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Research

Impact of school vaccination mandates on pediatric vaccination coverage: a systematic review

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Abstract

Background: Mandated vaccination for school attendance is a growing strategy internationally. Our aim was to investigate the effects of implementing school vaccination mandates on pediatric population vaccine coverage.

Methods: In this systematic review, we searched MEDLINE, Embase, CINAHL, the Education Resources Information Center (ERIC) and the PAIS Index for empirical studies of implementation of a primary or secondary school vaccination requirement published in any language through March 2019 with vaccination rates as an outcome. We sought additional studies by consulting experts, reference lists and grey literature sources. Included studies were too heterogeneous for meta-analysis; thus, we extracted data using a standardized rubric and synthesized the results narratively.

Results: Among the 4232 citations obtained, 20 studies met the inclusion criteria. Eighteen were conducted with US data, 1 with Italian data, and 1 with Australian data. Four studies examined school-entry mandates, and 16 examined adolescent requirements. An uncontrolled before–after design was used in 10 studies, cross-sectional analysis in 7, a retrospective cohort design in 2, and a prospective cohort in 1. In many cases, increased documentation of coverage followed the addition of new requirements. The exception to this was human papillomavirus vaccination mandates, which were highly controversial, in the United States. The studies contained notable risks of bias, with cointerventions rarely acknowledged or accounted for, and subpopulations often excluded. A substantial risk of ecological fallacy existed for most studies.

Interpretation: Vaccination mandates appear largely associated with increased vaccination coverage, but it is not possible to attribute causality to the mandate in most studies. High-quality implementation research that uses whole-population coverage data and takes into consideration cointerventions, confounders, clustering of unvaccinated populations and context is required.

Vaccination mandates for school attendance are ubiquitous in the United States and are growing as a strategy in Europe and Australia. Although the Canadian Medical Association passed a resolution in 2015 recommending that "governments authorize elementary and secondary schools to require a declaration of immunization status, to be followed by a conversation between public health officials and parents where children are shown to be inadequately immunized,"[1] school vaccination legislation currently exists in just 2 Canadian provinces, Ontario[2] and New Brunswick,[3] with intent to implement a policy in British Columbia recently announced.[4] Mandate policies vary in requirements (documentation, education, vaccination), schedule (which vaccines, when), restrictiveness (exemption processes),[5] and incentives (e.g., financial rewards) or penalties (e.g., fines, school exclusion). Debate regarding best practices for mandate policies tends to draw largely on ethical arguments[6] regarding the optimal legislation to achieve maximum pediatric vaccine coverage with minimal violation of parental civil liberties, with some voices advocating strict policies permitting few exemptions, others favouring a more libertarian approach, and many aiming to strike a balance.[7] Often in these debates, the effectiveness of vaccination mandate laws in increasing population vaccine coverage is assumed; however, recent systematic assessment of the literature regarding the impacts of school mandates on vaccine coverage in Canada and other wealthy countries has not, to our knowledge, been done.

To assess the effectiveness of school vaccination mandates in real-life settings, studies with appropriate methods and outcomes must be examined. Cross-sectional studies have documented associations between the existence (or strictness) of a

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child vaccination mandate and population coverage, suggesting that restrictive policies around exemptions from vaccination mandates may increase compliance.[8–11] These studies alone, however, cannot determine causality and are vulnerable to ecological biases. Other studies have explored the influence of mandates on outcomes such as exemption rate[12,13] and disease occurrence,[14] but disease is affected by many factors including temporal trends, and overall exemptions may mask clustering of unvaccinated populations that may raise the risk of disease outbreak. A focused systematic review comparing studies assessing the preferred outcome of population vaccination coverage is required to assess evidence for or against implementing new vaccination mandate policies. Our aim in this analysis was to inform the ongoing discussion regarding optimal childhood vaccination policy by systematically identifying and synthesizing the existing evidence to answer the question: What is the impact of implementation of school vaccination mandate policies on school-age population vaccine coverage?

Methods

Research design

This systematic review with narrative synthesis is reported according to PRISMA guidelines.[15] In designing and implementing this review, we referred to the *Cochrane Handbook for Systematic Reviews of Interventions*[16] for guidance. The protocol for this nonclinical review of policy interventions was not registered.

Selection criteria

We sought studies published in any language, using any empirical method, to obtain evidence on the effects of implementation of school vaccination mandates on the outcome of population vaccine coverage. Appropriate comparison groups included same-time comparators in locations without mandate changes or pre–post intervention comparisons. Studies that focused on individual school rules rather than regional/government policy, mandates for nonpediatric or nonschool populations, or outbreak-specific policies were excluded, as were nonempirical papers and studies that examined only outcomes other than population vaccine coverage.

Data collection/search strategy

Two of the authors (C.V.-M. and D.G.) searched MEDLINE, Embase, CINAHL, the Education Resources Information Center (ERIC) and the PAIS Index in March 2019 to identify potentially relevant articles (search details provided in Appendix 1, available at www.cmajopen.ca/content/7/3/E524/suppl/DC1). Searches combined database-specific subject headings and keywords for the concepts vaccination, law/policy and schools. Our MEDLINE search strategy was peer reviewed through Peer Review of Electronic Search Strategies (PRESS).[17] We conducted limited searches for grey literature in thesis and dissertation databases, and databases that include conference abstracts and working papers (Appendix 1). References were searched and experts consulted to identify studies, including grey literature, missed by database searching.

Screening and abstraction

Titles and abstracts were independently screened in duplicate by 2 authors (C.V.-M. and D.G.) for relevance. Full texts of potentially includable articles were obtained, and all of the authors reviewed them independently in triplicate. Discrepancies were resolved by discussion among the authors to reach consensus. Included articles were then subjected to a data-extraction process independently in duplicate by 2 authors (D.G. and J.A.B.) (see Appendix 2, available at www.cmajopen.ca/content/7/3/E524/suppl/DC1, for data extraction fields).

Risk of bias

Although we were unable to find a tool to assess the risk of bias that directly applied to all the included studies, 2 authors (J.A.B. and D.G.) independently and in duplicate assessed each included study for potential bias in methods using the bias categories from the ROBINS-I (Risk Of Bias In Non-randomised Studies – of Interventions) tool,[18] adapted for relevance to this specific body of literature.

Data analysis

We synthesized the findings in a narrative manner using methods influenced by Popay and colleagues.[19] Two authors (J.A.B. and D.G.) developed a preliminary textual synthesis of the characteristics and findings of the included studies, based on the tabulated extracted data. In an iterative manner, we explored relations within these data, grouping studies to examine the influence of heterogeneity (e.g., when looking by vaccine, target age group, location, data source, study design or type of mandate) on outcomes due to policy or setting details. We then incorporated our data on assessment of risk of bias into the descriptive synthesis of the included evidence to describe the robustness of the findings and temper the weight of the conclusions.

Ethics approval

As this study was solely literature based, it was not eligible for institutional ethics approval, and none was sought.

Results

Database searches resulted in 4232 unique citations to screen and assess for eligibility, and consulting experts and reference lists revealed 2 additional studies. After screening for relevance and applying inclusion and exclusion criteria, we selected 20 studies for inclusion in the review (Figure 1).

Heterogeneity

Of the 20 included studies, 18 were conducted with US data, 1 was from Italy,[20] and 1 was from Australia.[21] In 4 studies, the investigators looked at school-entry mandates implemented from 1970 to 2017,[20–22] and the remaining 16 (all set in the US) examined adolescent mandates (sometimes referred to as "middle school" requirements) from the 1990s to 2015.[23–38] An uncontrolled before–after design was used in 10 studies, cross-sectional analysis in 7 and retrospective

cohort design in 2, and 1 study was a prospective cohort study. Population size ranged from 583[23] to 954 973,[22] and time frames ranged from single cross-sectional surveys[27,31,38] to a 17-year span.[22] Types of data included parental report, administrative data sets and clinician-verified records, and sources included various iterations of the US National Immunization Survey-Teen,[24,25,30,33,34,37] state/national vaccine registries,[20,22,35,36] school immunization databases,[21,28,29] clinical registries,[26,32] clinic and school sampling,[27,38,39] random-digit-dial survey[23] and the US Health Plan Employer Data and Information Set.[31] The most commonly used data source, the US National Immunization Survey-Teen, is a random-digit-dial telephone survey of parents of adolescents aged 13–17 years in 50 US states and the District of Columbia that been conducted since 2006. Most of the included studies assessed coverage following the addition of new vaccines in a setting with existing mandates (e.g., addition of an adolescent pertussis vaccine dose), although 1 examined a new documentation mandate,[21] 1 examined a tightened exemption procedure,[22] 2 included education mandates,[24,33] and 1 reported on added vaccines combined with stricter enforcement.[20] Table 1 summarizes the methods and findings of included studies.

Risk of bias

Owing to the high degree of heterogeneity, it was difficult to quantitatively compare studies' risk of bias. Drawing on the categories for assessment of risk of bias in the ROBINS-I v.19 tool,[40] we systematically assessed all 20 included articles for potentially biasing limitations in the domains of confounding, comparison groups, data collection, lack of intervention detail and outcome assessment. We found that common biases to

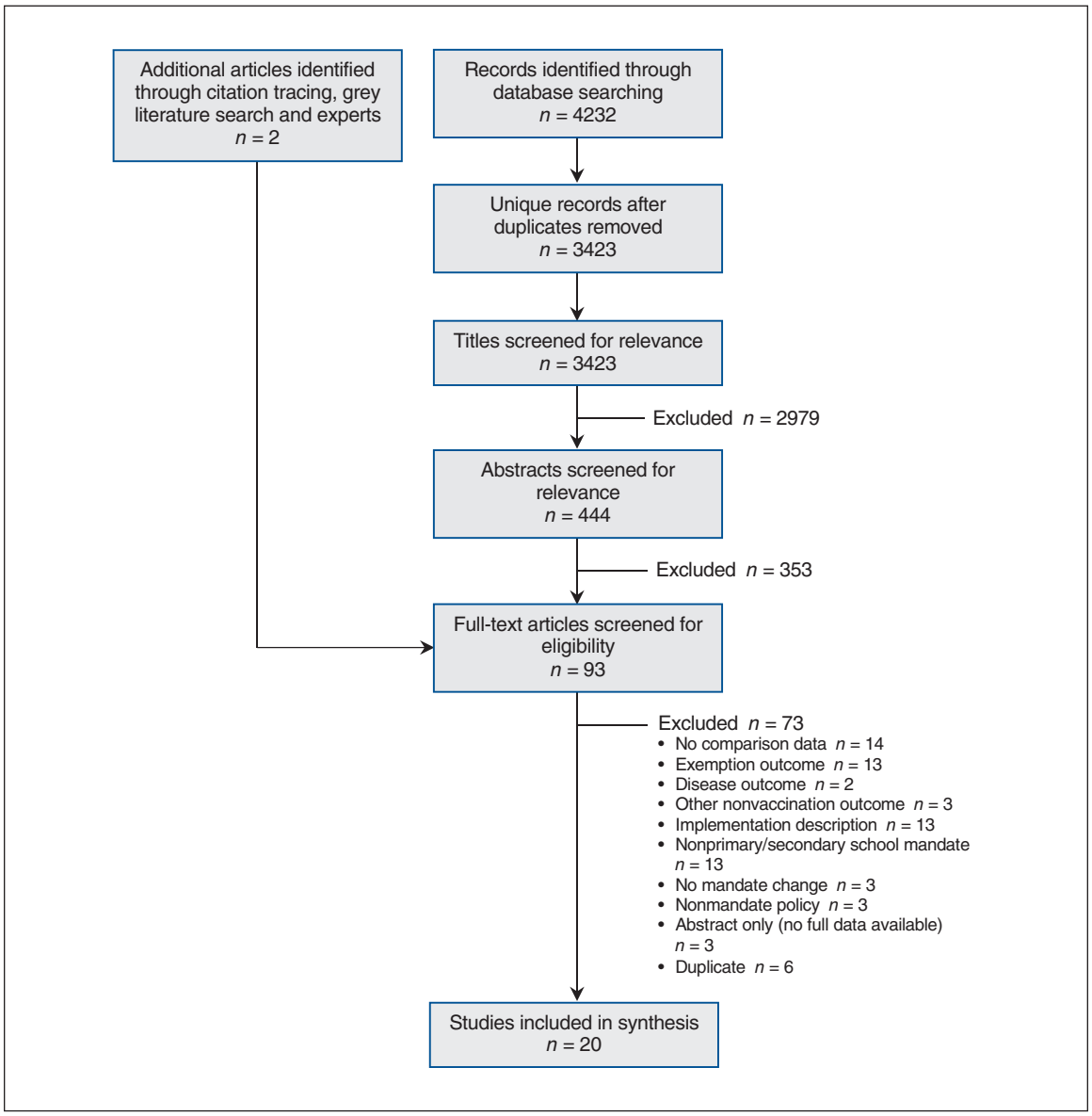

Figure 1: Flow diagram showing study selection.

Table 1 (part 1 of 4): Methods and findings of included studies

Investigator/ year	Setting	Method	Data source (population)	Mandate change studied (year)	Outcome of interest	Main findings
Averhoff et al.,[23] 2004	San Diego, Calif., US	Uncontrolled before–after study using survey data	Random-digit-dial telephone survey in 1998 (*n* = 205) and 1999 (*n* = 378)	7th grade hepatitis B and MMR mandate (1999)	3-dose hepatitis B and 2-dose MMR	• In year mandate took effect, 7th grade students more likely to be vaccinated than other cohorts not subject to mandate • Effect was larger for hepatitis B, which had lower uptake before mandate • No other factors found to be significantly associated with being vaccinated
Bugenske et al.,[24] 2012	US	Retrospective analysis of data from cross-sectional vaccination coverage survey	NIS-Teen 2008–2009 (landline only, provider-verified records only) (2008 *n* = 17 835; 2009 *n* = 20 066)	Middle school vaccination mandate (2008–2009)	Increase in coverage of Tdap, HPV and MCV vaccines, and increase of all recommended vaccines in adolescents 13–17 yr of age	• Tdap and MCV coverage increased from 2008 to 2009 in all states • States with existing or new mandates had higher coverage of Tdap and MCV than states without mandate; however, coverage did not differ among states with new and old mandates • HPV and MenACWY coverage did not differ in states with educational requirements compared to states without educational requirements (no states had educational requirements for Tdap) • Presence of vaccine mandates was not associated with increase in up-to-date status for all vaccines
Carpenter et al.,[25] 2019	US	Difference-in-differences analysis based on retrospective analysis of data from cross-sectional vaccination coverage survey	NIS-Teen 2008–2013 (including cellphone from 2011 onward) (*n* = 116 403)	Middle school Tdap vaccination mandate (2005–2015)	Increase in Tdap coverage at age 10–13 yr in states with Tdap mandates	Tdap uptake about 13% higher in states with mandates, with spillover effects to other vaccines (HPV and MCV)
Cuff et al.,[26] 2016	Virginia, US	Prospective cohort study using administrative data and telephone survey	University of Virginia Clinical Data Repository 2014 (*n* = 908 girls)	6th grade HPV mandate for girls (2009)	HPV vaccine initiation (≥ 1 dose) in girls 11–12 yr of age and proportion vaccinated in 2009 and 2014 cohorts	Mandate had no effect on HPV coverage 5 yr after mandate implementation

Table 1 (part 2 of 4): Methods and findings of included studies

Investigator/ year	Setting	Method	Data source (population)	Mandate change studied (year)	Outcome of interest	Main findings
D'Ancona et al.,[20] 2018	Italy	Uncontrolled before–after study of administrative data	Administrative information database collected by local health units for the Ministry of Health 2013–2017 (entire population; *n* unspecified)	Increase from 4 to 10 required vaccines; imposition of fines up to age 16 yr and exclusion up to age 6 yr for noncompliance (2017)	Polio and measles vaccine by age 7 yr	• Early results indicated slight increase in 2017; statistical significance of change and trends not tested • Increases in uptake of some vaccines among younger children as well
Jackson et al.,[39] 1972	Oklahoma, US	Uncontrolled before–after study of administrative data	1st grade students in 33 randomly selected counties (*n* = 8762)	School entry mandate for diphtheria, tetanus, pertussis, measles and rubella (1970)	3 doses DTP and orally administered polio, 1 dose rubella and measles or record of disease, smallpox vaccine	Increase in vaccination completion in first year of mandate, including for nonmandated smallpox; statistical significance of change not tested
Jacobs et al.,[27] 2004	US	Cohort study using clinical data sample	Practices (*n* = 53) recruited through mailing to doctors in AMA master file and enrolling first practices to respond; 20 adolescent patients (11–15 yr) per pediatric or general practice (*n* = 982 patients)	Middle school entry hepatitis B mandates (pre-2000)	Completion of 2- or 3-dose hepatitis B series	Presence of mandate was strongest predictor of completion of hepatitis B series
Karikari et al.,[28] 2017	Illinois, US	Uncontrolled before–after study of administrative data	Illinois State Board of Education database 2012–2013 and 2014–2015 (*n* = 1 151 993) and CDC survey data from 2012–2014 (*n* not unspecified; data source unclear)	Tdap mandate for 6th–12th grade (2013)	Adolescent Tdap vaccination	Both data sources showed higher Tdap coverage after the mandate, although numbers varied greatly between the 2 data sources
Kharbanda et al.,[32] 2010	New York, NY, US	Uncontrolled before–after study using administrative data from a clinical network	EzVAC, a hospital- and clinic-based vaccination registry, 2006–2008 (*n* = 2577)	6th grade entry Tdap mandate (2007)	Tdap and MCV4 coverage in 11- to 14-year-olds enrolled in EzVAC network	• Tdap coverage increased in both years after mandate, including some shift from Td to Tdap • MCV4 coverage (nonmandated) also increased
Morita et al.,[29] 2008	Chicago, Ill., US	Uncontrolled before–after study of administrative data	Chicago public schools' vaccination database 2000–2005 (*n* = 106 541)	5th grade hepatitis B mandate (1997)	Hepatitis B coverage by grade 12 (overall, and racial/ethnic disparities in coverage)	• Postmandate cohorts had higher hepatitis B coverage rates than premandate cohorts • Disparities in coverage rate by race and ethnicity also decreased after mandate
Moss et al.,[30] 2016	US	Retrospective analysis of data from cross-sectional vaccination coverage survey	NIS-Teen 2009–2012 (unspecified whether provider-verified or all, or whether cellphone included from 2011 on) (*n* = 99 921)	Middle school Tdap, MCV and HPV mandates (various)	Adolescent (13–17 yr) coverage of Tdap booster and MCV, and HPV among girls (1-dose series)	• Tdap and MCV mandates were associated with higher coverage of those vaccines and also of HPV for girls • HPV mandates had no effect

Table 1 (part 3 of 4): Methods and findings of included studies

Investigator/ year	Setting	Method	Data source (population)	Mandate change studied (year)	Outcome of interest	Main findings
Olshen et al.,[31] 2007	27 US states + DC	Cross-sectional study	Health Plan Employer Data and Information Set 2003 (*n* = 100 000)	Mandates for hepatitis B and varicella before 2003 (various)	Policy attribute that is associated with higher mean coverage	• Mandate policy at middle school level was associated with higher mean hepatitis B and varicella coverage • Other policy attributes (e.g., exemptions, payment and deductibles, universal purchasing) not associated
Omer et al.,[22] 2018	Washington State, US	Uncontrolled before–after study using administrative data	Washington State Department of Health 1997–1998 to 2013–2014 (*n* not reported)	New procedures requiring certificate signed by health care provider for medical exemptions (2011)	Kindergarten vaccination rates	• Vaccination rates for each vaccine stayed the same or increased slightly after the policy • Proportion of students up to date for all vaccines increased
Perkins et al.,[33] 2016	US	Retrospective analysis of data from cross-sectional vaccination coverage survey	NIS-Teen 2009–2013 (provider-verified responses only; unspecified whether cellphone included from 2011 on) (*n* = 47 845 parents of girls)	Middle school HPV mandate for girls (DC, Virginia) and HPV education mandate (Louisiana, Michigan, Colorado, Indiana, Iowa, Illinois, New Jersey, North Carolina, Texas, Washington) (various)	HPV vaccine coverage (series initiation, completion) in girls	No difference in HPV coverage between girls in states with school entry vaccine mandates or education mandates compared to no mandates
Pierre-Victor et al.,[34] 2017	Virginia, Tennessee, and South Carolina, US	Retrospective analysis of data from cross-sectional vaccination coverage survey	NIS-Teen 2008–2012 (landline only; excluding those who did not respond about HPV) (*n* = 3203 parents of girls)	Middle school HPV mandate for girls (Virginia) (2009)	HPV vaccine initiation	Trends were not different in Virginia with mandate compared to Tennessee and South Carolina without mandate
Potter et al.,[35] 2014	Michigan, US	Uncontrolled before–after study using administrative data	Michigan Care Improvement Registry (statewide vaccination registry) 2009 and 2010 (2009 *n* = 133 738; 2010 *n* = 131 051)	New mandate at 6th grade entry for Tdap, MCV4, varicella (2010)	Completion of all required vaccines (as a single variable); time to completion (up-to-date status) of all required vaccines; initiation of HPV vaccine (girls only)	Vaccine completion (up to date for all) was higher in year after mandate, and time to completion was shorter
Simpson et al.,[36] 2013	Arizona, US	Uncontrolled before–after study using administrative data	Arizona State Immunization Information System 2006–2011 (*n* = 954 953 records)	New mandate for MCV4 for 6th grade entry if aged ≥ 11 yr (2008)	MCV4 coverage	Vaccine coverage for 12-year-olds was higher after mandate than before mandate

Table 1 (part 4 of 4): Methods and findings of included studies

Investigator/ year	Setting	Method	Data source (population)	Mandate change studied (year)	Outcome of interest	Main findings
Thompson et al.,[21] 1994	Victoria, Australia	Uncontrolled before–after study using administrative data	Victoria Directorate of School Education mid-year census 1991 and 1992 (1576 schools included; 1992 *n* = 45 049 students)	Documentation mandate for school entry (1992)	Submitted documentation of immunization status; documentation of complete (up-to-date) vaccination for age	Small increase in submitted documentation after policy mandate, including small increase in documentation of fully vaccinated students and larger increase in documentation of incompletely vaccinated students
Thompson et al.,[37] 2018	Rhode Island, US	Retrospective analysis of data from cross-sectional vaccination coverage survey	NIS-Teen 2010–2016 (unspecified whether cellphone included from 2011 on; parent report only) (*n* unspecified)	HPV mandate for initiation by 7th grade and completion by 9th grade (2015)	Initiation of HPV series	• Only initiation in boys showed small increase after mandate; no change among girls • No increase among boys in other states
Wilson et al.,[38] 2005	Kansas City, Mo., and Kansas City, Kan., US	Retrospective cohort study of school samples	Random sample of vaccine records from purposive sample of 11 high schools in 2003 (*n* = 2230)	Hepatitis B mandate for elementary school (1997) and middle school (1999) (Missouri)	3 hepatitis B vaccine doses at 9th grade	• Students affected by middle school hepatitis B mandate were more likely to have been vaccinated than earlier cohort in same area or contemporaries in comparison area without mandate • No spillover differences observed for MMR or Td vaccines

Note: AMA = American Medical Association, CDC = Centers for Disease Control and Prevention, MCV = meningococcal vaccines, MenACWY = meningococcal conjugate vaccine for protection against serogroups A, C, W and Y, MMR = measles/mumps/rubella, NIS-Teen = National Immunization Survey-Teen,[40] Td = tetanus/diphtheria, Tdap = tetanus/diphtheria/acellular pertussis.

which this body of literature is vulnerable include confounding, selection bias, measurement bias and bias due to deviation from/variation in implementation of the interventions. All of the included studies were observational assessments of natural experiments rather than studies of interventions designed to be implemented in a controlled manner. Fifteen studies used ecological designs, which are prone to confounding and bias, including ecological fallacy, in which associations identified at a group level are extrapolated to apply to individuals[41] and cannot be relied on as evidence of causality,[42] as an increase or decrease in individual coverage may be due to factors other than the mandate. Several of the nonecological studies, however, recruited study populations that were unlikely to be representative of the larger population, which limited the external validity (generalizability) of the findings. Although some studies described cointerventions, others made no mention of common cointerventions (e.g., outreach programs to improve vaccination awareness, education and access, or changes in vaccine purchasing, coverage and distribution) that may accompany mandatory policies, and little effort was made across all studies to measure or account for the impact of such potential confounders. Studies with pre–post designs varied greatly in the length of baseline and follow-up data, and some had such short periods that a trend could not reliably be established. Any National Immunization Survey-Teen sample is vulnerable to response bias owing to the moderate response rate (55.5% for the landline sample and 29.5% for the cellphone sample in 2016).[43] Landline-only samples (including all pre-2011 surveys) are vulnerable to additional selection bias, non–provider-verified data (including nearly half of National Immunization Survey-Teen responses) are vulnerable to recall bias and social desirability bias by the respondent, and using only provider-verified data risks additional selection bias. Finally, although implementation elements such as messaging parents and consistency of enforcement likely matter greatly in a policy's success, details or measures of implementation factors were rarely mentioned in the studies and were never accounted for in analyses. Table 2 presents this assessment for each study individually, and discussion of these potentially biasing limitations is integrated into the findings below.

Study findings

School entry mandates (typically for age 5–7 yr and applying to a large array of vaccines scheduled from birth to school entry) were found to be associated with increased documentation and/or vaccination in diverse settings. The earliest study

Table 2 (part 1 of 3): Potentially biasing limitations of included studies

Investigator	Confounders, including cointerventions (ecological fallacy, confounding)	Bias in comparison groups (selection bias)	Data collection issues and missing data (selection bias, nonresponse bias, information biases including recall bias and reporting bias)	Lack of detail regarding intervention or implementation (bias due to deviation from or variation in interventions)	Outcome assessment methods or measures (measurement bias)
Averhoff et al.[23]	No measurement or adjustment for important potential confounders (e.g., home learning rates, noncompliance)	–	Self-reported vaccination data from single school district; response rate unknown	Exemption process, consequences for noncompliance and other implementation factors not specified	No external verification of vaccination status
Bugenske et al.[24]	• Ecological study • No measurement or adjustment for important potential confounders	May have been unobserved differences in individuals between states with and without mandates	Analysis limited to landline telephones and responses accompanied by provider-verified records; may not be representative	Policies were grouped together, not allowing for analysis of subtle differences in implementation or context	Follow-up time for policies limited; up-to-date vaccination status defined as 1 dose
Carpenter et al.[25]	Ecological study	• May have been unobserved differences in individuals between states with and without mandates • Age groups as proxy for middle school enrolment may not reflect actual grades affected by mandates in every state	Used 2008 data as proxy for premandate 2004/05 vaccination status; no middle school enrolment data; no premandate data	Multiple state policies grouped together; no accounting for differences	–
Cuff et al.[26]	No measurement or adjustment for important potential confounders	–	Single-centre study; low response rate; participants included only parents seeking care for well-child care visits; may not be representative	–	Only 1 yr of baseline (premandate) data
D'Ancona et al.[20]	• Ecological study • Media campaign cointervention not accounted for	–	–	–	Lack of reliable denominator; no testing for statistical significance of changes; only 1 yr of postmandate data
Jackson et al.[39]	• Ecological study • Known cointerventions included awareness campaigns to public and doctors, improving access through increased clinic days and free vaccines, special measles vaccination campaign in preintervention year, rubella vaccine shortage in preintervention year; effects not measured separately	–	Convenience sample of schoolchildren (not random) from a random sample of school districts	–	No external verification of vaccination status (parent report); no testing for statistical significance of changes; only 1 yr of pre- and postmandate data

Table 2 (part 2 of 3): Potentially biasing limitations of included studies

Investigator	Confounders, including cointerventions (ecological fallacy, confounding)	Bias in comparison groups (selection bias)	Data collection issues and missing data (selection bias, nonresponse bias, information biases including recall bias and reporting bias)	Lack of detail regarding intervention or implementation (bias due to deviation from or variation in interventions)	Outcome assessment methods or measures (measurement bias)
Jacobs et al.[27]	Ecological study	May have been unobserved differences in individuals between states with and without mandates	• Convenience sample of pediatric and family practices; adolescents enrolled only after visiting doctor; 7% excluded owing to incomplete records; unclear how representative this clinical sample is of population • Lack of clarity regarding data collection timelines	Policies grouped together, not allowing for analysis of subtle differences in implementation or context	–
Karikari et al.[28]	• Ecological study • No measurement or adjustment for important potential confounders	–	Included only school-enrolled children in vaccination registry; 2 different data sources for outcome had different results; unclear why differences existed; lack of detail on CDC survey	No information on implementation or context	Unknown to what extent findings can be extrapolated to larger population
Kharbanda et al.[32]	No measurement or adjustment for potential confounders, although did look at spillover effect on nonmandate vaccination	–	• Population from system of only 1 hospital; not representative of larger population; may not be generalizable • Data missing on any vaccines given outside participating hospital system • Only included those with sufficient vaccination information	No information on implementation or context	–
Morita et al.[29]	Ecological study	–	Losses to follow-up (e.g., students leaving school) excluded from analysis	Likely inconsistent enforcement of policy, not captured by study data collection methods	Only 2 yr of postmandate data
Moss et al.[30]	• Ecological study • No measurement or adjustment for important potential confounders	May have been unobserved differences in setting between states with and without mandates	–	Likely inconsistent enforcement of policy, not captured by study data collection methods	Unspecified/ unadjusted for state differences in age/ grade of mandate
Olshen et al.[31]	Ecological study	May have been differences in population with study insurer and population as a whole (representativeness and generalizability)	–	Policies grouped together, not allowing for subtle differences in implementation or context	Full model information not provided
Omer et al.[22]	Other known changes (e.g., in vaccination schedule, exemption forms) before policy change appear to have affected trends	–	Home learners may not have been included	–	–

Table 2 (part 3 of 3): Potentially biasing limitations of included studies

Investigator	Confounders, including cointerventions (ecological fallacy, confounding)	Bias in comparison groups (selection bias)	Data collection issues and missing data (selection bias, nonresponse bias, information biases including recall bias and reporting bias)	Lack of detail regarding intervention or implementation (bias due to deviation from or variation in interventions)	Outcome assessment methods or measures (measurement bias)
Perkins et al.[33]	Ecological study	May have been unobserved differences in setting between states with and without mandates	Included only respondents with adequate provider-verified vaccination history	Policies grouped together, not allowing for subtle differences in implementation or context	Only 1 yr of baseline (premandate) data
Pierre-Victor et al.[34]	Ecological study	May have been unobserved differences in setting between states with and without mandates	Landline-only sample; analysis included only those who responded about HPV	–	–
Potter et al.[35]	Ecological study	–	Home learners may not have been included	–	Only 1 yr of baseline (premandate) and follow-up (postmandate) data
Simpson et al.[36]	• Ecological study • No measurement or adjustment for important potential confounders; known potential confounders include 2005 ACIP recommendation and education/awareness campaign that accompanied mandate	–	Comparison with census data indicates registry may have underestimated coverage	–	–
Thompson et al.[21]	Ecological study	–	Data not available from nongovernmental schools; only schools with kindergarten enrolment included	Not possible to know reason for missing documentation, so unclear whether this represents bias in coverage outcome; some schools may have been more compliant than others	Limited pre- and postmandate data
Thompson et al.[37]	• Ecological study • No measurement or control for potential confounders • Insurance coverage for HPV for boys in other states unknown and may have confounded uptake	"All other states" comparator includes states both with and without mandates	Parent report only (no provider verification)	Implementation details not specified other than difficult to opt out	Only 1 yr of postmandate data
Wilson et al.[38]	Many cointerventions described; no measurement or control for potential confounders	Small school-based population may not be representative; combination of random and purposive sampling; 1 school excluded owing to improper documentation; nonenrolled students excluded (potential selection bias; enrolment in rural areas below target	–	Implementation details not specified	Small sample, insufficient statistical power

Note: ACIP = Advisory Committee on Immunization Practices, CDC = Centers for Diseases Control and Prevention, HPV = human papillomavirus.

showed increased coverage for all vaccines, including one not required by the mandate, in the first year of a 1970 vaccine mandate compared to the previous year.[39] Thompson and colleagues'[21] evaluation of an Australian mandate for school entry vaccination certificates in the 1990s showed increased documentation for all students, with greatest effect among those not up to date with vaccines. Omer and colleagues[22] studied changes to a Washington State vaccine mandate that introduced a requirement for a health care provider signature for exemptions in 2011 and found an increase in the proportion of students who were up to date for all vaccines after implementation. D'Ancona and colleagues[20] reported preliminary numbers following Italy's 2017 decision to add vaccination to an existing mandate and enforce it. They found a small increase in measles/mumps/rubella and polio vaccination among 7-year-old children. Jackson and Carpenter,[39] Thompson and colleagues[21] and D'Ancona and colleagues[20] did not assess the statistical significance of the observed changes. All 3 studies were ecological studies and, thus, vulnerable to confounding, and the investigators reported varying numbers of cointerventions such as awareness campaigns, and reduction of cost and access barriers. The mandate change studied by Omer and colleagues[22] was accompanied by other changes in vaccination education and access, which were not controlled for or assessed. Although the evidence for causality in this group of studies was not strong, all associations were positive.

Twelve of the included studies focused primarily or entirely on adolescent mandates (commonly for grades 5–9, or middle school populations) for vaccines other than human papillomavirus (HPV). These vaccines included hepatitis B, tetanus/diphtheria/acellular pertussis, meningococcal vaccines, measles/mumps/rubella and varicella. All 12 studies were conducted in the US, in jurisdictions with preexisting school entry mandates. These studies showed no increase in uptake associated with educational mandates,[24] but vaccination mandates for these vaccines were positively associated with higher coverage after implementation,[23–25,27–30,32,35,36,38] regardless of data source or study design. Effect sizes varied greatly; in some studies, larger increases were associated with mandates for vaccines whose coverage was lower before the intervention[23,32] or for low-income students,[25] and in 1 study, racial/ethnic disparities in coverage were smaller after the intervention.[29] Spillover effects were observed from 1 mandated vaccine (e.g., tetanus/diphtheria/acellular pertussis) onto other adolescent vaccines (e.g., meningococcal vaccines) in 3 of the 4 studies in which this was examined.[25,30,32] The 1 study that showed no spillover effects from tetanus/diphtheria/acellular pertussis mandates involved a small school-based sample that was unlikely to be representative of the entire population.[38]

The evidence on adolescent HPV mandates in the US told a different story. Four studies did not show an association between HPV vaccine education or mandates for girls and an increase in HPV vaccine coverage.[24,26,33,34] Pierre-Victor and colleagues[34] did find that, independent of mandates, physician recommendation and health care contacts were predictors of HPV vaccination. Thompson and colleagues[37] studied a later-implemented mandate for both girls and boys in a state with high coverage in girls before the mandate and found that rates increased among boys but not girls following the mandate. The study did not disentangle the effect of the mandate and the expanded insurance coverage for boys, which happened at the same time. Three studies showed a small spillover effect of new adolescent mandates for other vaccines onto HPV vaccine uptake,[25,30,35] but only if HPV vaccination was not mandated.[30] This spillover effect was most pronounced among low-income students.[25] The HPV mandate literature consisted of ecological studies and did not examine or control for other contextual or implementation factors, with the exception of the study by Cuff and colleagues,[26] which was a single-centre study of well-child clinic patients and may not be representative of the larger population.

Interpretation

New or tightened requirements for vaccination of schoolchildren were usually associated with increased coverage of the affected populations, with effects appearing larger when preintervention vaccination rates were low. Mandates for HPV vaccination in the US, where there was a high degree of population hesitancy and politicization around the vaccine, were notably ineffective. Spillover effects indicate that health care interactions may be more important than the compulsory nature of mandates and notably had greater impact on HPV vaccine uptake than direct mandates for education or vaccination. The vast majority of the studies were ecological and, thus, vulnerable to confounding and ecological fallacy. Although ecological analyses are important for generating hypotheses and are widely used in epidemiology, they are vulnerable to identifying associations between factors that may be correlative, bidirectional, mediated by other factors, or confounded by unobserved cointerventions or population attributes. Such studies are therefore not typically considered capable of drawing causal conclusions. Few studies examined or accounted for the influence of common cointerventions such as improved access, education, insurance coverage, and changes in vaccine purchasing or costs. Furthermore, implementation and enforcement of vaccine mandates were not examined in most studies, yet poor implementation and/or uneven enforcement may render a policy ineffective.[44]

MacDonald and colleagues[45] outlined 3 reasons jurisdictions implement vaccination mandates: failure of less-coercive methods of encouraging vaccination, outbreak of vaccine-preventable disease and as a final stage in a global disease-eradication project. Mandates considered in the current analysis — whether for documentation, education or vaccination — were enacted in 1 or both of the first 2 of these scenarios, when policy-makers decided such laws were ethically permissible given the safety profile of vaccine supplies and general population acceptance of vaccination.[46] Although school vaccine mandates are commonly considered to have made a major, if not essential, contribution to US vaccine coverage, the causal relations between mandates and population vaccination remain unclear owing to myriad cointerventions and

confounding factors. For example, in cases in which US insurance companies have been reluctant to cover nonmandated vaccines (e.g., HPV vaccine for boys), mandates can increase vaccination rates by acting indirectly on insurers through school vaccine requirements. Therefore, implementing a mandate in a setting in which public coverage for vaccines is already universally offered may not result in an increase in coverage comparable to that seen in jurisdictions with more privatized coverage.

Policy-makers must consider many factors, including the variety of possibilities for exemptions, penalties and rewards, and how the mandate may be implemented, when weighing implementation of new or revised mandates — issues Attwell and colleagues[5] classified as matters of severity and enforcement. Given the potential for a policy to fail to gain compliance, as seen with the US HPV mandates for girls,[24,26,30,33,34,37] such issues are real and present in today's policy landscape. Our findings are largely congruent with those of Lee and Robinson,[47] who found that, in most cases, childhood vaccination mandates through 2015 were associated with higher coverage in the US, with limited evidence of transferability to other settings. A review by the US Community Preventive Services Task Force that included studies published through 2012[48] advised that interventions such as reminder systems and school-based vaccination clinics were cost-effective interventions to promote pediatric vaccine coverage[49] and that such strategies to increase awareness of and access to vaccination could be attempted before proposing or strengthening a mandate.

Limitations

No search is exhaustive, so although we endeavoured to be systematic, transparent and comprehensive in our data collection and inclusion screening, it is possible we may have missed studies that may have been eligible for inclusion. At least 2 reviewers assessed for inclusion at every stage of review, but errors in judgment are possible. In addition, with nearly half of the included studies published within the past 3 years, there may be new studies currently under way that would contribute valuable information to our findings. Older studies, particularly those conducted before the mid-1990s, would have been conducted in an era of substantially different disease prevalence, vaccine products, vaccine schedules, data sources, data management practices and public health policies, which may limit the transferability of their findings to contemporary settings.

Conclusion

Adding well-accepted vaccines to an existing mandate, introducing a mandate in concert with reduction of structural barriers to vaccination or adding documentation requirements all appear to be associated with increased vaccination and/or documentation in most cases. It is unclear, however, to what extent such increases are due to the compulsory nature of the policies or to cointerventions that increase access and awareness. Education or vaccination mandates for highly politicized vaccines are more risky and may fail to be followed by the desired increase or even decrease uptake relative to nonmandate jurisdictions. To further the science of vaccination levers, high-quality implementation research that uses whole-population coverage data and takes into consideration cointerventions, confounders, clustering of unvaccinated populations and context is required. Owing to the risk of backlash, in cases of highly politicized vaccines or jurisdictions without a tradition of mandates, other approaches such as improving access, education and documentation might be tried before moving to mandated vaccination.

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