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Review

Factors associated with incomplete or delayed vaccination across countries: A systematic review

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ABSTRACT

Background: Despite the significant decline in the incidence of vaccine-preventable diseases as a result of increased vaccination coverage worldwide, there are many children with delayed vaccination and a marked heterogeneity in vaccination coverage.
Objective: The aim of this study was to review factors that influence the adherence to childhood immunization schedule in different countries, especially related to socioeconomic conditions and health care system characteristics.
Methods: Pubmed and Web of Science databases were searched systematically for observational studies published in peer-reviewed journals in English, Spanish and Portuguese languages from January 1992 to June 2014. We included original articles that assessed vaccination schedule with at least three diphtheria–tetanus–pertussis, three polio and one measles vaccines in children aged 0–24 months.
Results: 491 articles were identified and 23 met the inclusion criteria and were reviewed. The most cited factors reported by countries with distinct characteristics were higher birth order (9 articles, 39.1%), and low maternal education/socioeconomic status (7 articles each one, 30.4%). Irregular monitoring by the health care services was reported by countries with "mainly private" health care system. Out-of-hospital birth, no reminder(s) about the next follow-up visit, and mother working outside the home were cited by countries with low/medium Human Development Index (HDI). Ethnicity, use of private health care services, and no health insurance were cited by countries with very high HDI. The role of migration on vaccination coverage was reported by three studies conducted in countries with distinct characteristics.
Conclusions: The factors are complex and driven by context. Overall, strengthening the contacts and relationships between the health care services and mothers with several children and families with low educational level/low socioeconomic status appear to be an important action to improve vaccination coverage.

1. Introduction

Immunization is one of the most successful and cost-effective public health intervention for reducing infant and child morbidity and mortality globally [1,2]. The Expanded Program on Immunization (EPI) was launched by the World Health Organization (WHO) in 1974 with the goal of vaccinating children throughout the world. In 1999, the Global Alliance for Vaccines and Immunization (GAVI) was created to increase access to new vaccines for the poorest countries [3]. The first diseases targeted by the EPI were diphtheria, whooping cough, tetanus, measles, poliomyelitis and tuberculosis. Global policies for immunization and the establishment of the goal for providing universal immunization for all children by 1990 were concerted in 1977. This goal was considered an essential element of the WHO strategy to achieve health for all by 2000. In 2010, an estimated 85% of children under one year of age globally had received at least three doses of DTP vaccine (DTP3) against diphtheria, tetanus and whooping cough [4].

Despite the significant decline in the incidence of vaccine-preventable diseases, there is a considerable number of children with delayed vaccination and a marked heterogeneity in vaccination coverage worldwide, which represents a risk to the resurgence of infectious diseases that are under control and to the reintroduction of infectious diseases already eliminated, requiring different vaccination strategies [5,6]. Previous studies suggest that

Abbreviations: EPI, Expanded Program on Immunization; GAVI, Global Alliance for Vaccines and Immunization; WHO, World Health Organization; DTP, diphtheria, tetanus and pertussis vaccine; HDI, Human Development Index; USA, United States of America; PHC, Primary Health Care service.

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vaccination status is influenced by factors related to the child, parental attitude or knowledge, social context of the family and health care services [7–9].

Some factors associated with the child involve prematurity and having older siblings. Reasons related to parental attitude or knowledge include lack of knowledge on the role of vaccinations for disease prevention, fear of adverse reaction, belief that vaccination is not beneficial or causes damage, lack of motivation, mistrust of health care system and social or cultural pressure against vaccinations [6,10]. Factors previously associated with the family social context are; education level of caregivers, socioeconomic status, family composition, belonging to a minority ethnic or religious group, single mother and young mother or caregiver. Some reasons related to the health care services include access or distance from vaccination services, missed opportunities to vaccinate, limited availability and knowledge of health workers, costs for vaccinations, inadequate vaccine supply, incorrectly applied contraindications, mothers with limited access to prenatal care and infants born at home [6,10].

However, these factors may be different depending on the context [10]. Therefore, the aim of this study was to review in the literature, studies undertaken in different countries, which investigated factors that influence the adherence to childhood immunization schedule (measured by completeness and/or timeliness) in children aged 0–24 months, especially related to socioeconomic conditions (family features, parents' knowledge and attitudes, the Human Development Index/income) and health care system characteristics.

2. Methods

This systematic review was written in accordance with the PRISMA guidelines [11]. The search strategy was designed to retrieve observational studies looking at the factors that influence the adherence to childhood immunization schedule in children aged 0–24 months, published from January 1, 1992 to June 31, 2014. The Pubmed and Web of Science databases were searched for relevant articles between July 17 and July 21, 2014, using the key words "vaccination" AND ("delay" OR "timeliness" OR "completeness" OR "age-appropriate") AND ("factors" OR "predictors"). All databases in the Web of Science website were selected. Articles in English, Spanish and Portuguese were eligible for inclusion. Two authors (MCT and APSS) conducted the database search and data extraction independently. Duplicated articles obtained from different databases were excluded. Manual searching was used in reference lists of the obtained articles.

Due to the different vaccination schedules across countries, we included original articles that assessed vaccination schedule with at least three diphtheria–tetanus–pertussis (DTP3), three polio and one measles vaccine in children aged 0–24 months. We also included articles that reported factors independently associated with complete/incomplete or timely/delayed vaccination using Cox or logistic regression analysis. Literature reviews and articles that reported only associated factors with a specific vaccine were excluded.

Completeness was defined as receiving the basic series of vaccines recommended by the National Immunization Program [12]. Timeliness was based on minimum ages at which doses are considered valid and minimum acceptable intervals between doses [13]. The factors were classified into three categories [6]:

1. Family features: socioeconomic status (including community unemployment rate, interaction between literacy and wealth index, families with dependent children receiving aid), mother working outside the home, birth order (including parity and family size, more than one child in the house), maternal education, ethnicity, living in a rural area, migrant family (including recent and settled migrants, rural–urban and international migration), age and marital status of the mother.
2. Parents' knowledge and attitudes: premature child, lack of information about vaccination, and vaccination delay at three months of age.
3. Health care services: type of health care service (public/private), access to health services (including distance from the health unit, additional visit to a doctor), irregular monitoring by the health care services (including antenatal care visits), multiple vaccination providers, health insurance, out-of-hospital birth, no reminder(s) about the next follow-up visit, being vaccinated by a family doctor (not a pediatrician), and delay in being seen in the last vaccination.

Information about Human Development Index (HDI)/income, countries health care system and vaccination strategies and coverage were selected from articles, manuals and official sites. The HDI is a summary measure that includes the following indicators: life expectancy at birth, mean years of schooling and gross domestic product per capita. According to the 2013 HDI, countries with less than 0.550 are considered with low human development; between 0.550 and 0.700, medium human development; between 0.700 and 0.800, high human development; and with 0.800 or more, very high human development [14]. The health care system was categorized as "mainly public", "mainly private" and "mixed" (nearly half public and private). Additionally, we verified if the country receives investments of the GAVI, whether the country's vaccination was free of charge (at least for the vaccines included in this review – DTP, polio and measles vaccines), how many immunogens were offered to children aged 0–24 months and about the DTP3 coverage.

3. Results

Four hundred ninety-one papers were identified as fulfilling the initial search criteria (Fig. 1). After removing duplicate papers (104 articles) and those that did not meet the inclusion and exclusion criteria (345 articles), 91.4% (449 articles) of the studies were discarded. Forty-two articles had full text screening and another 13 articles were further included after searching the references of the pre-selected articles. Among the 55 articles, 58.2% (32 manuscripts) were excluded due to: lack of report of associated factors related to all vaccines included (DTP, polio and measles) (21.9%); inclusion of broader age group than 0–24 months (34.4%); inaccessibility of the manuscript (9.4%); language – one article was in French (3.1%); and lack of information about all the vaccines included (31.2%). A total of 23 articles were selected for this review. Of these, 19 (82.6%) were cross-sectional studies, two (8.7%) were retrospective cohort studies and two (8.7%) were case–control studies.

Table 1 describes the HDI/income, the health care system characteristics and the vaccination program of the countries with manuscripts included. The 23 selected studies were done in 13 different countries. Seven countries (53.8%) have "mainly public" health care system, three (23.1%) "mainly private" health care system and three (23.1%) have "mixed" health care system. In the United States of America (USA), very high HDI, where the health care system is "mainly private", the vaccination is not free of charge for the majority of the population.

The number of immunogens applied to children aged 0–24 months ranges from seven in India to 16 in Brazil. Countries with lower HDI such as, Mozambique, Uganda and Kenya, have lower vaccination coverage for DTP3 than the countries with higher HDI

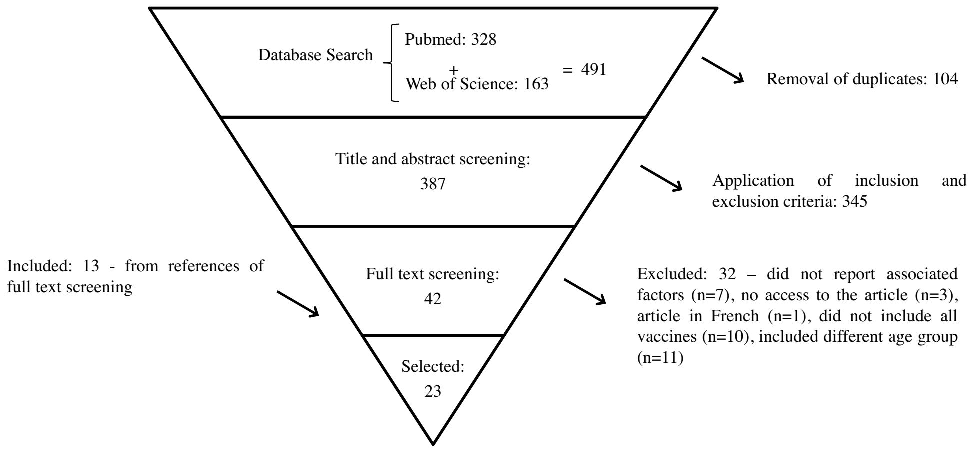

Fig. 1. Flow chart of included and excluded articles.

such as, China, Brazil, Belgium, Canada, USA and Australia. In addition, countries with low HDI have "mainly public" or "mixed" health care system.

Tables 2 and 3 describe the factors associated with incomplete or delayed vaccination in different countries and the 23 studies included, respectively. Factors associated with incompleteness resembled those associated with delay. Among the 23 reviewed studies, 14 (60.9%) referred to completeness, seven (30.4%) to timeliness and two (8.7%) to both.

The most cited factor was higher birth order, nine articles (39.1%), followed by low maternal education and low socioeconomic status, seven articles each one (30.4%). Both factors were reported by countries with distinct characteristics. Migration (rural–urban and international migration) was cited as a factor independently associated to incomplete or delayed vaccination by three studies conducted in India (rural–urban), Brazil (rural–urban) and Australia (international migration) with medium, high and very high HDI, respectively [12,35,36].

Table 1
Human Development Index, type of health care system and vaccination program in different countries.

Country	HDI/Income [14–16]	Type of health care system	Vaccination [33,34]
Burkina Faso	0.388 (181°-low)/Low-income Receives investments by GAVI[a]	Mainly public [17]	Free of charge 11 immunogens until 24 months DTP3 coverage: 88%
Mozambique	0.393 (178°-low)/Low-income Receives investments by GAVI[a]	Mainly public [18]	Free of charge 9 immunogens until 24 months DTP3 coverage: 78%
Uganda	0.484 (164°-low)/Low-income Receives investments by GAVI[a]	Mixed [19]	Free of charge 9 immunogens until 24 months DTP3 coverage: 78%
Kenya	0.535 (147°-low)/Low-income Receives investments by GAVI[a]	Mixed [20]	Free of charge 10 immunogens until 24 months DTP3 coverage: 76%
India	0.586 (135°-medium)/Middle-income Receives investments by GAVI[a]	Mainly private [21]	Free of charge 7 immunogens until 24 months DTP3 coverage: 72%
Philippines	0.660 (117°-medium)/Middle-income	Mainly private [22]	Free of charge 11 immunogens until 24 months DTP3 coverage: 94%
China	0.719 (91°-high)/Middle-income	Mainly public [23,24]	Free of charge 13 immunogens until 24 months DTP3 coverage: 99%
Brazil	0.744 (79°-high)/Middle-income	Mainly public [25]	Free of charge 16 immunogens until 24 months DTP3 coverage: 95%
Argentina	0.808 (49°-very high)/Middle-income	Mixed [26,27]	Free of charge 13 immunogens until 24 months DTP3 coverage: 87%
Belgium	0.881 (21°-very high)/High-income	Mainly public [28,29]	Free of charge 12 immunogens until 24 months DTP3 coverage: 99%
Canada	0.902 (8°-very high)/High-income	Mainly public [30]	Free of charge 13 immunogens until 24 months DTP3 coverage: 96%
USA	0.914 (5°-very high)/High-income	Mainly private [31]	Not free of charge 13 immunogens until 24 months DTP3 coverage: 94%
Australia	0.933 (2°-very high)/High-income	Mainly public [32]	Free of charge 12 immunogens until 24 months DTP3 coverage: 91%

[a] The Global Alliance for Vaccines and Immunization.

Table 2
Factors associated with incomplete or delayed vaccination in different countries.

	Completeness	Timeliness	Both
Family features			
High socioeconomic status	Barata et al. (Brazil, 2012) [37], Dummer et al. (Canada, 2012) [38]	–	–
Low socioeconomic status	Suarez et al. (USA, 1997) [39], Sanou et al. (Burkina Faso, 2009) [40], Kawakatsu et al. (Kenya, 2012) [41]	Babirye et al. (Uganda, 2012) [42], Williams et al. (USA, 1995) [43], Cui and Gofin (China, 2007) [23]	–
Mother does not work outside the home	Calhoun et al. (Kenya, 2014) [44]	–	Theeten et al. (Belgium, 2007) [28]
Mother working outside the home	–	Barman and Dutta (India, 2013) [45]	–
Low maternal education	Jani et al. (Mozambique, 2008) [46], Bondy et al. (Philippines, 2009) [47], Suarez et al. (USA, 1997) [39], Calhoun et al. (Kenya, 2014) [44], Bobo et al. (USA, 1993) [48]	Luman et al. (USA, 2005b) [52], Kusuma et al. (India, 2010) [36]	–
Ethnicity (not Hispanic/Black)	Suarez et al. (USA, 1997) [39]	Luman et al. (USA, 2005b) [49]	Cotter et al. (USA, 2002) [50]
Living in rural area	–	–	Cotter et al. (USA, 2002) [50]
Higher birth order	Barreto and Rodrigues (Brazil, 1992) [12], Bondy et al. (Philippines, 2009) [47], Barata et al. (Brazil, 2012) [37], Maina et al. (Kenya, 2013) [51], Kawakatsu et al. (Kenya, 2012) [41], Calhoun et al. (Kenya, 2014) [44], Bobo et al. (USA, 1993) [48]	Babirye et al. (Uganda, 2012) [42], Luman et al. (USA, 2005b) [49]	–
Single mother	Suarez et al. (USA, 1997) [39]	Babirye et al. (Uganda, 2012) [42], Luman et al. (USA, 2005b) [49]	–
Mother under 20 years of age	Herceg et al. (Australia, 1995) [35]	Kusuma et al. (India, 2010) [36]	Cotter et al. (USA, 2002) [50]
Migrants	Barreto and Rodrigues (Brazil, 1992) [12], Herceg et al. (Australia, 1995) [35]	Kusuma et al. (India, 2010) [36]	–
Caregiver different from child's parents	Fiks et al. (USA, 2006) [52]	–	–
Parents' knowledge and attitudes			
Not premature child	Fiks et al. (USA, 2006) [52]		-
Lack of information about vaccination	Kawakatsu et al. (Kenya, 2012) [41], Sanou et al. (Burkina Faso, 2009) [40]	Gentile et al. (Argentina, 2011) [53], Cui and Gofin (China, 2007) [23]	-
Vaccination delay at 3 months of age	Fiks et al. (USA, 2006) [52], Wood et al. (USA, 1995) [54]	Williams et al. (USA, 1995) [43], Cui and Gofin (China, 2007) [23]	-
Health services			
Use of public health care services	–	Luman et al. (USA, 2005b) [49]	–
Use of private health care services	Wood et al. (USA, 1995) [54], Dummer et al. (Canada, 2012) [38]	–	Cotter et al. (USA, 2002) [50]
Low access to health care services	Wood et al. (USA, 1995) [54], Jani et al. (Mozambique, 2008) [46]	–	–
Irregular monitoring by the health care services	Bondy et al. (Philippines, 2009) [47]	Kusuma et al. (India, 2010) [36]	–
Multiple vaccination providers	–	Luman et al. (USA, 2005b) [49]	–
No health insurance	Wood et al. (USA, 1995) [54], Fiks et al. (USA, 2006) [52]	–	–
Out-of-hospital birth	Jani et al. (Mozambique, 2008) [46], Maina et al. (Kenya, 2013) [51]	Babirye et al. (Uganda, 2012) [42], Barman and Dutta (India, 2013) [45], Kusuma et al. (India, 2010) [36]	–
No reminder(s) about the next follow-up visit	Maina et al. (Kenya, 2013) [51]	–	–
Being vaccinated by a family doctor	–	–	Theeten et al. (Belgium, 2007) [28]
Delay in being seen at the last vaccination	–	Gentile et al. (Argentina, 2011) [53]	–

Some factors such as out-of-hospital birth, no reminder(s) about the next follow-up visit, and mother working outside the home were cited by countries with low or medium HDI – Mozambique ("mainly public", low-income, GAVI), Kenya ("mixed", low-income, GAVI), Uganda ("mixed", low-income, GAVI) and India ("mainly private", middle-income, GAVI) [36,42,45,46,51].

Other factors such as ethnicity (not Hispanic/Black), caregiver different from the child's parents, use of private health care services, existence of multiple vaccination providers, lack of health insurance, being vaccinated by a family doctor (not a pediatrician), and delay in being seen in the last vaccination were cited by countries with very high HDI – USA ("mainly private", high-income), Belgium ("mainly public", high-income), Argentina ("mixed", middle-income), Australia ("mainly public", high-income) and Canada ("mainly public", high-income) [28,38,39,49,50,52–54].

In two articles done in the Philippines and India (middle-income countries) [36,47], with "mainly private" health care system, irregular monitoring by the health care services was found as a factor independently associated with incomplete vaccination.

Low maternal education was independently associated with incomplete or delayed vaccination in studies conducted in Kenya, Mozambique, USA, India, and Philippines [36,39,44,46–49], with different HDI and type of health care systems (Tables 1 and 2).

Two high-income countries showed opposite results to socioeconomic status: while the study conducted in Canada [38], with

Table 3
Description of the studies.

Reference	Setting	Year of data	Sample size	Type of study	Statistical analysis	Results
Babirye et al. [42]	Kampala, Uganda	2010	821	Cross-sectional	Cox regression	Untimely vaccination: increasing number of children per woman (AHR: 1.84, 95%CI 1.29–2.64); non-delivery at health facilities (AHR: 1.58, 95%CI 1.02–2.46); being unmarried (AHR: 1.49, 95%CI 1.15–1.94); being in the lowest wealth quintile (AHR: 1.38, 95%CI 1.11–1.72)
Barata et al. [37]	Brazil	2007–2008	17,295	Cross-sectional	Logistic regression	Incomplete vaccination: higher birth order (OR: 1.5, 95%CI 1.3–1.8); highest socioeconomic stratum (OR: 1.4, 95%CI 1.1–1.8)
Barman and Dutta [45]	West Bengal, India	2007–2008	1338	Cross-sectional	Logistic regression	Timely vaccination: delivered at any institution (OR: 1.6, 95%CI 1.1–2.4); mother employed (OR: 0.66, 95%CI 0.4–1.0)
Barreto and Rodrigues [12]	Santo André, Brazil	1971–1981	455	Case–control	Logistic regression	Incomplete vaccination: third or later born child (OR: 1.73, 95%CI 1.08–2.75); migrant mother (OR: 2.40, 95%CI 1.29–4.49)
Bobo et al. [48]	Oregon/Washington, United States	1984–1987	1163	Case–control	Logistic regression	Delayed vaccination: mother completed high school (OR: 0.6, 95%CI 0.4–0.8); not first-born (OR: 1.7, 95%CI 1.2–2.3)
Bondy et al. [47]	Philippines	2003	1324	Cross-sectional	Logistic regression	Full vaccination: higher maternal education (OR: 2.3, $p < 0.05$); 3 or more children (OR: 0.6, $p < 0.05$); at least 4 antenatal visits (OR: 1.4, $p < 0.05$)
Calhoun et al. [44]	Gem, Kenya	2003	244	Cross-sectional	Logistic regression	Full vaccination: 3 or more children in the family (OR: 0.27, 95% CI 0.13–0.65); mothers with lower education (OR: 0.35, 95%CI 0.13–0.97); working spouse in the home (OR: 0.40, 95%CI 0.17–0.91)
Cotter et al. [50]	United States	1993–1994	5598	Cross-sectional	Logistic regression	Full vaccination: served by public provider (OR: 2.41, 95%CI 2.00–2.90); African American children (OR: 0.56, 95%CI 0.49–0.65); mothers over the age of 20 years (OR: 1.25, 95%CI 1.06–1.48) Timely vaccination: reside in urban areas (OR: 3.24, 95%CI 1.38–7.59)
Cui and Gofin [23]	Gansu, China	1997	1025	Cross-sectional	Logistic regression	Delayed vaccination: delayed immunization at 3 months (OR: 14.1, 95%CI 7.63–28.57); high socioeconomic level (OR: 0.30, 95%CI 0.14–0.64); no source of information (OR: 6.46, 95%CI 1.97–21.16)
Dummer et al. [38]	Nova Scotia, Canada	2006	8245	Cross-sectional	Logistic regression	Full vaccination: public health administered vaccines (OR: 1.8, 95%CI 1.6–2.1); least-educated communities (OR: 2.0, 95%CI 1.7–2.3); areas with higher unemployment (OR: 1.7, 95%CI 1.4–2.0)
Fiks et al. [52]	Philadelphia, United States	2003	5464	Retrospective cohort	Logistic regression	Delayed vaccination: immunization delay at 3 months (OR: 4.54, 95%CI 3.98–5.19); prematurity (OR: 0.40, 95%CI 0.23–0.68); no health insurance (OR: 1.53, 95%CI 1.14–2.05); nonparent caregiver (OR: 1.39, 95%CI 1.10–1.76)
Gentile et al. [53]	Buenos Aires, Argentina	2008	1591	Cross-sectional	Logistic regression	Delayed vaccination: lack of information about vaccination (OR: 1.77, 95%CI 1.14–2.73); delay in being seen at the last vaccination (OR: 1.59, 95%CI 1.17–2.16)
Herceg et al. [35]	Newcastle, Australia	1994	187	Cross-sectional	Logistic regression	Incomplete vaccination: principal carer aged <25 years (OR: 4.24, 95%CI 1.55–11.54); principal carer born outside Australia (OR: 5.81, 95%CI 1.93–17.52)

Table 3 (*Continued*)

Reference	Setting	Year of data	Sample size	Type of study	Statistical analysis	Results
Jani et al. [46]	Magude, Mozambique	2001	668	Cross-sectional	Logistic regression	Incomplete vaccination: time to arrive to health facility (OR: 3.64, 95%CI 1.71–7.74); low maternal education (OR: 3.38, 95%CI 2.30–4.97); home delivery (OR: 1.78, 95%CI 1.28–3.36)
Kawakatsu et al. [41]	Nyanza Province, Kenya	2011	1965	Cross-sectional	Logistic regression	Full vaccination: higher knowledge of vaccination schedule (OR: 8.12, 95%CI 5.51–11.98); first birth (OR: 2.15, 95%CI 1.20–3.84); interaction between literacy and weath (OR:1.38, 95%CI 1.09–1.76)
Kusuma et al. [36]	Delhi, India	2009	746	Cross-sectional	Logistic regression	Full vaccination: higher maternal education (OR: 4.04, 95%CI 2.04–8.00); mothers over the age of 25 (OR: 3.60, 95%CI 1.26–10.30); settled migrants (OR: 1.93, 95%CI 1.18–3.14); reception of 3 or more antenatal care visits (OR: 3.89, 95%CI 2.07–7.31); hospital delivery (OR: 1.95, 95%CI 1.27–2.98)
Luman et al. [49]	United States	2003	14,810	Cross-sectional	Logistic regression	Delayed vaccination: single mother (OR: 1.3, 95%CI 1.1–1.6); low maternal education (OR: 2.3, 95%CI 1.9–3.0); 2 or more children in household (OR: 1.8, 95%CI 1.5–2.2); non-hispanic black (OR: 1.3, 95%CI 1.1–1.6); 2 or more vaccination providers (OR: 1.2, 95%CI 1.1–1.4); public vaccination provider (OR: 1.6, 95%CI 1.3–1.9)
Maina et al. [51]	Kaptembwo, Kenya	2011	380	Cross-sectional	Logistic regression	Full vaccination: less than 4 children within the family (OR: 2.67, 95%CI 1.50–4.74); both at health facility (OR: 2.26, 95%CI 1.36–3.76); advice on date of next visit (OR: 2.94, 95%CI 1.45–5.95)
Sanou et al. [40]	Nouna district, Burkina Faso	2004	476	Cross-sectional	Logistic regression	Full vaccination: perception of communication problem (OR: 0.46, 95%CI 0.28–0.75); highest socioeconomic stratum (OR: 2.1; 95% CI 1.24–3.55)
Suarez et al. [39]	Texas, United States	1994	4431	Cross-sectional	Logistic regression	Full vaccination: receiving Aid to Families with Dependent Children (OR: 0.67, 95%CI 0.53–0.84); higher educational level (OR: 1.48, 95%CI 1.17–1.89); African Americans (OR: 0.70, 95%CI 0.56–0.87); divorced mother (OR: 0.75, 95%CI 0.59–0.95)
Theeten et al. [28]	Flanders, Belgium	2005	1349	Cross-sectional	Logistic regression	Full vaccination: children vaccinated in a well baby clinic or day-care center (OR: 3.0, 95%CI 2.0–4.7) Timely vaccination: full-time working mother (OR: 1.8, 95%CI 1.3–2.4); children vaccinated in a well baby clinic or day-care center (OR: 2.4, 95%CI 1.7–3.4)
Williams et al. [43]	Virginia, United States	1992	2519	Retrospective cohort	Logistic regression	Delayed vaccination: low socioeconomic status (RR: 1.36, 95%CI 1.03–1.78); vaccination delay at 3 months of age (RR: 5.68, 95%CI 4.28–7.54)
Wood et al. [54]	Los Angeles, United States	1992	1025	Cross-sectional	Logistic regression	Full vaccination: up-to-date vaccination status at 3 months (OR: 5.56, 95%CI 1.43–21.6); uninsured (OR: 0.47, 95%CI 0.20–1.09); private health care service (OR: 0.45, 95%CI 0.26–0.79); additional visit to a doctor (OR: 1.13, 95%CI 1.01–1.27)

"mainly public" health care system, high socioeconomic status was associated with incomplete or delayed vaccination, in the study performed in the USA [43], with "mainly private" health care system, low socioeconomic status was associated with incomplete or delayed vaccination (Tables 1 and 2). In Brazil (middle-income country with "mainly public" health care system), one study conducted in 2007–2008 in all Brazilian capitals presented that children residing in census tracts in the highest socioeconomic stratum had the lowest percentage of complete immunizations by 18 months of age [37]. Conversely, in China (middle-income country with “mainly public” health care system), a study done in Gansu Province with children born in 1997, found that low socioeconomic level was associated with delay at 12 months [23].

4. Discussion

Identifying and understanding the factors related to social determinants and to health services on routine immunization programs in various countries are important to improve vaccination coverage [10]. Our findings show that these factors are complex and driven by context.

Some social determinants may be similar in countries with any income level while others may be population-specific [10]. Moreover, a factor can be changed by the context, for example, a low education level in Kenya, for instance, is not the same as in the USA [44,49]. In our revision, some factors associated to failure to adhere to vaccination were similar in countries with distinct HDI and health care system, but others were not. Socioeconomic status was associated with incomplete or delayed vaccination, but the direction of the association may be paradoxical among the countries studied. In the USA and Canada (high-income countries), it could be related to the type of health care system funding (“mainly private” or “mainly public”), and it warrants more research.

Several studies used education level as a proxy for socioeconomic status. For example, a study conducted in the USA showed similar conclusions for these two factors; i.e., low education level and low socioeconomic status were both associated with incomplete or delayed vaccination [39,40,48,49]. It corroborates with a systematic review (studies undertaken in low and middle-income countries) which pointed out that low education level and low socioeconomic status were often highly correlated, and were associated with under-vaccination; however, the underlying explanations for these associations were rarely investigated [6].

Although only two articles took into account both, completeness and timeliness, most of the studies reported similar associated factors between these categories. Suarez et al. chose to use an “up-to-date” immunization indicator rather than an “age-appropriate” indicator, because they believe that the “up-to-date” indicator provides comparable information about important predictors [39]. Another study that included both found that, in general, the factors associated with high vaccination coverage were similar [8].

A review including studies undertaken in low and middle-income countries found that approximately 44% of the reasons linked to being under-vaccinated were related to health care system, and 28% to parental attitudes and knowledge [6]. The authors reported that some factors related to health care system (missed opportunities to vaccinate, geographic barriers to receive immunization services) may be feasible to develop approaches that can be adapted to and implemented in a range of settings, such as training of health workers to reduce missed opportunities, improve communication, and remove barriers by enhancing outreach services [6]. A study that evaluated the immunization program for 12 and 24-month-old children in Curitiba, Brazil, found that groups with the highest coverage included children with three or more appointments at the Primary Health Care service (PHC), and children followed at the PHC with the Family Health Strategy [55]. All these factors depend on the tight integration between the health care service and the community.

On the other hand, in our review most factors were linked with family features and parents’ knowledge and attitudes. This is complex and more difficult to address, requiring targeted intervention. An article about vaccine hesitancy reported that different attitudes tend to assort into specific profiles; for example, anti-vaccination attitudes could be attributed to ignorance, misinformation, irrationality or it could be positively correlated with vaccine-related knowledge [56].

Migration was cited as a factor associated with incomplete or delayed vaccination by different countries. The role of migration (rural–urban and international migration) on vaccination coverage has been addressed in few studies. Vaccination coverage of migrants might be associated with their level of integration in the new society [57]. Canavati et al., in a study of migrant workers from Myanmar to Thailand, reported that it was important to involve the migrant parents in the development of the immunization program as they are key to deciding whether to immunize their children [57]. Kusuma et al. attribute low uptake of immunization to migrants’ vulnerability and marginalization in the new sociocultural environment. They believe that if these groups are not specifically addressed, immunization rates in urban areas may fall further, as rural–urban migration is an ongoing process [36].

It is important to note that according to some authors, when there is a health intervention, such as vaccination, at first the high socioeconomic population may benefit more than the low socioeconomic population, that is, the inequality increases. Then, when the high socioeconomic population reaches low levels of disease or condition in question, this starts to occur with the low socioeconomic population, that is, the inequality decreases [58].

Beyond the equity in access to vaccination, the safety of vaccines administered also influences vaccination coverage. Although the increased number of immunogens have not been cited as a factor associated with non-adherence to vaccination schedule, it should be considered in future studies about vaccination coverage. Maybe, we have missed these studies because we limited the search to all basic childhood vaccines, rather than specific vaccines versus all basic childhood vaccines.

Chen et al. presented the potential stages in the evolution of an immunization program, showing the dynamics of the interaction between vaccine coverage, disease incidence and the incidence of adverse reaction due to vaccination. They proposed five stages: pre-vaccine, increasing coverage, loss of confidence, resumption of confidence and eradication. At stage three, an increased focus on adverse reaction, often intensified by media coverage of one or a few case reports, may lead to a loss of confidence in the vaccine by the public, a reduction in vaccine coverage, and a resurgence of the disease to higher or even epidemic levels [59].

There were several limitations in our review. Although efforts were made to include all relevant articles, the review methodology might have been unable to identify every relevant article published during the specified review period. Due to the number and variability of articles identified by database search, some subjective judgment was employed in selecting relevant articles for full review. Peer reviewing and using a set of pre-defined inclusion criteria minimized this subjectivity.

Another limitation is related to the use of the HDI. Given the complexity of social reality this indicator is always imperfect and insufficient. So, it can hide large disparities intra-country. However, it is available for all countries and still considered a global working tool.

5. Conclusions

In conclusion, to achieve high and homogeneous vaccination coverage we must take into account the knowledge produced, which identifies the factors that influence the adherence to vaccination and it is fundamental to interpret them according to the characteristics of each context. Overall, higher birth order, low maternal education, and low socioeconomic status were the most frequently cited factors. Therefore strengthening the contacts and relationships between the health care services and mothers with several children and families with low educational level/low socioeconomic status appear to be an important action to improve vaccination coverage. Thereby, to intensify vaccination coverage taking into account the factors identified in the selected articles becomes a challenge for the different countries. However, it is through these factors that vaccination programs should be guided.

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