SECTION 2. THEORETICAL MEDICINE: BASIC DEVELOPMENT TRENDS

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MATHEMATICAL MODEL FOR CALCULATING THERAPEUTIC DAMAGE TO THE TUMOR AFTER NEOADJUVANT THERAPY FOR BREAST CANCER WITH OR WITHOUT METFORMIN MODIFICATION

МАТЕМАТИЧНА МОДЕЛЬ РОЗРАХУНКУ ТЕРАПЕВТИЧНОГО УШКОДЖЕННЯ ПУХЛИНИ ПІСЛЯ НЕОАД'ЮВАНТНОЇ ТЕРАПІЇ РАКУ МОЛОЧНОЇ ЗАЛОЗИ З МОДИФІКАЦІЇЮ МЕТФОРМІНОМ, АБО БЕЗ НЬОГО

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Creating a mathematical model for predicting outcomes in oncological research is relevant due to the increasing need to improve the accuracy and efficiency of cancer diagnosis and treatment. Such models help identify potential risks of disease development, predict their course, and choose the most effective treatment methods, which can significantly improve a patient's quality of life and chances of recovery [1, 2].

The mathematical model for calculating therapeutic damage to the tumor after neoadjuvant therapy for breast cancer, with or without the modification of metformin, incorporates an analysis based on 148 cases. This model utilized multiple regression to assess the impact of various independent

variables such as `control group=0, experimental group=1`, `Tumor grade`, `ER`, `PR`, `Ki-67`, `Cyclin D1`, and `AR` on the outcome, specifically the pathomorphosis of the tumor as per Lavnikova's classification. The regression coefficients, determined through the least squares method, minimize the sum of squared differences between observed and predicted values of the dependent variable based on the values of independent variables.

The coefficients, each signifying a one-unit change in the dependent variable for a one-unit change in the respective independent variable, were calculated using statistical analysis methods, mainly functions from Python's `sklearn` library. The mean squared error (MSE) was 1.24, and the coefficient of determination (R^2) was 0.21, indicating that the model explains approximately 21% of the variation in "Pathomorphosis."

In the context of our model, the dependent variable is «pathomorphosis», and the independent variables include «control group=0, experimental group=1», «Grade», «ER», «PR», «Her-2/neu», «Ki-67», «Cyclin D1», «AR».

How coefficients are formed:

1. The estimation of coefficients (beta coefficients) in linear regression is determined in such a way as to minimize the sum of squared differences between observed values and the values predicted by the model. For a linear model, the general form of the equation:

$$y = \beta 0 + \beta 1x1 + \beta 2x2 + \ldots + \beta nxn + \epsilon$$

Where «y» is the dependent variable, « $\mathbf{x_i}$» are the independent variables, «$\mathbf{B_i}$» are the regression coefficients, and « ϵ » is the model error.

2. For calculation through matrices, the coefficients can be found by applying matrix algebra using the formula:

$$\beta = (X^T X)^{-1} X^T Y$$

Where (**X**) is the matrix of observations of independent variables (with an added column of ones for the intercept $\boldsymbol{\beta_0}$), **γ** is the vector of observed values of the dependent variable, and **β** is the vector of regression coefficients.

3. Interpretation of coefficients: Each coefficient indicates the change in the dependent variable for a one-unit change in the corresponding independent variable, assuming the values of all other variables remain unchanged [3].

Specific coefficients in the model:

– Intercept (constant β_0=1.73): represents the expected value of `Pathomorphosis` when the values of all independent variables are zero.

The coefficients for independent variables (βi) reflect the change in the dependent variable for a one-unit change in the corresponding independent variable, ceteris paribus, and determine the impact of each on "Pathomorphosis". The coefficients are as follows: transition from control to experimental group (control group=0, experimental group=1) =0.919, Grade=0.188, ER=0.002, PR=0.010, Her−2/neu= 0.097, Ki−67=0.002, CyclinD1=0.006, AR=0.006.

These coefficients were calculated using statistical analysis methods, functions explicitly from the « sklearn » library in Python (Figure 1), which automatically apply the least squares method to determine the optimal coefficients based on the provided training data.

```
From sklearn.metrics import mean_squared_error, r2_score
# Calculation MSE
mse = mean_squared_error(y_test, y_pred)
# Calculation R²
r2 = r2_score (y_test, y_pred)
```

Where **y_test** are the actual values of the dependent variable from the test dataset, and **y_pred** are the corresponding predicted values generated by the multiple linear regression model.

After conducting statistical analysis using multiple linear regression on updated data, the following results were obtained:

– The Mean Squared Error (MSE) was 1.24, using the formula:

$$\boldsymbol{MSE = \frac{1}{n}\sum_{i=1}^{n} (yi - \hat{y}i)^2}$$

– The coefficient of determination (R^2) was 0.21, using the formula:

$$\boldsymbol{R^2 = 1 - \frac{\sum_{i=1}^{n} (y_i - \hat{y}i)^2}{\sum_{i=1}^{n} \left(y_i - \underline{y}\right)^2}}$$

To calculate these metrics in Python, the functions **mean_squared_error** and **r2_score** from the **sklearn.metrics** module are used. These functions take the actual and predicted values as input and automatically perform the aforementioned calculations, providing the MSE and R^2 values. The results suggest that the model with new data explains approximately 21% of the variation in the outcome, "Pathomorphosis."

The calculator for predicting the expected pathomorphological response is based on the following formula:

Pathomorphosis = 1.73+0.92 × (control group=0, experimental group=1) + 0.19 × Grade + 0.002 × ER−0.01 × PR + 0.097 × Her-2/neu + 0.0024 × Ki-67 − 0.0058 × CyclinD1 + 0.0056 × AR

Where:

– "control group=0, experimental group=1": 0 for the control group (metformin not added) and 1 for the experimental group (metformin added).

– Grade, ER, PR, Ki-67, Cyclin D1, AR – values of the respective variables in percentages.

The integration of linear regression coefficients into the code and its adaptation for a visual interface was done to calculate the probable indicator in the study of metformin in neoadjuvant chemotherapy for breast cancer.

However, these results provide insight into the studied variables' impact on pathomorphosis. A deeper understanding would require further analysis, using other statistical methods, including additional variables, and increasing the sample size for more accurate statistical indicators.

These findings provide preliminary insights into the impact of variables on tumor pathomorphosis following neoadjuvant therapy, with or without the combination of metformin. However, a deeper understanding requires further analysis, potentially employing other statistical methods, incorporating more variables, and expanding the sample size to obtain more reliable statistical indicators. This research highlights the complexity of predicting therapeutic outcomes in breast cancer treatment and illuminates the potential for integrating metformin as a modifying agent to enhance therapeutic efficacy.

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