Hrynkevich Christina I.

VACCINATION AND REDUCING MORTALITY AND MORBIDITY OF DIPHTHERIA, PERTUSSIS AND TETANUS IN UKRAINE (1944-2015)

Content

Introduction

Over the last hundred years in North America and Europe, there has been a significant reduction in mortality and an increase in longevity [1]. The "Theory of the epidemiological transition" links those trends with the transition from the " Age of Pestilence and Famine ", in which infectious diseases predominate in the mortality structure, especially among the yang people, to the present " Age of Degenerative and Man-Made Diseases", in which mortality from chronic disease prevails [2, 3]. According to a study by the World Health Organization (WHO) “Global Cancer Burden”, infectious diseases today account for only 4.2% of all disability in developed countries population, such as the United States, whereas chronic and neoplastic diseases make up 81.0% [4].

It is believed that vaccination programs in the United States have made a significant contribution to the elimination of many diseases that can be prevented by vaccination, and significantly reduced the number of other diseases. Cases of diseases decreased by more than 92% and mortality decreased by 99% or more due to the diseases that can be prevented by the use of vaccines recommended prior to 1980, such as diphtheria, epidemic mumps, pertussis and tetanus. For example, in the United States, the endemic transmission of poliomyelitis, measles and rubella viruses was eliminated. Also, through the world, natural pox was eliminated [5]. It is clear that the reduction of infectious mortality, compared with this, was also observed in countries with a lower level of development.

However, in addition to vaccination, other factors probably have impact to decreasing mortality from infections. These factors included improvements in sanitation, nutrition, labor legislation, the level of medical care, an introduction epidemiological surveillance, demographic changes, electrification, chlorination of water, cooling and freezing of food, pasteurization and much more.

We believe that there are many causes for reducing infectious mortality rates over the past 70-100 years, which are not related to vaccines. The reason for such assertion is that the scientific papers, known to us, do not indicate the proportion (contribution) or quantitative assessment of the effect of vaccines among other causes of mortality reduction. Moreover, it is generally accepted, that the vaccine is almost the only or main reason for reducing the overall infectious mortality. We believe that this opinion is not supported by the necessary evidence and the true contribution of vaccines to reducing mortality has not been evaluated properly.

The advantage of our approach is that on the example of a large European country (Ukraine) with a population up to 52 million people we used nationally representative data for the long period (1944-2015). Our data contain complete information about incidence (Cumulative Incidence-CI), mortality (Mortality Rate-MR) and lethality (Case Fatality Rate-CFR) of the total population and infant population in Ukraine for 3 vaccine-preventable infections (diphtheria, tetanus, and pertussis).

Our main methodological contribution is that we proposed an algorithm for calculating the contribution (%) or the quantitative effect of vaccines among other causes for reducing infectious mortality. This algorithm is based on the logical, epidemiological and mathematical relationship of speed or the multiplicity of declines in annual CI, MR, and CFR.

Material and methods

Our work is a retrospective epidemiological analysis of the dynamics and structure of annual CI, MR, and CFR indicators for three infections (diphtheria, tetanus, and pertussis) that can be prevented by vaccines (vaccine-preventable infections - VPI) in Ukraine in period 1944-2015.

Basic data on the annual number of death from these infectious diseases in Ukraine until 2000 are taken from several paper sources [6, 7, 8]. Date on the annual number of deaths from infectious diseases in Ukraine for the period 2001-2015 are taken from the statistical P-8 format "Distribution of the deceases by sex, age groups and causes of deaths " provided by the State Institution "Ukrainian Center for Monitoring and Disease Control of the Ministry of Guard health of Ukraine ".

Data on the annual number of cases of diseases from these infectious diseases in Ukraine until 2009, obtained from paper sources [6, 7, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20]. Data on the annual number of cases of three infectious diseases in Ukraine for the period 2010-2015 are derived from the statistical form number 2 (annual) "Report on certain infections and parasitic diseases" of the Ministry of Health of Ukraine.

The data we have used is not fully available in the public domain. In part, there is free access to data on mortality and morbidity in Ukraine for some periods in the WHO electronic databases [21, 22]. Data on the vaccine coverage of in Ukraine until 1972, obtained from a paper source [6]. Some disease data in Ukraine from 1981 to 2015 were obtained from the WHO electronic database [21].

For the convenience of data analysis, we split the entire study period into 4 separate periods: 1944-1964, 1965-1991, 1992-2005, and 2006-2015.1944-1964 years were the last decades of the pre-vaccination period, but in different years of this period, the gradual introduction of routine vaccination against diphtheria, tetanus, and pertussis. 1965-1991 - these are the years of economic growth, the formation, and functioning of sufficiently effective vaccination programs. In 1992-2005, there was a sharp drop in the economy and a deterioration in living standards, which was accompanied by a marked increase in the mortality rate of the total population from infectious diseases. The period 2006-2015 was characterized by an alternation of economic growth and its decline, but the level of the economy has not yet reached even the level of 1991.

In this study, our goal was to determine the percentage (%) or the quantitative effect of the vaccination impact, among other reasons, for reducing the mortality of the three VPIs (diphtheria, tetanus and pertussis). The design of our study is a comparative retrospective population study on the epidemiological indicators of annual CI, MR, and CFR for the VPI. Comparison of morbidity, mortality and lethality rates of VPI may help indirectly determine the proportion of the vaccine's impact on reducing mortality for each of the three infections.

Initially, we organized data on the incidence of coverage in Ukraine during four periods of time and built a continuous dynamic series of their annual CI, MD, and CFR. For each period, we calculated the minimum, maximum and mean values of the annual epidemiological indicators for vaccine coverage, CI, and MR. We calculated the CFR for each infection and for each period by dividing the total number of deaths by the number of cases for a certain period, then multiplying by 100%. Next, we calculated the ratio of the average values of each epidemiological indicator as a relation of the distribution of the average for the first period to the average of the last period. Thus, we have identified a reduction rate for morbidity, mortality, and mortality from each infectious disease in Ukraine for the period 1944-2015.

The incidence of infectious disease is a complex biological and mathematical parameter, defined as a product of the risks of two simple events, for the case when they are simultaneously present in one place. These probabilities or necessary conditions for the emergence of an infectious disease are specific sensibility and the probability of transmission or infection by a specific infectious agent. Thus, the incidence risk is equal to the product of the risk of sensibility and the risk of transmission of an infectious agent.

The sensibility risk in the population is represented by the percentage (%) of the susceptible population. The incidence is 0 if the sensibility and/or transmission risk are equal to 0, but in fact, they almost never equal 0 and their true ratio is never known.

The number of death depends on the proportion of persons (CFR, %), which inevitably die if they are ill. This is a true CFR. Probably, the true CFR is a biological constant that is almost unchanged and determines the minimum possible mortality rate in the presence of incidence. On the other hand, the actual CFR can vary substantially and differ from the true CFR, but the actual CFR is tied to a true CFR. The actual CFR depends on the ratio of registered deaths and sicknesses from each disease. In most cases, mortality is recorded more completely than morbidity, so the actual CFR will always be higher than the true CFR.

To calculate the contributions of vaccination in the mortality reduce, we used indicators of the frequency or rate of reduction of incidence of mortality. Our algorithm for calculating the contribution of vaccination to reduce mortality for each infection is based on the assumption about direct epidemiological and proportional relationship between the rates of decrease in these indicators in time. If the vaccine is effective, its use reduces the proportion (or percentage) of the susceptible population. Morbidity and mortality should decrease with other equal conditions in proportion to the decrease in the proportion of susceptible populations, but under real conditions, the incidence of registered mortality may not be equal to the coefficients of decrease in morbidity and the proportion of susceptible populations. We want to emphasize that the share of the susceptible population is not the only necessary risk factor for the emergence of an infectious disease. Another necessary risk factor is the probability of infection by an infectious agent. In real conditions, the occurrence of morbidity is possible only with the simultaneous presence and interaction of both of these factors. At the same time, the probability or risk of the disease is equal to the product of the risk of susceptibility and risk of infection. Thus, the proportion of the vaccine contribution to reducing the proportion of susceptible populations, incidence and mortality can range from 0 to 100%, and its precise value is unknown, but can be estimated approximately.

If the incidence reduction factor is divided by the mortality reduction factor and multiplied by 100%, then we obtain the maximum possible approximate (estimated) percentage contribution of the vaccination and / or the proportion of the susceptible population to reduce mortality from infection, for the case when the mortality reduction factor exceeds the multiplicity of the incidence reduction factor.

If the incidence reduction factor exceeds the mortality reduction factor, then it is correct to assume that the contributions of vaccination to the mortality reduce may be 100% and/or not all deaths have been recorded. Otherwise, if the incidence reduction factor was less than the mortality reduction factor and/or the mortality is decreased, then it is correct to assume that, apart from vaccination, other non-vaccine-related factors also occurred.

Thus, the maximum possible contribution of vaccination to mortality reduction is equal to the product of the CFR change rate and the ratio of the CI reduction factor to the MR reduction factor multiplied by 100%, if the CI decrease factor is less than the MR reduction factor. If the rate of incidence reduction is higher than the mortality decrease rate and/or an increase in lethality (CFR), then the maximum possible contribution of vaccination to a reduction in mortality is approximately equal to the mortality change rate multiplied by 100%. Both methods for calculating the contribution of vaccination to mortality reduce do not take into account the effect of changing the risk of transfer of agent, therefore actual and/or the true contribution of vaccination can be significantly lower than calculated by our algorithm.

The calculations of the average values were performed using the Microsoft Office Exel 2003 computer program. We used methods of statistical analysis without calculating confidence intervals of averages, but with the definition of minimum and maximum indicators. We believe that this is quite enough to achieve the goals of our evaluation study.

Results

Data on the vaccines coverage in Ukraine are presented in Table 1. Certain levels of vaccination against diphtheria and reduced diphtheria incidence were achieved in Ukraine before the Second World War. During the Nazi occupation (1941-1944) no vaccinations were carried out. In the years 1944-1950, the level of vaccination against diphtheria and tetanus increased but was insufficient. In this regard, the incidence of diphtheria in 1944 was 150.0 per 100,000, which is more than in 1939 (26.0 per 100,000) [6]. Figure 1 shows that the number of deaths caused by diphtheria, tetanus, and pertussis was greatest during the period 1944-1964.

According to Table 1 data, the high level of vaccination against diphtheria, tetanus, and pertussis was achieved for the first time only in the 1960s. The high level of vaccination against these infections was maintained until 1980s, but the level of vaccination against diphtheria, tetanus, and pertussis decreased somewhat in the late 1980s. Further, the level of vaccination against diphtheria, tetanus, and pertussis increased significantly from the 1990s to the middle of the 2000s, but then it decreased significantly in the 2010s. A comparative analysis of the average annual mortality rates between the two extreme periods (1944-1965 and 2006-2015) according to tables 2 and 3 showed a significant decrease in the mortality of the total population for pertussis only (a decrease of 3.9 times). For diphtheria, the mortality decreased by 1.4 times, but the tetanus showed even a slight increase in lethality.

According to the data of Table 3, the average mortality rate from pertussis decreased 216 times in 2006-2015 compared to 1944-1964, but the incidence decreased only 47 times. If the morbidity reduction factor is divided by the mortality reduction factor and multiplied by the lethality reduction factor, and then multiplied by 100%, then we will receive 84.9% (47/216 * 3.9 * 100% = 84.9%) or maximal possible contribution of vaccination to pertussis mortality reduce (provided that the risk of infection remained unchanged during 1944-2015). Table 3 presents data on the contribution of vaccination to mortality reduce from two other VPIs. Generally, for the population, it varied from 80% (tetanus) to 100% (diphtheria). It is obvious that the contribution of vaccination to mortality reduce for certain age groups can be significantly different from the contribution for the total population.

Analyzing chart 2 and 3, we tracked some discrepancies between the incidence of diphtheria and the immunization coverage by the 90s and 2010s. Thus, in 1995, the percentage of implementation of the plan of DTP vaccination population (third dose) was 98%, and in 2015, 23%. At the same time, in 1995, the intensive rate of incidence was 10.29 per 100,000 for diphtheria, that is, the epidemic of this infection took place, and in 2015, the incidence rate was 0.005 per 100,000. Also, it is noteworthy that in the 90s, with the same the level of vaccination against diphtheria, tetanus, and pertussis, a significant increase in morbidity occurred only for diphtheria, and the other two infections (tetanus and pertussis) tended to decrease. If you compare the dynamics of morbidity on tetanus, diphtheria, and pertussis, then it is clearly seen that the mortality reduction rate from tetanus is significantly inferior to the morbidity reduction rate from diphtheria and pertussis (especially in the period up to 1991). In addition, in the 2000s-2010s, there is a pronounced tendency to drop diphtheria and tetanus in the background of some raising of pertussis at the same levels of grafting against all three infections.

Discussion

A serious constraint for our algorithm for assessing the contribution of vaccination to reducing mortality is that we do not know the true correlation between cases and deaths. Moreover, we think that the only available and reliable data to evaluate the contribution of vaccination to the reduction of morbidity and mortality is the historical data of their dynamics, which are presented in our work. This is due to the fact that there are irreversible ethical constraints on conducting placebo-controlled experiments on the study of the epidemiological efficacy of vaccines. Moreover, even the absence of ethical constraints will not allow such experiments to be carried out in many cases because of the inability to determine susceptibility to an infectious agent without prior infection of the subjects.

Our research also has some methodological limitations that are associated with the presence of classification errors. We compare morbidity and mortality for various diseases that are not identical with each other. Any VPI is different from any other VPI. We also do not know the degree of difference between them. However, we assume that there is a small degree of difference between the natural properties of the infectious diseases we are investigating. All epidemics of these diseases are exposed to the same factors of the external and internal environment.

The strength of these factors or their contribution to the incidence and mortality of these infections may vary for different time periods that are being compared. Thus, it can be assumed that the difference in morbidity and mortality of VPI can be explained by the presence or absence of vaccinations. This methodological approach takes precedence over a historical comparison of morbidity and mortality before the introduction of vaccination and after its introduction into routine practice. Formally, the time between the introduction of vaccination and the reduction in morbidity and mortality [5] is insufficient evidence of the effects of vaccinations, so it is also necessary to assess the dynamics of morbidity and mortality and compare the rate of their decline.

We presented some data on the incidence of vaccination and the dynamics of infectious mortality in Ukraine in the second half of the 20th and early 21st centuries.

But our assessment of the impact of vaccines on infectious mortality is based not on comparing the dynamics of vaccination coverage and infectious mortality, but on the comparison of the dynamics of infectious mortality and morbidity. We a priori assume that vaccination reduces infectious mortality due to reduced morbidity. Thus, we estimate the impact of vaccinations on epidemiological indicators indirectly, that is, taking into account the rate or multiplicity of the risk change of the disease and the risk of death after the introduction of routine vaccination. The greater the risk of falling sick, the more likely the vaccine effects will be on reducing mortality, as the rates of morbidity, mortality, and lethality are related to each other as epidemiological, logical and mathematical values. If vaccination is effective, mortality should be reduced in proportion to the reduction in morbidity. In turn, the incidence is reduced due to the fact that vaccination reduces the proportion of susceptible individuals and, in the case of some infections (for example, pertussis), also prevents the spread of the pathogen. The latter, probably, does not apply to diphtheria, tetanus and acellular pertussis component of the vaccine DTP. In addition, our study finds a discrepancy between the percentage of vaccinated individuals and the level of morbidity. This is due to the fact that the level of morbidity and mortality depends not only on the coverage by vaccination in the year in which they were registered, but also on the coverage of the population by vaccination over the years and the effects of other factors not related to the action of the vaccine, such as sanitary conditions, medical care, effective epidemiological surveillance and others.

If for some infections the multiplicity of mortality reduction exceeds the multiplicity of reduction in morbidity, then we can call such reduction of mortality "excessive" in relation to the multiplicity of reduction of morbidity. If we proceed from our hypothesis about the direct proportionality of the relationship between morbidity and mortality, then the presence of "excessive" mortality is likely to indicate a contribution to reducing the mortality of those factors that do not depend on vaccination coverage and/or indicate a significant underestimate of morbidity. This may mean that after the introduction of mass vaccination, its contribution to reducing mortality from some VPIs may be less than 100% predicted.

We believe that the accuracy of our calculations for this kind of indicators is quite acceptable for a rough estimate of the contribution of vaccinations to reducing mortality, but if we consider the presence of a fairly significant variability of annual epidemiological indicators, then the reliability of our assessment is more likely to derive from natural (epidemiological) and logical preconditions than from the actual reliability of the data used. In our opinion, the presence of an almost directly proportional relationship between the gradients of morbidity, mortality for diphtheria, tetanus and pertussis is not accidental, but it is likely to indicate that vaccination can be an important factor in the pressure on the epidemic process, which reduces the natural, cyclic and accidental manifestations of epidemics. The more severe such an addiction is the more controllable is the infection. To protect our hypothesis, it is also important to emphasize that data on the number of diseases and deaths have been obtained from various sources independent of each other. Registration of infectious diseases was carried out by the sanitary-epidemiological service of the Ministry of Health of Ukraine, and registration of deaths was a function of the State Statistics Department.

Our hypothesis suggests that proportion of dead persons among patients or true lethality, in other equal conditions, slowly changing over time (years and decades) for each infection and for each country. The assumption that vaccination directly reduces mortality is likely to contradict our data for infections like diphtheria, tetanus, and pertussis in the event that these data are completely reliable. We think that vaccination does not reduce lethality directly if the incidence is not equal to 0. We believe that vaccination can not prevent death faster than the disease that causes this death. It is biologically unlikely. We think this can be explained by the incomplete registration of the disease and/or the effect of other causes that are not related to the effect of vaccines. This can be seen very well on the example of diphtheria, pertussis and tetanus, because these infections show a relatively small decrease in mortality after the introduction of vaccination (1.4 times in diphtheria and 3.9 times in the case of a pertussis) or even an increase in it (tetanus), which is quite possible to explain not the influence of proper vaccination, but the completeness of the records of these diseases and the effectiveness of treatment of patients. In our opinion, these disadvantages can be offset to a certain extent due to the high power of the presented data array and the considerable time interval of individual periods on which the average mortality, mortality and morbidity rates were calculated.

We established some discrepancies between the relatively high level of vaccination against diphtheria in the 1990s and the high levels of morbidity and mortality from diphtheria in this period, as well as low incidence of diphtheria at very low levels of vaccination in 2010, obviously, need additional research and explanation. A study of this issue will be the subject of our next searches.

Conclusion

The contribution of vaccination to reducing mortality from VPI is characterized by statistical and causal (epidemiological) coherence of indicators of morbidity, mortality, and mortality. During the period 1944-2015 in Ukraine, the multiplicity of reduction in the mortality rate for vaccine-preventing infections was quite impressive. It could range from 40.5 fold (tetanus) to 656.3 times (diphtheria), but the multiplicity of the reduction in the overall morbidity was significantly lower and ranged from 47 times (pertussis) to 471.1 times (diphtheria), that is, it is likely that the reduction in mortality was largely due to factors not related to vaccines. More significant was the contribution of vaccination to reducing infectious mortality for the infant population, among which currently the annual death rate from the VPI is absent or presented in isolated cases. In Ukraine, vaccination continues to be a powerful factor in the pressure on the epidemic process of some VPIs. It promotes the maintenance of a low level of infectious mortality over the last 30-50 years and prevents the rebirth of epidemics, but unfortunately, not in the case of diphtheria (the 1990s).

Thus, vaccination in Ukraine for some infections is definitely low and in the future, it will also be important for the control of infectious morbidity and mortality. Moreover, vaccination continues to be the most affordable and effective intervention to achieve global or regional elimination of some infections (for example poliomyelitis, measles, tetanus). But given current historical and epidemiological data on the dynamics of mortality from vaccine-preventing infections, we assume, which may be in the next few decades, the impact of vaccination programs on reducing infectious mortality in Ukraine will be significantly lower than in the previous 70-100 years.

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Table 1. Some data on the state of vaccination among the population of Ukraine (1936 - 2015)

	Diphtheria	Tetanus	Pertussis
Years of introduction of routine vaccination	1936 (D) 1963 (DTP, DT)	1952 (T) 1963 (DTP, DT)	1960 (P) 1963(DTP)
Immunization data (before 1965)	1948-64: 70.883.824doses	1952-64: 24.980.038vaccinated	1961-62: 2.537.912 doses
Immunization data (1965-1991),% coverage (min / max / mean)	1965: 4.571.641 doses	1965-72: 69.346.107 doses	1965-72: 69.346.107 doses
	42/99/63*	42/99/63*	42/99/63*
Immunization data (1992-2005),% coverage (min / max / mean)	88/99/97	88/99/97	88/99/97
Immunization data (2006-2015),% coverage (min / max / mean)	23/98/66	23/98/66	23/98/66

Table 2. The Cumulative Incidence, Case Fatality Rate and Mortality Rate for vaccine-preventable infections in Ukraine by periods (1944-1964, 1965-1991, 1992-2005, 2006-2015)

Indicators	Periods	Diphtheria	Tetanus	Pertussis
Mortality Rate (minimum / maximum / mean)per 100,000 in all ages	1944-1964	0,044/17/ 2,41	0,29/1,5/ 0,63	0,49/1,36 /0,902
	1965-1991	0/0,097/ 0,0147	0,10/0,37/ 0,177	0,004/0,14 /0,032
	1992-2005	0,004/0,5/ 0,111	0,02/0,12/ 0,06	0/0,035/ 0,008
	2006-2015	0/0,017/ 0,0037	0,01/0,04/ 0,016	0/0,011 /0,0042
Cumulative Incidence (minimum / maximum / mean) per 100,000 in all ages	1944-1964	0,66/180/ 27,79	0,7/2,73/ 1,76	25/441/ 183,9
	1965-1991	0,016/3/ 0,197	0,18/0,92/ 0,36	4,42/67,9/ 19,59
	1992-2005	0,21/10,3/ 2,76	0,034/0,2/ 0,099	0,84/13,4/ 4,34
	2006-2015	0,05/0,17/ 0,06	0,02/0,06/ 0,037	1,51/6,42/ 3,92
Case Fatality Rate (minimum / maximum / mean), %in all ages	1944-1964	3,5/13,9/ 8,5	26,8/53/ 35,1	0,23/0,7/ 0,42
	1965-1991	0/37,5/ 7,42	37,2/67,4/ 49,3	0,075/0,24 /0,163
	1992-2005	1,27/4,57/ 4,03	50/70,6/ 61,7	0/0,259/ 0,183
	2006-2015	0/50/ 6,23	18,8/79,2/ 43,4	0/0,293/ 0,106
Mortality Rate (minimum / maximum / mean) per 100,000, ages0-14	1965-1991	0/0,067/ 0,032	0/0,37/ 0,058	0,018/0,5/ 0,13
	1992-2005	0/0,551/ 0,144	0/0,018/ 0,018	0/0,165/ 0,039
	2006-2015	0/0,061/ 0,0136	0/0/ 0	0/0,077/ 0,029
Mortality Rate (minimum / maximum / mean) per 100,000, ages 15 & ↑	1965-1991	0/0,096/ 0,0093	0,1/0,41/ 0,21	NC
	1992-2005	0,002/0,45 /0,103	0,03/0,15/ 0,08	NC
	2006-2015	0/0,01/ 0,002	0,01/0,05/ 0,02	NC

Notes

NC – No cases

Table3. The ratio of Indicators of Cumulative Incidence, Case Fatality Rate and Mortality Rate in vaccine-preventable infections in Ukraine by periods (1944-1964, 1965-1991, 1992-2005, 2006-2015)

The ratio of Indicators	Ratio of Periods	Diphtheria	Tetanus	Pertussis
The ratio of mean Mortality Rate between different periods (all ages)	(1944-1964)/(1965-1991)	164,5	3,6	28,3[*]
	(1944-1964)/(1992-2005)	21,7	10,4	114,6[□]
	(1944-1964)/(2006-2015)	656,3	40,5	216[‡]
The ratio of mean Cumulative Incidence between different periods (all ages)	(1944-1964)/(1965-1991)	141,3	4,9	9,4
	(1944-1964)/(1992-2005)	10,1	17,8	42,4
	(1944-1964)/(2006-2015)	471,1	47,7	47
The ratio of mean Case Fatality Rate between different periods (all ages)	(1944-1964)/(1965-1991)	1,1	0,7	2,6[*]
	(1944-1964)/(1992-2005)	2,1	0,6	2,3[□]
	(1944-1964)/(2006-2015)	1,4	0,8	3,9[‡]
The ratio of mean Mortality Rate between different periods (ages 0-14)	(1965-1991)/(1992-2005)	0,2	3,2	3,3
	(1965-1991)/(2006-2015)	2,3	To 0	4,5
The ratio of mean Mortality Rate between different periods (ages 15& ↑)	(1965-1991)/(1992-2005)	0,1	2,8	NC
	(1965-1991)/(2006-2015)	4,6	11,6	NC
The maximum estimated proportion of the contribution of the share of susceptible (and/or vaccine) among all causes of mortality,%		100.5	80	84.9

Notes

TB – Tuberculosis

[*](1953-1964)/(1965-1991), [□](1953-1964)/(1992-2005), [‡](1953-1964)/(2006-2015)

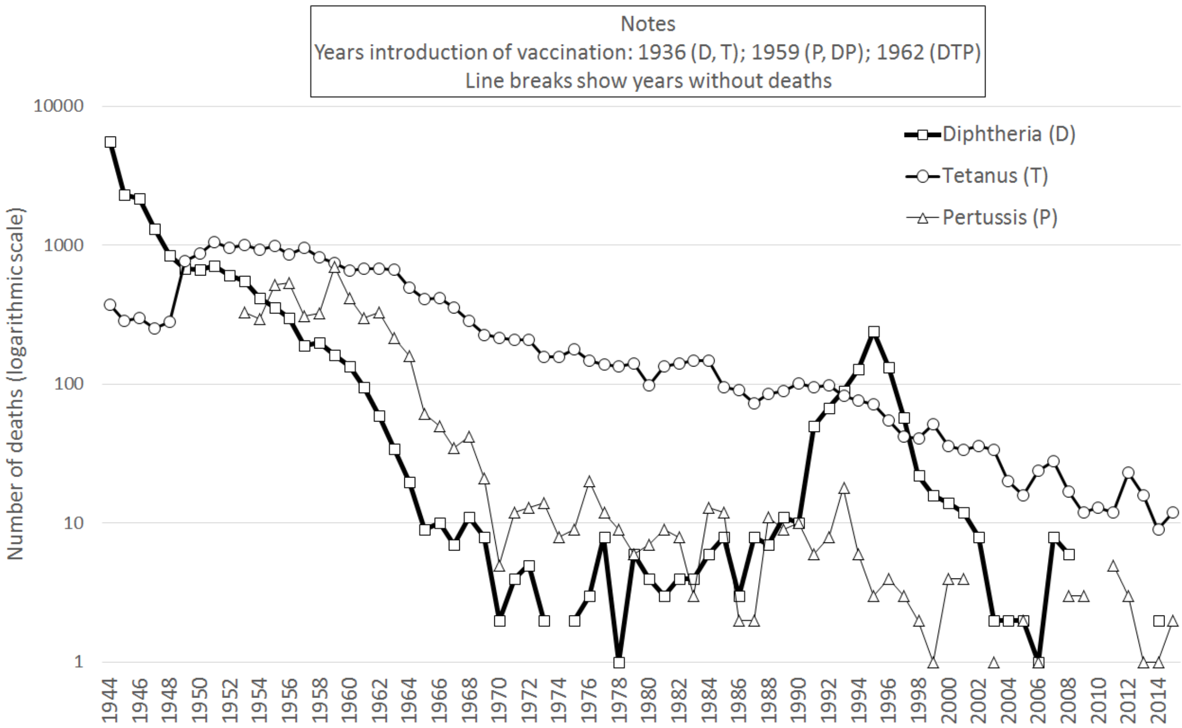

Figure 1. Number of deaths from diphtheria, tetanus, pertussis in 1944-2015 years and years the introduction of vaccination against them in Ukraine

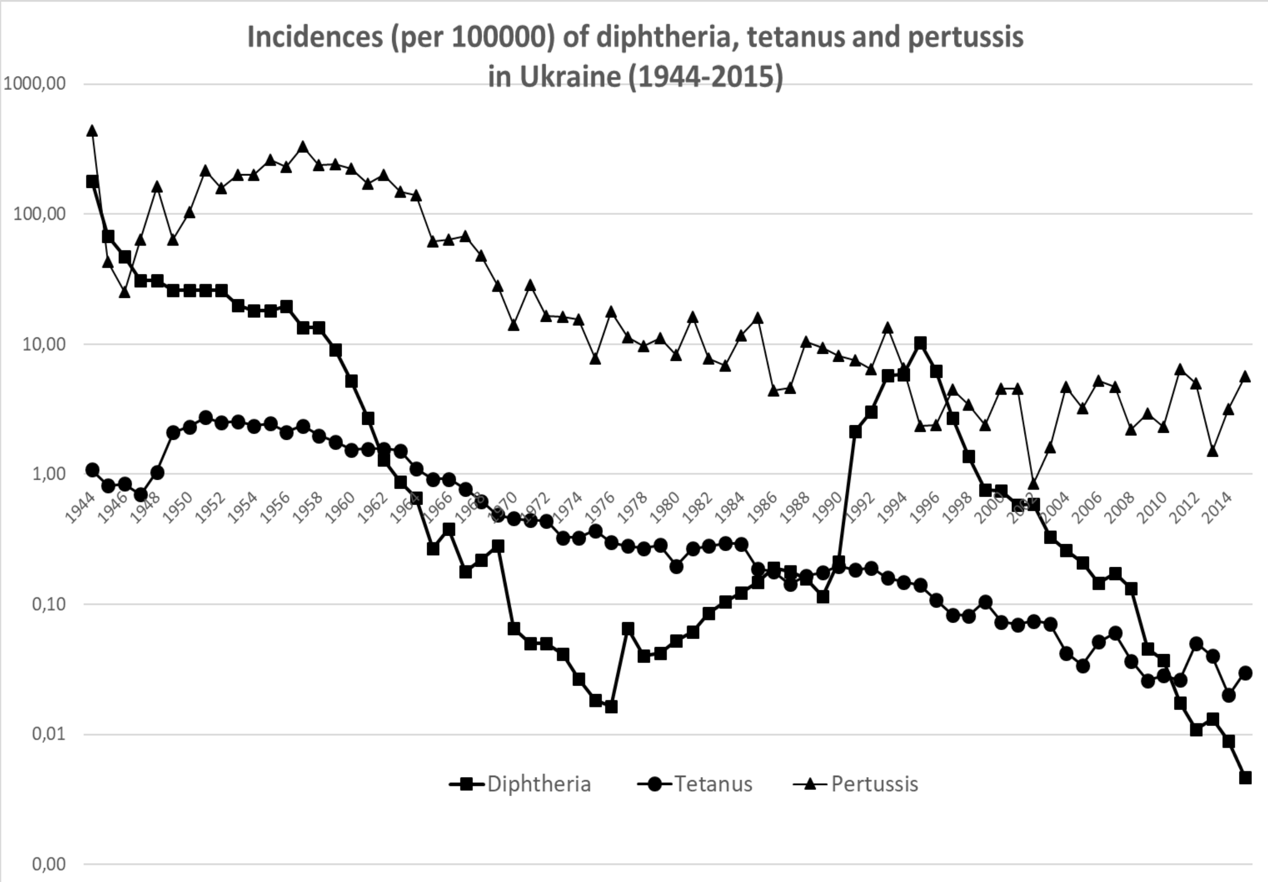

Figure 2. The incidence of diphtheria, tetanus and pertussis in Ukraine (1944-2015)

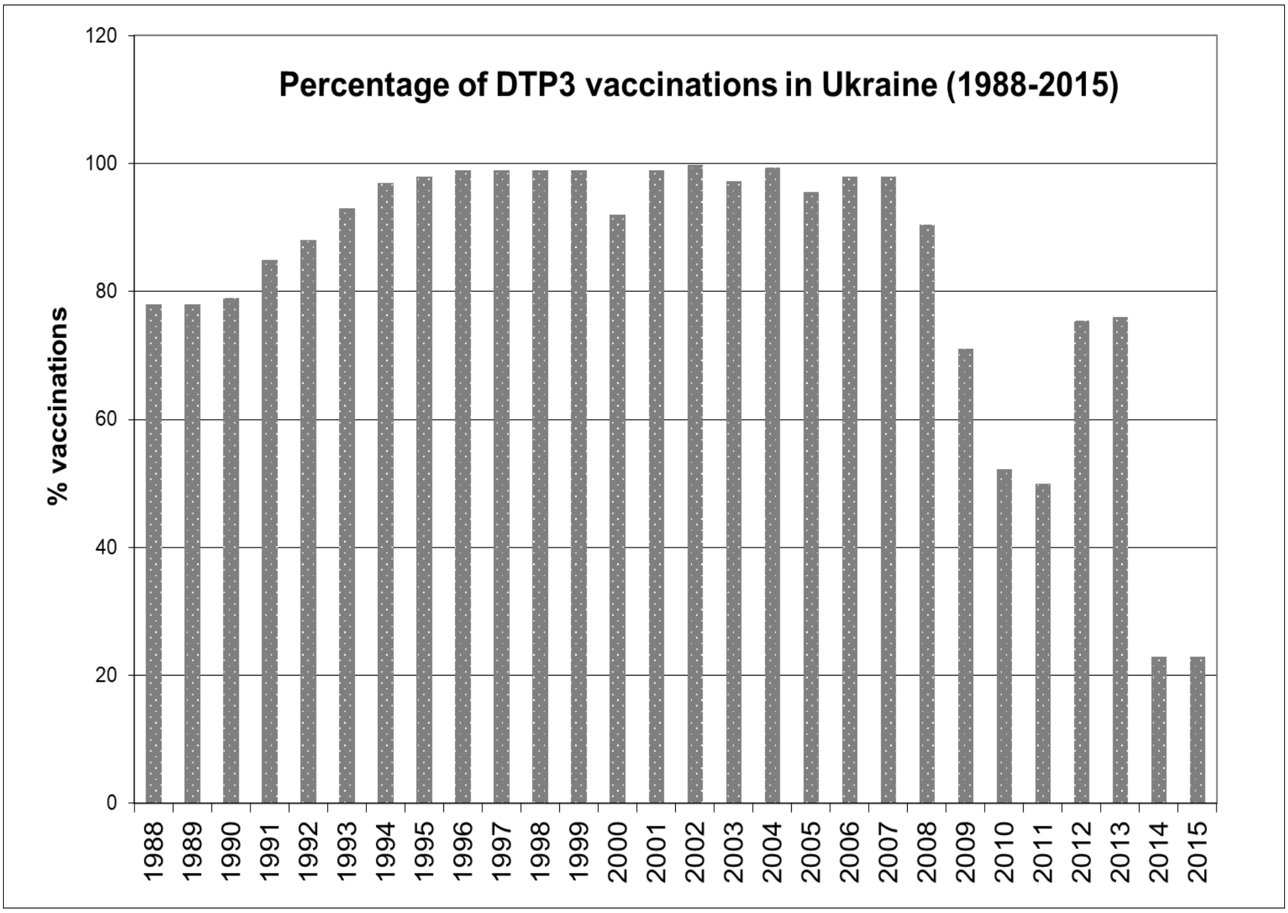

Figure 3. Data coverage of the third dose of DTP in Ukraine (1988-2015)