

**PUBLIC
HEALTH
CENTER**

ANALYSIS OF THE HIV MORTALITY SURVEILLANCE SYSTEM AND HOSPITAL-BASED MONITORING OF HIV-ASSOCIATED MORTALITY IN UKRAINE

Odesa



2024

AUTHORS

Svitlana Baltina¹, Natalia Buhaienko¹, Violetta Martsynovska¹, Anna Meteliuk³, Ludmyla Dobrovolska², Marianna Azarskova², Iryna Adrianova¹, Oleksandra Sheiko¹, Oleksandra Sadkova³

(1) Public Health Center of the Ministry of Health of Ukraine

(2) U. S. Centers for Disease Control and Prevention

(3) Independent consultants

ACKNOWLEDGEMENTS

We would like to express our sincere gratitude to the hospital staff in Odesa (site coordinators) who participated in the study for their dedication to the process despite the difficult times:

Feodora Dimitrova	Head of Pathology Department and pathologist, Odesa City Clinical Hospital No. 1
Maryna Mosina	Pathologist, Odesa Regional Clinical Hospital
Serhii Shaposhnikov	Head of the Pathology Department, Odesa City Clinical Hospital No. 5
Olha Zaporozhets	Pathologist, Odesa Regional Clinical Oncology Center
Svitlana Moskalenko	Pathologist, Odesa Regional Clinical Oncology Center
Petro Kuzyk	Associate Professor, Department of Pathology, O.O. Bohomolets National Medical University

DISCLAIMER

Support for the HIV epidemiological surveillance system and laboratory management/quality improvement system of the Ministry of Health of Ukraine, improvement of strategic information use and public health capacity building within the framework of the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) and the Cooperation Agreement NU2GGH002375 "Strengthening HIV Treatment, Laboratory Network Capacity Building, Substitution Therapy and Programme Monitoring in Ukraine within the framework of the U.S. President's Emergency Plan for AIDS Relief (PEPFAR)" are implemented by the Public Health Center of the Ministry of Health of Ukraine.

The findings and conclusions presented in this report are those of the author(s) and do not necessarily reflect the official position of the agencies providing project funding.

CONTENTS

Authors	2
Acknowledgements	2
Disclaimers	3
Abbreviations and acronyms	5
Abstract	6
1 Introduction	7
1.1 Reference information	8
1.2 Rationale.....	9
1.3 Purpose	10
1.4 Tasks.....	10
2 DESIGN AND METHODOLOGY	11
2.1 Rationale for conducting the study in Odesa.....	11
2.1.1 Site selection	11
2.1.2 Population, inclusion and exclusion criteria	12
2.1.3 Sample size calculation	12
2.1.4 Sampling method.....	13
2.1.5 Data sources.....	13
2.1.6 Variables.....	14
2.1.7 Procedures in pathology departments and laboratories	14
2.1.8 Ethical considerations.....	18
3 Data management and analysis	18
4 Results	19
4.1 Study population.....	20
4.2 HIV-positive cases	21
4.3 Bivariate analysis	22
4.4 Multivariate analysis	24
4.5 Quality assessment of testing	24
4.6 Features of death registration documentation and information flow.....	24
5 Discussion	27
5.1 Brief summary of findings and comparison with other studies.....	27
6 Recommendations and next steps	29
Appendix	31
Table 1. Characteristics of study participants who died in the period from August 2023 to March 2024, Odesa (n = 1502).....	31
table 2. Causes of death, viral load, and diagnosis of hiv among deceased hiv-positive individuals based on testing results (n = 53).....	33
table 3. Characteristics of study participants, stratified by sex, who died in the period from August 2023 to March 2024 in Odesa (n = 1502)	34
table 4. Age characteristics of study participants who died in the period from August 2023 to March 2024, Odesa (n = 1502)	36
table 5. Independent correlates of a positive HIV test result after death (n = 1502).....	38

ABBREVIATIONS AND ACRONYMS

AIDS	acquired immunodeficiency syndrome
ART	antiretroviral therapy
DBS	dried blood spots
HIV	human immunodeficiency virus
ICD-10	International Classification of Diseases, 10th Revision
MOH	Ministry of Health
PEPFAR	The US President's Emergency Plan for AIDS Relief
PLHIV	people living with HIV
RDT	rapid diagnostic test
SOP	standard operating procedure
IS	Information System
MSSDIS	Monitoring Information System
MSSD	Monitoring Socially Significant Diseases
UPHC	Public Health Center of the Ministry of Health of Ukraine
VL	viral load

ABSTRACT

All-cause and cause-specific mortality rates are important indicators of population health status. Mortality surveillance provides key data for monitoring public health trends and strategic planning and can support advocacy efforts for vital public health interventions. It also allows tracking the epidemiology of mortality over time and documenting the impact of diseases and public health interventions on population health. Comprehensive mortality surveillance typically requires public health infrastructure, including a civil registration and vital statistics system.

In Ukraine, the system for monitoring HIV-related mortality has significant shortcomings, particularly due to imperfect death registration and inaccuracies in determining the causes of death, including those related to HIV. In the absence of an effective civil registration and vital statistics system, pathology departments in healthcare facilities may serve as a valuable alternative for collecting data on the causes of mortality. Therefore, to gain a deeper understanding of the impact of HIV/AIDS on mortality rates and overcome existing difficulties in data registration, a study on HIV-related mortality was conducted for the first time in Ukraine in from July to December 2021 in the pathology departments of healthcare facilities in Kyiv. In 2024, the study was extended to Odesa, a location with a high burden of HIV in Ukraine.

The purpose of the study "Analysis of the HIV Mortality Surveillance System and Hospital-based Monitoring of HIV-Associated Mortality in Ukraine (Odesa)" was to assess the feasibility of integrating HIV mortality surveillance into routine pathology service operations. In this study, we aimed to determine the proportion of diagnosed and undiagnosed HIV-associated deaths among adults using minimally invasive but highly sensitive methods. To confirm the HIV status of deceased individuals, we used three different rapid tests according to the national testing algorithm. Three consecutive reactive results indicated the HIV-positive status of the deceased.

Among the 1502 deceased individuals in the study cohort, HIV status at the time of death was missing from medical records for 81.3%, indicated as HIV-positive for 3.4%, and as HIV-negative for 15.3%. The majority of the deceased were older than 65 years (69.2%), 20.1% belonged to the 55-64 age category, 8.9% to the 36-50 age category, and 1.7% were aged 18-35 years. Approximately half of the study participants were women (52.2%), the majority lived in Odesa or the Odesa region (96.1%), and died in a healthcare facility where they were treated (82.6%). Medical records for a very small proportion of participants (1.3%) indicated the use of injectable drugs. Autopsies were performed on 65.2% of the deceased, with the predominant causes of death being diseases of the circulatory system (55.2%) and neoplasms (18%). Testing of 1502 blood samples identified 53 HIV-positive deceased individuals, of whom women (52.2%) and individuals under 65 years of age (69.2%) predominated, and 1.3% had a history of injecting drug use. Fifty-one of the 53 HIV-positive participants (96.2%) were aware of their HIV status before death, and two (3.8%) were diagnosed with HIV postmortem. Overall, 3.5% of the entire study cohort were HIV-positive. Most HIV-positive individuals died as a result of HIV progression (79.2%).

Building on the previous [research experience in Kyiv](#), we hope to contribute to expanding the surveillance of HIV-related hospital mortality in Ukraine.

Ukraine is among the countries with the highest burden of HIV/AIDS in the Eastern Europe and Central Asia region. As of January 2023, the estimated number of people living with HIV (PLHIV) was 248,000, including the non-government-controlled areas.¹

In 2023, 11,658 new cases of HIV, 3,351 cases of AIDS, and 1,474 deaths from AIDS-related diseases were registered in Ukraine²[1] The HIV incidence rate was 28.4 per 100,000 population and varied by region: more than 70% of all people newly diagnosed with HIV were concentrated in a few regions (Dnipropetrovsk region (88.6 per 100,000 population), Odesa region (78.3), Mykolaiv region (42.1), Kyiv region (42), Chernihiv region (38.6), Kirovohrad region (37.2) Kyiv city (36.8).¹

As of January 1, 2024, there were 157,435 PLHIV (384 per 100,000 population) registered in healthcare facilities providing medical services to PLHIV, of whom 48,541 people were currently diagnosed with AIDS (118.4 per 100,000 population). In 2023, the percentage of individuals with a baseline CD4 count <200 cells/ mm³ was 38.4%, and the antiretroviral therapy (ART) coverage rate for individuals involved in the HIV care system was 77%.

The majority of PLHIV live in urban areas, where 70% of new HIV cases were registered in 2023; most of them are men (55%), and most cases occur in the 25-49 age group (70%). It is important to note that the epidemic is gradually aging (17.4% of PLHIV are people aged 50 years and older). There is a high proportion of PLHIV diagnosed at late stage of infection: 39% had a baseline CD4 count <350 cells/ mm³ in 2023³.

According to official statistics, the most common route of HIV transmission is unprotected heterosexual contact (65% of new HIV cases in 2023), although risky behavior among populations at high risk to HIV, especially people who inject drugs (PWID), remains a significant factor in HIV infection (22.5%). A study on the assessment of HIV transmission routes, conducted by the International Charitable Foundation "Alliance for Public Health", indicates a potential misclassification of HIV transmission routes in the routine case registration system and estimates that the proportion of HIV-positive PWID reaches 60% of newly registered HIV cases⁴.

Monitoring HIV-related mortality is part of HIV surveillance and, when compared with other data, allows for a comprehensive assessment of HIV epidemic control measures. An increase in this indicator may reflect delayed HIV diagnosis and late initiation of antiretroviral therapy, resulting in a higher proportion of individuals progressing to advanced stages of infection. Conversely, a decrease may indicate earlier testing, timely initiation of treatment, and improved effectiveness of HIV care services. In Ukraine, monitoring deaths among HIV-positive people has been a routine practice since 1987 and is regulated by the legal framework. Since the beginning of the epidemic, as of January 1, 2024, a total of 58,242 AIDS-related deaths have been officially registered in Ukraine.

1 Predicting results using Spectrum software

2 Operational information on officially registered cases of HIV and AIDS and the number of AIDS-related deaths [hiv_aids_statistics_operinfo_2023.12](#)

3 Reporting form No. 2 HIV/AIDS "Report on individuals with conditions and diseases caused by the human immunodeficiency virus (HIV), for the year 20____" (annual), 2017-2021.

4 <https://bmcpublihealth.biomedcentral.com/track/pdf/10.1186/s12889-020-09373-2.pdf>

Between 2018 and 2023, more than 13,219 PLHIV died from AIDS-related causes, accounting for 22.6% of all recorded deaths among PLHIV in Ukraine. Over the last ten years, there has been a decrease in the number of new AIDS-related deaths. This trend is estimated to continue in the projected period until 2025⁵², indicating an increase in the life expectancy of people living with HIV due to expanded access to ART.

Available information on causes of death from various data sources indicates that there is a problem of underreporting of HIV-related deaths in Ukraine⁶. The HIV surveillance system should include the monitoring of deaths among both diagnosed and undiagnosed HIV-positive people who were not linked to treatment. In this context, improving approaches to the diagnosis and registration of HIV-related deaths remains one of the most important areas for improving the reliability of data in the current HIV-associated mortality surveillance system in Ukraine.

1.1 REFERENCE INFORMATION

According to the latest available data collected at the planning stage of this study, 42,422 people died in the Odesa region in 2021 (1805 per 100,000 population). Of these deaths, 465 were among PLHIV (19.6 per 100,000 population). In 2023, there were 355 deaths among PLHIV (15 per 100,000 population).⁷⁸

In 2021, 14,348 autopsies were performed in Odesa region (in 2020- 12,693 autopsies performed), of which 2,895 autopsies were performed by pathologists (in 2020 - 2,952 autopsies were performed by pathologist) and 11,453 (in 2020 - 9,741) by forensic medical experts. The largest number of autopsies was performed by facilities that provide general inpatient and emergency medical care, as well as anesthesiology and intensive care units.

At the end of 2021, the city of Odesa had 9 pathological facilities organized as follows:

4 pathology departments of the Municipal Institution "Odesa Regional Pathology Bureau" of the Odesa Regional Council:

Suvorov Pathology Department,

Central Pathology Department,

Slobidka Pathology Department,

Oncology Pathology Department

And 5 departments based in healthcare facilities located within the city, which are not part of the Municipal Institution "Odesa Regional Pathology Bureau" of the Odesa Regional Council:

Municipal Non-profit Enterprise (MNE) "City Clinical Hospital No. 1;

⁵ National Assessment of the HIV/AIDS Situation in Ukraine as of the beginning of 2022: https://npsi.phc.org.ua/HIV_Monitoring?indicator=100&tab=description

⁶ Assessment of the current status of epidemiological surveillance of HIV-related mortality in Ukraine as of 2020: https://aph.org.ua/wp-content/uploads/2020/10/Otsinka-smertnosti_2020_web.pdf

⁷ <https://www.ukrstat.gov.ua>

⁸ Reporting form No. 2 HIV/AIDS "Report on persons with conditions and diseases caused by the human immunodeficiency virus (HIV) for 20____"

MNE "Odesa City Clinical Hospital No. 3 named after Professor L. Aleinikova" of the Odesa City Council;

MNE "City Clinical Infectious Diseases Hospital" of the Odesa City Council;

MNE "Odesa Regional Clinical Medical Center" of the Odesa Regional Council;

University Clinic of Odesa National Medical University

A reorganization occurred within the Odesa region in 2022, whereby the Municipal Institution "Odesa Regional Pathology Bureau" of the Odesa Regional Council was restructured and incorporated into the MNE "Odesa Regional Hospital" of the Odesa Regional Council and the MNE "Odesa Regional Clinical Oncology Center" of the Odesa Regional Council.

1.2 RATIONALE

Accurate data on mortality among PLHIV are crucial for planning interventions aimed at increasing survival rates. Accurate cause-of-death data, used within mortality surveillance, allow for the tracking of HIV-related deaths, which is an important indicator when evaluating the impact of HIV/AIDS response interventions. Correct data on causes of death are essential for defining public health strategies, research agendas, and program planning.

Guidelines on autopsy procedures for monitoring HIV-related mortality and determining the cause of death have yet to be approved at the national level. Surveillance form 502-2/o is based on the ICD-10 classification of causes of death, whereas cause-of-death coding in subsequent reporting forms (quarterly form No. 1 on HIV/AIDS and annual form No. 2 on HIV/AIDS) is not consistent with ICD-10, making it impossible for the State Statistics Service to properly verify the data. Mortality statistics for HIV-positive individuals are not systematic, and information verification between pathology institutions, healthcare facilities providing medical supervision for PLHIV, and the statistics service is complex and not performed regularly. This leads to an underestimation of HIV-related mortality rates and causes of death. Given that the imperfect overall system for registering deaths is imperfect and the problematic issues regarding the reliability of the HIV-associated mortality rate, this study will help the country to collect data and information on HIV-related mortality, identify and address gaps in cause-of-death coding, enable the tracking of mortality among undiagnosed PLHIV, and assess progress in implementing the HIV/AIDS response program. All this will allow for obtaining accurate data for responding to and monitoring the HIV epidemic. The study will focus on measuring HIV-related mortality in the city of Odesa and will subsequently be expanded to other regions of Ukraine.

1.3 PURPOSE

The main purpose is to provide information on the overall improvement of the standard routine approach to HIV-associated mortality surveillance in Ukraine.

1.4 TASKS

The main task

The main task is to establish appropriate procedures for measuring HIV-associated mortality in Ukraine.

Specific tasks

1. Identify the main data sources for HIV-associated mortality, understand the data flow and approaches to reporting, and compare data obtained from different sources.
2. Assess the current situation regarding the registration of deaths among HIV-positive people, practices of determining the underlying cause of death, and cross-checking and validation of data.
3. Evaluate existing practices of HIV diagnosis among deceased individuals.
4. Analyze current trends in HIV-related and non-HIV-associated mortality rates.
5. Determine the presence of HIV infection and the level of HIV-1 viral load (VL) among the deceased with unknown HIV status in Odesa.
6. Establish the causes of death among the deceased individuals with HIV-positive status at surveillance sites in Odesa.
7. Identify HIV-related correlations among the data obtained during the study in Odesa.
8. Estimate the percentage of HIV cases that were not diagnosed during their lifetime.
9. Develop recommendations for improving HIV-associated mortality surveillance based on routine practices and data.

2 DESIGN AND METHODOLOGY

2.1 RATIONALE FOR CONDUCTING THE STUDY IN ODESA

2.1.1 SITE SELECTION

Odesa, a port and resort city, was selected as the study site because it has the resources for thorough monitoring, a developed infrastructure, and a diverse socio-demographic population representing different regions of Ukraine. Only pathology departments, under the authority of the Departments of Health of the Odesa City Council and Odesa Region State Administration, were selected for the study, excluding national-level facilities.

The selection was based on the number of deceased individuals admitted to the Pathology Department of the facility (the hospital with the largest caseload) and the representation of various population groups and city districts.

Specifically, according to Table 1, the following sites were selected:

- City Clinical Hospital No. 1, where deceased homeless people and those brought in by ambulance are taken;
- City Clinical Hospital No. 5, where individuals deceased with a COVID-19 diagnosis and those who died in the neurology department and the department of internal medicine are taken;
- Suvorov Department of the Odesa Regional Pathology Bureau, where people who were admitted to the Odesa Regional Clinical Hospital for treatment before death (after the reorganization in 2022, Odesa Regional Clinical Hospital) are taken;
- Central and Slobidka Departments of the Odesa Regional Pathology Bureau: (after the reorganization in 2022, Departments No. 1 and No. 2 of the Odesa Regional Clinical Oncology Center), where deceased HIV-positive individuals who were under medical supervision at the Odesa Regional Center for Socially Significant Diseases, and those who died from infectious, oncological, and mental diseases are taken.

2.1.2 POPULATION, INCLUSION, AND EXCLUSION CRITERIA

Population: The study population included deceased adults aged 18 years and older who were consecutively admitted to the pathology departments of 4 selected hospitals in Odesa during the study period (August 2023 – March 2024).

Inclusion criteria:

- Bodies of deceased adults aged 18 years and older
- Possibility of collecting blood samples

Exclusion criteria:

- Bodies of deceased individuals younger than 18 years
- Bodies of deceased individuals from whom blood samples could not be taken and/or whose condition deteriorated at the time of blood collection.

2.1.3 SAMPLE SIZE CALCULATION

The sample size was calculated to estimate the HIV seroprevalence among deceased adults (aged 18 years and older) in Odesa with adequate precision. The primary criterion used for this calculation was the overall HIV seroprevalence rate among deceased individuals aged 18 years and older.

Using data from 2021, the total number of registered adult deaths in Odesa was $N = 18,426$. Assuming a conservative estimated HIV prevalence (p) of 50%—which maximizes sample size when the true prevalence is unknown—a 95% confidence level, and a 5% margin of error ($d = 0.05$) were applied. To account for the use of cluster sampling, a design effect (DEFF) of 3 was incorporated.

The sample size was calculated using OpenEpi (Version 3), with the *SSPropor* tool, based on the following formula:

$$n = [\text{DEFF} \times N \times p(1-p)] / [(d^2 / Z_{1-\alpha/2}^2) \times (N-1) + p(1-p)]$$

Where:

- **N** – total population size (18,426, the number of registered adult deaths in Odesa in 2021)
- **p** – estimated HIV prevalence (0.5)
- **d** – margin of error (0.05)
- **Z_{1- α /2}** – Z-score corresponding to a 95% confidence level (1.96)
- **DEFF** – design effect (3)

This yielded an initial required sample size of 1,152 deceased individuals. Accounting for an expected 20% sample loss, the final target sample size was adjusted to $1,152 / 0.80 = 1,440$ deceased individuals. To facilitate comparison with the results of a similar study conducted in Kyiv, the sample size for Odesa was rounded up to 1,500 deceased individuals.

The total sample size was proportionally distributed among the participating institutions, taking rounding into account, as detailed below.

Table 1. Selected facilities and sample distribution

List of healthcare facilities	Number of autopsies per year	% per facility	Sample distribution (N=1500)
City Clinical Hospital No. 1	1101	20 %	298
City Clinical Hospital No. 5	1323	24 %	359
Suvorov Department of the Odesa Regional Pathology Bureau (Odesa Regional Clinical Hospital)	1038	19 %	281
Central Department of the Odesa Regional Pathology Bureau, (Odesa Regional Clinical Oncology Center)	856	15 %	232
Slobidka Department of the Odesa Regional Pathology Bureau, (Odesa Regional Clinical Oncology Center)	1219	22 %	330
Total	5537	100 %	1500

2.1.4 SAMPLING METHOD

We used consecutive sampling of all deceased bodies eligible for autopsy that were delivered to the designated pathology departments. The sampling duration was consistent across all departments to ensure the proportionality of the sample. The process of collecting blood samples for the study continued until the target sample size for each facility was reached.

2.1.5 DATA SOURCES

Most of the data were collected by a pathologist at the site involved in the study by filling out a data collection form on causes of death and HIV status (hereinafter – Data Collection Form). Information accessible to the pathologist was obtained from primary medical record forms: No. 003/o "Inpatient Medical Record ____ " and No. 013/o Autopsy Report No. __ ". The Data Collection Form also included fields for recording HIV test results and for the collection of dried blood spot (DBS) samples intended for VL testing. To determine if the deceased individual had been previously registered as HIV-positive, we used the National Information System Monitoring Socially Significant Diseases (IS MSSD) to check for existing records in the registry. The Case++¹⁰³ code was used to search for data on HIV-positive deceased individuals in the IS MSSD, allowing obtaining information for the "Registered in IS MSSD" (yes/no) variable in the Data Collection Form.

2.1.6 VARIABLES

Social and demographic, clinical, and laboratory data were collected and recorded, which included the following information: date of birth, place of residence, sex, occupation, social status, dates of death and autopsy, clinical and pathological diagnoses, cause of death, information on HIV status, HIV testing date and result, viral load testing date and result, and registration of the individual in the IS MSSD.

2.1.7 PROCEDURES IN PATHOLOGY DEPARTMENTS AND LABORATORIES

Blood Sample Collection

Standard operating procedures (SOPs) were developed and used for blood collection and laboratory procedures during the study. A pathologist involved in the study, during the examination of the deceased body and the autopsy procedure, collected blood samples from deceased individuals who met the inclusion criteria of the study, according to the Study Protocol. Blood collection was performed from the heart or large blood vessels using an 18-gauge, 12 cm long intravenous cannula needle attached to a 20 ml syringe. The volume of the blood sample was at least 1 ml.

Afterward, the blood sample was transferred into a 600 µl microtube containing the anticoagulant – potassium salt K2 (K3) ethylenediaminetetraacetic acid (EDTA). Blood collection was performed as soon as possible after the body arrived at the pathology department, usually within 48 hours. A 600 µl sample of unclotted blood was considered

¹⁰ Individual number of the deceased individual, generated by the algorithm of the Case++ database: Code generation rule: 1-3 - first three letters of the surname; 4-5 - first two letters of the name; 6-7 - first two letters of the patronymic; 8-9 - birthday; 10-11 - month of birth; 12-13 - year of birth; 14 - client's sex (m/f)

acceptable for further research. The blood collection procedure was documented in the "Log of Blood Collection and Results of Tests for HIV Serological Markers Using Rapid Diagnostic Tests" (form № 498-5/o16). Blood samples were used for HIV testing using different types of rapid diagnostic tests (RDTs). In the event of receiving three consecutive positive HIV test results using RDTs, the sample was considered to contain HIV markers and was used to prepare DBS samples for VL determination.

For the preparation of DBS, blood samples from individuals with confirmed HIV-positive status were used; they were placed on special filter paper and dried. To ensure the quality of the study, this procedure was practiced by pathologists performing autopsies and by the Reference Laboratory for Diagnosis of HIV/AIDS, Viral and Especially Dangerous Pathogens of the UPHC, which monitored sample collection. In addition, DBS samples were collected from HIV-negative deceased individuals (10% of the total number), in which the VL was also determined.

HIV testing

The determination of the deceased individual's HIV status using RDTs was carried out on-site immediately after blood collection by sequentially using a combination of three immunochromatographic tests. HIV testing was carried out in accordance with the Procedure for HIV Infection Testing and Quality Assurance of Tests approved by Order No. 794 of the Ministry of Health of Ukraine dated 2019 (as amended). The testing algorithm is shown below (Fig. 1).

The first RDT was used during screening to detect serological markers of HIV, namely HIV-1/2 using an HIV antibody rapid test, colloidal gold device (Beijing Wantai).

To confirm an HIV-positive result of the first screening RDT, immunochromatographic antibody test kits (First Response HIV-1/2 v.3.0) were used.⁴

If both the initial screening and the confirmatory RDTs were positive, a third immunochromatographic antibody assay (HIV-1/2 Bioline 3.0) was performed for final confirmation.

All tests used in this algorithm detect HIV antibodies, not antigen.¹¹

¹¹The original name of all tests and their characteristics in terms of sensitivity and specificity:

Algorithm HIV testing:

1 st test: RT for Antibody to HIV (Colloidal Gold Device), Wantai: sens 100% (95%CI 99.2-100) spec 99.9% (95% CI 99.2-100)

If 1st + - 2 nd test; if - -Final

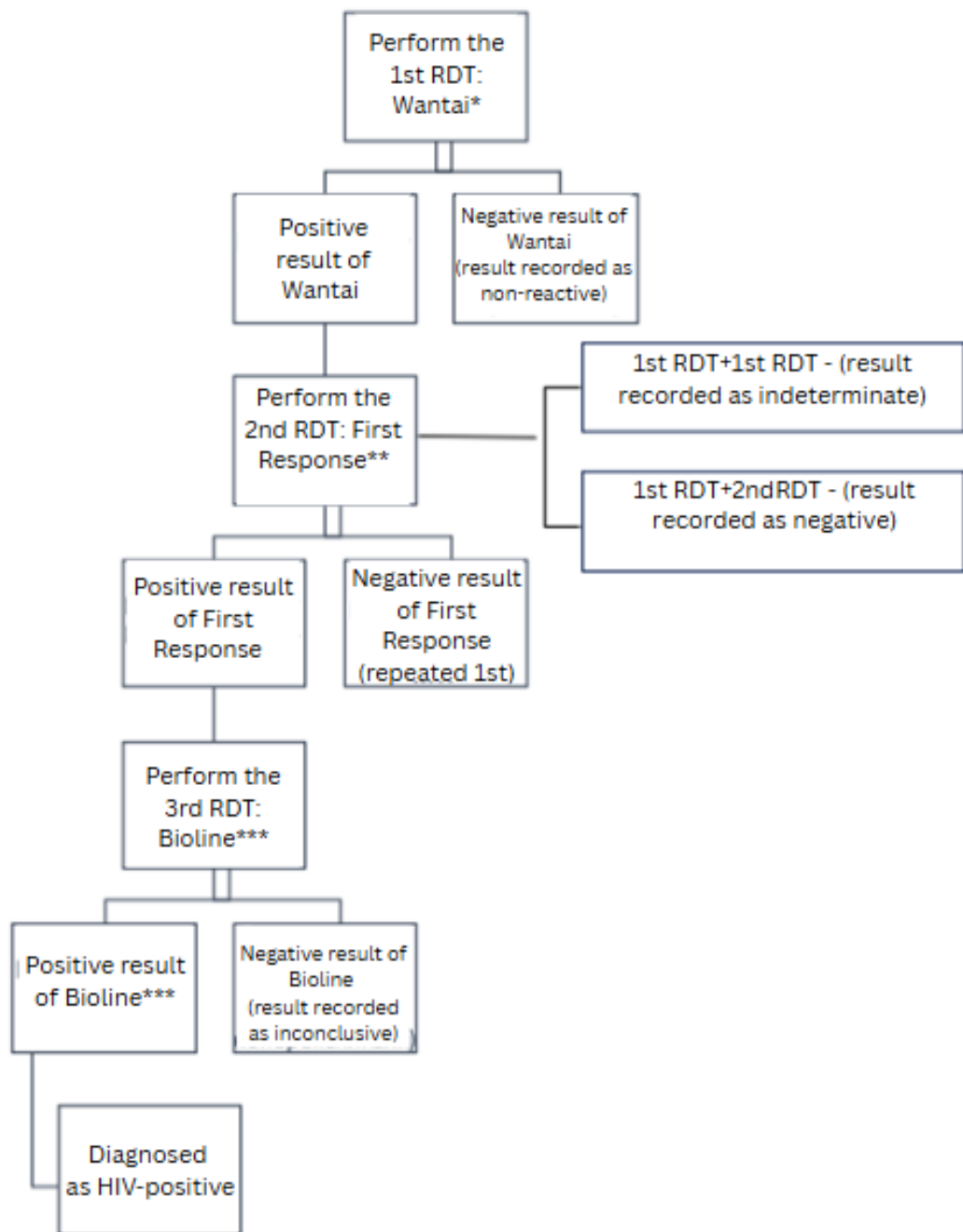
2 nd test First Response HIV 1-2-0 Card Test, Premier Medical Corp. Private Limited): sens 99.6% (95%CI 98-100) spec 100% (95% CI 98.4-100)

If 2nd + - 3 rd test; if - -repeat 1st test. If 1st test is + - inconclusive result; If 1st test is -, final negative result of testing

3 rd test BioLine HIV ½ 3.0, Abbott: sens 100% (95%CI 99.2-100) spec 99.9% (95% CI 99.2-100)

If 3rd + - final reactive result of testing (HIV status confirmed); if 3rd - inconclusive result

Fig. 1. Algorithm for using RDT in establishing the HIV status of a deceased individual



* HIV-1/2, rapid diagnostic test (RDT) for Antibody to HIV (Colloidal Gold-based rapid immunoassay kit), 10 tests (Wantai RDT, No.10, Beijing) screening tests.

** HIV-1/2 FIRST RESPONSE® HIV 1-2/O Rapid Test Cassette (Premier Medical Corporation Private Limited, India, No.5)

*** HIV-1/2, Bioline 3.0, No.25

The following procedure was applied:

After receiving a negative result of the first rapid test for HIV serological markers, the result was entered into the Data Collection Form as "negative" (HIV status negative). No further tests were performed.

If a reactive result was obtained from the first rapid test, the result was entered into the Data Collection Form, and a second rapid test for HIV serological markers was performed.

If an invalid result was obtained from the first or any subsequent (second or third) rapid test for HIV serological markers (absence of the control line), the testing procedure was repeated using a test of the same type

The results of the second rapid test could be positive or negative:

- If the second test result was negative (contradictory test results: first test positive, second test negative), repeat testing was performed using the first rapid test type; If the result of this repeat test (using the first test type) was negative, the final testing result was recorded as "negative".
- If the first test result was positive, the second test result was negative, and the repeat test using the first test type for HIV serological markers was positive, the final testing result is recorded as "indeterminate".
- If a positive result was obtained from the second test for HIV serological markers, testing continues using the third rapid test for HIV serological markers;

The results of testing using the third rapid HIV test can be positive or negative:

- If a positive result was obtained from the third test for HIV serological markers (meaning the results of the first and second tests were also positive), an HIV-positive status is registered.
- If a negative result was obtained from the third test for HIV serological markers (meaning the results of the first and second tests were positive), the final result is recorded as "indeterminate".

Collection and preparation of dried blood spot (DBS) samples

DBS samples were prepared from the blood samples of deceased individuals in the following cases:

- If positive results were obtained from all three RTs when testing the deceased person's blood;
- From 10% of participants with HIV-negative results on the first RT, selected randomly in each designated medical facility involved in the study, to ensure quality control of HIV testing using RDTs.

Laboratory testing

All DBS samples were tested to determine the HIV-1 viral load (using the Abbott Real Time HIV-1 Test) at the Reference Laboratory for Diagnosis of HIV/AIDS, Viral, and Especially Dangerous Pathogens of the UPHC, according to SOP.

2.1.8 ETHICAL CONSIDERATIONS

The Study Protocol was approved by the Ethics Committee of the UPHC (Kyiv, Ukraine; FWA00026980, valid until June 20, 2023). The Protocol was also reviewed in accordance with the UPHC procedures for the protection of human rights. The conclusions of the Ethics Committee comply with the requirements of: the Regulation on Medical Ethics of the MOH of Ukraine No. 281 dated November 1, 2002; the provisions and principles of the Declaration of Helsinki, adopted by the General Assembly of the World Medical Association (1964-2000); the International Code of Medical Ethics (1983); the Convention on Human Rights and Biomedicine of the Council of Europe (1997); relevant regulatory acts of the WHO and the Council for International Organizations of Medical Sciences.

All participating institutions administratively approved the activities conducted as part of the study "Analysis of the HIV-associated Mortality Surveillance System and Hospital-based Monitoring of HIV-associated Mortality in Ukraine (Odesa)".

The study was approved by the Centers for Disease Control and Prevention, USA, in accordance with CDC human research protection procedures and was determined to be research; however, CDC investigators were not engaged because they did not interact with human subjects and did not have access to identifiable data or specimens for research purposes (dated June 9, 2021, ID 0900f3eb81d41884).

3 DATA MANAGEMENT AND ANALYSIS

The CDC-approved English version of the Protocol with Appendices was translated into Ukrainian and verified for accuracy by both principal investigators.

All personnel involved in the study implementation received training on ensuring participant confidentiality and signed the Data Use and Personnel Confidentiality Agreement, which provided clarification on the procedures for handling confidential data and the responsibilities for breaching such procedures.

The study coordinator at each healthcare facility (participating hospital) entered data directly into the Qualtrics system (electronic data collection form) in accordance with the designated format. Specialists from the Reference Laboratory for Diagnosis of HIV/AIDS, Viral, and Especially Dangerous Pathogens of the UPHC provided data on VL results, which were also entered into the Qualtrics system. Two data registries, based on the Qualtrics Data Collection Forms and the VL results, were exported from the Qualtrics system and merged into a single analytical dataset in Excel format for further analysis.

During the study, the national research team conducted monthly monitoring visits to participating hospitals to verify study data and improve its quality.

For the preparation of this report, we conducted a descriptive analysis to review the main findings of the study. A more comprehensive manuscript analysis will be conducted based on the study.

4 RESULTS

The field stage of the study was conducted from August 2023 to March 2024.

The final distribution of the study sample and the number of collected samples was as follows (Table 2):

Table 2. Final distribution of the study sample

List of healthcare facilities	Number of deceased individuals tested for HIV	Of these, number of HIV-positive individuals	Proportion (%) of HIV-positive individuals	Number of collected DBS samples
City Clinical Hospital No. 1	586	21	3.6	60
City Clinical Hospital No. 5	72	1	1.3	7
Suvorov Department of the Odesa Regional Pathology Bureau (Odesa Regional Clinical Hospital)	281	1	0.3	28
Central Department of the Odesa Regional Pathology Bureau, (Odesa Regional Clinical Oncology Center)	330	4	1.2	33
Slobidka Department of the Odesa Regional Pathology Bureau, (Odesa Regional Clinical Oncology Center)	233	26	11.1	26
Total	1,502	53	3.5	154

4.1 STUDY POPULATION

General characteristics of all study participants

Table 1 of the Appendix presents the characteristics of the study participants who died during the period from August 2023 to March 2024 in Odesa, including demographic data and data on HIV-related mortality. Among the 1502 study participants, the majority were aged 65 years and older (69.2%), 20.1% were aged 51-64 years, 8.9% were aged 36-50 years, and 1.7% were aged 18-35 years. Women accounted for half (52.2%) of the study participants; the vast majority lived in Odesa city or Odesa region (96.1%) and died in healthcare facilities where they had been receiving treatment (82.6%). A small proportion of participants (1.3%) had a documented history of injecting drug use in their medical records. Autopsies were performed on 65.2% of the deceased individuals.

Characteristics of study participants related to HIV testing

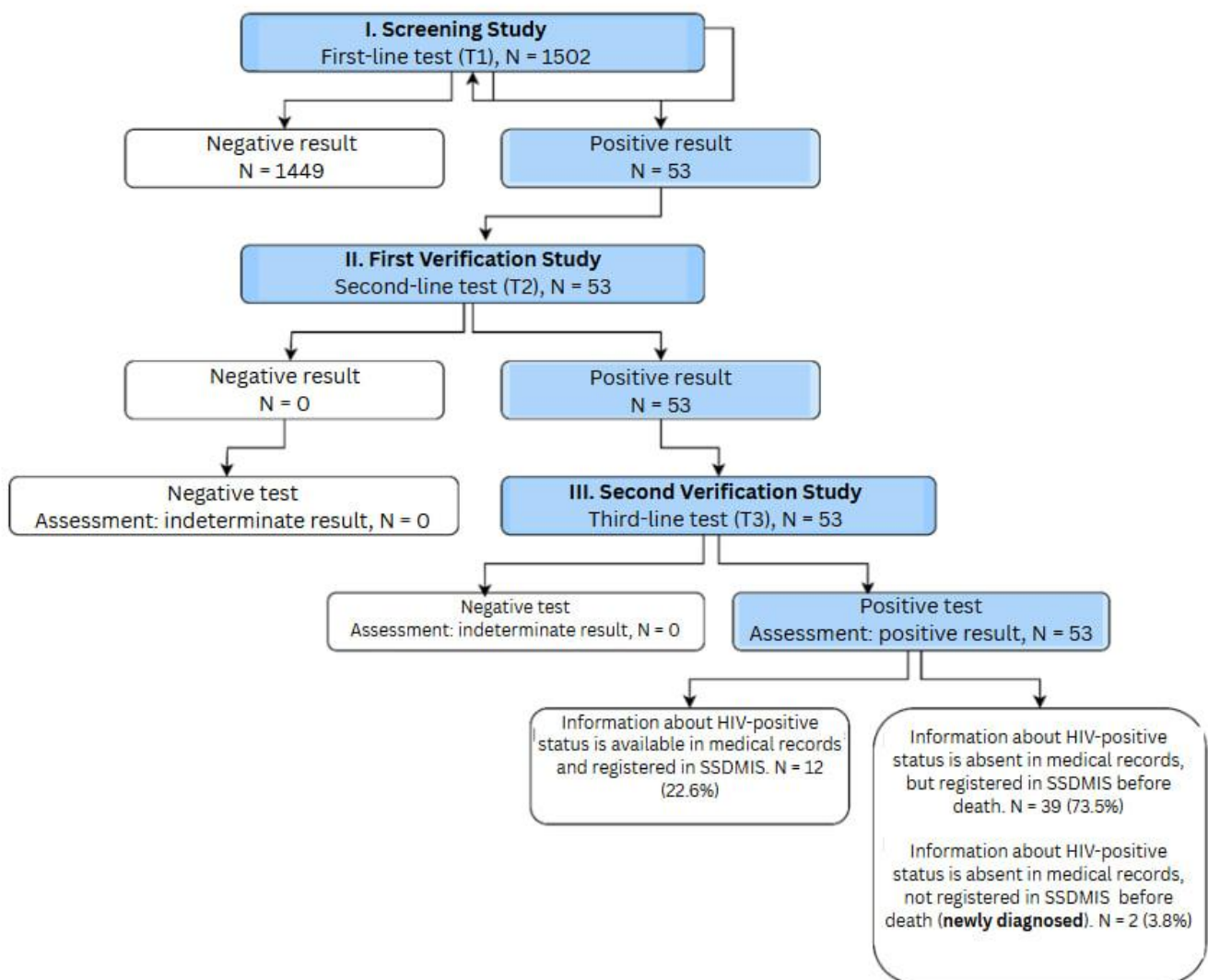
The medical records of the vast majority of study participants (81.2%; N = 1221) did not have information about their HIV status; 15.3% (N = 230) had information indicating an HIV-negative status before death, and 3.4% (N = 51) of participants were known to be HIV-positive before death. Fig. 2 presents the results of postmortem HIV testing.

Of the 1502 HIV tests conducted, 53 participants were HIV-positive on the initial screening test. According to the HIV testing algorithm outlined in Figure 1, second and third tests were conducted. Based on the testing results, 53 HIV-positive cases were confirmed, including:

- 12 (22.6%) deceased individuals with a known HIV-positive status before death according to medical records;
- 39 (73.6%) deceased individuals diagnosed with HIV postmortem who had no HIV status data in their medical records but were registered as HIV-positive in the IS MSSD;
- 2 (3.8%) deceased individuals diagnosed with HIV postmortem who had no HIV status data in their medical records and no record in the IS MSSD.

Overall, among the 53 deceased individuals with HIV-positive status, 51 were registered in the IS MSSD and therefore knew their HIV-positive status during their lifetime. Information on the HIV infection status of the remaining two HIV-positive deceased individuals was missing from both their medical records and the IS MSSD. Therefore, it can be assumed that in our study, the 2 deceased individuals with HIV-positive status represent previously undiagnosed cases of HIV infection, suggesting that the proportion of undiagnosed cases among the HIV-positive deceased in this sample was 3.8%. Overall, 3.5% of the deceased individuals in the study sample were HIV-positive.

Fig. 2. Results of postmortem HIV testing among deceased study participants (N = 1502)



4.2 HIV-POSITIVE CASES

Characteristics of individuals who received a positive HIV test result postmortem

Characteristics of individuals with HIV-positive status (N = 53), including demographic and other data related to the cause of death, are presented in **Table 1 of the Appendix**. Nearly 98% of the deceased HIV-infected individuals lived in the city of Odesa or the Odesa region during their lifetime, and the majority of them died in healthcare facilities (94.3%). More than half of the study participants were in the age group of 36-50 years (58.5%) and were male (52.8%).

In more than 90% of cases, information about the occupation of the deceased was not available, and the distribution by social status was as follows: injecting drug users accounted for 35.8% (n = 19), non-injecting drug users – 14.8% (n = 8), people with a history of imprisonment – 10.5% (n = 6), people with alcohol dependence – 31.6% (n = 17), homeless individuals – 5.5% (n = 3).

DBS samples were prepared for 53 HIV-positive deceased individuals, but a VL determination test was not performed for one DBS sample due to its untimely dispatch to the Reference Laboratory for Diagnostics of HIV/AIDS, Viral and Especially Dangerous Pathogens of the UPHC. In 27 (52.0%) deceased individuals, the VL was below 1,000 copies/mL, consistent with the standard threshold for viral suppression. In 25 (48%) individuals, the VL ranged from 839 to 3,189,247 copies/mL of plasma, of which in 11 (21%) deceased individuals, it was over 10,000 RNA copies/mL of blood. In one newly diagnosed HIV-positive deceased individual, VL was not determined.

Autopsies were performed on 31 (58.5%) HIV-positive deceased individuals. The majority of individuals died as a result of HIV-related causes (42 individuals; 79.2%).

AIDS-defining conditions identified at autopsy included:

- Cerebral toxoplasmosis – 57.1%
 - Multiple concurrent infections – 12.0%
 - Pneumocystis pneumonia – 9.5%
 - Extrapulmonary cryptococcosis – 9.5%
 - HIV-associated encephalopathy – 7.1%
 - Cervical cancer – 4.7%
- Corresponding causes of death and VL in HIV-positive deceased individuals (N = 53) are presented in **Table 2 of the Appendix**.

4.3 BIVARIATE ANALYSIS

Comparison of HIV-Positive and HIV-Negative Cases

Pearson's chi-square test was used for the categorical variables and the Fisher's exact test was used for the variables with small numbers for the bivariate analyses. The results of the bivariate analysis for comparing HIV-negative and HIV-positive cases are also presented in **Table 1 of the Appendix**. Statistically significant characteristics were:

- (a) age ($p < 0,0001$);
- (b) injecting drug use ($< 0,0001$);
- (c) place of death (0,0218);
- (d) autopsy ($p < 0,0001$);
- (e) whether the person's HIV-positive status was known before death ($p < 0,0001$);
- (f) infectious and parasitic diseases as the immediate cause of death ($p < 0,0001$);
- (g) diseases of the blood and blood-forming organs as the immediate cause of death (0,0256).

Stratified analysis by sex

The results of the bivariate analysis for comparing the characteristics of men and women are presented in **Table 3 of the Appendix**. Age was the only statistically significant characteristic ($p < 0.0001$).

Stratified analysis by age

The results of the bivariate analysis for comparing characteristics between individuals younger and older than 65 years are presented in **Table 5 of the Appendix**. Statistically significant characteristics were:

- (a) sex ($p < 0,0001$);
- (b) postmortem HIV status ($< 0,0001$);
- (c) injecting drug use ($< 0,0001$);
- (d) place of residence ($< 0,0001$);
- (e) place of death ($0,0004$);
- (d) autopsy ($p < 0,0001$);
- (e) confirmed COVID-19 diagnosis ($p < 0,0001$);
- (f) HIV status before the time of death ($p < 0,0001$);
- (g) immediate cause of death ($p < 0,0001$).

Causes of death

A list of all causes of death within this study, with a detailed breakdown by all disease categories according to ICD-10, is presented in **Table 4 of the Appendix**. Overall, the most common causes of death were diseases of the circulatory system (55.2%; $N = 829$) and neoplasms (18.0%; $N = 270$).

Among the 53 deceased individuals with HIV-positive status, the majority (42 individuals; 79.2%) died from causes directly related to HIV.

4.4 MULTIVARIATE ANALYSIS

All variables with a p-value less than 0.20 in the bivariate analysis were entered into a logistic regression model with backward prediction. The results of the multivariate analysis of adjusted models are presented in **Table 6 of the Appendix**. In addition, Table 6 presents independent correlates of a positive postmortem HIV test result within the overall sample ($N = 1502$):

- (a) age of 65 years or older ($p = 0,0001$);
- (b) history of injecting drug use ($p = 0,0001$);
- (c) autopsy ($p = 0,0212$);
- (d) infectious diseases as the immediate cause of death ($p < 0,0001$).

4.5 QUALITY ASSESSMENT OF TESTING

Postmortem diagnosis of HIV within the study was based on laboratory testing to detect serological markers of HIV using RDTs, the results of which are interpreted visually. Therefore, it was critically important to ensure the quality of such testing to obtain correct results, which formed the basis of conclusions about detected cases of HIV infection among the deceased.

Quality control of HIV testing and the correctness of establishing HIV-positive status were ensured by determining the VL in blood samples of HIV-negative deceased individuals. In 10% of cases with HIV-negative results from the initial RDT, DBS samples were randomly selected at each study site for further determination of HIV-1 viral load in them.

According to the results of VL determination, it was established that in all 101 DBS samples obtained from HIV-negative individuals, the VL was at an undetectable level.

Thus, the correct interpretation of HIV test results using RDTs was confirmed, with HIV-negative status correctly identified in 100% of deceased individuals.

4.6 FEATURES OF DEATH REGISTRATION DOCUMENTATION AND INFORMATION FLOW

Within the framework of the study, the algorithm for documentation procedures and the flow of information regarding death cases was examined (Fig. 4).

The algorithm for completing death registration documentation included the following stages:

1. In the event of conducting a pathological examination, a pathologist of the healthcare facility documented the autopsy results in the Pathological Examination Report (primary record-keeping document form No. 013/o). The protocol indicated the final diagnosis and the date of its establishment, clearly stated the primary disease, its complications, and comorbidities. The pathological diagnosis was also recorded, further categorized into the primary disease, complications, and comorbidities. Diseases etiologically and pathogenetically unrelated to the primary disease or complication were listed as comorbidities. The pathological diagnosis was formulated based on etiopathogenetic principles, considering current legal regulations and the requirements of ICD-10. The report included results from 20 clinical laboratory tests. Necessary clinical data and examination results extracted from the inpatient medical record, were provided as appendices to this form. In cases of a combined primary disease, its components were indicated. In such cases, the ICD-10 code was determined based on the first disease listed. Complications were listed in chronological order, considering their mutual pathogenetic relationship. In cases of death due to infectious pathology, the results of microbiological (virological) tests were included. In the "Cause of Death" section of the report, the pathologist indicated data according to paragraph 11 of the primary record-keeping document form No. 106/o, "Death Certificate No. __". Following this, the pathologist filled out an extract from the Pathological Examination Report. The extract from form No. 013/o, including the pathological diagnosis and data comparing clinical and pathological diagnoses, and the cause of death according to paragraph

11 of form No. 106/o, was filled out on the last page of form No. 003/o, "Inpatient Medical Record".

2) After performing the autopsy, the pathologist prepared the paper version of primary documentation form No. 106/o "Death Certificate No. ____" and the Certificate of Cause of Death (form No. 106/o No. _____, issued for burial) in accordance with the order of the MOH of Ukraine dated August 8, 2006, No. 545.

3) The first copy of the death certificate was issued for state registration of the death to the deceased's relatives or other persons responsible for burial. The second copy remained in the pathology department or the location of medical practice Of an individual entrepreneur (in cases of death at the place of residence when an autopsy was not performed).

4) If a pathological examination was not ordered (subparagraph 2, paragraph 2 of this section) (in cases specified by Article 6 of the Law of Ukraine "On Burial and Funeral Affairs"), the death certificate was issued by the doctor under whose supervision the deceased was, or another healthcare facility doctor (on-call doctor in cases of death during holidays and weekends or a pathologist).

5) State registration of the death was conducted by the civil registry authorities or the executive body of the village, town, city (except for cities of regional significance) council, upon the request of the deceased's relatives, representatives of the guardianship and custody authority, or other persons responsible for burial. After the state registration of death, the relatives or other persons were issued a death certificate and an extract from the State Register of Civil Status Acts regarding the death for burial assistance or the corresponding burial certificate. Civil registry authorities sent death certificates to the relevant territorial offices of the State Statistics Service of Ukraine.

6) A doctor of the healthcare facility indicated the cause of death according to paragraph 11 of form No. 106/o and the pathological diagnosis (in cases of autopsy) in form No. 066/o "Inpatient Discharge Record No. ", which is recorded in the statistical office (informational and analytical medical statistics department) of the healthcare facility. Based on forms No. 066/o and No. 013/o, the corresponding sections of the report form No. 20 "Report of a legal entity, regardless of its organizational and legal form, and individual entrepreneur engaged in medical practice, for the year 20__" (annual) were completed.

As part of the study, the pathologist also filled out:

7) Data collection form on the causes of death and HIV status for deceased adults aged 18 and older, and, if possible, blood sample collection, as indicated in subparagraphs 2.1.5;

8) Blood sample collection register and HIV serological marker rapid test results (form 498-5/o).

9) Forms for monitoring studies using the DBS method:

- DBS Sample Log Form
- Rejected DBS Sample Log Form
- DBS Sample Dispatch Form

Fig. 4. Information flow on deceased individuals within the study "Analysis of the HIV Mortality Surveillance System and Hospital-based Monitoring of HIV-Associated Mortality in Ukraine."



5 DISCUSSION

According to data from the Ministry of Justice of Ukraine on regional departments of civil registration of vital records concerning birth and death records for 2023, the Odesa region, along with Kyiv, Dnipropetrovsk, Kharkiv, and Donetsk regions, is among the regions of Ukraine with a high general mortality rate [1]. This trend has been consistent in these regions since 2021.

In total, in 2023, 32,057 people died in the Odesa region (6.5% of the total number of deaths in Ukraine), of which 786 had a diagnosed HIV infection, making up 2.4% of the total number of deaths in the region or 17.5% of the total number of people with HIV who died in Ukraine.

In Kyiv, in 2023, the number of deaths was nearly the same as in the Odesa region — 34,546 (7.0% of the total number of deaths in Ukraine). However, the proportion of HIV-positive individuals among the deceased was significantly lower both among the total number of deaths in Kyiv (1.1%) and among the deaths of people living with HIV in Ukraine (8.6%). Data from the seroepidemiological monitoring on testing for HIV using section material (postmortem blood) confirm that, over the past decade, the highest number of HIV tests among the deceased in Ukraine has been conducted in the Odesa region. According to 2023 data, 57% (196) of HIV tests were conducted in the Odesa region, accounting for 86% (86) of all HIV-positive deceased individuals in Ukraine for code 119, while in Kyiv, this was 16.0% and 2.3%, respectively. Fourteen regions did not conduct any tests under code 119^[2]. Thus, the targeted laboratory testing policy for the presence of HIV infection in deceased individuals with unknown HIV status and clinical and pathological manifestations of HIV infection varies significantly by region. Only in some regions of the country is there an established exchange of data between healthcare facilities that provide medical supervision of people living with HIV and AIDS, forensic medical examination bureaus regarding the diagnosis of HIV infection among the deceased, with the Odesa region being the most effective.

^[1] https://dostup.org.ua/request/statistika_narodzhuvanosti_i_smi_3#incoming-395806

^[2] Reporting form No. 2 HIV/AIDS "Report on individuals with conditions and diseases caused by the human immunodeficiency virus (HIV) for the year 2023" (annual).

According to the Study Protocol, the study endpoints involved obtaining and discussing the results for the tasks related to assessing cases of undiagnosed HIV infection, based on the study results (paragraphs 5.1-5.2).

5.1 BRIEF SUMMARY OF FINDINGS AND COMPARISON WITH OTHER STUDIES

Social and demographic data

Among all study participants, the majority were women (52.2%) and individuals aged 65 and older (69.2%). About 96.1% lived in Odesa or the Odesa region; 1.3% had a history of injecting drug use; 82.6% died in healthcare facilities where they were inpatients.

The study in Kyiv¹²⁵ was conducted from July to December 2021, during a period of increased COVID-19 incidence in Ukraine, including in Kyiv. Therefore, a substantial proportion of deaths in the Kyiv study were associated with COVID-19. In contrast, the study conducted in Odesa was implemented in a later period, when the epidemiological situation related to COVID-19 had significantly stabilized and the number of confirmed cases had markedly decreased. This difference in the timing of the studies should be taken into account when comparing the results between Kyiv and Odesa.

In the Kyiv study, nearly one-third of the participants (29.0%; N=440) had documented confirmed COVID-19 cases, 42.2% (N=638) had a confirmed negative COVID-19 test result, and in 28.8% (N=435) of cases the COVID-19 status was unknown. Among all deceased individuals with confirmed COVID-19 (N=440), four were HIV-positive (0.9%). In the vast majority of cases (98.6%), the underlying cause of death was a disease associated with SARS-CoV-2 infection. Among individuals with a negative COVID-19 status, 28 were HIV-positive, while among those with unknown COVID-19 status, seven individuals had a positive HIV test result.

These findings should be interpreted in the context of the Kyiv study conducted during an active COVID-19 epidemic wave, which explains the high proportion of COVID-19–related deaths observed in that analysis.

HIV status

In both Odesa and Kyiv, most study participants had no information on their HIV status in their medical records at the time of death.

In Odesa, 81.2% of the deceased had no HIV status information. HIV-positive status was recorded for 3.4% (51 individuals), and HIV-negative for 15.3% (230 individuals). HIV infection was diagnosed in 53 deceased individuals (3.5%) through testing. Of these, 51 already had a confirmed status in the IS MSSD, while 2 were newly identified as HIV-positive.

In Kyiv, 94.4% of participants also had no information on HIV status. Only 2.1% (31 individuals) were HIV-positive, and 3.5% (53 individuals) were HIV-negative. HIV infection was identified in 39 deceased individuals (2.6%) through testing. Of these, 33 had a confirmed HIV status in the IS MSSD, and 6 individuals were newly diagnosed.

The actual underdiagnosis rate of HIV during life was 3.8%. In our study based on pathology departments in four healthcare facilities in Odesa, the number of HIV tests conducted on deceased individuals (N=1502) exceeded the total annual number of tests recorded under code 119 in Ukraine (344 in 2023). According to 2023 data, 6,688 people died in Odesa (20.9% of all

¹² https://phc.org.ua/sites/default/files/users/user90/2021_Ukraine_MS_report.pdf

deaths in the Odesa region). Among them 429 with diagnosed HIV (6.4% of all deaths in Odesa and 54.6% of all deceased PLHIV in the region).

If we assume that all deceased individuals in Odesa in 2023 had been tested for HIV, the number of deceased PLHIV would have been 445 instead of 429 (by 3.8% more). And the proportion of PLHIV among the deceased would have remained nearly the same—6.7%—supporting targeted laboratory testing policy in Odesa and the region as a whole, in contrast to the lack of unified national approaches to HIV postmortem diagnosis.

HIV-positive cases

Among all HIV-positive study participants (N=53), the majority were men (52.8%) and individuals aged 36–50 (58.5%). A history of injecting drug use was recorded in 35.8% of cases. According to 2023 official data, among deceased PLHIV in Ukraine and Odesa, men also predominated (66% and 63%, respectively), as did individuals of working and reproductive age (25–49 years) — 68% and 62%, respectively. People who injected narcotic drugs accounted for 33% of HIV-related deaths in Ukraine and 25% in Odesa.

Among HIV-positive deceased individuals, 48% had a detectable viral (e.g. VL>839 copies/ml), and 21% had >10,000 copies/ml. The remaining HIV-positive individuals (N=27), as well as all HIV-negative individuals from whom DBS samples were taken (N=101), had undetectable VL.

Leading causes of death

Autopsies were performed on 31 (58.5%) HIV-positive individuals. The majority died from HIV-related causes (42 people; 79.2%). Among AIDS-defining illnesses, the most common were:

- Toxoplasmosis of the brain (57.1%)
- Multiple infections (12%)
- Pneumocystis pneumonia and extrapulmonary cryptococcosis (each 9.5%)
- Encephalopathy (7.1%)
- Cervical cancer (4.7%)

In the general study cohort, the leading causes of death were diseases of circulatory system (55.2%) and neoplasms (18%). In the Kyiv study, leading causes of death were diseases of circulatory system (37.3%) and COVID-19 (28.7%).

The majority of HIV-positive individuals in both Odesa and Kyiv died as a result of HIV progression — **58.5%** and **56.4%**, respectively.

Separately, among all HIV-positive individuals who were removed from medical supervision in 2023 due to death, 38% of deaths were directly attributed to HIV infection, and among them, **86%** were AIDS-related.

In this study, autopsies were performed on 65.2% of deceased individuals, including 31 (58.5%) of the HIV-positive individuals in the study cohort.

6 RECOMMENDATIONS AND NEXT STEPS

To strengthen the mortality surveillance system in Ukraine, the following actions are recommended:

Improve monitoring of HIV-positive patients who are registered in but do not attend healthcare facilities, have low adherence to antiretroviral therapy, or have been lost to follow-up with healthcare facilities. This requires enhanced efforts to attract and retain patients under medical supervision, including the implementation of practical, evidence-based measures such as case management and peer support programs to improve linkage to care and adherence, the use of digital tools (SMS reminders, phone calls, telemedicine) to reduce missed visits and improve communication, as well as community-based ART delivery and differentiated care models to increase accessibility and continuity of treatment..

Ensure electronic monitoring of deaths among PLHIV in the IS MSSD as a key surveillance event based on an HIV case and establish data exchange between healthcare facilities providing care to PLHIV, pathology services, and the state statistics authorities to verify death information, which will ensure proper quality and reliability of data for further analysis.

Enhance collaboration with healthcare facility doctors to ensure routine HIV testing for all inpatients, with mandatory documentation of test results or known HIV status in medical records.

Develop educational materials and/or an online course on determining and documenting pathological diagnoses in HIV-related deaths, reporting practices, for physicians in pathology services and public health institutions.

To assess mortality risks among PLHIV, future epidemiological studies should expand the range of relevant research questions.

TABLE 1. Characteristics of deceased study participants, Odesa (August 2023 – March 2024, N=1,502) *

Characteristic	Total (N=1,502) n (%)	HIV-Positive (N=53) n (%)	HIV-Negative (N=1,449) n (%)	p-value
Age group (years)				
18 - 35	26 (1.7)	8 (15.1)	15 (1.0)	< 0.0001
36 – 50	134 (8.9)	31 (58.5)	101 (7.0)	
51 – 64	302 (20.1)	9 (17.0)	293 (20.2)	
65+	1040 (69.2)	5 (9.4)	1040 (71.8)	
Sex				
Men	718 (47.8)	28 (52.8)	690 (47.6)	0.2804
Women	784 (52.2)	25 (47.2)	759 (52.4)	
Place of residence				
Odesa city and Odesa region	1444 (96.1)	52 (98.1)	1392 (96.1)	0.6828
Other	38 (2.5)	1 (1.9)	37 (2.6)	
Unknown	20 (1.4)	0	20 (1.3)	
Injecting drug use				
No	1483 (98.7)	34 (64.2)	1449 (100.0)	< 0.0001
Yes	19 (1.3)	19 (35.8)	0	
Place of death				
Healthcare facility	1241 (82.6)	50 (94.3)	1191 (82.2)	0.0218
Home	262 (17.4)	3 (5.7)	258 (17.8)	
Was an autopsy performed?				
No	523 (34.8)	22 (41.5)	501 (34.6)	< 0.0001
Yes	979 (65.2)	31 (58.5)	948 (65.4)	
Confirmed COVID-19 diagnosis				

No	43 (3.9)	2 (3.8)	41 (2.8)	0.7829
Yes	3 (0.20)	0	3 (0.2)	
Unknown	1456 (97.1)	51 (96.3)	1405 (97.0)	
HIV status before death				
Positive	51 (3.4)	51 (96.2)	0	< 0.0001
Negative	230 (15.3)	0	230 (15.9)	
Unknown	1221 (81.3)	2 (3.8)	1219 (83.1)	
Immediate cause of death				
Some infectious and parasitic diseases (A00 B99)	62 (4.1)	42 (79.2)	20 (1.4)	< 0.0001
Neoplasms (C00 D48)	270 (18.0)	2 (3.8)	268 (18.5)	0.2418
Diseases of the circulatory system (I00 I99)	829 (55.2)	1 (1.9)	828 (55.1)	0.0356
Diseases of the genitourinary system (N00 N99)	55 (3.4)	1 (1.9)	54 (3.7)	0.0256
Endocrine, nutritional and metabolic diseases (E00 E90)	18 (1.2)	3 (5.7)	15 (1.0)	0.2913
Diseases of the respiratory system (J00 J99)	67 (4.5)	2 (3.8)	65 (4.3)	0.0641
Diseases of the digestive system (K00 K93)	118 (7.8)	2 (3.8)	116 (7.7)	0.4315
Multiple organ failure	29 (1.9)	0	29 (2.0)	0.3217
Other	54 (3.6)	0	54 (3.6)	0.0854

**Pearson's chi-square test was used for the categorical variables and the Fisher's exact test was used for the variables with small numbers*

TABLE 2. Causes of Death, Viral Load, and Timing of HIV Diagnosis Among Deceased HIV-Positive Individuals, Odesa (August 2023 – March 2024, N=53)

Causes of death	ICD-10 code	Total (N=53)	RNA copies/mL			Timing of HIV Diagnosis	
			>10,000*	1,000-10,000	< 1000	Antemortem**	Postmortem**
HIV diseases, including	B20— B24****	42	42	11	14	33	9
<i>cerebral toxoplasmosis</i>	<i>B20.8</i>	24	24	5	12	19	5
<i>pneumocystis pneumonia</i>	<i>B20.6</i>	4	4	2	0	3	1
<i>cryptococcosis</i>	<i>B20.5</i>	4	4	2	1	2	2
<i>multiple infections</i>	<i>B20.7</i>	5	5	0	0	3	2
<i>cervical cancer</i>	<i>B21.8</i>	2	2	0	0	1	1
<i>encephalopathy</i>	<i>B22.0</i>	3	3	2	1	2	1
pneumonia	<i>J18.9</i>	2	2	0	0	0	2
liver cirrhosis	K74.6	4	4	0	0	3	1
diseases of the gallbladder, bile ducts and pancreas	K86.3	2	2	0	0	2	0
lung cancer	C34.8	2	2	0	0	1	1
brain tumor	C71.0	1	1	0	0	0	1
Total		53	53	11	14	36	17

*VL = Viral Load, based on DBS testing; values <1,000 copies/mL considered “Not Detected”

**Antemortem diagnosis = HIV status known before death

***Postmortem diagnosis = newly diagnosed after death

****AIDS-defining illnesses indicated under ICD-10 codes B20–B24

TABLE 3. Characteristics of Deceased Study Participants Stratified by Sex, Odesa (August 2023 – March 2024, N=1,502)*

Characteristic	Total (N=1,502) n (%)	Men (N=718) n (%)	Women (N=784) n (%)	p-value
Age group (years)				
18-35	26 (1.7)	12 (1.7)	14 (1.8)	< 0.0001
36-50	134 (8.9)	88 (12.2)	46 (5.9)	
51-64	302 (20.1)	179 (25.0)	123 (15.7)	
65 +	1040 (69.2)	439 (61.1)	601 (76.7)	
HIV status before death				
Positive	36 (2.4)	15 (2.1)	21 (2,7)	0.999
Negative	230 (15.3)	112 (16.0)	118 (15.1)	
Unknown	1236 (82.3)	591 (82.3)	645 (82.3)	
Postmortem determination of HIV status				
HIV-negative	1449 (97.4)	690 (96.1)	759 (96.8)	0.2815
HIV-positive*	53 (2.6)	28 (3.9)	25 (3.2)	
Place of residence				
Odesa city and Odesa region	1444 (96.1)	700 (97.5)	744 (94.5)	0.6512
Other	38 (2.5)	17 (2.4)	21 (2.7)	
Unknown	20 (1.4)	1 (0.1)	19 (2.4)	
Injecting drug use				
No	1483 (98.)	705 (98.2)	778 (99.2)	0.4210
Yes	19 (1.3)	13 (1.8)	6 (0.8)	
Place of death				
Healthcare facility	1241 (82.6)	584 (81.3)	657 (83.8)	0.4209
Home	262 (17.4)	134 (18.7)	128 (16.2)	
Was an autopsy performed?				
No	523 (34.8)	234 (32.6)	289 (36.9)	0.5198
Yes	979 (65.2)	484 (67.4)	495 (63.1)	
Confirmed COVID-19 diagnosis				
No	43 (3.9)	22 (3.1)	21 (2.7)	0.3612
Yes	3 (0.20)	1 (0.1)	2 (0.3)	
Unknown	1456 (97.1)	695 (96.8)	761 (97.0)	

Causes of death				
<i>Some infectious and parasitic diseases (A00 B99)</i>				0.0001
No	1440 (95.9)	689 (96.0)	751 (95.8)	
Yes	62 (4.1)	29 (4.0)	33 (4.2)	
<i>Neoplasms (C00 D48)</i>				0.0019
No	1232 (82.0)	589 (82.0)	643 (82.0)	
Yes	270 (18.0)	129 (18.0)	141 (18.0)	
<i>Diseases of the circulatory system (I00 I99)</i>				0.3712
No	673 (44.8)	351 (48.9)	322 (41.0)	
Yes	829 (55.2)	367 (51.1)	462 (59.0)	
<i>Diseases of the genitourinary system (N00 N99)</i>				0.6989
No	1447 (96.3)	691 (96.2)	756 (96.4)	
Yes	55 (3.4)	27 (3.8)	28 (3.6)	
<i>Endocrine, nutritional and metabolic diseases (E00 E90)</i>				0.4207
No	1484 (98.8)	713 (99.3)	771 (98.3)	
Yes	18 (1.2)	5 (0.7)	13 (1.7)	
<i>Diseases of the respiratory system (J00 J99)</i>				0.5514
No	1435 (95.)	676 (94.2)	759 (96.8)	
Yes	67 (4.5)	42 (5.8)	25 (3.2)	
<i>Diseases of the digestive system (K00 K93)</i>				0.3968
No	1384 (92.2)	663 (92.3)	655 (83.5)	
Yes	118 (7.8)	55 (7.7)	63 (8.0)	
<i>Multiple organ failure</i>				0.0543
No	1473 (98.1)	702 (97.8)	771 (98.3)	
Yes	29 (1.9)	16 (2.2)	13 (1.7)	
<i>Other</i>				0.4814
No	1448 (96.4)	670 (93.3)	778 (99.2)	
Yes	54 (3.6)	48 (6.7)	6 (0.8)	

**Pearson's chi-square test was used for the categorical variables and the Fisher's exact test was used for the variables with small numbers*

TABLE 4. Age characteristics of study participants who died in the period from August 2023 to March 2024, Odesa (N=1,502)*

Characteristic	Total (N = 1,502) n (%)	Aged < 65 years (N = 462) n (%)	Aged ≥ 65 years (N = 1,040) n (%)	p-value
Sex				
Men	718 (47.8)	279 (60.4)	439 (42.2)	< 0.0001
Women	784 (52.2)	183 (39.6)	601 (57.8)	
HIV status before death				
Positive	36 (2.4)	33 (7.1)	3 (0.3)	< 0.0001
Negative	230 (15.3)	70 (15.2)	160 (15.4)	
Unknown	1236 (82.3)	359 (77.7)	877 (84.3)	
Place of residence				
Odesa city and Odesa region	1444 (96.1)	439 (95.0)	1005 (96.7)	0.939
Other	38 (2.5)	19 (41.1)	19 (1.8)	
Unknown	20 (1.4)	4 (0.9)	16 (1.5)	
Injecting drug use				
No	1483 (98.7)	445 (96.3)	1038 (99.8)	< 0.0001
Yes	19 (1.3)	17 (3.7)	2 (0.2)	
Place of death				
Healthcare facility	1241 (82.6)	407 (88.1)	834 (90.1)	0.089
Home	262 (17.4)	55 (11.9)	207 (19.9)	
Was an autopsy performed?				
No	523 (34.8)	246 (53.2)	277 (26.6)	< 0.0001
Yes	979 (65.2)	216 (46.8)	763 (73.4)	
Confirmed COVID-19 diagnosis				
No	43 (3.9)	15 (3.2)	28 (2.7)	< 0.0001
Yes	3 (0.20)	2 (0.4)	1 (0.1)	
Unknown	1456 (97.1)	445 (96.3)	1011 (97.2)	
Causes of death				
Some infectious and parasitic diseases (A00 B99)				0.0001
No	1440 (95.9)	409 (88.5)	1031 (99.1)	
Yes	62 (4.1)	53 (11.5)	9 (0.9)	

Neoplasms (C00 D48)				0.0023
No	1232 (82.0)	343 (74.2)	889 (85.5)	
Yes	270 (18.0)	119 (25.8)	151 (14.5)	
Diseases of the circulatory system (I00 I99)				0.0034
No	673 (44.8)	295 (63.9)	378 (36.3)	
Yes	829 (55.2)	167 (36.1)	662 (63.7)	
Diseases of the genitourinary system (N00 N99)				0.6989
No	1447 (96.3)	449 (97.2)	998 (96.0)	
Yes	55 (3.4)	13 (2.8)	42 (4.0)	
Endocrine, nutritional and metabolic diseases (E00 E90)				0.4309
No	1484 (98.8)	456 (98.7)	1028 (98.8)	
Yes	18 (1.2)	6 (1.3)	12 (1.2)	
Diseases of the respiratory system (J00 J99)				0.6754
No	1435 (95.5)	439 (95.0)	996 (95.8)	
Yes	67 (4.5)	23 (5.0)	44 (4.2)	
Diseases of the digestive system (K00 K93)				
No	1384 (92.2)	411 (89.0)	973 (93.6)	
Yes	118 (7.8)	51 (11.0)	67 (6.4)	
Multiple organ failure				0.0874
No	1473 (98.1)	454 (98.3)	1019 (98.0)	
Yes	29 (1.9)	8 (1.7)	21 (2.0)	
Other				0.5617
No	1448 (96.4)	441 (94.5)	1007 (96.8)	
Yes	54 (3.6)	21 (4.5)	33 (3.2)	

**Pearson's chi-square test was used for the categorical variables and the Fisher's exact test was used for the variables with small numbers*

TABLE 5. Independent Correlates of a Positive HIV Test Result After Death (N=1,502)

Covariates	Crude model			Adjusted model		
	Crude odds ratio	95 % CI	<i>p-value</i>	Adjusted odds ratio	95 % CI	<i>p-value</i>
Age (years)						
18-35		Reference			Reference	
36-50	2.180	1.354, 4.018	0.0001	0.496	0.277, 2.928	0.9355
51-64	0.065	0.023, 0.099	0.8345	0.180	0.098, 2.210	0.0819
≥ 65	0.021	0.004, 0.089	0.3424	0.453	0.018, 0.467	0.0001
Injecting drug use						
No		Reference			Reference	
Yes	5.648	3.121, 6.243	< 0.0001	4.965	2.234, 6.397	0.0001
Was an autopsy performed?						
No		Reference			Reference	
Yes	0.078	0.042, 0.087	< 0.0001	0.067	0.034, 0.089	0.0212
Immediate cause of death						
Other		Reference			Reference	
Infectious diseases	6.297	2.739, 7,112	< 0.0001	12.098	4.299, 18.056	< 0.0001