INTRODUCTION

According to the World Health Organization, there is a rapid population aging throughout the world. In Ukraine, the proportion of people over 65 in 2016 was almost 16% while by the United Nations scale, the old population considered with the proportion of people over 65 more than 7%. Demographic changes caused by aging lead to a numerous consequences for society that have repercussion to all spheres of our lives. Delay in economic development, declining household incomes, lack of investment, reduction of consumer basket, employment problems, insufficient pension provision, tax increase, family composition, deterioration of living conditions, increased emigration movements, increased need for medical care and social services for the elderly, etc. Therefore, the modern concept of the health system goes along with “healthy aging” and requires comprehensive measures, both from the state and from the health care system. Among such measures should be the prevention of the incidence and exacerbations of chronic diseases.

According to the data of Health Ministry of Ukraine [1], circulatory system diseases occupy the first place in the structure of the morbidity prevalence in Ukraine. For example, in 2012 this indicator reached 31.48% (58 385.70 per 100 thousand), in 2015 - 30,95% (52 956.9 per 100 thousand), in 2016 - 30,67% (52,970.4 per 100 thousand).

ASSESSMENT OF THE EFFECTIVENESS OF THE GASTROPATHY RISK REDUCTION PROGRAM IN PATIENTS WITH ARTERIAL HYPERTENSION

OCENA SKUTECZNOŚCI PROGRAMU ZMNIEJSZENIA RYZYKA ROZWOJU GASTROPATII U PACJENTÓW Z NADCIŚNIENIEM TĘTNICZYM

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ABSTRACT

Introduction: For primary health care patients with concomitant morbidity are usual phenomena. Combination of gastropathy with arterial hypertension is increasingly being studied. However, the assessing of the medical and economic effectiveness of treatment of patients with concomitant morbidity still methodologically challenging. The issue aggravated by different cushion programs aimed to alleviate financial burden to indigent population. These cover non-expensive drugs with probable hazard to concomitant morbidity.

The aim: to evaluate the effectiveness of the gastropathy risk reduction program in patients with arterial hypertension (AH).

Materials and methods: data on 150 patients with AH collected by panel design with dynamic cohort traced up to 17 years. We have elaborated a program for the prevention of gastropathy in patients taking antihypertensive therapy. Program is based on regulations of the Ministry of Health of Ukraine, adapted clinical guidelines, and other official sources of information, since holistic prevention of gastropathy is not depicted in any source. Two main cohorts were distinguished: those in prevention program (PP) and patients with usual treatment. 6 built in cohorts (Group№0-№5) helped to diversify PP across groups of different severity. Event of interest was incidence or aggravation of gastropathy (gastroduodenitis mainly). We used Poisson model to study average treatment effect of PP on annual number of aggravations.

Results: The main effect of program participation is significant in a model of fixed effects ($β = -0.269; p = 0.0156$), and even more supportive in the mixed model ($β = -0.282; p = 0.0097$). Other components with a variable “PP participation”, namely participation in the program given the group, participation in the program given GP duration, participation in the program given compliance, appeared to be nonsignificant, that suggest absence of substantial selection bias due to non-randomness of allocation. The greatest risk reduction due to program participation was in patients of Group0, that is, in patients with hypertension who do not receive antihypertensive therapy. In groups №1-№5 with more aggressive hypertension treatment the effects of program participation are obvious but less pronounced.

Conclusions: The elaborated program differentiates patients by groups and furthermore allows one to consider each patient characteristics, taking into account income, age, gender, progression of the disease, comorbidity, drugs the patient takes. The established program based on cooperation of patient, general practitioner, and gastroenterologist. We reduced selection bias due to possible randomness blemishes in allocation to the PP by control function method. The main effect of program participation is significant in a model of fixed effects ($β = -0.269; p = 0.0156$), and even more supportive in the mixed model ($β = -0.282; p = 0.0097$).

KEY WORDS: program of prevention, risk, assessment of efficiency
At the same time, the third place was occupied by diseases of the digestive system: in 2012 – 9.74% (18 058.10 per 100 thousand), in 2016 – 9.93% (16 998.1 per 100 thousand) and 2016 – 9.74% 16 825.5 per 100 thousand).

With an increase in the life expectancy the probability of simultaneous existence of different diseases is increasing, which leads to a number of issues that are needed to be addressed. The problem of polymorbidity is one of the most difficult in medical practice. Mutual influence of diseases and medical pathomorphosis significantly change the clinical manifestation, the natural course of each, and the probabilities of complications. In addition, it causes deterioration in the quality of life, difficulties in the diagnostic and treatment. Prescribing the drug, it is necessary to keep in mind its possible positive or negative impact on the concomital pathology.

For primary health care patients with concomitant morbidity are usual phenomena. Combination of gastropathy with arterial hypertension is increasingly pervasive. It is obvious that, with high blood pressure as conspicuous symptom, arterial hypertension is diverse and multifaceted. The diversity of the course of arterial hypertension and its combination with other diseases are among most common topics for research, still the assessment of effectiveness of combined pathologies treatment faces challenges on methodological ground [2].

THE AIM
The aim was to evaluate the effectiveness of the gastropathy risk reduction program in patients with arterial hypertension.

MATERIALS AND METHODS
Data on 150 patients with AH collected by panel design with dynamic cohort traced up to 17 years. Two main cohorts were distinguished: those in prevention program (PP) and patients with usual treatment. Event of interest was incidence or aggravation of gastropathy (gastroduodenitis mainly). We also discerned sub-cohorts: (i) patients with hypertension that did not receive antihypertensive therapy and without complaints related to the organs of the gastrointestinal tract (group 0), (ii) those treated with anticoagulants and (or) with antiaggregates (group 1), (iii) patients treated with non-steroidal anti-inflammatory drugs (group 2), (iv) patients with resistant AH (group 3), (v) patients on medications that did not receive antihypertensive therapy and without complications. The main cohort included 100 patients of respectively examined followed by prospective observation for 4), (vi) patients treated with antihypertensive drugs only.

In the course of the study, outpatient cards were retrospectively examined followed by prospective observation of patients. The main cohort included 100 patients of retirement age with arterial hypertension with different duration (at most 17 years) complicated by gastropathies originated in the course of antihypertensive therapy. The control cohort included 50 retirement age patients with arterial hypertension of varying duration (at most 17 years old) but without gastropathy developed. Data on the natural course of both diseases were collected with the assistance of attending physician.

PROGRAM DESCRIPTION
We have elaborated a program for the prevention of gastropathy in patients taking antihypertensive therapy. Program is based on regulations of the Ministry of Health of Ukraine, adapted clinical guidelines, and other official sources of information, since holistic prevention of gastropathy is not depicted in any source.

The program differentiates patients by groups and furthermore allows one to consider each patient characteristics, taking into account income, age, gender, progression of the disease, comorbidity, drugs the patient takes. The general principles are the same for all patients aimed to prevent the incidence and following exacerbations of gastropathy are balanced nutrition, normalization of body weight, active lifestyle, abstaining from bad habits, reduction of psycho-emotional overload.

The established program based on cooperation of patient, general practitioner, and gastroenterologist. The general approaches are complemented with particular activities identified under delineated groups of patients with essential hypertension. One of the prime goal is to achieve compliance.

We used mixed Poisson model to study average treatment effect of PP on annual number of aggravations. The statistical justification for the testing of the effectiveness of the prevention program (PP) based on the methods of eliciting “Average treatment effect” (ATE). These methods are called to correct the bias of treatment effects estimators primarily due to violation of the randomness of the program’s assignment, in particular the bias imposed by self-selection.

TREATMENT EFFECT ESTIMATION
The general rule of the techniques is to take into account unobserved heterogeneity, which, in particular, leads to a biased test of the effectiveness of the treatment in case of its correlation with selection into treatment regiment, say, into main and control cohorts. If the PP performance indicator is y, and the vector w contains PP components, we are interested in the effect w on y in the structural model

\[ E(y | w, c) = a + bw \]

where a and b may be confounded with both observed (covariates) and unobserved heterogeneity and c represents such heterogeneity.

b is not a constant because of the conditioning on unobserved heterogeneity, that is, we estimate the average (partial) treatment effect (ATE) averaged over the sample:

\[ b \equiv E(b_{population}) = E(b_{sample}) \]

In the presence of the set of covariates x, which include, in particular, the components of the program, we can identify the average partial effect given x: E(b|x). To validate the use of independent variables x as proxy variables to c, it is necessary to fulfill 2 conditions of redundancy x and c. 1. The vector x is redundant (or ignorable) given w and c:

\[ E(y | w, c, x) = E(y | w, c) = a + bw \]

2. In the first two conditional moments of w, c is redundant given x:

\[ E(w | c, x) = E(w | x); \]
\[ Var(w | c, x) = Var(w | x) \]
As was demonstrated by Wooldridge, J.M. (2004, f.3.1) under these conditions ATE of w on y has unbiased estimator [3]:

\[ \text{ATE} = E[(w - \mu(x))y/\text{Var}(x)] \quad (4) \]

with \( \mu(x) \) and \( \text{Var}(x) \) are respectively the mean and the variance of vector \( w \).

There are several types of ATE appraisers (4) for meeting the conditions (2) and (3). We chose an evaluator based on the redundancy of the vector \( w \) given covariates \( x \) present due to the lack of reliable instrument variables. Analytical techniques are based on the proposals of Rosenbaum and Rubin (1983), known as ignorability of treatment conditioned on covariates \( x \) namely:

(a) \( E(y|a,x,w) = E(y|a,x) \); (b) \( E(y|x,w) = E(y|x) \quad (5) \)

where \( y \) and \( y_a \) are the values of dependent variable (annual number of gastroduodenitis aggravations) in patients allocated to control and experimental (treatment) cohorts.

The idea (5) is straightforward: if there is sufficient information in the variable \( x \) about the allocation to PP, the expected values of dependent variable do not depend on the allocation status in the presence of \( x \). In other words, even if \( y \) and \( y_a \) are correlated with \( w \), this correlation is explained by \( x \), and, consequently, is not necessary in the presence of \( x \).

An effective method for evaluating ATE given ignorability of treatment conditions (5) is a control function method [4]. By this method, the control functions of \( x (g(x)) \) are added to the linear predictor \( 1 \), \( w \) to control the violation of the randomized allocation of the program, that is:

\[ E(y|x,w) = \mu + \alpha w + g(x) + w[g(x) - g(x)] \quad (6) \]

The coefficient \( \alpha \) evaluates ATE. If the control functions are linear in \( x \), then the expression (6) is simplified to:

\[ E(y|x,w) = \mu + \alpha w + \beta x + w(x - x) \theta \quad (7) \]

with the normalization of the values of the covariates \( x \) by the means \( x \). Decentralization is important to ensure unbiased estimation of \( \alpha \) (ATE), which is confounded with \( wx\theta \) otherwise.

The type of model is determined by the nature of the effect measurement and the link function \( y = f(w|\theta, x) \). In the study the effectiveness of PP \( (y_j) \) is measured in annual number of gastroduodenitis aggravations in the patient \( i \) in the year \( j \), that calls for Poisson model with the dependent variable “annual number of exacerbations”. The specification of the model depends on the organization of the data, which in the study for \( N \) patients have a panel structure:

\[
\begin{align*}
&y_{11} 
&y_{12} 
&\vdots 
&y_{1k} 
&y_{N1} 
&y_{N2} 
&\vdots 
&y_{Nl}
\end{align*}
\]

\[
\begin{align*}
x_{11} & \quad x_{12} & \quad \cdots & \quad x_{1p} \\
x_{12} & \quad x_{12} & \quad \cdots & \quad x_{1p} \\
\vdots & \quad \vdots & \quad \cdots & \quad \vdots \\
x_{1k} & \quad x_{1k} & \quad \cdots & \quad x_{1p} \\
\vdots & \quad \vdots & \quad \cdots & \quad \vdots \\
x_{N1} & \quad x_{N1} & \quad \cdots & \quad x_{N1p} \\
x_{N2} & \quad x_{N2} & \quad \cdots & \quad x_{N2p} \\
\vdots & \quad \vdots & \quad \cdots & \quad \vdots \\
x_{Nl} & \quad x_{N1l} & \quad \cdots & \quad x_{Nlp}
\end{align*}
\]

where the first index indicates the patient’s number, and the second denotes the year of observation; for predictors the third indicates the predictor number (1, ..., \( p \)). So, the first patient is traced \( k \) years. Accordingly, the number of exacerbations of duodenitis is indicated by \( y_{1k}, \ldots, y_{1p} \). In the first year, the values of \( p \) predictors for the first patient are \( x_{1k}, \ldots, x_{1p} \), while in the last year they are \( x_{1k}, \ldots, x_{1p} \).

Given the Poisson distribution of dependent variable we opted for log link function.

The basic equation of logistic regression for such a plan has the form:

\[ y_i \sim \text{Poisson}(\mu_i) \]

\[ \mu_i = \log(b_0 + b_1 x_{ik} + b_2 x_{ip} + \ldots + b_p x_{ip}) \quad (8) \]

where \( x_{ik} \) – independent variables (factors of patient and aggravation episode),

\[ y_i \] – the number of exacerbations of gastroduodenitis, observed in the patient \( i \) in the period \( t \)

\( \log \) – function of natural logarithm,

\( b_j \) – regression coefficient on \( j \) variable.

Estimation of the model parameters was carried out by MCMC algorithms using Gibbs sampler realized in WinBUGs software.

The composition of predictor set was determined by their suggested effects on the incidence and aggravations of gastroduodenitis. Predictors organized as follows:

- patient characteristics: age, gender, marital status, smoking status, obesity, comorbidity load measured by Charlson index, PP allocation (participation) status, AH duration;
- patient by year data: annual income, occupation status, served by the social welfare status, stage and degree of hypertension, annual expenses for treatment of hypertension, annual number of AH related hospitalizations, annual size of reimbursement, annual costs of AH treatment, main drug for the treatment of hypertension, doctor’s note of patient non-compliance, GP related complaints;
- patient by year by exacerbation data: erosion presence, \( H_p \) presence.

In the hierarchical mixed model, we also included design elements such as: serial index (patients are organized in series by the place and time of inclusion in the study), physician’s code to make allowance for physician practice, patient’s number.

**FIXED EFFECTS AND MIXED MODELS**

To measure risk shifts due to participating in the program, we have applied fixed effects and mixed models. The mixed model is padded out by three additional variables: the index of series, the number (code) of the district (doctor’s code), the patient’s number. The sample formed in series by time and place of inclusion in the study, presumably heterogeneous by composition, in particular by the ratios of patients with GP. Of course, accounting for such heterogeneity of the fragments of the general sample is desirable to accurate assessment of the risk of GP aggravation and its shift due to PP participation. It is hard-to-tackle with fixed effects model, since the series capture random effect nature (lack
of clear sensible gradations or expected deviations from the mean, though so called pulling toward mean tendency is obvious). Analytically, for each series, its effect on the risk of GP is estimated, provided normal distribution with zero mean. That is, the random effects inclusion does not shift the expected risk, but modifies its value in each of the series. That is why the effect is estimated by the sigma parameter. The larger the sigma, the greater the risk deviations in individual series.

A similar logic of inclusion the site (physician) and the patient's personal effects as random. It is not possible to take into account the peculiarities of the individual medical practice and the patient's individual response to the proposed treatment otherwise. Therefore, we processed data both by the fixed effects model and by mixed model.

Randomized effects rendered by a complex covariance matrix structure with a clear hierarchical nesting effects, namely: the model's residuals are nested into the individual effects of patients due to panel data organization, the latter are nested into physician effects which in turn are nested into series.

ATE IDENTIFICATION
The identification of ATE is implemented in the linear predictor of the models as:

\[ \beta^* \text{Treatment} + \beta_1^* \text{Treatment} \times \text{Group} + \beta_2^* \text{Treatment} \times \text{bi} + \]

\[ \beta_3^* \text{Treatment} \times \text{AH duration} + \beta_4^* \text{Treatment} \times \text{Complaints} + \ldots \]

where Treatment is participation in PP, bi is individual patient i effect, \ldots stands for other predictors.

The main parameter of ATE test is the \( \beta \) coefficient, whose identification from the bias due to violation of the randomization of allocation into PP is ensured by including constituents of \( w [x - \bar{x}] \theta \) in (7):

- component \( \beta_2^* \text{Treatment} \times \text{bi} \), which expresses the individual effect of the patient, which is centered by assigning the function generating its prior values a normal law with zero mean \( b[i] \sim \text{dnorm} (0, \tau) \) in the text of the code. In fact, the individual patient effect absorbs all possible patient's characteristics not included into model (unobserved heterogeneity), thus providing a powerful proxy variable for unbiased test of ATE. Having \( \beta_2 \) insignificant indicates absence of substantial bias in the ATE estimation due to the randomness violation of the allocation to PP by unobserved patient's characteristic;

- participation in the program, given sub-cohort \( (\beta_1^* \text{Treatment} \times \text{Group}) \), the positive effect shows smaller PP effect (compared to the standard program) in a given group against “healthiest” Group 0 used as reference;

- participation in the program, given AH duration \( (\beta_3^* \text{Treatment} \times \text{AH duration}) \), the negative effect indicates the augment in gain due to participation in the program (compared with effect of the standard program) given progressed in time (presumably more serious and resistant to manage) AH;

- participation in the program given complaints \( (\beta_4^* \text{Treatment} \times \text{Complaints}) \), the positive effect of the effect indicates the additional gain due to participation in the program (compared with the standard program) given progressed in time (presumably more serious and resistant to manage) AH;

In addition to the important content, these effects are parts of \( w [x - \bar{x}] \theta \) in (7) to identify the ATE effect.

IMPLEMENTATION AND SOFTWARE
The powerful modern driver for the implementation of hierarchical mixed models, which includes our model...
structure, are MCMC algorithms. We chose the most elaborate and powerful Gibbs sampler. The analytical program module is written in WinBUGS, which is the abbreviation for Bayesian inference using Gibbs (software). The processing of mixed model was carried out in the WinBUGS package version 1.4. Preliminary data preparation, as well as the study of convergence in the Markov chains, was carried out in the framework of the mathematical analytical system R version 3.1.0 on the basis of the CODA package. All of the above graphic images are also created in the R environment (GRAPHICS package). Fixed effect Poisson model was processed by GLM procedure.

**RESULTS AND DISCUSSION**

To evaluate the effectiveness of the proposed PP for patients with hypertension in terms of GP risk reduction, we first applied a simpler Poisson fixed effects model. To focus on significant effects with meaningful interpretation, we used function STEP of the statistical system R. The procedure reduced the set of predictors from 27 to 16 without significant reduction of AIC (the value decreased from 1557.4 to 1540.3) with the difference $\Delta = 17.1$, which defines the 0.895 area of hi-squared distribution $\chi^2 (11) = 17.1$, that is, $p = 0.895$ being insignificant. The estimations of a model with a reduced set of predictors are given in Table I.

**REGRESSION EFFECTS ESTIMATIONS**

In order to more accurately estimate ATE effect and increase the power of the test, we applied a mixed Poisson model with complete and reduced sets of predictors to study the robustness of the effects. Mixed model enabled to include the effects of design elements. Estimates of hierarchical mixed Poisson model with complete and selected set of predictors are shown in Tables I and II.
There is no significant bias effect (PP*bi) due to non-randomness of allocation into PP correlated with unobservable patients characteristics, $\beta = 0.008 \pm 0.742 p = 0.999$ by the mixed model (Table II), which advocates the redundancy of the effect. Thus, the estimation of ATE effect is unbiased even in the absence of corrective control function. Thus, the randomness of allocation into PP is tenable. That is, allocation was independent of the unobserved characteristics of the natural course of the disease and the individual characteristics of the patient. Randomization of the allocation to treatments compared is a requirement of evidence-based medicine, in case of randomness violation there is a possibility of biased estimation of the treatment effect.

The main effect of ATE is significant in a model of fixed effects ($\beta = -0.269; p = 0.0156$), and even more supportive in the mixed model ($\beta = -0.282; p = 0.0097$). Other components with a variable “PP participation”, namely participation in the program given the group, participation in the program given GP duration, participation in the program given compliance, appeared to be nonsignificant and excluded from the reduced set of predictors. Insignificance of mentioned effects bear evidence on independency of allocation from these observed characteristics.

Effect of marital status indicates a substantial reduction in the risk of GP exacerbations in single patients. This may be explained by the opportunity to allocate the income, efforts and time to personal needs, health related needs in particular.

There is substantial increased risk of gastropathy exacerbation in patients with higher grades of hypertension as the consequence of more intensive treatment regimens.

### Table I. Estimations of regressors effects on annual number of GP exacerbations in patients with AH by fixed effects and mixed Poisson models

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Poisson model</th>
<th>mixed Poisson model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\beta$</td>
<td>$m$</td>
</tr>
<tr>
<td>Constant</td>
<td>-0.539</td>
<td>0.269</td>
</tr>
<tr>
<td>Age</td>
<td>-0.018</td>
<td>0.051</td>
</tr>
<tr>
<td>Gender</td>
<td>0.253</td>
<td>0.092</td>
</tr>
<tr>
<td>Marital status (Single)</td>
<td>-0.238</td>
<td>0.161</td>
</tr>
<tr>
<td>Occupation (Works)</td>
<td>-0.070</td>
<td>0.153</td>
</tr>
<tr>
<td>Served by the social welfare</td>
<td>-0.014</td>
<td>0.184</td>
</tr>
<tr>
<td>AH Stage</td>
<td>-0.094</td>
<td>0.209</td>
</tr>
<tr>
<td>AH Grade 2</td>
<td>0.119</td>
<td>0.215</td>
</tr>
<tr>
<td>AH Grade 3</td>
<td>0.692</td>
<td>0.468</td>
</tr>
<tr>
<td>Smoking (Smoke)</td>
<td>-0.248</td>
<td>0.183</td>
</tr>
<tr>
<td>Obesity (present)</td>
<td>-0.241</td>
<td>0.114</td>
</tr>
<tr>
<td>AH related expenses</td>
<td>0.051</td>
<td>0.076</td>
</tr>
<tr>
<td># of AH related hospitalizations</td>
<td>-0.040</td>
<td>0.079</td>
</tr>
<tr>
<td>Reimbursement</td>
<td>0.001</td>
<td>0.004</td>
</tr>
<tr>
<td>Income</td>
<td>0.024</td>
<td>0.046</td>
</tr>
<tr>
<td>GP related complaints</td>
<td>14.914</td>
<td>1.980</td>
</tr>
<tr>
<td>PP participant</td>
<td>0.063</td>
<td>0.246</td>
</tr>
<tr>
<td>PP*bi</td>
<td>0.008</td>
<td>0.742</td>
</tr>
<tr>
<td>Group (2-5 against 0)</td>
<td>-2.596</td>
<td>0.402</td>
</tr>
<tr>
<td>Compliance</td>
<td>0.085</td>
<td>0.051</td>
</tr>
<tr>
<td>AH duration</td>
<td>-0.018</td>
<td>0.009</td>
</tr>
<tr>
<td>Complaints*Group1</td>
<td>-10.896</td>
<td>1.618</td>
</tr>
<tr>
<td>Complaints*Group2</td>
<td>-7.799</td>
<td>1.228</td>
</tr>
<tr>
<td>Complaints*Group3</td>
<td>-5.833</td>
<td>0.854</td>
</tr>
<tr>
<td>Complaints*Group4</td>
<td>-3.250</td>
<td>0.437</td>
</tr>
<tr>
<td>PP*Group</td>
<td>-0.041</td>
<td>0.060</td>
</tr>
<tr>
<td>PP*Complaints</td>
<td>-0.418</td>
<td>0.258</td>
</tr>
<tr>
<td>PP*AH duration</td>
<td>-0.029</td>
<td>0.023</td>
</tr>
</tbody>
</table>

None: Residuals st.dev. (sigma) = 0.514894; Patients effects sigma = 0.53429; Physicians effects sigma = 0.09999; Subsample (series) effects sigma = 3.66673; AICfixed= 1557.4, df=27; AICmixed = 1421.2, df=28

414
We obtained surprisingly insignificant effect of the compliance. The possible explanation is confounding compliance effect with PP effect for one of the improvement related to compliance support. PP effect captures the effect of compliance on GP exacerbations risk reduction. Assessing risk in groups 2-5, we see that they have significantly lower risk compared to group 1, which is due to the fact that the first group is the most resistant and difficult to treat, since this contingent experienced the longest treatment with drugs that increase the risk of gastropathy.

The “Complaints*Group” effect represents the set of contrasts with no complaints and Group0 as reference levels. Significant positive effects bear evidences on the marginal increase in risk due to presence of complaints in the groups 1-5 compared to that in Group0 patients. Since Group0 patients had no complaints by definition, in fact the contrasts “Complaints*Group1” - “Complaints*Group5” express the increased risk of joining complaints in groups (1-5). The estimates suggest a significant increase in the risk in the presence of complaints across all groups (1-5) with the largest increase in the 5th, the least severe group.

The analysis of the information values of the research design and its individual elements is given in Table III. In the fixed effects model it is not possible to estimate the components of variation because they are merged with the model residual term, inflating the residual variance and undermining power of study. The advantage of the mixed model is the ability to identify the variation structure and evaluate its components, formed by design elements.

Afterward residual component is small, its share does not exceed 2% in the total variance. The share of the variation across patients is slightly higher (up to 2.5%). The low proportion of dispersion of physician individual effects suggests homogeneity of physicians practices. The greatest portion takes the series variance across subsamples. That is, a series of patients clump in time and locations is an important element of the design, having been accounted for it increases the power of statistical tests of hypotheses. In addition, the apparent dominance of the variances of the design elements over residual variance indicates improvement in information value of the mixed model over fixed effect counterpart.

INDIVIDUAL EXPECTED RISK ESTIMATIONS
The emphasis of the study is on the expected shifts in individual risks due to participation in the PP (Δπᵢ). The problem is that the patient can participate in one alternative only, and the risk for the other is a marginal expected value that was not directly observed. Given the panel design, we have Δπᵢ notation, that is, individual risks by the years of observation.

We evaluated Δπᵢ both by the model of fixed effects and by the mix model. Histograms of distributions of the modeled values Δπᵢ are displayed (Figure 1) with the basic distribution statistics as follows: Table IV.

The two-sided criterion for the significance of the differences asserts the identity of the mean two distributions: t = 1,14, df = 2522, p = 0,253.
These findings support dominating effectiveness of participation in PP over usual treatment, since in fact all $\Delta \pi_t$ are negative. However, the dispersion of the estimates $\Delta \pi_t$ based on the mixed model is significantly higher: $F(1346, 1346) = 1.7021$, $p<2.2e-16$ with a dispersion ratio of 1.7, which is typical for the mixed formulations.

To visualize a joint distribution of estimates $\Delta \pi_t$ for the two models, we demonstrate their biplot (Figure 2). Coincidence of the ranks, as well as the tight linear correlation ($r = 0.883$) are obvious. The difference is only in the scaling, with greater variation in the mix model estimates.

We also investigated the distributions of PP participation related individual risk shifts for important factors. Particularly, we were interested in the patterns across sub-cohorts (Group0-Group5).

The greatest PP related risk reduction was in patients of Group 0, that is, in patients with hypertension who do not receive antihypertensive therapy (Figure 3). In groups №1-№5 the effects of program participation are obvious but less pronounced, especially in the first two groups as the most complicated. One-way ANOVA Fisher test shows a high significance of the demonstrated regularities: $F(5,1344) = 26.67$ with $p = 1.1e-11$ (Figure 6).

The risk augmentation due to presence of complaints is another important issue to consider. However, there is no significant difference in distributions, since the notches of two box plots overlap (Figure 4). This is also evident from one-way ANOVA Fisher test: $F(1,1345) = 0.56$ with $p = 0.4529$.

We observed distributions of risk reduction due to PP participation by presence of complaints across sub-cohorts Group0-Group5. Distribution pattern is alike to distribution across sub-cohorts.

We also studied the distributions of risk reduction due to PP participation across AH grades, since patients with higher grades subjected to more intensive AH therapy and, therefore, to a higher risk of induced exacerbations of GP which is confirmed by correspondent significant effects (Tables I and II) (Figure 5). The greatest risk reduction due to PP participation observed in patients with first grade of blood pressure, while the second and especially third degrees reduced the gain due to participation in the PP, one-way ANOVA Fisher test suggests significance of findings: $F(2.1344) = 26.67$ with $p = 1.1e-11$ (Figure 6).

**CONCLUSIONS**

1. We have elaborated a program for the prevention of gastropathy in patients taking antihypertensive therapy. Program is based on regulations of the Ministry of Health of Ukraine, adapted clinical guidelines, and other official sources of information, since holistic prevention of gastropathy is not depicted in any source.

2. The program differentiates patients by groups and furthermore allows one to consider each patient characteristics, taking into account income, age, gender, progression of the disease, comorbidity, drugs the patient takes. The established program based on cooperation of patient, general practitioner, and gastroenterologist. The general approaches are complemented with particular activities identified under delineated groups of patients with essential hypertension. One of the prime goal is to achieve compliance.

3. Data on 150 patients with AH collected by panel design with dynamic cohort traced up to 17 years. Two main cohorts were distinguished: those in prevention program (PP) and patients with usual treatment. Event of interest was incidence or aggravation of gastropathy (gastroduodenitis mainly). The numbers of exacerbations were analyzed by the Poisson regression. Model parameters were estimated by MCMC algorithms with the Gibbs sampler using WinBUGS.

4. The main effect of program participation is significant in a model of fixed effects ($\beta = -0.269; p = 0.0156$), and even more supportive in the mixed model ($\beta = -0.282; p = 0.0097$). Other components with a variable “PP participation”, namely participation in the program given the group, participation in the program given GP duration, participation in the program given compliance, appeared to be nonsignificant, that suggest absence of substantial selection bias due to non-randomness of allocation.

5. The greatest risk reduction due to program participation was in patients of Group0, that is, in patients with hypertension who do not receive antihypertensive therapy. In groups №1-№5 with more aggressive hypertension
treatment the effects of program participation are obvious but less pronounced.

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