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INCIDENCE OF VACCINE PREVENTABLE DISEASES IN PEDIATRIC POPULATION OF LATVIA

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Abstract

Childhood and adolescent immunizations are one of the most effective means of preventing such serious diseases as diphtheria, pertussis, rubella, etc. These infectious diseases are termed as vaccine preventable diseases because vaccination continues to be the most effective strategy to reduce morbidity and mortality from these diseases. Despite this, immunization is an emotional issue for many parents. As vaccine preventable diseases become less common and parents have little familiarity with the devastating effects of vaccine preventable illnesses, the benefits of immunization may seem less important than the potential adverse effects.

Keywords: *diphtheria, pediatric, pertussis, vaccine.*

Introduction

The history of infectious diseases shows unequivocally that vaccination is the cheapest and most effective form of medical intervention ever devised (Doherty, 2011). Application of the original strategy, developed (in 1796) when Edward Jenner scarified pustular material recovered from the teat of an infected cow into the arm of a young boy, James Phipps, then challenged him later with virulent smallpox virus, led to the global elimination of that terrible disease some 200 years later (Doherty, 2011). Between 1913 and 1997, new vaccines for 20 diseases became available that provided defence against feared childhood diseases, such as diphtheria, pertussis, measles and *Haemophilus influenzae* type b infection, and other worldwide killers, including influenza, polio and hepatitis B virus (Garçon, Stern, Cunningham, & Stanberry, 2011). Medical advances in immunization led to the development of national vaccine immunization programs, directed principally at children in order to reach protective vaccination coverage in populations. The use of combination vaccines (e.g., diphtheria, tetanus, acellular pertussis (DTaP)) can help to reduce the number of inoculations at each visit and improve vaccination coverage (Drutz, 2016a). However, outbreaks of vaccine preventable diseases continue to occur even in countries with well-established vaccination programs. Reasons include the existence of under-vaccinated populations, the increasing anti-vaccination movement and the increasing movement of populations. Ensuring adequate levels

of herd immunity is the only reliable method for preventing epidemics and a re-emergence of vaccine preventable diseases (Wicker, 2014). Community immunity or herd immunity provides protection to individuals who cannot develop immunity. This indirect measure of protection raises an important issue about individual and public values. When immunization rates fall below these thresholds (90-95%), the risk of infectious outbreaks increases (measles and pertussis outbreaks have been attributed to declining herd immunity) (Barbacariu, 2014).

Parents can elect to exempt their children from immunizations. There are three types of exemption: 1) Medical exemptions are for children who have a valid medical contraindication to a vaccine or vaccine component; 2) Religious exemptions are for individuals whose religious beliefs oppose immunizations; 3) Philosophical exemptions are for individuals with a personal, moral, or philosophical belief against some or all immunizations (Boom & Healy, 2016). Because of exceptions children become under-vaccinated (children who have received fewer than the recommended number of vaccines) or unvaccinated (children who have received no vaccines). Parents who seek vaccine exemptions may have a low level of trust in the government and healthcare professionals and may use complementary or alternative medicine professionals whom they consider to be reliable sources of vaccine information (Boom & Healy, 2016).

All vaccine preventable diseases can be divided in two groups by epidemiologic cause – virus or bacteria. Diphtheria is an acute respiratory or cutaneous illness caused by bacteria *Corynebacterium diphtheriae*. Respiratory diphtheria has a case fatality rate of 5 to 10 percent. Mortality is increased (up to 20 percent) among children younger than five years (Drutz, 2016b). Pertussis, or "whooping cough", is an acute respiratory illness caused by bacteria *Bordetella pertussis*. The case fatality rate for pertussis is approximately 0.2 percent. Mortality is increased among infants younger than three months of age (Drutz, 2016b).

In Latvia the Centre for Disease Prevention and Control (CDPC) was established on 1st April 2012 (Republic of Latvia, Ministry of Health). The CDPC of Latvia is Institution aimed at strengthening Latvia's public health system, preventing diseases, including infectious and rare diseases (Republic of Latvia, Ministry of Health). The Centre's mission is to implement public health policy in the field of epidemiological safety and disease prevention (Republic of Latvia, Ministry of Health). Reports of social media and the CDPC about outbreaks of diphtheria in pediatric population of Latvia contribute interest of health care providers and researchers to carry out the research on pediatric immunization.

The aim of the study is to collect statistics about incidence of vaccine-preventable diseases in Latvia and to demonstrate that vaccine-preventable diseases still emerge among children and is a pressure to health care budget in Latvia.

Research objectives:

1. To estimate the incidence of vaccine preventable diseases in pediatric population of Latvia.
2. To analyze the intensity of health care provided due morbidity with vaccine preventable diseases.

Methodology

Materials

The retrospective study took place in Children's Clinical University Hospital (CCUH) in Riga, Latvia. The statistical data were collected in CCUH about the period from 2005 to 2014 year. Medical histories of pediatric patients were used to collect statistics. Selection of patients was made according to the code of diagnosis (all vaccine-preventable diseases that are

included in vaccination calendar 2014, except rotavirus and human papilloma virus infection). 731 cases conformed to selection criteria.

The statistics from CCUH were compared with data received from the CDPC of Latvia. Telephone survey was made to collect data from parents whose children were in hospital during 2014 year (in telephone survey were obtained data on 22 cases).

Methods

Values of incidence, mean, standard deviation (SD) were determined with confidence interval (CI) of 95%. With Shapiro-Wilk test both groups of patients with diphtheria and pertussis were tested for normal distribution (null hypothesis: distribution is normal). This test was chosen because the analyzed groups are small (n<50). The cases did not meet the criteria for a normal distribution ($P<0.05$ or $5.00x10^{-2}$). The Mann-Whitney (MW) test was chosen to compare the two groups on various factors. MW test is designed for small parametric groups with or without normal distribution. Indicator U and confidence interval $P_{MW}<0.05$ or $5.00 x10^{-2}$ was calculated to determine statistically significant difference between two groups.

Results

Despite the national immunisation program, data received from the CDPC of Latvia proves that vaccine preventable diseases are common in pediatric population of Latvia (see Figure 1). Varicella is not represented there. Vaccination against varicella was introduced in national immunisation program of Latvia in 2007. It is early to analyse the effect of vaccine efficacy. There was no one case of tetanus or acute poliomyelitis in Latvia during 2005-2013 year. Pertussis and tuberculosis was the most common diseases and most successful year of immunisation was 2009 (see Figure 1).

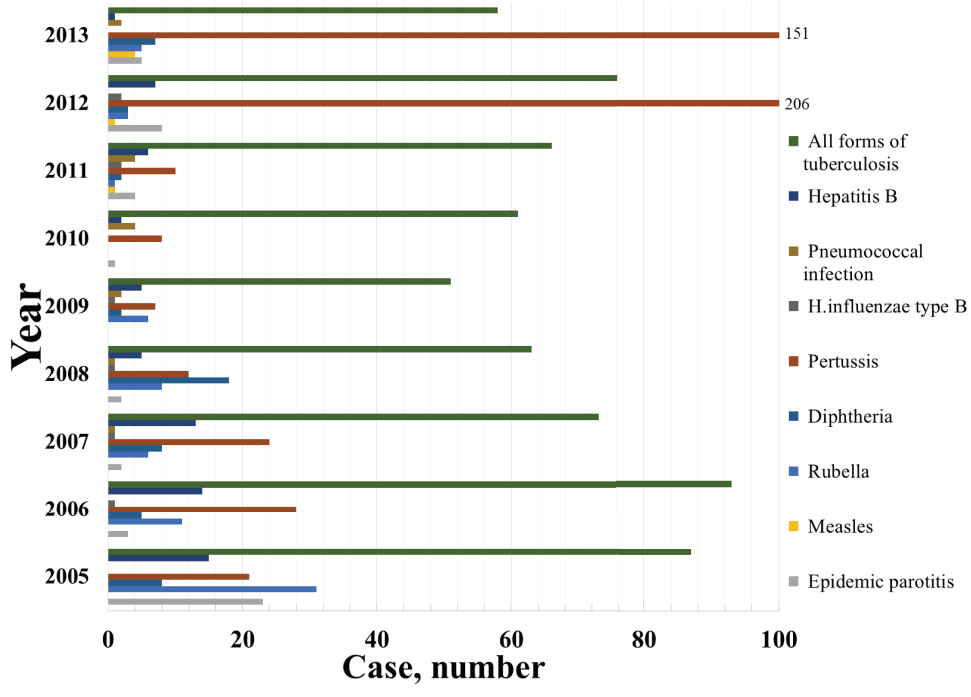

Figure 1. The distribution of vaccine preventable diseases (varicella, tetanus, acute poliomyelitis not included) according to the years in Latvia. Data received from the CDPC of Latvia

Vaccine preventable diseases treated in CCUH during 2005-2014 year are represented in Figure 2. There was no one case of tetanus or poliomyelitis. Varicella was excluded from the diagram. Vaccination against varicella was introduced in 2007. In 2007 CCUH faced 71 case of varicella, but in 2010 only 10 cases. During 2010 CCUH from all vaccine preventable diseases faced only varicella.

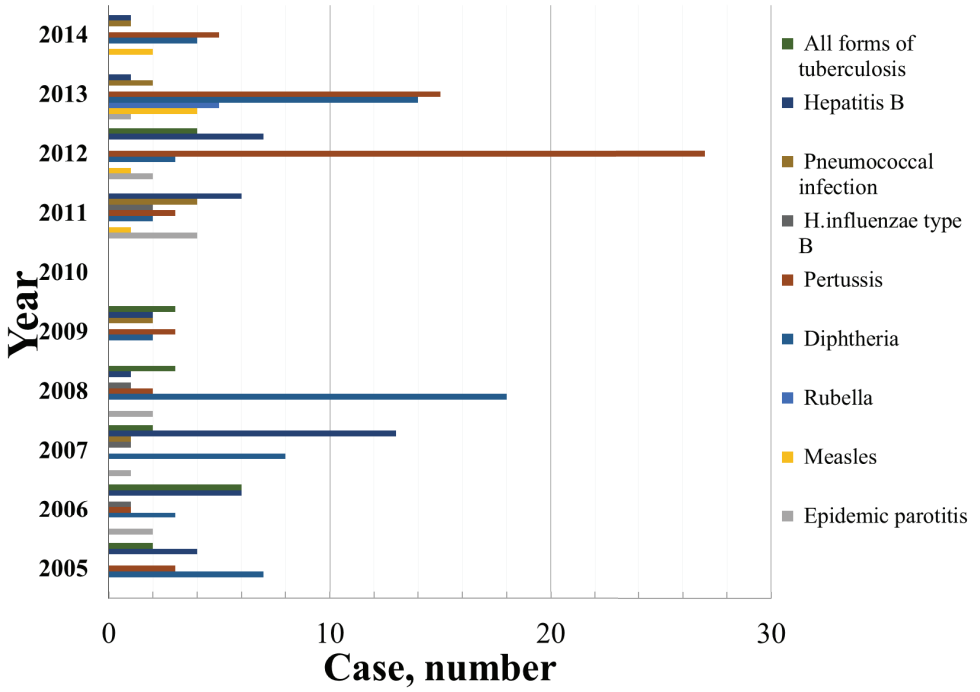

Figure 2. The distribution of vaccine preventable diseases (varicella, tetanus, acute poliomyelitis not included) according to years in CCUH

Detailed characteristic of patients with diphtheria or pertussis at CCUH

During the period from 2005 to 2014 year 61 patient with diphtheria and 59 patients with pertussis were hospitalized at CCUH. From all the patients 39.64% were girls, while 60.36% were boys. The mean age of patients (children) was 65.72 ± 65.01 months, with an interval from 1 to 215 months. Confidence interval (CI 95%) of age mean value is from 52.75 to 78.68 months. Looking at each individual disease (see Table 1) it shows that diphtheria is observed on mean for older children, and this difference is statistically significant.

Table 1. Patient age in months

Health status	Mean	SD	Interval		CI 95%			
			Lower border	Higher border	Lower border	Higher border	U	P_{MV}
Diphtheria	92.00	56.79	12	214	75.51	108.49	782.50	1.83 x10^{-5}
Pertussis	40.98	62.97	1	215	23.27	58.69		
Diphtheria/pertussis	65.72	65.01	1	215	52.75	78.68		

During the study health condition at the time of hospitalization of the patients were analysed. Such criteria were analysed: body temperature, heart rate, respiratory rate, blood

pressure, blood oxygen saturation, consciousness, diuresis, time of recapilarisation, skin turgor. Health condition was assessed as severe when such clinical signs as vital indicators, consciousness, diuresis were seriously alternated

At the admission to the hospital (see Table 2; Figure 3), most or 66.67% of the patients had moderate health condition.

Table 2. The patient's health condition at the time of hospitalization

Health status	Number of patients	Patient incidence, %	CI 95%	
			Lower border	Higher border
Mild or asymptomatic	31	27.93	19.82	36.91
Moderate	74	66.67	57.66	75.68
Severe	6	5.41	1.80	9.91

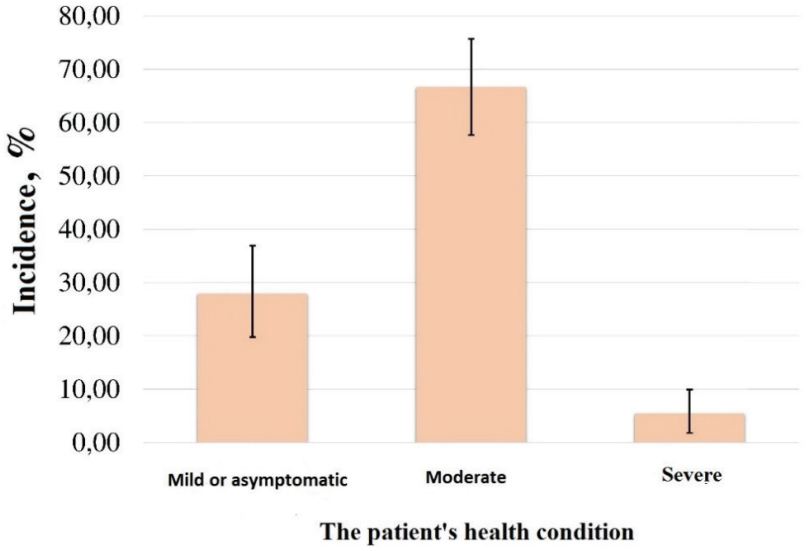

Figure 3. The patient's health condition at the time of hospitalization

The mean length of patient treatment in hospital (see Table 3, Figure 4) was 12.45 ± 7.10 days, with an interval from 2 to 31 days. Confidence interval (CI 95%) of the mean duration is from 11.04 to 13.87 days. If one compares the duration of hospitalization in patients with diphtheria or whooping cough, it is seen that diphtheria patients' hospitalization time is longer than for patients with whooping cough. This difference is statistically significant.

Table 3. Patient treatment in hospital in days

Health status	Mean	SD	Interval		CI 95%			
			Lower border	Higher border	Lower border	Higher border	U	P_{MV}
Diphtheria	15.54	6.89	2	31	13.54	17.54	590.00	5.22×10^{-6}
Pertussis	9.55	6.03	2	30	7.85	11.24		
Diphtheria/Pertussis	12.45	7.10	2	31	11.04	13.87		

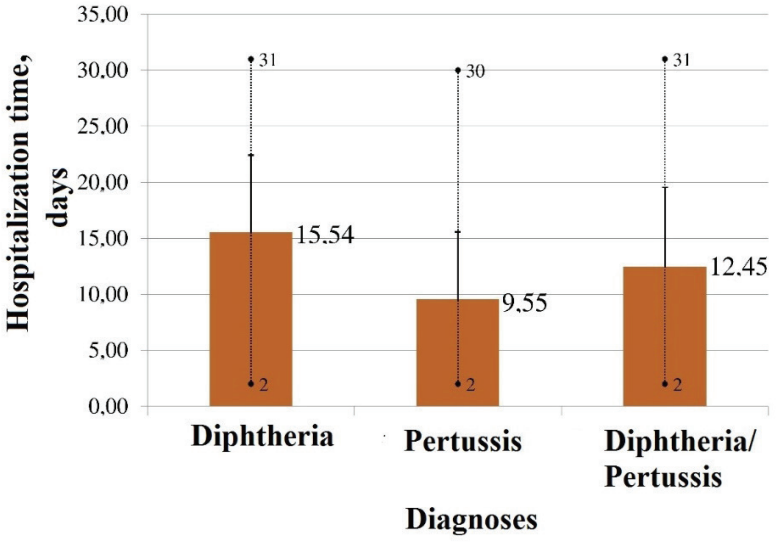

Figure 4. Patient treatment in hospital in days

Invasive manipulations made during treatment process of diphtheria and pertussis at CCUH

During hospitalisation patients received invasive manipulations for therapeutic or diagnostic purposes. Most frequently full blood count, blood biochemistry were taken and intravenous injection was made. Full blood count was taken from 108/120 patients for 192 times. Blood biochemistry from 98/120 patients for 181 times (see Table 4).

Table 4. Characteristics of the manipulation carried out during patient treatment

Manipulation	Number of patients	Number of manipulation	Mean for one patient	CI 95%*
Full blood count	108	192	1.78 ± 1.41	1.51 … 2.05
Blood biochemistry	98	181	1.85 ± 1.26	1.59 … 2.10
Antidiphtheria serum	16	16	1.00	-
Antidiphtheria antibody test	23	24	1.04 ± 0.21	0.95 … 1.13
Blood gas analysis	12	37	3.08 ± 1.68	2.02 … 4.15
Mechanical lung ventilation	10	10	1.00	-
Intravenous injection	76 (87.36%)	76	-	79.31% … 94.25%
Intravenous fluid infusion	61 (70.11%)	61	-	60.92% … 80.46%

*CI 95% – for the mean value or incidence

One part of scientific research was a survey that was sent to those parents whose child was hospitalised in CCUH in 2014 with vaccine preventable disease. 22 parents from 44 fulfilled the survey (see Figure 5 and 6).

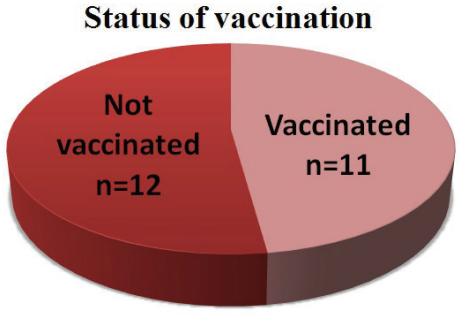

Figure 5. The vaccination status of children who were in CCUH during 2014 year (n – number of cases). From 22 patients with VPD in CCUH in 2014

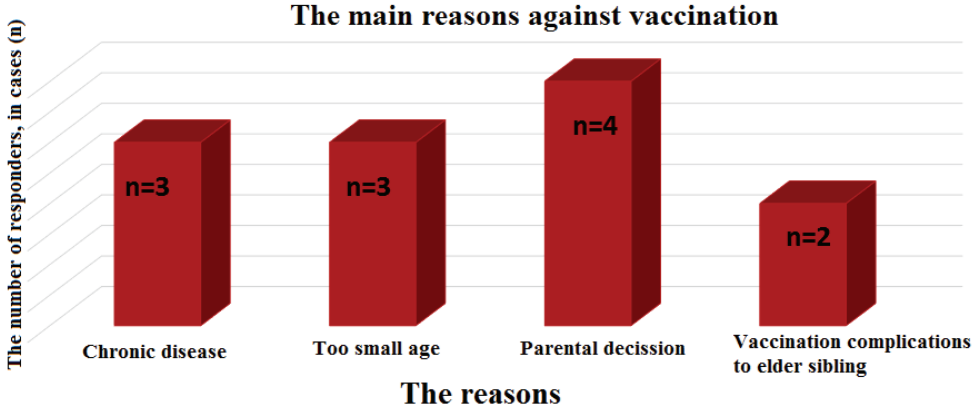

Figure 6. The reasons against vaccination in 2014 in CCUH for children with VPD

Discussion

In populations with high pertussis vaccine coverage in infants and children, infants usually acquire pertussis infection from adults, most often their parents (McIntyre PB, Elliott E, Morris A, et al., 2002). Acellular pertussis vaccines are highly immunogenic in adults (Mertsola et al., 1983) and appear to provide some protection following the first dose in infants, becoming maximal after two doses (Juretzko, 2002). Strategies to reduce mortality and morbidity from pertussis in infants too young to be vaccinated themselves include vaccination of their parents at, or shortly after, birth (to potentially reduce exposure to pertussis) and earlier vaccination of the infant (Scuffhama & McIntyreb, 2004.). Obtained data prove that patients with pertussis (M=40.98 ±62.97months) are younger than those with diphtheria and researchers suggest to use *cocoon strategy* described above to protect infant from pertussis.

Twenty-one out of all patients with diphtheria (21/61) were diphtheria bacteria carriers. That explains long time of hospitalization: they had to stay at hospital and receive treatment till negative bacterial culture was gained.

Pressure to health care budget is made not only from invasive manipulations but also by examinations necessary to make diagnosis, e.g., microbial cultures from throat, X-ray and ultrasound imaging, electroencephalogram etc. CCUH searched for solution and in April 2015 opened Child Vaccination Center where parents are able to meet health care specialist with questions about immunisation or for making vaccination.

Conclusions

1. Vaccine preventable diseases are important issue to deal with in Latvia.
2. In CCUH 731 patients in a 10 year period received medical treatment due to vaccine preventable diseases.
3. During 10 year period 61 patient with diphtheria and 59 patients with pertussis were hospitalized at CCUH. They mean age was 65.72 ± 65.01 months. At the admission to the hospital 66.67% of them had moderate health condition. The mean length of patient treatment in hospital was 12.45 ± 7.10 days. During hospitalisation children received painful invasive manipulations, e.g., full blood count was taken in 90% (from 108/120 patients).
4. Morbidity with vaccine preventable diseases makes pressure to the budget of Latvia in several ways: spends hospital resources and at least one parent is unable to work for 12.45 ± 7.10 days when children are at hospital.

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Summary

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Childhood and adolescent immunizations are one of the most effective means of preventing such serious diseases as diphtheria, pertussis, rubella, etc. These infectious diseases are termed as vaccine preventable diseases (VPD) because vaccination continues to be the most effective strategy to reduce morbidity and mortality from these diseases. Nevertheless, VPD still emerge in pediatric population of Latvia. The researchers in this study estimate the incidence of VPD in pediatric population of Latvia and analyze the intensity of health care provided due morbidity with vaccine preventable diseases.

The aim of the study is to collect statistics about incidence of VPD in Latvia and to demonstrate that VPD still emerge among children and is a pressure to health care budget in Latvia.

Materials and methods: The retrospective descriptive study took place in Children's Clinical University Hospital (CCUH) in Riga, Latvia. The statistical data were collected in CCUH from medical histories and received from the Centre for Disease Prevention and Control (CDPC) of Latvia about the period from 2005 to 2014 year. Telephone survey was made to collect data from parents whose children were in hospital during 2014 year (the data on 22 cases were obtained in a telephone survey).

Results. Retrospective descriptive study contains data about VPD registered in Latvia and in CCUH during the period from 2005 till 2014 year. During this period of time 731 patients were hospitalized in CCUH with such vaccine-preventable diseases as diphtheria 8.34% (n=61), hepatitis B 5.61% (n=41), tuberculosis 2.74% (n=20), tetanus 0% (n=0), pertussis 8.07% (n=59), poliomyelitis 0% (n=0), *Haemophilus influenzae* type B 0.68% (n=5), measles 1.10% (n=8), pneumococcal 1.37% (n=10), varicella 69.77% (n=510), mumps 1.64% (n=12), rubella 0.68% (n=5). Diptheria and pertussis were two most common VPD in CCUH except varicella. Vaccination against varicella was introduced in Latvia only in 2007. The mean length of patient treatment in hospital due to diphtheria or pertussis was 12.45 ± 7.10 days. At the admission to the hospital most or 66.67% of these patients had moderate health condition, mild or asymptomatic – 27.93%, but severe – 5.41%. Patients with severe health condition had seriously alternated such clinical signs as vital indicators, consciousness, diuresis. The prevalence of moderate health condition explains the amount of invasive manipulations done during hospitalisation: intravenous injections 76/120, intravenous infusion 61/120, complete blood count 108/120 and blood biochemistry 98/120 patients.

Parents whose children were treated with VPD in CCUH during 2014 were interviewed for specific VPD. From 44 parents 22 answered to questionnaire and it was found out that 12 out of 21 patients were not vaccinated according to vaccination calendar, 11 out of 21 patients answered that there was similar case of disease in their kindergarten, school, etc.

Conclusions. In spite of national immunization program, VPD are common in children of Latvia (731 patients in CCUH from 2005 to 2014 year) and is pressure to health care budget (mean 12.45 ± 7.10 bed days for one patient). Every hospitalization with VPD is painful for little patients because blood tests, intravenous medicaments or infusion are done. In 2014 10 out of 21 of patients with VPD were not vaccinated according to the vaccination calendar.