Vilnius University

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EPIDEMIOLOGICAL PATTERNS OF DIPHTHERIA IN LITHUANIA IN 1991–2011 AND ITS PREVENTION

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Vilniaus universitetas

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DIFTERIJOS EPIDEMIOLOGINIAI DĖSNINGUMAI LIETUVOJE 1991–2011 METAIS IR JOS PROFILAKTIKA

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1. INTRODUCTION

1.1. Problem under research

Diphtheria remains an important issue of public health in the XXI century both in Europe and worldwide. Even though diphtheria is an uncommon disease in the member states of the European Union, the defined goal of the World Health Organisation to eliminate the indigenous cases of diphtheria in the European region till the year 2000 has been achieved in the Western and Central Europe. However, the this goal has not been achieved throughout the whole WHO European region. Local cases of diphtheria disease are registered in Latvia, Ukraine and the Russian Federation. Almost annually, in the member states of European Union cases of diphtheria are notified to be imported not only from the countries of Eastern Europe, but also from the countries of the Hindustan peninsula, South-east Asia and South America. Increased number of cases of *C. ulcerans* aetiology diphtheria related to the infection reservoir of domestic animals is identified in certain European and other (USA, Japan) countries. Cases of diphtheria becoming a rare instance in European countries led to the lower awareness of the health care specialists as well as their ability to diagnose and manage this disease. Vaccinations against diphtheria are included in all of the national vaccination schedules for children and adult revaccination against diphtheria and tetanus is recommended by many countries. However, since these vaccinations only create an antitoxic and not an antibacterial immunity to diphtheria, it does not eliminate the circulation of the microorganism in population. Therefore, risk of new cases and outbreaks in case of a decrease of the herd immunity level are still exists. In the last 20 years, diphtheria incidence manifested throughout the periods of epidemic and post-epidemic incidence, during which, sporadic cases of this disease were notified. Epidemiological patterns of diphtheria have changed, differences of the manifestation of the epidemic process were revealed by comparing these time periods.

The specific feature of the causative organism of diphtheria is that non-toxigenic toxin-gene bearing causative organism can still circulate in population causing diphtheria cases. However, after beginning the production of the toxin, it can cause cases and outbreaks of the disease.

Diphtheria is caused by the identical toxin of several causative organisms (*C.diphtheriae, C.ulcerans, C.pseudotuberculosis*). Even though, children vaccination coverage are sufficiently high, adult vaccination coverage are relatively low. Prior experiences in Lithuania and other countries indicate that the highest diphtheria incidence and case-fatality rate appear within susceptible groups of the population which have insufficient herd immunity. The antitoxic immunity to diphtheria is wanning over time, therefore, revaccinations are recommended. Herd immunity level of the adult

population in Lithuania has been unknown, therefore, it is unknown which age groups are the most susceptible and are at risk of outbreaks and epidemics.

Application of behaviour theories for analysing the behaviour is one of the main tools for the assessment of the interventions that are used in order to try and change the behaviour. The main measure for diphtheria prevention is children and adult vaccination. The vaccination coverage rely on the attitude to vaccination. Attitude is one of the determinants of appropriate behaviour. Determinants of certain behaviour (intentions) have been studied applying the theories and models explaining behaviour (extended Theory of Planned Behaviour, Health Belief Model).

1.2. Relevance of the study

The European Centre for Disease Prevention and Control defines diphtheria as a communicable disease that could once again cause an epidemic in the European region. The raised goal of the World Health Organization to eliminate local cases of diphtheria in the European region should be achieved by sustained high children vaccination coverage, increased adutd accessibility to vaccinations as well as vaccination coverage, assurance of proper management of diphtheria cases, and the capacity of laboratory diagnostics. In order to control diphtheria successfuly, more research allowing the identification of the risk groups and determinants of diphtheria are required. It is necessary to identify the epidemiological patterns of diphtheria, define the risk and most important issues in order to control diphtheria in Lithuania.

Cases of diphtheria becoming a rare instance in European countries led to a decrease of laboratory testing for diphtheria on patients with upper respiratory tract infections, therefore, the toxigenicity and ribotypes of the diphtheria agent strain circulating within the population were unknown.

Many factors have a decisive influence on the formation and the level of the herd immunity to diphtheria, such as schemes and the coverage of children vaccination, revaccinations, circulation of the causative organism playing the role of "buster dose", etc.

Data on the actual seroprofile is required in order to predict diphtheria epidemic, identify the susceptible age groups of the adult population which are at risk and would be prioritized during the organization of preventive vaccinations. The findings of this study are useful for a substantiated statement on the intervals for adult revaccination.

One of the most important issue for the control of the disease is the attitude of the population to vaccination and their intention to be vaccinated. In order to create a herd immunity, high vaccination coverage are necessary, therefore, even a marginal change to the negative side of the attitude of the population to vaccination can essentially impact the coverage of the vaccination programme and influence the increase of risk of outbreaks and epidemics.

Vaccine preventable diseases are became quite rare in the countries that implemented well organised vaccination programmes, therefore, it is complicated to comprehend the significance of the vaccinations and the risks of the diseases to population and the health specialists. One of the factors influencing the behaviour of an individual is their belief (attitude). Beliefs are dependent on various factors, primarily on the comprehension of the threat to their health and that certain preventive measures could lower this threat. Provided that the belief is based on false (not evidence based) information or a wrong interpretation, a false (negative) behaviour model starts to form. In order to organise an effective vaccination programme, it is important to have data on not only what the attitude of the population to vaccination is, but also on the identification of the dterminants influencing their intentions and decisions following from these intentions, i.e. to be vaccinated or not (to vaccinate their children or not). The identification of populations' attitude to vaccination should be the basis for the organization of a successful vaccination intervention.

Determinants of the attitude and intentions to be vaccinated of the adult population in Lithuania were not examined using the behaviour models.

1.3. Scientific novelty of the study

Diphtheria– communicable disease manifesting in epidemic in the past. After the appearance of the presumptions (formation of susceptible population groups, circulation of the virulent strains), threat of a diphtheria epidemic that affects the most vulnerable population group arises. The results of this study allowed to assess the long-term results of applied diphtheria control measures of the massive vaccination campaign for adults. Contemporary epidemiological patterns of diphtheria (by gender, age, season, geographical distribution, diphtheria causative organisms, case-fatality rate, etc) are revealed in this study.

For the first time in Lithuania, study on the circulation of diphtheria causative organisms was conducted assessing the circulation of both the toxigenic and non-toxigenic strains in the population, toxigenicity, bearing of toxin-gene, and the ribotypes. Therefore, this allowed to assess the potential of the infection reservoir compared to the situation in other countries. According to the study findings, Lithuania remains as a country with the risk of diphtheria, within which, an virulent *Sankt-Peterburg* ribotype *gravis* biotype *C.diphtheriae* is circulating that is responsible for the diphtheria epidemic in the former countries of the Soviet Union during 1990s. The study findings revealed that the circulation of the toxigenic causative organisms of diphtheria in Lithuania and Latvia differ substantially compared to other countries.

The conducted study after nearly 20 years since the last study on the herd immunity to diphtheria of the adult population in Lithuania, allowed to compare the current data and age groups which are at risk and the ones from the year 1997. The study findings allowed to identify age groups within the population which are susceptible to

diphtheria, efficiency of the conducted adult vaccination programmes, and to predict the guidelines for future implementations.

The study on determinants of the attitude to vaccinations and the intention to be vaccinated by use of the Theory of Planned Behaviour and Health Belief Model was conducted in Lithuania for the first time. It has been noted that there is only a small amount of publicised research findings in literature that use behaviour models (Theory of Planned Behaviour, Health Belief Model) to study the behaviour and attitude towards vaccinations as well as that there are no publicised results on the attitude and behaviour of the population towards "traditional" vaccines, i.e. vaccines which have been in use for a long period of time in accordance with the national vaccination programmes.

1.4. The aim and objectives of the study

The aim of the sudy is to evaluate epidemiological patterns of diphtheria in Lithuania in 1991–2011 and describe the risk of diphtheria and the possibility of elimination applying preventive measures..

Objectives of the study:

1. To evaluate epidemiological patterns of the diphtheria in Lithuania in 1991–2011.
2. To identify the prevalence of toxigenic and non-toxigenic *Corynebacterium* in the population of Lithuania.
3. To identify the herd antitoxic immunity to diphtheria and to assess the potential risk of the diphtheria outbreak within the adult population of Lithuania.
4. To assess the attitude of the adult population to vaccination, identify determinants of their intention to be vaccinated against diphtheria and tetanus, and the prior behaviour (vaccination against diphtheria and tetanus).

1.5. Defended statements

- The highest risk for the diphtheria epidemic arises when large groups of people, susceptible to the disease among children and adults, form within the population at the same time. Similar case-fatality rates and the same predominant strain of the diphtheria causative is evident during the period of diphtheria epidemic incidence and postepidemic period.
- The herd immunity level might have an impact to the circulation of the diphtheria causative organism in the population. Adults become the most important infection reservoir when a sufficient children vaccination coverage (at least 90%) is present. Insufficient herd immunity level in the adult population forms favourable conditions for the circulation of the toxigenic and non-toxigenic *C. diphtheriae* strains.
- Variables of extendedTheory of Planned Behaviour (attitude, subjective norm, sef-efficacy, perceived control, anticipated regret, past-related behaviour) and

Health Belief Model (perceived susceptibility, perceived severity, perceived benefits) are directly related to the intention of the adults to be vaccinated. These models could form a theoretical basis for the assessment of the efficiency and the organization of vaccination programmes for the population.

2. METHODS OF THE STUDY

2.1. Study on the epidemiological patterns of the diphtheriain Lithuania in 1991–2011

Descriptive analysis of epidemiological patterns was conducted, surveillance data were used. The trend of the diphtheria incidence during the years 1946–1990 was assessed using the historical data of the diphtheria incidence (data source – Centre for Communicable Diseases and Aids). Diphtheria case-based data during the years 1991–2011 was collected and analysed by time, place, and person.

In order to compare diphtheria epidemic process during the different incidence periods, the time period was divided into diphtheria epidemic incidence period of 1991–1996 (incidence rate varied from 0.24 to 1.18 / 100 thousand people), and the postepidemic period of 1997–2011 (incidence varied from 0 to 0.17 / 100 thousand population).

Maps were created for the assessment of the dispersion of the disease cases according to the territories. GADM (*Database of Global Administrative Areas*) spatial database was used for the creation of maps. Data from the statistical report forms was used for the evaluation of the vaccination coverage. The vaccination coverage against diphtheria was assessed in accordance with age groups and the number of doses

2.2. Study on the prevalence of toxigenic and non-toxigenic Corynebacterium within the patients with upper respiratory tract infections in Lithuania

The study on the prevalence was conducted as an integral part of the DIPNET study (Screening for *Corynebacterium diphtheriae* and *Corynebacterium ulcerans* in patients with upper respiratory tract infections 2007–2008: a multicentre European study) that was funded by the European Commission. 10 countries (Estonia, Latvia, Lithuania, Finland, Ireland, United Kingdom, Italy, Greece, Bulgaria, and Turkey) participated in the study.

The author of tis study was the national focal point of the DIPNET network in Lithuania and the member of Steering Committee of the DIPNET network.

13 laboratories (8 of hospitals and 5 microbiology laboratories of public health centres) participated in the study in Lithuania. The sampling size (at least 2700 swabs) were accounted based on the presumption that the prevalence of the diphtheria causative organism could be similar to the case in Latvia (3.7/1000 population). The study was conducted from December of 2007 to June of 2008. The initial laboratory testing on the

diphtheria causative organism in the participating laboratories was using the *Hoyle* agar. All suspected cultures from the participating laboratories were sent to the National Public Health Surveillance Laboratory for further confirmation of identification and toxigenity by use of the *Elek* test. 2988 swabs were screened. Isolates of the toxigenic diphtheria causative organism were sent to Health Protection Agency (United Kingdom) for ribotyping.

2.3. Study on the herd immunity to diphtheria within the adult population in Lithuania

Serosurvey of adult population in Lithuania was conducted. Target population of the study– adult population (18 years old and over) of Lithuania. Population of the study– adults from various administrative territories of Lithuania whose blood samples were sent for testing to the National Public Health Surveillance Laboratory. Blood samples were collected from July of 2013 till June of 2014. The main presumption of the sampling size was blood samples that are sent to the laboratory are random.

Results of antibody testing were considered according to these values:

– seronegative person, antibody concentration– < 0.01 IU/ml;

– seronegative person, low antibody concentration– 0.01-0.09 IU/ml serum;

– Seropositive person, high antibody concentration– ≥ 0.1-0.99 IU/ml serum;

– Seropositive person, very high antibody concentration– ≥ 1 IU/ml serum.

Selected age groups: 18-29 years, 30-39 years, 40-49 years, 50-59 years, 60 and over.

The identification of the IgG level of diphtheria antitoxin in the blood serum was conducted by ELISA with assay – *Serion ELISA classic Diphtheria IgG test*®.

The sampling size (about 500 tests) was calculated according to presumption that the proportion of seronegative persons(diphtheria antitoxin level IgG is equal or lover than 0.01TV/ml) is 0.5 (50 percent).

2.4. Study on the attitude of the adult population in Lithuania to vaccination

The cross-sectional study was conducted.

The theoretical basis of the study was based on the Theory of Planned Behaviour *(I. Ajzen, 1988)* (Figure 1) and Health Belief Model *(M. H. Becker, 1974)*.

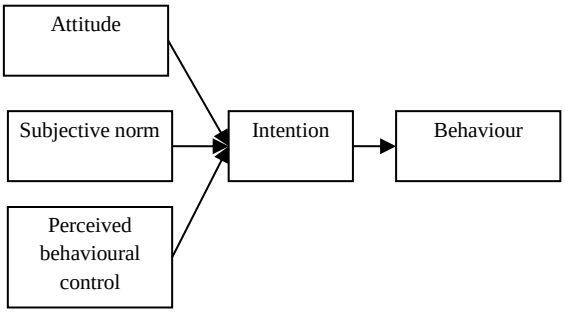


Figure 1. Theory of Planned Behaviour model.

At least 3 questions were dedicated to each variable of the study. 7-point (from 1 to 7) Likert scale was used in the study.

The variables were measured with these items:

I. Intention to be vaccinated. Do you intent to be vaccinated against diphtheria and tetanus once every 10 years? Do you intent to be annually vaccinated against influenza? Do you intent to be regularly vaccinated with other recommended vaccinations for adults? (Scale of possible answers: not at all likely (1) – very likely (7)).

II. Intention to be vaccinated against diphtheria and tetanus: Do you intent to be vaccinated against diphtheria and tetanus once every 10 years?

III. Prior behaviour towards vaccinations against diphtheria and tetanus: Have you been vaccinated against diphtheria and tetanus in the last 10 years?

IV. Variables Theory of Planned Behaviour.

1) Attitude. To be regularly vaccinated against diphtheria and tetanus in your opinion is;

To be regularly vaccinated against influenza in your opinion is; (scale of possible answers: foolish (1) – wise (7); not worth it (1) – worth it (7); harmful (1) – useful (7); bad (1) – good (7); view negatively (1) – view positively (7); wrong (1) – right (7); complicated (1) – simple (7); dangerous (1) – safe (7); disapprove (1) – approve (7)).

2) Subjective norm: My family approves of me being regularly vaccinated against diphtheria and tetanus; My family approves of me being regularly vaccinated against influenza; Majority of my friends approve of me being regularly vaccinated against diphtheria and tetanus; Majority of my friends approve of me being regularly vaccinated against influenza; I believe that majority of my friends are regularly vaccinated; In general, the society believes that every adult should be vaccinated; Opinions of important people for me impact my decision to be vaccinated against diphtheria, tetanus, and influenza (scale of possible answers: completely disagree (1) – completely agree (7)).

3) Perceived behavioural control:

a) Self-efficacy: To be vaccinated against diphtheria and tetanus for me is; To be vaccinated against influenza for me is (scale of possible answers: complicated (1) –

simple (7)); I am the person who is always vaccinated on time (scale of possible answers: completely agree (1) – completely disagree (7)); If I wanted to be vaccinated, I would be able to do it easily (simply) (scale of possible answers: absolutely disagree (1) – absolutely agree (7)); Are you positive on the fact that you are able to be vaccinated? (scale of possible answers: completely unconvinced (1) – completely convinced (7)).

b) Perceived control: Various factors and events that obstruct me from being vaccinated exist (scale of possible answers: a lot (1) – almost none (7)); Being vaccinated or not is entirely dependent on my own decisions (scale of possible answers: (completely agree (1) – completely disagree (7)).

V. Additional variables of the Theory of Planned Behaviour.

1) Anticipated regret: If I was not vaccinated on time, I would regret it in the future (scale of possible answers: completely agree (1) – completely disagree (7)).

2) Past related behaviour: Have you been vaccinated against diphtheria and tetanus in the last 10 years? Have you been vaccinated against influenza prior to the current season of influenza? Is your child vaccinated in accordance with the children vaccination schedule? (possible answers: yes, no, do not know).

VI. Variables of the Health Belief Model:

1) Perceived susceptibility: I would be at a high risk of contracting diphtheria and tetanus if I would not have been vaccinated against these diseases; I would feel anxious about the fact that I could contract a disease in the near future if I would not have been vaccinated against diphtheria and tetanus; It is possible that, exactly, I would contract diphtheria and tetanus if I would not have been vaccinated against these diseases (scale of possible answers: completely disagree (1) – completely agree (7)),

2) Perceived severity: Diphtheria and tetanus are serious diseases that could even cause fatalities; If would contract diphtheria or tetanus, I would become seriously ill; I am afraid of contracting diphtheria or tetanus: (scale of possible answers: completely disagree (1) – completely agree (7)).

3) Perceived benefits. Vaccination is a good idea, because you do not have to worry about contracting a disease after being vaccinated; Vaccination lower the risk of contracting diseases; I would have to visit the doctor's office a lot less if I had been vaccinated (scale of possible answers: completely disagree (1) - completely agree (7)).

4) Perceived barriers. Side effects from being vaccinated could obstruct the rhythm of my everyday life; I am scared of injections (needles), therefore, I am afraid of being vaccinated (scale of possible answers: completely disagree (1) - completely agree (7)).

These variables were formed for the dispersion of the answers according to the Likert scale. Answers of 1-3 points were evaluated as negative, answer of 4 points neither as negative, nor positive, and answers of 5-7 points as positive.

For the binomial logistical regression answers of 1-4 points were recoded as negative and answers of 5-7 points as positive.

The target population of the study was comprised of 18 years old and over, permanent citizens of Lithuania. The selection was formed according to the data on the permanent citizens of the Republic of Lithuania of the Statistics Lithuania. The respondents were selected using the multi-level (location, house and apartment number, respondent) randomised selection. In June 2013, 945 respondents were interviewed face to face.

2.5. Statistical analysis

Descriptive and analytical statistics methods were used for the analysis of the data.

Proportions were compared by using Fisher exact or chi-square tests were used for the analysis of category variables, Mann-Whitney test was used as appropriate. Hetvis and Rachet tests were used for the examination of the seasonality.

Joinpoint Regression Program, Version. 4.0.1. was used for calculations of the analysis of the time-serries (1946–1972) *January 2013; Statistical Research and Applications Branch, National Cancer* Institute.

Binomial logistical regression analysis was used to explore which variables of extended Theory of Planned Behaviour and Health Belief Model predicted intention to be vaccinated.

Direct method (variables are selected, removed, and changed by the researcher themselves) was chosen for forming of the binomial logistical regression. Variables for the model were selected not only by the statistical, but also by epidemiological principles. For the creation of the logistical regression model (selection of variables), the plausibility ratio test was used. The variable (regressor) was left in the model when the test $p \leq 0.3$, removed when the test $p > 0.3$ or if the removal of the regressor lowered the amount of properly classifiable cases.

The suitableness of the model was assessed in accordance with the statistics of the highest probable proportion of the chi-square, Hoshmer Lemesh chi-square statistics (compatibility test), determination of (pseudo) coefficients, classification table, and ROC area.

After the formation of the preliminary model, diagnostics of the model were concluded. Identification problems were verified (assessed according to the downward multiplier of the dispersion, VID), exclusions assessed by calculating the standardised deviations and tolerance for the deviation of the statistics, leverage assessed by the impact of the index.

Specification errors were examined by Linktest. The final model was formed after conducting diagnostics of the preliminary model and removing all of the identified issues.

0.05 significance level was chosen for the assessment of the hypothesis. Zero hypothesis is rejected when $p \leq 0.05$.

Data analysis was conducted using Stata IC/12.1 (StataCorpLP).

3. RESULTS OF THE STUDY

3.1. Epidemiological patterns of diphtheria in Lithuania during the years 1991–2011

3.1.1. Trends of diphtheria and their changes

Several periods of diphtheria incidence can be distinguished from the trends of the years 1946–1991. Period of high diphtheria incidence was during the years 1946-1955 when the incidence rate ranged from 42.6 to 57.7 cases / 100 thousand population. After the increase of vaccination coverage up to 60-70%, the incidence rate decreased sharply. Significant change in the dynamics of the diphtheria morbidity was notified in the year 1955. From the year 1955 to 1970, annual percentage of the decrease in incidence rate comprised -40.0 (95% CI -44.9 – (-34.6), $p < 0.0001$). During the years 1971–1990 sporadic cases of diphtheria occured (Figure 2).

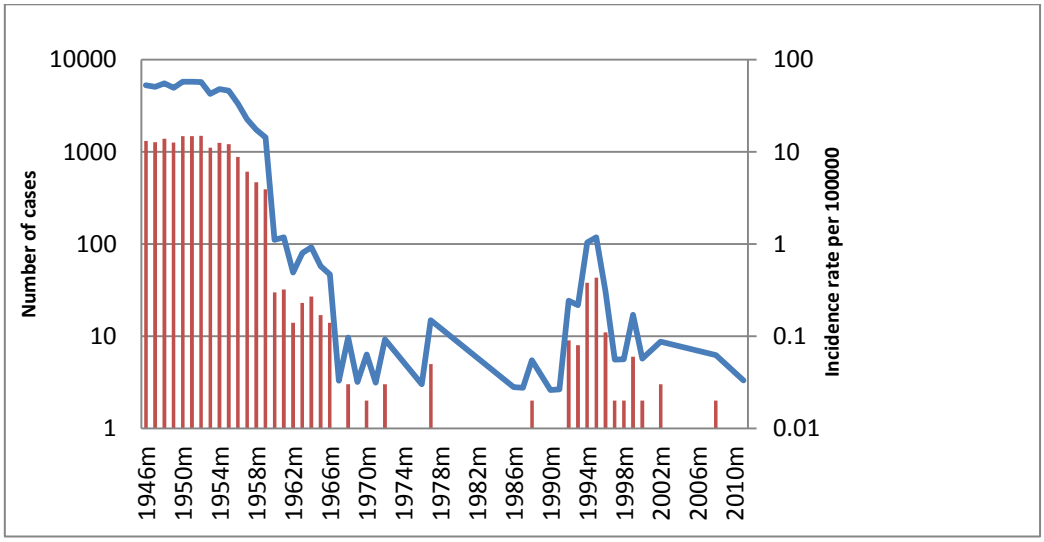


Figure 2. Diphtheria incidence and the number of cases in Lithuania in 1946–2011 (logarithmic scale).

In the year 1992, diphtheria incidence was 0.24 / 100 thousand, in the year 1993– 0.22 / 100 thousand. The peak of the diphtheria incidence was observed in 1994–1995 when the incidence rate was 1.04 / 100 thousand population (38 cases) and 1.18 / 100 thousand population (43 cases). The average annual change of diphtheria incidence in 1991–1995 was 146.34% (95% CI 53.05 – 296.50).

In order to control the diphtheria epidemic vaccination campaign of adults was organized with the help of international organisations. After the vaccination campaign, the average annual change of diphtheria incidence in the period 1995–1997 was –78.27%

(95% CI –87.98 – (–60.71)). The period in 1997–2002 can be interpreted as an "epidemic tail". During the years 1997–1998, two cases of the disease were notified each year. In the year 1999, 6 cases of diphtheria were reported, 3 of which occured in the same family. In the years 2000 and 2002, two and three cases of the disease were reported appropriately. From the year 2003 to 2007, no cases of the disease were notified. In the year 2008, 2 cases of diphtheria occurred in Lithuania, however, one of the cases was diagnosed during the study on the screening of the diphtheria causative organism. This diphtheria case would have been missed in the absence of this screening study. In the year 2011 in Lithuania, 1 case of diphtheria was notified (Figure 2).

3.1.2. Case-fatality rate

The diphtheria occurence was characterized by high case-fatality rates both in the period of epidemic incidence and the postepidemic period. During different years, the rates of case-fatality ranged from 16.7 to 50.0%. Dduring the postepidemic period, there was a lower number of diphtheria cases, however, the case-fatality rate (16.67%) was similar to the period of the epidemic incidence (15.54%) (Table 1). Case-fatality rates during the periods of diphtheria epidemic and postepidemic period were similar, no significant statistical difference estimated ($p = 0.13$).

Table 1. Diphtheria incidence and case-fatality rates in Lithuania, 1991–2011

Period	Number of diphtheria cases	Average incidence rate / 100 thousand population	Number of deaths from diphtheria	Case-fatality rate (%)
Epidemic incidence period, 1991–1996	110	2.76	17	15.45
Postepidemic period, 1997–2011	18	0.49	3	16.67

3.1.3. Seasonality

Diphtheria incidence was characterized by clearly expressed seasonality during diphtheria epidemic incidence period in 1991–1996. Seasonal peak lasted for 6 months (August-January). 70.8% of all diphtheria cases were notified during this time period. Statistically significant disease occurence peaks lasting for 2, 3, 4, 5, and 6 months were identified using the Hewitt and Ratchet tests.

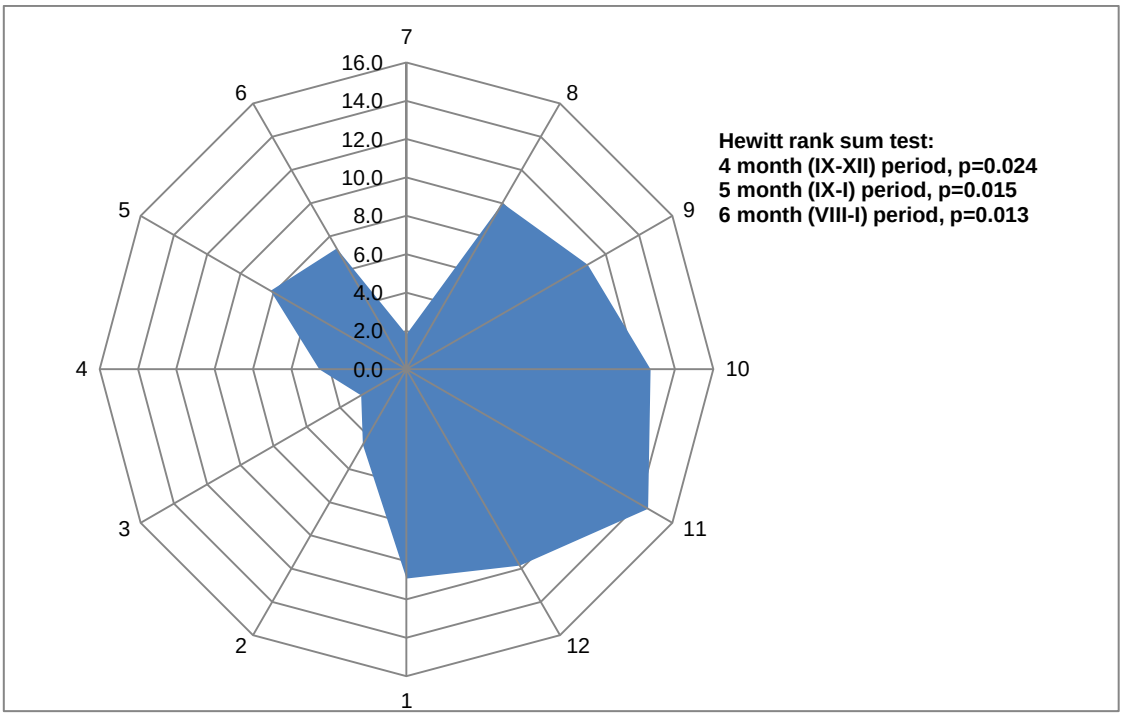


Figure 3. Diphtheria seasonality in Lithuania, 1991–1996

November was the month with the highest incidence. During seasonal peak, the most high diphtheria incidence was observed during the months of October-November (27.3% of cases). No statistically significant seasonality was identified during the postepidemic period in 1997–2011.

3.1.4. Diphtheria occurrence by place of residence

The most of diphtheria cases were occured in western and south-eastern parts of Lithuania during epidemic incidence period in 1991–1996. Sporadic diphtheria cases were also observed in other parts of Lithuania (Figure 4). Diphtheria cases more often occured within the major cities of Lithuania, 60.9% of all cases (67 cases) were diagnosed within the major cities. 42.7% of all cases (47 cases) were reported in Vilnius. Diphtheria cases were reported both in the city of Vilnius and (or) the districts in bordering territories, such as district of Trakai, Švenčionys, Šalčininkai. 15.5% of all the cases (17 cases) were notified in the city of Kaunas. Proportion of diphtheria cases within major cities of Lithuania during the epidemic incidence and postepidemic period were similar, no significant statistical difference was identified (p = 0.21). During the postepidemic period the family cluster of diphtheria cases (3 cases) was reported in the Šilutės district, majority of the cases in Vilnius city (Figure 5)

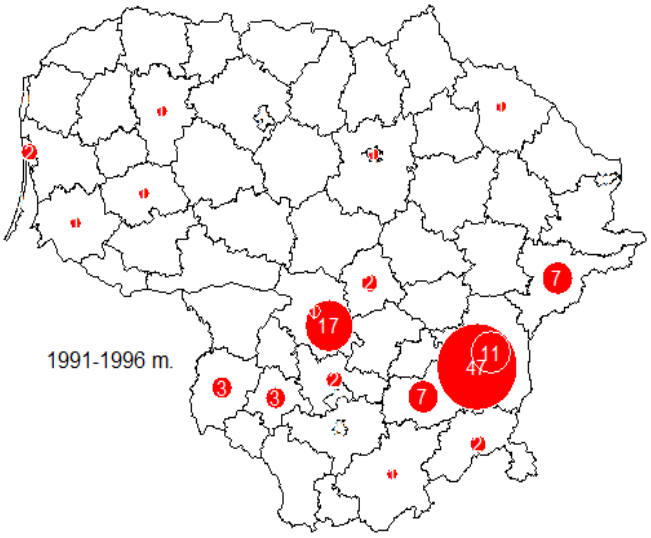


Figure 4. Diphtheria cases by the administrative territories in Lithuania, 1991–1996

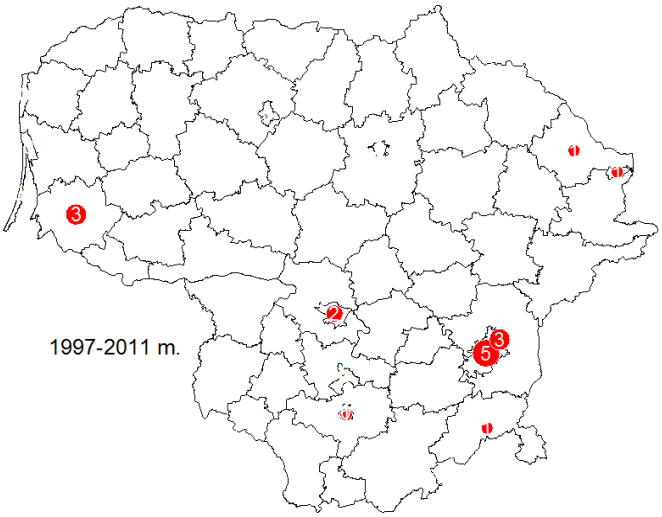


Figure 5. Diphtheria cases by the administrative territories in Lithuania, 1997–2011.

3.1.5. Diphtheria incidence by gender, age, vaccination status, time before seeking medical care, diphtheria risk factors and causative organism

The proportion of the diphtheria incidence according to gender during the diphtheria epidemic incidence period and postepidemic period was similar, no significant statistical difference was identified (p = 0.43). During epidemic incidence period the average incidence was 0.48 / 100 thousand population in males, 0.62 / 100 thousand population in females. The incidence rate of males (0.04 / 100 thousand population) was higher than the incidence rate of females (0.03 / 100 thousand population) during the postepidemic period in 1997–2011. No significant difference of incidence of genders has been identified during the epidemic incidence and postepidemic periods. The ratio of incidence rate among male and female was 0.77 (95% CI 0.52 - 1.15, p = 0.22) in

epidemic incidence period and 1.33 (95% CI 0.47 - 3.79, p = 0.70) in postepidemic period (Table 2). However, while analysing the incidence according to genders within the groups of children and adults, certain differences were observed within the adult group. The risk of diphtheria was 36% lower for males than females. The incidence ratio across males and females comprised 0.64 (95% CI 0.40 - 1.00), p = 0.052).

Table 2. Diphtheria incidence by gender in Lithuania, 1991–2011

Period	Males		Females		RR*	95% CI	p
	Number of cases	Incidence rate / 100 thousand of males	Number of cases	Incidence rate / 100 thousand of females			
Epidemic incidence period	44	0.48	66	0.62	0.77	0.52 - 1.15	0.22
Postepidemic period	9	0.04	9	0.03	1.33	0.47 - 3.79	0.70

* rate ratio

The age of diphtheria cases varied from 3 to 64 years, median was 39 years (average – 34.5 years) during the epidemic incidence period. During postepidemic period the age diphtheria cases varied from 5 to 68 years, median was 38.5 years (average – 37.7 years). No significant statistical difference comparing the age distribution of diphtheria cases during the different periodswas identified (p = 0.51).

Adults were predominant within diphtheria cases during the epidemic incidence period and postepidemic period. People of 18 years and over comprised 82.8% of all diphtheria cases during epidemic incidence period and 72.4% during the postepidemic period (p = 0.21). The highest proportion of disease during epidemic incidence period was observed within the 30-40 years age group. Especially high incidence rate of diphtheria was identified within the 40-49 years age group (1.5 / 100 thousand population). The incidence rate within this group was 5 times higher than within the 20-29 and 50-59 years age groups. Case-fathality rate during epidemic incidence period was 15.5%, however, within the 40-49 years age group it reached 31.8%. During the postepidemic period higher diphtheria incidence was also observed within the 30-49 years age group (Table 3).

Table 3. Diphtheria incidence and case-fatality rate by age in Lithuania, 1991–2011.

		Age groups, years							Total
		0-14	15-19	20-29	30-39	40-49	50-59	60 and >	
Epidemic incidence period, 1991–1996	Number of diphtheria cases	19	8	8	22	44	8	1	110
	Proportion of diphtheria cases (%)	17.3	7.3	7.3	20.0	40.0	7.3	0.9	100.0
	Average incidence rate / 100 thousand population	0.6	0.5	0.3	0.8	1.5	0.3	0.02	0.6
	Number of deaths	0	0	0	2	14	1	0	17
	Proportion of deaths (%)	0	0	0	11.8	82.4	5.9	0.0	100.0
	Case-fatality rate (%)	0	0	0	9.1	31.8	12.5	0.0	15.5
Postepidemic period, 1997–2011	Number of diphtheria cases	3	1	2	4	4	1	3	18
	Proportion of diphtheria cases (%)	16.7	5.6	11.1	22.2	22.2	5.6	16.7	100.0
	Average incidence rate / 100 thousand population	0.04	0.03	0.03	0.06	0.05	0.02	0.03	0.04
	Number of deaths	1	0	0	0	1	0	1	3
	Proportion of deaths (%)	33.3	0.0	0.0	0.0	33.3	0.0	33.3	100.0
	Case-fatality rate (%)	33.3	0.0	0.0	0.0	25.0	0.0	33.3	16.7

During the years 1991–2011 the majority of diphtheria cases in Lithuania have not been vaccinated or the status of the vaccination was unknown. The prevalence of people who have not been vaccinated within the group of patients during epidemic incidence period and postepidemic period comprised 77.3% and 72.2% appropriately (p = 076). Children and adults who have not been vaccinated comprised 24.0% of the children group and 89.3% of the adult group. The proportion of diphtheria cases who have not been vaccinated within the groups of adults and children during epidemic incidence period and postepidemic period was similar (Table 4). Risk of death within unvaccinated diphtheria cases was 6.6 times higher, compared to the one of vaccinated cases (RR (Relative risk) = 6.60; 95% CI 1.24 - 38.79, p = 0.021).

Table 4. Diphtheria cases by vaccination status in Lithuania, 1991–2011

Period	Total:	Unvaccinated		p	Children (0-17 years old)			p	Adults (18 years old and over)			p
		No of cases	%		Total	Unvaccinated			Total	Unvaccinated		
						No of cases	%			No of cases	%	
Epidemic incidence period, 1991–1996	110	85	77.3	0.76	21	4	19.0	0.23	89	81	91.0	0.17
Post epidemic period, 1997–2011	18	13	72.2		4	2	50.0		14	11	78.6	

The median for seeking medical care from the first day of disease was 2 days (average 2,5 days) in epidemic incidence period,. During the postepidemic period the median was 1 day (average 2.7 days). No significant statistical difference between the time period for seeking medical help from the first day of disease during the epidemic incidence period of and postepidemic period was identified (p = 0.24).

Table 5. Diphtheria cases by risk factors in Lithuania, 1991–2011

Diphtheria risk factors	Epidemic incidence period, 1991–1996		Postepidemic period, 1997–2011	
	Number of cases	%	Number of cases	%
Travelling to endemic countries (Russia, Belarus) or close contact to people travelling from these areas	11	10.0	1	5.6
Living in closed settings (boarding school)	3	2.7	0	0.0
Homeless, antisocial type of life	4	3.6	2	11.1
Chronic alcoholism, drug addiction	4	3.6	3	16.7
Epidemiological link to laboratory confirmed cases of diphtheria (carriers)	15	13.6	3	16.7
Unemployed	43	39.1	0	0
Work in closed settings	4	3.6	0	0

Treatment using a specific antitoxinwas applied to less than a half of patients during epidemic incidence periodand postepidemic period (42.2% of cases, 54 cases). However, for 13 of them were lethal cases.

The diphtheria risk factors were prevalent among diphtheria cases during epidemic incidence period and postepidemic period (Table 5).

During 1991–2011 years 86.7% of diphtheria (111 cases) were confirmed laboratory confirmed, diphtheria diagnosis for the rest was confirmed by clinical picture and (or) epidemiological link. Toxigenic causative organism was isolated in 75% (96 cases) of all cases, from 9.4% (12 cases) were identified non-toxigenic *C.diphtheriae* (Table 8). Toxigenic *C.diphtheriae* was identified in 85% (16 cases) of all diphtheria lethal cases.

46.1% (59 cases) of all diphtheria cases and 55.0% (11 cases) of lethal cases were caused by toxigenic *gravis* biotype *C. diphtheriae* and 2.3% (3 cases) by non-toxigenic *gravis biotype C. diphtheriae* . *Gravis* biotype *C.diphtheriae* was identified in 48.4% (62 cases) of all diphtheria cases (Table 6).

Table 6. Diphtheria cases of (lethal cases) by causative organism and diagnosis confirmation in Lithuania, 1991–2011

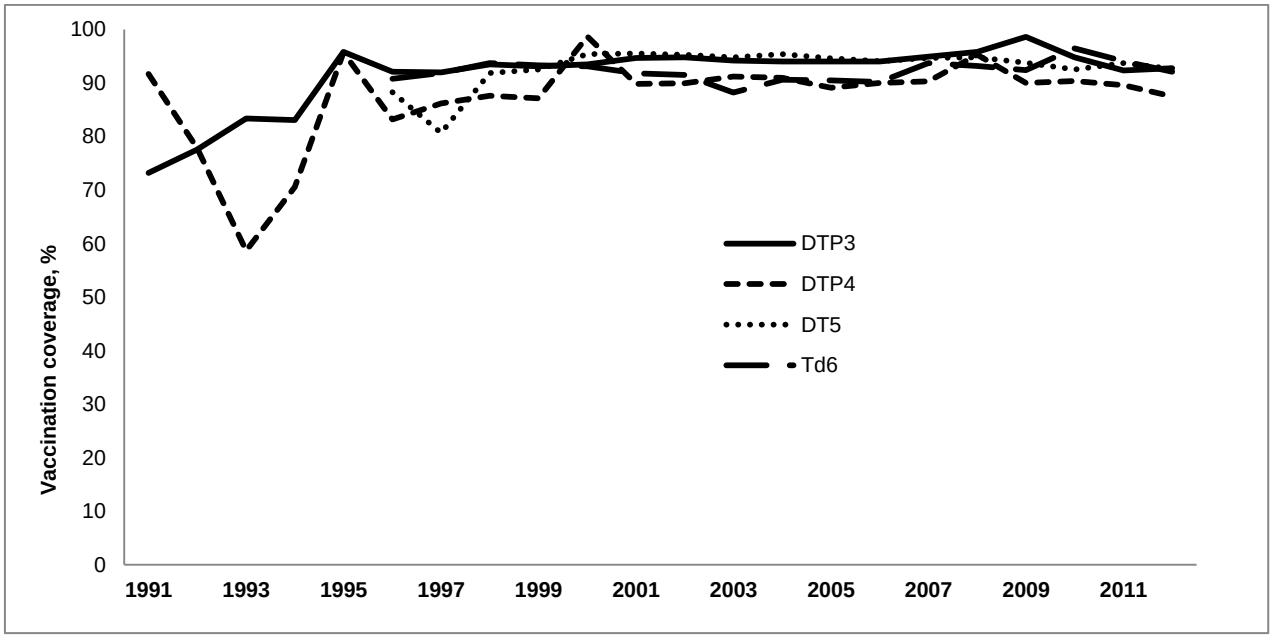
		Diagnosis of diphtheria								
		Isolated *Corynebacterium diphtheriae*								Not laboratory confirmed
		Toxigenic				Notoxin-toxigenic				
		biotype *gravis*	biotype *mitis*	not typed	Total	biotype *gravis*	biotype *mitis*	Not typed	Total	
Epidemic incidence period, 1991–1996	Cases (cases of death)	48 (8)	27 (4)	9 (2)	84 (14)	3	3	6 (1)	12 (1)	13 (2)
	%	43.6	24.5	8.2	76.4	2.7	2.7	5.5	10.9	11.8
Post-epidemic period, 1997–2011	Cases (cases of death)	11 (3)	2	1	14 (3)	0	0	0	0	4
	%	61.1	11.1	5.6	77.8	0	0	0	0	22.2

During the years 1991–2011 in Lithuania, 79.7% (102 cases) of all cases were diagnosed with throat diphtheria, 14.1% (18 cases) of patients with combined diphtheria of respiratory tracts and a lot less with diphtheria manifesting in other parts of the respiratory tracts– larynx (4.7% of patients, 6 cases), nasal (1.6% of patients, 2 cases). In the cases of death from diphtheria, 90% (9 cases) of all the patients who died were diagnosed with throat diphtheria, combined throat diphtheria, and diphtheria manifesting in other parts of the respiratory tract (9 cases). In 2 cases, the death was caused by larynx diphtheria. 94.4% (17 cases) of all the identified cases during the post-epidemic period were diagnosed with throat diphtheria and 1 patient was diagnosed with a combined form of diphtheria.

3.1.6. Vaccination

One of the main indicators on children vaccinationcoverage – the vaccination coverage comprised of three vaccination doses against pertussis, diphtheria, and tetanus (DTP3) for children of age 1 year. DTP3 vaccination coverage during the years 1991–1994 was insufficient, reaching from 73.2 to 83.4%. After the year 1995, vaccination coverage reached higher than 90% annually and remained at this level for many years. During the later years, DTP3 vaccination coverage slightly decreased, if DTP3 vaccination coverage was 98.6% in 2009, in 2010, it reached only 94.8% and decreased to 92.4% in 2011.

DTP4 vaccination coverage was lower than DTP3, and did not reach 90% during the years 1991–2011 (i.e., WHO recommendations), except certain years when very high vaccination coverage was reached (e.g., 95.3% in 2008). After the time period in 2003–2010 when DTP4 vaccination coverage reached or was higher than 90%, DTP4 vaccination coverage once again decreased to lower than 90% in the year 2011. (Picture 6).



Picture 7. Vaccination coverage in Lithuania, 1991–2012.

After conducting the mass vaccination campaign for adult in the years 1996–1997 till the year 2009, adults were not vaccinated from diphtheria free of charge.

After 2009, in accordance with National Immunization Programme, the adult revaccination against diphtheria and tetanus every 10 years was funded by the state. Even though, adults were vaccinated against diphtheria and tetanus free of charge, high vaccination coverage was not achieved. During the time period 2010–2012, 195.4 thousand were vaccinated against diphtheria and tetanus (9.1% of adult population). Adults vaccination coverage ranged between the counties. For example, in 3 years

15.1% of adult population 26 years old and over were vaccinated in Panevežys county, 11.7% in Kaunas county, and 6.8% in Marijampolė county.

3.2. Prevalence of toxigenic and non-toxigenic Corynebacterium within the population of Lithuania

13 laboratories from different regions of Lithuania (Vilnius, Klaipėda, Šiauliai, Panevežys, Alytus, Marijampolė counties) participated in screening for diphtheria causative organisms in patients with upper respiratory tract infections. 3 toxigenic strains of *Corynebacterium diphtheriae* were identified in Vilnius (2 in the National Public Health Surveillance, 1 in Vilnius University Children's Hospital) and 1 toxigenic strain of diphtheria causative agent in Kaunas (in Kaunas division of National Public Health Surveillance Laboratory).

2988 swabs were examined during the screening on diphtheria causative organisms. The majority of the examined swabs were collected from females (58.7% of all swabs (n = 1755)) (Table 6). 4 toxigenic *C.diphtheriae* strains were isolated during the study. Carriage of toxigenic *C. diphtheriae* rate was 1.3 cases per 1000 tested swabs (95% CI 0.4 - 3.4).

Table 6. Carriage of diphtheria causative organism rate by age and gender

		Toxigenic			Non- toxigenic		
	Number of swabs (%)	Number of isolated strains	Carriage per 1000	95%CI	Number of isolated strains	Carriage per 1000	95% CI
Total	2988 (100.0)	4	1.3	0.4 - 3.4	4	1.3	0.4 - 3.4
By age groups							
0-14 years	1430 (47.9)	0	0	0	0	0	0
15-19 years	364 (12.2)	1	2.7	0.1 - 15.2	1	2.7	0.1 - 15.2
20-29 years	265 (8.9)	1	3.8	0.1 - 20.8	0	0	0
30-39 years	338 (11.3)	0	0	0	3	8.9	1.8 - 25.7
40-49 years	236 (7.9)	1	4.2	0.1 -2 3.4	0	0	0
50-59 years	185 (6.2)	0	0	0	0	0	0
60+ years	170 (5.7)	1	5.9	0.1 - 32.3	0	0	0
By gender							
Males	1233 (41.3)	1	0.8	0.02 -4.51	2	1.6	0.2 - 5.8
Females	1755 (58.7)	3	1.7	0.4 - 5.0	2	1.1	0.1 - 4.1

Higher toxigenic *C.diphtheriae* carriage rate was identified between females and between age groups of 40-49 and 60 years old and over, however, no statistically significant difference between genders and age groups was identified.

Out of the four cases, where the toxigenic *C.diphtheriae* was isolated, 2 were diphtheria cases and 2 healthy carriers. Both diphtheria cases presented with classic respiratory diphtheria with a pseudomembranes Neither one of them had travelled to other countries nor had epidemiological link to other diphtheria case. The fatal case of diphtheria was unvaccinated 61 years old woman (case no. 1) who lived in crowded conditions with inadequate nutrition (Table 7).. Eighty contacts were swabbed, two of whom were carriers of toxigenic *C.diphtheriae* (case no. 2 and no. 3). One of them was unvaccinated against diphtheria and other with unknown vaccination status. The second diphtheria case was a 15 year old female, was vaccinated (completed primary immunization, last high dose booster was received in 2001, next booster would be scheduled at 15–16 years of age) with no other known risk factors.

The girl was suffering from a mild form of diphtheria that was cured during the course of the treatment. All 22 close contacts were swabbed and were negative for diphtheria causative organisms.

All 4 of toxigenic C.diphtheriae isolated strains were of *gravis biotype Sankt-Peterburg* ribotype.

Identification of the ribotype and biotype of isolated non-toxigenic strains was conducted. Three out of four isolated non-toxigenic *C.diphtheriae* strains were of *mitis* biotype (two of them were of *Moskva* ribotype, one *Otchakov*), one of them was of the *belfanti* biotype, *Romania* ribotype. Non-toxigenic isolates of *C.diphtheriae* were tested for toxin-gene bearing, it appears that two out of four isolated non-toxigenic *C.diphtheriae* strains were bearing toxin-gene, even though, they did not produce the toxin (*mitis* biotype, *Moskva* ribotype).

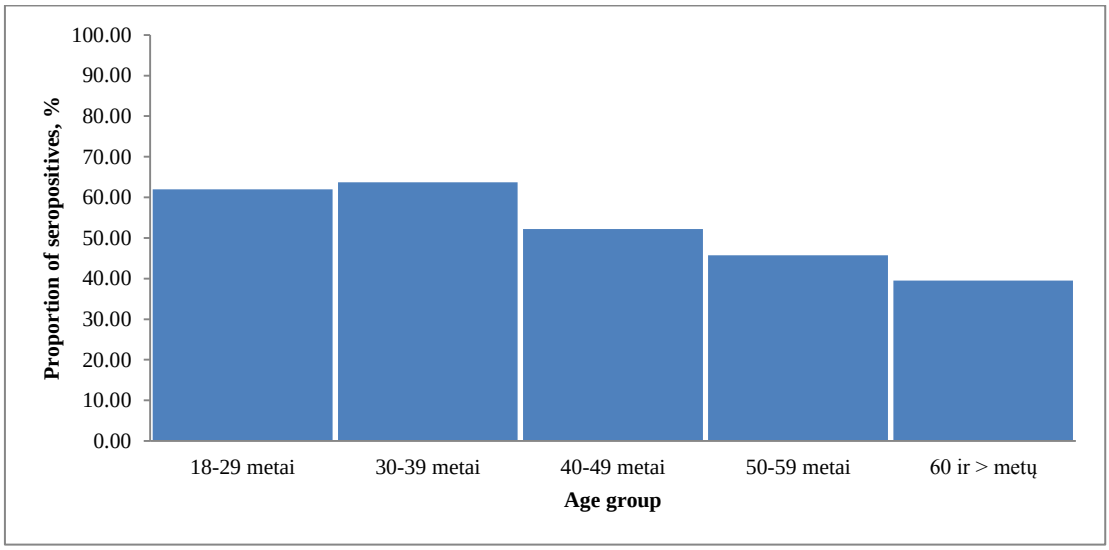
Table 7. Isolates detected during screening period

Case No.	Age group (years)	Gender	Organism	Biotype	Ribotype	Comment
Toxigenic isolates						
1.	60 and >	F	*C.diphtheriae*	*gravis*	*Sankt-Peterburg*	Case of diphtheria (death)
2.	15-19	F	*C.diphtheriae*	*gravis*	*Sankt-Peterburg*	Case of diphtheria, identified during screening
3.	20-29	M	*C.diphtheriae*	*gravis*	*Sankt-Peterburg*	Carrier, epidemiological link
4.	40-49	F	*C.diphtheriae*	*gravis*	*Sankt-Peterburg*	Carrier, epidemiological link
Non- toxigenic isolates						Identification toxin-gene bearing (PCR)
1.	15-19	M	*C.diphtheriae*	*mitis*	*Moskva*	Positive, non-toxigenic toxin-gene bearing
2.	30-39	M	*C.diphtheriae*	*mitis*	*Otchakov*	Negative
3.	30-39	F	*C.diphtheriae*	*mitis*	*Moskva*	Positive, non-toxigenic toxin-gene bearing
4.	30-39	F	*C.diphtheriae*	*belfanti*	*Romania*	Negative

3.3. Herd antitoxic immunity to diphtheria of the adult population in Lithuania

In total, 495 were enrolled and tested for diphtheria antibodiesstudy, 41.8% (n = 207) were males and 58.2% (n = 288) females. The average age of the tested subjects was 47.5 years (46.5 for males, 48.2 for females).

During the study, it was identified that 51.92% (95% CI 47.51 – 56.30) of the tested participants were seropositive, i.e., had a protective antitoxic immunity to diphtheria (Table 15). The proportion of seronegativeparticipants decreased respectively with age. (p = 0.001) (Figure 7).



Picture 8. Seropositivity for diphtheria by age group

Diphtheria seropositivity was highest within the 18-29 and 30-39 age groups, appropriately – 61.97% (95% CI 50.30 - 72.68) and 63.72% (95% CI 54.55 - 72.19) (Table 8).

The lowest proportion of seropositive participants was observed within the age groups of 40 years old and over.

55.07% (95% CI 48.25 – 61.76) of males and 49.65% (95% P.I. 43.90 – 55.92) of females were seropositive. However, no significant difference between the groups of different gender was identified.

Diphtheria antibody concentration 0.01–0.09 IU/ml were detected for 44.2% of participants (95% CI 39.91 – 48.65). 3.84% (95% CI 2.40 – 5.82) of the tested participants had no detectable antibodies (i.e., concentration lower than 0.01 IU/ml).

47.47% (95% CI 43.10 - 51.88) of seropositive participants had a concentration of the protective level of diphtheria antitoxin antibodies (0.1-0.99 IU/ml), however, the concentration of the antibodies that is interpreted as a long-term protection was identified for 4.44% (95% CI 2.88 - 6.54) of the tested participants. The decrease in the concentration of the diphtheria antitoxin antibodies is related to age (p = 0.044). The proportion of participants with very low concentration of diphtheria antitoxin antibodies

(lower than 0.01 IU/ml) increased proportionally to age and, vice versa, the proportion of participants with the concentration of antibodies that ensures long-term protection (> 1 IU/ml) decreased within the older age groups.

Table 8. Diphtheria seropositivity by age and gender

Variable	Number of tested participants	Seropositive (≥ 0.1 IU/ml)		
		No.	%	95% CI
Total	495	257	51.92	47.51 - 56.30
By age group				
18-29 years	71	44	61.97	50.30 - 72.68
30-39 years	113	72	63.72	54.55 - 72.19
40-49 years	92	48	52.17	41.98 - 66.24
50-59 years	105	48	45.71	36.37 - 55.30
60 and > years	114	45	39.47	30.82 - 48.66
By gender				
Males	207	114	55.07	48.25 - 61.76
Females	288	143	49.65	43.90 - 55.92

3.4. Attitude, intentions to be vaccinated of the adult population in Lithuania

3.4.1. Description of respondents

945 respondents participated in the study, 46.2% (n = 437) of them were males and 58.2% (n = 508) females. The average age of the repondents was 48.0 years (45.8 for males, 49.8 for females). 3.1% of the respondents had obtained a primary education, basic education– 9.9%, secondary education– 39.0% post-secondary/ higher education– 27.0%, university degree– 21.0%. 47.4% of the respondents were residents of city municipalities, 52.6% of district municipalities. The majority of the respondents (58.7%) indicated that the average monthly income of a single family person was ≤1000 Lt, 25.0% indicated that it was above 1000 Lt.

3.4.2. Prevalence of variables of the extended Theory of Planned Behaviour and the Health Belief Model

21.4% of respondents indicated a positive intention to being vaccinated. While analysing the attitude of the respondents toward the vaccinations against diphtheria and tetanus, 49.8% of the respondents expressed a positive attitude, while 22.7% had a positive attitude towards the questions illustrating the subjective norms. During the assessment of perceived behavioural control, 59.6% of the respondents answered the questions positively. As a past-related behaviour, 13.1% of the respondents indicated that in the last 10 years they had been vaccinated against diphtheria and tetanus while 14.1% indicated that they had been vaccinated against influenza during the last influenza season. Positive comprehension on the perveived susceptibility), i.e., comprehension that exactly they can be the ones who could contract the disease, expressed 28.3% of the respondents, while 50.3% believed that it is not possible for them to be exactly the ones who could contract the disease. Perceived severity was assessed positively by more than half of the respondents (59.2%).

Perceived benefits of the vaccinations was assessed positively by the majority of the respondents– 42.7%, negatively– 35.5%.

3.4.3. Demographical determinants of the intention to be vaccinated

Intention to be vaccinated was dependant on the gender. Males had a 50% lower odd to be vaccinated compared to females (OR (odds ratio) = 0.50, 95% CI 0.32 - 0.78, p = 0.002).

Intention to be vaccinated was related to age, statistically significant differences were identified between different age groups (p = 0.024).

No statistically significant correlation to family status, average amount of the income of a single family member, working capacity, residence (city or district) of the respondents, was identified. Social-demographic factors explained only a relatively small variance (7.0 - 13.2%) in intention.

3.4.4. The extended Theory of Planned Behaviour determinants of the intention to be vaccinated

A strong correlation between a positive attitude and the intention to be vaccinated was identified (OR = 39.25, 95% CI 4.27 - 360.83, p = 0.001) (Table 9). Study results showed that a social environment has a direct effect on the intention to be vaccinated. The respondents who assessed the subjective norm positively, had a 3.49 times higher odd of the intention to be vaccinated compared to the ones who assessed the subjective norm negatively, (OR = 3.49, 95% CI 1.42 - 8.59), p = 0.007).

Perceived behavioural control (i.e., does a person feel that he can control his own actions) was associated to the intention to be vaccinated. The odd to be vaccinated of the

respondents who assessed the perceived behavioural control was 6.16 times higher (OR = 6.16, 95% CI 1.10 - 34.55, p = 0.039) compared to the group of respondents which assessed the perceived behavioural control negatively.

Intentions to be vaccinated were assessed by connecting additional variables to the Theory of Planned Behaviour– anticipated regret in the future for not being vaccinated and past-related behaviour (i.e., if a person had been vaccinated against diphtheria and tetanus in the last ten years and vaccinated against influenza during the influenza season). Additional variables significantly improved the model (AIC = -0153), the sensitivity of the model increased (from 65.22 to 76.74%) and the specificity increased (from 93.57 to 96.10%), the proportion of correctly classified cases increased from 85.92 to 90.85 Study results showed that these additional variables of the Theory of Planned Behaviour are important for the study on behaviour, i.e., intention to be vaccinated.

Table 9. The extended Theory of Planned Behaviour determinants of the intention to be vaccinated

Variable	OR_b	OR_p	95 % CI	p
Variables of the Theory of Planned Behaviour.				
Attitude				
Positive attitude *	85,14	39,25	4,27–360,83	0,001
Negative attitude **	1,00	1,00	–	–
Subjective norm				
Positive subjective norm *	13,37	3,49	1,42–8,59	0,007
Negative subjective norm **	1,00	1,00	–	–
Perceived behavioural control				
Positive perceived behavioural control *	16,48	6,16	1,10–34,55	0,039
Negative perceived behavioural control **	1,00	1,00	–	–
Additional variables				
Past-related behaviour				
Have been vaccinated against diphtheria and tetanus in the last 10 years	7,67	1,08	0,34–3,37	0,90
Have not been vaccinated against diphtheria and tetanus in the last 10 years	1,00	1,00	–	–
Have been vaccinated against influenza prior to influenza season	30,43	16,47	5,02–54,08	<0,0001
Have not been vaccinated against influenza prior to influenza season	1,00	1,00	–	–
Anticipated regret				
Positive anticipated regret *	15,64	7,51	2,92–19,33	<0,0001
Negative anticipated regret **	1,00	1,00	–	–

Controlled variables: gender, age, average monthly income of a single family member, working capacity, family status, residence, education, and occupation.

N = 317. Chi-square ratio of the model probability 222.36, llsk. 18, p < 0.001, chi-square of Hosmer-Lemeshow test 10.92, llsk. 8, p = 0.206, R^2 (McFadden) 0.600, R^2 (McKelvey and Zavoina) 0.810, model correctly classified 90.85% of the respondents, area under the ROC – 0.95.

* 5-7 points on the Likert scale, * 1-4 points on the Likert scale.

No significant correlation between the intention be vaccinated and past-related vaccinations against diphtheria and tetanus was identified, although, the odds for the intention to be vaccinated within the group of respondents which were vaccinated against influenza were 16.47 times higher compared to the group which have not been vaccinated against influenza (OR = 16.47, 95% CI 5.02 - 54.08), $p < 0.0001$).

Intention to be vaccinated is directly associated to the anticipated regret in the future for not being vaccinated. The intention to be vaccinated within the respondents who anticipated that they will regret not being vaccinated in the future was 7.51 times higher (OR = 7.51, 95% CI 2.92 - 19.33, $p < 0.0001$) compared to the respondents who believed that they will not regret not being vaccinated in the future.

3.4.5. The Health Belief Model determinants of of the intention to be vaccinated

A significant correlation between the intention to be vaccinated and the variables of the Health Belief Model (perceived susceptibility, perceived severity and perceived benefits) was identified. Odds of intention to be vaccinated of the respondents who positively assessed the perceived susceptibility to diphtheria and tetanus, i.e., comprehend the personal risk of contracting these diseases, was 2.25 times higher (OR = 2.25, 95% CI 1.04 - 4.83, $p = 0.038$) compared to the respondents who expressed a negative opinion on the susceptibility, i.e., who do not believe that exactly they could be the ones who could contract diphtheria and tetanus (Table 10). Odds of intention to be vaccinated of the respondents who positively assessed the perceived severity of the disease were 3.80 times higher (OR = 3.80, 95% CI 1.49 - 9.71, $p = 0.005$) compared to the respondents who assessed the perceived severity of the disease negatively, i.e., they did not believe that exactly they could be the ones who could contract diphtheria and tetanus. Intention to be vaccinated was directly related to the positive assessment of the perceived benefits between respondents (it is beneficial to receive vaccinations because there would be no more worries of contracting a disease, no more visits to the doctor, etc.). The odds ratio for the intention to be vaccinated was 14.07 (OR = 14.07, 95% CI 7.07 - 51.16), $p < 0.0001$). No significant correlation between the intention to be vaccinated and perceived barriers was identified (OR = 047, 95% CI 0.20 - 1.79), $p = 0.40$).

The Health Belief Model explained 41.5-60.5% of the variance in intention to be vaccinated.

Table 10. The Health Belief Model determinants of the intention to be vaccinated

Variable	OR_b	OR_p	95% CI	p
		Perceived susceptibility		
Positively perceived susceptibility*	9.04	2.25	1.04 - 4.83	0.038
Negatively perceived susceptibility**	1.00	1.00	–	–
		Perceived severity		
Positively perceived severity *	7.60	3.80	1.49 - 9.71	0.005
Negatively perceived severity**	1.00	1.00	–	–
		Perceived benefits		
Positively perceived benefits*	14.07	19.02	7.07 - 51.16	<0.0001
Negatively perceived benefits**	1.00	1.00	–	–
		Perceived barriers		
Positively perceived barriers *	0.47	0.47	0.20 - 1.79	0.40
Negatively perceived barriers **	1.00	1.00	–	–

Controlled variables: gender, age, average monthly income of a single family member, working capacity, family status, residence, education, and occupation.
N = 367. Chi-square ratio of the model probability 136.91, llsk. 16, $p < 0.001$, chi-square of Hosmer-Lemeshow test 6.42, llsk. 8, $p= 0.601$, R^2 (McFadden) 0.415, R^2 (McKelvey and Zavoina) 0.605, model correctly classified 83.95% of the respondents, area under ROC curve– 0.90.
* 5-7 points on the Likert scale.
** 1-4 points on the Likert scale.

3.4.6. Demographical determinants of the intention to be vaccinated against diphtheria and tetanus

Intentions to be vaccinated against diphtheria and tetanus were dependent on the gender. Males had a 53% lower odd to be vaccinated compared to females (OR = 0.53, 95% CI 0.35 - 0.81, p = 0.003).

The intention to be vaccinated against diphtheria and tetanus was related to age, the younger the age groups had the higher the odds to be vaccinated compared to other age groups. The odd of intention to be vaccinated against diphtheria and tetanus within the 18-24 age group was 2.93 times higher (OR = 2.93, 95% CI 1.17 - 7.30, p = 0.021) compared to the 65-74 age group. Intention to be vaccinated against diphtheria and tetanus was also related to the monthly income of a single family member and their occupation. The odd of intention to be vaccinated against diphtheria and tetanus for people whose monthly income was higher than 1000 Lt was 2.59 higher (OR = 2.59, 95% CI 1.16 - 4.79, p = 0.021) compared to the people whose monthly income of a single family member was lower than 1000 Lt. The odd of intention to be vaccinated against diphtheria and tetanus of people who are employed was 2.81 times higher (OR = 2.81, 95% CI 1.57 - 5.02, p = 0.0001) compared to the people who are unemployed.

3.4.7. The extended Theory of Planned Behaviour determinants of the intention to be vaccinated against diphtheria and tetanus

A strong direct correlation between a positive attitude and the intention to be vaccinated against diphtheria was identified (OR = 12.88, 95% CI 3.74 - 44.42, p = 0.0001) (Table 11). Study results showed that a social environment has an effect on the intention to be vaccinated against diphtheria and tetanus. Respondents who positively assessed the subjective norm, had a 2.11 times higher odds of intention to be vaccinated against diphtheria and tetanus compared to the ones assessing the subjective norms negatively, (OR = 2.11, 95% CI 1.02 - 4.35), p = 0.043).

Table 11. The extended Theory of Planned Behaviour determinants of the intention to be vaccinated against diphtheria and tetanus

Variable	OR_b	OR_p	95 % CI	p
Variables of the Theory of Planned Behaviour.				
Attitude				
Positive attitude *	19.69	12.88	3.74 - 44.42	< 0.0001
Negative attitude **	1.00	1.00	–	–
Subjective norm				
Positive subjective norm *	7.19	2.11	1.02 - 4.35	0.043
Negative subjective norm **	1.00	1.00	–	–
Perceived behavioural control				
Positive perceived behavioural control *	5.99	2.05	0.68 - 6.12	0.20
Negative perceived behavioural control **	1.00	1.00	–	–
Additional variables				
Past-related behaviour				
Have been vaccinated against diphtheria and tetanus in the last 10 years	7.67	8.43	3.92 - 18.10	< 0.0001
Have not been vaccinated against diphtheria and tetanus in the last 10 years	1.00	1.00	–	–
Have been vaccinated against influenza prior to influenza season	30.43	1.72	0.78 - 3.81	0.18
Have not been vaccinated against influenza prior to influenza season	1.00	1.00	–	–
Anticipated regret				
Positive anticipated regret *	15.64	2.49	1.22 - 4.79	0.012
Negative anticipated regret **	1.00	1.00	–	–

Controlled variables: gender, age, average monthly income of a single family member, working capacity, family status, residence, education, and occupation.
N = 3800. Chi-square ratio of the model probability 186.65, llsk. 6, p < 0.001, chi-square of Hosmer-Lemeshow test 9.89, llsk. 6, p = 0.129, R2 (McFadden) 0.426, R2 (McKelvey and Zavoina) 0.620, model correctly classified 85.26% of the respondents, area under ROC curve– 0.89.
* 5-7 points on the Likert scale.
** 1-4 points on the Likert scale.

Perceived behavioural control was not directly related to the intention to be vaccinated against diphtheria and tetanus.

Intention to be vaccinated against diphtheria and tetanus was assessed by adding additional variables to the variables of the Theory of Planned Behaviour, such as anticipated regret in the future for not being vaccinated and past-related behaviour (i.e., the person has been vaccinated against diphtheria, tetanus in the last 10 years and against influenza prior to the influenza season). No significant correlation between the intention to be vaccinated and prior vaccinations against influenza was identified, although, the odds of intention to be vaccinated against diphtheria and tetanus of the group of respondents which has been vaccinated against these diseases in the last 10 years was 8.43 times higher compared to the group which has not been vaccinated in the past (OR = 8.43, 95% CI 3.92 - 18.10), $p < 0.0001$).

Intention to be vaccinated against diphtheria and tetanus was directly related to the anticipated regret in the future. The odd of the intention to be vaccinated between the respondents who predicted that they will regret not being vaccinated in the future was 2.49 times higher (OR = 2.49, 95% CI 1.22 - 4.76, $p < 0.012$) compared to the respondents who believed that they will not regret not being vaccinated in the future.

3.4.8. The Health Belief Model determinants of the intention to be vaccinated against diphtheria and tetanus

A significant correlation between the intention to be vaccinated against diphtheria and tetanus and variables of the Health Belief Model was identified. Odds of the intention to be vaccinated against diphtheria and tetanus between the respondents who positively assessed the susceptibility to the diphtheria and tetanus, i.e., comprehend the personal risk to contract these diseases was 3.31 times higher (OR = 3.31, 95% CI 1.88 - 5.80, $p < 0. 0001$) compared to the respondents who expressed a negative opinion on the susceptibility (Table 12). Odds of intention to be vaccinated against diphtheria and tetanus of the respondents who positively assessed the perceived disease severity were 3.80 times higher (OR = 3.03, 95% CI 1.55 - 5.91, $p = 0.001$) compared to the respondents who assessed the perceived disease severity negatively, i.e., who do not believe that they could be exactly the ones who could contract a severe case of diphtheria and tetanus or could even die from it. Intention to be vaccinated against diphtheria and tetanus was directly related to the positive assessment of the perceived benefits of the respondents. The odds ratio of the intention to be vaccinated was 3.95 (OR = 3.95, 95% CI 2.17-7.19, $p < 0.001$) between the ones who assessed the perceived benefit positively and negatively. No significant correlation between the intention to be vaccinated against diphtheria and tetanus, and perceived barriers was identified (OR = 0.62, 95% CI 0.32 - 1.22), $p = 0.17$).

Table 12. The Health Belief Model determinants of the intention to be vaccinated against diphtheria and tetanus

Variable	OR_b	OR_p	95% CI	p
Perceived susceptibility				
Positively perceived susceptibility*	8.22	3.31	1.88 - 5.80	< 0.0001
Negatively perceived susceptibility**	1.00	1.00	–	–
Perceived severity				
Positively perceived severity *	6.13	3.03	1.55 - 5.91	0.001
Negatively perceived severity**	1.00	1.00	–	–
Perceived benefits				
Positively perceived benefits*	5.35	3.95	2.17 - 7.19	< 0.0001
Negatively perceived benefits**	1.00	1.00	–	–
Perceived barriers				
Positively perceived barriers *	0.52	0.62	0.32 - 1.22	0.17
Negatively perceived barriers **	1.00	1.00	–	–

N = 384. Chi-square ratio of the model probability 102.14, llsk. 4, p < 0.001, chi-square of Hosmer-Lemeshow test 12.88, llsk. 6, p = 0.601, R^2 (McFadden) 0.232, R^2 (McKelvey and Zavoina) 0.362, model correctly classified 83.95% of the respondents, area under ROC curve– 0.81.
* 5-7 points on the Likert scale.
** 1-4 points on the Likert scale.

3.4.9. Demographical determinants of past-related behaviour (vaccination against diphtheria and tetanus in the last 10 years)

Past-related behaviour (vaccination against diphtheria and tetanus in the last 10 years) was related to age. The younger the age group had the higher odds of vaccinations against diphtheria and tetanus in the last 10 years compared to other age groups. The chance of past-related vaccination against diphtheria and tetanus within the 18-24 age group was 8.40 times higher (OR = 8.40, 95% CI. 2.88 - 24.49, p = 0.0001) compared to the 65-74 age group. Past-related vaccination against diphtheria and tetanus was also related to the monthly income of a single family member and their occupation. The odd of prior vaccinations against diphtheria and tetanus in the last 10 years for people whose monthly income was higher than 1000 Lt, was 2.77 higher (OR = 2.77, 95% CI 1.36 - 6.78, p = 0.025) compared to people whose monthly income of a single family member was lower than 1000 Lt. Higher odds of past-related vaccination were estimated within the respondent groups which lived and worked in the district municipalities.

3.4.10. The extended Theory of Planned Behaviour determinants of past-related behaviour (vaccinations against diphtheria and tetanus in the last 10 years)

A strong, direct correlation between positive attitude and past related behaviour (vaccination against diphtheria and tetanus in the last 10 years) was identified (OR = 2.29, 95% CI 1.06 - 4.97, p = 0.036) (Table 13). Study results showed that there were no

significant relation of subjective norm and perceived behavioural control to past-related behaviour (vaccination against diphtheria and tetanus in the last 10 years).

Table 13. The extended Theory of Planned Behaviour determinants of past-related behaviour (vaccination against diphtheria and tetanus in the last 10 years)

Variable	OR_b	OR_p	95 % CI	p
Variables of the Theory of Planned Behaviour.				
Attitude				
Positive attitude *	6.01	2.29	1.06 - 4.97	0.036
Negative attitude **	1.00	1.00	–	–
Subjective norm				
Positive subjective norm *	4.99	1.85	0.94 - 3.62	0.08
Negative subjective norm **	1.00	1.00	–	–
Perceived behavioural control				
Positive perceived behavioural control *		1.24	0.53 - 2.91	0.63
Negative perceived behavioural control **	1.00	1.00	–	–
Additional variables				
Past-related behaviour				
Have been vaccinated against influenza prior to influenza season	2.52	1.61	0.53 - 4.88	0.40
Have not been vaccinated against influenza prior to influenza season	1.00	1.00	–	–
Anticipated regret				
Positive anticipated regret *		0.98	0.43 - 2.25	0.96
Negative anticipated regret **	1.00	1.00	–	–

N = 407. Chi-square ratio of the model probability 77.22, llsk. 6, $p < 0.001$, chi-square of Hosmer-Lemeshow test 0.32, llsk. 4, $p = 0.989$, R^2 (McFadden) 0.191, R^2 (McKelvey and Zavoina) 0.255, model correctly classified 84.28% of the respondents, area under ROC curve– 0.77.
* 5-7 points on the Likert scale.
** 1-4 points on the Likert scale.

No significant correlation between prior vaccinations against diphtheria and tetanus to prior vaccinations against influenza was identified.

3.4.11. The Health Belief Model determinants of past-related behaviour (vaccination against diphtheria and tetanus in the last 10 years)

A statistically significant direct correlation between past-related behaviour (vaccination against diphtheria and tetanus in the last 10 years) and the variables of the Health Belief Model, such as perceived susceptibility, perceived severity and perceived benefits was identified. Odds of prior vaccinations against diphtheria and tetanus of the respondents who positively assessed their susceptibility to diphtheria and tetanus, i.e., comprehend the personal risk of contracting these diseases was 2.27 times higher (OR = 2.27, 95% CI 1.24 – 4.17, p = 0.008) compared to the respondents who expressed a negative opinion on susceptibility (Table 13). Odds of past-related vaccination against diphtheria and tetanus of the respondents who assessed the perceived severity positively

were 2.94 times higher (OR = 2.94, 95% CI 1.44 - 6.01, p = 0.003) compared to the respondents who negatively assessed the perceived severity. Past-related vaccination against diphtheria and tetanus was directly related to positive assessment of the perceived benefits of the respondents, the odds ratio of past-related vaccination against diphtheria and tetanus within them was 2.19 times higher (OR = 2.19, 95% CI 1.17 - 4.11, p < 0.015) compared to the respondents who assessed the perceived benefits negatively. No statistically significant correlation between past-related vaccination and perceived barriers was identified.

Table 13. The Health Belief Model determinants of past-related behaviour (vaccinations against diphtheria and tetanus in the last 10 years)

Variable	OR_b	OR_p	95% CI	p
Perceived susceptibility				
Positively perceived susceptibility*	4.89	2.27	1.24 - 4.17	0.008
Negatively perceived susceptibility**	1.00	1.00	–	–
Perceived severity				
Positively perceived severity *	4.52	2.94	1.44 - 6.01	0.003
Negatively perceived severity**	1.00	1.00	–	–
Perceived benefits				
Positively perceived benefits*	30.8	2.19	1.17 - 4.11	0.015
Negatively perceived benefits**	1.00	1.00	–	–
Perceived barriers				
Positively perceived barriers *	0.46	0.53	0.26 - 1.09	0.08
Negatively perceived barriers **	1.00	1.00	–	–

N = 384. Chi-square ratio of the model probability 51.00, llsk. 4, p < 0.001, chi-square of Hosmer-Lemeshow test 4.87, llsk. 6, p = 0.561, R^2 (McFadden) 0.134, R^2 (McKelvey and Zavoina) 0.243, model correctly classified 81.75% of the respondents, area under ROC curve– 0.75.
* 5-7 points on the Likert scale.
** 1-4 points on the Likert scale.

4. CONCLUSIONS

1. The period of epidemic diphtheria incidence in1991–1996 is characterized by clearly expressed seasonality, higher female incidence compared to males, very high case-fatality rate between those who start seeking medical care in the later stages of the disease. Other epidemiological patterns during the postepidemic period in 1997–2011 remain similar to the period of epidemic incidence in 1991–1996: same affected age groups , high case-fatality rate, the most of cases in major cities, prevalence of the *gravis* biotype *C.diphtheriae* strain.

2. A higher incidence rate within children of 14 years old and younger and within people of age 30-50 during the diphtheria epidemic incidence period in 1991–1996,

shows that the highest risk for the diphtheria epidemic arises when large groups of susceptible people between children and adults exist in population at the same time.

3. Non-toxigenic toxin-gene bearing strains and toxigenic strains of the diphtheria causative organism are circulating in Lithuania. Virulent *Sankt-Peterburg* ribotype *gravis* biotype *C.diphtheriae* continue to circulate.. Lithuania remains a territory of increased risk compared to other European countries.

4. The level of herd antitoxic immunity to diphtheria within adult population of Lithuania is insufficient. Adults of older age (40 years old and over) are the main risk group. The circulating diphtheria causative organisms in the population and the insufficient herd immunity of adults form favourable conditions for the diphtheria epidemic process to become more active.

5. The interval between adults revaccinations against diphtheria and tetanus cannot be longer than 10 year, thus ensuring a protective concentration of diphtheria antibodies in blood.

6. The prevalent attitude to vaccination within the adult population of Lithuania is negative. Negative attitude is prevalent in groups of males and people of older age. Past-related behaviour and anticipated regret are significant , independent variables increasing the prognostic value of the model of Theory of Planned Behaviour in explaining the intention of the adult population to be vaccinated.

7. The variables of the Theory of Planned Behaviour and Health Belief Model are directly related to the intention of the adult population to be vaccinated and the intention to be vaccinated against diphtheria and tetanus. Past-related behaviour is correlated with the attitude to vaccination and the variables of the Health Belief Model.

5. LIST OF PUBLICATIONS

1. Wagner KS, White JM, Neal S, Crowcroft NS, Kupreviciene N, Paberza R, Lucenko I, Joks U, Akbas E, Alexandrou-Athanassoulis H, Detcheva A, Vuopio J, von Hunolstein C, Murphy PG, Andrews N, Members of the Diphtheria Surveillance Network (DIPNET), Efstratiou A. Screening for Corynebacterium diphtheriae and Corynebacterium ulcerans in patients with upper respiratory tract infections 2007–2008: a multicentre European study. Clin Microbiol Infect. Clin Microbiol Infect 2011 Apr; 17(4):519–25

2. Kuprevičienė Nerija, Žagminas Kęstutis, Razmuvienė Daiva, Griškevičius Algirdas. Difterijos epideminio proceso dėsningumai Lietuvoje 1991–2011 metais. Visuomenės sveikata. 2014, Nr. 2. ISSN 1392-2696 p. 45–54. = Patterns of the diphtheria epidemic process in Lithuania during 1991–2011, 45–54 p.

3. Kuprevičienė Nerija, Žagminas Kęstutis. Lietuvos suaugusiųjų gyventojų ketinimas skiepytis ir jį lemiantys veiksniai. Visuomenės sveikata. 2014, Nr. 3. ISSN 1392-2696 p. 56–67. = Influencing factors and intention to be vaccinated of the adult population in Lithuania. Public Health, 56–67 p.

6. PRESENTATIONS

1. Kuprevičienė, Nerija, Žagminas, Kęstutis, Daukšienė, Snieguolė, Razmuvienė, Daiva, Savickienė, Daiva Diphtheria in Lithuania: risk of re-emergence. New Technologies, Healthy Human Being and Environment: IFEH 12th World Congress on Environmental Health, Vilnius, Lithuania, And 22-27 May, 2012: abstract book. ISSN 13929786094600395 p. 4535. (Oral presentation)
2. Kuprevičienė Nerija, Žagminas Kęstutis. Diphtheria in the post-epidemic period in Lithuania. Evoliucinė medicina: nauji senųjų problemų sprendimai: [tarptautinė konferencija, 2012 m. birželio mėn. 12–15 d., Vilnius] = Evolutionary medicine: new solutions for the old problems: the p. 63. (Presentation)
3. Kuprevičienė Nerija, Lucenko I., Perevoscikovs J., Žagminas K., Kanstone I., Razmuvienė D. Diphtheria is still seen disease in Lithuania and Latvia. ESPID 2014: 32th annual meeting of European Society for paediatric infectious diseases: Abstracts, Ireland, 2014, May 6-10. p [1] (presentation)
4. Kuprevičienė Nerija, Žagminas Kęstutis, Tutkuvienė Janina. Determinants related to adult's intention to be vaccinated. Evoliucinė medicina: sveikos sampratos ir ligų suvokimo perspektyvos = Evolutionary medicine: perspectives in understanding health and disease: [tarptautinė konferencija, 2014 m. birželio mėn. 12–15 d., Vilnius]. p. 70. (presentation)
5. Kuprevičienė Nerija, Griškevičius Algirdas, Lipnickienė Vilnelė, Žagminas Kęstutis. Immunity to diphtheria of adult population in Lithuania. ECCMID 2015 Congress, 25-28 April 2015 in Copenhagen, Denmark. Abstracts, p 1] (presentation)

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REZIUME

Tiriamoji problema: Difterija išlieka svarbi XXI amžiaus visuomenės sveikatos problema Europoje ir visame pasaulyje. Nors difterija yra reta liga Europos Sąjungos (ES) šalyse, o Pasaulio sveikatos organizacijos (PSO) apibrėžtas tikslas – iki 2000 metų Europos regione pašalinti vietinius difterijos atvejus Vakarų ir Centrinėje Europoje yra pasiektas, tačiau šis tikslas nėra įgyvendintas visame PSO Europos regione. Difterijai tapus reta liga Europos valstybėse, mažėja sveikatos priežiūros specialistų budrumas, o tuo pačiu ir gebėjimas diagnozuoti ir valdyti šią ligą. Skiepijimai nuo difterijos įtraukti į visų šalių nacionalinius vaikų skiepijimo kalendorius, daugelyje šalių rekomenduojama revakcinacija suaugusiems nuo difterijos ir stabligės. Per pastaruosius 20 metų difterijos sergamumas pasireiškė epideminio sergamumo laikotarpiu ir poepideminiu laikotarpiu, kai buvo registruojami pavieniai šios ligos atvejai. Keitėsi difterijos epidemiologiniai ypatumai, išryškėjo epideminio proceso pasireiškimo skirtumai, lyginant šiuos laikotarpius.

Difterija, kaip liga kurią sukelia keleto mikroorganizmų (*C.diphtheriae, C.ulcerans, C.pseudotuberculosis*) gaminamas identiškas toksinas pasižymi skirtingais klinikiniais ligos pasireiškimais bei kintančiais epidemiologiniais ypatumais. Lietuvoje nebuvo tyrinėta kokie difterijos sukėlėjai cirkuliuoja ir koks jų toksigeniškumas, be to nebuvo aišku, ar pasikeitė cirkuliuojančių sukėlėjų pasiskirstymas lyginant su epideminio sergamumo laikotarpiu.

Atsižvelgiant į tai, kad difteriją sukelia ne tik *C.diphtheriae*, bet ir kitų sukėlėjų (*C.ulcerans, C.pseudotuberculosis*) gaminamas toksinas, aktualu įvertinti realų difterijos sukėlėjų paplitimą tarp gyventojų.

Pastaruoju metu Lietuvoje suaugusių gyventojų kolektyvinio imuniteto lygis nebuvo žinomas, todėl nežinoma, kurios gyventojų amžiaus grupės yra imliausios ir galėtų nulemti epideminio proceso suaktyvėjimą, pasireiškiantį protrūkiais ir epidemijomis.

Elgesio teorijų taikymas, nagrinėjant gyventojų elgesį, yra vienas pagrindinių įrankių įvertinti intervencines priemones, kuriomis siekiama pakeisti gyventojų elgesį. Tam tikrą elgesį (ketinimus) nulemiantys veiksniai tyrinėti atsižvelgiant į elgesį paaiškinančias teorijas ir modelius (Planuoto elgesio teorija su papildomais kintamaisiais, Įsitikinimų apie sveikatą modemis).

Tyrimo privalumas ir naujumas: Disertaciniame darbe pirmą kartą išanalizuoti ir kompleksiškai įvertinti difterijos epidemiologiniai dėsningumai ir jų kaita, realus difterijos sukėlėjų paplitimas tarp Lietuvos gyventojų ir Lietuvos suaugusių gyventojų kolektyvinis imunitetas. Tyrimai leido įvertinti nustatyti šiuolaikinius difterijos epideminio proceso dėsningumus, apibūdinti difterijos riziką ir svarbiausias difterijos pašalinimo kliūtis.

Gyventojų požiūrio į skiepijimus ir ketinimų skiepytis lemiančių veiksnių, naudojant Planuoto elgesio teoriją ir Įsitikinimų apie sveikatą modelį, Lietuvoje atliktas pirmą kartą. Atliktas Lietuvos suaugusių gyventojų požiūrio ir ketinimo skiepytis veiksnių tyrimas, naudojant Planuoto elgesio teoriją ir Įsitikinimų apie sveikatą modelį, leido įvertinti ne tik gyventojų požiūrį į skiepijimus, bet ir ketinimus (elgseną) lemiančius veiksnius.

Tyrimo tikslas: Nustatyti difterijos epideminio proceso pasireiškimo dėsningumus Lietuvoje 1991–2011 metais ir apibūdinti difterijos riziką bei pašalinimo galimybę, taikant profilaktines priemones.

Tyrimo uždaviniai:

1. Apibūdinti difterijos epideminio proceso pasireiškimo dėsningumus Lietuvoje 1991–2011 metais.

2. Nustatyti toksigeninių ir netoksigeninių *Corynebacterium* paplitimą Lietuvos gyventojų populiacijoje.

3. Nustatyti kolektyvinį antitoksinį imunitetą difterijai ir įvertinti, kokia yra potenciali difterijos protrūkių rizika suaugusių Lietuvos gyventojų populiacijoje.

4. Įvertinti suaugusiųjų požiūrį į profilaktinius skiepijimus, nustatyti, kokie veiksniai lemia ketinimą skiepytis nuo difterijos ir stabligės bei ankstesnę elgseną, susijusią su skiepijimusi nuo difterijos ir stabligės.

Ginamieji teiginiai:

- Didžiausia difterijos epidemijos rizika kyla tada, kai visuomenėje tuo pačiu metu susiformuoja didelės imlių vaikų ir suaugusių žmonių dalys. Epideminio sergamumo difterija ir poepideminiam laikotarpiams būdingas panašus mirštamumas ir ta pati vyraujanti difterijos sukėlėjo padermė.
- Kolektyvinio imuniteto lygis gali turėti įtakos difterijos sukėlėjų cirkuliacijai populiacijoje. Esant pakankamiems vaikų vakcinacijos mastams (ne mažiau kaip 90 proc.), svarbiausiu infekcijos rezervuaru tampa suaugę asmenys. Nepakankamas suaugusių žmonių kolektyvinio imuniteto lygis sudaro palankias sąlygas toksigeninėms ir netoksigeninėms, bet turinčioms toksiną lemiantį geną, *C. diphtheriae* padermėms cirkuliuoti.
- Planuoto elgesio teorijos su papildomais kintamaisiais (požiūris, subjektyvi norma, elgesio valdymo suvokimas, nujaučiamas apgailestavimas, ankstesnė elgsena) ir Įsitikinimų apie sveikatą modelio (suvokiamas pažeidžiamumas (imlumas), suvokiamas sunkumas (rimtumas), suvokiama nauda) kintamieji yra tiesiogiai susiję su suaugusių gyventojų ketinimu skiepytis. Šie modeliai galėtų sudaryti teorinį gyventojų skiepijimo programų organizavimo ir jų efektyvumo vertinimo pagrindą.

Tyrimo medžiaga ir metodai: Nagrinėjant Difterijos epideminio proceso pasireiškimo 1991–2011 metais Lietuvoje dėsningumų atliktas aprašomasis tyrimas, epideminio proceso pasireiškimas vertintas pagal Lietuvos valstybinės epidemiologinės

priežiūros duomenis. Daugiametė sergamumo difterija už 1946–1990 metų dinamika vertinta naudojant istorinius sergamumo difterija duomenis. Difterijos susirgimų atvejų duomenys surinkti už 1991–2011 metų laikotarpį ir analizuoti laiko, vietos ir gyventojų grupių atžvilgiu.

Siekiant palyginti difterijos epideminio proceso pasireiškimą skirtingo sergamumo laikotarpiais, tiriamasis laikotarpis pagal sergamumo lygį buvo suskirstytas į 1991–1996 metų difterijos epideminio sergamumo laikotarpį (metinis sergamumo rodiklis svyravo nuo 0,24 iki 1,18 atvejų 100 tūkst. gyventojų) ir 1997–2011 metų poepideminį laikotarpį (metinis sergamumo rodiklis svyravo nuo 0 iki 0,17 atvejų 100 tūkst. gyventojų). Skiepijimo apimčių nustatymui naudoti statistinės ataskaitos formos Nr. 7 duomenys.

Vertinant toksigeninių ir netoksigeninių Corynebacterium paplitimą tarp pacientų, sergančių viršutinių kvėpavimo takų infekcijomis Lietuvoje atliktas paplitimo tyrimas kaip sudėtinė EK finansuoto DIPNET tyrimo (multicentrinis Europos tyrimas „Pacientų, sergančių viršutinėmis kvėpavimo takų infekcijomis patikra dėl *C.diphtheriae* ir *C.ulcerans* 2007–2008 metais) dalis. Autorė buvo DIPNET tinklo nacionalinis atstovas Lietuvoje bei DIPNET tinklo organizacinio komiteto (angl. *DIPNET steering committee*) narė. Lietuvoje tyrime dalyvavo 13 laboratorijų (8 ligoninių ir 5 mikrobiologijos laboratorijos visuomenės sveikatos centruose). Tyrimo imtis (ne mažiau 2700 ėminių) buvo apskaičiuota remiantis prielaida, kad difterijos sukėlėjo paplitimas gali būti panašus kaip Latvijoje (3,7 / 1000 gyventojų). Tyrimas buvo atliekamas nuo 2007 m. gruodžio mėn. iki 2008 m. birželio mėn. Dalyvaujančiose laboratorijose buvo atliekamas pirminis tyrimas dėl difterijos sukėlėjo, tepinėlių mežiaga buvo sėjama ant *Hoyle* agaro. Esant augimui ant *Hoyle* agaro visos kultūros iš dalyvaujančių laboratorijų buvo siunčiamos į Nacionalinę visuomenės sveikatos priežiūros laboratoriją tolimesniam tyrimui – identifikavimui ir toksigeniškumo nustatymui *Elek* metodu. Buvo ištirti 2988 ėminiai. Nacionalinėje visuomenės sveikatos priežiūros laboratorijoje išskirtos toksigeninės difterijos sukėlėjo padermės buvo išsiųstos į Sveikatos Apsaugos Agentūrą Jungtinėje Karalystėje ribotipavimui.

Vertinant difterijos kolektyvinį antitoksinį imunitetą Lietuvos suaugusių gyventojų populiacijoje atliktas momentinis paplitimo tyrimas. Tikslinė tyrimo populiacija – Lietuvos suaugę (18 metų ir vyresnio amžiaus) gyventojai. Tyrimo populiacija: iš įvairių Lietuvos administracinių teritorijų suaugę asmenys, kurių kraujo ėminiai buvo atsiųsti tyrimui į Nacionalinę visuomenės sveikatos priežiūros laboratoriją infekcinių ligų diagnostikai (išskyrus difterijos diagnostiką) arba tyrimams imuninei būklei nustatyti (išskyrus specifinio difterijos imuniteto nustatymą). Kraujo serumų ėminiai buvo renkami nuo 2013 metų liepos mėn. iki 2014 metų birželio mėn. Tyrimo metodikos pagrindinė prielaida – kraujo ėminiai patenkantys į laboratoriją yra atsitiktiniai, nesusiję tarpusavyje, nesusiję su difterijos židiniu ar pacientų skiepijimo nuo

difterijos būkle. Taikyti šie atrankos kriterijai: amžius (18 metų amžiaus ir vyresni), Lietuvos gyventojas.

Tyrimų rezultatai vertinti pagal šias reikšmes:

– serologiškai neigiamas asmuo, antitoksino koncentracija – < 0,01 TV/ml serumo;

– serologiškai neigiamas asmuo, maža antitoksino koncentracija – 0,01–0,09 TV/ml serumo;

– serologiškai teigiamas asmuo, didelė antitoksino koncentracija – ≥0,1–0,99 TV/ml serumo;

– serologiškai teigiamas, labai didelė antitoksino koncentracija – ≥1 TV/ml serumo.

Duomenų analizei pasirinktos šios amžiaus grupės: 18–29 metų, 30–39 metų, 40–49 metų, 50–59 metų, 60 ir daugiau metų.

Difterijos antitoksino IgG lygio nustatymas kraujo serume buvo atliekamas imunofermentiniu (*ELISA*) metodu. Imunodiagnostiniai preparatai – *Serion ELISA classic Diphtheria IgG test*®) (difterijos antitoksino (IgG) lygio nustatymui). Tyrimo imčiai (apie 500 tyrimų) apskaičiuoti naudota prielaida, kad serologiškai neigiamų (difterijos antitoksino IgG lygis yra lygus arba mažesnis 0,01 TV/ml) suaugusių gyventojų paplitimas kiekvienoje amžiaus grupėje yra 0,5 (50 procentų).

Vertinant suaugusių Lietuvos gyventojų požiūrį į profilaktinius skiepijimus atliktas momentinis skerspjūvio tyrimas (suaugusiųjų Lietuvos gyventojų apklausa).

Tyrimo teorinį pagrindą sudarė Planuoto elgesio teorija (*angl. Theory of Planned Behaviour, I.Ajzen, 1988*) ir Įsitikinimų apie sveikatą modelis (*angl. Health Belief Model, M.H. Becker, 1974*).

Apklausos anketoje kiekvienam kintamajam buvo priskirti ne mažiau kaip 3 klausimai. Anketoje naudota 7-balė Likerto skalė (nuo 1 iki 7).

Kintamieji: ketinimas skiepytis, ketinimas skiepytis nuo difterijos ir stabligės, ankstesnė elgsena dėl skiepijimosi nuo difterijos ir stabligės. Planuoto elgesio teorijos kintamieji: požiūris, subjektyvi norma, elgesio valdymo suvokimas (paties asmens veiksmingumas, suvokiama kontrolė). Papildomi Planuoto elgesio teorijos kintamieji: nujaučiamas apgailestavimas, ankstesnė elgsena. Įsitikinimų apie sveikatą modelio kintamieji: suvokiamas pažeidžiamumas (imlumas), suvokiamas sunkumas (rimtumas), suvokiama nauda, suvokiamos kliūtys.

Atsakymų pasiskirstymo pagal Likerto skalę analizei buvo sudarytos šie kintamieji: atsakymai 1–3 balai buvo vertinti kaip neigiami, atsakymas 4 balai – kaip nei neigiamas, nei teigiamas, atsakymai 5–7 balai – kaip teigiami. Dvinarei logistinei regresijai atsakymai 1–4 balai buvo perkoduoti kaip neigiami, atsakymai 5–7 balai – kaip teigiami.

Anketos patikimumui (angl. *reliability*) įvertinti buvo atliktas bandomasis tyrimas. Tyrimo populiaciją sudarė 18 metų ir vyresni Lietuvos nuolatiniai gyventojai.

2013 m. birželio mėn. tiesioginio interviu žodžiu metodu buvo apklausti 945 respondentai. Apklausa buvo atliekama kaip Omnibus tyrimo. Apklausą atliko sociologinių tyrimų kompanija UAB „Rait“, specialiai parengti interviuotojai tiesioginio interviu metu apklausė respondentus ir pildė apklausos anketas.

Duomenų analizei buvo taikyti aprašomosios ir analitinės statistikos metodai.

Hipotezių tikrinimui pasirinktas 0,05 reikšmingumo lygmuo. Nulinė hipotezė buvo atmetama kai $p \leq 0,05$.

Duomenų analizė atlikta Stata IC/12.1 (StataCorpLP).

Tyrimams atlikti gauti Vilniaus regiono bioetikos komiteto leidimai biomedicininiams tyrimams vykdyti (2-4 priedai).

Rezultatai:

1992 metais sergamumo difterija rodiklis 100 tūkst. gyventojų buvo 0,24, 1993 metais atitinkamai – 0,22. Sergamumo difterija pikas stebėtas 1994–1995 metais, kai sergamumas buvo atitinkamai 1,04 atvejo 100 tūkst. gyventojų (38 atvejai) ir 1,18 difterijos atvejai 100 tūkst. gyventojų (43 atvejai). Metinio sergamumo rodiklio santykinis augimas 1991–1995 m. sudarė 146,34 proc. (95 proc. P.I. 53,05 – 296,50). Difterijos epidemijai suvaldyti su tarptautinių organizacijų pagalba buvo organizuota suaugusiųjų skiepijimo nuo difterijos kampanija. 1995–1996 metais įvyko 2 suaugusiųjų skiepijimo nuo difterijos kampanijos etapai.

Metinio sergamumo rodiklio santykinis sumažėjimas 1995–1997 metų laikotarpiu sudarė –78,27 proc. (95 proc. P.I. –87,98 – –60,71). 1997–2002 m. laikotarpį galima būtų traktuoti kaip „epideminę uodegą“. 1997–1998 metais registruota po 2 susirgimo atvejus. 1999 metais buvo nustatyti 6 difterijos atvejai, 3 iš jų vienoje šeimoje.

Difterijos epideminio proceso pasireiškimas Lietuvoje pasižymėjo dideliu letališkumu tiek epideminio sergamumo, tiek poepideminiu laikotarpiais. Skirtingais metais difterijos letališkumas svyravo nuo 16,7 iki 50,0 proc. Poepideminiu laikotarpiu susirgimų buvo registruota mažiau, tačiau letališkumas buvo panašus kaip ir epideminio sergamumo laikotarpiu, atitinkamai 16,67 ir 15,54 proc.

Difterijos epidemio pakilimo laikotarpiu 1991–1996 metais stebėtas sergamumo sezoniškumas. Sezoninis sergamumo pakilimas tęsėsi 6 mėnesius (rugpjūčio–sausio mėn.). 70,8 proc. visų susirgimų difterija buvo nustatyti šiuo laikotarpiu.

Difterijos epideminio sergamumo laikotarpiu 1991–1996 metais susirgimai difterija buvo registruoti Vakarų ir Pietryčių Lietuvoje, pavieniai atvejai kitose Lietuvos teritorijose.

Difterijos pasireiškimas labiau išreikštas buvo didžiuosiuose Lietuvos miestuose, 60,9 proc. visų susirgimų (67 atvejai) buvo diagnozuoti didžiuosiuose mietuose, daugiausia 42,7 proc. (47 atvejai) – Vilniuje. Poepideminiu laikotarpiu difterijos šeiminis židinys (3 difterijos atvejai) buvo registruotas Šilutės rajone, dauguma atvejų – Vilniaus mieste, pavieniai – kitose Lietuvos teritorijose.

Epideminio sergamumo laikotarpiu vyrų vidutinis sergamumo rodiklis buvo 0,48 susirgimų 100 tūkst. vyrų, moterų – 0,62 atvejų 100 tūkst. moterų. Poepideminiu laikotarpiu 1997–2011 metais vyrų sergamumo rodiklis nežymiai viršijo moterų sergamumą, atitinkamai 0,04 ir 0,03 difterijos atvejų 100 tūkst. atitinkamos lyties gyventojų. Tačiau analizuojant sergamumą pagal lytį vaikų ir suaugusių grupėse nustatyta tam tikra priklausomybė epideminio sergamumo laikotarpiu suaugusių grupėje. Vyrams difterijos tikimybė buvo 36 proc. mažesnė nei moterims. Vyrų ir moterų sergamumo rodiklių santykis sudarė 0,64 (95 proc. P.I. 0,40–1,00, p = 0,052).

Epideminio sergamumo ir poepideminiu laikotarpiais tarp sirgusių difterija vyravo suaugusio amžiaus asmenys. 18 metų ir vyresni asmenys epideminio sergamumo laikotarpiu sudarė 82,8 proc. sirgusiųjų, poepideminiu – 72,4 proc. (p = 0,21) sirgusiųjų. Didžiausias sergamumas epideminio sergamumo laikotarpiu buvo stebimas 30–49 metų amžiaus grupėje. Ypač didelis sergamumas nustatytas 40–49 metų amžiaus grupėje (1,5 atvejo 100 tūkst. gyventojų). Šioje amžiaus grupėje sergamumas buvo 5 kartus didesnis nei 20–29 ir 50–59 metų amžiaus grupėse.

Lietuvoje 1991–2011 metų laikotarpiu didžioji dauguma (76,6 proc.) sirgusių difterija buvo neskiepyti arba skiepijimo anamnezė nebuvo žinoma. Rizika mirti neskiepytų ligonių grupėje buvo 6,6 karto didesnė, nei skiepytų ligonių (SR (santykinė rizika) = 6,60; 95 proc. P.I. 1,24 – 38,79, p = 0,021).

Lietuvoje 1991–2011 metų laikotarpiu difterijos diagnozė laboratoriškai (išskiriant sukėlėjo kultūrą) buvo patvirtinta 86,7 proc. (111 atvejų) susirgusiųjų, likusiems difterijos diagnozė buvo nustatyta pagal klinikinį ligos vaizdą ir (ar) epidemiologinę anamnezę. 75 proc. ligonių (96 atvejams) buvo išskirtas sukėlėjas gaminantis difterijos toksiną, 9,4 proc. (12 ligonių) buvo nustatyta toksino negaminanti *C.diphtheriae*. Didžioji dauguma mirties nuo difterijos atvejų buvo sąlygoti toksiną gaminančios *C.diphtheriae* bakterijos (75 proc. visų susirgimų, 96 atvejai), dalis susirgimų (12 atvejų, 9,4 proc. visų susirgimų) buvo patvirtinti laboratoriškai išskyrus *C.diphtheriae* kultūrą, tačiau toksino išskyrimas nenustatytas. Mirties nuo difterijos atvejais 85,0 proc. atvejų (16 susirgimų) buvo nustatyta toksiną gaminanti *C.diphtheriae*.

46,1 proc. visų susirgimų (59 atvejai) ir 55,0 proc. mirčių nuo difterijos (11 atvejų) buvo sąlygoti *gravis* biotipo *C. diphtheriae* gaminačios toksiną ir 2,3 proc. susirgimų (3 atvejai) *gravis* biotipo *C. diphtheriae* negaminančios toksino. *Gravis* biotipo *C.diphtheriae* buvo nustatyta 48,4 proc. (62 atvejai) visų susirgimų.

Tyrimo dėl difterijos sukėlėjo paplitimo metu buvo išskirtos 4 toksigeninės *C.diphtheriae* kultūros, toksigeninių *C. diphtheriae* bakterijų nešiojimo paplitimas buvo 1,3 atvejo 1000 ištirtų tepinėlių (95 proc. P.I. 0,4 – 3,4). Visos 4 išskirtos toksigeninės C.diphtheriae kultūros buvo *gravis* biotipo, *Sankt-Peterburg* ribotipo. Tyrimo metu buvo išskirtos 4 netoksigeninės difterijos sukėlėjų padermės, nešiojimo dažnis buvo 1,3 atvejo 1000 ištirtų tepinėlių (95 proc. P.I. 0,4–3,4). Trys iš keturių išskirtų netoksigeninių *C.diphtheriae* kultūrų buvo *mitis* biotipo (dviejų ribotipas – *Moskva*, vienos – *Otchakov*),

viena – *belfanti* biotipo *Romania* ribotipo. Netoksigeninės *C.diphtheriae* kultūros buvo ištirtos dėl difterijos toksiną lemiančio geno turėjimo, pasirodė, kad dvi iš keturių nustatytų netoksigeninių *C.diphtheriae* turėjo toksino gamybą lemiantį geną, nors toksino ir negamino (*mitis* biotipas *Moskva* ribotipas).

Lietuvos suaugusių gyventojų kolektyvinio imuniteto tyrimo metu nustatyta, kad 51,92 proc. (95 proc. P.I. 47,51–56,30) tiriamųjų buvo serologiškai teigiami, t.y. turėjo apsauginį antitoksinį imunitetą nuo difterijos. Serologiškai teigiamų tiriamųjų dalis mažėjo su amžiumi, kuo vyresnės amžiaus grupės tuo mažesnė dalis tiriamųjų turėjo apsauginį antitoksinį imunitetą prieš difteriją (p=0,001). Vyresnėse nei 40 metų amžiaus grupėse turinčių apsauginį imunitetą prieš difteriją tiriamųjų dalis mažėjo didėjant amžiui.

Lietuvos suaugusių gyventojų ketinimo skiepytis tyrimas parodį, kad teigiamą ketinimą skiepytis išreiškė 21,4 proc. respondentų, 14,7 proc. išreiškė nei teigiamą, nei neigiamą ketinimą skiepytis, 63,9 proc. – neigiamą ketinimą skiepytis.

Ketinimas skiepytis priklausė nuo lyties. Vyrai turėjo 50 proc. mažesnį ketinimo skiepytis šansą lyginant su moterimis (ŠS=0,50, 95 proc. P.I. 0,32 – 0,78, p = 0,002). Ketinimas skiepytis buvo susijęs su amžiumi, stebėti statistiškai reikšmingi skirtumai tarp amžiaus grupių (p = 0,024). Kuo jaunesnė amžiaus grupė, tuo ketinimo skiepytis šansų santykis, lyginant su kitomis amžiaus grupėmis, buvo didesnis.

Vertinant Ketinimo skiepytis ryšys su Planuoto elgesio teorijos ir papildomais kintamaisiais, Nustatytas stiprus tiesioginis teigiamo požiūrio ryšys su ketinimu skiepytis (ŠS=39,25, 95 proc. P.I. 4,27 – 360,83, p = 0,001), subjektyvia norma (teigiamai vertinę subjektyvią normą respondentai turėjo 3,49 kartus didesnį ketinimo skiepytis šansą (ŠS=3,49, 95 proc. P.I. 1,42–8,59, p = 0,007), elgesio valdymo suvokimi (respondentų teigiamai vertinusių savo elgesio valdymą ketinimų skiepytis šansas buvo 6,16 kartus didesnis (ŠS=6,16, 95 proc. P.I. 1,10–34,55, p = 0,039)).

Ketinimas skiepytis tiesiogiai susijęs su nujaučiamu apgailestavimu ateityje (tarp respondentų kurie vertino, kad ateityje jaus apgailestavimą (teigiamas vertinimas) ketinimo skiepytis šansas buvo 7,51 karto (ŠS = 7,51, 95 proc. P.I. 2,92–19,33, p < 0,0001) didesnis).

Nustatytas ketinimo skiepytis tiesioginis statistiškai reikšmingas ryšys su Įsitikinimų apie sveikatą modelio kintamaisiais: suvokiamu pažeidžiamumu (imlumu), suvokiamu ligos sunkumu (rimtumu), suvokiama skiepijimosi nauda.

Ketinimas skiepytis nuo difterijos ir stabligės priklausė nuo lyties (vyrai turėjo 53 proc. mažesnį ketinimo skiepytis šansą lyginant su moterimis (ŠS = 0,53, 95 proc. P.I. 0,35 –0,81, p = 0,003)) ir nuo amžiaus, kuo jaunesnė amžiaus grupė, tuo ketinimo skiepytis šansų santykis, lyginant su kitomis amžiaus grupėmis, buvo didesnis.

Nustatytas stiprus tiesioginis teigiamo požiūrio ryšys su ketinimu skiepytis nuo difterijos ir stabligės (ŠS = 12,88, 95 proc. P.I. 3,74–44,42, p < 0,0001) (24 lentelė). Teigiamai vertinę subjektyvią normą respondentai turėjo 2,11 kartus didesnį ketinimo

skiepytis nuo difterijos ir stabligės šansą, lyginant su neigiamai vertinusiais subjektyvią normą, (ŠS = 2,11, 95 proc. P.I. 1,02–4,35, p = 0,043).

Respondentų grupės, kuri per pastaruosius 10 metų skiepijosi nuo difterijos ir stabligės, ketinimo skiepytis nuo šių ligų vėl šansas buvo 8,43 karto didesnis nei nesiskiepijusių anksčiau grupėje (ŠS = 8,43, 95 proc. P.I. 3,92–18,10, p < 0,0001).

Ketinimas skiepytis nuo difterijos ir stabligės tiesiogiai susijęs su nujaučiamu apgailestavimu ateityje. Tarp respondentų kurie vertino, kad ateityje jaus apgailestavimą, ketinimo skiepytis šansas buvo 2,49 karto (ŠS = 2,49, 95 proc. P.I. 1,22–4,76, p = 0,012) didesnis, nei tarp tų, kurie manė, kad ateityje nesigailės, jei nesiskiepys.

Nustatytas ketinimo skiepytis nuo difterijos ir stabligės tiesioginis statistiškai reikšmingas ryšys su Įsitikinimų apie sveikatą modelio kintamaisiais: suvokiamu pažeidžiamumu (imlumu), suvokiamu ligos sunkumu (rimtumu), suvokiama skiepijimosi nauda.

Ankstesnė elgsena (skiepijimasis nuo difterijos ir stabligės per pastaruosius 10 metų) buvo susijęs su amžiumi. Kuo jaunesnė amžiaus grupė, tuo šansai, kad skiepijosi nuo difterijos ir stabligės per pastaruosius 10 metų, lyginant su kitomis amžiaus grupėmis, buvo didesnis.

Nustatytas stiprus tiesioginis teigiamo požiūrio ryšys su ankstesne elgsena (skiepijimasis nuo difterijos ir stabligės per pastaruosius 10 metų) (ŠS = 2,29, 95 proc. P.I. 1,06–4,97, p = 0,036) (27 lentelė). Tyrimo rezultatai parodė, kad subjektyvi norma ir elgesio valdymo suvokimas nebuvo statistiškai reikšmingai susiję su ankstesne elgsena (skiepijimasis nuo difterijos ir stabligės per pastaruosius 10 metų).

Nustatytas ankstesnės elgsenos (skiepijimasis nuo difterijos ir stabligės per pastaruosius 10 metų) tiesioginis statistiškai reikšmingas ryšys su Įsitikinimų apie sveikatą modelio kintamaisiais: suvokiamu pažeidžiamumu (imlumu), suvokiamu ligos sunkumu (rimtumu), suvokiama skiepijimosi nauda.

Išvados:

1. Epideminio sergamumo difterija laikotarpiui 1991–1996 metais būdingi šie bruožai: akivaizdus sezoniškumas, didesnis suaugusių moterų sergamumas nei vyrų, labai didelis mirštamumas tarp vėlai besikreipiančių medicinos pagalbos. Kiti epidemiologiniai dėsningumai poepideminiu laikotarpiu 1997–2011 metais išliko panašūs kaip epideminio sergamumo laikotarpiu 1991–1996 metais: tos pačios paveiktos gyventojų amžiaus grupės, didelis mirštamumas, didžioji dalis susirgimų registruoti didžiuosiuose miestuose, potencialiai epideminį sergamumą linkusio sukelti *gravis* biotipo *C. diphtheriae* ir didesnės dalies nei epideminio sergamumo laikotarpiu atvejų, nepatvirtintų laboratoriniais tyrimais, vyravimas.

2. Epideminio sergamumo difterija 1991–1996 metais laikotarpiu vaikų iki 14 metų amžiaus ir 30–50 metų amžiaus suaugusiųjų didesnis nei kitų amžiaus grupių sergamumas rodo, kad didžiausia rizika difterijos epidemijai kilti atsiranda, kai

visuomenėje tuo pačiu metu susiformuoja didelės imlių žmonių dalys tarp vaikų ir suaugusiųjų.

3. Lietuvoje cirkuliuoja netoksigeninės, bet turinčios difterijos toksino gamybą lemiantį geną, ir toksigeninės difterijos sukėlėjo padermės, tarp jų ypač virulentiška *Sankt-Peterburg* ribotipo *gravis* biotipo *C. diphtheriae*. Palyginti su kitomis Europos šalimis, Lietuva pagal difterijos sukėlėjų cirkuliavimo lygį išlieka padidėjusios rizikos teritorija.

4. Suaugusių Lietuvos gyventojų antitoksinis kolektyvinis imunitetas difterijai yra nepakankamas. Vyresnio amžiaus (vyresni nei 40 metų amžiaus) suaugusieji yra pagrindinė rizikos grupė. Visuomenėje cirkuliuojantys difterijos sukėlėjai, nepakankamas suaugusių gyventojų kolektyvinis imunitetas sudaro palankias sąlygas difterijos epideminiam procesui suaktyvėti.

5. Laikotarpis tarp suaugusiųjų revakcinacijų nuo difterijos ir stabligės negali būti ilgesnis nei 10 metų, – taip užtikrinama difterijos antikūnų apsauginė koncentracija kraujyje.

6. Lietuvos suaugusių gyventojų populiacijoje vyrauja neigiamos nuostatos dėl skiepijimosi. Tokio pobūdžio nuostatos būdingos vyrų ir vyresnio amžiaus žmonių grupėms. Ankstesnė elgsena ir nujaučiamas apgailestavimas yra reikšmingi papildomi nepriklausomi kintamieji, padidinantys Planuoto elgesio teorijos modelio prognozinę vertę, aiškinant suaugusių gyventojų populiacijos ketinimą skiepytis.

7. Planuoto elgesio teorijos ir Įsitikinimų apie sveikatą modelio pagrindiniai kintamieji yra tiesiogiai susiję su suaugusių gyventojų ketinimu skiepytis ir ketinimu skiepytis nuo difterijos ir stabligės. Ankstesnė elgsena dėl skiepijimosi nuo difterijos ir stabligės susijusi su požiūriu į skiepijimus ir Įsitikinimų apie sveikatą modelio kintamaisiais.

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Gimimo data		1970 m. vasario 26 d.
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Išsilavinimas		
	1988-1994	Vilniaus universitetas Medicinos fakultetas Gydytoja higienistė
	1994-1996	Vilniaus universitetas Medicinos fakultetas Epidemiologijos rezidentūra Gydytoja rezidentė
	2011-2015	Vilniaus universitetas Medicinos fakultetas Visuomenės sveikatos institutas, doktorantūra
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	1996-1997	Respublikinis imunoprofilaktikos centras Gydytoja epidemiologė
	1997-2008	Užkrečiamųjų ligų profilaktikos ir kontrolės centras Skyriaus vedėja, gytoja epidemiologė
	2008-2012	Valstybinė visuomenės sveikatos priežiūros tarnyba prie Sveikatos apsaugos ministerijos Skyriaus vedėja
	Nuo 2011	Vilniaus universitetas Medicinos fakultetas Visuomenės sveikatos institutas Asistentė
	Nuo 2012	Sveikatos apsaugos ministerija Vyriausioji specialistė