Vaccine 35 (2017) 443–451

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Vaccine coverage and adherence to EPI schedules in eight resource poor settings in the MAL-ED cohort study

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ARTICLE INFO

Article history:
Received 5 April 2016
Received in revised form 17 November 2016
Accepted 18 November 2016
Available online 18 December 2016

Keywords:
Public health
Vaccine coverage
Vaccine timing
EPI
Socioeconomic factors
Measles

ABSTRACT

Background: Launched in 1974, the Expanded Program on Immunization (EPI) is estimated to prevent two-three million deaths annually from polio, diphtheria, tuberculosis, pertussis, measles, and tetanus. Additional lives could be saved through better understanding what influences adherence to the EPI schedule in specific settings.

Methods: The Etiology, Risk Factors and Interactions of Enteric Infections and Malnutrition and the Consequences for Child Health and Development (MAL-ED) study followed cohorts in eight sites in South Asia, Africa, and South America and monitored vaccine receipt over the first two years of life for the children enrolled in the study. Vaccination histories were obtained monthly from vaccination cards, local clinic records and/or caregiver reports. Vaccination histories were compared against the prescribed EPI schedules for each country, and coverage rates were examined in relation to the timing of vaccination. The influence of socioeconomic factors on vaccine timing and coverage was also considered.

Results: Coverage rates for EPI vaccines varied between sites and by type of vaccine; overall, coverage was highest in the Nepal and Bangladesh sites and lowest in the Tanzania and Brazil sites. Bacillus Calmette-Guérin coverage was high across all sites, 87–100%, whereas measles vaccination rates ranged widely, 73–100%. Significant delays between the scheduled administration age and actual vaccination date were present in all sites, especially for measles vaccine where less than 40% were administered

Abbreviations: MAL-ED, The Etiology, Risk Factors and Interactions of Enteric Infections and Malnutrition and the Consequences for Child Health and Development; EPI, Expanded Program on Immunization; BGD, Dhaka, Bangladesh; BRF, Fortaleza, Brazil; INV, Vellore, India; NEB, Bhaktapur, Nepal; PEL, Loreto, Peru; PKN, Naushero Feroze, Pakistan; SAV, Venda, South Africa; TZH, Haydom, Tanzania; BCG, Bacillus Calmette-Guérin; DPT, Diphtheria, Pertussis, and Tetanus; OPV, Oral Polio Vaccine; IPV, Inactivated Polio Vaccine; LTF, lost to follow up; WAMI, Water/sanitation, Assets, Maternal education and Income; DHS, Demographic Health Survey; WHO, World Health Organization; UNICEF, United Nations Children's Fund.

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http://dx.doi.org/10.1016/j.vaccine.2016.11.075
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on schedule. A range of socioeconomic factors were significantly associated with vaccination status in study children but these results were largely site-specific.
Conclusions: Our findings highlight the need to improve measles vaccination rates and reduce delayed vaccination to achieve EPI targets related to the establishment of herd immunity and reduction in disease transmission.
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1. Introduction

The Expanded Program on Immunization (EPI) was established to ensure that all children have access to and receive basic immunizations [1]. Vaccination schedules are designed to balance maximizing vaccine efficacy (i.e. targeting the ages for optimal immunological response) with high population coverage (i.e. leveraging frequent contacts with healthcare providers during the first months of life) to achieve high levels of vaccine effectiveness [2]. The EPI prevents an estimated two to three million child deaths annually; however, despite near global adoption of EPI recommendations, schedules and vaccination rates vary greatly by country. Steady increases in global vaccination rates since 1990 [3] suggest that the overall EPI target, that 90% of children in the world should be vaccinated with Bacillus Calmette-Guérin (BCG), 3rd dose of Diphtheria, Pertussis, and Tetanus (DPT3), 1st dose of measles vaccine (MCV1), and 3rd dose of Oral Polio Vaccine (OPV3) by 2020, is within reach [4]. This progress can be accelerated and significant disease burden reduced by better understanding the factors associated with vaccine coverage and timeliness. However, few studies have addressed the extent of delayed vaccination across multiple regions of the world [5,6].

The Etiology, Risk Factors and Interactions of Enteric Infections and Malnutrition and the Consequences for Child Health and Development (MAL-ED) Study is a multi-site cohort study investigating the effects of undernutrition, gut function, and enteric disease on child development, growth, and vaccine response [7]. Children in the MAL-ED cohorts, located in Dhaka, Bangladesh (BGD), Fortaleza, Brazil (BRF), Vellore, India (INV), Bhaktapur, Nepal (NEB), Loreto, Peru (PEL), Naushero Feroze, Pakistan (PKN), Venda, South Africa (SAV), and Haydom, Tanzania (TZH), were followed for the first two years of life providing an opportunity to assess adherence to national EPI schedules in diverse settings [8–15]. Here we describe vaccination coverage in the MAL-ED cohorts and examine adherence to country-specific EPI schedules. Additionally, we evaluate how socioeconomic and demographic factors are associated with vaccination and schedule adherence.

2. Methods

2.1. EPI schedule

Country-specific EPI schedules and vaccine information were collected by study personnel. For several countries, the EPI schedule was modified during the study period of 2009–2014; changes were accounted for where appropriate. Additionally, vaccine campaigns conducted throughout the study period were documented.

2.2. Child vaccination histories

Data collection methods have been previously described [16]. Briefly, the MAL-ED cohorts consisted of approximately 200 children per site followed from birth to 24 months of age [7]. The study was observational and vaccines were not administered by the study. A structured vaccine history questionnaire was administered during home visits on the monthly anniversary of the child's birth (±2 days) to collect information on vaccine receipt. The mother/caregiver was asked to provide information on vaccinations since the previous visit, using the vaccine card issued by the health provider when possible or based on mother/caregiver recollection if no vaccine card was available. Additionally, a quarterly vaccine information form recorded vaccines received and date of administration based on the child's vaccination card if present, clinical records or mother/caregiver's best recollection; the source of the vaccination history was also noted and the records were furthermore used to confirm data from the monthly questionnaire. Approval to access health records of study children for vaccination information was received from local Internal Review Board. Extensive quality control activities were coordinated uniformly across all sites in real time. Vaccinations occurring outside the expected site-specific EPI schedule and vaccinations inconsistently reported on the two forms (monthly and quarterly) were reported back to the sites where study personnel made appropriate corrections after confirming the information with the source.

2.3. Analytical methods

Children with $\geqslant$12 months of follow-up were included in the primary analysis. Depending on the country-specific schedule, regardless of vaccination age, children were considered fully vaccinated at 12 months of age with a minimum of 1 dose of BCG, 3 doses of DPT, 1 dose of measles vaccine, and 3–5 doses of Oral/Inactivated Polio Vaccine (OPV/IPV). For schedule adherence analyses, vaccinations were considered 'on time' if administered within 7 days of the scheduled time (14-day window). Per EPI recommendations, for vaccines with multiple doses, the scheduled interval between initial and subsequent doses was considered more important than the specific age at receipt of subsequent doses if the initial dose was off schedule. To assess bias in the sample due to drop outs, the proportion of children who adhered to the schedule prior to being lost to follow up (LTF) was estimated.

Student's *t*-tests and tests to compare two proportions were used to compare fully vaccinated versus non-fully vaccinated children for overall socioeconomic status (the Water/sanitation, Assets, Maternal education and Income [WAMI] index) [17], and factors including household income in US dollars, maternal age, years of maternal education, number of siblings in the household, sex, whether the child was first born, and place of delivery. Proportions tests were used to examine timeliness of vaccination; age at the first dose of BCG, DPT, OPV, or measles were indicators for schedule adherence. p-Values equal to or below 0.10 were considered significant. All analyses were performed using STATA version 13 (StataCorp LP. College Station, TX).

3. Results

The MAL-ED cohorts were selected to represent a broad range of low and middle income country settings including a mix of urban and rural locations where malnutrition and enteric disease burden were high [8–15]. The median monthly household income across all sites was $113 (range $0–1648/month) ranging from $14 in

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