

BREAST CANCER IN UKRAINE: The Continuum of Care and Implications for Action

Breast cancer (BC) is the leading cancer in Ukrainian females.^{1,2} Ukraine has seen little change in BC burden in the last 25 years: BC remained the 4th most important non-communicable disease (NCD) cause of years of life lost (YLL) in 2016, responsible for 3.4% of all YLL in 2016 (3.5% of YLL in 1990). BC was also the 5th cause of NCD-related death in 2016 (rank 6 in 1990). Population ageing, changing childbearing patterns and adoption of modern lifestyles affect BC risks.

However, there is evidence of programmatic progress with a shift to earlier BC detection, possibly supported by more effective treatment. Some stage shifting occurred in the last 15 years with **76%** of BC cases detected at stages I–II in 2015 compared to **69%** in 2003.³ Conversely, **9.7%** of cases were only diagnosed at stage IV in 2015, down from **14.5%** in 2000. And first year mortality post diagnosis was down from 14.5% in 2000 to 9.7% in 2015.

KEY MESSAGES

1. Analysis of the continuum of care highlights breakpoints in patients' journeys from screening to diagnosis, treatment and longer-term monitoring.
2. Public sector routine data in two Ukraine Regions show that only 36% (Lviv) and 61% (Poltava) of eligible women were screened for breast cancer in 2016 (screening gaps of 64% and 39%, respectively). At least 3 of 10 positive screens were followed up with diagnostic tests.
3. Among the diagnosed cases, negative outcomes (death, loss to care, treatment refusal, and withdrawal from treatment) were not sufficiently documented in both regions, calling for urgent attention to outcomes. In the 2015 treatment cohorts, 56% (Lviv) and 25% (Poltava) had no record of breast cancer treatment completion.
4. Understanding of diagnosis and treatment gaps and delays from cascade analysis helps identify solutions ranging from simplified decision-making for cancer treatment, to improved pharmaceutical supplies and access to diagnostic equipment.
5. Systems for age- and risk-appropriate screening invitations and recalls need to be developed in Ukraine for earlier detection of cases and an overall more efficient breast cancer program.

¹ http://www.ncru.inf.ua/publications/BULL_18/PDF_E/05_struct10.pdf

² <https://vizhub.healthdata.org/gbd-compare>

³ <http://unci.org.ua/en/for-specialists/national-cancer-registry/>

BACKGROUND AND RATIONALE

The main strategy in Ukraine to detect BC early is to offer to all females aged 18 years and above an annual preventive gynaecological examination, which include a clinical breast exam.

The main strategy in Ukraine to detect BC early is to offer to all females aged 18 years and above an annual preventive gynaecological examination, which include a clinical breast exam. About 50% of BC cases are found during these preventive exams.³ Females with a positive clinical breast screen should be followed-up with diagnostic mammography and breast ultrasound. In 2016, based on long-standing international evidence of the effectiveness of screening mammography for earlier BC detection, stage shifting and reduced mortality, some Ukraine Regions started to develop a system of mammography screening, accompanied by awareness and public education interventions and health sector support activities.

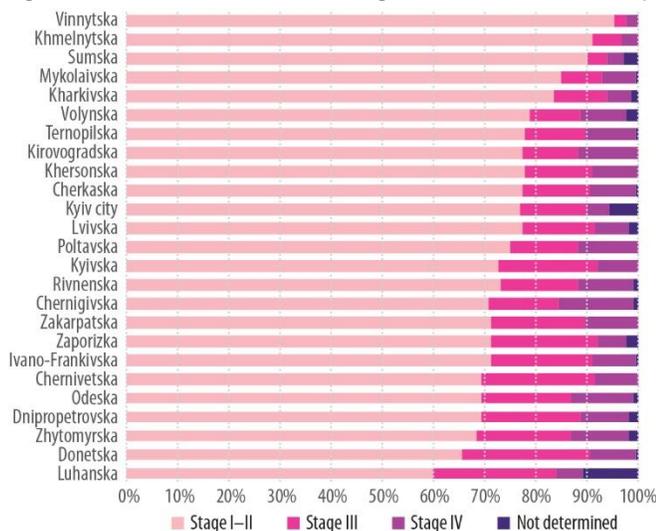
The World Bank, with support from the Swiss Development Cooperation, implements the technical assistance program “Support to Reforms and Governance in the Health Sector in Ukraine”. In 2017, an analysis was conducted on the continuum of care for BC in two Ukrainian Regions, Lviv and Poltava, to determine the breakpoints in the care cascade and opportunities for action.

The analysis also provided a 2016 baseline prior to the introduction of a BC prevention, screening and health sector strengthening program in Lviv Region. The Program was developed after consultation with specialists from the International Agency for Research on Cancer in 2015, taking into account the recommendations from the Ministry of Health on BC screening issued in February 2018.⁴

FINDINGS

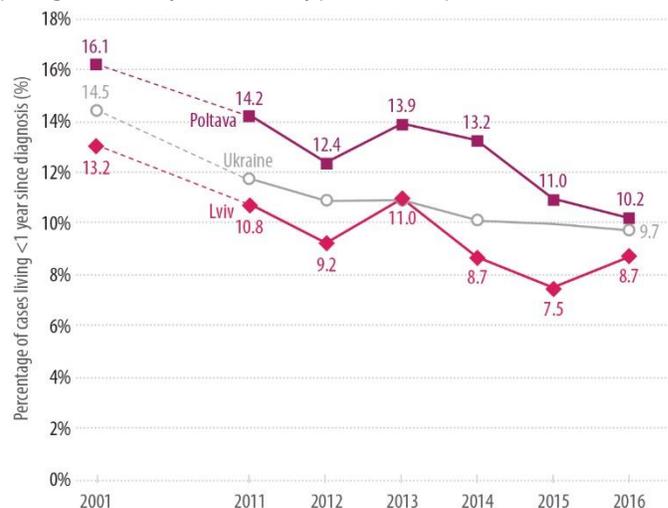
Early BC detection varies widely between regions, from 95% of all BC cases detected at TNM stages I and II in Vinnytska Region to only 60% detected early in Luhanska Region in 2016 (Figure 1). Lviv and Poltava Regions were within the national average.

Figure 1 Tumour, node and metastasis⁵ stage distribution of new BC cases (2016)



Source: National cancer bulletin on CSO (2016)

Figure 2 First year BC mortality (2001, 2011–16)



Source: National cancer bulletins 2001, 2011–16

⁴ Ustinov O.V. (2018). Recommendations for disease screening and periodic examinations at the primary health care level developed by the Ministry of Health of Ukraine. *Medychny Chasopys (Medical Bulletin) Online* dated 2018-02-13.

⁵ <http://www.cancerresearchuk.org/about-cancer/breast-cancer/stages-types-grades/tnm-staging>.

In both regions, there was also a gradual decline of first year BC mortality over the last 15 years (Lviv: 37% reduction from 2001 to 2016, Poltava: 34%, see Figure 2). This likely reflects progress associated with the introduction of immunohistochemical testing, targeted and modern anti-estrogen drugs, and the inclusion of patients in international clinical trials.

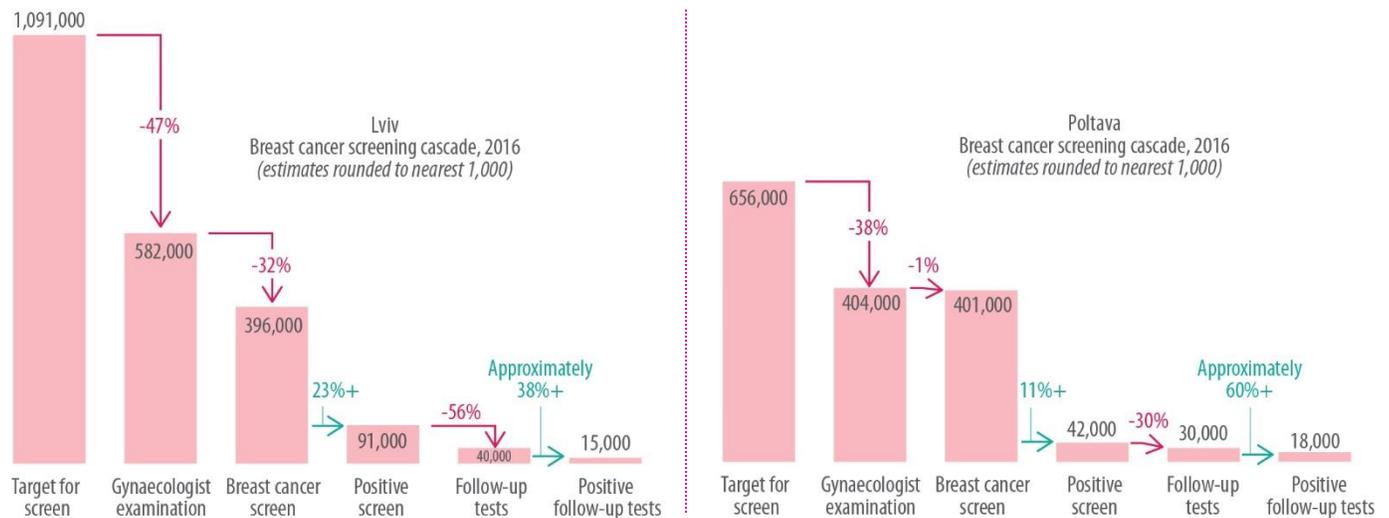
SCREENING CASCADE: ISSUES OF COVERAGE AND RECORD KEEPING

Of all eligible females, 47% in Lviv Region and 38% in Poltava Region did not have a gynaecological examination.

The screening cascade was in both regions determined by the coverage of the annual preventive examination, which is the entry point to the clinical breast screen (Figure 3). Of all eligible females, 47% in Lviv Region and 38% in Poltava Region did not have a gynaecological examination according to the Health Index Survey 2016 (the national value is 45%).⁶ According to ambulatory patient card data, there was another breakpoint in the cascade in Lviv Region with 32% of women not undergoing the clinical breast screen during the gynaecological exam. However, this might be due in part to poor recording of negative screens (indicated by a high proportion of positive screens at 23% in Lviv, versus 11% in Poltava).

In Poltava, the clinical breast screen was well recorded with only 1% of women with gynaecological exams lacking a record of the breast screening result.

Figure 3 Breast cancer screening cascades for 2016 in Lviv and Poltava Regions



Sources: Lviv and Poltava regional demographic statistics (target to screen), Health Index Report 2016 (gynaecologist exam), ambulatory care data from women's consultation units form O25 (mammary palpitation screen, screening result, diagnostic mammography and breast ultrasound for follow-up of suspects, follow-up test results)

DIAGNOSIS: IMPORTANT LOSSES TO FOLLOW-UP

Positive breast screens require follow-up with diagnostic mammography or breast ultrasound and verification with biopsy, however, 56% (Lviv) and 30% (Poltava) had no evidence of such follow-up examinations in their patient cards (Figure 3). These follow-up tests move women closer to a diagnosis, including mastopathy, cysts, breast calcifications, lipogranuloma, and benign and malignant breast changes. The follow-up data probably lack some test data from the tertiary level of care which are not always captured in the primary level medical cards of patients.

⁶ Health Index Survey Report 2016.

BREAST CANCER CASES: MOST CASES REGISTERED IN STAGE II WERE AGED 50 YEARS AND ABOVE

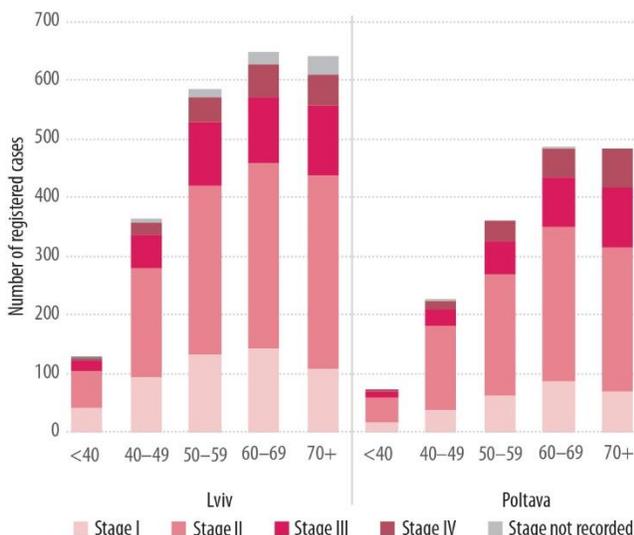
BC incidence per 100,000 females was 68.5 in Lviv Region, and 71.3 in Poltava.

BC incidence per 100,000 females was 68.5 in Lviv Region, and 71.3 in Poltava.⁷ Assessing the age pattern and staging results of registered first time episodes of BC can inform screening strategies. About one in five cases diagnosed was aged below 50 (Lviv: 21%, Poltava: 18%, 2015-mid 2017 data) (Figure 4). Invasive, stage IV cancer was diagnosed in 7% (Lviv) and 11% (Poltava) of all registered BC cases, respectively. Stage II cancers were the most frequently diagnosed in both regions. According to the 2018 cancer screening recommendations for the Ukraine Ministry of Health⁴, females aged 50–69 years should receive mammography screening every two years, and women with risk factors⁸ should commence screening from age 40. This is not fully consistent with the Gail model for BC risk assessment, and the National Comprehensive Cancer Network guidelines recommended by the Ministry of Health as one of the sources of clinical protocols in oncology in Ukraine). Also, the role of the clinical breast exam in not explicitly provided in the 2018 recommendations (see also Box 1 on global lessons).

TREATMENT STRATEGIES: THE VARIATION OF TREATMENT OBSERVED IN TWO REGIONS IN PARTICULAR IN STAGES II AND IV IS MOSTLY EXPLAINED BY AVAILABLE EQUIPMENT AND TREATMENT OPTIONS

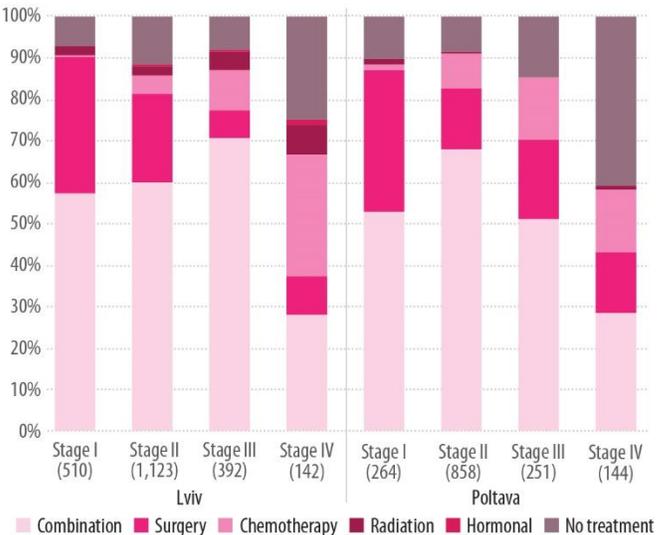
Most cases received combination treatment (Figure 5). The treatment patterns for each stage were comparable between the two regions, but the local oncology teams concluded that a further reduction of surgery mono-therapy of stage III cancers is important for appropriate patient care.

Figure 4 Breast cancer cases registered 2015 to mid-2017 in Lviv and Poltava in Regions by age group and cancer stage



Source: Cancer registries 2015 to mid-2017 Lviv and Poltava Regions

Figure 5 Breast cancer treatment in Lviv and Poltava in Regions by cancer stage, 2015 to mid-2017



The cancer registry data were analysed for “time-to-treatment”, another parameter not routinely reviewed by the Oncology Teams. In 2016, the average interval between diagnosis

⁷ Breast cancer statistics, Bulletin of National Cancer Registry of Ukraine № 18, 2015–16.

⁸ Risk factors listed in the guidance note are: Confirmed BRCA-1/2 mutation, burdened hereditary anamnesis (BC of relative in 1–2 degree of relationship), radiation therapy of chest in anamnesis, late first giving birth to a child (≥30 years), infertility, late menopause (≥55 years old), prolonged hormone replacement therapy for menopause, postmenopausal obesity, drinking alcohol, smoking, sedentary way of life, and background precancerous diseases.

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and treatment start was 28 days in Lviv Region and 20 days in Poltava Region. In Lviv, the interval was slightly longer for more advanced BC (30 days for stage III treatment initiation, 32 days for stage IV). This was likely due to the multi-step decision-making processes associated with complex, individualized treatment plans. The need for improved pharmaceutical supplies for cancer units was emphasized, especially by the Lviv Oncology Team. In both regions, the required diagnostic equipment was in some instances not available or outdated. The local oncologists found that time-to-treatment could potentially be reduced for stage I cancers, down from 22 days (Lviv) and 19 days (Poltava) due to the simpler treatment regimens.

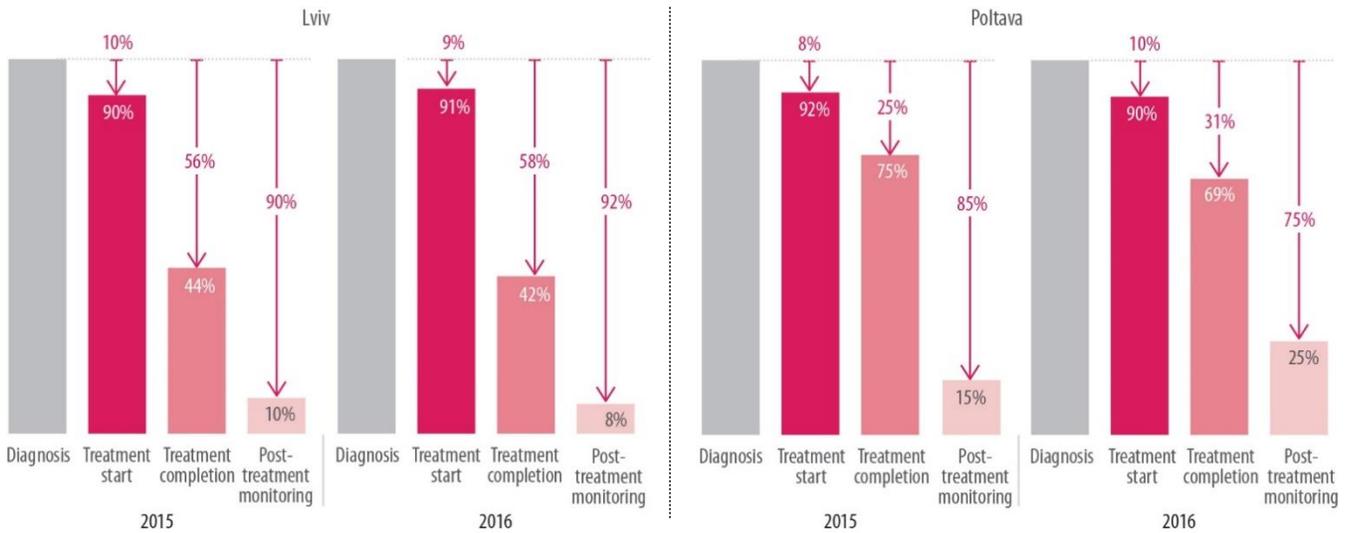
TREATMENT CASCADE: PATIENT-LEVEL DATA ON CONFIRMED FIRST EPISODES OF BC WERE ASSESSED FOR THE CONTINUUM OF CARE.

The main three stages assessed were:

1. The percentage of diagnosed breast cancer cases initiated on treatment
2. The percentage of cases with confirmed treatment completion (first episode only)
3. The percentage of cases who had evidence of post-treatment monitoring

Data were analysed for two annual cohorts, 2015 and 2016, to prevent truncated data due to insufficient follow-up time (data extracted from registries in Oct 2017) (Figure 6).

Figure 6 Breast cancer treatment cascades for 2015 and 2016 as per cancer registry data in Lviv and Poltava Regions



Sources: Cancer registries, breast cancer cases newly registered in 2015 and 2016 Lviv and Poltava Regions.

In both regions and annual cohorts, about 1 in 10 cases had no record of treatment initiation in the cancer registry.

In both regions and annual cohorts, about 1 in 10 cases had no record of **treatment initiation** in the cancer registry (Figure 6 – 10% and 9% in Lviv, 8% and 10% in Poltava). In Lviv, about 4% of cases had evidence of linkage to care after diagnosis but did not start treatment. According to the oncologists, this was due to high age, advanced cancer and treatment refusal, but the entries in the registry were not systematic. Another 4% of cases seemed lost to care with no registry entries after diagnosis. There were also a few out-transfers (9 of 2,367 total cases). Finally, about 2% of cases lacked treatment information most likely due to pre-treatment death. In Poltava, almost all patients foregoing treatment had evidence of linkage to care. Again, reasons for not receiving treatment were not systematically recorded. In both regions, it was often unclear at what stage of the continuum of care a patient’s death occurred.

TREATMENT COMPLETION WAS POORLY RECORDED IN THE REGISTRY (FIGURE 6)

56% and 58% of Lviv’s annual cohorts lacked data on the status or date of treatment completion, and 25% and 31% of Poltava’s cohorts. In Lviv, a small number (14 of 2,113 treatment initiated cases) withdrew from treatment, and therefore did not have a treatment completion date. In Poltava, no data could be found on withdrawal while on treatment.

POST-TREATMENT MONITORING WAS ALMOST NOT DOCUMENTED

About 9 of 10 Lviv cases and 8 of 10 Poltava cases had no evidence in the registry of being monitored. This was explained by the lack of information from family doctors to flow back to the registry, including information on patient death. Five-year survival could therefore not be calculated. The lack of following patients through also means that women with BC history may not be systematically recalled for high-frequency screening.

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IMPLICATIONS FOR ACTION

- ▶ The study, conducted in collaboration with the regional Oncology Teams, demonstrated the value of **analyzing cancer registry data on strategic key information** such as time-to-treatment, treatment coverage, loss to care and treatment patterns (each by cancer stage) to guide quality improvements
- ▶ In order to **initiate cancer treatments without delay**, the oncology teams need to have clear procedures, improved pharmaceutical supplies and access to reliable diagnostic equipment
- ▶ Coordination of care between levels and follow-up of cancer cases needs strengthening
- ▶ Better data flow to the Cancer Registry Units would improve the understanding of **timing and prevalence of death** and ultimately provide estimates of 5-year survival, it would also strengthen data on treatment completion and post-treatment monitoring, which the Oncology Teams consider important
- ▶ The recently published National Guidance on Cancer Screening⁵ needs to be translated into **systems of targeted invitations and patient recall**, bearing in mind individuals’ age and risk (Box 1).

Box 1 Global lessons on successful screening and early detection of breast cancer

STRATEGIC MIX OF EARLY DETECTION METHODS

- ▶ Mammography, clinical breast examination, breast self-examination, and other screening and investigative methods (such as 3D-tomosynthesis, ultrasound, MRI)
- ▶ Chosen method must be based on clients’ profile, on-the-ground capacity and local resources

TARGET GROUPS FOR MAMMOGRAPHY

- ▶ Should consider breast cancer demographics (many European programs have chosen the starting age of mammography screening at 45-47 years)
- ▶ Pre-menopausal women have a higher rate of false positives with mammography (digital mammography or tomosynthesis are preferred options).

Box 1 Global lessons on successful screening and early detection of breast cancer (continued)

- ▶ Consider enhanced screening strategy for women with known inherited susceptibility (possibly using MRI-mammography)

EFFECTIVENESS OF MAMMOGRAPHY SCREENING

- ▶ Lower in younger women – 19% reduction of BC in women 40-49 (evidence inconsistent), 25% in women 50-69
- ▶ “Number needed to screen” to prevent one BC death highest in women <50 (~1900), lowest at age 60-69 (~380)

QUALITY OF THE SCREENING PROGRAM

- ▶ Impact reduced if mammograms are of inferior quality, and if those reading mammograms are not adequately trained and assessed ongoingly
- ▶ Requires screening registers and invitation/recall system

Sources: Gelband et al 2015 (DCP3), Anderson et al. 2008, ARC 2008, Nelson et al. 2009.

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