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Uptake and timeliness of rotavirus vaccination in Norway: The first year post-introduction

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ABSTRACT

Background: To minimise vaccine-associated risk of intussusception following rotavirus vaccination, Norway adopted very strict age limits for initiating and completing the vaccine series at the time rotavirus vaccination was included in the national immunisation programme, October 2014. Although Norway has a high coverage for routine childhood vaccines, these stringent age limits could negatively affect rotavirus coverage. We documented the status and impact of rotavirus vaccination on other infant vaccines during the first year after its introduction.

Methods: We used individual vaccination data from the national immunisation register to calculate coverage for rotavirus and other vaccines and examine adherence with the recommended schedules. We identified factors associated with completing the full rotavirus series by performing multiple logistic regression analyses. We also evaluated potential changes in uptake and timeliness of other routine vaccines after the introduction of rotavirus vaccine using the Kaplan-Meier method.

Results: The national coverage for rotavirus vaccine achieved a year after the introduction was 89% for one dose and 82% for two doses, respectively. Among fully rotavirus-vaccinated children, 98% received both doses within the upper age limit and 90% received both doses according to the recommended schedule. The child's age at the initiation of rotavirus series and being vaccinated with diphtheria, tetanus, pertussis, polio and Haemophilus influenzae type b (DTaP/IPV/Hib) and pneumococcal vaccines were the strongest predictors of completing the full rotavirus series. No major changes in uptake and timeliness of other paediatric vaccines were observed after introduction of rotavirus vaccine.

Conclusions: Norway achieved a high national coverage and excellent adherence with the strict age limits for rotavirus vaccine administration during the first year of introduction, indicating robustness of the national immunisation programme. Rotavirus vaccination did not impact coverage or timeliness of other infant vaccines.

1. Introduction

In October 2014, the two-dose oral Rotarix® vaccine (GlaxoSmithKline Biologicals, Rixensart, Belgium) was introduced in the Norwegian immunisation programme. Current European guidelines from 2014 recommend initiating rotavirus vaccination between 6 and 8 weeks of age and completing the entire series by 24 weeks of age due to age-specific vaccine-associated risk of intussusception following vaccination [1,2]. The previous version of these guidelines recommended the first rotavirus dose to be given between 6 and 12 weeks of age and completing the entire vaccine series by the age of 27 weeks [3]. The World Health Organization recommends an upper age limit of 15 weeks for the first rotavirus dose and a maximum age of 36 weeks to complete the full series [4]. The upper age limits for vaccination are recommended because of a risk of intussusception following rotavirus vaccination [5–7]. The baseline annual incidence of intussusception in Norway before rotavirus vaccine introduction was estimated at 3.7 (95% CI 3.3–4.2) cases per 10,000 children <2 years of age [8]. To minimise vaccine-associated risk of intussusception, Norway was the first among all industrialised countries to adopt the *strictest* age limits for initiating and completing the vaccine series. Thus, the initiation of rotavirus vaccination is recommended at 6 weeks of age with the second dose given at 12 weeks of age. The Norwegian absolute upper age limit for the first dose is 12 weeks (84 days) and for the second dose is 16 weeks (112) days. An interval of at least 4 weeks (28 days) is recommended between the two doses.

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At the time rotavirus vaccination was introduced in October 2014, Norway had a consistently high uptake for other childhood vaccines included in the national immunisation programme (e.g. ⩾93% for the third dose of diphtheria, tetanus, pertussis, polio and Haemophilus influenzae type b vaccine (DTaP/IPV/Hib) at 2 years of age). However, a recent study found that at least one routine vaccination was slightly delayed in 45% of Norwegian children aged ⩽2 years [9]. The stringent age cut-offs for rotavirus vaccine administration could negatively affect its uptake, but delayed rotavirus vaccination could affect vaccine safety and potentially jeopardize sustainability of the entire immunisation programme. Thus, a timely assessment of both vaccine coverage and adherence with the recommended age limits is crucial to ensure the adequate implementation, performance and safety of a newly introduced immunisation programme.

The aim of this study was to document the status and impact—on other vaccines—of rotavirus vaccination in Norway during the first year after its inclusion in the national immunisation programme, and to identify predictive factors for completion of the two-dose vaccination course.

2. Materials and methods

2.1. Data source and study population

We obtained data from the Norwegian Immunisation Register (SYSVAK), a national, electronic immunisation register which uses population census data as a denominator to estimate vaccine coverage [10]. Reporting to SYSVAK is mandatory for all programme vaccines and is based on a unique personal identification number assigned to all legal residents in Norway. Immunisation providers report the following data to SYSVAK: personal identification number, birth date, sex, administration date for each vaccine dose, vaccine-specific code (a reporting code assigned by the register to differentiate between various vaccines), name and municipality of the immunisation provider, and reporting date. Nearly all providers (99%) report data electronically in real time by transferring information to SYSVAK through a secure link. The remaining 1% report by using paper forms; these data are entered manually. The completeness of reported data is high, as 98% of the annual birth cohorts ($n \sim 60{,}000$) are registered in SYSVAK.

For this study, we used two cohorts of children: a pre-rotavirus vaccine cohort and a post-rotavirus vaccine cohort. The pre-rotavirus vaccine cohort consisted of all children born from 1 September 2009 through 31 August 2014 or during five years before the introduction of rotavirus vaccine. The post-rotavirus vaccine cohort includes children born from 1 September 2014 through 31 August 2015; the first annual cohort eligible to receive rotavirus vaccine within the national programme. For the post-rotavirus vaccine cohort, data extraction and evaluation was done on a weekly basis during January–December 2015 to ensure that the each member of the cohort was age-eligible for vaccination. Immunisation status and time of vaccination for each child were first evaluated when the child had reached 16 weeks of age and re-evaluated on a weekly basis until the end of study period.

If multiple vaccinations targeting the same diseases were recorded on the same date, only one vaccination was included in the analysis. If more than two rotavirus doses were recorded for the same child, information about only the first two doses was included in the analysis. This is because multiple reporting to SYSVAK is possible even though the national programme offers only a two-dose rotavirus vaccine. We calculated age at vaccination for all received doses and intervals between doses using the birth date and administration dates for each dose.

2.2. Coverage, timeliness and completeness of rotavirus vaccination

Rotavirus vaccine coverage was calculated from January 2015 to December 2015 using the post-rotavirus vaccine cohort. We calculated the general coverage for rotavirus vaccination by using the total number of children who had received the vaccine as the numerator and the number of children born in Norway during the study period as the denominator. Both the numerator and the denominator included only children who were 16 weeks and older at the time of each data extraction because 16 weeks is the maximum recommended age for a two-dose rotavirus vaccine course in Norway [8]. We examined timeliness of rotavirus vaccination by calculating a time-dependent coverage. The latter was calculated by restricting the numerator to children who received dose one by age 12 weeks and dose two by 16 weeks of age. We assessed adherence with the recommended schedule by restricting the numerator to children who received dose one between 6 and 12 weeks of age and dose two by age 16 weeks, including an interval of at least 4 weeks between the doses. The proportions of children vaccinated before reaching the lower age limit of 6 weeks or outside the upper age limit of 16 weeks were also calculated.

We evaluated differences in the rotavirus vaccine coverage by sex and geographic regions using a chi-square test. For the latter, data were divided into five regions: Northern, Central, Western, Southern and Eastern. In addition, we assessed the relationship between completeness of rotavirus schedule and a set of predictor variables. Rotavirus vaccination status was defined as partially vaccinated if only one rotavirus dose was administrated or fully vaccinated if two rotavirus doses were administrated. The set of predictor variables included age at administration for rotavirus dose one, sex, geographical region, having received at least one dose of DTaP/IPV/Hib, pneumococcal or hepatitis B vaccines, and having received one dose of Bacillus Calmette-Guerin (BCG) vaccine. Socio-economic characteristics such as parental educational status or household income are not available in the immunisation register. To explore the association between rotavirus vaccination status and each of these predictor variables, we first performed a univariate logistic regression analyses; Odds Ratios (ORs) and their 95% confidence intervals (95% CIs) were calculated. Variables found to be associated in the univariate models at the threshold of $p < 0.1$ were entered into multiple logistic regression models through a forward stepwise selection process and retained if their inclusion produced a significant likelihood ratio test result ($p < 0.05$) as compared to the previous model. ORs and their 95% CIs were calculated for the final adjusted model. Statistical significance for the multiple logistic regression model was determined by setting a conservative Bonferroni corrected threshold of $p < 0.05/M$, where M denotes the number of explanatory variables included in the final adjusted model.

2.3. Comparison between rotavirus vaccine and other programme vaccines

We assessed uptake for other childhood programme vaccines such as the BCG and hepatitis B vaccines, which Norway offers to children whose parents originate from areas with high endemicity of tuberculosis or hepatitis B virus infection. Simultaneously with the introduction of rotavirus vaccine, timing of BCG vaccination was moved from birth to 6 weeks of age per modified national recommendations. In addition, we calculated coverage of dose one for DTaP/IPV/Hib vaccine and dose one of pneumococcal vaccine and compared coverage for these vaccines with a two-dose coverage for rotavirus vaccine. Both DTaP/IPV/Hib and pneumococcal vaccines should be administered concomitantly with the second rotavirus dose before age 16 weeks in the Norwegian programme. Coverage for these vaccines was calculated by using the same