years global reductions were seen.^[2]

UNICEF regards protection from vaccine-preventable diseases as a child's fundamental right and states that right now is 'time to vigorously monitor the impact on immunisation and plan for services that reach the most vulnerable once restrictions are lifted.'^[3] We, therefore, set out to synthesise the published literature on the impact of the COVID-19 pandemic restrictions on vaccination coverage for children.

Methods

We performed a rapid review using a flexible framework for restricted systematic reviews.^[4] For the initial search, we restricted the results to peer-reviewed articles using the LitCovid database. LitCovid is a curated literature hub for tracking up-to-date scientific information about SARS-CoV-2 (<https://www.ncbi.nlm.nih.gov/research/coronavirus/>). It is a comprehensive resource on the subject, providing central access to relevant articles in

PubMed. We searched for various terms/phrases associated with childhood vaccinations, e.g., 'vaccines', 'vaccination' or 'immunisation' and 'children' or 'infants'. We screened the title and abstract for inclusion and extracted data into templates on the study identifier, country, the type of vaccination, the study type, the age of the included populations, the primary methods and the main results. We did not formally assess quality as studies were retrospective reviews of records that involved an active lockdown phase and a historical control period, surveys or modelling studies. The quality of included studies was instead assessed using an adapted version of the Oxford Centre for Evidence-Based Medicine Levels of Evidence (<https://www.cebm.ox.ac.uk/resources/levels-of-evidence/ocebml-levels-of-evidence>)

We also included reports by national or international agencies that included original data on vaccination uptake. We summarised data narratively and reported the outcomes as stated, including quantitative estimates, where feasible and relevant. We presented the data by disruption of services and by diphtheria tetanus pertussis, BCG, measles and polio vaccine uptake. We also extracted up to date numbers from the Global Polio Eradication Initiative (GPEI) database to assess the latest impact of polio vaccination disruptions in Afghanistan and Pakistan, where polio is endemic (<https://polioeradication.org/>). Our review process, strategy and rationale can be accessed at <https://collateralglobal.org/article/what-is-a-rapid-review/>.

Results

Figure 1 reports the Identification of Childhood Vaccination studies via databases. From 389 records identified, we found 35 published studies that compared changes in the pattern of childhood vaccinations before and during the pandemic. 32 studies assessed evidence from 22 countries: Afghanistan, Bangladesh, China, Germany, India, Indonesia, Japan, Kuwait, The Netherlands, Portugal, Rwanda, Scotland, Senegal, Sierra Leone,

South Korea, Spain (16 countries, one study each); England, Ethiopia, Italy, Pakistan, Saudi Arabia (five countries, two studies each). For the USA, there were six studies. Three studies reported on multiple countries: two were done in Africa [Masresha 2020 and Abbas K 2020] and one in South-East Asia and the Western Pacific (SEAR/WPR) [Harris 2021].

In terms of methods, thirteen studies were surveys; two were mixed-methods surveys and interviews, three studies were models (one provided data on a retrospective cohort), and 17 were retrospective cohort studies.

We also included ten reports by national or international agencies that had original data on vaccination uptake: one each for Blue Cross, the Nuffield Trust, PAHO and Public Health England, two reports for UNICEF (one jointly with PAHO) and four WHO reports. (See TABLE 2)

Disruption to services

Data collated by the WHO, UNICEF, Gavi, and the Sabin Vaccine Institute show that pandemic restrictions substantially reduced the delivery of immunization services in at least 68 countries affecting over 80 million children under the age of one. [UNICEF 2020] According to the WHO's first pulse interim survey published in August 2020, 16/91 (18%) of countries reported severe/complete disruption of routine mobile immunization services, and 10% reported disruption to static routine immunisation services. About half of the countries reported partial disruptions of routine immunisation for both health facilities and mobile services. [WHO first-round survey 2020] On May 15, the pulse survey reported that more than half (53%) of the 129 countries with available data had moderate-to-severe disruptions or a total suspension of vaccination services from March to April 2020. [WHO pulse survey 15 May 2020] The WHO's second round national pulse survey from January to March 2021 reported that more than one-third of 135 countries experienced disruptions to immunisation services: routine facility-based disruption occurred in 35 (34%) countries surveyed

and outreach immunisation services occurred in 35 (39%) countries. [WHO second-round survey 2021]

Africa

A review of the administrative routine immunisation data from 15 **African** countries in 2020 revealed that 13 countries experienced declines in the monthly average number of vaccine doses provided from January to June compared with 2018 and 2019. [Masresha BG 2020]. In **Ethiopia**, 633 children and their mother/caregiver were interviewed from Jul 22 to Aug 7, 2020. Based on their recall, plus vaccination cards, 350 (57%) children finished all recommended vaccines. Vaccination coverage during the outbreak was 12.5% lower than before the outbreak. [Miretu DG 2021]

Asia

Twenty percent of child immunisation services in **Bangladesh** were cancelled in April 2020 and 25% in May. The most significant disruption occurred in remote subdistricts: Hijla (57%), Agailjhara (25%) and Mehendiganj (20%). Improved coverage appeared in the post-disruption months (July to October 2020), with about 99% of immunisation sessions held. [Rana S 2021] In **India**, survey data of paediatric healthcare providers from April to June and September 2020 reported a greater than 50% drop in vaccination services by 83% of the respondents in June (n=424 respondents) and 33% in September (n=141). [Shet 2021] In **Indonesia**, 42% (480/1137) of survey respondents reported disruption of childhood vaccination services in local health facilities and 13% (193/1137) of respondents explained that their children could not be vaccinated because a healthcare facility temporarily stopped vaccination service. Of all respondents, 312 (27%) delayed vaccinating their children for a compulsory vaccination shot. [Fahriani M 2021] In **South Korea**, during the outbreak, the vaccination rate in children aged <35 months did not decrease significantly, whereas the vaccination rate for children aged 4 to 6 decreased

by 1.4 to 1.9%. [Yu 2020] In **Japan**, COVID-19 resulted in decreases in the vaccination rate for Haemophilus influenza type b in <5-year-olds from approximately 97% each in 2013 and 2019 to 87% and 73% in 2020 for primary and booster doses, respectively. [Kitano 2021]

Middle East

At the King Saud University Medical City, Riyadh, in **Saudi Arabia**, electronic health records reported drops in vaccination visits of 50%, 72% and 68% in March, April, and May 2020 compared with the same months in 2017 to 2019. [Alrabiaah 2020] Furthermore, in the Qassim region of **Saudi Arabia**, a questionnaire for parents of children under two years of age conducted between 1 May to 30 June 2020 reported that 23% had a delay of more than one month in the immunisation of their child. The most common reason for delay was fear of COVID-19 infection. [Alsuhaibani M 2020]

Europe

Weekly survey data from roughly 1,000 participants in **Germany** reported on 14 April 2020 that 31 of 73 scheduled childhood vaccinations were cancelled within the previous six weeks - 26 (84%) because of the pandemic. Nearly half of the parents (46%) indicated that their paediatrician cancelled the appointment. According to the survey, two-thirds of the cancelled vaccination appointments had been caught up, but appointments had not been scheduled for roughly one in five. [Schmid-Küpke 2021] In Lothian, **Scotland**, fixed-point clinics delivered infants' first vaccinations at various locations accessible by public transport, leading to stable attendance rates. [Jarchow-MacDonald 2021] In **Spain**, a review of data from Autonomous Communities reported that vaccination coverage in all communities decreased by between 5% and 60%, depending on the age and type of vaccine. The first dose of meningococcal vaccine B decreased by 68.4% in the Valencian Community, and Andalusia observed a 39% decrease in the total doses of this vaccine [Moraga-Llop FA 2020]. In

Portugal, survey responses for 19,745 children reported that 21.6% of planned vaccinations were missed. [Poppe M 2021] Similarly, a survey among **Italian** families on childhood vaccinations during the lockdown period reported that out of 1474 responders, 34% skipped vaccine appointments because they were afraid of the SARS-CoV-2 virus, the vaccination provider postponed the appointment, or the service was closed. [Russo R 2021]

USA

US CDC Data indicated that three million fewer doses of non-influenza vaccines were ordered from 6 January to 19 April 2020, compared with the previous year. [Santoli JM 2020] A decrease was seen in the number of vaccine doses administered in **New York City** in March and April 2020. In children <24 months of age, the largest relative decrease occurred between 5 to 11 April with a 62% decrease - from 33,261 doses in 2019 to 12,746 doses in 2020. In those aged 2 to 18 years, a 96% decrease was observed - from 23,631 doses in 2019 to 1,054 doses in 2020. Vaccine administration in children <24 months returned to levels comparable with 2019 in May 2020, but in those aged 2 to 18 years, levels had not returned to normal by the end of June. [Langdon-Embry 2020] Blue Cross Blue Shield, which insures 1 in 3 **Americans**, reported a drop of up to 26% in MMR, DTP & polio vaccines between January and Sept 2020. [Blue Cross 2020]

Latin America and the Caribbean

In **Latin America and the Caribbean**, difficulties caused by public transport limitations, confinement and physical distance policies, along with fear of COVID, led to a decrease in demand for vaccination services in half of the 38 countries that reported information to the Pan American Health Organization [PAHO] in June 2020. ^[5] [PAHO 2020] Initiatives to increase vaccination rates included institutional drive-through vaccination, mobile vaccination centres, vaccination in homes and

strategic locations, follow-up vaccinations using the electronic immunisation registry and emphasis on the importance of maintaining immunisation during a pandemic.

BCG vaccination

Data from the **Rwanda** Health Management Information System from March and April 2019 showed significant reductions in bacille Calmette–Guérin (BCG) compared with 2020. [Wanyana 2021] In **Pakistan**, there was a 53% decline in the daily average total vaccinations administered. Provincial electronic immunisation registry data reported about 8,400 children per day missed immunisation during the lockdown phase [Chandir S 2020], with the highest decline seen for BCG immunisation 958/2360). **Ethiopia** reported that of 1,110 children who started their BCG vaccination, only 798 (72%) completed their immunisations. [Wale 2020] From January to June 2020, **Burundi, CAR, Chad, DR Congo, Eritrea, Rwanda** and **Senegal** managed to maintain cumulative numbers of vaccinated children for BCG, compared to the mean of 2018/2019. [Masresha BG 2020]

Diphtheria, Tetanus, Pertussis [DTP]

The **Rwanda** data also showed significant reductions in DTP vaccination rates. [Wanyana 2021] Analysis of children receiving the first and third doses of DTP-containing vaccines in Guinea, Nigeria, Ghana, Angola, Gabon, and South Sudan showed drops in monthly vaccination in the second quarter of 2020 for the third dose compared with 2018-19. **Burundi, CAR, Chad, DR Congo, Eritrea, Rwanda** and **Senegal** managed to maintain the number of vaccinated children for DPT1 and DPT3. [Masresha BG 2020] Declines were seen in Pakistan, with the likelihood of Penta-3 immunisation, which includes the DTP-containing vaccines, reduced by 5% for each week of delay. Retrospective data from a vaccination unit of a hospital centre in **Senegal** comparing data for 2018,

2019 and 2020, reported pentavalent vaccine reductions in ten-week-olds. [Sow A 2020]

Measles

Eleven studies assessed measles vaccination rates: Abbas 2020, Bechini 2020, Bramer 2020, Carias 2021, Masresha 2020, McDonald 2020, Middeldorp 2021, Santoli 2020, Seither 2021, Sow 2020, and Wale 2020.

Two surveys [Bechini 2020 and Wale 2020] reported reductions in vaccine uptake. Nearly a third (32%) of 223 paediatricians in Tuscany, **Italy**, reported declines in mandatory vaccination, including the measles and rubella vaccine (MMR). Postponements were mainly due to safety fears. [Bechini 2020] A survey in **Ethiopia** including 1,300 children aged 10 to 23 months reported 798 (61%) had received the measles vaccine. Women who could not read and write were five times more likely to have an incompletely immunised child than those educated with a diploma, degree, and above (Adjusted Odds Ratio = 5.1, 95% CI 2.3 - 11.1). [Wale TA 2020]

Retrospective data from **US** states on local immunisation programs among kindergarten children (age 5-6 years) reported 95% had two doses of measles, mumps, and rubella vaccine in the 2019/20 school year. COVID disruptions were expected to reduce vaccination coverage in the 2020/21 school year. [Seither R 2021] Data from the Michigan Care Improvement Registry in the US reported that disruptions impacted coverage. For 16-month-olds, measles vaccination coverage decreased from 76.1% in May 2019 to 70.9% in May 2020. [Bramer CA 2020] Data from the **US** CDC reported significant reductions in measles vaccines over 15 weeks. The greatest reduction in orders was reported in the week beginning 13 April, with a cumulative decrease of approximately 400,000 measles doses compared to 2019. Smaller declines were seen in children aged ≤ 24 months than in older children. [Santoli JM 2020]

A review of routine immunisation data from 15 **African** countries showed that thirteen saw drops in the monthly average vaccine doses

provided. Nine countries had lower monthly first dose measles vaccinations in the second quarter of 2020 compared to the first quarter. Those countries with more inadequate coverage before COVID-19 reported more significant drops in the number vaccinated after the pandemic was declared. [Masresha BG 2020] A retrospective study in a hospital vaccination unit in Senegal comparing measles vaccinations, amongst others, reported significant reductions in coverage. [Sow 2020] On 15 May 2020, as part of the pulse survey, the WHO reported that measles campaigns were suspended in 27 countries. [WHO pulse survey 15 May report 2020]

Electronic health records of children <1-year-old in **England** reported measles-mumps-rubella vaccination was 20% lower in the first three weeks of restrictions than the same period in 2019, before improving in mid-April. [McDonald 2020] The Nuffield Trust reported the number of vaccinations decreased in the week beginning 23 March 2020 (week 13) when lockdown measures began. [Nuffield Trust 2021] Vaccination numbers then increased from week 16 and remained relatively stable at pre-pandemic levels. Public Health **England** [Public Health England 2021] reported that vaccine coverage for MMR1 between September and December 2020 was lower than 2019 estimates and that coverage was already below the WHO target of 95% in 2019. [5] In the **Netherlands**, the first MMR vaccination from March to September 2020 dropped by between 6 and 14% compared with the previous year. After catch-up vaccinations, a difference in the first MMR vaccination of -1% to -2% remained. [Middeldorp M 2021]

There were two modelling studies. Abbas K et al. 2020 modelled a high-impact scenario and a low-impact scenario in **Africa** to approximate child deaths relating to measles that immunisation coverage reductions could cause during COVID-19 outbreaks. Carias C et al. 2021 modelled projected **US** measles vaccination coverage for one-year-olds in 2020 for different durations of stay-at-home orders.

Polio

A Review of the Global Polio Eradication Initiative (GPEI) reported a halt to polio vaccination until the second half of 2020. GPEI comprises six organisations: the WHO, the US CDC, UNICEF, Rotary International, the Bill & Melinda Gates Foundation, and the Global Alliance for Vaccines and Immunisations. Data from **Afghanistan** reported 21 confirmed polio cases in 2018, 29 in 2019, and, in 2020, 34 confirmed cases were reported as of August 1, 2020. [Ahmadi 2020]

We reviewed the latest **Afghanistan** data from GPEI (<https://polioeradication.org/>). As of 16 June, one case of wild poliovirus type 1 (WPV1) has been reported for 2021 and a total of 56 cases in 2020.^[6] The latest status for Afghanistan suggests that the country remains affected by WPV1 and circulating vaccine-derived poliovirus type 2 (cVDPV2). In March 2021, 6.6 million children were vaccinated against polio during the National Immunisation Days.^[7] There were forty cases of circulating cVDPV2 reported in 2021 and 308 cases in 2020.

An overview of the impact of COVID-19 on polio vaccination in **Pakistan** reported that vaccination campaigns in Pakistan were suspended in April 2020. Due to COVID-19-related disruptions to services, 40 million children missed polio vaccinations. [Din M 2020]. In Sindh, **Pakistan**, one in every two children in the province missed their routine vaccinations during the lockdown period. [Chandir S 2020]

We similarly reviewed the latest data on the GPEI from **Pakistan**. In 2020, through September, 73 cases of WPV1 were reported in Pakistan and 62 cases of cVDPV2. Cases in Pakistan dropped to eight in 2017, 12 in 2018, and then increased to 147 in 2019. [Chandir S 2020] The latest data from Pakistan as of June 16 reports one case of WPV1 in 2021 and 84 cases in 2020. The number of cVDPV2 cases so far in 2021 is eight; in 2020, there were 135 cases. In March 2021, a national Immunisation campaign ran from 29 March to 2 April 2021, with 40.1 million children vaccinated.^[8]

Data from the **Rwanda** Health Management Information System from March and

April 2019 compared to 2020 showed significant reductions in polio 1 and 2 vaccinations. [Wanyana 2021] In a hospital centre in **Senegal**, polio vaccination was reduced from March to August 2020. [Sow A 2020] Data from **Sierra Leone** on five common vaccinated diseases from Mar 1, 2020, to Apr 26, 2020, compared with 2019, reported decreases in vaccination ranging from 50 to 85% depending on the individual vaccine analysed, including the OPV1 vaccine. [Buonsenso D 2021]

In April 2020, The WHO reported that **Niger** had an outbreak of vaccine-derived poliovirus that affected two children—having suspended the vaccination campaign due to the pandemic. Niger's last wild polio case was in 2012^[9]. Niger joins 15 countries experiencing vaccine-derived poliovirus outbreaks in Africa. No wild poliovirus has been detected in **Africa** since 2016. Niger joins the list of countries experiencing vaccine-derived poliovirus outbreaks in Africa. The other countries are Angola, Benin, Burkina Faso, Cameroon, Central African Republic, Chad, Côte d'Ivoire, the Democratic Republic of the Congo, Ethiopia, Ghana, Mali, Nigeria, Togo and Zambia.

Discussion

The evidence in this review comes from a wide range of conditions and countries that highlight significant disruptions to childhood vaccine services. We found reductions in diphtheria tetanus pertussis, BCG, measles and polio vaccine uptake, as well as a range of other vaccines regularly given to children. Reductions in many settings were reversed once restrictions were lifted. However, not all settings reported a return to complete normality. Smaller declines were seen in younger children than older children. In addition, children born to women who could not read and write were more likely to be incompletely immunised. Barriers to access and maintaining public transport infrastructure impacted uptake of childhood vaccinations as well.

The true impact of COVID-19 disruptions on childhood vaccination services is yet to be determined. Two years after reductions in measles

vaccination during the Ebola outbreak in Guinea, the incidence of measles increased from 2.7 per million in 2015 to 11.5 per million in 2016 and 52.5 per million in 2017, of which 65% of cases were confirmed in those aged < 5 years. ^[10] Worldwide measles deaths climbed by 50% from 2016 to 2019, with over 200,000 lives lost in 2019. ^[11]

Low levels of polio vaccination and a lack of immunity can leave countries at risk of polio returning. Indonesia, Mozambique, Myanmar, Papua New Guinea, and the Philippines are currently considered key-at-risk countries by GPEI, Afghanistan, and Pakistan affected by ongoing endemic WPV1 and cVDPV2. ^[11] There is a concerted effort underway to eradicate polio. The GPEI reports fewer cases in 2021 compared to the same period last year. This is promising, despite the lockdowns; however, the potential for underreporting exists due to the pandemic. The effects of Polio can be devastating: in 1996, wild poliovirus paralysed more than 75,000 children in Africa. ^[12] Therefore, maintaining sustained vaccination levels and disease surveillance remains a priority for at-risk countries. Furthermore, several barriers were reported to vaccination, including a lack of clarity around whether vaccination services were operating, as usual, difficulties in organising vaccination appointments, and fears around contracting COVID-19. [Bell S 2020]

Limitations

We did not formally assess the quality of the included studies. However, clinical audit and service evaluation remain valuable for analysing and targeting improvements in healthcare. Publication bias will favour studies that highlight disruptions and account for excess reporting of decreases in vaccination levels. However, alongside those studies, reviews by international bodies highlight consistent drops in vaccination uptakes during the restrictive phases of the pandemic. Studies that report no reductions in vaccination are essential; they highlight strategies that can overcome disruptions during restrictions

and – crucially – after they have been lifted. Reports of vaccine coverage may not be 100% accurate, particularly during periods of upheaval such as in a pandemic.

Conclusions

COVID-19 pandemic measures caused significant disruption to childhood vaccination services and uptake. In future pandemics, and for the remainder of the current one, policymakers must ensure access to vaccination services and provide catch-up programs to maintain high levels of immunisation, especially in those most vulnerable to childhood diseases in order to avoid further inequalities.

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Competing Interest Statement

TJ was in receipt of a Cochrane Methods Innovations Fund grant to develop guidance on the use of regulatory data in Cochrane reviews (2015 to 2018). From 2014 to 2016, he was a member of three advisory boards for Boehringer Ingelheim. TJ is occasionally interviewed by market research companies about phase I or II pharmaceutical products for which he receives fees (current). TJ was a member of three advisory boards for Boehringer Ingelheim (2014 to 16). TJ was a member of an independent data monitoring committee for a Sanofi Pasteur clinical trial on an influenza vaccine (2015 to 2017). TJ is a relator in a False Claims Act lawsuit on behalf of the United States that involves sales of Tamiflu for pandemic stockpiling. If resolved in the United States favour, he would be entitled to a percentage of the

recovery. TJ is coholder of a Laura and John Arnold Foundation grant for the development of a RIAT support centre (2017 to 2020) and Jean Monnet Network Grant, 2017 to 2020 for The Jean Monnet Health Law and Policy Network. TJ is an unpaid collaborator to the project Beyond Transparency in Pharmaceutical Research and Regulation led by Dalhousie University and funded by the Canadian Institutes of Health Research (2018 to 2022). TJ consulted for Illumina LLC on next-generation gene sequencing (2019 to 2020). TJ was the consultant scientific coordinator for the HTA Medical Technology programme of the Agenzia per i Servizi Sanitari Nazionali (AGENAS) of the Italian MoH (2007 to 2019). TJ is Director Medical Affairs for BC Solutions, a market access company for medical devices in Europe. TJ was funded by NIHR UK and the World Health Organization (WHO) to update Cochrane review A122, Physical Interventions to interrupt the spread of respiratory viruses. TJ is funded by Oxford University to carry out a living review on the transmission epidemiology of COVID 19. Since 2020, TJ receives fees for articles published by The Spectator and other media outlets. TJ is part of a review group carrying out a Living rapid literature review on the modes of transmission of SARS CoV 2 (WHO Registration 2020/1077093 0). He is a member of the WHO COVID 19 Infection Prevention and Control Research Working Group, for which he receives no funds. TJ is funded to co-author rapid reviews on the impact of Covid restrictions by the Collateral Global Organisation.

CJH holds grant funding from the NIHR, the NIHR School of Primary Care Research, the NIHR BRC Oxford and the World Health Organization for a series of Living rapid review on the modes of transmission of SARs-CoV-2 reference WHO registration No2020/1077093. He has received financial remuneration from an asbestos case and

given legal advice on mesh and hormone pregnancy tests cases. He has received expenses and fees for his media work, including occasional payments from BBC Radio 4 Inside Health and The Spectator. He receives expenses for teaching EBM and is also paid for his GP work in NHS out of hours (contract Oxford Health NHS Foundation Trust). He has also received income from the publication of a series of toolkit books and appraising treatment recommendations in non-NHS settings. He is the Director of CEBM and is an NIHR Senior Investigator. He is co-director of the Global Centre for healthcare and Urbanisation based at [Kellogg College](#) at Oxford, and he is a scientific advisor to Collateral Global.

JB is a major shareholder in the Trip Database search engine (www.tripdatabase.com) and an employee. In relation to this work, Trip has worked with many organisations over the years; none have any links with this work. Their main current projects are with AXA and Collateral Global.

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Ethics Committee Approval

No approval was necessary.

Data Availability

All data included in the review is provided in the tables and text.

Appendices

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TABLE 1: Primary Studies on Childhood Vaccination Uptake During the COVID-19 Pandemic

Author	Country	Type of Vaccine	Type of Evidence	Methods	Population	Impact
Abbas K 2020	Africa	General	Modelling	Modelling of a high-impact scenario and a low-impact scenario to approximate child deaths that could be caused by immunisation coverage reductions during COVID-19 outbreaks.	< 5 years	High-impact scenario: for every one excess COVID-19 death related to SARS-CoV-2 acquired during routine vaccination visits, 84 (95% UI 14–267) deaths in children could be prevented by sustaining routine immunisation in Africa. In the low-impact scenario that approximates the health benefits to only the child deaths averted from measles the benefit-risk ratio to the households of vaccinated children is 3 (0.5–10); if the risk to only the vaccinated children is considered, the benefit-risk ratio is 3000(182–21 000).
Alrabiah AA 2020	Saudi Arabia	General	Retrospective cohort	At the King Saud University Medical City, Riyadh, Saudi Arabia electronic health records were reviewed for children at birth and at 2, 4, 6, 9, and 12 months during Mar-May 2017- 2020 (sample =15,870 children).	0-12 months	In March, April, and May 2020 there were respective drops in vaccination visits of 50%, 72% and 68% compared with the mean numbers of vaccination visits during the same months from 2017 to 2019.
Alsuhaibani M 2020	Saudi Arabia	General	Survey	In the Qassim region, Saudi Arabia a cross-sectional study using an online self-administered questionnaire for parents of children under two years of age during the period from 1 May to 30 June 2020.	< 2 years	Nearly three-quarters (73.2%) of the parents had appointments scheduled for their child's vaccination during the pandemic, and approximately 23.4% of the parents reported a delay of more than one month in the immunization of their child. The most common reason for the delay was the fear of being infected by COVID-19 (60.9%).
Bechini A 2020	Italy	General	Survey	Four hundred members belonging to the Italian Federation of Paediatricians (FIMP) in Tuscany were invited to answer a semi-structured online survey.	Paediatricians	Among 223 respondent 93% (208) guaranteed vaccination activities; 66 paediatricians (32%) reported a reduction in the compliance of parents to mandatory vaccination (hexavalent and MMRV vaccines), and 88 paediatricians (42%) to non-mandatory vaccinations.
Bell S 2020	England	General	Survey & semi-	1252 parents and guardians in England with a child aged under 18 months completed	≤18 months	86% of survey respondents considered it important for their children to receive

			structured interviews	the survey and 19 respondents took part in follow-up interviews.		routine vaccinations on schedule. Several barriers to vaccination were identified. These included a lack of clarity around whether vaccination services were operating as usual; difficulties in organising vaccination appointments; and fears around contracting COVID-19
Bramer CA 2020	USA	General	Retrospective cohort	Cohorts for 2016-2019 compared with 2020 using data from the Michigan Care Improvement Registry (the state's immunization information system)	1, 3, 5, 7, 16, 19, and 24 months	Among children aged 5 months, recommended vaccines declined from an average of 67% in 2016-2019 to 50% (absolute reduction 17.6%) in May 2020. For 16-mth olds, measles vaccination coverage decreased from 76% in 2019 to 71% in 2020. Non-Influenza vaccine doses administered for children aged ≤24 months decreased 15.5% during Jan-Apr 2020.
Buonsenso D 2021	Sierra Leone	General	Retrospective cohort	Review at the Kent Community Health Post, Sierra Leone (estimated popn. 5,000) from Mar 1 to Apr 26, 2020 and compared with 2019.	< 5 years	A lower number of children received vaccination in 2020 compared with 2019, ranging from 50 to 85% depending on the individual vaccine analysed, including BCG and OPV1. Second measles vaccinations dropped by 84% from 49 children in 2019 to 8 in 2020.
Chandir S 2020	Pakistan	General	Retrospective cohort	Individual immunization records from real-time Electronic Immunization Registry from Sep 23, 2019, to Jul 11, 2020, comparing baseline (6 months before lockdown and lockdown period.	Children	A 53% decline in the daily average number of vaccinations administered during lockdown compared to baseline. The highest decline was for BCG (40.6% (958/2360). Around 8438 children/day were missing immunization during the lockdown. Enrollments declined furthest in rural districts, urban sub-districts with large slums, and polio-endemic super high-risk sub-districts. Pentavalent-3 (Penta-3) immunization rates were higher in infants born in hospitals (RR: 1.09; 95% CI: 1.04–1.15) and those mothers with higher education (RR: 1.19–1.50; 95% CI: 1.13–1.65).
Fahriani M 2021	Indonesia	General	Survey	A nationwide, online, cross-sectional study. A set of questionnaires assessed the disruption of childhood	Children	Disruption of childhood vaccination service was reported in 42% (480/1137) of respondents and 13.3%

				vaccinations and possible explanatory variables.		(193/1137) explained that their children could not be vaccinated because a facility temporarily stopped the vaccination service. Of all respondents, 312 (27.4%) delayed vaccinating their children for a compulsory vaccination shot.
Harris RC 2021	South-East Asia and Western Pacific	General	Survey	Sanofi Pasteur teams from 19 countries in SEAR/WPR completed a structured questionnaire reporting on COVID-19 disruptions for 13–19 routinely delivered antigens per country, based on sales data, government reports, and regular physician interactions.	Children	95% (18/19) of countries reported vaccination disruption. Infancy and school-entry age vaccinations were most impacted. Vaccination rates had not recovered for 39% of impacted antigens by 1 June 2020. Fear of infection, movement/travel restrictions, and limited healthcare access were the highest-ranked reasons for disruption. The highest-scoring solutions were separating vaccination groups from unwell patients, non-traditional vaccination venues, virtual engagement, and social media campaigns. Many of these solutions were under-utilised.
Hou Z 2021	China	General	Survey	An online survey in mid-March 2020 using proportional quota sampling in Wuhan (the epicentre) and Shanghai (a non-epicentre)	3-17 years	Parent-reported vaccination behaviours showed 75% delayed scheduled vaccines and 81% planned to have their children get the influenza vaccine after the epidemic.
Jarchow-MacDonald 2021	Scotland	General	Retrospective cohort	Analysis In Lothian, Scotland of first vaccinations delivered by fixed-point clinics	Children	Attendance rates were stable.
Langdon-Embry 2020	USA	General	Retrospective cohort	Routine childhood vaccination was monitored by the NYC Department of Health and Mental Hygiene (DOHMH) using the Citywide Immunization Registry (CIR),* a population-based immunization information system with high data quality and provider participation	<24 months & 2–18 years	A decrease in the number of vaccine doses administered in NYC was detected beginning the week of Mar 8, 2020; numbers declined further after March 22 when New Yorkers were required to stay at home The largest relative decrease was observed Apr 5–11 and was less pronounced in <24 months (62% decrease, from 33,261 doses in 2019 to 12,746 doses in 2020) than in 2–18 years olds (96% decrease, from 23,631 doses in 2019 to 1,054 doses in 2020). Vaccine administration increased <24 months starting Apr 19–25, and returned to

						levels comparable with 2019 on May 17. Vaccine administration among 2–18-year-olds increased April 26–May 2 and continued to rise, but as of June 27 still had not reached levels comparable with 2019.
Masresha BG 2020	Africa	General	Retrospective cohort	Review of the administrative routine immunization data from 15 African countries for the period from January 2018 to June 2020 and compared with the first three months of the COVID-19 pandemic.	Children receiving BCG, DPT1 & DPT3, MCV1 and MCV2.	13/15 countries showed a decline in the monthly average number of vaccine doses provided, with 6 countries having more than 10% decline. Nine countries had lower monthly mean recipients of first dose measles vaccination in the second quarter of 2020 compared to the first quarter. Guinea, Nigeria, Ghana, Angola, Gabon, and South Sudan experienced a drop in the monthly number of children vaccinated for DPT3 and/or MCV1 of greater than 2 standard deviations at some point in the second quarter of 2020 as compared to the mean for the months January–June of 2018 and 2019.
McDonald 2020	England	General	Retrospective cohort	Using electronic health records, we assessed the early impact of coronavirus disease (COVID-19) on routine childhood vaccination in England by 26 April 2020.	< 1 year	MMR vaccination counts fell from Feb 2020, and in the 3 weeks after physical distancing measures were 19.8% lower (95%CI, –20.7 to –18.9) than 2019, before improving in mid-April. The MMR vaccination counts also followed a similar pattern in 2020 until week 11 when they fell and remained low for several weeks before rising in week 16.
Middeldorp M 2021	Netherlands	General	Retrospective cohort	Data on the monthly number of cases reported from January 2019 through September 2020 were compared with data from the five preceding years.	Children	The incidence of various VPDs initially decreased by 75–97% after the implementation of measures. The participation in MMR1 vaccination in Mar–Sep 2020 initially dropped by 6–14%. After catch-up, a difference in MMR1 participation of –1% to –2% remained.
Miretu DG 2021	Ethiopia	General	Survey	633 children with their mother/caregiver were interviewed from Jul 22 to Aug 7, 2020, in Dessie town, Ethiopia. The response rate was 96.4%.	15 - 23 months	Based on the vaccination card plus recall, 350 (57.4%) of children finished all recommended vaccines. Age-eligible vaccination coverage during the COVID-

						19 outbreak was 12.5% lower than before the outbreak.
Moraga-Llop FA 2020	Spain	General	Survey	Review of data from Autonomous Communities depending on the age and type of vaccine	Children	Despite health authority recommendations vaccination coverage decreased in all Autonomous Communities between 5% and 60%, depending on the age and type of vaccine. School vaccinations were suspended and only vaccination of pregnant women against tetanus, diphtheria and pertussis was maintained. The first dose of meningococcal vaccine B has decreased by 68.4% in the Valencian Community, and Andalusia has observed a 39% decrease in the total doses of this vaccine and of 18% for that of rotavirus.
Poppe M 2021	Portugal	General	Survey	An anonymous online survey via social media. Data was collected between the 16th of March and the 17th of May 2020.	Children	Responses for 19 745 children were obtained and 21.6% of planned vaccinations were missed. Parents expressed concerns regarding psychological, social, and physical consequences for their children due to the pandemic
Rana S 2021	Bangladesh	General	Retrospective cohort with historical controls	Retrieved annual data for 2019 and 2020 from Bangladesh's district health information system (DHIS) for child immunisation and sick children's care-seeking in six subdistricts of Barishal, Bangladesh.	< 5 years	Child immunisation services were mostly disrupted in April and May 2020, when 20% (280 of 1414) and 25% (346 of 1395) of planned outreach immunisation sessions were cancelled, respectively. On average, the greatest disruption was observed during these months in three remote subdistricts: Hijla (57% [185 of 322]), Agailjhara (25% [69 of 275]), and Mehendiganj (20% [135 of 660]).
Russo R 2021	Italy	General	Survey	A survey among Italian families on children vaccination during lockdown period.	Children	Out of 1474 responders, 34% skipped the vaccine appointment as they were afraid of SARS-CoV-2-virus (44%), vaccination services postponed the appointment (42%) or were closed (13%).

Santoli JM 2020	USA	General	Retrospective cohort with historical controls	Data analyses from CDC's Vaccine Tracking System and Vaccine Safety Datalink (VSD) vaccine administration data. Cumulative doses of Vaccines ordered by health care providers weekly from Jan 7, 2019–Apr 21, 2019 [period 1] and Jan 6, 2020–Apr 19, 2020 [period 2]) were compared between two age groups: aged ≤24 months and >24 months through 18 years.	≤24 months & aged >24 months through 18 years	A notable decrease in orders for VFC-funded was noted, ACIP-recommended non-influenza childhood vaccines and for measles-containing vaccines during period 2 compared with period 1. Approx reduction of 3 million doses ordered for non-influenza vaccines and 400,000 measles-containing diseases over 15 weeks.
Schmid-Küpke NK 2021	Germany	General	Survey	Data within three waves (waves 7, 9, and 14) of COSMO, a serial cross-sectional survey monitoring public perceptions of risk, trust, knowledge, and misinformation on COVID-19 measures. Since Mar 3, 2020, about 1000 participants weekly (since June, fortnightly)	Children	The 1st data collection (14th April) indicated that 73/306 children had vaccination appointments in the last six weeks, and 31/73 (43%) were cancelled. Nearly all because of the pandemic 26/31 (84%). Half indicated their paediatrician cancelled the appointment (12/26 = 46%), The remaining by the patients themselves (14/26 = 53.9%). In June 48/82 = 59% vaccinations in children took place.
Seither R 2021	USA	General	Retrospective cohort	Retrospective data collected by state and local immunization programs* vaccination coverage among children in kindergarten in 48 US states, exemptions for kindergartners in 49 states, and provisional enrollment and grace period status for kindergartners in 28 states for the 2019–20 school year.	First-year of primary education in the US (5-6 years)	Vaccination coverage was 94.9% for the state-required number of doses of diphtheria and tetanus, and acellular pertussis vaccine (DTaP); 95.2% for 2 doses of measles, mumps, and rubella vaccine (MMR); and 94.8% for the state-required number of varicella vaccine doses. (2.5% of kindergartners had an exemption from at least one vaccine; 2.3% were not up to date for MMR and did not have a vaccine exemption).
Shet A 2021	India	General	Survey	Surveyed paediatric healthcare providers in India in 2 rounds in April-June and September 2020 to understand how COVID-19 control measures may have impacted routine vaccination.	Children	Among the 424 (survey 1) and 141 (survey 2) respondents, 33.4% and 7.8%, respectively, reported near complete suspension of vaccination services due to COVID-19. A 50% or greater drop-in vaccination services was reported by 83% of respondents in June, followed by 323% four months later.

Sow A 2020	Senegal	General	Retrospective cohort with historical controls	Analysis in the vaccination unit of the Abass NDAO hospital centre in Senegal comparing 2020 data from Mar to Aug to the last three years of vaccine administered at birth (BCG, poliomyelitis), at 6 weeks at 10 weeks (pentavalent, pneumococcal, rotavirus and polio vaccine), at 14 weeks and 9 months (measles, rubella and yellow fever).	6 weeks to 9 months	For the vaccines administered in the sixth week in April, the number of doses was 36 in 2018, 29 in 2019 and 15 in 2020, a decrease of 50% compared to March. In July, the number of doses administered was 40 in 2018, 35 in 2019 and 15 in 2020, i.e. a reduction of 42% compared to 2019.
Vogt TM 2020	USA	General	Survey	A May 2020 survey of 1,933 practices participating in the Vaccines for Children program	Children	1,727 (89.8%) of 1,993 practices were currently open, including 1,397 (81%) offering immunization services to all paediatric patients. Among responding practices, 1,135 (59%) were likely able to provide immunization services to new paediatric patients if necessary.
Wale TA 2020	Ethiopia	General	Mixed methods survey and interviews	Community-based mixed quantitative and qualitative cross-sectional study in southwest Ethiopia. Data was collected using semi-structured questionnaires and in-depth interviews.	Children aged 10–23 months	Of the total respondents, 1,110 (85%) took both BCG and OPV vaccine, from 1,110 BCG started children only 798 (71.8%) completed their immunization. Of 1,300 children, 190 (14.6%) were not taking any vaccine at all. Overall 1,088 (84%) received both PCV one and Penta one, 1082 (83%) received rota1 and 798 (61%) received measles vaccine. The coverage rate declined for the consecutive dose, such as OPV zero (85.4%) to OPV three (73.7%), both Penta and PCV one (83.7%) to Penta and PCV three (71.9%). The percentage of incomplete immunization among children aged from 10 to 23 months was found to be 809 (62.2%, 95% CI: 59.5, 64.8).
Wanyana D 2021	Rwanda	General	Retrospective cohort with historical controls	Analyzed data from the Rwanda Health Management Information System (HMIS) estimated 2020 population: 12,663,117. Analysis from Mar and Apr 2019 (before the COVID-19 outbreak) were compared with Mar and Apr 2020.	12–23 months	Vaccinations: bacille Calmette–Guérin (BCG) from 1.06 in 2019 to 0.95 in 2020 ($P = 0.002$), polio zero from 0.97 to 0.86 ($P = 0.001$), polio 1 from 0.97 to 0.89 ($P = 0.008$), polio 2 from 0.95 to 0.88 ($P = 0.008$), diphtheria, tetanus, pertussis, hepatitis B and haemophilus influenzae (DTP_HepB_Hib) 1 from 0.97 to 0.89 ($P = 0.007$), DTP_HepB_Hib 2 from 0.95

						to 0.88 (P = 0.007), pneumococcus 1 from 0.97 to 0.89 (P = 0.007), pneumococcus 2 from 0.95 to 0.88 (P = 0.007), rotavirus 1 from 0.98 to 0.89 (P = 0.006) and rotavirus 2 from 0.95 to 0.88 (P = 0.009).
Yu JH 2021	South Korea	General	Retrospective cohort with historical controls	National vaccination coverage of 10 essential children vaccines between Jan–June 2019 and 2020. Coverage was based on the resident population data of the Korean Ministry of Public Administration and Security, which covers 100% of national immunization in the country.	< 6 years	During the COVID-19 outbreak, the vaccination rate in children aged 0 to 35 months in Korea did not decrease significantly, whereas the vaccination rate for children aged 4 to 6 decreased by 1.4–1.9%. The overall incidence of VPDs decreased by 10–50% between 2019 and 2020, especially varicella.
Kitano T 2021	Japan	Haemophilus influenza type b	Model and Retrospective cohort with historical controls	Incidences of invasive Hib disease among 0–4-year-olds in the pre-vaccine (2008–2010) and post-vaccine period (2013–2019) before the COVID-19 outbreak were compared	< 5 years	The national Hib vaccination rate after the impact of COVID-19 reduced to 87% and 73% in 2020 from approximately 97% each in 2013–2019 for primary and booster doses.
AlHajri B 2021	Kuwait	Influenza	Survey	online survey to adults in Kuwait between Aug 26 and Sep 1 2020 (n = 2368; 1038 participants with children aged <18 years).	< 18 years	17.6% of parents (183/1038) reported their children received the influenza vaccine in the last season. Of the participating parents, 33% (342/1038) indicated they definitely/probably will vaccinate their children in the coming influenza season.
Carias C 2021	USA	Measles	Modelling	Projected measles vaccination coverage for one-year-olds in 2020 in the US, for different durations of stay-at-home orders.	Infants born in 2019 aged 12 months	For a two-month 2020 stay-at-home order with a reduction in measles-containing vaccine administration by 50% (base-case), estimated a decline in vaccination coverage for infants born in 2019 from 90% to 82% for the first dose of the measles-containing vaccine with no catch-up. In scenarios with catch-up vaccination after stay-at-home orders are lifted, the projected coverage would increase to 90% with a 15% increase in the number of well-child visits over baseline for the rest of the year.

Ahmadi A 2020	Afghanistan	Polio	Retrospective cohort	Review of WHO GPEI polio data and Afghanistan policies (data is up to August 2020); however, there is now data till March 2021	Children	National immunization days aim to cover around 10 million children against polio. However, in 2020, only two programs were conducted before the outbreak of COVID-19 in the country. Vaccine stocks ran precariously low as supply chains were disrupted by travel bans. Many health facilities where children were normally vaccinated were closed. Polio cases have recently emerged in three provinces, Balkh, Herat, and Badakhshan, which had not reported any cases in the past 5 years. On May 21, 2020, the government of Afghanistan ratified an initial plan for loosening restrictions and allowing some businesses, including money exchange markets and shops, to reopen. However, this plan did not include restarting nationwide polio vaccination, and as of August 1, 2020, the program remains suspended.
Din M 2020	Pakistan	Polio	Retrospective cohort	Surveillance for acute flaccid paralysis (AFP) done for primary detection of cVDPV and WPV transmission. Within the Global Polio Laboratory Network, stool specimen testing is done in WHO-accredited laboratories for confirmation	< 15 years	In 2020, up to September 73 cases of Wild Polio Virus were reported in Pakistan. and 62 cases of circulating vaccine-derived poliovirus (cVDPV2) have been detected.

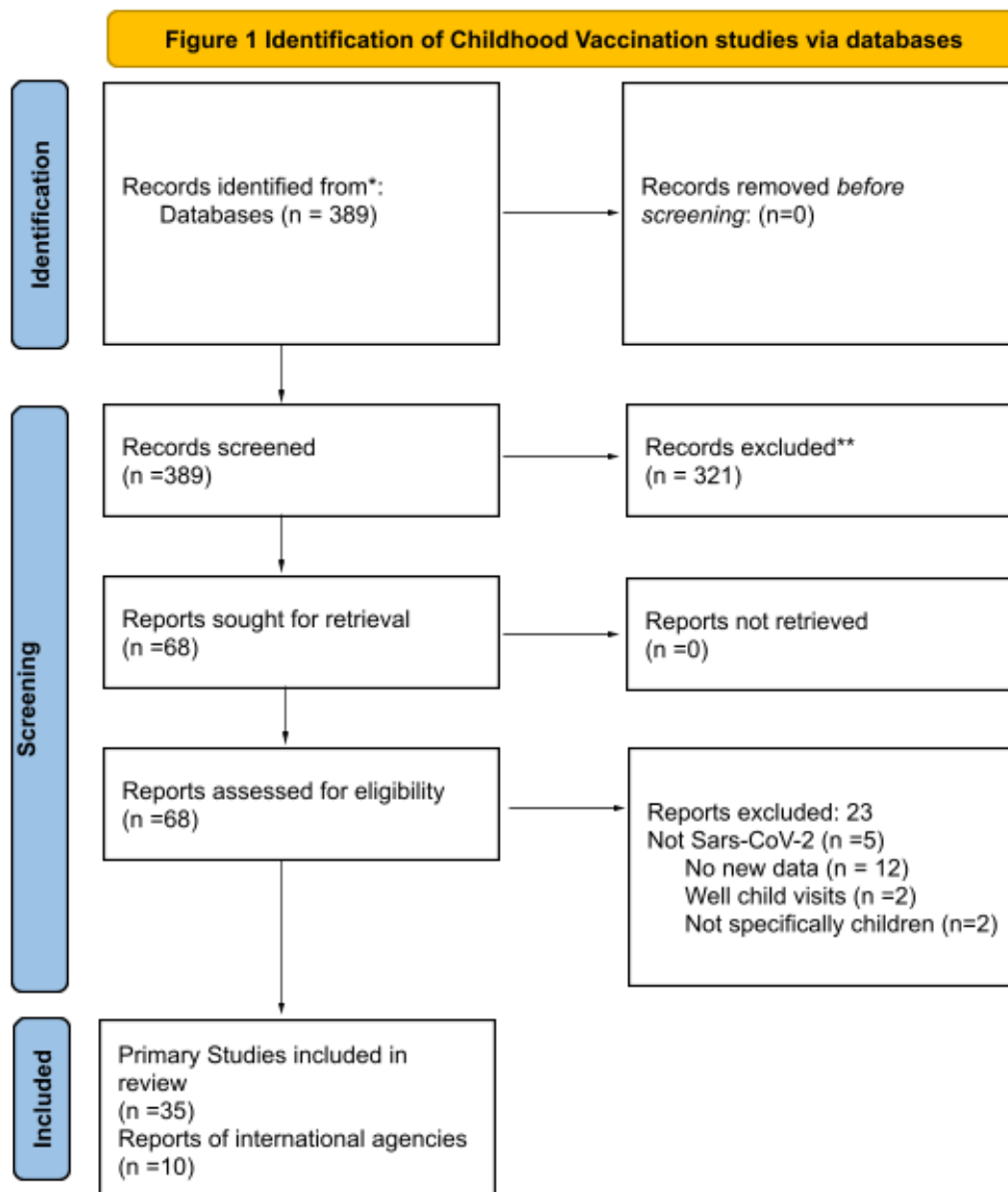
TABLE 2: Reports by National and International Agencies on Childhood Vaccination Uptake During the COVID-19 Pandemic

Organization and Year of Publication	Title	Summary	Link
Blue Cross 2020	Blue Cross Blue Shield. Missing vaccinations during COVID-19 puts our children and communities at risk	Reports up to 26% drop in MMR, DTP & polio vaccines between Jan-Sept 2020 in America.	https://www.bcbs.com/the-health-of-america/infographics/missing-vaccinations-during-covid-19-puts-our-children-and-communities-at-risk
Nuffield Trust 2021	Vaccination coverage for children and mothers	Indicators that look at vaccination coverage for children and mothers in the UK and internationally during the coronavirus (Covid-19) pandemic, coverage was largely maintained when compared to coverage in 2019/20.	https://www.nuffieldtrust.org.uk/resource/vaccination-coverage-for-children-and-mothers-1
Public Health England 2021	Impact of COVID-19 on childhood vaccination counts to week 4 in 2021, and vaccine coverage to December 2020 in England: interim analyses	Hexavalent and MMR vaccination counts fell at the time of the introduction of physical distancing measures in March 2020 (week 13) compared to the same period in 2019. This was followed by a rise from weeks 16 onwards which has stabilised and is comparable to vaccination counts prior to the COVID-19 pandemic.	Impact of COVID-19 on childhood vaccination counts to week 4 in 2021, and vaccine coverage to December 2020 in England: interim analyses
UNICEF 2020	Challenges posed by the COVID-19 pandemic in the health of women, children, and adolescents in Latin America and the Caribbean	During the pandemic, the population's fear of COVID-19 and public transport limitations and confinement and physical distance policies led to a decrease in the demand for vaccination services in half of the 38 countries in the region that report information to the Pan American Health Organization (PAHO).	https://www.unicef.org/lac/media/16376/file/undp-rblac-CD19-PDS-Number19-UNICEF-Salud-EN.pdf
PAHO* 2020	Summary of the Status of National Immunization Programs during the COVID-19 Pandemic, July 2020.		https://iris.paho.org/handle/10665.2/52544
UNICEF 2020	Immunization coverage Are we losing ground?	Lockdown measures had substantially hindered the delivery of immunization services in at least 68 countries, putting approximately 80 million children under the age of 1 at increased risk of contracting vaccine-preventable diseases.	https://data.unicef.org/resources/immunization-coverage-are-we-losing-ground/

WHO pulse interim survey 2020	Pulse survey on continuity of essential health services during the COVID-19 pandemic: interim report, 27 August 2020	105 countries responded. Severe/complete disruption of outreach routine mobile immunization services occurred in 18% of 91 countries and in 10% disruption to static routine immunization occurred.	https://www.who.int/publications/i/item/WHO-2019-nCoV-EHS_continuity-survey-2020.1
WHO pulse second-round survey 2021	The second round of the national pulse survey on continuity of essential health services during the COVID-19 pandemic	In January-March 2021 for 135 countries surveyed more than one-third were reporting disruptions to immunization services.	https://www.who.int/publications/i/item/WHO-2019-nCoV-EHS-continuity-survey-2021.1
WHO pulse survey 15 May report 2020	At least 80 million children under one at risk of diseases such as diphtheria, measles and polio as COVID-19 disrupts routine vaccination efforts, warn Gavi, WHO and UNICEF	More than half (53%) of the 129 countries where data were available reported moderate-to-severe disruptions or a total suspension of vaccination services during March-April 2020.	https://www.who.int/news/item/22-05-2020-at-least-80-million-children-under-one-at-risk-of-diseases-such-as-diphtheria-measles-and-polio-as-covid-19-disrupts-routine-vaccination-efforts-warn-gavi-who-and-unicef
WHO Niger 2020	Niger reports a new polio outbreak.	Niger has reported a new polio outbreak that has affected two children in Niamey and Tillaberi region,	https://www.afro.who.int/news/niger-reports-new-polio-outbreak

* Pan American Health Organization

Figure 1. PRISMA 2020 Flow Diagram



*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).

**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

Figure 2. PRISMA Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	0
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	1
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	1
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	1
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	1
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	1
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	1
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	1
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	1
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	1

Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	N/A
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	1
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	1
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	1
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	N/A
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	1 / 2
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	1 / 2
Study characteristics	17	Cite each included study and present its characteristics.	1 / 2
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	1
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	2-5
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	N/A
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	2-5
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A

	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	2-5
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	6
	23b	Discuss any limitations of the evidence included in the review.	6
	23c	Discuss any limitations of the review processes used.	6
	23d	Discuss implications of the results for practice, policy, and future research.	6
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	N/A
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	1
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	1
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	7
Competing interests	26	Declare any competing interests of review authors.	7
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	8

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71

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