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The impact of the recommendation of routine rotavirus vaccination in Germany: An interrupted time-series analysis

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ABSTRACT

Background: Rotavirus is a highly contagious virus causing gastroenteritis, mostly in children under the age of 5. Since 2006, two vaccines are available in Germany. In 2013, these were included into the German national vaccination schedule. The aim of this intervention is to reduce the incidence and hospitalization among children under 5 years caused by rotavirus. The effectiveness of the intervention was analyzed in this study.

Methods: National surveillance data of laboratory confirmed rotavirus infections among children under the age of 5 were analyzed using interrupted time-series analysis. Weekly incidence from 2011 to 2017 and monthly hospital discharge rates from 2005 to 2015 were analyzed using a segmented generalized linear model with Poisson distribution.

Results: After adjusting for seasonal effects the incidence were approximately 22% (95% CI: 13.2–30.1) lower than expected following the intervention. The hospitalizations were approximately 27% (95% CI: 14.9–39.7) lower than expected following the intervention. The long-term effects of the intervention were nearly zero. The incidence changed in trend by −0.2% (95% CI: −0.1 to (−0.3)) and the hospitalizations by +0.2% (95% CI: 1.2–(−0.8)) following the intervention.

Conclusion: After the inclusion of the vaccines into the national vaccination schedule significant immediate effects of this intervention were found. The weekly incidences and monthly hospitalization caused by the rotavirus were more than 20% lower than expected. The long-term effects of the intervention however were found to be nearly zero. This could be caused by a low vaccination rate in the German population.

1. Introduction

Rotaviruses are a common cause of gastroenteritis [8, p. 483]. "Most infections occur in children under 2 years of age; by 3 years of age more than 90% of the children have been infected (...)" [3, p. 624]. The agent is highly contagious, 10 ingested particles are enough to cause an infection [1, pp. 300–301].

In 2006, two vaccines against rotavirus were approved and licensed for the European market [2, pp. 1946–1948]). They have since been available in Germany. An adoption of these vaccines into national vaccination schedules was recommended by the WHO in 2009 [4, pp. 1160–1161]). But it was not until 2013 that the Standing Committee on Vaccinations STIKO) in Germany included these vaccines into the national vaccination schedule for children [16], making them available free of charge.

This large scale public health intervention aims at reducing the incidence of infections caused by rotavirus and especially at reducing the number at hospitalizations among children under the age of 5 [16]. In January 2017, an overview of the rotavirus vaccination rates was published. Overall, the average vaccination rate against rotavirus in 2014 in Germany was 66%. Hence, one third of the children did not receive the vaccine [14, pp. 2–5].

Every intervention needs to be evaluated to estimate whether and to what extend it was effective. To investigate whether this intervention was effective meeting its goals, a retrospective study of observational data was conducted.

Since the infection results in vomiting and diarrhea, especially the bodies of infants are exposed to a large amount of stress due to dehydration. The lack of water and electrolytes can be life-threatening. Currently, there is no antiviral therapy available, only supportive therapy to correct fluid and electrolyte imbalances is in use [8, p. 484]. In the world's northern hemisphere rotavirus infection follow a strong seasonal pattern with more cases in the cold seasons [4].

Since 2001, rotavirus gastroenteritis is a notifiable disease in Germany. Based on the laboratory confirmations [5, p. 957], a large

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surveillance database was established. Therefore, numbers on incidences are available. In 2009, 62,207 cases were reported. 61% 37,822) of these occurred among children under the age of 5 of which 49% 18,621) were hospitalized [12]. Between 2008 and 2012 RVGE was the third most common disease among children <5 years of age [4, p. 1156]). The highest incidence occurred among infants and children under the age of 2 [11, p. 444]. These surveillance data were analyzed using an interrupted time-series analysis, which allows the researcher to draw conclusions on a casual impact of an intervention. A segmented generalized linear model with Poisson distribution was fit to perform the statistical analyses. The aim of this study is to estimate the effectiveness of the public health intervention of including them into the vaccination schedule.

2. Methods

2.1. Study design

The aim of vaccination programs is the reduction of incidences. The STIKO stated, that the rotavirus vaccine is recommended because other preventive measures, such as hand sanitizing, are ineffective. Moreover, the reduction of severe cases that lead to hospitalizations is a goal of the intervention [16].

Therefore, the aim of this study was to investigate the effectiveness of the German rotavirus vaccination recommendation in terms of meeting its predefined goals – reducing RVGE incidences and hospital admissions in infants and small children.

The core of the study conducted to answer the research question consists of two major parts.

- (1) The change of incidences prior to and after the intervention is investigated.
- (2) The change of hospital admissions prior to and after the intervention is investigated.

A population based retrospective observational analysis of the RVGE incidences and hospital admission time-trends was performed.

The analyses have been adjusted for seasonal effects by using the user written circulation package in Stata.

2.2. Data collection and variables

The secondary quantitative data on RVGE incidences for this study was obtained from the RKI's national surveillance database. The time span is coded weekly and reaches from 2001 to week 13 of 2017 [15]. Data on the number of hospital admission due to RVGE was provided by the German federal statistics office. The time span is coded monthly and reaches from 2005 to 2015 [17].

2.3. Statistical analysis

A powerful tool for estimating the impact of an intervention/policy is the ITS analysis. This method is a quasi-experimental research design using observational data. It enables the researcher to draw conclusion on the causal impact of an intervention on an outcome without randomization or a case-control design [6, p. 1]. A time series is a sequence of values of a particular outcome observed continuously and ordered at equally spaced intervals e.g. weeks). This sequence is divided into two or more segments. These are defined by change points, the interruptions. At the change points, the previously established pattern of events is expected to change due to events, such as interventions or policy changes [18, pp. 299–300]. The time series must cover the period before and after the interruption [10, p. 39].

Each segment is defined by two parameters, level and trend. The level is the y-axis-intercept at which each segment begins. The trend is the slope inclining, declining or stable) by which the observations change over the period in the segment [10, p. 39].

Changes in level and slope in the segment following a change point indicate that the intervention had an effect on the outcome. Level-changes indicate an immediate effect while slope-changes indicate a gradual/long-term effect [18, p. 300].

Since rotavirus infection follow a seasonal pattern, this needs to be taken into account when calculating the effects of the intervention. The user-written "circulation" package in STATA was used to adjust for the recurring patterns by using Fourier-terms.

3. Results

3.1. Incidence

The time series of the incidences was divided into three segments accounting for an impact of the commercialization as well (see Fig. 1 and Table 1).

The table and graph above present the results of the regression with three segments. The trend in the pre-commercialization period shows a weekly IRR of 1.0007. Every week the predicted mean rate increases by 0.07%. This result is statistically significant (see Tables 1 and 2).

The level change at the date of the commercialization shows an IRR of 1.0884. A level change of approximately +8.84% at the first change point, the commercialization, occurred. This finding is statistically significant.

The period following the commercialization and preceding the recommendation has an estimated weekly IRR of 0.9977. This indicates a declining trend in the predicted mean rates by approximately −0.23% per week compared to the previous segment. This finding is also statistically significant.

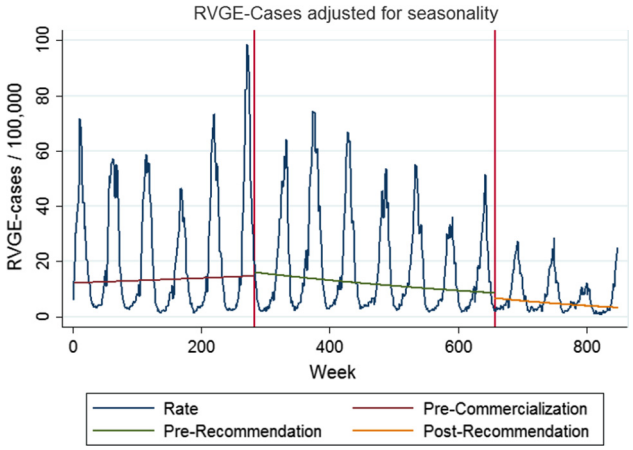

Fig. 1. RVGE-cases adjusted, own creation.

Table 1
Results from adjusted analysis of RVGE-cases, own creation.

Variables	IRR	p-value	(95% CI)	
Trend pre-commercialization	1.0007	0.000	1.0004	1.0010
Change in level at commercialization	1.0884	0.011	1.0194	1.1620
Trend pre-recommendation	0.9977	0.000	0.9973	0.9980
Change in level at recommendation	0.7831	0.000	0.6987	0.8776
Trend post-recommendation	0.9980	0.000	0.9970	0.9990

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