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# Impact of COVID-19 on Oncology

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June 12, 2020

# Contents

# 1. Abstract

The coronavirus pandemic of 2019–2020 is an infectious disease caused by extreme acute respiratory coronavirus syndrome 2 (SARS-CoV-2). The virus primarily spread among people when they closely meet each other.

Due to the decreased immune-compromised state, cancer patients are known to be at greater risk among community-acquired respiratory viruses such as influenza, SARS CoV-2 virus, etc. The treatment regimens of cancer such as chemotherapy, immunotherapy, and radiation therapy harm patient's immunity making them more prone to the risk of getting infected with COVID-19 virus.

COVID-19 pandemic is impacting at every stage of cancer care i.e. screening, diagnosis, treatment, research, and development. Through this whitepaper, we have enlighted about the effect COVID-19 virus in cancer patients.

# 2. Introduction

The unprecedented worldwide occurrence of the coronavirus SARS-CoV-2 (COVID-19) pandemic has a profound impact on the management of cancer patients. The COVID-19 crisis started in China in December 2019 with a cluster of pneumonia cases from an unknown pathogen firstly identified in Wuhan, China. There have been no specific clinical features identified till now that can yet reliably distinguish COVID-19 from other viral respiratory infections. Additionally, there are no specific symptoms identified for COVID-19 virus infection in cancer patients. The most prevalent clinical signs of infection are fever, dry cough, fatigue, anorexia, myalgia, dyspnea, sputum production, and kidney failure. Cancer patients receiving systemic anti-cancer treatments are at great risk as a comparison to the counterparts who are not receiving such treatments.

COVID-19 has caused a tremendous shift in the medical focus concerning many other serious diseases, including cancer. According to the American Cancer Society, more than a quarter of patients with active cancer are reporting delays in treatment. The countries where coronavirus has been increasing rapidly, many hospitals in those regions have been forced to stop such treatments. Therefore, due to the increase in pandemic situations, many cancer patients have been finding it difficult to receive the cure. And the cancer screenings are dramatically decreased so that conditions of cancer patients did not have a negative impact while the health system diverts to fight the virus.

Countries that are most affected by this coronavirus pandemic are the United States, Brazil, Russia, Spain, Italy, United Kingdom, India, etc. It has been observed that each step in the cancer management pathway has been disrupted by COVID-19 virus i.e. diagnosis, screening, treatment, research, and development.

**Screening**: Due to the coronavirus outbreak and lockdowns in various countries, screening has been diminished significantly because people with no symptoms or fewer symptoms are not visiting the hospitals for health check-ups, screening programs, routine checkups, or monitoring activity. These screening programs are necessary for the early detection of these cancer types before the presentation of symptoms that can result in a better prognosis for the patient.

**Diagnosis:** Cancer diagnosis has been significantly disrupted as patients with possible signs of cancer have been staying away from health services due to fear of getting infected with COVID-19 infection. For this reason, urgent referrals by general physicians of people with symptoms of cancer have been dropped by 75% as compared to the usual levels in England. Consequently, more than 2,300 cancer cases are likely to be going undiagnosed every week in the UK leads to a significant build-up of cases.

Similarly, a huge population of the world could not be diagnosed at an early stage which could be a serious problem for patients getting their condition worse.

**Treatment**: Cancer treatment therapies like chemotherapies have been highly impacted as they are prone to corona virus infections due to the low immunity. Oncologists have seen a lower number of patients with acute symptoms arriving to the hospitals. In United States, almost 80,350 oncology treatments have been delayed. A recent study of four hospitals across England has found that chemotherapy attendances have decreased by 60% amid the COVID-19 pandemic. The measures for the COVID-19 pandemic has also been applied to cancer research centers leading to the decline of the activity due to quarantine measure, working in shifts and lacking supplies. Patients who usually travelled abroad for their cancer treatment have quietly stopped receiving treatment as border of almost every country are closed and flights are not operational. Whereas, many high authorities such as FDA has issued guidelines to be followed being more flexible about their protocols. Various other measures have also been adopted by clinical physicians like remote communication with cancer patients for follow-up, reducing multiple hospital visits or routine follow-ups by making some changes and exceptions to trials protocols.

**Research & Development:** Cancer clinical research activities have been slowed down or suspended as research has been shifted to ongoing COVID-19 virus research. Recruitment of participants and new trials has been put on hold and results of the trials have undergone significant delays in clinical research and drug development timelines. Due to COVID-19 pandemic, more impact on designing, executing, gathering data, and reporting results have been observed.

### Design

- Define patient set
- Determine recruitment numbers
- Select trial location
- Establish treatment protocols

### Execute

- Coordinate with providers
- Manage enrollment
- Determine dosing administration
- Monitor Patients
- Manage timelines

## Gather Data

- Record patient data
- Coordinate with ground staff
- Collaborate on analysis

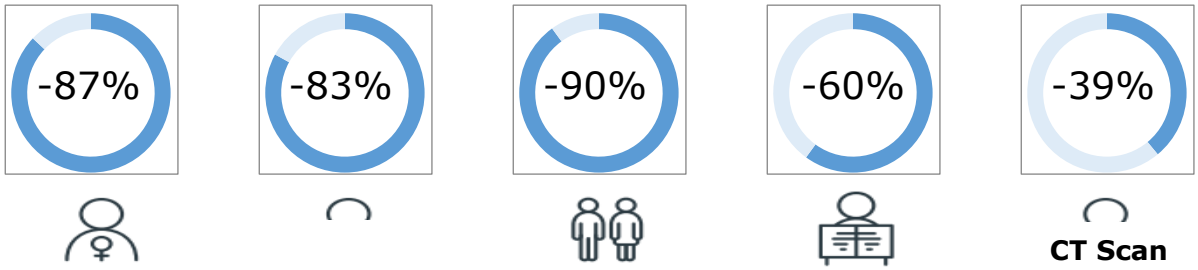
## Report Data

- Report procedures
- Present data at conferences
- Publish data in journals

## 3. How is Diagnosis and Screening Impacted?

Screening and diagnosis by several tests in suspected cases of cancer have been substantially disrupted because of COVID-19 pandemic due to which thousands of cancer cases are going undiagnosed or untreated.

Cancer Research UK (CRUK) has teamed up with charity partners to provide support to cancer patients. Many countries like Scotland, Ireland, England has put a pause to the screening services. Screening for breast, bowel, and cervical cancer can detect the disease before any symptoms show, in the early stages when treatment is more effective. But with around 200,000 people per week no longer being screened for bowel, breast, and cervical cancer across the UK, there are a significant number of early cancers left undetected before these programs can be reintroduced. As per IQVIA Real World Claims, United States has seen up to 90% reduction in diagnostic test procedures when compared from April to February. The data suggested from the current positivity rates, there could be 36,000 missed or delayed diagnoses of breast cancer during the 3-month period from early March through early June. Estimates for missed diagnosis of the four other cancers analyzed include 450 for lung cancer, 2,500 for cervical cancer, 18,800 for colorectal cancer, and 22,600 for prostate cancer.

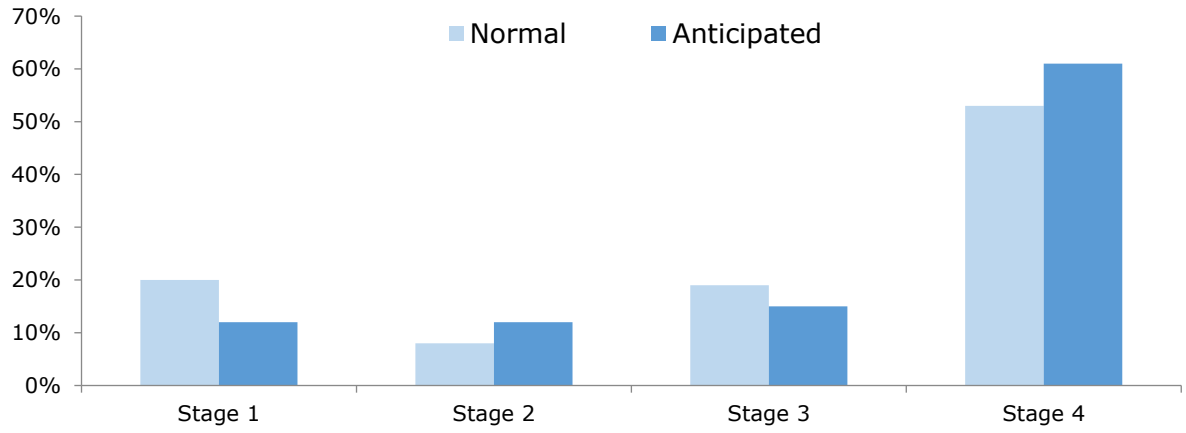



***Source:*** *IQVIA Real World Claims, April 17, 2020*

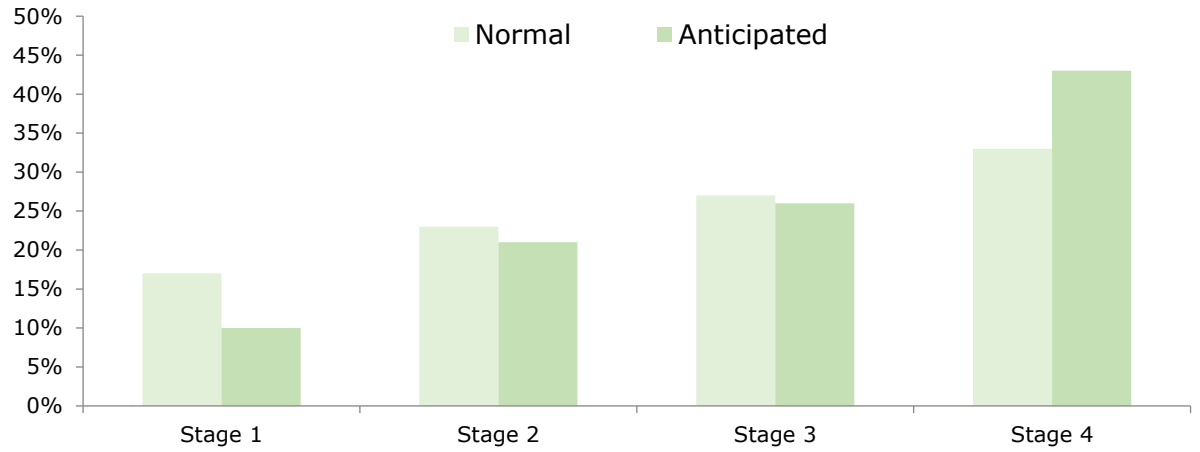
## 4. Impact on Patient Outcome

Amid the COVID-19 pandemic, there has been a significant decrease in number of patients diagnosed with cancer worldwide. The major disruption in the cancer management pathway has likely result in diagnosis of cancer at later stage leading to worsen the situation. Patients diagnosed at later stages have fewer treatment options and have a less survival rate. Data obtained from many countries affected by the pandemic suggest that the most COVID-19 patients who require hospitalization are suffering from heart disease, cancer, diabetes, and hypertension.

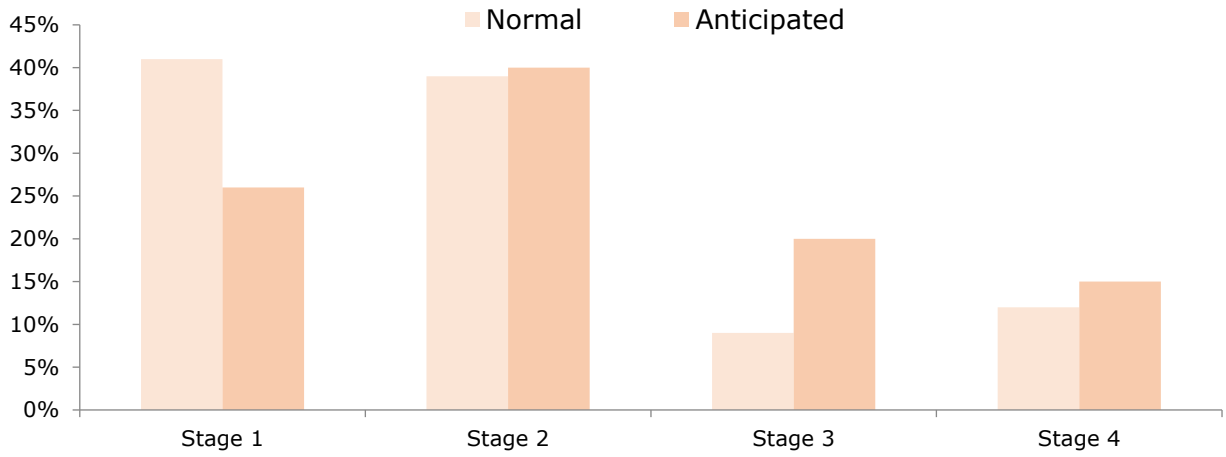
According to National Cancer Registration and Analysis Service (UK) it has been proposed that if the disruptions to the cancer pathway were to mean that people who would have otherwise been diagnosed during the COVID-19 period end up being diagnosed a stage later, then the stage shift in the three biggest cancers will look like this:




**Lung Cancer**



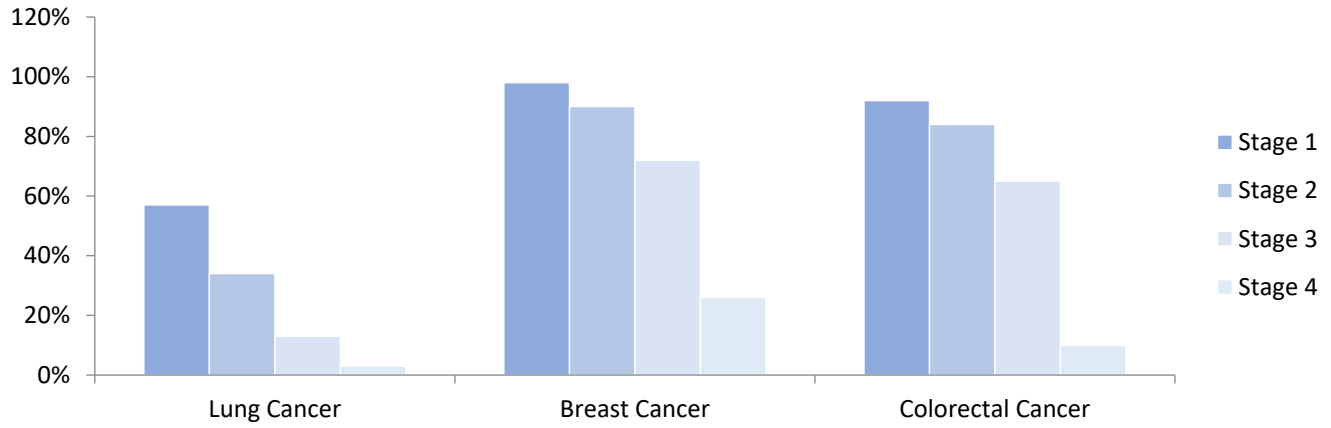

**Colorectal Cancer**




**Breast Cancer**

***Normal and Anticipated Stage Distribution for 2020, by Cancer Type***

As shown in the below figure, it has been said that due to the shift in the stages of cancer diagnosis because of Covid-19 situation then the anticipated percentage for each type of cancer stage 4 will be much higher than normal. This implies that such people with cancer will have lesser chances of survival rate to 2025. Thus, the increase in patients who are diagnosed at a later stage will most likely result in unnecessary deaths.




***Source:*** *Cancer Post-COVID: Impact, Outcomes and Next Steps by Carnall Farrar*

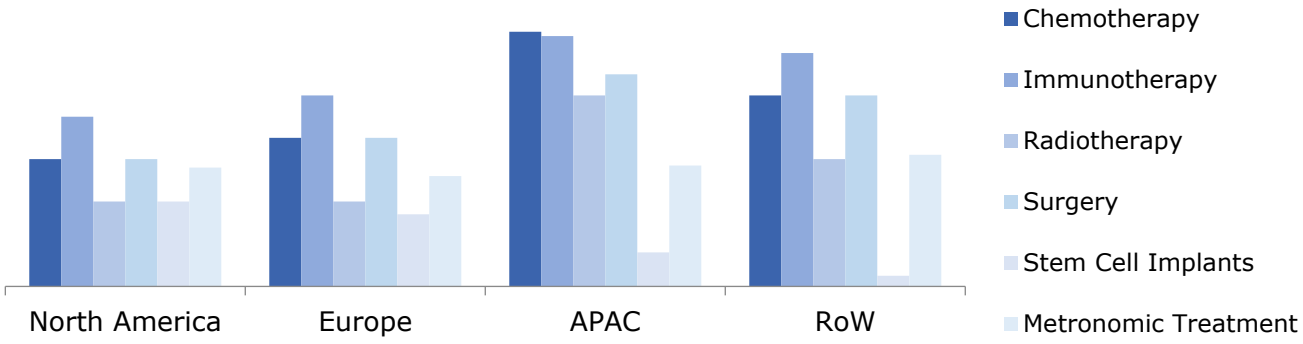
# 5. Impact on Treatment Modalities

COVID-19 is complicating life, including cancer treatment plans. Therefore, doctors are realizing that it is difficult to have a universal set of recommendations for all cancer patients and treatment decisions need to be customized for individuals. Cancer patients are at risk of being immune-compromised depending on the type of cancer they have, treatment modality they are undergoing, age, other associated medical co-morbidities, and other health-related factors.

Major treatment modalities for cancer include chemotherapy, immunotherapy, radiotherapy, surgery, stem cell implants, and metronomic treatments. Many electrical surgeries have been delayed due to the pandemic condition whereas, patients with cancer are being advised for the avoidance of the non-essential hospital visits and switching to the telecommunication for such problems.

Chemotherapy uses anti-cancer (cytotoxic) drugs to destroy cancer cells. Other cancer drugs include targeted cancer drugs and immunotherapy. Cancer drug treatments can increase the risk of complications from COVID-19 because they can harm the patient by attacking his immunity. The immune system protects the body against illness and infection caused by viruses like coronavirus. Having a weak immune system can mean you are less able to fight this infection.

Due to coronavirus outbreak, many cancer organizations and institutes have recommended not to use chemotherapy, immunotherapy, radiotherapy, and a few drugs unless or until they are the only option for cancer treatment because they affect the immunity of patients which makes them prone to getting infected with COVID-19 virus. Thus, many cancer patients particularly those, currently being treated or with certain medical histories are at increased risk of complications of COVID-19 infection. Multiple studies suggest that the outcomes of cancer patients are also dependent on social infrastructure. Managing cancer patients during the COVID-19 outbreak has created many challenges and oncology therapies are acceptable only to patients with mild infections



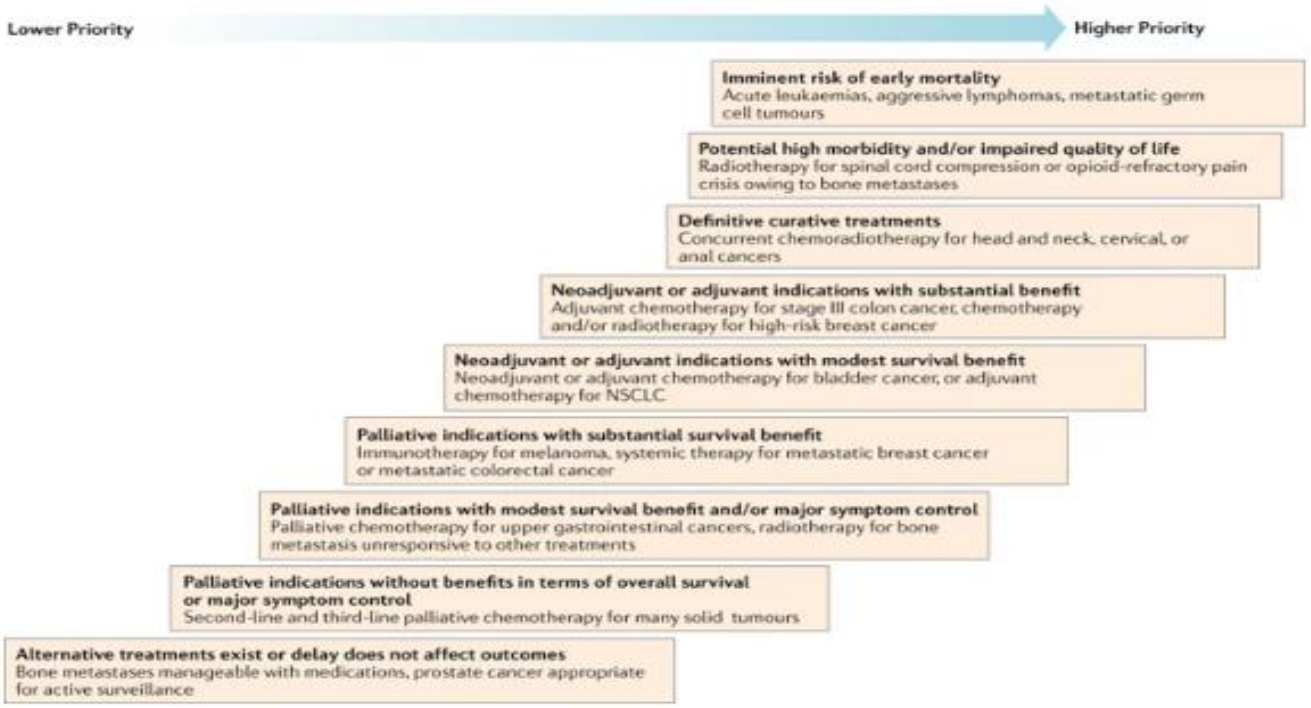
***Source:*** *Coronavirus and Cancer- Latest Updates by Cancer Research UK*

"It's devastating to see the impact that COVID-19 is already having on the lives of cancer patients, and these new figures highlight a concerning picture for projected cancer deaths. We can only estimate how many avoidable deaths there might be based on a number of assumptions, but if the government acts now, they can prevent more lives being lost. The sooner we have adequate testing for all NHS staff and patients, including those without symptoms, the sooner COVID-free cancer hubs can diagnose and treat cancer effectively, and patients can be reassured it's safe to go to hospital. And by ensuring there's enough staff and kit to work through the growing backlog of patients, the better equipped the NHS will be to deliver vital cancer care."

- Sarah Woolnough, Cancer Research UK's Executive Director

## 6. Conceptual framework for prioritizing the use of radiotherapy and systemic treatments during the COVID-19 pandemic

Researchers of Queen's University have proposed a conceptual framework for prioritizing cancer treatment during pandemic involving the radiotherapy and systemic therapy. This system is mainly focused on three scenarios (1) preparedness (with no confirmed cases); (2) Moderate health-care resource limitation; and (3) severe health-care resource limitation.

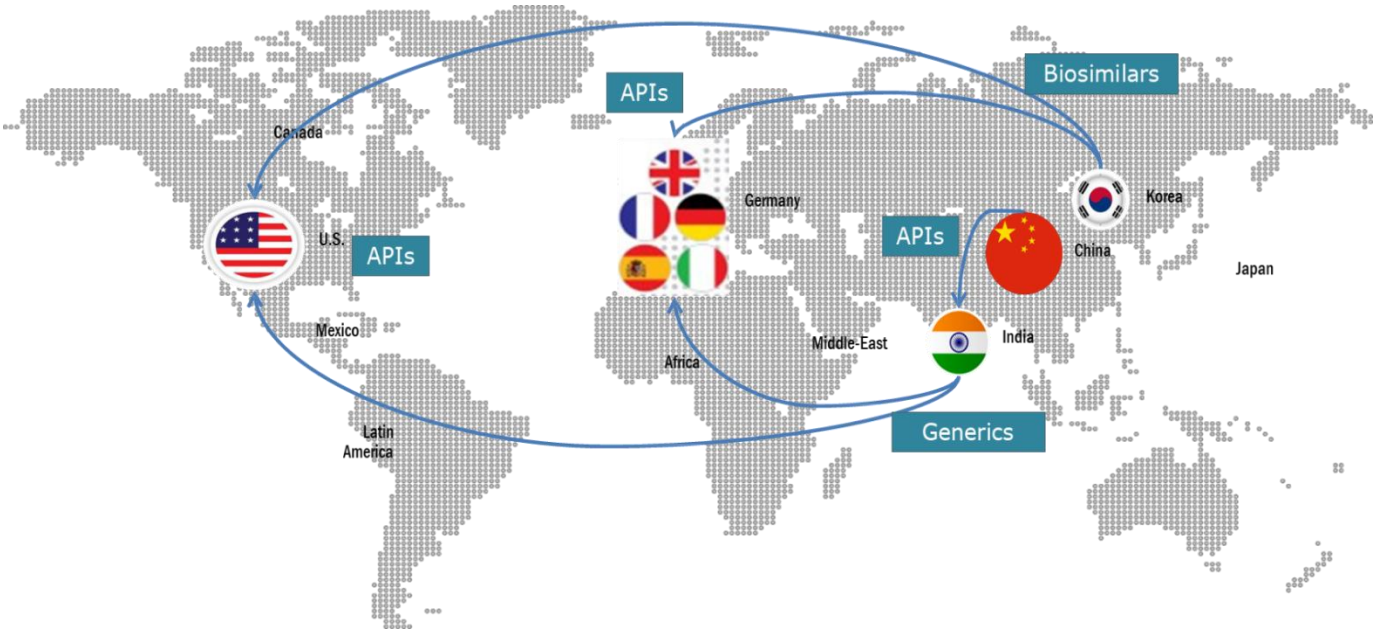



It includes the magnitude of treatment benefit, possible effects of treatment delays or interruptions on outcomes, patient-specific considerations and the availability of staff and resources to safely deliver treatment.

***Source:*** *Cancer, COVID-19 and the precautionary principle: prioritizing treatment during a global pandemic*

# 7. Impact on Availability of Drugs and API to the World

COVID-19 has caused an increase in demand for APIs and drugs that are used as anti-malarial, followed by bronchodilators, antibiotics, and antivirals. Also, there are shortages for sedatives, painkillers, anesthetics, muscle relaxants, and other steroids that are required for patients on a ventilator. These ongoing shortages have increased the need for generics, resulting in an accelerated approval by the FDA and the lifting of existing import alerts. Around 48 percent of the world's pharmaceutical ingredients used to make generics come from India and China.




***Major Exporters of API, Generics and Biosimilars in the World***

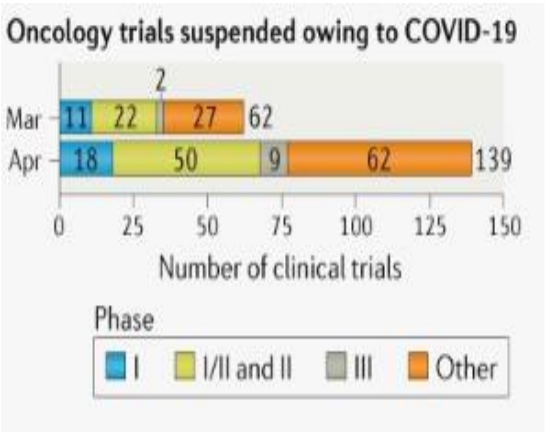
China, India, and Korea are the major exporters of API, generics, and biosimilars to the world and during this outbreak due to various government restrictions on export, import, and manufacturing shortage because of the decreased workforce has caused a shortage of oncology drugs in many countries.

## 8. Impact on Oncology Clinical Trials

COVID-19 outbreak has disrupted clinical research in almost every part of the world; from the enrollment of patients into a clinical trial to reporting the data for the final report of the trial every step of clinical trials has been affected. The redials which are ready to review should be submitted online. If a breach occurs during the pandemic, then the investigator should have to communicate with the sponsor, record, and report the situation to the ethics committee.

As medical infrastructure became increasingly overwhelmed with COVID-19-related illnesses, investigators are dealing with new regulatory and operational hurdles. Nearly 60% of investigators reported that the COVID-19 pandemic had a moderate or high impact on patient visits (delayed or canceled).

As per clinicaltrials.gov, due to COVID-19, more than 130 oncology clinical trials have been affected. Mostly affected trials were of either IV$^{th}$stage or stage of trial was not stated. In future, there is possibility that the COVID-19 pandemic could have a lasting impact on clinical research and the practice of medicine moving forward, with new approaches such as telemedicine possibly being adopted with increased frequency.




***Source:*** *Impact of COVID-19 on Oncology Clinical Trials by, S Upadhaya et al 2020*

***Number of interventional oncology trials suspended in March and April owing to COVID-19***

# 9. Clinical Advancements in Medical Oncology

In recent years, astonishing progress has been made to understand, prevent, diagnose, and treat cancer because of which cancer death rate has dropped from 2015 to 2019. But due to coronavirus pandemic, this cancer death rate is anticipated to rise this year and in coming few years because patients with acute symptoms or no symptoms are not getting proper screening and diagnosis which is causing a delay in diagnosis and finally leading to diagnosis at later stages where treatment is either not much effective or not proper to sustain patient for longer period of time.

The following are some evolving advances that offer great promise for patients living with cancer:

1. Cardio-Oncology: Given the prevalence of cardiovascular disease and the potential cardiac toxicity of many cancer treatments, cardio-oncology is becoming an important emerging field in cancer care.

   Cardio-oncology helps assess any heart issues, a patient may have prior to cancer therapy, as well as any side effects that occurs during and following chemotherapy and radiation. Through screening and monitoring, patients' cardiac needs are addressed, allowing a clinical team, in coordination with the patient's oncologist, to prevent and proactively manage any heart conditions that may arise.

1. Immunotherapy: Another rapidly emerging method of treating cancer is immunotherapy, a form of treatment that harnesses an individual's own immune system to recognize, control, and potentially cure cancers. It is a different approach from conventional treatments such as chemotherapy or radiation. The latter attack the disease directly, while immunotherapy aims to empower the body's own immune system to recognize cancer and eliminate it.

   Immunotherapy comes in many forms, including treatment vaccines and drugs that are received intravenously. The side effects of immunotherapy drugs are often far more manageable than those of traditional chemotherapy.

2. Virotherapy: There is a new treatment for certain types of melanoma, and it works in an unusual way. Using a genetically engineered herpes virus, medical oncologists inject the virus directly into tumors. The virus is modified to the point where it recognizes the melanoma cells as a host.

   This unique drug, known as talimogenelaherparepvec (T-VEC), not only can kill the tumor cells where it is injected, but it also triggers the patient's immune system to recognize the virally infected melanoma cells leading to the death of other melanoma cells throughout the body. The application of this drug is for patients who have melanoma of the skin and lymph nodes that are too extensive to be removed surgically.

3. Targeted Therapies: Targeted therapy drugs are considered a special type of chemotherapy that targets cancer cells' inner makeup while leaving most healthy cells unaffected. While traditional chemotherapy drugs can be used for various types of cancer, targeted therapies have a specific effect on cancer cells with a mutation. This type of therapy can directly kill cancer cells, prevent cancer cells from dividing, or even inhibit blood vessel formation by tumors. Although, targeted therapy is often used alone; it is sometimes used in conjunction with other cancer treatments.

## 10. Precautions cancer patients take amidst the corona virus crisis:

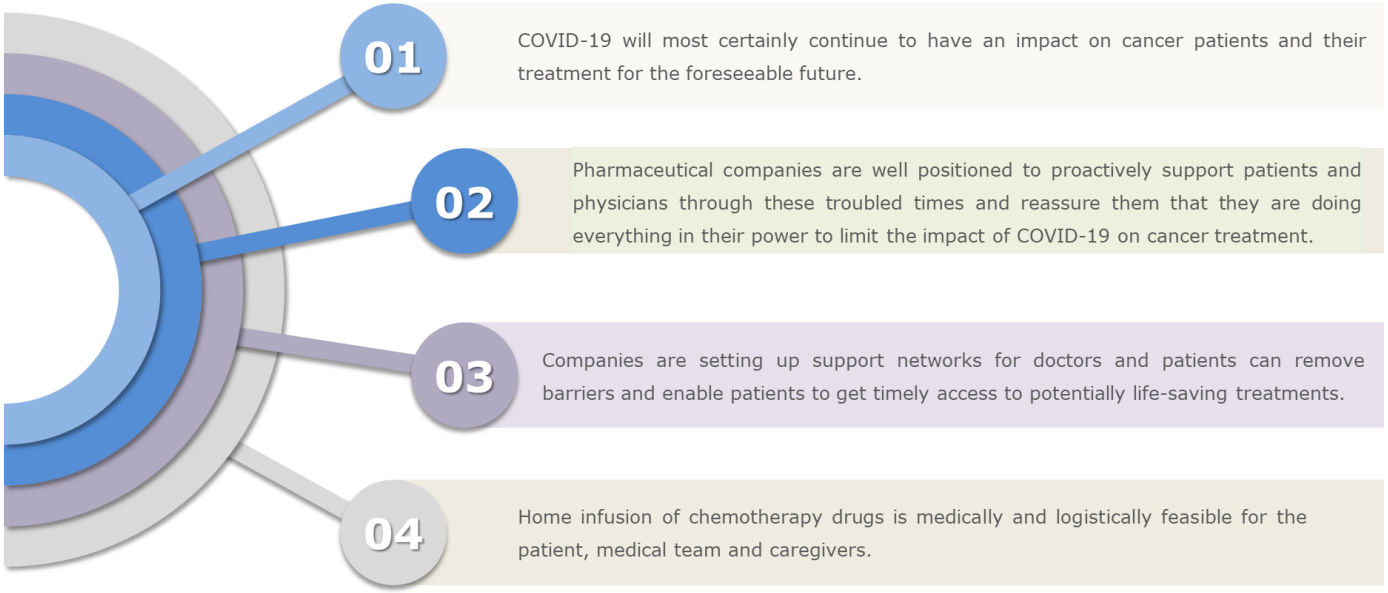
- Cancer patients are advised to maintain social distancing.
- Regular handwashing with soap or alcohol-based hand rub.
- Patients are advised to avoid crowded places and stay in well-ventilated rooms.
- Patients are advised not to shake hands and organize longer prescriptions for regular medicines well in advance of running out.
- If a member of your household develops Covid-19 symptoms such as cold, cough, or fever they should self-isolated themselves.

## 11. What Pharmaceutical Companies are doing to Fight COVID-19 Pandemic?

Pharmaceutical companies, biotech companies, research institutes, cancer associations, and every associated organization are giving their best to fight COVID-19 pandemic and providing the best possible care to cancer patients by taking new initiatives, launching new products, collaborating with other for research and development, conducting clinical researches and more. Below are the few examples of the initiatives taken by such organizations:

- Fred Hutchinson Cancer Research Center has collaborated with Roche for leveraging digital technology to help cancer patients undergoing chemotherapy. The project will focus on reducing unplanned emergency department visits through remote monitoring systems.
- Varian launches "Noona", to meet the growing demand for remote cancer patient monitoring in response to COVID-19 impact.
- TERAVOLT (Thoracic cancers international COVID 19 collaboration) registry for thoracic cancers has been formed to gather information on patients with thoracic cancer patients infected with COVID-19. This registry is designed to capture patients with thoracic malignancies regardless of therapies administered.
- Evotec has allied with Takeda to expand into gene therapy research.

# 12. Conclusion



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