THESES OF THE DOCTORAL (PhD) DISSERTATION

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FACULTY OF ECONOMICS AND BUSINESS

IHRIG KÁROLY DOCTORAL SCHOOL OF MANAGEMENT AND ORGANIZATIONAL STUDIES

Head of the Doctoral School: **Prof. Dr. Balogh Péter, Professor, DSc**

SEASONAL INFLUENZA VACCINE ECONOMIC MODELING THROUGH ECONOMIC AND SOCIAL BENEFIT ANALYSIS OF VACCINATION

Written by:
Vajó Péter, MSc

Thesis supervisor:
Bács Zoltán, PhD
Professor
University of Debrecen

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1. BACKGROUND, OBJECTIVES AND PRESENTATION OF THE THESES

1.1. Hypothesis

My hypothesis is that greater emphasis should be placed on vaccinating the active (19-60 years of age), as well as the children and adolescent (3-18 years of age) population groups, while maintaining the supply of free vaccines to the age group of 60 and older that current Hungarian regulations define as one of the most vulnerable groups. I suppose that the same level of vaccination coverage amongst children and adolescents and active population groups would lead to much greater economic benefits compared to the current vaccination strategy surplus.

The primary aim of my dissertation is to present the economic impact of the actual vaccination strategy which is focusing on the vaccination of 60 and older population group. After identifying the outcomes of the primary aim the next goal of my dissertation is to present the economic impact in case of a new suggested vaccination strategy, assuming that the same vaccination coverage would be applied in population groups of active (19-60 years of age) and children and adolescents (3-18 years of age) as in the elderly age group. I intend to justify this hypothesis with figures and facts.

1.2 Areas of focus

My study is focused on seasonal influenza and its impacts on the national (domestic) healthcare and social security system; I do not aim at exploring the effects and economic correlations of pandemics (including the current Covid-19 pandemic). Thus, I will not quantify the economic consequences of the collapse of tourism and aviation, the closure of factories and shops, the lack of construction investments, or the unemployment resulting from the pandemic. These impacts are so severe and complex that they affect all areas and actors of the economy. In such a situation, general interest in tourism, hospitality, event organization or transport services decreases due to people’s cautiousness and the lockdowns or limitation of movements. These steps might lead to further factory closures, service outages, and in some cases supply difficulties. These economic problems already pose real challenges to industries other than tourism and hospitality reaching far beyond the direct economic impacts. Prolonged uncertainty and deteriorating business confidence will reduce consumer spending and investments, which could lead to a further and wider-scale decline in economic performance. Production disruptions and weak economic activity threaten the stability of corporate management, productivity growth is stopped, and lost revenues can push indebted companies to insolvency. A global economic crisis is unfolding.

I will describe the different aspects of the impact of seasonal influenza on the national economy (employees, employers, social security expenditure aspects, variables within individuals and social groups, variables within age groups) based on international and national data, my own and previously published research results, and publications.

With the help of the conclusions drawn from the international and national comparison of influenza vaccination data, I intend to prove that the only available effective "antidote" to this infectious disease and the negative healthcare, economic and market impacts it generates is regular and increasing degree of vaccination.

The currently available most effective method to fight influenza is prevention, that is, **annual vaccination.**

There are several types of influenza vaccines currently in use that are grouped as follows:

1. Live (reproducible), weakened (attenuated) virus vaccines,
2. Inactivated virus or virus component vaccines.

My dissertation processes data available regarding the nationally produced, inactivated, whole virion, adjuvanted (the adjuvant has potency-enhancing properties) 3Fluart seasonal influenza vaccine.

2. MATERIAL AND METHODS

2.1. Cost-minimization analysis

The cost-minimization analysis is the right choice provided that the clinical results of the compared processes (e.g. number of saved years or improvement in life quality) are equal in controlled or routine curative activities based on the available and reliable scientific results (e.g. randomized clinical trials with an appropriate number of subjects, or systematic literature reviews). In other words, the benefits (health improvement) and costs (e.g. adverse effects) they generate are corresponding. In such case the analysis should focus on comparing the costs.

Cost minimization analysis is required in case the effectiveness of the comparative interventions is equal or they result in equivalent health gains under routine circumstances (clinical efficiency).

Cost minimization analysis is one of the fastest and cheapest studies to perform, yet this method can be used only in an extremely small percentage of cases. This analysis can only be performed in case the health gains associated with the healthcare technologies to be compared are identical and this condition is rarely met.

While all other full-scale economic analysis methods give high importance to the unit which measures health gains, cost minimization analysis does not give any relevance to the unit that measures changes in health status. Therefore, health improvement can be measured by a natural unit, that is Quality-adjusted Life Year (QALY), or even in Forint (the Hungarian national currency); the most important aspect is equality. Decision-makers can easily interpret the result of the cost minimization analysis since they have to choose the less expensive process out of the alternative possibilities after they have compared the expenses. It is important to stress that inexpensiveness alone is not a sufficient reason to apply a given healthcare technology. A common mistake in economic analyses or analysis-based decision-making is to compare the costs only but to not provide sufficient evidence of equal health improvement. This is an incorrect method as in most cases the “no-intervention” alternative is the less expensive. Accordingly, cost minimization analyses would constantly suggest downsizing healthcare services and products and terminating their support.

The cost minimization analysis can be applied with one extended condition. If a new healthcare technology produces demonstrably higher healthcare gains than the comparator procedure, but at the same time the costs associated with its application are lower, it is sufficient for the cost minimization analysis to justify the cost-effectiveness of the new technology. However, this is only a coincidence for innovative technologies, since if a new healthcare technology has proven health benefit surplus, manufacturers would rarely make the mistake to offer their product cheaper than the widely used technology that is the basis for the comparison. This pricing decision would inevitably result in a loss of profit for them plus a reducing rate of return on research and development.

Cost minimization analyses are most commonly applied for decision-making related to the funding of generic drugs. In case of undoubted bioequivalence study results of drugs with identical active substance, therapeutic equivalence - i.e. the equality of health benefits – is assumed, thus the cheaper product is considered cost-effective.

Outpatient surgery and conventional surgery can also be compared by cost-minimization analysis. However, the cost-efficiency of outpatient surgery can only be assessed with this method if evidence proves that the cost-savings from reduced nosocomial infections due to shorter hospital stays outweigh the extra costs caused by complications observed only later due to the shorter post-operative monitoring period. Outpatient surgery is a good example of how the methodology of cost-minimization analysis seems simple only at first sight.

2.2. Cost-effectiveness analysis

Cost-effectiveness analysis measures clinical efficiency in so-called natural units (e.g. physiological parameters, adverse effects, number of asymptomatic days, number of lives saved, number of years saved, patient satisfaction indices, etc.). Cost-effectiveness analyses include studies that measure health improvement by means of patient-specific or generic (general) quality of life questionnaires that are based on scores independent of utility values and measurements of the occurrence of clinically minimal changes. There are a number of life quality questionnaires that are perfectly suitable for cost-effectiveness analyses, for example, the SF-36 questionnaire, which also has a validated Hungarian version.

If the efficacy of the interventions to be compared is different or produces different health benefits under routine circumstances, a cost-effectiveness analysis is required.

Using cost-effectiveness analysis, we compare the extra cost generated by a new healthcare technology (D-cost) to the extra health benefits generated by the same technology (D-effectiveness). The analysis measures costs and savings in monetary units, and health benefits in natural biological or medical units (e.g. mmol / l cholesterol reduction, Hgmm blood pressure reduction, life years saved, number of healthy days). The evaluation is based on a quotient, the incremental cost-effectiveness ratio (ICER), where the increase in costs and effectiveness is compared to a benchmark, such as the cost-effectiveness rate of an already funded healthcare technology. ICER = D-cost/ D-effectiveness.

The cost-effectiveness indicator shows the extra costs required to achieve one unit of efficiency change; that is, the specific costs of achieving one effect unit. Depending on the point of view of the analysis, the costs can involve healthcare or total social expenditure. The perspective of financiers (in Hungary the NEAK - National Health Insurance Fund Management) is most commonly applied to study decisions on introducing new healthcare technologies.

Basically, there are two limits to cost-effectiveness analyses, which define their application scope as well. Since cost-effectiveness analysis can only measure changes in health benefits in a specific dimension, it does not allow for the comparison of technologies that generate changes in health status in different dimensions (hip replacement vs. lung transplantation vs. new antihypertensive). Thus, this method of analysis can only compare the cost-effectiveness of healthcare technologies that result in a change in health status in identical medical or biological parameters. These can be ranked depending on which procedure can generate one unit of health gain at lower costs. Consequently, the application of cost-effectiveness analyses is limited for preparing decisions on acceptance policy, since they are not suitable, for example, for defining the full scope of publicly funded benefits or for redefining the basic plan for the insured. However, the method may be appropriate for preparing individual acceptance decisions that, for example, assess funds for a new antihypertensive taking into account the cost-effectiveness analyses of previous antihypertensive drugs.

Another limitation of cost-effectiveness analysis is that it can measure changes in health status in only one dimension; even if a given healthcare procedure causes obvious changes in health status in other dimensions. For example, chemotherapeutic drugs that prolong survival or progression-free survival also have serious adverse effects, yet these cannot be included in a single natural health dimension. However, it is also possible to include adverse events in the costs (i.e. in the numerator) and not in the health status changes (i.e. in the denominator of the cost-effectiveness rate). The effect of nausea associated with chemotherapeutic treatments can be considered, for example, by including the cost of antiemetic drugs administered for the symptomatic treatment of the adverse effect. Other effects are thus indicated in the change in costs, i.e. the numerator: positive effects are accompanied by a cost-decreasing sign and negative effects are indicated by a cost-increasing sign. Although this method can extend the scope of cost-effectiveness analyses, the outcome will be results that are more difficult to interpret in case of several common adverse effects and less reliable conclusions.

As for cost-effectiveness analyses, it is best to measure health gains at hard endpoints (e.g., years of life gained, number of lethal heart attacks, etc.). In the case of an intermediate endpoint (e.g. Hgmm decreased blood pressure or mmol/l decreased cholesterol), the model will only provide a reliable result if the intermediate endpoint has been validated by means of a reliable test for the given drugs class, i.e. the improvement at the intermediate endpoint will certainly increase the expected survival and/or patients' overall life quality. Due to the detailed limitations, standard cost-effectiveness analysis is neglected as a method of assessment used in decision-making. At the same time, the concept of cost-effectiveness analysis is increasingly applied in a broader sense, as a synonym for comprehensive economic analysis.

2.3. Cost-benefit analysis

The cost-benefit analysis (CBA) is a type of comprehensive economic analysis that can be applied to any investment decision.

When used for funding decisions in healthcare technologies or programs, it compares the net cost of interventions with the change in health status and other consequences resulting from the intervention.

For this type of full-scale economic analysis, both costs and health gains should be expressed in monetary terms. The evaluation is based on the difference between the yield and cost of the processes to be compared: $(B1 - C1) - (B2 - C2) > 0$, where B is the benefit from the alternatives and C is the cost. The formula helps compare the net benefits from the alternatives, which eases the choice between two procedures with positive net benefits.

If the effect of the technology or program to be assessed extends over several years, a present value calculation should be used to aggregate net costs and benefits. Costs include healthcare costs and, in the case of social analyzes, the direct and indirect costs outside the healthcare system. In addition to health gains, benefits include avoided expenses. The difficulty of the analysis lies in how express the health gains generated by healthcare technologies in monetary terms.

The main advantage to cost-benefit analysis is that enables the comparison of any program or intervention on a purely financial basis, regardless of their nature or purpose. From an economic perspective, the investment with the highest net return should be selected. Another advantage is that this method not only enables the comparison of two or more options, but also makes it possible to decide if a given investment is worth realizing, i.e. whether it has a positive net return. Thus, the cost-benefit analysis may be relevant to all social investment related decisions. The practical application of cost-benefit analyzes can make allocation decisions for “publicly available” resources more impartial and well-founded. It can also help with funding policy decisions related to new technologies and the development of social care packages.

Cost-benefit analyses express the value of health improvement in money. The most common method for this is contingency assessment, which examines how much society would be willing to pay for a certain degree of health improvement associated with a particular healthcare service.

Measuring the extent of health improvement in monetary terms may seem unrealistic at first. Nevertheless, several methods have already emerged to quantify the value of life years. These include:

a) The human capital approaches

- net current value of future earnings over the years of life gained
- net current value of products consumed during the years of life gained
- gross domestic product (GDP)

b) Past decisions of the public sector

- court rulings in forensic assessment of health damage (e.g. legal proceedings due to medical malpractice, damages paid due to adverse effects)
- general court rulings on damages (e.g. compensation for unjustified imprisonment)
- insurance decisions (e.g. costs of general insurance payable for a specific risk)
- health insurance financing decisions (e.g. one year costs of persistent disease)

c) Implicit preferences

- how much we are willing to pay to reduce certain risks (e.g. safety helmet, airbag)
- related to the market assessment of a certain product (e.g. to what extent air pollution can reduce the value of a given plot)

d) Hedonistic pricing

• wages in high-risk workplaces (amount of hazard allowance compared to normal risk workplaces)

e) Contingency assessment

• willingness to pay – assessment by means of questionnaire of how much people are willing to pay to avoid certain health damage or to reduce the risk of the disease

• willingness to accept – how much people are willing to accept in exchange for a certain extent of health damage or for increased risk of the disease.

Certain international guidelines (Lisa A. Robinson, 2019) accept the use of cost-benefit analysis in making decisions on the use of public funds as a possible type of economic analysis, while other guidelines do not recommend its application in healthcare. Despite the increasing use of cost-benefit analyses within the healthcare sector, its methodology is not yet fully developed, and very little experience is available in Hungary.

2.4. Cost-utility analysis

Cost-utility analyses measure health gains in life years weighed by health status and expressed in terms of utility. Cost-utility analyses are recommended to be performed to supplement cost-effectiveness analyses (in parallel with them) provided that the required data are available or can be generated. For example, a life expectancy calculation can be supplemented with a QALY calculation (provided changes in utility values are also known from basic research or literature), and thus the cost / QALY ratio can also be defined.

When applying cost-utility analysis, health improvement is measured in QALY units. QALY is a unit of measure that combines health improvement with regard to life expectancy and quality of life (based on utility).

Quality of life adjustments can be obtained primarily through the use of utility-based health questionnaires in which individual values were defined using surveys of the general population. Such internationally accepted questionnaire is e.g. EQ-5D (EuroQol-5D).

If healthcare interventions relate to diseases for which the dimensions of quality-of-life questionnaires (e.g., pain, physical function) do not adequately monitor changes in the patients' health status, direct utility measurement methods (scale method, forced selection of time length, standard game) can be used to assess patient utility values.

There might be several reasons to introduce Quality-adjusted Life Year (QALY) calculations into the analysis as supplementary information:

- It considers quality of life in addition to mere prolongation of life or avoided death, thus reflects both dimensions that are important to individuals.
- The cost-effectiveness of supplies with different purposes (e.g. related to other diseases and patient groups) is comparable, which helps optimize the allocation of resources within healthcare.
- A cost-threshold can be established that indicates how much society is able and willing to spend on a quality life year that can be gained through a given curative-preventive procedure in addition to the country's economic development. This cost threshold facilitates explicit decision-making.

Despite the scarcity of experience with cost-utility analyses in Hungary, and due to the challenges, it raises, I consider this analysis type closest to my own methodology, therefore I use some methods from this type of analyses in my dissertation to present the use and economic effects of nationally produced influenza vaccines.

3. MAIN FINDINGS AND CONCLUSIONS, RECOMMENDATIONS

3.1. Main Findings

While examining in my study the number of vaccines administered and number of influenza-like illnesses I have divided the total population of Hungary into three age groups: the age group of minors (0-18 years), the age group of economically active (19-59 years) and the age group of elderly (60 years and older).

From statistical data I have stated that in the 2018/2019 influenza season almost 20% of the age group of 60 years and older have been vaccinated with seasonal influenza vaccine, while the ratio of the illnesses in the same age group was only 1.7%.

The level of vaccination was the lowest in case of minors (1.1%), while at the same time the number of illnesses was the highest (10.1%). With the help of statistical data I managed to demonstrate, that there is an inverse relationship between the level of vaccination and the number of influenza-like illnesses, which leads to a conclusion that in case the level of vaccination is increased the number of illnesses is decreasing.

With comparison of data on illnesses of the least vaccinated group of minors against the highly vaccinated age group of 60 years and older I have determined the effectiveness of the vaccine against seasonal influenza through a mathematical calculation. The value I have reached is 44.68% which is in correlation with the efficacy data to be found in different sources of the scientific literature.

Based on this efficacy value I have made an estimation on the number of non-occurred illness cases avoided due to the vaccination. As a result of this estimation I have concluded that in 2018/2019 influenza season there were a total of 321,000d non-occurred influenza-like illness cases in Hungary.

By the age-group distribution of the above number of avoided cases I have quantified the economic benefit in billion HUF gained due to the non-occurrence of the illnesses. I have concluded that the vaccination triggered savings i.e., economic benefit in magnitude was 15,550 billion in terms of the Hungarian national economy. This savings value represents as a share of the GDP 0.4 parts per thousand.

In the next part of my study I have made a proposal on a new vaccination strategy where the focus should not be solely on the vaccination of the elderly but there is a need for increasing the level of vaccination of the whole population to the level of vaccination coverage of the age group of 60 years and older. In case of this suggested new vaccination strategy I have used the same methodology for calculations and I have concluded that with the implementation of a new vaccination strategy there would be further 78,000 cases avoided.

The positive impact on the national economy calculated with the higher number of avoided cases (taking into consideration the costs of the extra vaccination, as well) is 7,7 billion HUF higher compared to the benefits achievable by the current vaccination strategy, in figures 23,2 billion HUF. The share of the GDP has raised with 0.2 parts per thousand.

As a next part of my study I have determined the number of the Quality-adjusted Life Years (QALY) both in cases of the present and recommended vaccination strategies. In case of the present vaccination strategy it was 3,190 years while in case of the recommended one it turned out as 3.965 years, therefore the extra years of life value in case of the recommended vaccination strategy represents 775 years.

In the closing part of my study I have calculated the incremental cost-effectiveness ratio (ICER), as well, which represents 961,000 HUF/life years in Hungary. I have made a comparison of this value to the figures of some developed countries and with the WHO recommendation. I have concluded that the above Hungarian ICER data is below these threshold values and recommendation therefore it is justified that the newly suggested vaccination strategy is worth to be implemented both from the perspective of healthcare and economic aspects.

3.2. Conclusions

The goal I set in my dissertation has had no precedent either in the Hungarian literature: my intention was to present the impact of influenza vaccination on the economy and the national gross product.

My hypothesis was that greater emphasis should be placed on vaccinating the active (19-60 years of age), as well as the children and adolescent (3-18 years of age) population groups, while maintaining the supply of free vaccines to the age group of 60 and older that current Hungarian regulations define as one of the most vulnerable groups.

I managed to prove that the same level of vaccination coverage amongst children and adolescents and active population groups would lead to much greater economic benefits compared to the current vaccination strategy surplus.

The primary aim of my dissertation was to present the economic impact of the actual vaccination strategy which is focusing on the vaccination of 60 and older population group. After identifying the outcomes of the primary aim the next goal of my dissertation was to present the economic impact in case of a new suggested vaccination strategy, assuming that the same vaccination coverage would be applied in population groups of active (19-60 years of age) and children and adolescents (3-18 years of age) as in the elderly age group. I managed to justify this hypothesis with figures and facts.

For the specific calculation, I took data from the Central Statistical Office and the Influenza Surveillance System of the Epidemiology and Infection Control Department of the National Public Health Center as basic data, and I used international comparative data to determine the final result for factors with no available national data.

Based on the available basic data, I also had to make estimates during the calculation; I always carefully considered the circumstances and set the most accurate end-result as a purpose. One of the most important calculations was to find out how many cases of the disease were avoided through vaccination. There have been no former attempts in this regard so my dissertation can be considered innovative in this area.

I evaluated data from the influenza season of 2018/2019 in my dissertation. I analyzed the available data on population, vaccination and the number of diseases, and drew conclusions therefrom. It was a problem that the basic data appeared in different data sets for different age groups, so I had to find a consensus between them, and establish comparable age groups. Ultimately, I defined three distinct age groups: the age group of minors (0-18 years), the economically active (19-59 years) and the age group of 60 and older. These three age groups became well distinguishable by population, vaccination, and morbidity.

During the study period (2018/2019 influenza season), 1.1 percent of the minor age group, 3.5 percent of the economically active age group, and almost twenty percent (19.8%) of those 60 and older received influenza vaccinations. In terms of morbidity data, 10.11 per cent of the age group of minors, 4.95 per cent of the economically active age group, and only 1.74 per cent of those over the age of 60 became ill. It is evident that compared to all members of this age group, the rate of vaccination and the number of cases are strongly opposite.

The detailed data described the preventive effect and the effectiveness of vaccines. My calculation made on the basis of facts resulted in vaccine effectiveness of 44.68 percent compared to the fifty percent estimated by scientific literature.

The effectiveness value calculated on the basis of real data helped define the number of illnesses that did not occur due to vaccination: it is 8,992 cases in the minor age group, 83,804 cases in the active age group and 228,200 cases in the elderly age group, i.e. a total of 320,996 non-occurred illnesses.

Since there are no reliable national and processed data on the further history of patients visiting their doctor with flu-like symptoms, I applied international data in my work. The CDC report reflects data on influenza morbidity, the symptoms of the disease, medical visits, and the number of hospital cases over the past nine years. Based on the published data, the number of doctor visits and the number of subsequent hospitalizations could also be determined.

Based on the rate of hospitalization in the United States and the number of illnesses avoided in Hungary, I could draw conclusions on the number of hospital care that could be avoided in Hungary. This represents 3,777 hospital cases avoided in the active population group and 7,009 in the passive population group.

Based on the data of the CSO, the total health expenditure of hospitals and healthcare institutions as well as all days of care can be determined. From the quotient of these two numbers it can be stated that the health care expenditure per day of care is HUF 49,801.

When examining the impact on the gross national product, I calculated the loss of income for employees and the savings for employers and the budget. Overall, it can be concluded that gross earnings for the entire duration of non-occurred diseases appear as an economic benefit.

To summarize the results of my dissertation, it can be stated that the disease-preventing property of influenza vaccination has a total economic benefit of HUF 15,550 billion (fifteen billion five hundred and fifty million HUF) for the national economy. The value of GDP (gross domestic product) in Hungary in 2018 was HUF 42,661,805 million. The economic benefit of influenza vaccination in case of the present vaccination strategy as a share of the GDP is 0.4 parts per thousand.

Results might be achieved in case of the suggested vaccination strategy: the suggested vaccination strategy generates plus economic benefit both in active and passive population groups. The results clearly show that more than three-quarters of all economic benefits are generated in the active population group, although they only account for only one-third of non-occurred diseases. Consequently, higher degree of vaccination in the active population is strongly justified as the resulting economic benefit is cumulative in their case.

During calculations the same methodology was used for the suggested strategy as in case of the present one and it resulted almost 24 billion HUF. It means that the suggested vaccination strategy ensures more than 50% economic benefit compared to the current vaccination strategy. The economic benefit of influenza vaccination in case of the suggested vaccination strategy as a share of the GDP is 0.6 parts per thousand.

3.3. Recommendations

The data listed above on the disease caused by the influenza virus, the course and frequency of influenza infections, and the specific characteristics of influenza virus clearly accentuate the extreme hazards of the influenza virus and the disease it causes, the high level of national and global health risks due to the regularity of seasonal epidemics and pandemics, as well as the paramount importance of protection against the virus.

Since there are currently no widely used traditional drugs that could be used effectively against the influenza virus, the most effective way to control the virus and the disease is by means of vaccination.

The production and use of influenza virus vaccines produced by vaccine manufacturers using different technologies is therefore of strategic importance for all countries and the world's population.

Therefore, all nations and all vaccine manufacturers must make every effort to ensure that the vaccines they manufacture are the most effective in protecting against viral infection, regardless of the manufacturing technology or the composition.

It is necessary to extend the scope of vaccinations in order to prevent severe consequences that could easily become unpredictable. Vaccination should cover not only people in the hazard age groups and those already suffering from other diseases but also minors (they typically socialize in large "groups" where they can spread the virus effectively) and those in the active age group. The anti-vaccination sentiments typical of our age need to be addressed assertively. Vaccine acceptance can make a major contribution to mitigating the devastating consequences of a severe pandemic predicted by the WHO.

What are the possibilities of increasing vaccine acceptance?

WHO lists vaccine hesitancy among the 10 most dangerous global health threats in its study published in 2019. The importance of this problem is emphasized by many publications and studies available. Vaccination is referred to as one of the most important achievements of public health, yet there have always been certain groups (e.g., religious, political, scientific) that question its significance for some reason. Another problem is that information (and false information) is shared quickly in versatile communication channels, which might undermine confidence in vaccines or strengthen sentiments against immunization. There are several different reasons for vaccination hesitancy, the mapping of which is the first step toward increasing vaccine propensity and to persuading hesitant members of the population by effective means.

Literature data reveal that active participation by healthcare professionals and doctors in supporting vaccination, answering questions that arise, and providing information is essential. According to a study conducted in Hungary, training and actively involving pharmacists in the recommendation of vaccinations would also contribute to increasing vaccine propensity not only in at-risk groups but also in the active adult population.

There should be campaigns to increase vaccine propensity so that professionals can share information and knowledge to hesitant people to build confidence and reinforce the importance of vaccination. In addition to explaining the patient information leaflet, they should also provide an overview of the vaccination procedure itself as well as its background.

The below list contains some but not all methods taken from literature that help increase vaccine propensity:

- Continuous training for healthcare professionals, doctors, and pharmacists
- Briefing, brochures and posters to GPs
- Informing parents
- More information on vaccines, the importance of vaccines, the influenza virus, and the disease, shared on social media (internet, tv, radio)
- Influencing perceptions of the effectiveness, safety, and adverse events of vaccines; consultation
- Free vaccination
- Sending reminders (phone, email)
- Easily accessible vaccines (designated vaccination points, simple and quick procedure without waiting times).

4. NEW AND NOVEL RESULTS OF THE DISSERTATION

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New and novel results

- Until now there were only medical-professional data available regarding the efficacy of vaccines against influenza. In my study I managed to prove the effectiveness of influenza vaccine on the basis of statistical data for the first time.
- On the basis of quantified efficacy, the first time estimation has been made on the number of avoided cases due to the vaccination.
- Also, this was the first estimation on impact of the vaccination on national economy.
- Furthermore, there was the first quantification of Quality-adjusted Life Years (QALY) gained by the vaccination.
- Finally, the value of cost-increase necessary to reach one unit of health gains in course of protection against influenza was demonstrated for the first time in Hungary.

SUMMARY

I believe that my dissertation examining the impact of vaccination on economic performance is innovative as for both its approach and methodology. It does not match any type of health economics analysis (cost-minimization analysis, cost-effectiveness analysis, cost-utility analysis, cost-benefit analysis), yet it is closest to cost-utility analysis. However, the methodology of the latter is not yet fully sophisticated, and there is little experience with it in Hungary. I hope my study can fit into the line of cost-utility analyses and serve as a basis for future economic analyses that go deeper than my dissertation.

In my dissertation I could prove my initial hypothesis that – in addition to maintaining the supply of free vaccines to the age group 60 and older being one of the vulnerable groups defined in the current regulations for influenza vaccinations – more emphasis should be placed on increasing vaccination in the active (18-60 years) and the pediatric and minors age groups (3-18 years).

The presented facts, numbers, the results of the calculations, and the conclusions drawn clearly show the preventive effect and effectiveness of vaccination, which was quantified for the first time in Hungarian literature. The economic benefit of influenza vaccination in case of present vaccination strategy as a percentage of GDP is 0.4 parts per thousand, while in case of the recommended vaccination strategy is as a percentage of GDP is 0.6 parts per thousand. These values might seem only mathematically small, but in reality it is quite significant.

Nevertheless, for the first time, the positive impact of a vaccine on the economy has been quantified on the basis of specific statistics.

In addition to the new viruses that are emerging today, the old enemy, the flu, is still the greatest threat. Even a one-year seasonal flu epidemic kills half a million people every year around the world. Drug researchers are working on a general influenza vaccine that would be able to catch the virus at the genetic level, making it much more effective than vaccines currently available on the market. Although many formulations are in the clinical trial phase, none of them offer fully universal protection. WHO

experts believe that the most devastating disease with the most widespread consequences in the world could be a severe influenza pandemic.

It is necessary to extend the scope of vaccinations in order to prevent severe consequences that could easily become unpredictable. Even the CDC and EMA agrees that the only and best way to fight influenza is by means of annual vaccination. Vaccination should cover not only people in the hazard age groups and those already suffering from other diseases but also minors (they typically socialize in large “groups” where they can spread the virus effectively) and those in the active age group. The anti-vaccination sentiments typical of our age need to be addressed assertively. Vaccine acceptance can make a major contribution to mitigating the devastating consequences of a severe pandemic predicted by the WHO.

5. PUBLICATIONS

1. **Vajó, P.** (2021): Az influenza elleni védőoltás hatása egyes más egészségügyi tényezőkre. Economica, Debreceni Egyetem Publikációs Platform. Economica XII. Új évf., 1-2. sz. (2021) ISSN 2560-2322

2. **Vajó, P.** – Bács, Z. (2021): Influenza elleni védőoltás. Gazdasági modellalkotás a védőoltás gazdaságossági és társadalmi hasznossági elemzése útján. Régiókutatás Szemle, 2021/1. DOI: 10.30716/RSZ/21/1/1.

3. Vajo, Z. – Kalabay, L. – **Vajo, P.** – Balaton, G. – Rozsa, N. – Torzsa, P. (2019): Licensing the first reduced, 6 µg dose whole virion, aluminum adjuvanted seasonal influenza vaccine – A randomized-controlled multicenter trial. VACCINE 37 : 2 pp. 258-264., 7 p. (2019)

4. Vajo, Z. – Balaton, G. – **Vajo, P.** – Kalabay, L. – Erdman, A. – Torzsa, P. (2017): Dose sparing and lack of dose response relationship with an influenza vaccine in adult and elderly patients - a randomized, double-blind clinical trial. BRITISH JOURNAL OF CLINICAL PHARMACOLOGY 83 : 9 pp. 1912-1920., 9 p. (2017)

5. **Vajo, P.** – Gyurjan, O. – Szabo, A.M. – Kalabay, L. – Vajo, Z. – Torzsa, P. (2017): Az új, csökkentett dózisú, hazai gyártású influenzavakcina (FluArt) forgalomba hozatalát követő első szezonjának biztonságossági vizsgálata [Safety data of the new, reduced-dose influenza vaccine FluArt after its first season on the market] ORVOSI HETILAP 158 : 49 pp. 1953-1959. , 7 p. (2017)

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Doctoral School: Károly Ihrig Doctoral School of Management and Business

MTMT ID: 10059780

List of publications related to the dissertation

Articles, studies (5)

1. **Vajó, P.**: Az influenza elleni védőoltás hatása egyes más egészségügyi tényezőkre.
   Economica. 12 (1-2), 36-50, 2021. ISSN: 2560-2322.
2. **Vajó, P.**, Bács, Z.: The Calculation of Social Benefits of Influenza Vaccination based on Statistical Data.
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3. Vajó, Z., Kalabay, L., **Vajó, P.**, Balaton, G., Rózsa, N., Torzsa, P.: Licensing the first reduced, 6??g dose whole virion, aluminum adjuvanted seasonal influenza vaccine - A randomized-controlled multicenter trial.
   Vaccine. 37 (2), 258-264, 2019. ISSN: 0264-410X.
   DOI: http://dx.doi.org/10.1016/j.vaccine.2018.11.039
   IF: 3.143
4. **Vajó, P.**, Gyurján, O., Szabó, Á. M., Kalabay, L., Vajó, Z., Torzsa, P.: Az új, csökkentett dózisú, hazai gyártású influenzavakcina (FluArt) forgalomba hozatalát követő első szezonjának biztonságossági vizsgálata.
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   DOI: http://dx.doi.org/10.1556/650.2017.30877
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Address: 1 Egyetem tér, Debrecen 4032, Hungary Postal address: Pf. 39. Debrecen 4010, Hungary
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5. Vajó, Z., Balaton, G., **Vajó, P.**, Kalabay, L., Erdman, A., Torzsa, P.: Dose sparing and the lack of a dose-response relationship with an influenza vaccine in adult and elderly patients - a randomized, double-blind clinical trial.
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   DOI: http://dx.doi.org/10.1111/bcp.13289
   IF: 3.838

Total IF of journals (all publications): 7,303
Total IF of journals (publications related to the dissertation): 7,303

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Address: 1 Egyetem tér, Debrecen 4032, Hungary Postal address: Pf. 39. Debrecen 4010, Hungary
Tel.: +36 52 410 443 Fax: +36 52 512 900/63847 E-mail: publikaciok@lib.unideb.hu, ¤ Web: www.lib.unideb.hu