



## Current Perspective

## Far-reaching impact of the Russian invasion of Ukraine on global cancer research



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**Abstract** Clinical research is crucial for national cancer control plans. Prior to the Russian invasion on 24th Feb 2022 both Russia and Ukraine were significant contributors to global clinical trials and cancer research. In this short analysis we describe this and the impact that the conflict has had with wider consideration of the global cancer research ecosystems © 2023 The Author(s). Published by Elsevier Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

The Russian invasion of Ukraine on February 24 2022 has set in motion a series of catastrophic events. For the aggressor Russia, economic sanctions, including reduced imports of pharmaceuticals, will directly impact

the health of the country's most vulnerable [1]. For Ukraine, population displacement within and across national boundaries, destruction of healthcare facilities, displacement of healthcare workforce and damage to healthcare logistics will have serious long-term consequences that will only be mitigated by an end to the conflict and reconstruction of Ukraine's health system. Overall, around 1100 medical facilities were damaged, 144 among those were completely destroyed. Hospitals and clinics in 17 regions of Ukraine suffered from shelling and air strikes. Most affected regions are as

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Table 1  
Top 5 country-level participation in global randomised clinical trials (RCTs) published 2014–2017 by United Nations income category compared to their total cancer research outputs over same period.

	Global RCTs		Total cancer research output	
	No. of RCTs	% of RCTs	No. of publications	% of publications
<b>Lower Middle <math>n = 84</math> RCTs</b>				
India	42	50	27,601	67
Ukraine	39	46	801	2
Philippines	23	27	384	1
Egypt	12	14	6262	15
Georgia	6	7	78	0.2
<b>Upper Middle <math>n = 182</math> RCTs</b>				
Russian Fed.	115	63	4835	2
Brazil	94	52	15,272	7
Romania	62	34	3457	2
China	56	31	154,373	69
Mexico	56	31	4126	2

follows: Kharkivska oblast – 249 medical facilities, Donetsk oblast – 210, Mykolaivska oblast – 148 and Kyivska oblast – 121. Life in Ukraine changes on an almost daily basis as Ukrainian citizens move to safer places or return homes. Nevertheless, figures show that about 7.5 million Ukrainians have left the country and approximately 3.0 million returned. Almost 7 million citizens are considered internally displaced. It is hard to say the exact number because Ukrainian counterattacks, liberation of captured cities and winter conditions constantly change patients place of residence, particularly in the Eastern Oblasts (see Table 1).

The impact of Ukrainian refugees in Europe will also create new challenges for health systems capacity, especially for Central and Eastern European countries, particularly for non-communicable diseases. While there has been substantial discourse on this already [2,3], what has gone relatively unnoticed is the profound impact the war is having on cancer clinical research. Both Russia (upper middle-income) and Ukraine (lower middle-income) are unusual in their global cancer research activities. Both are two of the largest contributors to clinical cancer research, especially to industry-sponsored randomised clinical trials (RCTs).

Ukrainian clinical cancer research, in particular, has enjoyed a long history. Between 2014 and 2017, a total of 636 cancer RCTs were published. Ukraine contributed to 39 of these, one of the highest lower middle-income contributors, placing it only just behind India, a country over thirty times its size. Moreover the quality of RCT remains high; Ukraine is the only one post-Soviet country which is represented in the “Clarivate Analytics” ranking (2022) among the 19 leading countries of the world with highly cited publications in clinical oncology. For upper middle income countries, Russia was by far the largest contributor to 115 cancer RCT over this period. At the start of the war, an

analysis of [ClinicalTrials.Gov](https://clinicaltrials.gov) on February 24 2022 indicated that Ukraine had  $n = 245$  active pharmaceutical cancer clinical trials, of which 127 were actively recruiting. Corresponding figures for Russia were  $n = 667$  and 352, respectively.

Beyond the numbers, clinical cancer research finds itself in uncharted territory. The loss of centres which are such major recruiters to global RCTs will have significant impact worldwide. It has taken many years for Ukraine to develop its strong cancer clinical trials ecosystem including research ethics processes, contract research organisations and high public trust. Such developments have been put at grave risk by the ongoing conflict. The loss of the opportunity to participate in RCT is a significant loss for Ukrainian patients who thereby lose access to innovative cancer treatment. In addition, since the start of the war, Ukraine has lost a large number of clinical research specialists. Human capital that will need to be rebuilt in the post-conflict era.

Many major clinical trials will be delayed as new centres elsewhere are brought online and some will undoubtedly fail to recruit. Pharmaceutical companies are struggling to balance ethical duties to patients with broader security and geopolitical realities. Even if the legal, ethical and security issues can be surmounted, the war has created massive logistical barriers to supplying basic standard-of-care cancer medicines. Sponsors are also grappling with serious moral issues, for example, do they have an obligation to continue ongoing cancer clinical trials in conflict settings?

As the extent of Russian violations against international humanitarian law has become apparent, multinational corporations have come under increasing pressure to withdraw all engagement with Russia. Additional pressure has been applied to these companies through the so-called Yale List [4], which has illuminated which companies have/have not withdrawn from Russia. Many of the major pharmaceutical companies on the Yale (AstraZeneca, Pfizer, Glaxo Smith Kline (GSK) et al) have taken the position to stop new investment and new clinical trials but to continue both preexisting trial recruitments and supplying standard cancer medicines as per contractual arrangements.

The situation in Ukraine is very different. While many cancer centres in Kyiv and the more Western and Central Oblasts are still functioning at time of writing, many centres in the East and South have been destroyed/occupied by Russian forces or rendered unsafe by proximity of the fighting [5]. The massive displacement of the Ukrainian population, coupled to hospitals having to orientate themselves to a war footing, has meant that many cancer trials have had to be suspended, although anecdotal reports reflect attempts by many cancer centres still operating in Kyiv and Western, Central Ukrainian Oblasts and even those

close to front-line continue to retain a lot of active clinical cancer research.

Ukrainian centres and research sites have gained priceless experience around the logistics and ethics in the continuation of clinical research activity in conflict. For example, Dnipro State Medical University, located relatively close to the front line that arcs up from Kherson in the south, passes through the Donbas and ends further north, near Kharkiv, has provided treatment for about 200 patients in 28 clinical trials with more than 3000 completed patient visits and 100% source data verification since the start of the conflict. The cancer centre has learnt invaluable lessons for conducting clinical cancer research in high risk environments, germane to many conflict countries around the world, e.g., MENA region.

The experience of Ukraine has shown that it is necessity of investing in the development and training of research sites, using the latest site management systems. Such systems should have deep planning of all activities, including major crisis, and automated performance control, remote data entry and remote monitoring. All of which have proven to be practically valuable for conducting clinical research in conflict for Ukrainian centres.

What then of the future? This crisis could precipitate a permanent move of cancer clinical research activities away to other countries, leaving Ukraine and the surrounding region bereft of clinical trial capacity. How the global cancer community meets not just its humanitarian obligations during conflict but also its development obligations in the post conflict space is a critical issue. Reconstruction and recovery of Ukraine's cancer services and systems must take account of and include research. (Re)strengthening clinical cancer research across all the major Oblast cancer centres has to be planned for at the earliest opportunity, and in parallel with systems strengthening. The European Cancer Organisation – American Society For Clinical Oncology (E.C.O – ASCO) Special Network on the

Impact of the War in Ukraine on Cancer has pledged its support to overcoming this challenge. The global oncology community needs to address these questions and others as a matter of urgency, as we consider how to best support clinical research in Ukraine and the integrity of research systems in the region.

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### Author contributions

IB, RS, ML developed the proposal and analysis.

All authors co-drafted the manuscript.

All authors finalised the manuscript.

### Conflict of interest statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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