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Socioeconomic differences in childhood vaccination in developed countries: a systematic review of quantitative studies

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Abstract)

Introduction

The reasons for vaccine hesitancy and its relation to individual socioeconomic status (SES) must be better understood.

Areas covered

This review focused on developed countries with programs addressing major financial barriers to vaccination access. We systematically reviewed differences by SES in uptake of publicly funded childhood vaccines and in cognitive determinants (beliefs, attitudes) of parental decisions about vaccinating their children.

Using the PRISMA statement to guide this review, we searched three electronic databases from January 2000 through April 2016. We retained 43 articles; 34 analyzed SES differences in childhood vaccine uptake, 7 examined differences in its cognitive determinants, and 2 both outcomes.

Expert commentary

Results suggest that barriers to vaccination access persist among low-SES children in several settings. Vaccination programs could be improved to provide all mandatory and recommended vaccines 100% free of charge, in both public organizations and private practices, and to reimburse vaccine administration. Multicomponent interventions adapted to the context could also be effective in reducing these inequalities. For specific vaccines (notably for measles, mumps, and rubella), in UK and Germany, uptake was lowest among the most affluent. Interventions carefully tailored to respond to specific concerns of vaccine-hesitant parents, without reinforcing hesitancy, are needed.

Keywords

Child; Child, Preschool; Developed Countries; Infant; Social Determinants of Health; Socioeconomic Factors; Vaccination; Vaccine Hesitancy

1. Introduction

Childhood vaccination is a highly cost-effective intervention that has made it possible to control and even eliminate many vaccine-preventable diseases [1]. Despite the overall high vaccination coverage in children in developed countries [2], several vaccine-preventable diseases (e.g., measles, mumps, and pertussis) have re-emerged [3–6] and pose threats at the individual and community level [3]. This re-emergence has been linked mainly to the persistence of insufficient vaccination coverage among children, due in part to a loss of public confidence in some vaccines or vaccination in general [3,7,8], in a context where controversies have multiplied [9–11]. Today, the public health literature increasingly uses the term vaccine hesitancy (VH) to denote this spreading reluctance toward vaccines [9,12,13]: VH “refers to delay in acceptance or refusal of vaccines despite availability of vaccine services” [14]. Improving our knowledge about the particular population groups most susceptible to VH is a prerequisite for designing suitable interventions to address VH. Reducing social health inequalities among children has become a priority worldwide, including in developed countries [15,16]. It is thus particularly important to examine whether childhood vaccination coverage and parental VH regarding childhood vaccines vary according to parental socioeconomic status (SES) [17], and to explore the reasons for these variations. To help understand them, the World Health Organization Commission on Social Determinants of Health (WHO CSDH) has developed a conceptual framework [18] that shows how structural determinants (e.g., social class) shape health outcomes through intermediary determinants (e.g., material circumstances, behaviors, and the health system, Figure 1) [18,19].

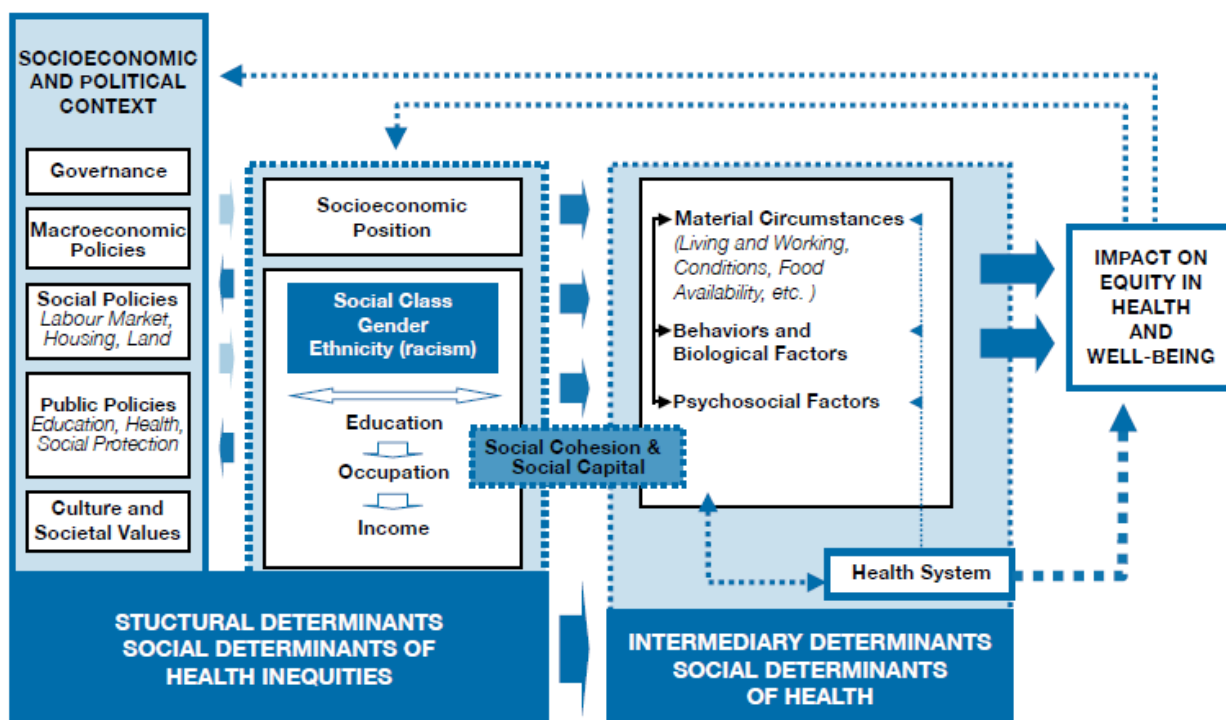


Figure 1. Diagram of the conceptual framework for action on the social determinants of health, World Health Organization Commission on Social Determinants of Health (WHO CSDH). Reprinted with permission from WHO from “A Conceptual Framework for Action on the Social Determinants of Health. Social Determinants of Health Discussion paper 2”, Solar O and Irwin A, Executive summary, Page 6, Copyright (2010) [18].

Note for the reader: In the far left column, the CSDH framework shows how social, economic and political contexts together give rise to a set of socioeconomic positions, whereby populations are stratified according to income, education, occupation, gender, race/ethnicity, and other factors (structural determinants). Moving to the right, this framework depicts how these socioeconomic positions in turn shape specific determinants of health status (intermediary determinants). Intermediary determinants of health include material and psychosocial circumstances, behavioral and/or biological factors, and the health system. This framework also shows that illness can “feed back” into a given individual’s social position (e.g. by compromising employment opportunities and reducing income) and into

socioeconomic and political contexts (e.g., certain epidemic diseases can affect the functioning of social, economic, and political institutions).

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At the health system level, most developed countries have implemented publicly funded national vaccination programs to address financial barriers to access to vaccination (overview of childhood vaccination policies by country available on request). Some of these programs are universal and provide all (or almost all) recommended vaccines free of charge (or at reduced charges) to all children [20,21]. Other programs are addressed to disadvantaged groups, such as the US Vaccine for Children Program (VFC), in effect since October 1, 1994 [22,23]. Individual-level intermediary determinants include in particular parental beliefs, attitudes, and perceptions towards vaccines and vaccination [24,25] (also referred to as cognitive factors in other models [26,27]). Evidence about their social differentiation is mixed [12,13,28].

Our bibliographic search (see next section) found a lack of systematic reviews specifically designed to document the extent of SES inequalities in childhood vaccine uptake in developed countries where major financial barriers to access vaccination have been addressed or to explore the potential mediating effect of cognitive determinants where such inequalities are observed. We thus performed this systematic review to analyze evidence about the associations between parental SES and 1) childhood vaccine uptake, distinguishing types of vaccines; and 2) cognitive determinants of parents' decisions about childhood vaccination.

2. Methods

We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [29] as a guide to design, conduct, and report the results of this systematic review (completed PRISMA checklist in Supplementary Table 1).

2.1 Search strategy

We searched Medline, the Web of Science Core Collection, and PsycINFO from January 1, 2000, to April 12, 2016, for original articles in English, using a combination of terms referring to childhood vaccination uptake, its cognitive determinants [30], and SES [31]

(Supplementary Table 2). The reference sections of the articles for review were also examined to supplement the search. We began the search in 2000 to include studies conducted after the implementation of some major national vaccination programs.

2.2 Study selection

As recommended by the PRISMA statement, we defined the following criteria for this review:

- Population: Children (birth to 12 years) [32] (with the exception of very specific groups, such as exclusively low-SES or chronically ill children) and their parents living in developed countries ranked “very high” in the 2014 United Nations (UN) Human Development Index (HDI) [33];
- Intervention: Not applicable;
- Comparator: SES (education, occupation, income, or any combination of these variables);
- Outcomes: Childhood vaccine uptake and cognitive determinants of the parental decision about their child’s vaccination (Supplementary Text 1) [26], with the exception of outcomes for the human papillomavirus vaccine (reviews examining social inequalities in its uptake already available [34–36]) and for vaccines not publicly funded during the study period.
- Study design: Longitudinal, cross-sectional, case-control studies.

Additional criteria were: results from multivariate analyses; data collected in 2000 or later (see Supplementary Text 2 for detailed explanations of these criteria); and at least a moderate global quality rating according to an adaptation of the Effective Public Health Practice Project, a quality tool for quantitative studies (Supplementary Text 2 and Supplementary Table 3) [37,38].

Two authors (AB, with either PV or PPW) independently assessed abstracts and then full texts against these criteria. Differences between authors were resolved by consensus.

2.3 Data extraction

We extracted information about study design and population, vaccines, outcome measures, SES measures, the main results regarding associations between SES and vaccination uptake or its cognitive determinants, and factors examined in multivariate analyses and recorded it in a standardized form (see Supplementary Table 4).

3. Results

3.1 Articles identified

The database search generated 1096 articles; another 14 were identified from other sources (Figure 2). After removing duplicates, we reviewed 882 abstracts, assessed 148 full-text articles for eligibility, and finally included 43 articles from 41 studies.

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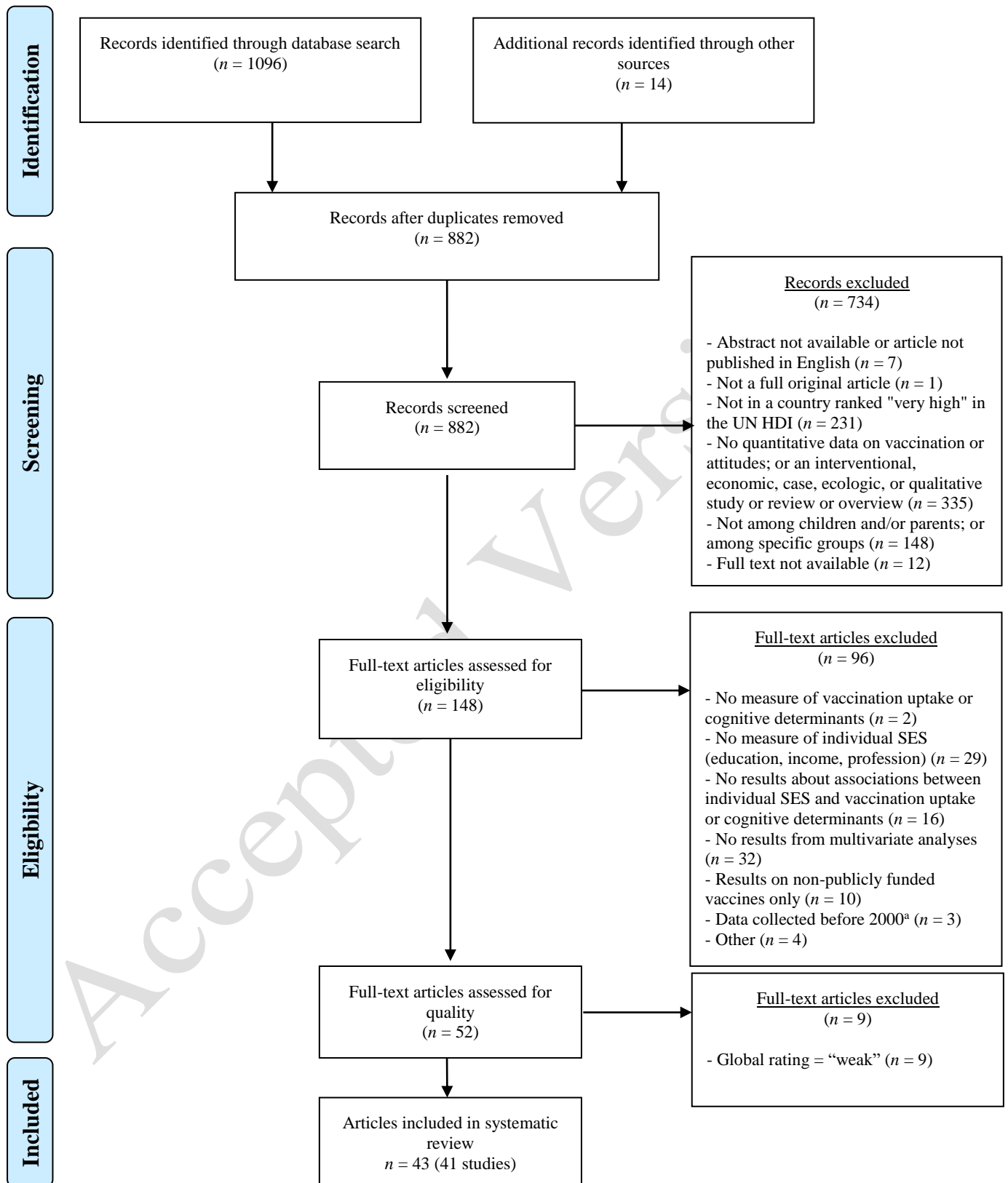


Figure 2. Flow diagram of study selection procedure for this systematic review of the association between socioeconomic status (SES) and childhood vaccination uptake and/or its cognitive determinants

UN HDI: United Nations Human Development Index

^aWe began the search in 2000 to include studies conducted after the implementation of some major national vaccination programs; in the United States, for example, Vaccine For Children Program began in the mid-1990s.

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3.2. SES and childhood vaccination uptake

3.2.1 Study characteristics

Of these 43 articles, 36 (34 studies) reported results about associations between parental SES and childhood vaccination uptake; global quality was rated strong for 19 [39–57] and moderate for 17 [58–74]. North America accounted for 16 articles (US: 13 [39–45,56,60,61,71,72,74]; Canada: 3 [58,59,70]). The others (18) came from Europe (Belgium:5 [46,47,52,57,73]; the UK: 5 [50,66–69]; Ireland [49,55], Germany [53,54], Greece [48,62], and Italy [63,65]: 2 each), and Australia (2 [51,64]). Study design was cross-sectional in 27 articles [39–44,46–50,52–54,56,57,61–65,68–70,72–74], cohort in 6 [45,51,55,66,67,71], and case-control in 3 [58–60]; 15 used data representative at the national level (US: 9 [39–44,56,60,61]; UK: 2 [50,67]; Australia [64], Germany [54], Greece [48], and Ireland [49]: 1 each); others were conducted at the state/regional (8) [45–47,52,57–59,73] or local level (municipality: 11 [51,55,62,63,65,66,68–72]; county/district: 2 [53,74]). Only one study used an SES composite indicator combining information on parents' educational level, occupation, and household income [54]. Vaccination data came from medical records or databases in 20 articles [39–45,49,51,55,56,58–60,65,66,68,69,71,73], from children's vaccination booklets transcribed by investigators in 9 [46–48,52–54,57,61,62], from parents using their children's vaccination booklets in 2 [64,74], and from parent-reported data alone in 5 [50,63,67,70,72]. Twenty studies analyzed completion of series of several recommended vaccines, i.e., completion of the vaccine schedule for all included vaccines with no detail on which specific vaccines of the series had or had not been administered; seven also focused on at least one other vaccine not included in the series (see references below in sections 3.2.2 to 3.2.7). Thirteen studies reported results on MMR vaccine, and 8 on pneumococcal, meningococcal C, and/or varicella vaccines. Other specific vaccines studied were those against seasonal influenza (3), rotavirus, hepatitis B, and polio (2 each), hepatitis A, pertussis, and

Haemophilus influenzae type b (Hib) (1 each). Vaccination program and market types differed according to country and vaccine (overview available on request). In the US, recommended vaccines are delivered free of charge only to children from disadvantaged families (non-universal program), except in a few states with universal purchase policies. All of the other countries included in this review have implemented universal vaccination programs and deliver vaccines free of charge to all children during the relevant study periods, with a few exceptions (see details below in sections 3.2.2 to 3.2.7).

3.2.2 Series of recommended vaccines

Twenty studies [39–51,58–64] reported completion of series of vaccines (Table 1 and Supplementary Table 4). Series included at least the DTP, polio, and Hib vaccines in 13 studies; the other vaccines included in series were for hepatitis B (12), MMR (10), varicella (4), and pneumococcal and meningococcal C infections (3 each). Sixty percent of the 20 studies found higher completion rates among high-SES children, and 30% found no significant association for any outcomes (the remaining two studies found lower rates among high-SES children). These percentages were respectively 50% and 42% in the 12 studies of countries/states where these series are provided in universal programs [45–51,58,59,62–64]; and 75% and 13% among the 8 nationwide US studies [39–44,60,61]. For instance, results from the 2007 US National Immunization Survey showed a lower probability of full vaccination for series of recommended vaccines among children whose mothers had less than 12 years of education compared to those whose mothers had a college degree (aOR [95% CI] = 0.73 [0.63-0.84]) [43].

To analyze SES differences in vaccine uptake according to the type of outcome, we focused on 4 studies that examined both completeness and timeliness of vaccination during the recommended time periods: children were old enough to have received complete series of recommended vaccines (from 18-24 months to 6 years, depending on the study). One US

study [39] reported higher vaccination rates among high-SES children for both outcomes; 2 (1 Belgian, 1 Greek) [46,48] found that the timeliness of vaccination was better among high-SES children but found no significant association for complete vaccination; and 1 Greek study [62] found no significant association for timeliness_or completion rates at different ages (12 and 24 months).

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Table 1. Number of studies reporting results about various associations between socioeconomic status (SES) and vaccination uptake, by type of vaccine and country^a

Vaccine/country	Higher rates of vaccine uptake among high-SES children	Lower rates of vaccine uptake among high-SES children	No significant association	Mixed results^b	Total
Series of recommended vaccines	12	2	6	0	20
Canada	1 [58] ^{F-all}	0	1 [59] ^{F-all}	0	2
US	6 [39,41–44,60] ^{F-lowSES}	1 [40] ^{F-lowSES}	2 [45] ^{F-all} , [61] ^{F-lowSES}	0	9
Belgium	2 [46,47] ^{F-all}	0	0	0	2
Greece	1 [48] ^{F-all}	0	1 [62] ^{F-all}	0	2
Ireland	1 [49] ^{F-all}	0	0	0	1
Italy	0	0	1 [63] ^{F-all}	0	1
UK	0	1 [50] ^{F-all}	0	0	1
Australia	1 [64] ^{F-all}	0	1 [51] ^{F-all}	0	2
<u>MMR</u>	2	5	5	1	13
US	1 [44] ^{F-lowSES}	0	0	0	1
Belgium	1 [46,52] ^{F-all, c}	0	1 [47] ^{F-all}	0	2
Germany	0	2 [53,54] ^{F-all, d}	0	0	2
Ireland	0	0	0	1 [55] ^{F-all, b}	1
Italy	0	0	2 [63,65] ^{F-all}	0	2
UK	0	3 [66–68] ^{F-all}	1 [69] ^{F-all}	0	4

Australia	0	0	1 [51] ^{F-all}	0	1
Pneumococcal					
infections,	4	1	3	0	8
meningitis C,					
varicella					
US	3 [39,41,56] ^{F-lowSES}	0	0	0	3
Belgium	1 [47] ^{F-all}	0	1 [46] ^{F-all}	0	2
Greece	0	1 [62] ^{partial-F, e}	0	0	1
Italy	0	0	1 [63] ^{F-all}	0	1
Australia	0	0	1 [51] ^{F-all}	0	1
Seasonal					
influenza	1	1	1	0	3
Canada	0	1 [70] ^{F-all}	0	0	1
US	1 [71] ^{F-lowSES}	0	1 [72] ^{F-lowSES}	0	2
Rotavirus					
Belgium	2 [57,73] ^{partial-F}	0	0	0	2
Hepatitis B					
Belgium	1 [46] ^{F-all}	0	0	0	1
Germany	0	1 [53] ^{F-all}	0	0	1
Hepatitis A					
US	0	1 [74] ^{F-lowSES}	0	0	1
Polio,					
pertussis, Hib	3	0	0	0	3
separately					
US	1 [44] ^{F-lowSES}	0	0	0	1

Belgium	1 [46] ^{F-all}	0	0	0	1
UK	1 [66] ^{F-all}	0	0	0	1

Hib: *Haemophilus influenzae* type b

MMR: measles, mumps and rubella

UK: United Kingdom

US: United States

F-all: Vaccines free for all children.

F-lowSES: Vaccines free for disadvantaged children only.

Partial-F: Vaccines partially free.

^aCountries are sorted by World Health Organization (WHO) region, and then by alphabetic order.

^bResults differed with the SES indicator used (Ireland, 2007, children aged 5 years: higher odds of not receiving MMR vaccine among children with mothers who had a higher level of education, and with a family income <£300 per week) [55].

^cTwo articles from the same study.

^dIn 1 [54] of these 2 German studies, the association between a high SES and non-immunization against MMR was no longer significant when parental reservations about vaccination were included in the model.

^eIn this study, the outcome was: “age-appropriate immunization with three vaccines (meningococcal C, 7-valent pneumococcal, varicella) at 24 months.”

3.2.3 Vaccines against measles, mumps, and rubella

Combined MMR vaccine

Thirteen studies reported results about associations between SES and uptake of MMR vaccine [44,46,47,51–55,63,65–69] vaccines. These 13 studies took place in countries where the MMR vaccine was provided free of charge to all children, except one in the US [44]. Two studies (1 Belgian, 1 US) found a lower vaccine uptake in children from low-income households, and one Irish study found mixed results (Table 1). Five studies found no SES differences in vaccine uptake, regardless of outcome (e.g., on-time doses 1 and 2 [69]). Finally, 5 studies reported lower vaccine uptake among high-SES children (Table 1): 3 in the UK and 2 in Germany. For example, results from the Millennium Cohort Study (UK, 2000-2005) showed that children were at a higher risk of being unimmunized by age 3 if their mother had at least a degree vs no diploma (aRR [95% CI] = 1.41 [1.05-1.89]) [67]. One of the German studies [54], focusing on measles vaccine, also included monovalent vaccines; but they were not analyzed separately from combined MMR vaccines (personal communication from the author). In this study, the initial association was no longer significant after adjustment for parental beliefs about vaccination (Supplementary Table 4).

At least one monovalent vaccine

One of the British studies cited above [67] also focused on monovalent vaccines (measles, mumps, or rubella), and found that highly educated mothers used at least one these self-paid vaccines more frequently than less educated ones (aRR [95% CI] = 3.15 [1.78-5.58]) as did those from the wealthiest households compared to those from the poorest (aRR [95% CI] = 2.98 [2.05-4.32]).

3.2.4 Vaccines against pneumococcal infections, meningitis C, varicella, or series of these 3 vaccines

Eight studies focused on pneumococcal, meningococcal C, and/or varicella vaccines [39,41,46,47,51,56,62,63]. In the US, all 3 national studies providing results on these vaccines found lower rates of pneumococcal [41,56] and varicella [39] vaccine uptake among low-SES children. For example, results from the 2004 US National Immunization Survey showed a lower probability of age-appropriate receipt of 4 doses of pneumococcal vaccine (PCV7) at 24 months among children whose mothers had less than 12 years of education vs a college degree (aOR [95% CI] = 0.63 [0.48-0.83]) [56]. Conversely, in Greece, where these vaccines were only partially free of charge during the study period (2010-2011), children of highly educated mothers were less likely to be immunized against these diseases at 24 months (>13 years vs ≤ 12 years: aOR [95% CI] = 0.42 [0.19-0.94]) [62]. Four other studies took place in countries where these vaccines were provided free of charge to all children, and three found no significant association between SES and vaccine uptake; another found lower uptake rates among low-SES children (Table 1).

3.2.5 Vaccine against seasonal influenza

In the US, vaccination against seasonal influenza (free for disadvantaged children only) has been recommended to all children aged 6-23 months since 2004; this recommendation was expanded in 2008 to all children aged 6 months to 18 years [75]. In Canada, vaccination against influenza is also recommended for all those aged 6 months and older (since 2000 in some jurisdictions) and is provided free of charge for those aged 6 months to 17 years [70]. One Canadian [70] and two US [71,72] studies (conducted between 2004 and 2008) showed inconsistent results for an association between parental SES and childhood vaccination against seasonal influenza (Table 1).

3.2.6 Vaccine against rotavirus

In Belgium, the rotavirus vaccine has been recommended since 2007 and is only partially free of charge. Two Belgian studies focusing on this vaccine found higher vaccination rates among

high-SES children [57,73]. For example, in 2012, in Flanders, children of unemployed mothers were at higher risk of incomplete vaccination against rotavirus than children whose mothers received full-time salaries (aOR [95% CI] = 2.56 [1.35-5.00]) [57].

3.2.7. Other, less frequently studied/recommended vaccines

Few studies analyzed other recommended vaccines separately, although some were included in series (see section “Series of recommended vaccines”). Two studies found inconsistent results about SES differences in vaccine uptake for hepatitis B [46,53] (Table 1). One US study conducted in San Diego County focused on vaccination against hepatitis A, recommended on a routine basis there; it found lower rates of vaccine uptake among children whose mothers had a high educational level [74]. Finally, 3 studies (1 Belgian, 1 UK, 1 US) that analyzed vaccines against polio, pertussis, and Hib separately found higher rates of vaccines uptake among high-SES children [44,46,66] (Table 1).

3.3 SES and cognitive determinants of parents’ decisions about childhood vaccination

3.3.1 Study characteristics

Nine studies reported information about associations between SES and cognitive determinants of parents’ decisions about their children’s vaccinations. The global quality rating was strong for 3 [54,76,77] and moderate for 6 [60,78–82]; 5 took place in the US [60,76,79,80,82], and the others in Austria [81], Germany [54], Italy [77], and Australia [78] (1 each). Four were representative at the national level (US: 3 [60,76,79]; Germany: 1 [54]); others were conducted at the regional/state (2 [78,82]) or municipal level (3 [77,80,81]). Participants were mostly mothers. One study used an SES composite indicator [54].

3.3.2 Confidence in vaccines

Three studies (2 from the US, conducted in 2001 and 2004 [60,79], and 1 Australian, conducted in 2011 [78]) found higher levels of confidence in vaccine safety among people with higher educational levels [78] or income [60] or both [79]. One Austrian study (Vienna,

2008-2009) found a lower level of confidence in vaccines among people with high educational levels [81]. In a German survey (2003-2006), preference for natural immunity was more frequent among parents with high vs low SES (aOR [95% CI] = 4.76 [3.50-6.46]) [54].

3.3.3 Behavioral intention

One Italian study (Milan, 2013) found that willingness to have their children vaccinated with the new-generation MenB vaccine was lower among mothers with a high educational level (degree vs middle school: aOR [95% CI] = 0.68 [0.47-0.97]) but did not vary according to father's educational level or parents' employment status [77].

3.3.4 Other cognitive/behavioral elements

A study of a representative sample of the US general population conducted in 2004 [76] distinguished four subgroups of parents according to their beliefs and behaviors in past vaccinations: one subgroup had had their children vaccinated despite uncertainty about whether this was the right thing to do (9% of the sample); another had delayed their children's vaccinations (13%); the third had refused any childhood vaccinations (6%); and the fourth group accepted childhood vaccinations without any doubts (72%). The study found no SES difference between any of these groups. Similarly in the US (Seattle, 2010-2012) [80], no significant association was found between parental SES and VH, measured by the Parent Attitudes About Childhood Vaccines (PACV) questionnaire. On the contrary, in two other US studies, parents with a high educational level were the most likely to have ever refused or delayed a vaccine for their child (US, 2001, college vs high school: aOR [95%CI] = 2.8 [1.2-6.5] [60]; North Carolina, 2010, at least college vs high school or less: aOR [95% CI] = 2.45 [1.30-4.63]) [82]).

3.3.5 Contribution of SES differences in parental beliefs to SES differences in childhood vaccination uptake

One study carried out in Germany between 2003 and 2006 [54] found an association between a high SES and non-immunization against MMR that was no longer significant after adjustment for parents' preferences for natural immunity (mostly reported by high-SES parents). The authors concluded that parents' preferences for natural immunity may play a mediating role between parental SES and children's vaccination against MMR.

4. Discussion

4.1 Methodological issues in the studies

First, we must note that most of the studies included in this review came from the US, especially those with nationally representative results. Fewer studies were available in other developed countries, and they most frequently reported regional/local findings. This prevents us from drawing any general conclusions about the existence and patterns of social differentiation in childhood vaccination at the national level in many countries or about their potential subnational geographical variation.

Four studies [63,67,70,72] used parent-reported data on childhood vaccination uptake. The validity of Texan parents' recall of their child's immunization history (compared with provider records) depended on the vaccine (overestimation for one dose of MMR, underestimation for total doses of DTP and polio) and the child's age, but not on parental SES [83]. It is nonetheless difficult to generalize from this study to the others using self-reported data in different contexts. Validation studies comparing parents' self-reported data and objective uptake data should be encouraged in countries where vaccination records are lacking or not routinely accessible.

One problem we faced in comparing the 9 studies of cognitive determinants of parents' decisions about childhood vaccination included in this review was the great variability of the questionnaires used to measure these aspects, in terms of the type and number of questions and in the modes of response. An instrument (PACV [84]) of verified validity and reliability

was used in only one study [80]. Few instruments assessing cognitive factors associated with vaccine behaviors and/or vaccine hesitancy have thus far been validated [30,85].

Another problem stems from the lack of a theoretical framework in most studies included in this review; when one was mentioned, it was most frequently the Health Belief Model [43,51,71,72], as noted in another public health field (HPV vaccination) [86].

Finally, we found no studies exploring SES differences in other potentially important determinants of childhood vaccination (e.g., trust toward health authorities or interpersonal factors such as peer influence or medical advice) [87].

4.2 Understanding the variation in childhood vaccine uptake according to parental SES

The WHO Commission of Social Determinants of Health conceptual framework [18,19] underlies our discussion of the role of two types of intermediary factors: those related to the health system, especially vaccine accessibility, and parental cognitive determinants of childhood vaccination.

4.2.1 Factors related to the health system: vaccine accessibility

Publicly funded national vaccination programs are intended to address problems of vaccine affordability and reduce SES differences in childhood vaccine uptake. We found higher completion rates among high-SES children for series of vaccines in about half of the studies from countries/states with universal access to free vaccines, and in two thirds of the studies focusing on partially free vaccines. In the US, where programs are non-universal except in a few states, completion rates are higher for high-SES children in three quarters of nationwide studies (including the 2013 National Immunization Survey [44]). This suggests that residual financial constraints persist despite these national vaccination programs. These constraints may exist especially where vaccines are provided at reduced cost but not entirely free of charge (e.g., rotavirus vaccine in Belgium), or when programs are not universal (e.g., in the US). Financial barriers may also remain despite universal programs, especially when these

programs do not cover the costs of the fees to providers for vaccine administration (e.g., in Australia [21] or in Belgium when vaccine is administered by a private physician [47]). Other barriers to vaccination access can include the travel and time costs of taking the child to the doctor. These barriers may be particularly acute when pathways to this access are complex. In France for example, most parents have their children vaccinated in the private sector. They must first see the physician to obtain a prescription for the vaccine, visit the pharmacy to pick up the vaccine, and then return to the physician's office for the vaccination [88]. Beyond these convenience factors, as they are labeled by the WHO Sage group [14], the role of other factors should be stressed, and there is a need for a better understanding of how they affect uptake [44].

4.2.2 Intermediate factors: parental cognitive determinants of childhood vaccination

The results of our review are in line with those of previous studies (including overviews and qualitative studies) [28,89,90] that suggest the coexistence of different patterns of social differentiation of parental beliefs toward vaccination according to type of belief, vaccine, and country. Moreover, consistently with previous studies in other health fields (e.g., cancer screening [91] and sun-protection behaviors [92]), there is some evidence that cognitive factors play a role in mediating SES differences in childhood vaccination [54,93].

First, some studies included in our review suggested that low-SES parents are less confident about the safety of childhood vaccination than high-SES parents [60,78,79]. This finding, common to numerous risk perception studies in various fields including vaccination [34–36], shows that, generally speaking, lower SES is associated with perceptions of higher risks [94]. Material deprivation and social isolation can fuel a feeling of powerlessness and vulnerability when faced with any kind of threat [95]. However, such theories fail to explain results of other studies suggesting lower level of confidence in vaccines in general [54,81] and greater reluctance about new vaccines (e.g., meningococcal B) [77] among high-SES parents. Nor do

they explain the lower rates of MMR vaccine uptake among high-SES children reported in 5 of 6 UK and German studies included in this review [53,54,66–68]. Sociological theories developed in the tradition of the sociology of risk [95–97] offer potential explanations for understanding these observations. These theories posit that high-SES parents are more committed than low-SES parents to “healthism”, a cultural trend in which individuals are encouraged to exercise control over their own behaviors and use information disseminated by health authorities to maximize their life expectancy [98]. The link between healthism and vaccine reluctance is quite obvious in several studies [99–101]. Moreover, in contemporary “risk societies”, wealthier and more educated people have a stronger perception of “manufactured risks” (i.e., risks produced by science and industry) and may develop a sense of distrust toward science, especially “official” science and experts [97]. A theoretical framework is needed to improve our understanding of the variability of social differentiation of parental beliefs toward childhood vaccination. A recent article proposes building such a framework by considering simultaneously the levels of parent confidence in health authorities and commitment to healthism [13].

4.3 Implications for health policy and future research

In some but not all settings where programs exist to reduce the out-of-pocket costs of childhood vaccinations, children from lower SES backgrounds remain less completely vaccinated than those from higher SES backgrounds. This suggests two main avenues of intervention and research. First, efforts should be made to further address and reduce the residual financial and convenience barriers that may remain for some low-SES families. This may include providing all mandatory and recommended vaccines 100% free of charge, regardless of place of care (public organization or private practices); for instance, this was one of the main recommendations produced by the recent French public debate on vaccination [88]. Including the reimbursement for vaccine administration in the vaccination program

[102,103] and facilitating access to vaccination in countries where pathways are complex (e.g., making vaccines available at the physician's office) [88] may also reduce convenience barriers. Universal programs appear more effective in reducing SES inequalities in vaccine uptake than non-universal ones [41]. These necessary efforts may not be sufficient, however, without addressing appropriately the cognitive barriers that may hamper vaccination uptake in low-SES people.

Second, this review suggests the existence of different patterns of social differentiation of parental beliefs toward vaccination. This finding relies on a limited number of studies with some methodological limitations, and further research is needed, including efforts at methodological improvements (especially the development of validated instruments). More research is needed to document the reasons for these socioeconomic differences in developed countries. Guidelines to develop and validate instruments are warranted to improve the reliability and comparability of results [85].

As already underscored, given the variability of contexts throughout developed countries, an effective "one size fits all" intervention is unlikely to exist [104]; interventions adapted to the context and the target populations are needed and should apply promising strategies and evaluate them rigorously [104]. In particular, context-driven, multicomponent interventions (including especially parents education, home visits, telephone reminders, healthcare workers' training and prompts) have proved to be effective in increasing vaccine uptake among low-SES children [105]. There is also an urgent need to revise communication strategies about vaccines and to move beyond "knowledge deficit models of communication" [106]. For high-SES parents who decline some vaccines (MMR in particular), interventions tailored to respond to specific concerns and beliefs are necessary, despite the current lack of evidence about what actually works [104]. Such interventions must be carefully designed since

messaging that advocates vaccination too strongly may reinforce the vaccine hesitancy of already hesitant parents [104].

Moreover, health care professionals, especially pediatricians and primary-care practitioners, play a key role in parental decisions about vaccination [107], and recent studies have emphasized that cognitive barriers may also exist among some of them [108]. Interventions and strategies to address these issues are also necessary [109]. Finally, a complete revision of the content of education about vaccination during initial medical training and the methods used to teach it in both initial and continuing medical education is necessary. New methods are required to help physicians develop the skills to respond to their patients' vaccine hesitancy [109].

4.4 Strengths and limitations of this systematic review

This systematic review has several strengths: 1) it specifically addresses SES differences in both childhood vaccine uptake and its cognitive determinants and thus enables a detailed analysis of types of vaccines and of outcomes; 2) it follows a standard process, applying the PRISMA statement and the PICOS checklist; additionally, two authors independently assessed the quality of the selected studies; 3) it is limited to studies reporting results from multivariate analyses, to control for some potential confounders of the associations between parental SES and childhood vaccine uptake, such as parental age; 4) by focusing on countries ranked “very high” on the UN HDI that have implemented national vaccination programs, and in those countries, on vaccines at least partly publicly funded, we were able to limit heterogeneity in socioeconomic contexts and vaccine availability and affordability across countries. Nonetheless, differences in vaccination policies and programs remained (e.g., universal programs *versus* programs targeting disadvantaged children) and justified stratification by country (Table 1).

Nevertheless, our results should be interpreted with the following limitations in mind: 1) despite a systematic search, we might have missed some articles; 2) as in any systematic review, we cannot exclude a publication bias — overrepresentation of positive, statistically significant results; this is unlikely, however, since most studies in this review were not intended to examine specifically the associations between SES and vaccine uptake and/or its cognitive determinants; 3) we focused on articles in English, but this should not explain the underrepresentation of several developed countries since only 4 articles were published in another language (French: 2; German: 1; Chinese: 1); 4) 33 of the 43 studies included in the review used data collected in 2010 or before, which raises a question about whether our conclusions apply today and highlights the need for new studies based on recent data. Nonetheless, one study published in 2016 and based on one of the most recent US National Immunization Surveys has confirmed the persistence of social inequality in childhood vaccination in the US [44].

5. Conclusion

This systematic review focused on developed countries with publicly funded national vaccination programs (universal or not) and on vaccines delivered free or at least at reduced cost. It identified 36 articles analyzing SES differences in childhood vaccine uptake. Results varied across types of vaccines and countries. For series of recommended vaccines, we found some evidence of higher completion rates among high-SES children in several settings where universal programs provide 100% free vaccines to all children; this inequality was still more notable in the US where 100% free vaccines are delivered to disadvantaged groups only. Such a gradient was also found for some vaccines only partially free of charge (e.g., rotavirus in Belgium). For the MMR vaccines, we found some evidence of an inverse relation (i.e., lower vaccine uptake among high-SES children) in several settings, especially the UK and Germany.

We identified only 9 studies (from 5 different countries) analyzing SES differences in cognitive determinants of parents' childhood vaccination decisions, and results were inconsistent. The only study that analyzed the potential mediating effect of parental beliefs on the relation between SES and childhood vaccine uptake found such an effect.

Expert commentary

Reducing social health inequalities among children remains a priority in many developed countries. Given the context in the field of vaccination – persistence of insufficient vaccination coverage among children and spreading reluctance to use vaccines — it is particularly challenging to determine whether childhood vaccination coverage and parental vaccine hesitancy vary according to parental socioeconomic status (SES) and to understand the reasons for these variations. Financial barriers to access to care are traditionally strong determinants of social health inequalities. In the field of vaccination, however, most developed countries have implemented publicly funded national vaccination programs to address these barriers and reduce socioeconomic inequalities in vaccine uptake. We found some evidence in these settings and especially in the US that children from lower SES background remain less completely vaccinated than those from higher SES background, notably for vaccine series: this finding might be due to residual financial barriers and other economic constraints in developed countries. It also raises the question of whether other key determinants of parents' decisions about their children's vaccinations, especially cognitive ones (e.g., attitudes, beliefs about vaccination, vaccine safety, and efficacy) are socially differentiated and may contribute to SES differences in childhood vaccine uptake. The results of this review suggest that the patterns of social differentiation of parental beliefs toward vaccination differ according to context and vaccine. A few studies suggest lower levels of confidence about the safety of childhood vaccination among low-SES parents while others

report greater reluctance about specific vaccines (notably those including measles) among high-SES parents, especially in Germany and the UK.

Several recommendations for policy makers and public health specialists can be drawn from this review. Residual financial barriers to access to childhood vaccination could be reduced by programs to provide all mandatory and recommended vaccines 100% free of charge, regardless of the place of care (public organization or private practices) and by reimbursing costs of vaccine administration (when not already done). Universal programs seems more effective in reducing inequalities in childhood vaccination than non-universal ones. In countries where pathways to access to vaccination are complex, efforts should be made to simplify them (e.g., making vaccines available at the physician's office). Context-driven, multicomponent interventions including parent education, reminders, home visits and physician training should be implemented to increase vaccine uptake among low-SES children. Also needed are interventions carefully tailored to respond to specific concerns and beliefs of vaccine-hesitant parents, without reinforcing hesitancy, especially among high-SES vaccine-hesitant parents. The impacts of such interventions on vaccine uptake and parental beliefs must be rigorously evaluated.

Further research is needed to improve knowledge about SES differences in childhood vaccine coverage and to document the reasons of these differences in various settings and for different vaccines in developed countries. First, most of the studies included in this review come from the US, and reliable data on social differentiation in childhood vaccination are lacking in many other developed countries, especially in Europe. Second, guidelines to develop and validate instruments and to improve the comparability of results across studies are warranted. This is a prerequisite to the ultimate goal in this field, which is to design interventions adapted to the context and the target populations to improve vaccine coverage while reducing social inequalities.

Five-year view

We may assume that, as in the past, new controversies will emerge in the next few years, and will spread rapidly due to their propagation on the Internet. These controversies will probably affect social differentiation of childhood vaccination in different ways, according to the context (e.g., vaccine, country/region), as previously observed. Additional data on the social differentiation of childhood vaccination coverage, parental vaccine hesitancy, and its cognitive determinants will become available, especially in countries where no results are available today (e.g., in France, through data from the *2016 Health Barometer*).

Key issues

- The re-emergence of various vaccine-preventable diseases linked to the spread of vaccine hesitancy among parents in many developed countries is worrisome.
- No previous studies have systematically reviewed the socioeconomic differences in childhood vaccine uptake and parental beliefs/attitudes towards vaccination — key determinants of parents' decisions in this field.
- This review shows an increasing socioeconomic gradient in vaccine uptake – for vaccine series — in several settings with publicly funded national vaccination programs, and an inverse gradient for specific vaccines, such as that for measles, mumps, and rubella.
- It suggests that the patterns of social differentiation of parental beliefs toward vaccination differ according to context and vaccine.
- Further research is needed to document the reasons for these socioeconomic differences and to develop validated instruments to assess determinants of parents' decisions about childhood vaccination.

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• = of interest

•• = of considerable interest

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