

## ANALYTICAL STUDY OF THE LEADING CAUSES OF DEATH OF PALLIATIVE PATIENTS

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### ABSTRACT

**Background.** Palliative and Hospice Care (PHC) aims to prevent premature death of patients from complications of serious illnesses and their comorbid impact on vital functions. As well as adequate pain relief, treatment should be aimed at alleviating suffering and improving the quality of life of such patients. The causes of death of palliative patients, which are closely related to the PHC organization, in particular to the package budget financing of inpatient and mobile palliative care for adults and children, the leading needs of palliative patients, remain insufficiently studied.

**Aim.** Analysis of the main causes of death of palliative patients depending on the diagnosis and determination of their impact on the organization of palliative and hospice care.

**Materials and Methods.** The method of system analysis, comparative method and bibliosemantic method were used for the research.

**Results and Conclusions.** Causes of death were studied for diseases listed as palliative in severe cases and in the presence of complications. The analysis allows us to deepen our understanding of the practical aspects of organizing palliative and hospice care in meeting the needs of palliative patients, adults and children. The summary of the causes of death allows us to group these causes into organ and system failure; vascular crises; asphyxia; thromboembolic conditions; infectious complications up to sepsis; chronic intoxication; tumor growth in other organs with disruption of their vital functions, metastasis; malignancy of benign tumors; complications of treatment; brain and spinal cord lesions due to epileptic seizures, injuries, inflammatory processes; endocrine comas; gangrene and bedsores; severe immunodeficiency; underdevelopment or absence of organs in congenital malformations; prematurity; suicides in depressive states.

**Keywords:** *palliative and hospice care, primary palliative diagnosis, comorbidity.*

### Introduction

Palliative and Hospice Care (PHC) is provided to terminally ill patients in the last days of their lives and is intended to reduce their suffering, the feeling of pain and to prepare for a dignified death. Modern development of medical technologies theoretically allows to ensure painless dying, which is possible with the correct organization of medical care. The countries with developed PHC systems offer patients recognition of their palliative status, stay in specialized institutions (hospices, palliative departments and wards) or in "hospices at home", adequate pain relief, euthanasia as an op-

tion, as well as social support and spiritual support, which extend to both the patient himself and his loved ones (caregivers) [1–3].

A significant part of palliative diseases belongs to the category of disabling and is accompanied by chronic intense pain [4; 5]. Depending on the main palliative diagnosis and comorbid pathology, in severe palliative conditions, nociceptive (associated with nerve irritation), neuropathic (associated with organic nerve damage) type of pain prevails, or a combination of these types of pain is present. Depending on the intensity of pain, which is derived from the characteristics of the pathological process and individual perception of pain, narcotic drugs (morphine, oxycodone, buprenorphine, etc.), non-narcotic drugs (primarily Nonsteroidal Anti-Inflammatory Drugs, NSAIDs) and adjuvants (not intended for direct pain relief, but capable of enhancing the effect of analgesic drugs – sedatives, hypnotics, anticonvulsants, neuroleptics, etc.)

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are used for pain relief [2; 6; 7]. The recent legalization of medical cannabis theoretically significantly expands the possibilities of adequate pain relief. However, to practically realize this opportunity, Ukraine needs to accelerate the adoption of by-laws regulating cultivation of cannabis, production of cannabis-based drugs, and simplify the procedures for obtaining these drugs by palliative patients [8; 9].

Pain in severe palliative conditions is not a "signal" pain, i.e., it does not indicate a previously unknown health problem. On the contrary, it is emotionally debilitating and depletes the immune and endocrine systems. Its impact on inflammatory processes is negative due to its participation in "pathological circles" [2; 4; 5; 10]. This indicates the need for constant adequate pain relief for palliative patients, but taking into account the risks of excessive sedation, which can lead to death. It is these risks that allow us to talk about the need to prevent premature death in patients who already expect it to be imminent. In the ongoing debate about the risks and benefits of long-term pain relief with narcotic drugs, it is necessary to focus on evidence collected according to the rules of evidence-based medicine [11; 12].

In recent years, researchers from the Ukrainian Center for Public Data (Kyiv, Ukraine) and Kharkiv National Medical University have made progress in determining the list of palliative diseases in Ukraine [13–16]. Representatives of the first organization calculated the need for PHC and determined the list of main palliative diagnoses of adults and children for 2018. Representatives of the second organization expanded this list, calculated the need for PHC for 2019–2020 and forecasted this need for 2021–2022. Subsequently, this forecast was checked and revised retrospectively using the creeping trend method with a constant smoothing segment. The method itself was also improved [16; 17].

In their further studies, representatives of the Kharkiv group studied the features of the organization of PHC at the regional level [18; 19], improved the questionnaire on the quality of life of palliative patients of neurological and oncological profiles [20; 21], studied the issues of types of pain in different palliative diagnoses, features of pain relief [4; 6; 7], attitudes towards the possibility of legalizing euthanasia [22–25]. To date, the causes of death of palliative patients, which are closely related to the organization of PHC, in particular, with the package budget financing of stationary and mobile palliative care for adults and

children [26], and the leading needs of palliative patients [1; 8], remain insufficiently studied in the works of the authors and according to the results of searches on PubMed, Google and Google Scholar.

The **aim** of the study was to analyze the main causes of death of palliative patients depending on the diagnosis and to determine their impact on the organization of palliative and hospice care.

### Materials and Methods

The research used methods of systematic analysis, comparative and bibliosemantic, with a search for sources on PubMed, Google and Google Scholar using the keywords "palliative and hospice care", "causes of death of palliative patients", "comorbidity of palliative diseases" in Ukrainian and English. In connection with the theoretical approach to the research, bioethical examinations of the research materials were not conducted. Statistical methods were also not used.

### Results and Discussion

The causes of death of cancer patients (C00–C97, D00–D48 according to the International Statistical Classification of Diseases and Related Health Problems, 10<sup>th</sup> revision, ICD-10) are cancer intoxication, failure of affected organs and systems (respiratory, cardiovascular, renal, hepatic failure), cachexia, metastasis and germination of tumors to other organs with disruption of their vital functions, thromboembolism, infectious complications (sepsis, infection of decaying tumors). Treatment complications are also possible. For example, death due to excessive sedation with narcotic analgesics [7; 27; 28]. Cancer patients with malignant neoplasms accounted for (36.3–40.4)% of all palliative adult patients and (13.5–17.8)% of children with palliative diagnoses in Ukraine for the period 2018–2020, according to the calculation of the need for PHC in Ukraine performed by Nesterenko V.G. et al. (2021) [14–17].

The causes of death from cardiovascular diseases (I00–I99 according to ICD-10) are usually acute and chronic heart failure, circulatory failure due to myocardial infarction and stroke of the brain vessels (hemorrhagic and ischemic), chronic heart failure, thromboembolic conditions and cardiac arrhythmias. Rupture of aneurysms against a background of hypertension with internal bleeding is also possible [29–33]. Cardiovascular diseases accounted for (32.8–40.1) % of all palliative adult patients and (1.6–2.3) % of children with palliative diagnoses in Ukraine for the period 2018–2020 according to the calculation of the need for PHC in Ukraine.

The causes of death in adult dementia (F72–F79 according to ICD-10) and severe and profound mental retardation in children (F00–F03 according to ICD-10) are swallowing disorders and related asphyxia and aspiration pneumonia; urinary tract infections up to septic conditions; pressure ulcers and their infectious complications; anorexia; treatment complications [34–37]. An important aspect of organizing PHC for these categories of palliative patients is the resumption of the collection of statistical data on morbidity, which was discontinued in Ukraine in 2019.

The causes of death from tuberculosis (A15–A19 according to ICD-10) are bronchial obstruction and respiratory failure; massive pulmonary hemorrhage; HIV infection (in combination with tuberculosis, the stage of this disease is defined as AIDS); meningitis. The infectious process threatens the life of the patient when infected with a pathogen with multidrug resistance to antibiotics [38–41]. In 2022, tuberculosis was the second leading cause of death from infectious diseases in the world, second only to COVID-19 (7.5 million new cases of infection). In 2023, it was in first place (8.2 million new cases of infection). At the same time, the elderly and people with disabilities are at risk and often require palliative care [42–45].

The causes of death in diabetes mellitus (E10–E14 according to ICD-10) are diabetic coma, vascular crises, renal failure, infectious complications (up to sepsis) due to the development of gangrene of the lower extremities, and pressure sores [46].

The causes of death in rheumatoid arthritis (M05–M06 according to ICD-10) are mainly infectious complications (up to sepsis) of immobility caused by the disease (bedsores, pneumonia) and complications of treatment (primarily immunosuppressants, which reduce the body's resistance to infectious diseases and can cause liver fibrosis) [47–49]. Fibrosis and cirrhosis of the liver (K74 according to ICD-10) are also considered as palliative conditions in adults and children. Most often, their occurrence is associated with chronic hepatitis (K73, K75.2, K75.3 according to ICD-10), and death is caused by liver failure, bleeding, malignancy (liver cancer), infectious complications of immobility in these diseases (skin infections, pneumonia), which can cause sepsis [50].

The causes of death in HIV infection are the development of the final stage of the disease (AIDS) and related infectious and oncological processes (B20–B24 according to ICD-10). Due to the ineffectiveness of immune defense, even

opportunistic infections can cause severe consequences, and the range of possible oncological diagnoses is significantly expanded (for example, due to Kaposi's sarcoma). NeuroAIDS can also be a direct cause of death. In war conditions, temporarily displaced persons and migrants with HIV-positive status may be deprived of access to antiretroviral therapy, which can accelerate the development of AIDS and its fatal complications [51–53].

The causes of death in Chronic Obstructive Pulmonary Disease (COPD) (J43–J47 according to ICD-10) are respiratory failure due to pneumonia, bronchial obstruction, destruction of lung tissue affected by the infectious process, and tumor destruction. Treatment complications are also possible: allergic reactions up to anaphylaxis, cardiac arrhythmias, thromboembolism, steroid insufficiency due to long-term treatment with inhaled corticosteroids. Chronic lack of oxygen can cause heart failure. The onset of death is significantly accelerated by the widespread use of tobacco smoking in the world [54–57]. Even before the start of the COVID-19 pandemic, COPD was one of the leading causes of death in the world. Thus, in 2016, the disease caused more than 3 million deaths and took 3rd place among the 10 leading causes of death [56]. When collecting data on causes of death, COPD should be counted separately from deaths caused by COVID-19. But in practice, these causes were often not separated.

The causes of death in kidney diseases (N00–N15, N20–N23 according to ICD-10) are renal failure, uremia, infectious complications of inflammatory processes in the kidneys. Severe complications of treatment are also possible: the development of an infectious process at the site of access to the vessels during dialysis, malignancy of kidney tumors during dialysis, gastrointestinal bleeding from damage to the mucous membranes by oral drugs, cardiac arrhythmias due to deviations from the norm of potassium content in the blood caused by treatment with loop and thiazide diuretics, angiotensin-converting enzyme inhibitors [58–63].

The causes of death in cystic fibrosis (E84 according to ICD-10) are respiratory, cardiovascular and hepatic failure, cystic fibrosis of the pancreas and infectious complications of the disease, up to sepsis [64; 65]. Insufficiency of organs and organ systems is also a cause of death in children with mucopolysaccharidosis (E76 according to ICD-10), but in addition to cardiovascular, respiratory and hepatic failure, renal failure should be added.

Other causes of death are seizures that damage the brain, arrhythmias and infectious complications [66; 67].

The causes of death in congenital malformations of newborns (Q00–Q99 according to ICD-10) are the absence or underdevelopment of organs, causing all possible types of organ failure, immediately after birth or during the growth and development of the child. Malformations that are present in the nervous system can cause seizures and paralysis. Complications of surgical treatment of these patients can also affect vital signs [68–71].

Perinatal conditions that lead to death and require palliative care for children (P05–P96 according to ICD-10) may be associated with congenital malformations [72], prematurity, pathology of pregnant women (including extragenital), fetal asphyxia, bleeding of pregnant women and women in labor, infections of pregnant women, fetus and newborn [73–75].

The causes of death in cerebral palsy (G80 according to ICD-10) may include decompensation of the underlying disease with impaired nervous regulation of the respiratory process and the development of acute heart failure, aspiration pneumonia, thromboembolic conditions, seizures, tumor malignancy, infectious processes of the urinary system up to sepsis [76–78].

Inflammatory diseases of the Central Nervous System (CNS) (E70.0 according to ICD-10) lead to death due to depression of the respiratory center, additional damage to nerve structures during epileptic seizures, as well as suicides in a state of depression, malignancy of tumors and complications of treatment [79–81]. In turn, epilepsy (G40 according to ICD-10) can cause Sudden Unexpected Death in Epilepsy (SUDEP) due to damage to nerve centers during an attack with a stroke, trauma (especially when falling during an attack). Drowning during an attack and suicide in depressive states are also possible [82; 83].

Multiple sclerosis (G35 according to ICD-10) can cause death due to the development of pneumonia, vascular crises, pulmonary embolism, infectious complications of immobility (bedsores, urinary tract infections), up to sepsis, and suicide in depressive states [84–87].

The medical and social component of preventing most premature deaths of palliative patients consists of promoting timely examination and treatment of diseases with controllable and condi-

tionally controllable risk factors, promoting vaccinations, safe sex, quitting tobacco smoking, recreational drug use and alcohol abuse, implementing anti-epidemic rules, and building partnerships between patients and doctors in health care [88–93].

### Conclusions

The causes of death have been studied for diseases listed as palliative in severe cases and in the presence of complications. The analysis allows us to deepen our understanding of the practical aspects of organizing palliative and hospice care in terms of meeting the needs of palliative patients, adults and children. The summary of determining the causes of death allows us to group these causes into organ and system failure (cardiovascular, respiratory, hepatic and renal); vascular crises (cerebral strokes and myocardial infarctions, cardiac arrest due to rhythm disturbances); asphyxia (fetal, adults due to food aspiration, bronchial obstruction); thromboembolic conditions (including pulmonary embolism); infectious complications up to sepsis, chronic intoxication (cancerous, including during tumor decay; uremia; against the background of multi-resistance of microflora to antibiotics); tumor growth in other organs with disruption of their vital functions, metastasis; malignancy of benign tumors; complications of treatment (including excessive sedation, which caused premature death; electrolyte imbalance; anaphylaxis of unsuccessful surgical interventions and resuscitation); brain and spinal cord lesions due to epileptic seizures, injuries, inflammatory processes; endocrine comas; gangrene and bedsores; severe immunodeficiency; underdevelopment or absence of organs in congenital malformations; prematurity; suicides in depressive states.

### DECLARATIONS:

#### Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

#### Statement of Ethics

The authors have no ethical conflicts to disclosure.

#### Data Transparency

The data can be requested from the authors.

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All authors give their consent to publication.



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