

The Armed Conflict and the Impact on Patients With Cancer in Ukraine: Urgent Considerations

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On February 24, 2022, a war began within the Ukrainian borders. At least 3.0 million Ukrainian inhabitants have already fled the country. Critical infrastructure, including hospitals, has been damaged. Children with cancer were urgently transported to foreign countries, in an effort to minimize interruption of their life-saving treatments. Most adults did not have that option. War breeds cancer—delaying diagnosis, preventing treatment, and increasing risk. We project that a modest delay in care of only 4 months for five prevalent types of cancer will lead to an excess of over 3,600 cancer deaths in the subsequent years. It is critical that we establish plans to mitigate that risk as soon as possible.

JCO Global Oncol 8:e2200123. © 2022 by American Society of Clinical Oncology

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WAR AND CANCER

A broad group of medical oncologists and cancer researchers joined together from different countries and continents to discuss and assess the devastating consequences that the unexpected armed conflict currently occurring within Ukraine's boundaries might have to the general civilian population and in particular to patients with cancer. We would like to bring awareness to the impact of this armed conflict on this vulnerable population.

Since this warfare began, there has been a mass exodus to neighboring countries of more than three million people from Ukraine. It is expected that approximately five million people will leave the country to escape from the war by year end. There are countless tragedies that arise from war, such as death, disability, poverty, famine, and many types of cancer. All of these are intensified by the destructive impact that war has on access to health care. In many ways, war and cancer are linked.

As a consequence of the Second World War, 35-60 million people died. By the end of the War, atomic bombs dropped in Japan directly killed up to 210,000 persons.¹ A tumor registry from survivors of the nuclear bombs in the Japanese cities of Hiroshima and Nagasaki, including almost 80,000 people, revealed 8,613 documented cases of new cancer diagnoses between 1958 and 1987.² The herbicide named Agent

Orange that was used during the Vietnam War has been associated with the development of multiple types of cancer, including cancers of the head and neck, thyroid, esophagus, stomach, small intestines, and liver.^{3,4} In 1986, at Chernobyl in the former Soviet Union (current Ukraine), an accident in a nuclear power plant, from official information, immediately took the lives of 31 persons. In the years that followed, more than 4,000 deaths have since been attributed to the subsequent radiation and secondary cancers.⁵ In March 2011, Japan was the victim of one of the most powerful earthquakes ever reported that resulted in an accident in the nuclear power plant of Fukushima. Although the accident itself was a major catastrophe, even higher mortality because of thyroid cancer has been linked to this event.⁶

According to The Armed Conflict Location & Event Data Project information, during the period 2020-2021, because of different types of armed conflicts worldwide, including wars between countries, civil war, the drug war, terrorist insurgency, political unrest, and ethnic violence, thousands of casualties have occurred. In countries such as Afghanistan, Ethiopia, Mexico, and Yemen, more than 10,000 deaths were reported. During the same period and for the same reasons, between 1,000 and 10,000 casualties were also reported in countries such as Algeria, Burkina Faso, Cameroon, Chad, Colombia, DR Congo, Iraq, Libya, Mali, Mozambique, Myanmar, Niger, South

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Accepted on July 11, 2022 and published at ascopubs.org/journal/go on August 22, 2022; DOI <https://doi.org/10.1200/GO.22.00123>

CONTEXT

Key Objective

Several reports of the current and devastating situation in Ukraine have been published; nevertheless, the excess of cancer deaths because of consequences of the armed conflict in that country had not been estimated previously.

Knowledge Generated

Currently, there is a lack of access to minimal conditions to assure proper diagnosis and treatments within Ukrainian borders.

Including only the five more frequent cancer types among Ukraine inhabitants with a 4-month delay for initial diagnosis and/or for starting treatment, we estimate a minimum of 3,600 excess of deaths because of cancer in the following years.

Relevance

International community awareness of the risk of a previously unexpected excess of cancer deaths may help people who are under the effects of this armed conflict to have a chance of an earlier diagnosis and proper cancer treatment.

Sudan, Syria, Tanzania, and Tunisia.⁷ These warlike situations not only affect those who are directly involved in the conflict itself but unfairly most of the time also affect civilians who are directly harmed, inflicting to them serious severe damage, many times unrecovered. At the end of 2020, 82.4 million people were forcibly displaced worldwide, including 6.7 million from Syria, four million from Venezuela, 2.6 million from Afghanistan, 2.2 million from South Sudan, and 1.1 million from Myanmar. During the period 2018-2020, up to 340,000 children per year were born as refugees.⁸

There is also evidence that persons involved in armed conflicts are more likely to develop cancer. Examples include the higher incidence of cervical cancer in Vietnam and breast cancer in the former Yugoslavia after the wars that involved those countries. During the immediate postwar period in Croatia, an increase in gastric and testicular cancer was noted. In Iraq, cancer-related deaths increased by 4.9 cases per year, equivalent to a 50% increase in mortality from 2001-2002 to the period 2003-2010, which includes the prewar period and the armed conflict's period.⁹

Adding to the clear and present dangers of war are the threats of multiple variants of SARS-CoV-2. Under peaceful conditions, the pandemic has caused more than six million deaths.¹⁰ Beyond the deaths that are directly related to this infectious disease, there is excess mortality because of delays in cancer diagnosis and treatment. For example, in the United Kingdom, an increase in cancer mortality is estimated for the following years, up to 9.6% for breast cancer, 16.6% for colorectal cancer, 5.3% for lung cancer, and 6% for esophageal cancer.¹¹ The safeguards and precautions that have saved lives disappear during the war, and among refugees and survivors, the higher infections of SARS-CoV-2 will exacerbate the situation further. This too will disproportionately affect patients with cancer. Early data suggest that patients with lung cancer who are infected with COVID-19 disease have a seven-fold higher risk

of developing a severe acute respiratory syndrome, with an estimated increase in mortality of up to 30% or more.¹²

One of the ways that war takes lives is through cancer. War increases the risk of cancer. War interrupts and prevents effective treatment for cancer. War exposes vulnerable patients with cancer to infections and threatening conditions. War diverts resources from cancer care. War leads to delays in diagnosis—as those involved seek shelter and safety, ignoring concerning signs and symptoms, and the very hospitals and clinics are overrun, damaged, or destroyed. These delays in cancer diagnosis and care increase mortality. Up to an 8% increase in the risk of death has been reported for every 4 weeks of delay in cancer surgeries. A 12-week delay in surgery for breast cancer is associated with a 26% increase in mortality. Similar correlations have been reported for bladder, colorectal, head and neck, and non-small-cell lung cancer. Delays in neoadjuvant and/or adjuvant treatments have also been related to a statistically higher risk of death among bladder, breast, colorectal, non-small-cell lung cancer, and cervical cancer.¹³

CANCER IN UKRAINE

Ukraine is located in Eastern Europe, with approximately 44 million people living there in February 2022. After the post-independence period from the former Soviet Union, Ukraine has made efforts to improve its centralized health system. Unfortunately, because of several circumstances, the improvement has been slow.¹⁴ Ukrainian cancer reports show some lack of information from some cities and regions considered by Ukrainian authorities as part of the country.¹⁵ According to the Globocan database, the age-standardized incidence of cancer in Ukraine was 180/100,000 and 240/100,000 for females and males, respectively, in 2015. Reported mortality for both sexes was 102.5/100,000 in 2020. The estimated 5-year prevalence of cancer cases for all ages is 927.6/100,000 in the country. Lung cancer, colorectal cancer, and gastric cancer are the most common cancers among men; breast cancer, colorectal cancer, and cervical cancer are the most frequent types of cancer

among Ukrainian women.¹⁶ Cancer is the second most common cause of mortality in Ukraine, with 15% of the total deaths from cardiovascular diseases.

One of the most relevant institutions for patients with cancer in Ukraine, founded in 1920, is the National Cancer Institute, located in the capital city of Kyiv. This institute established the Ukrainian Cancer Registry in 1966. They also promoted the National Programme Control of Cancer until 2016. Before February 24, 2022, this institute had more than 1,000 employees and 95 researchers, 600 swing beds, and accommodated 400 patients with cancer each day.¹⁷ According to the Ukrainian Society of Surgical Oncology, there are at least 150 acting members. This society strongly cooperates with the National Cancer Institute of Ukraine.¹⁸ On the basis of UATOM information, Ukraine has at least 40 radiotherapy centers with 133 gamma therapy units and 24 electron accelerators.¹⁹ By 2018, 1935 clinical oncologists were working in Ukraine with a ratio of new cancer cases per clinical oncologist of 73.²⁰ The Organization of European Cancer Institutes, OEI, also has one Ukrainian member, the Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology of National Academy of Sciences of Ukraine (IEPOR), in Kyiv.²¹

WAR AND CANCER: THE NEW REALITY IN UKRAINE

At the onset of the current armed conflict in Ukraine, there was an international concern that the local health system could be irrevocably damaged or destroyed. Those fears are becoming a reality. Critical health infrastructure has already been affected with reports of entire hospitals being destroyed, tragedies with countless current and future victims.

Despite the urgent health needs for acute injuries, including corporal trauma in the context of war, cancer treatments must continue uninterrupted, lest the mortality of battle be amplified. Significant plans to do just that are being made. There are an estimated 1,500 pediatric patients currently undergoing oncologic treatment in Ukraine, many of whom have been transported in adapted trains to neighboring countries, such as Poland, to assure the continuation of their treatments. Efforts are underway to send some of these children to highly qualified hospitals in Germany, Italy, Spain, and the United States as well.²² Several international societies aiming at childhood cancer have openly declared their solidarity with health care workers and patients with cancer from Ukraine.²³

Adult patients with cancer face inconceivable challenges. Loss of family structure and support with an uncertain future, war-related stress, lack of access to facilities and infrastructure, lack of transportation, shortage of essential medicines and medical equipment and teams, financial devastation, and inability to provide basic, much less optimal, cancer care are among the many issues that patients face war. Because of the instructions from Ukrainian

authorities, the male population age between 18 and 60 years is not permitted to flee the country. The female population and older men with cancer from Ukraine will face difficulties properly continuing their cancer treatments in their homeland. Those who have left or will leave will certainly prioritize food and shelter for themselves and their families in the short term. Cancer, however, will show no sympathy or patience and will not kindly accommodate delays in treatment.

Delays in cancer treatment in Ukraine are inevitable. Medical supplies, including chemotherapy and other treatments, will be hard to obtain and administer to patients. Oncologic surgeries will be postponed while the strained health care system cares for those injured in battle. Damages to infrastructures, such as power, transportation, and supply chain, stand as insurmountable barriers to even basic health care. Protracted courses of therapy are difficult to imagine against the backdrop of daily uncertainties. It is critical to ensure that WHO essential medicines, including cancer treatments for adults²⁴ and children,²⁵ remain available for the people who cannot or will not leave the country. It is just as critical to continue providing palliative care to all patients suffering from cancer-related pain or who are in terminal conditions requiring essential analgesics and other supportive medications, oxygen, psychologic support, and other care.

As mentioned earlier, Hanna et al¹³ published a systematic review whose purpose was to estimate the impact of delaying the application of interventions for cancer treatment in terms of survival. For this aim, they selected 34 primary studies that included surgery, radiotherapy, and systemic treatments as curative options, involving or not neoadjuvant or adjuvant indications in distinct types of malignancies, such as cancers of the bladder, breast, colon, rectum, lung, cervix, and head and neck. Considering the limitations of this study and using only the risk parameter of those indications that were significant and consistent in the meta-analyses, we theoretically estimated the effect of the delay in cancer treatment on the basis of the Ukrainian reported population and cancer rates by Globocan.¹⁶ To do this, we corrected mortality by the corresponding hazard ratio and then projected the differences between the corrected mortality and the data reported by GLOBOCAN for Ukraine. [Table 1](#) shows the potential deaths attributable to a 4-month delay in applying cancer treatment in some cancers for the Ukrainian population.

Assuming the current situation, it is extremely hard to believe that cancer treatments in Ukraine will not be extremely altered or interrupted. Medical supplies, including chemotherapy and other treatments, will be hard to obtain and administer to patients. Oncologic surgeries will probably be postponed for a long time resulting in worsening of the prognosis of patients with cancer. Radiotherapy treatments will not be possible to provide if the current

TABLE 1. Estimated Excess of Deaths Attributable to a 4-Month Delay in Applying Therapeutic Indications in Some Cancers, Considering the Population of Ukraine in 2021 and the Mortality Reported by GLOBOCAN for Neoplasms

Type of Cancer	Treatment	Estimated Deaths by 4 Months of Delay
Bladder	Surgery	119
Bladder	Systemic neoadjuvant	557
Colon	Surgery	663
Breast	Systemic adjuvant	1,118
Nasopharynx	Radiotherapy	306
Cervix	Radiotherapy adjuvant	848

situation does not improve and the armed conflict is promptly stopped. By now, all the efforts must be made to attempt assuring that WHO essential medicines, including cancer treatments for adults²⁴ and children,²⁵ stay available for the people who will not leave the country, understanding that disruption of supply chains is a fact. It is mandatory to provide palliative care to all those patients who are suffering from cancer-related pain and/or patients who are in terminal conditions requires essential analgesics and other medications, oxygen, hydration, psychologic support, and other care as well.

It has been reported that patients with cancer and SARS-CoV-2 infection have higher mortality rates.²⁶ Latest reports from Ukraine including the number of deaths because of COVID-19 showed 112,459 victims since the pandemic began, but with no updates during the last few weeks.²⁷ With more active cases of this disease currently in Europe, the risk of acquiring SARS-CoV-2 may also increase the risk of death among the Ukrainian cancer population, especially among those patients who will not have the chance to get medical care and also for those who are subjected to cramped conditions.

CANCER RESEARCH IN UKRAINE

Cancer research has been negatively affected because of armed conflicts in different low- and middle-income countries.²⁸ Lack of safe conditions and environment; lack of personnel; alteration in the chain of supplies for devices, drugs, and others; and improper conditions for meetings, suboptimal communication systems, and networks are few examples that limit the options to develop research. Unexpectedly, only 1 month ago, similar situations because of this war are affecting cancer research in both Ukraine and Russia. A recent statement from the American Association for Cancer Research addressing this war supports the safety and integrity of scientists and clinicians from Ukraine and notifies about risk that present research efforts in Ukraine and Russia might be jeopardized or hampered.²⁹ At this moment, it is probable that most or all cancer investigations in Ukraine are paralyzed. Cancer research does not lend itself to interruptions, and the loss of animal models, cell lines, and the vital continuity of experiments and analyses will cripple cancer research in

all involved countries. This loss is hard to see and impossible to quantify but could set researchers back decades. This affects us all.

FINAL REMARKS

Pandemics, natural catastrophes, and wars have been part of history since its beginnings. Immediate casualties in armed conflict are always anticipated. What is often hidden or forgotten are the indirect deaths, including those from cancer—when treatment is abruptly stopped by war or when war leads to the disease itself. Ukraine has been involved in an unexpected armed conflict resulting in less than three weeks in partially destroyed critical infrastructure for many cities, including health services and hospitals. Hundreds of civilians have already died, and more than 2.5 million fled. Patients with cancer, who have fled or who remain in Ukraine, will see their care interrupted, and this will cost countless lives in the coming years. A nonprompt stop in this conflict also raises the concern on a hypothetical risk of using nuclear weapons. We cannot fathom the direct and indirect costs and the threat to our very existence.

Plans for mitigation must be implemented to provide as much help as possible to the Ukrainian war-affected cancer population. The global oncologic community, including societies, associations, private cancer institutions, networks, public health systems, universities, medical schools with oncologic education and cancer-related programs, and nongovernmental organizations (such as International Red Cross, Doctors Without Borders, and the WHO) must work together to help these patients and provide the care they deserve and that urgently require. Medical journals should allow spreading original reports and editorials that not only enhance awareness concerning the impact in science and health care of the war that is affecting Ukraine, but also any other armed conflict worldwide that threatens innocent persons including health care workers, researchers, and patients.

The conflict in Ukraine has captured headlines, but sadly, it is not the only recent or ongoing war. Many armed conflicts, ethnic violence, terrorism, political unrest, and other types of crisis are affecting many countries and territories of the world, resulting in deaths and forced displacement that may have similar consequences as the current situation in Ukraine, including a higher risk of cancer-related mortality.

In the past decade, we have made remarkable progress in cancer care, delivering outcomes previously unimaginable. The towers of progress, however, crumble at the hands of a cruel war. We speak in solidarity with the victims of that war, including patients already embattled in a war of their own—a war on cancer where the tools needed for victory have already been forged but now lay just out of reach. We long for a peaceful end to the conflict and when that day comes, which will not be soon enough, it will be vital that we all mobilize to regain whatever ground we can with regard to health care access and proper cancer treatment.

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Manuscript writing: All authors

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The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/go/authors/author-center.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

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Travel, Accommodations, Expenses: AstraZeneca, Roche

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Travel, Accommodations, Expenses: Pfizer, Boehringer Ingelheim, Roche

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Research Funding: Pfizer (Inst), Bristol Myers Squibb (Inst), AstraZeneca (Inst), Merck Sharp & Dohme (Inst)

Patents, Royalties, Other Intellectual Property: Patent Property, Imugene

No other potential conflicts of interest were reported.

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