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ІСТОРІЯ СТАНОВЛЕННЯ ТА РОЗВИТКУ БІОСТАТИСТИКИ

Анжела БІДУЧАК, Маряна ГРИЦЮК, Жанетта ЧОРНЕНЬКА, Тетяна ДОМАНЧУК
ВДНЗ України „Буковинський державний медичний університет”, Чернівці (Україна)
biduchak5@gmail.com

HISTORY OF FORMATION AND DEVELOPMENT OF BIOSTATISTICS

Anzhela BIDUCHAK, Maryana GRYTSIUK, Zhanetta CHORNENKA, Tetyana DOMANCHUK
Higher State Educational Establishment of Ukraine „Bukovinian State Medical University”, Chernivtsi (Ukraine)

Бидучак Анжела, Грицюк Марьяна, Чорненькая Жанетта, Доманчук Татьяна. История становления и развития биостатистики. В последние 20-30 лет медицина и биология вступили в новую фазу своего развития. Накопление огромных массивов количественных данных в связи с доступностью вычислительной техники усилило математизацию биологии и медицины. В подавляющем большинстве медицинских научных работ авторы используют (в том или ином объеме) методы статистики. **Цель исследования.** Проанализировать исторические этапы становления биостатистики, как науки. **Методология исследования.** В статье использованы описательный, библиосемантичний и историко-сравнительный методы. **Обсуждение результатов исследования.** В статье отражена история развития биостатистики в мире. Сбор статистических данных начался с самой глубокой древности. А к более позднему периоду относятся обработка и анализ статистических данных, т. е. зарождение биостатистики как науки. **Выводы**. К какой бы области знаний ни относился предмет исследования статистики (население, промышленность, торговля и т.п.), метод ее везде одинаков, т.е. везде используются массовое наблюдение, группировки и обобщающие показатели, в которых взаимопогашается влияние случайных причин и выявляется типичное и закономерное. Иначе говоря, метод биостатистики обусловлен спецификой ее предмета.

Ключевые слова: *биостатистика, история, этапы становлення биостатистики, история медицины.*

Introduction. The term “statistics” comes from the Latin word status, which first denoted a situation, a state of things. From this came the Italian word stato, which was first understood as a governed area or state, and later on as a practical policy, which consisted in the knowledge of Euro-European states. Those who possessed such knowledge were called statista, which meant a statesman, an expert on the state. In the XVII century, statista, goes into German and Latin with the same name. Later, in the second half of the 17th century and at the beginning of the 18th century, the adjective statisticus comes from this word, which was included in the name of the new discipline. For the first time this word was introduced as a scientific term by Herm-Hermann Conring in his lectures on “Notitia rerum publica-publicarum”. As the term was first used by G. Achenvall in 1743 in the work "Notitia politica vulgo statistica". Statist-Statistics at that time was understood as the totality of kno-knowledge about the state structure necessary for a govern-government official[1]. Thus, the term “statistics”, formed for the first time at German universities, gradually found its practical application, became commonly used and gained universal recognition and distribution.

Biological statistics as a methodology of biomedicine in its historical development has gone a long and difficult way from a purely verbal description of biological objects to their objective measurement, from simple statistical summaries and tables to a systematic statistical analysis of mass phenomena in biology and medicine[2].

Aim of investigation. To analyze the historical stages of biostatistics as a science.

Setting the main material. At the initial stages of its formation, biostatistics could not be a separate science, it developed over a long period of time in the structure of general statistics and only in the 19th century received the right to independent existence in biomedicine.

The first stage is the initial one. The first statistical studies were carried out not for the sake of science, but mostly for a practical purpose, most often to determine the military and tax ability of the population. It is known that as early as 550 BC in China, a population census was conduct-conducted for this. This is evidenced by the collection “Shu -King”, compiled by Confucius. It contains information on the population (its distribution according to sex, age), on the profitability of land, on the movement of trade, etc. Statist-Statistical observations in Persia are also discussed in Herodotus’s work, which provides data that characterize state activity. There is also evidence of the existence of administrative statistics in ancient Egypt. Similar statistical observations were made in ancient Greece. The Greeks understood that without statistical accounting it was impossible to ensure the high development of the state. Reforms of Lycurgus and Solomon, based on the division

[1] Abdrakhmanova G. I. Statistika informatsionnogo obshchestva-sovremennoye sostoyaniye i perspektivy razvitiya [Statistics of the information society - current status and development prospects], *Voprosy statistiki* [Statistics issues], 2008. N 1. P. 20–31 [in Russian].
[2] Yeliseyeva I. I., Yuzbashev M. M. Obshchaya teoriya statistiki [General Theory of Statistics], Moskva, Finansy i statistika, 2001, 480 p. [in Russian].

of the population into classes, are known from the same positions. At that historical time, there were official lists in which all freely born children were entered immediately after birth, as well as when they reached the age of 18 (lists of militaries) and after 20 years (lists of full members)[3]. In Greece, the first attempts are made to process statistical material: for example, Aristotle (384-322 BC) gives a broad demographic description of 157 different states and the bridge of Greece. The Romans were practical in these matters, and therefore drew attention to the need to collect various information about the population. To this end, they organized a statistical organization – the so-called qualification introduced by Servius Tullius (550 BC). The censorship organization had its own strict rules: each independent Roman citizen was obliged to inform the censor of his full name, the community (tribe) to which he belongs, the name and age of his father or master (who let him go free), the names, gender, age of all family members. All these data were sealed. Censorship was repeated every 5 years. In parallel, there were also other qualifications, for example, on property. In Rome, there were land cadastres for collecting land tax. In addition to periodically maintaining qualifications and cadastres, the Romans conducted an ongoing population census: official birth records, late registration of deaths.

Since the Middle Ages, much less information about statistical observations has come to us than from ancient times, because the fragmentation of states then limited the development of statistics. At the same time, statistical work is known, carried out according to the order of Charlemagne, "Breviaris rerum fiscalium". It included a description of royal and feudal estates (buildings, land, profitability, livestock, etc.). A similar description was compiled by William the Conqueror in England (between 1083-1086) and is known as the "Doomsday-Book" ("Doomsday Book"). The clergy played an important role in the development of statistics, because churches regularly kept records of burial, baptism, and marriage. Certain statistical studies were conducted in Ancient Russia. So, in the XIII century, the census was carried out twice by the Tatars, and at the end of the XIV century – by Russian princes. In the Middle Ages, special attention was paid to the systematization of statistical material. In Italy, in the 15th century, collections of demographic descriptions of modern states appeared (the Piccolomini collection – with the time of Pope Pius II, the Sansovino collection). The latest collection has survived 5 editions and enjoyed great popularity for 40 years, has been translated into many languages of the world. In France, the collection of d'Avity (1614) was well known, which included a description of the states not only of Europe, but also of Asia, Africa, and America. It should be noted that all the statistical studies carried out during that period, according to methodology and content, were unsystematic, disordered and scientifically of little value, therefore we cannot call them scientific in the modern sense[4].

The **second stage** in the development of biological statistics, as well as statistics in general, entered the history of science as descriptive. Methods of descriptive statistics are still relevant today, because many biological scientific studies are descriptive. So, when describing plants and animals, their shape, size, color, behavior, distribution, similarity with other organisms, or difference are characterized. In its simplest form, such a description was mainly of a verbal nature. Descriptive statistics as a science of state studies originated in Germany. German researchers, developing the method according to the needs of practice, elevated state studies from a simple description of states to the level of pure science, introducing it into the compulsory university program. Professor of Helmstadt University G. Conring is considered to be the founder of descriptive statistics.

G. Konring, a well-known German physician, historian and state expert, was a professor of medicine and politics in Helmstadt. In 1658, the Swedish king Charles X made G. Conring his adviser and life physician. Since 1669, he was a state adviser to the Danish king. His advice was needed in deciding the most important state affairs. He took part in the preparation of the Westphalian Peace Treaty. A study by G. Konring ("De origine juris germanici", Helmstadt, 1643) gives reason to consider him the founder of the history of German law. In philosophy, G. Conring was a follower of Aristotle; in theology, he shared the views of Calixtus. In medicine, he disseminated Harvey's teaching on blood circulation, fought alchemy, and established the importance of chemistry for pharmacy. G. Conring was the first to give a public lecture course on state studies at the university (in 1660). His lectures were a huge success, and state studies became a popular subject of teaching. Unfortunately, the works of Hermann Conring were published only 50 years after his death (in 1730) in 6 volumes on the basis of 5 handwritten notebooks of his listeners[5].

Later, one of the talented university teachers of statistics G. Aachenvall (1719-1772), who was born in Elbing, studied in 1738-1743 in Jena, Halle, Leipzig, continued to develop this direction, which quickly gained popularity and universal recognition. The study of statistics has become considered mandatory for every educated person. G. Aachenwall began lecturing in 1748 as a privat-docent at the University of Marburg and Gottingen. His works were published in 1749 ("Abriss der neuesten Staatswissenschaft der vornehmsteneuropaischen Reiche"). This work is a code of German university statistics[6].

Assessing the role of G. Conring and G. Achenvall in the development of statistics, G. Conring should be given an undoubted advantage, although his works were less known and accessible, since they were published in Latin. G. Aachenwall published his works in German, which attracted a large readership. But the merit of G. Achenwall is that he first introduced a new terminology and made statistics popular.

Of the followers of the Achenwall school, A. Schletser (1735-1809) is known, who is called the first theorist of descriptive statistics. A. Schletser was not only a brilliant scientist in statistics, but also an excellent publicist. He was the first to publish in his journal data on the state, acts of government that were previously inaccessible to many readers, which is why he gained popularity. He wrote

[3] Ploshko B. G. Iz istorii ucheniy o predmete statistiki [From the history of the teachings on the subject of statistics], *Vestnik statistiki* [Bulletin of statistics], 1964, N 5, P. 28–33 [in Russian].
[4] Sheynin O. B. "Teoriya statistiki: istoricheskiy eskiz" [Theory of statistics: historical sketch], *Voprosy statistiki* [Questions of statistics], 2002, N 9, P. 64–69 [in Russian].
[5] Kaganovich I. "K voprosu o sovetskoy statistiki kak nauke" [On the question of Soviet statistics as a science]. *Vestnik statistiki* [Bulletin of statistics], 1952, N. 6, P. 30–38 [in Russian].
[6] Surinova A.Ye. Statystika [Statistics], Moskva, Izd-vo RAGS, 2005, 656 p. [in Russian].

sharply, witty, knew how to interest the public, which allowed him to introduce a new science to the public. A. Schletser worked at that historical time, when the ideas of English "political arithmetic" began to spread (this direction was later called mathematical statistics, or political arithmetic). A. Schletser, remaining a supporter of descriptive statistics, understood the prospects for science and society of the ideas and methodology of mathematical statistics. He understood the special scientific and practical significance of the law of large numbers, in connection with which he emphasized that small numbers are not decisive, and only a large number of observations will make them such that objectify the reliability of the phenomenon under investigation as much as possible[7].

In the future, among the researchers in the field of statistics, it is necessary to name the geographer Anton Friedrich Buesching (1724–1793), who proposed comparative methods of statistics[8]. Although he was a representative of descriptive statistics, the subject of his study is state science. However, Bushing does not analyze the material by state, but according to the requirements of statistics separately for the subjects and the phenomena studied. So, he described the population of not one state, but at the same time a whole group, and he systematized digital material, especially in matters of mortality and fertility, which made it possible to conduct a comparative maximum objective analysis and contributed to the formation of practically necessary tabular or linear statistics.

The founder of tabular or linear statistics is the Danish historian and geographer Rudolf Martin Andersen. It was he who, in his work Descriptio statuum cultiorum in tabulus (1741), proposed to submit material on significant events for a comprehensive analysis in the form of generalized tables, hence the name of the proposed method. Thus, tabular statistics completes the logical development of descriptive statistics (the science of significant events in the state). So descriptive statistics has existed for more than 150 years, without changing its theoretical foundations and its characteristic methodology, and has retained its relevance to this day[9].

The **third (decisive) stage** in the development of biostatistics is the use of quantitative data to describe states, which led to the formation of a new direction in general statistics – mathematical statistics, or political arithmetic. The most important representatives of this direction were John Graunt, William Patty, Edmund Galle, Jacob Bernoulli and others.

The cradle of the mathematical direction of statistics and probability theory in the 17th century was the advanced countries of trade capital and manufactories – England, Holland, France. As early as 1662, the English merchant, over time, Lord Mayor of London John Graunt (1620–1674) published in London his wonderful book, "Natural and Political Observations of the Lists of the Dead in London". In his work, using the data of church records about the born and the dead, he first determined the specific patterns of population reproduction. His work on demographic issues has survived several reprints and was a huge success[10]

.Another representative of this trend is William Patty (1623–1687). In his famous work "Several Essays in Political Arithmetic" ("Experience of Political Arithmetic"), he gives the name of the direction of statistics – political arithmetic, in which D. Graunt's methodology was used. His work is the first big attempt to solve the main problems of the economy with the help of statistics. Unlike D. Graunt, he freely operates with numbers, often uses different calculations[11].

William Patty collected a huge statistical material about the most important states of Europe. The work of D. Graunt and W. Patty was based on quantitative characteristics. "I choose", said V. Patty, "the language of numbers, measures and weights..., taking into account only those reasons that, obviously, exist only in the very nature of things, contrasting them with those that depend on thoughts that change, inclinations and passions of individuals". The subject of their study was mainly social phenomena.

An important representative of this direction was also the famous English astronomer and mathematician Edmund Halley (1656–1742), who greatly used the work of William Patty. In the memoirs of E. Halley "On the degrees of mortality of mankind" is one of the first attempts to apply statistics to the insurance business[12].

Subsequently, the method of E. Halley was improved by V. Kerseboom, a Dutch researcher, an official of the finance and control department in The Hague, who in 1740 calculated age-specific mortality for one generation. In his mortality table, he used data on life annuity and in this way obtained valuable material, because annuity indicated the age of each person entering the society and the year of his death. The disadvantage of his research is that the mortality table included only selected wealthy citizens. Other categories of the population were not taken into account. V. Kerseboom was the first to point out that in order to compile an objective «correct» mortality table, it is necessary to trace successively the extinction rates of the population of one generation[13].

This problem was solved by his follower K. F. Herman (1767–1838), he proposed a direct observation method to compile a table that characterizes the natural movement of the population. With this in mind, he ensured continuous monitoring of the extinction of a generation for a long time. To implement the method, it would be necessary to have at least 100 years, and, of course, to implement it with K. F. Herman did not have enough life. Its results apply only to young people. K. F. Herman emphasized the importance of a large number of observations in a statistical study[14].

[7] Karpenko B. I. Razvitiye idey i kategoriy matematicheskoy statistiki [The development of ideas and categories of mathematical statistics], Moskva, Nauka, 1979, 376 p. [in Russian].
[8] Sheynin O. B. "Teoriya statistiki: istoricheskiy eskiz" [Theory of statistics: historical sketch], *Voprosy statistiki* [Questions of statistics], 2002, N 9, P. 64–69 [in Russian].
[9] Gromyko G. L. Teoriya statistiki [Theory of statistics], Moskva, INFRA-M, 2005, 476 p. [in Russian].
[10] Gozulov A.I. Ocherki istorii otechestvennoy statistiki [Essays on the history of domestic statistics], Moskva, Vyd-vo "Statistika", 1972, 312 p. [in Russian].
[11] Kaganovich I. "K voprosu o sovetskoy statistiki kak nauke" [On the question of Soviet statistics as a science], *Vestnik statistiki* [Bulletin of statistics], 1952, N 6, P. 30–38 [in Russian].
[12] Abdrakhmanova G. I. "Statistika informatsionnogo obshchestva-sovremennoye sostoyaniye i perspektivy razvitiya" [Statistics of the information society - current status and development prospects], *Voprosy statistiki* [Statistics issues], 2008, N 1. P. 20–31 [in Russian].
[13] Sheynin O. B. "Teoriya statistiki: istoricheskiy eskiz", Op. cit., P. 64-69.
[14] Afanas'yev V.N., Markova A.I. Kurs lektsiy po istorii statistiki [Lecture course on the history of statistics], Orenburg: Izdatel'skiy tsentr OGAU, 2003, 376 p. [in Russian].

The first technical processing of statistical mortality tables was done by the French researcher Deparsier (1703–1868). His works were distinguished by clarity, harmony and novelty. It was he who first calculated the average statistical probability of life expectancy for each age[15].

Among population researchers, it is also necessary to recall the Prussian chaplain (military pastor) Johann Süssmilch. In 1741, his work Die gottliche Ordnung (Divine Order in Changing the Human Race) was published. It contained 3 sections: mortality, fertility and reproduction of the human race. From this perspective, he systematized the material, conducted a comparative statistical analysis and made conclusions about stillbirth, about the birth of twins, the birth of children depending on gender in a certain proportion, and revealed the causes of higher mortality in cities than in villages. The results of his work, he undoubtedly surpassed political arithmetic. His work significantly influenced administrative statistics. Unfortunately, J. Süssmilch did not create his own scientific school, possibly because he was a visionary and talented pastor, and not a professional scholar[16].

The biggest fact in the development of statistics, including biostatistics as a science, is the law of large numbers discovered by Jacob Bernoulli (1654–1705). It is this law, also known as the theorem, that has become the basis in the construction of the theory of probability and statistics, which is used in modern biological statistics. In 1713, 8 years after the death of J. Bernoulli, his classic work "Ars conjectandi" was published in Basel. The fourth, most important, part of this work has remained unfinished. It contains the famous theorem of J. Bernoulli, called the law of large numbers. The most prominent followers of J. Bernoulli in the development of probability theory were Montmore (1678–1719) in France and De Moire (1667–1754) in England[17].

Based on the work of his predecessors, the famous French astronomer, physicist and mathematician Pierre Simon Laplace (1749–1827) publishes the work "Analytical Theory of Probability" and creates an error theory, that is, an application of probability theory to process the results of specific observations. In this work, P. Laplace describes, in particular, the practical application of probability theory to various phenomena of society, including the demographic analysis of mortality, average life expectancy, level of marriage, etc. Simultaneously with P. Laplace, Legendre also worked on the theory of errors, especially fruitfully – the German mathematician, astronomer and physicist Karl Friedrich Gauset (1777–1855) and the French mathematician, mechanic and physicist Simeon Denis Poisson (1781–1840)[18].

In his works P. Laplace at the beginning of the XIX century. made the result of all the previous development of probability theory and statistics, which opened a new period in the history of the development of statistical science. By increasing public interest in probability theory, by the nature and scope of work in the field of theoretical justification of science and its practical applications, the new period in its effectiveness significantly exceeds everything that was noted immediately after the publication of the works of J. Bernoulli. In 1837, S. Poisson's work "Research on Probabilities" (the best student of P. Laplace) appeared. This paper presents a theorem known as the law of large numbers. This is the biggest breakthrough after J. Bernoulli in developing the law of large numbers as a stage in the development of statistics[19].

The **fourth (fundamental) stage** of development of biostatistics began to take shape in the middle of the XIX century. and was marked by the work of the Belgian astronomer, mathematician, physicist and statistician Lambert Adolphe Jacques Quetelet (1796–1874). It was his work that laid the foundations of biometrics as a science. A. Ketle played a large role in the development of statistics, he called statistics the queen of all sciences, and he is rightly considered the father of modern statistics. In his "Letters on Probability Theorie", the scientist extensively develops the question of the practical application of probability theory with respect to the social sciences, primarily with regard to the study of socio-demographic phenomena[20]. A. Ketle was the first to combine the methods of anthropology and social statistics with the conclusions of probability theory and mathematical statistics.

In 1835, his work "On man and the development of his abilities, or the Experience of social physics" (2nd ed. In 1869) was published, where A. Ketle showed on various practical material that different physical characteristics of a person, including behavioral, obey the law of probability distribution. In another work "On the social system and the laws that govern it" (1848), he describes society not as a population, but as a single system, which is completely dependent on the laws of nature and does not obey the will of the population. In 1871, A. Quetelet published the following work, "Anthropology", in which he proved that statistical laws significantly affect not only the society of people, but also all living things. Thus, A. Ketle laid the foundations of biological statistics, which were independently developed primarily in the English school of biometrics. A. Ketle put forward the theory of the average person, which is a kind of statistical projection and combines physical, intellectual and moral qualities. This is a kind of person type of this or that country. The average person, in his opinion, is the center of weight around which all social phenomena are formed[21].

A. Ketle points out that it is possible to identify patterns that occur in society on the basis of mass statistical observations, only in this case the influence of random variables will disappear. To measure a large number of observations, he suggests introducing a special quantity, taken as a unit. This standardized value is the average value. Thanks to his work, criminal, then moral, and later biological statistics are successfully formed[22].

[15] Kremlev N.D. "Bez ucheta i statisticheskikh izmereniy nevozmozhno upravleniye" [Without accounting and statistical measurements, control is impossible], *Voprosy statistiki* [Statistics issues], 2008, N 5, P. 46–50 [in Russian].
[16] Mikhaylov N. "Nekotoryye voprosy teorii statistiki" [Some questions of the theory of statistics], *Vestnik statistiki* [Bulletin of statistics], 1952, N 3, P. 32–38 [in Russian].
[17] Shmoylovoy R. A. Teoriya statistiki [Theory of statistics], Moskva: Finansy i statistika, 2003, 656 p. [in Russian].
[18] Yeliseyeva I. I. "Kakuyu statistiku khotelos' by kmet'" [What statistics would like to be noted], *Voprosy statistiki* [Statistics issues], 2008, N 4. P. 13–15 [in Russian].
[19] Ploshko B.G. Iz istorii ucheniy o predmete statistiki [From the history of the teachings on the subject of statistics], *Vestnik statistiki* [Bulletin of statistics], 1964, № 5, P. 28–33 [in Russian].
[20] Shul'gin I. "K voprosu o predmete i metode statistiki" [On the subject and method of statistics], *Vestnik statistiki* [Bulletin of statistics], 1952, N 4, P. 42–50 [in Russian].
[21] Afanas'yev V. N., Markova A. I. Kurs lektsiy po istorii statistiki [Lecture course on the history of statistics], Orenburg: Izdatel'skiy tsentr OGAU, 2003, 376 p. [in Russian].
[22] Ibidem.

Among the Ukrainian followers of the ideas of A. Ketle, it is necessary to note the professor of Kharkov University O.P. Roslavsky-Petrovsky. In 1848 (2nd ed. In 1856) he published the "Guide to Statistics". The author, relying on the study of A. Quetelet, does not limit the task of statistics to a mere description of the state, but includes the objective laws of state life.

In 1846, an original and independent study by D. P. Zhuravsky (1810-1856) "On the sources and use of statistical information". The scientist graduated from the cadet corps, first served in the army, then switched to civil service. In the 50s. XIX century he was taken into service by an official of special powers of attorney under the Kiev governor Fundukleev. Under his leadership and with his personal participation, a description of the Kiev province in 3 volumes was compiled. This basic research was highly appreciated by contemporaries[23].

From compatriots, except O. P. Roslavsky-Petrovsky and D. P. Zhuravsky, an important role in the development of statistics was played by the works of N. Bunge, L. Fedorovich, A. N. Antsiferov, A. A. Rusov and others. Kiev professor N. Bunge in 1876 (2nd ed.) Published the work "Statistics Course". In this small but informative scientific work, detailed population statistics in Ukraine are presented in the spirit of a mathematical school. According to N. Bunge, the subject of statistics is primarily various social phenomena. In 1884, the History and Theory of Statistics was published by professor of Odessa University L. Fedorovich[24].

Among the textbooks of that time published in Ukraine, the works of professor of Kharkov University A. N. Antsiferov are of great importance. His work, The Elementary Statistics Course (2nd ed. 1910), considers statistics as a science of society, suggesting that statistics will necessarily come closer to sociology over time, or even merge with it[25].

In 1909, A. Z. Rusov, a well-known Zemstvo statistician at the Kiev Commercial Institute, published a Short Review of the Development of Russian Estimated Statistics, which provided a detailed description of the methods for collecting statistical data and the images of their development regarding zemstvo practice[26].

In this same period, the Russian mathematician P. L. Chebyshev (1821–1894), using the method of mathematical expectations of the classical theory of probability, gave a mathematical justification of the law of large numbers in its most general expression as the law of average values. Works of paramount importance for statistics are also the work of O.O. Chuprova (1874–1926), A.A. Markov (1856–1922), O. G. Lyapunova (18571919), O. A. Kaufman (1864–1919), A. M. Kolmogorov (1903–1987) and others[27].

The **fifth (formalistic) stage** is characterized by the emergence and development of the English biometric school. The application of statistics to biology was notably developed in the 19th century, and in this the leading role was played primarily by the English school of biologists Francis Galton and Karl Pearson. This school arose under the influence of the work of C. Darwin (1808-1882) "The Origin of Species" (1859), which made a revolution in biological science. It should be noted that at the beginning of the XVIII century. Reaumur tried, in particular, to find the mathematical laws for constructing bee honeycombs, and 30 years before him Borelli made mathematical calculations of animal movements, but the need for a quantitative analysis of wildlife using mathematical methods became real only at the end of the 19th century. Thus, in biology, statistical methods began to be used purposefully much later than in physics and chemistry. Biology has long developed on the basis of a qualitative analysis of natural phenomena. A serious reason for the emergence of biological statistics as a scientific methodology was the transition from a descriptive method in biology to experiment, because it required objectively comparable quantitative characteristics. An important circumstance is also the obligatory recognition of the fact that many biological phenomena have distinct statistical patterns.

Francis Galton (1822–1911), was a cousin of C. Darwin and took part in the discussion of the results of his research. The work of A. Ketle, especially his "Social Physics" and "Anthropology", made a strong impression on F. Galton, which served as the basis for the first time to use statistical methods in studying the processes of human heredity. Since 1865, F. Galton published several works on anthropology and genetics. On a large amount of factual material, he confirmed the conclusion of A. Quetelet that not only physical, but also mental abilities of a person are distributed according to the law of probability described by the Gauss-Laplace formula. Thus, he managed to instill in English biologists an interest in statistical methods[28].

Another representative of English biological statistics, Carl Pearson (1858-1936), a professor at the University of London (head of the Department of Applied Mathematics and Mechanics), has already founded a scientific school to develop biology issues using the statistical method. K. Pearson proved himself to be a talented mathematician and statistician, he managed to unite students around him who continued his research in various fields of science. He himself successfully studied the problems of heredity and variability of organisms[29].

To promote his ideas, K. Pearson published the journal "Biometrica" (1901) specifically for the statistical study of biological processes, the editor of which remained until the last days of his life.

The biometric methods developed by F. Galton and K. Pearson were included in the golden fund of mathematical statistics. However, their attempts to solve the problem of heredity of organisms only using the statistical method were unsuccessful. They mistakenly thought that the external similarity between relatives can be used to judge the degree of their relationship. But regardless of mistakes, according to the totality of ideas, views, approaches, Francis Galton and Karl Pearson are the founders of the new school of statistics – biometrics, in modern terminology – biostatistics[30].

The **sixth stage** in the development of biological statistics

[23] Gozulov A. I. Ocherki istorii otechestvennoy statistiki [Essays on the history of domestic statistics], Moskva: "Statistika", 1957, 356 p. [in Russian].
[24] Ptukha M. V. Ocherki po istorii statistiki v SSSR [Essays on the history of statistics in the USSR], Moskva, Izd-vo AN SSSR, 1955, 471 p. [in Russian].
[25] Yeliseyeva I. I., Yuzbashev M. M. Obshchaya teoriya statistiki, op. cit.
[26] Ptukha M.V. Ocherki po istorii statistiki v SSSR [Essays on the history of statistics in the USSR], op. cit. P. 450 p.
[27] Sheynin O. B. Teoriya statistiki: istoricheskiy eskiz [Theory of statistics: historical sketch], Op. cit., P. 64–69.
[28] Afanas'yev V. N., Markova A. I. Kurs lektsiy po istorii statistiki [Lecture course on the history of statistics], Orenburg: Izdatel'skiy tsentr OGAU, 2003, 376 p. [in Russian].
[29] Shmoylovoy R. A. Teoriya statistiki [Theory of statistics], Moskva: Finansy i statistika, 2003, 656 p. [in Russian].
[30] Tkach Ye. I. Zahal′na teoriya statystyky [General Statistics Theory], Ternopil′: Lider, 2004, 388 p. [in Ukrainian].

is called rational. It begins in 1902 with the classical studies of W. Johansen (1857–1927), which showed that in the field of biological research, the first place should belong to a biological experiment, and not to mathematics. Mathematical methods should be used as an auxiliary apparatus in the processing of experimental data, otherwise erroneous results may be obtained. W. Johansen reached this conclusion by experimenting with beans. Mathematics should help, not serve as a guiding idea. V. Johnsen published the results of his research in 1933 in his work "Elements of the exact doctrine of variability and heredity". This was a new, realistic approach to assessing the role of mathematical methods in biological research[31].

The **seventh (classical) stage** in the development of biometrics begins the work of the British V. Gosset and R. Fisher. William Gosset (1876-1937) – student of K. Pearson. He published in the journal "Biometrics" (1908) his work under the pseudonym Student. The work was devoted to the theory of small sampling and V. Gosset (student) became a pioneer in this field. It was then that the foundations of the theory of small sampling, the theory of planning experiments were created, new terms and concepts were introduced into the content of biometrics[32].

Famous scientists of the XX century in the field of biostatistics is Ronald Yelmer Fisher (1890–1962), who made a huge contribution to biometrics, enriching it with new methods of statistical analysis. G. Fisher was born and lived in England. For most of his life he remained a supporter of eugenics. R. Fisher noted his work in the field of mathematical statistics, enriched evolutionary genetics. His first book, Genetic Theory and Natural Selection (1930), was devoted to the synthesis of the Darwinian theory of selection and genetics. Fisher's theoretical and practical contribution to genetics is huge. He put forward the concept of progressive selection and inbreeding, tried to unify the doctrine of evolution. G. Fisher worked productively from 1912 to 1962[33]. Many of his studies positively influenced the development of statistics, including biological. For a long time R. Fisher worked as a researcher at the Rotamsted Agricultural Research Station, and since 1933, as a professor at the Department of Applied Mathematics, University of London. Later (1943–1957) R. Fisher – head of the Department of Genetics in Cambridge. Successfully combining in his person a biologist-experimenter and mathematics-statistician, Fisher brought into biometrics not only new methods, but also new ideas. He laid the foundations of the theory of experimental design, which in our time was further developed and became an independent section of biometrics[34].

All these innovations are connected with the revolution in biology, with the destruction of obsolete principles and concepts in the field of research, with the strengthening of the process of mathematization of biology. There is an ever more noticeable specialization of biometry, the targeted application of its methods in different areas of biology, medicine, anthropology and other related sciences.

Contribution of Ukrainian scientists to the development of biostatistics. Considering the history of biometrics, one cannot but note the enormous contribution to the development of biological statistics of such scientists of our country as S.G. Igumnov, O. V. Korchak-Chepurkovsky, S. A. Tomilin, A. M. Merkov, E. G. Kagan, S. S. Kagan, I. I. Ovsienko, K. F. Duplenko, E. Ya. Belitskaya, L. G. Lekarev, P. T. Petrov, S.M. Eckel, L.S. Kaminsky and others[35].

O. V. Korchak-Chepurkovsky (1857–1947) – an outstanding Ukrainian scientist, epidemiologist, hygienist, department head at the Institute of Demography and Sanitary Statistics. The main directions of his research related to the problems of epidemiology and the sanitary state of the population. Based on his own experience as a sanitary doctor and taking into account the scientific developments of that time, he singles out epidemiology as a separate scientific discipline, he assigns the main role according to the time and nature of the development of epidemics of smallpox, scarlet fever, diphtheria danger of plague, etc. According to Korchak-Chepurkovsky, the epidemiological tasks had to be addressed not separately, but as components of a study of the sanitary condition[36]. O.V. Korchak-Chepurkovsky combined practical work with the teaching: he gave lectures on epidemiology and medical statistics at the University of St. Vladimir.

Scientific heritage S.A. Tomilina (1877–1952) – an outstanding Ukrainian social hygienist, sanitary statistician, demographer, medical historian, phytotherapist – these are numerous works on social hygiene, sanitary statistics, demography, epidemiology, history of medicine and herbal medicine. S.A. Tomilin investigated the problems of fertility, marriage and family, the health status of the population and the improvement of medical care, the problems of morbidity and mortality, and the social aspects of human genetics. S. A. Tomilin is the first doctor-statistician who headed the statistics department in Ukraine in 1918, 1922–1930, laid the organizational and methodological foundations of its formation and development. He is the organizer of departmental health statistics in Ukraine. He took an active part in the development of its methodological provisions, and in a number of sanitary-statistical studies[37].

A. M. Merkov (1899–1971) – a well-known national statistician, a specialist in the field of social hygiene and medical demography – began his activities in Kharkov, and eventually worked in Russia. A large number of his works are devoted to the theory, methodology and history of sanitary statistics, which was the main theme of his scientific work[38].

A. M. Merkov was an extremely erudite and talented teacher. Numerous listeners – doctors of various specialties, who are sometimes skeptical of such a "dry and boring" subject as sanitary statistics – under the influence of his brilliant lectures changed their attitude towards the subject. And many of them became his students and followers. An independent direction in the scientific work of A.M. Merkova had demographic statistics. He wrote more than 200 works on the problems of social hygiene, sanitary statistics, the organization of healthcare and demography, including about 20 monographs and teaching aids[39].

[31] Shmoylova P.A. Praktikum po teorii statistiki [Workshop on the theory of statistics], Moskva: Finansy i statistika, 1998, 416 p. [in Russian].
[32] Matkovs′kyy C. O., Hal′kiv L. I., Hryn′kevych O. S, Sorochak O. Z. Statystyka [Statistics], L′viv, "Novyi Svit", 2009, 430 p. [in Ukrainian].
[33] Marmoza A. T. Statystyka [Statistics], Kyiv: El′ha, KNT, 2009, 896 p. [in Ukrainian].
[34] Luhinin O. S. Statystyka [Statistics], Kyiv: Tsentr uchbovoyi literatury, 2007, 608 p. [in Ukrainian].
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[36] Matkovs′kyy C. O., Hal′kiv L. I., Hryn′kevych O. S, Sorochak O. Z. Statystyka [Statistics], op. cit.
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Over the years, the teaching of medical statistics has been conducted in the modern higher medical school as a type of biological statistics. Today, a lot of work is underway to reform the institution of higher education, curricula, teaching technolotechnologies are being improved, new subjects are being introintroduced, including biological statistics. A lot of work is carcarried out by leading experts in the field of social medicine, healthcare, biostatistics, especially in the formation of it as a subject of teaching in higher medical school. Among them Corr. AMSU, prof. V. F. Moskalenko, Corr. AMSU, prof. Yu. V. Voronenko, prof. G. O. Weak, prof. A. R. Uvarenko, prof. O. G. Protsek, prof. B. O. Ledoschuk, prof. A. P. Mintzer, prof. V. M. Lehan, N. A. Galicheva and others[40].

The first Ukrainian special textbooks published were impimportant for the development of biostatistics: "Working MedMedical Statistics" (Є. G. Kagan, 1923), "Mortality in Russia and Ukraine" (M.V. Ptukha, 1928), "General Theory of SanitSanitary Statistics" (A. M. Merkov, 1935), "Workshop on SanSanitary Statistics" (L. A. Abramovich, M. Y. Kaminsky, P. T. Petrov, 1940), "General Theory and Methodology of SanitaryStatistical Research" (A. M. Merkov, 1960 and 1963), "Demographic statistics" (A. M. Merkov, 1959, 1965), "Processing of clinical and laboratory data (application of statistatistics in the work those of a doctor" (L. S. Kaminsky, 1959, 1964) and others[41].

Conclusions. Biostatistics developed in its own way, using its methods in research. But the subject of study was general – the state, society, as well as mass phenomena and processes taking place in it.

Thus, the history of the development of statistics shows that statistical science has developed as a result of theoretical enrichment of the advanced experience of accounting and statistical work accumulated by mankind; due primarily to the needs of managing the life of society.

Бідучак Анжела, Грицюк Мар'яна, Чорненька Жанетта, Доманчук Тетяна. Історія становлення і розвитку біостатистики. В останні 20-30 років медицина і біологія вступили в нову фазу свого розвитку. Накопичення величезних масивів кількісних даних і доступність обчислювальної техніки посилило математизацію біології і медицини. У переважній більшості медичних наукових робіт автори використовують в тому чи іншому обсязі методи статистики. **Мета дослідження.** Проаналізувати історичні етапи становлення біостітістікі, як науки. **Методологія дослідження.** У статті використано описовий, бібліосемантічній та історико-порівняльний методи. **Обговорення результатів дослідження.** У статті висвітлено історію розвитку біостатистики в світі. Збір статистичних даних почався з давніх-давен. А до більш пізнього періоду відносяться обробка і аналіз статистичних даних, т.б. зародження біостатистики як науки. **Висновки.** До якої б області не ставився предмет дослідження статистики (населення, промисловість, торгівля і т.п.), метод її скрізь однаковий, тобто всюди використовуються масове спостереження, угрупування і узагальнюючі показники, в яких вплив випадкових причин і виявляється типове та закономірне. Інакше кажучи, метод біостатистики обумовлений специфікою її предмета.

Ключові слова: *біостатистика, історія, етапи становлення, етапи становлення біостатистики, історія медицини.*

Анжела Бідучак *– кандидат медичних наук, доцент кафедри соціальної медицини та організації охорони здоров'я ВДНЗ України "Буковинський державний медичний університет". Автор понад 60 праць наукового та навчально-методичного характеру, з яких 2 монографії, 9 навчально-методичних посібників. Наукові інтереси: профілактика хронічних неінфекційних захворювань, історія медицини, конфліктологія.*

Anzhela Biduchak *– Candidate of Medical Sciences, Assistant Professor of the Department of Social Medicine and Public Health of the Higher State Educational Establishment of Ukraine "Bukovinian State Medical University", Chernivtsy. Is the author of more than 60 works of scientific and educational-methodical nature, including 2 monographs, 9 scientific-methodical manuals. Research interests: prevention of chronic non-communicable diseases, history of medicine, conflictology.*

Маряна Грицюк *– доктор медичних наук, доцент кафедри соціальної медицини та організації охорони здоров'я ВДНЗ України "Буковинський державний медичний університет". Автор понад 90 праць наукового та навчально-методичного характеру, з яких 2 монографії, 9 навчально-методичних посібників. Наукові інтереси: профілактика захворювань, проблеми цукрового діабету, історія медицини.*

Mariana Grytsyuk *– Doctor of Medical Sciences, Assistant Professor of the Department of Social Medicine and Health Care Institutions of the Academy of Medical Sciences of Ukraine "Bukowina State Medical University". Is the author of more than 90 works of scientific and educational-methodical nature, including 2 monographs, 9 scientific-methodical manuals. Scientific interests: disease prevention, diabetes problem, history of medicine.*

Жанетта Чорненька *– кандидат медичних наук, доцент кафедри соціальної медицини та організації охорони здоров'я ВДНЗ України "Буковинський державний медичний університет". Автор понад 85 праць наукового та навчально-методичного характеру, з яких 4 монографії, 9 навчально-методичних посібників. Наукові інтереси: профілактика захворювань, історія медицини, проблеми дерматовенерології.*

Janetta Chornenka *– Candidate of Medical Sciences, Assistant Professor of the Department of Social Medicine and Public Health of the Higher State Educational Establishment of Ukrain "Bukovinian State Medical University", Chernivtsy. Is the author of more than 85 works of scientific and educational-methodical nature, including 2 monographs, 9 scientific-methodical manuals. Scientific interests: disease prevention, history of medicine, problems of dermatovenereology.*

Тетяна Доманчук *– асистент кафедри соціальної медицини та організації охорони здоров'я ВДНЗ України "Буковинський державний медичний університет". Автор понад 20 праць наукового та навчально-методичного характеру, з яких 1 монографія, 5 навчально-методичних посібників. Наукові інтереси: профілактика захворювань, історія медицини, проблеми онкології.*

Tetyana Domanchuk *– assistant of the Department of Social Medicine and Public Health of the Higher State Educational Establishment of Ukraine "Bukovinian State Medical University", Chernivtsy. Is the author of more than 60 works of scientific and educational-methodical nature, including 1 monograph, 5 scientific-methodical manuals. Scientific interests: disease prevention, history of medicine, problems of oncology.*

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