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**GENERAL UNDERSTANDING OF THE ETIOLOGY OF DISEASES IN
MEDICINE****Tillayeva Zarina Zafarbekovna**zarina_tillyayeva@tues.uz<https://orcid.org/0009-0000-9394-5324>**Termez University of Economics and Service****Abstract**

A correct understanding of disease etiology is one of the fundamental requirements of modern medical science and clinical practice. Etiology examines the causes and determinants of disease, including biological agents, genetic susceptibility, immune dysregulation, metabolic disturbances, environmental exposures, behavioral risk factors, social determinants, and health system-related influences. In contemporary medicine, most diseases are no longer interpreted through a single-cause model. Instead, the development of disease is increasingly explained by complex interactions between host factors, external exposures, molecular mechanisms, and population-level determinants. This article provides a comprehensive academic overview of the general understanding of disease etiology in medicine, with emphasis on classification, epidemiological relevance, modern diagnostic tools, methodological approaches, and implications for prevention and personalized care. The article is based on recent evidence from the World Health Organization, CDC, NIH, PubMed-indexed literature, Cochrane Library, The Lancet, BMJ, Nature Medicine, New England Journal of Medicine, and health system data relevant to Uzbekistan. The analysis shows that etiological assessment is clinically meaningful only when genetic, infectious, environmental, behavioral, and social determinants are evaluated together. Multifactorial causation is especially important in cardiovascular diseases, diabetes mellitus, cancer, chronic respiratory diseases, infectious diseases, antimicrobial resistance, and mental health disorders. The article also discusses the role of artificial intelligence, real-world data, real-world evidence, genomics, multi-omics, and precision medicine in identifying causal pathways and improving clinical decision-making. A strong etiological framework supports early diagnosis, rational prevention, individualized treatment, and evidence-based health policy. Therefore, understanding disease etiology should be considered not only a theoretical medical concept but also a practical instrument for reducing disease burden and improving population health outcomes.

Keywords: disease etiology, causation, risk factors, pathogenesis, multifactorial diseases, genetic susceptibility, infection, environmental exposure, social determinants, non-communicable diseases, antimicrobial resistance, epidemiology, precision medicine, artificial intelligence, real-world evidence.

Introduction

The etiology of diseases is one of the oldest and most essential questions in medicine: why does a disease occur in one person, at one time, under certain conditions, but not in another? The answer to this question determines how physicians diagnose disease, how public health systems design prevention programs, how researchers develop new treatments, and how society understands responsibility for health. In classical medicine, the cause of disease was often interpreted in a narrow way, especially when a specific pathogen, toxin, trauma, or hereditary defect could be identified. However, modern biomedical science has demonstrated that the majority of diseases arise from layered and dynamic interactions between biological, genetic, environmental, behavioral, and social factors.

The global relevance of disease etiology has increased sharply in recent decades. Non-communicable diseases remain the leading cause of mortality worldwide, while infectious diseases, antimicrobial resistance, environmental pollution, climate-related health threats, occupational exposures, and social inequalities continue to shape disease patterns across countries. The same clinical disease may have different etiological structures in different populations. For example, ischemic heart disease may be driven mainly by hypertension, dyslipidemia, diabetes, smoking, poor diet, air pollution, chronic stress, genetic predisposition, or combinations of these factors. Similarly, cancer may result from inherited mutations, viral infections, carcinogenic exposures, immune changes, lifestyle factors, and random somatic mutations accumulated over time.

The epidemiological significance of etiological understanding is particularly clear in the Global Burden of Disease studies. These studies show that modifiable risk factors such as high systolic blood pressure, tobacco use, high fasting plasma glucose, high body mass index, air pollution, unhealthy diet, and kidney dysfunction contribute substantially to premature mortality and disability. At the same time, infectious etiologies remain central in tuberculosis, HIV/AIDS, viral hepatitis, respiratory infections, diarrheal diseases, and health care-associated infections. Antimicrobial resistance has further complicated the etiological landscape because treatment failure may occur not only due to the pathogen itself but also due to resistance mechanisms shaped by antibiotic misuse, inadequate infection control, agricultural antibiotic exposure, and weak surveillance.

In Uzbekistan, the etiological structure of disease reflects both global and regional characteristics. Non-communicable diseases, especially cardiovascular diseases, remain the dominant causes of mortality and morbidity. Important risk factors include unhealthy diet, high blood pressure, tobacco use, physical inactivity, air pollution, and metabolic disorders. At the same time, communicable diseases such as tuberculosis, including multidrug-resistant tuberculosis, continue to require etiological surveillance and public health attention. This dual burden creates a need for medical education and clinical practice to integrate classical etiological thinking with modern epidemiology and systems medicine.

The research problem is that the concept of etiology is sometimes taught or understood too simply. In many cases, students associate etiology only with “cause,” while in real clinical practice causation may be probabilistic, multifactorial, time-dependent, and mediated by biological mechanisms. A narrow understanding of etiology may lead to incomplete diagnosis, weak prevention, inappropriate treatment, and poor risk communication. Therefore, modern medicine needs a broader etiological framework that explains not only immediate causes but also predisposing, enabling, triggering, and maintaining factors.

The research gap lies in the insufficient integration of etiological theory with contemporary evidence from genomics, exposomics, social determinants of health, real-world data, and artificial intelligence. Although each of these fields contributes to understanding disease causation, they are often discussed separately. A comprehensive article is needed to connect these domains into a clinically useful model.

The aim of this article is to analyze the general understanding of disease etiology in medicine and to systematize the major etiological categories, mechanisms, methodological approaches, and practical implications for diagnosis, prevention, treatment, and health policy.

Materials and Methods

Study design

This article was prepared as a structured narrative review with an additional methodological framework for a model cross-sectional etiological risk assessment. The narrative review was selected because disease etiology is a broad concept that requires synthesis of biomedical, epidemiological, clinical, environmental, genetic, and social evidence. The proposed empirical model is included to demonstrate how etiological factors can be assessed in real clinical and public health settings.

Study setting

The theoretical review is based on international scientific literature and health system reports. The proposed field component may be conducted in primary health care

institutions, outpatient clinics, university hospitals, family polyclinics, and community-based medical centers. For adaptation to Uzbekistan, a suitable setting would include urban and rural primary care facilities where patients are routinely evaluated for chronic and infectious diseases.

Study period

The literature review focused primarily on sources published between 2020 and 2026. Earlier foundational sources were included only when they were methodologically important for understanding causality, epidemiology, genetics, or public health frameworks. For the empirical component, a recommended study period is 6 months, including participant recruitment, clinical measurements, laboratory testing, data verification, and statistical analysis.

Participants

For a model cross-sectional study, 400 adult participants aged 18 years and older may be included. This sample size allows assessment of the prevalence of major etiological risk factors and evaluation of associations between demographic, behavioral, metabolic, environmental, and family-history variables.

Inclusion criteria

Participants may be included if they meet the following criteria:

1. Age 18 years or older.
2. Permanent residence in the selected region for at least 6 months.
3. Ability to provide informed consent.
4. Attendance at a primary health care facility during the study period.
5. Availability for questionnaire completion and basic clinical examination.

Exclusion criteria

Participants should be excluded in the following cases:

1. Severe acute condition requiring emergency medical intervention.
2. Cognitive impairment limiting reliable communication.
3. Refusal to participate.
4. Incomplete clinical or questionnaire data.
5. Current pregnancy if metabolic parameters are analyzed without pregnancy-specific adjustment.
6. Recent major surgery or acute infection within the previous 2 weeks, if inflammatory biomarkers are included.

Research methodology

The literature review included scientific publications from PubMed, Scopus, Web of Science, Cochrane Library, WHO, CDC, NIH, The Lancet, BMJ, Nature Medicine, New England Journal of Medicine, and national health system sources. Search terms

included “disease etiology,” “causation in medicine,” “risk factors,” “multifactorial diseases,” “genetic susceptibility,” “infectious etiology,” “environmental determinants,” “social determinants of health,” “non-communicable disease risk factors,” “real-world evidence,” “multi-omics,” and “precision medicine.”

The proposed empirical component includes four major domains:

1. Sociodemographic data: age, sex, education, occupation, income category, residence.
2. Behavioral factors: smoking, alcohol intake, diet, salt consumption, physical activity, sleep pattern.
3. Biological and clinical factors: family history, body mass index, blood pressure, chronic disease history, medication use.
4. Environmental and social factors: air pollution exposure, occupational risks, access to health care, stress, housing conditions.

Laboratory and instrumental examinations

For etiological risk assessment, the following examinations may be used:

1. Complete blood count.
2. Fasting blood glucose.
3. HbA1c.
4. Lipid profile.
5. C-reactive protein.
6. Serum creatinine and estimated glomerular filtration rate.
7. Liver function tests.
8. Urinalysis.
9. Blood pressure measurement.
10. Body mass index and waist circumference.
11. Electrocardiography.
12. Spirometry in patients with respiratory symptoms or smoking history.
13. Chest X-ray or ultrasound only when clinically indicated.
14. Microbiological testing in suspected infectious diseases.
15. Molecular or genetic testing in selected cases, especially rare diseases, hereditary cancer syndromes, familial dyslipidemia, and unclear congenital disorders.

Statistical analysis

Data may be analyzed using SPSS, Stata, R, or Jamovi. Quantitative variables should be expressed as mean $\pm$ standard deviation or median with interquartile range depending on distribution. Categorical variables should be presented as frequencies and percentages. Normality can be assessed using the Shapiro–Wilk test. Between-

group comparisons may be performed using Student's t-test, Mann–Whitney U test, chi-square test, or Fisher's exact test.

Multivariable logistic regression may be used to identify independent etiological predictors of chronic disease risk. Results should be presented as odds ratios with 95% confidence intervals. A p-value of less than 0.05 should be considered statistically significant. For etiological modeling, population attributable fraction, adjusted odds ratio, and interaction analysis may be used when data quality permits.

Ethical considerations

The empirical component must be conducted according to the principles of the Declaration of Helsinki. Participants should receive clear information about study aims, procedures, potential risks, confidentiality, and voluntary participation. Written informed consent must be obtained. Personal data should be anonymized. The study protocol must be reviewed and approved by an institutional ethics committee before data collection. Genetic testing, if performed, requires additional ethical safeguards, including pre-test counseling, data protection, and careful interpretation of incidental findings.

Results

The review demonstrates that disease etiology in modern medicine can be divided into several major categories: genetic, infectious, immunological, metabolic, environmental, behavioral, occupational, iatrogenic, psychosocial, and social determinants. In real clinical practice, these categories rarely act in isolation. Most diseases develop through interaction between host vulnerability and external exposure.

General etiological classification

Etiological group	Examples	Clinical significance
Genetic factors	Monogenic disorders, polygenic risk, chromosomal abnormalities	Important for diagnosis, family screening, reproductive counseling
Infectious agents	Bacteria, viruses, fungi, parasites, prions	Important for microbiological diagnosis, vaccination, antimicrobial therapy
Immune mechanisms	Autoimmunity, allergy, immune deficiency	Relevant to chronic inflammatory and systemic diseases
Metabolic factors	Obesity, insulin resistance, dyslipidemia	Major drivers of diabetes, cardiovascular disease, fatty liver disease

Etiological group	Examples	Clinical significance
Environmental factors	Air pollution, toxins, radiation, climate-related exposure	Linked to respiratory, cardiovascular, oncological and developmental disorders
Behavioral factors	Smoking, alcohol, diet, physical inactivity	Strongly associated with preventable NCD burden
Occupational factors	Dust, chemicals, noise, ergonomic overload	Important for respiratory disease, cancer, hearing loss, musculoskeletal disorders
Iatrogenic factors	Drug reactions, hospital infections, procedural complications	Important for patient safety and quaternary prevention
Social determinants	Poverty, education, housing, food insecurity, access to care	Shape unequal distribution of disease risk

The strongest conclusion from recent epidemiological literature is that modifiable risk factors explain a substantial proportion of global disease burden. High blood pressure, tobacco use, unhealthy diet, high fasting plasma glucose, high body mass index, and air pollution remain among the most influential etiological contributors to premature mortality. These factors are especially important because they are not only associated with individual disease development but also measurable and preventable at population level.

Infectious etiologies remain clinically important despite the global rise of chronic diseases. Bacterial, viral, fungal, and parasitic agents are direct causes of many acute and chronic conditions. However, infection-related disease causation has become more complex because host immunity, vaccination status, microbiome composition, antimicrobial resistance, and social conditions influence clinical outcomes. For example, the same pathogen may cause mild disease in one person and severe disease in another due to differences in age, immune function, comorbidities, genetic susceptibility, and access to timely care.

Genetic etiology is also expanding as genome sequencing becomes more accessible. In monogenic diseases, a single pathogenic variant may be sufficient to cause disease. In complex diseases, however, genetic variants usually modify risk rather than determine outcome absolutely. Cardiovascular diseases, type 2 diabetes, many cancers, autoimmune diseases, and neuropsychiatric conditions are examples of disorders where polygenic predisposition interacts with lifestyle and environmental exposures.

The proposed empirical model may produce results such as the following if implemented in a real primary care setting. In a hypothetical sample of 400 adult participants, common etiological risk factors may include overweight or obesity in 45–55%, elevated blood pressure in 30–40%, low physical activity in 35–50%, high salt consumption in 50–65%, smoking in 15–25%, and family history of chronic disease in 25–35%. These values should not be interpreted as real study findings; they are shown only as an analytical framework for how final results may be presented after actual data collection.

Model table for empirical etiological assessment

Indicator	Model value	Interpretation
Mean age	46.8 ± 13.4 years	Middle-aged adult sample
Male participants	48.5%	Balanced sex distribution
BMI ≥25 kg/m ²	51.2%	High metabolic risk
Elevated blood pressure	36.7%	Major cardiovascular etiological factor
Current smoking	19.8%	Important behavioral risk
Low physical activity	42.5%	Modifiable lifestyle determinant
Family history of NCD	31.4%	Genetic and familial risk marker
High fasting glucose	18.6%	Early metabolic dysfunction
Dyslipidemia	39.1%	Atherogenic risk factor
Poor preventive awareness	44.3%	Barrier to risk reduction

In a model logistic regression analysis, elevated blood pressure, obesity, smoking, dyslipidemia, and family history may be independently associated with high cardiometabolic risk. For example, obesity may show an adjusted odds ratio of approximately 2.1 with a 95% confidence interval excluding 1.0 and $p < 0.01$, while smoking may show an adjusted odds ratio of approximately 1.8 with $p < 0.05$. In an actual article submission, these model outputs must be replaced by real statistical results derived from collected data.

From a clinical perspective, the most important finding is that etiological risk is cumulative. One risk factor may moderately increase disease probability, but the combination of several risk factors can substantially increase risk. This is why etiological assessment should not be limited to identifying a single cause. A patient with hypertension, obesity, smoking history, dyslipidemia, family history, and chronic stress has a fundamentally different etiological profile from a patient with only one isolated risk factor.

Discussion

The findings of this review confirm that disease etiology in modern medicine should be understood as a dynamic and multidimensional process. Classical medical thinking often searched for a single cause, but contemporary evidence shows that many diseases are produced by causal networks. These networks include biological susceptibility, environmental exposure, lifestyle patterns, social conditions, and health system performance.

The results are consistent with major international studies published in *The Lancet*, which demonstrate that preventable risk factors account for a large share of disability-adjusted life years and premature mortality worldwide. The Global Burden of Disease framework is especially useful because it does not reduce disease causation to one factor. Instead, it estimates the relative contribution of multiple exposures across countries, age groups, and time periods. This approach is highly relevant for countries such as Uzbekistan, where cardiovascular diseases, metabolic disorders, dietary risks, and environmental exposures coexist with infectious disease challenges.

Evidence from *BMJ* and public health literature supports the idea that social determinants are not secondary background variables but active etiological conditions. Poverty, low education, poor housing, food insecurity, limited access to care, and occupational vulnerability influence disease risk through biological pathways such as chronic stress, inflammation, poor nutrition, delayed diagnosis, and reduced treatment adherence. Therefore, etiological analysis should not stop at the level of individual behavior. For example, advising a patient to eat healthier is clinically correct, but incomplete if healthy food is economically inaccessible or if the patient lives in an environment that does not support physical activity.

Nature Medicine and other precision medicine sources show that genomics and multi-omics technologies are changing the way etiology is investigated. Genome sequencing can identify rare disease causes, inherited cancer syndromes, pharmacogenomic risks, and previously unknown pathogenic variants. Multi-omics approaches, including genomics, transcriptomics, proteomics, metabolomics, epigenomics, and microbiome analysis, allow researchers to examine disease mechanisms at multiple biological levels. This is important because the same clinical diagnosis may include several molecular subtypes with different causes and treatment responses.

New England Journal of Medicine discussions on social determinants and health system transformation emphasize that clinicians cannot fully understand disease causation without considering the patient's living environment. This does not mean that biological mechanisms become less important. Rather, modern etiology connects biological mechanisms with upstream determinants. A patient's inflammatory state,

glucose metabolism, blood pressure, immune response, and microbiome may all be influenced by nutrition, stress, sleep, pollution, infection history, and social conditions. The role of infectious etiology has also evolved. The discovery of microbes transformed medicine in the nineteenth and twentieth centuries, but the twenty-first century has added new complexity. Antimicrobial resistance illustrates this well. The etiological agent may be a bacterium, but the clinical problem is shaped by resistance genes, antibiotic exposure, hospital transmission, agricultural practices, diagnostic delays, and infection prevention failures. Therefore, AMR is simultaneously a microbiological, clinical, behavioral, agricultural, and policy-related etiological problem.

Artificial intelligence may strengthen etiological research by detecting patterns in large datasets, electronic health records, imaging, laboratory values, genomic data, and wearable devices. AI can identify risk clusters that may be missed by traditional analysis. However, AI-based etiological interpretation must be clinically validated. Correlation should not be confused with causation. Without careful study design, high-quality data, causal inference methods, and external validation, algorithmic models may produce misleading conclusions.

The strength of this article is its integrated approach. It explains disease etiology not only as a definition but as a practical clinical framework. It connects epidemiology, molecular medicine, infectious disease, chronic disease, environmental health, social determinants, AI, RWD, RWE, and precision medicine. This makes the concept useful for students, clinicians, researchers, and health policy planners.

The main limitation is the absence of original field data. The statistical results presented in the Results section are model examples and should not be used as actual evidence. A second limitation is that disease etiology is a very broad topic; each disease group requires separate detailed evaluation. A third limitation is that many etiological pathways are probabilistic, and proving causation requires stronger designs such as cohort studies, randomized interventions, Mendelian randomization, mechanistic laboratory studies, or triangulation of evidence.

Future studies should focus on etiological risk mapping in Uzbekistan, especially for cardiovascular disease, diabetes, chronic kidney disease, cancer, tuberculosis, antimicrobial resistance, and environmentally mediated diseases. Research should combine clinical data, laboratory biomarkers, lifestyle assessment, environmental exposure data, and digital health records. Such studies would help identify high-risk groups and support more precise prevention strategies.

Conclusion

The etiology of diseases in medicine is a broad and clinically important concept that explains why diseases occur, how risk factors interact, and how prevention and treatment should be organized. Modern etiology goes beyond the simple search for one cause. It includes genetic predisposition, infectious agents, immune mechanisms, metabolic disorders, environmental exposures, behavioral habits, occupational risks, social determinants, health system factors, and iatrogenic influences.

The main conclusion of this article is that disease causation should be evaluated through an integrated and evidence-based model. In clinical practice, this means that physicians should assess not only symptoms and laboratory findings but also family history, lifestyle, environment, occupation, social conditions, medication exposure, infection history, and access to care. In public health, etiological knowledge allows more accurate prevention programs, better screening strategies, and rational allocation of resources.

Practical recommendations include:

1. Strengthening etiological thinking in medical education.
2. Using structured risk assessment tools in primary care.
3. Integrating genetic and family-history data into clinical evaluation where appropriate.
4. Expanding screening for major metabolic and cardiovascular risk factors.
5. Improving infectious disease surveillance and antimicrobial resistance monitoring.
6. Considering environmental and occupational exposures during diagnosis.
7. Including social determinants in patient assessment.
8. Using real-world data and AI tools carefully, with clinical validation.
9. Developing population-specific etiological studies in Uzbekistan.
10. Linking etiological research with prevention, early diagnosis, and personalized treatment.

In future medicine, successful diagnosis and treatment will depend not only on recognizing the disease but also on understanding its causes at biological, social, environmental, and population levels. A deeper understanding of etiology is therefore essential for improving individual patient care and strengthening public health systems.

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