

LETTER



## HPV vaccine requirements, opt-outs and providers' support: Key studies missing from a recent systematic review

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Vaccination requirements are of perennial interest to parents, policymakers and researchers. In the last decade, school vaccination requirements have generated substantial media attention, with human papillomavirus (HPV) vaccination policies garnering perhaps the greatest attention. Thus, we read with interest the recent review on support for vaccination requirements by Gualano and colleagues<sup>1</sup> that identified 29 articles, including 9 articles on HPV vaccination. However, the review missed at least 8 additional articles on HPV vaccination requirements. The review's search of the literature appears to be the source of the omission.

Systematic reviews must balance *sensitivity*, making searches flexible enough to retrieve as many articles as possible that may be relevant to the research question, and *specificity*, making sure those articles are certainly relevant.<sup>2</sup> When formulating a search strategy, systematic reviews should line up on the side of sensitivity to avoid missing important articles.<sup>2</sup> To evaluate the review's likelihood of an inclusive search, we evaluated its search terms. They were brief: "Compulsory AND vaccination" OR "mandatory AND vaccination."

These search terms do not reflected at least 5 best practices for systematic searches.<sup>2,3</sup> First, the search terms did not include synonyms. "Vaccination" could also be "immunization" or "shots." More worrisome is the absence of the terms "requirements," "policy," and "law." Many researchers and advocates prefer the term "requirements" because it is descriptive without being pejorative. In comparison, the terms "compulsory" and "mandatory" have a negative connotation. Second, the search terms did not include alternative forms. These alternatives could include singular and plural forms (e.g., "vaccination" and "vaccinations") and verb forms (e.g., "vaccinate"). Third, the search terms did not include alternative spellings (e.g., "immunization," "immunisation"), limiting, for example, the representation of journals that use the British spelling for these terms. Fourth, the search terms did not leverage database indexes by using controlled terms (e.g., MeSH terms in Pubmed; Index terms in Scopus). Fifth, the search examined only two databases. Searching multiple databases, such as EMBASE, CINAHL, and

PsycInfo can identify articles in international journals and from disciplines not indexed in for example, traditional US-based biomedical databases such as PubMed. The result of not following these best practices is that the review missed important findings.

To illustrate the limitations of the search, we ran a new ad hoc search of free-text terms in PubMed: ("vaccine" OR "vaccination" OR "vaccinations" OR "immunize" OR "immunization" OR "immunizations" OR "immunise" OR "immunisation" OR "immunisations") AND ("requirement" OR "requirements" OR "compulsory" OR "mandate" OR "mandatory" OR "law" OR "laws" OR "policy" OR "policies"). Following the methods described by Gualano et al., we delimited our search to human vaccines, articles written in English, Italian or French, and articles published after 2000 (we searched records until September 27, 2018, the date when the manuscript was originally submitted to the journal, as the published work did not include the end date for the search). We did not search the Scopus database or MeSH terms in PubMed, nor did we use truncation (to include various word endings) or wildcard symbols (to substitute for any other character or characters in a word). Our search (conducted on June 17, 2019) resulted in 10,628 records, over twice as many as the 4,198 records identified by the published review. Thus, it appears that the review missed at least 6,400 records and did not screen them for inclusion.

To illustrate the limitations of the corpus of articles reviewed, we relied on our knowledge of research on support for HPV vaccine requirements. The review did not include at least 8 articles<sup>4–11</sup> from 8 unique studies that assessed support for HPV vaccination requirements in the US that we are aware of (Table 1). In contrast, the review identified 9 HPV vaccine-related articles, 5 from U.S. populations, 2 articles of which reported on the same study's data. Thus, the review omitted at least half of the relevant articles in this area.

The result of omitting these articles is that the review also missed several key insights. One insight missed by the review is that support for vaccination requirements is substantially higher when surveys describe an opt-out provision.<sup>5,7,8</sup> After describing a policy that allows parents to opt out, support

**Table 1.** Articles reporting support for school-entry requirements for HPV vaccination in the United States.

Author	Location	Sample	Study design & Period	Measure	% of Support
Califano, 2016 <sup>4</sup>	US	Representative sample of physicians who provide direct care in family medicine and pediatrics (N = 775)	Online survey with members of an existing national panel of physicians; April to June 2014.	The survey introduced items with the prompt, "Some states are trying to pass laws that would require all 11 and 12 year-olds to get HPV vaccine before they are allowed to start 6th grade." Respondents then said whether they agreed with the next two statements: "I think these laws are a good idea" and "It is okay to have these laws only if parents can opt out if they want to." Responses were dichotomized as agreeing (strongly agree or somewhat agree) or not agreeing (strongly disagree, somewhat disagree, or neither agree nor disagree).	74% supported laws, with or without opt-out provisions. When opt-out provisions were not specified, 47% agreed that such laws "are a good idea."
Calo, 2016 <sup>5</sup>	US	Representative sample of parents of children aged 11–17 years (N = 1,501)	Online survey with members of an existing national panel of adults; November 2014 to January 2015.	The survey introduced items with the prompt, "Some states are trying to pass laws that would require all 11 and 12 year-olds to get HPV vaccine before they are allowed to start 6th grade." Parents then said whether they agreed with the statement, "I think these laws are a good idea." Parents who did not agree with the previous statement received an additional item: "It is okay to have these laws only if parents can opt out if they want to." For each statement, responses were dichotomized as agreeing (somewhat or strongly agree) or disagreeing/neither (somewhat or strongly disagree, or neither disagree or agree).	21% agreed that laws "are a good idea." If laws included opt-out provisions, agreement increased to 57%.
Kahn, 2009 <sup>6</sup>	Texas	Representative sample of physicians who provide direct care in family medicine, pediatrics, obstetrics/gynecology, and internal medicine (N = 1,122)	Online survey of physicians for whom the Texas Medical Association had email addresses on file; September 2008.	Respondents said whether they agreed with the statement, "HPV vaccination should be mandated for 11–12-year-old girls in Texas." Responses were dichotomized as agreeing (strongly agree or somewhat agree) or not agreeing (strongly disagree, somewhat disagree, or neither agree nor disagree).	41.7% agreed with mandating HPV vaccination.
Robitz, 2011 <sup>7</sup>	Los Angeles, California	Parents of girls aged 11–18 years who were part of a larger study evaluating a pregnancy and STI prevention program in the Los Angeles Unified School District (N = 484)	Telephone survey in English and Spanish; October 2007 to June 2008.	After stating that "some states are trying to pass laws that would require all 11- and 12-year-old girls to get the HPV vaccine before they are allowed to start 6th grade," interviewers asked whether parents agreed with the next two statements, "I think these laws are a good idea" and "These laws are okay only if parents can opt out if they want to." Responses were dichotomized as agreeing (somewhat and strongly agree) or opposing (somewhat and strongly disagree).	58.5% agreed that laws "are a good idea." If laws included opt-out provisions, agreement increased to 92%.
Smith, 2011 <sup>8</sup>	North Carolina	Parents of girls aged 10–18 years who were part of the Carolina HPV Immunization Measurement and Evaluation (CHIME) study (N = 889)	Telephone survey in four rural counties and one urban county; July to October 2007.	After stating that "some states are trying to pass laws that would require all 11 and 12 year old girls to get the HPV vaccine before they are allowed to start 6th grade," interviewers asked whether parents agreed with the next two statements, "I think these laws are a good idea" and "It is okay to have these laws only if parents can opt out if they want to." Responses were dichotomized as agreeing (somewhat and strongly agree) or opposing (somewhat and strongly disagree).	46.4% agreed that laws "are a good idea." If laws included opt-out provisions, agreement increased to 83.6%.
Vercruysee, 2016 <sup>9</sup>	Massachusetts	Parents of girls aged 11–17 years who were seeking care at inner-city public clinic and private practices (N = 129); Primary care providers (N = 34)	Semi-structured interviews conducted in English, Spanish and Haitian Creole; September 2012 to July 2013.	Respondents answered, "Several vaccines are required for school, but the HPV vaccine is not required at this time. How would you feel about requiring children to get the HPV vaccine in order to go to middle school or high school? Why do you feel this way?" For parents, support was reported separately by girls' vaccination status.	Among parents, 63.8% in the Incomplete/Unsure group, 46% in the Not Initiated group, and 32% in the Complete group. Among providers, 32% were in favor, and another 21% would favor but believed the implementation would be difficult.
Wilson, 2017 <sup>10</sup>	Texas	Female college students aged 18–26 years (N = 1,105)	Online survey in two large Texas universities; February to March 2011.	Respondents answered, "A mandate is something that is required by law. Do you think the HPV vaccine should be mandated (e.g., required by law) for those ... ?" Respondents responded separately with "no" or "yes" to the age-groups provided, 9–11 and 12–17 years of age.	13.6% for those aged 9–11 years, and 47.5% for those aged 12–17 years.
Yeganeh, 2010 <sup>11</sup>	Los Angeles, California	Parents of girls aged 11–17 years who were seeking care at a free community clinic (N = 95)	Verbal survey in Spanish and English; May to June 2008.	Parents were asked about their opinions on mandating HPV vaccination for middle school with an opt-out clause giving parents the option of not vaccinating their child (no specific item/responses were described in article).	64% agreed with mandating HPV vaccination.

increased from 21% to 57% among a nationally representative sample of US parents;<sup>5</sup> from 46% to 84% among parents of girls in North Carolina, US;<sup>8</sup> and from 59% to 92% among a Hispanic-majority sample of parents in California, US.<sup>7</sup> This set of studies showed that support for requirements in the US continues to be contingent upon the inclusion of opt-out provisions that would clearly undermine the effectiveness of these laws.<sup>12</sup>

A second insight missed by the review is that providers look much like parents in their support for HPV vaccination school-entry requirements. Three of the missing articles surveyed health care providers.<sup>4,6,9</sup> Their support for laws requiring HPV vaccination ranged from 32% in a qualitative study with 34 providers<sup>9</sup> to 74% in a national sample of 775 physicians who practice pediatrics and family medicine.<sup>4</sup> This range is similar to that for parents. Healthcare providers can be potent advocates for promoting the adoption of vaccination policies (e.g., school-entry requirements) and educational campaigns, often leading or playing key roles in these efforts through their professional organizations.<sup>13</sup>

Our main point is that the previous review, at a minimum, missed many articles. That said, we acknowledge that our new ad hoc search was not exhaustive as we did not search several important databases and did not use, for example, MeSH terms. We also relied on our knowledge of the literature to identify some missing studies but did not systematically screen records using multiple reviewers and independent data extraction. Finally we did not include studies on vaccination requirements for general vaccines or non-U.S. studies. Using these additional approaches would likely reveal even more extensive omissions than we show.

A new systematic review is urgently needed to fully understand support for vaccine requirements. Working with a medical librarian would likely facilitate and improve the quality of reviews from early planning and question formulation stages to dissemination activities.<sup>14</sup> We encourage systematic reviewers to consult with a medical librarian prior to conducting their searches, which is also a best practice.<sup>14</sup> They should also consider preregistering the review using a standard system such as PROSPERO.<sup>15</sup> In the meantime, the current review is better viewed as a narrative review of a part of the vaccine requirements literature.

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Dr. Brewer has received research grants and served as a paid consultant for Merck and the U.S. Food and Drug Administration. Dr. Calo has no financial disclosures or potential conflicts of interest to report.

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