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MATHEMATICAL METHOD FOR FORECASTING AIDS PROGRESSION IN HIV-INFECTED PATIENTS

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Abstract: The article features a method developed for forecasting the development of AIDS in HIV-infected patients. Mathematical model is drafted and probability of the disease determined per stages. Method helps in the diagnosis and treatment of HIV infection and can be used in daily medical practice. Currently, the method is going through patent registration procedures (registration number of the application RU 2015123255 dated 18 June 2015). It is expected that the use of this technique will help penitentiary doctors take appropriate therapeutic measures for patients with high prognostic index on time thus preventing implementation of a negative prediction.

1 Introduction

A majority of people with HIV employed in the UK report that HIV has no impact on their working life at present, according to research conducted by City University on behalf of the National AIDS Trust. Although most of those who disclosed their HIV status at work had had a generally positive reaction, stigma and discrimination create more problems at work than ill-health. However, only a minority of people with HIV are fully aware of the provisions of the Disability Discrimination Act.

Although the quantitative findings only relate to gay and bisexual men living with HIV, the researchers also conducted focus group discussions with a more diverse mix of people with HIV, and they say that the points of similarity between the black Africans and the gay men were striking.

Previous research in other countries has identified barriers to employment for people with HIV, and levels of employment tend to be lower than in the general population. However improved treatments mean that more people with HIV are able to remain in employment.

While the experiences of people working in the UK remain under-researched, a previous study among HIV clinic attendees in East London did identify that white gay men were more likely to be in employment than heterosexual black African men and women. More part-

time working and financial problems were reported by Africans. White gay men reported higher rates of disclosure to employers than either black African heterosexuals or gay men from minority ethnic backgrounds.

The new research used focus groups to establish key themes. Three groups were held with black African heterosexuals, and two groups with gay and bisexual men (38 participants in total). Then, an online questionnaire was conducted with gay and bisexual men using the Gaydar website in order to quantify the insights of the focus groups. The researchers regret that there is no equivalent website which could be used to recruit a large convenience sample of black African people with HIV, and that other recruitment methods would have been too costly.

A total of 1830 HIV-positive gay male respondents took part in the online survey. (Moreover, some comparisons are made between these men and over 6000 HIV-negative gay men who also completed the survey.)

It's important to note that the research only included people with current employment, and the experiences of those who are no longer working are likely to be different. Twenty-five years ago the world received news about the previously unknown virus that destroys the human immune system - HIV (human immunodeficiency virus). This virus infection inevitably leads to incurable,

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fatal disease – AIDS and then death. In a short period of time in human history the virus carried thirty millions lives away and so far more than 80 millions people in the world live with HIV.

Over half the respondents (58%) said that living with HIV had no impact on their working life at the moment.

Of those who reported an impact, the most common responses were to report feeling very tired (20%) and feeling very stressed or anxious (13%). One in ten (11%) said that side-effects from treatment were having an impact on their work.

Seventy per cent of gay men living with HIV had taken no HIV-related sickness days in the last 12 months, and took no more sick days than HIV-negative men. Only a third had made any changes to their working lives because of their HIV status, with the most common change being alterations to working hours.

On the other hand, initial diagnosis of HIV was a time when many respondents did report an impact on their working life. Forty-two per cent reported stress or anxiety, 32% needed some time off, and 28% were very tired. However, it is important to note that almost a third of respondents said that their initial diagnosis had no impact on their working life. There was some suggestion from focus group discussions that starting or changing medication was another ‘flash point’ when HIV had an impact on their working lives [1], [2].

2 Solution design

By the number of HIV infection occurrences and the spreading velocity of infection Russia is ranked in the world ahead of countries such as China, India, Ethiopia and Nigeria etc. 60 percents of people living with the HIV-infection are concentrated in 10 Russian regions. 80 percents of HIV-infected people in Russia are young people between 18 and 30 years. More and more women are being involved in the epidemic process, a growing number of children are being born by infected mothers.

In the last few decades we can see the rapid spread of drug addiction in the Russian society, and reduction in the quality of life in Russia associated with the epidemic of HIV and TB. That led to the increase in the proportion of people suffering from co-infected (HIV + TB) [3], [4], [5]. This problem is very actual for penal system, where is a high concentration of these patients. Thus, over the last 20 years the number of HIV-infected people in prison have increased more than in 800 times. Nowadays about 56 thousand people with HIV -infection and about 30 thousand TB patients are contained in Russian prisons [5].

The dynamisc of number of patients with HIV in Russian prisons is shown in figure 1.

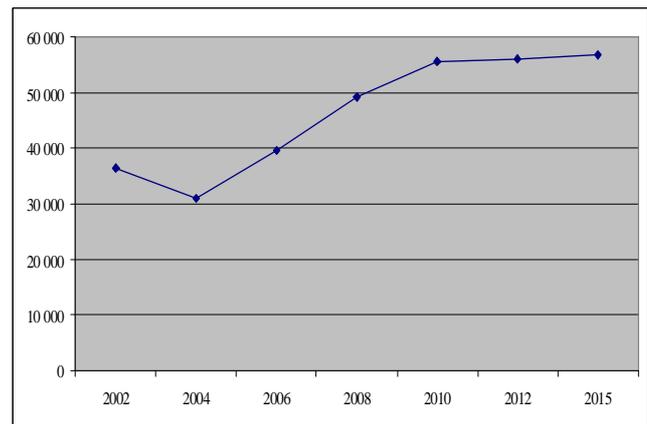


Figure 1. The dynamisc of number of patients with HIV in Russian prisons

It is widely known that the prediction of the final stage of HIV infection - Acquired Immune Deficiency Syndrome (AIDS) is not developed enough [6], [7] due to a large number of parameters that affect the course of HIV infection [8], [9], [10], [11]. This is especially significant for a prison, where there are many specific factors that might speed up the time of AIDS [12]. It is known that the combination of HIV and TB worsens the prognosis of the disease. The action of penitentiary factors in Russian prisons also leads to the progression of the disease and the onset of end-stage of HIV infection.

It is known that there are a number of indicators by which the medical men can determinate the risk of AIDS development in patient with HIV infection.

The aim of the study was to get a method of forecasting the development of AIDS in HIV-infected patients by means of mathematical modeling.

In accordance with the concept of developing the forecast [13], 49 covariates were initially considered as input variables (x_i) - the leading characteristics of the health status of HIV-infected people held in places of detention in the Russian Federation. Variable (y) is taken as a resulting factor reflecting the dynamics of the disease within a year upon completion of the study. The stable condition of a patient was taken as "1", and number "5" was to indicate the rapid development of AIDS, followed by lethal termination.

Statistical database on which the simulation was conducted according to function $y = f(x_i)$ included 30 observations. The review team included 37 observations.

Construction of a mathematical model in which factors x_i providing significant impact on the value of y were selected, was carried out by the procedure of stepped inclusion of the factor in the regression linear model $y = f(x_i)$. As a result, 4 of 49 variables were selected which make the largest contribution to the explanation of the variations in the dependent variable.

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3 Mathematical formula

Mathematical formula takes into account the formalization of the patient's complaints (the presence of cough, muscle pain, loss of appetite and other results of medical tests). In addition, the border of liver according to the mid-clavicular line based on the M.G.Kurlov classical technique (1927) was further measured by percussion [14].

The method of least squares has determined coefficients of the linear regression of the following (1) form:

$$y = \alpha_1 \cdot t_1 + \alpha_2 \cdot t_2 + \alpha_3 \cdot t_3 + \alpha_4 \cdot t_4 + \alpha_5 \cdot t_5 + \alpha_6 \cdot t_6 + \alpha_7 \cdot t_7 + e, \quad (1)$$

where y is integral index,

$\alpha_1, \alpha_2, \alpha_3, \alpha_4$ is weighting coefficients,

t_1, t_2, t_3, t_4 are measurable parameters,

e are residues.

The parameters of medical examination (such as the presence and stage of concomitant tuberculosis, severity of myalgia, increasing the degree of lymph nodes, presence of cough, liver size by Kurlov, laboratory tests, etc) as predictors in multiple regression formula used.

Calculations show that patients who have cough, are subject to AIDS progress risk by 0.352 units. Patients who have myalgia (muscle pain), are subject to AIDS progress risk by 69.7%, patients who have enlarged lymphnodes are subject to AIDS progress risk by 0.764 units. Stages of tuberculosis development also aggravate the situation of the patient.

The reseaches show that in case when the value of y was less than 3 units low risk of developing AIDS was predicted within the nearest year. While at a value within $3 \leq y \leq 4$ units the average risk of developing AIDS is determined within the nearest year, at a y value of more than 4 units a higher risk of developing AIDS within the nearest year of observation was predicted.

To assess the adequacy of the constructed model the coefficient of determination R^2 (the ratio of the explained dispersion to the total one) (2) (3) was used:

$$R^2 = \frac{RSS}{TSS} \quad (2)$$

$$\text{wherein } RSS = \sum_{t=1}^T (y_t^{mod} - \bar{y})^2,$$

$$TSS = \sum_{t=1}^T (y_t - \bar{y})^2 \quad (3)$$

If $R^2 = 0$ then the regression does not improve the quality of prediction y_t^{mod} as compared with the trivial prediction \bar{y} . If $R^2 = 1$, they say it means the

exact fit of the model, i.e., all observation points comply with the regression equation.

4 Known connection

The coefficient of determination $R^2 = 0,783$ shows that 4 of the variable estimates 78.3% of the variation of the result.

To determine the significance of the coefficients of the regression model, hence the importance of the entire model, the Fisher statistics (4) was used F :

$$F = \frac{R^2}{1 - R^2} \cdot \frac{n - k}{k - 1}, \quad (4)$$

where n is the number of observations,

k is the number of estimated parameters.

The main and alternative hypotheses are advanced (5), (6):

$$H_0 : \beta_i = 0 ; \quad (5)$$

$$H_1 : \beta_i \neq 0 . \quad (6)$$

When the main hypothesis statistics F has Fisher distribution with $(k - 1, n - k)$ degrees of freedom. Value F is compared with the tabulated value $F_\alpha(k - 1, n - k)$ at significance level α . If $F < F_{tab}(k - 1, n - k)$, then the main hypothesis that regression coefficients are equal to zero is accepted. If $F > F_{tab}(k - 1, n - k)$, then the main hypothesis is rejected in favor of an alternative.

For the estimated model Fisher test was 3.17. The probability to randomly get such a value of F-test does not exceed the acceptable level of significance of 5%. Therefore, the resulting value of the Fisher criterion confirms the statistical significance of the model.

Additionally, the average relative error of approximation has been calculated by (7) the formula:

$$\bar{\delta} = \frac{1}{N} \sum_{t=1}^N \left| \frac{y - y^{mod}}{y} \right| \cdot 100\% \quad (7)$$

Where N is the number of observations; y^{mod} is the model value of the index.

The average relative error of approximation was 8.2%. When checking the model on a test subgroup with HIV infection, acceptable values of correlation coefficient $r = 0,58$ between predicted and actual values of the prognostic index were observed.

Approximation error graph is shown in Figure 2.

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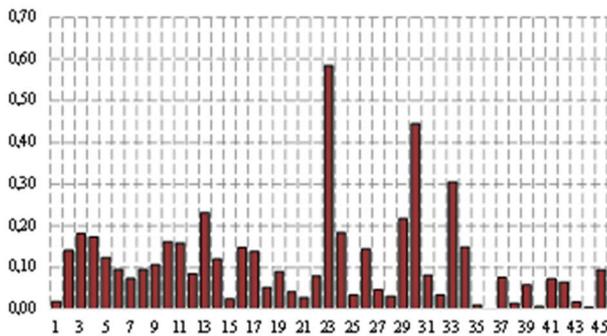


Figure 2. Approximation error for the multiple regression

Conclusions

In conclusion, in the course of research a methodology was obtained which, with reasonable accuracy, can indicate risk of AIDS development in HIV-infected patients who are serving their sentence of imprisonment in correctional facilities of the Federal Penitentiary Service of the Russian Federation. Currently, the method is going through patent registration procedures (registration number of the application RU 2015123255 dated 18 June 2015). It is expected that the use of this technique will help penitentiary doctors take appropriate therapeutic measures for patients with high prognostic index on time thus preventing implementation of a negative prediction. Mathematic method helps in the diagnosis and treatment of HIV infection and can be used in daily medical practice in prisons.

The advantages of the method are simplicity of definition, low cost, convenience, high accuracy, absence of threat to the patient health. Also there is no need for expensive equipment and the possibility of determining the risk of AIDS in HIV infected patient is high.

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Review process

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