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*Patients treated for cancer are at high risk for serious infections that increase suffering and delay essential cancer treatment. Effective antibiotic treatment is therefore lifesaving.*

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## Successful cancer treatment relies on effective antibiotics

- Infections are one of the most common complications faced by cancer patients.
- Antibiotics are crucial for safe cancer surgery.
- Multidrug-resistant infections are more common in patients treated for cancer than other patients.

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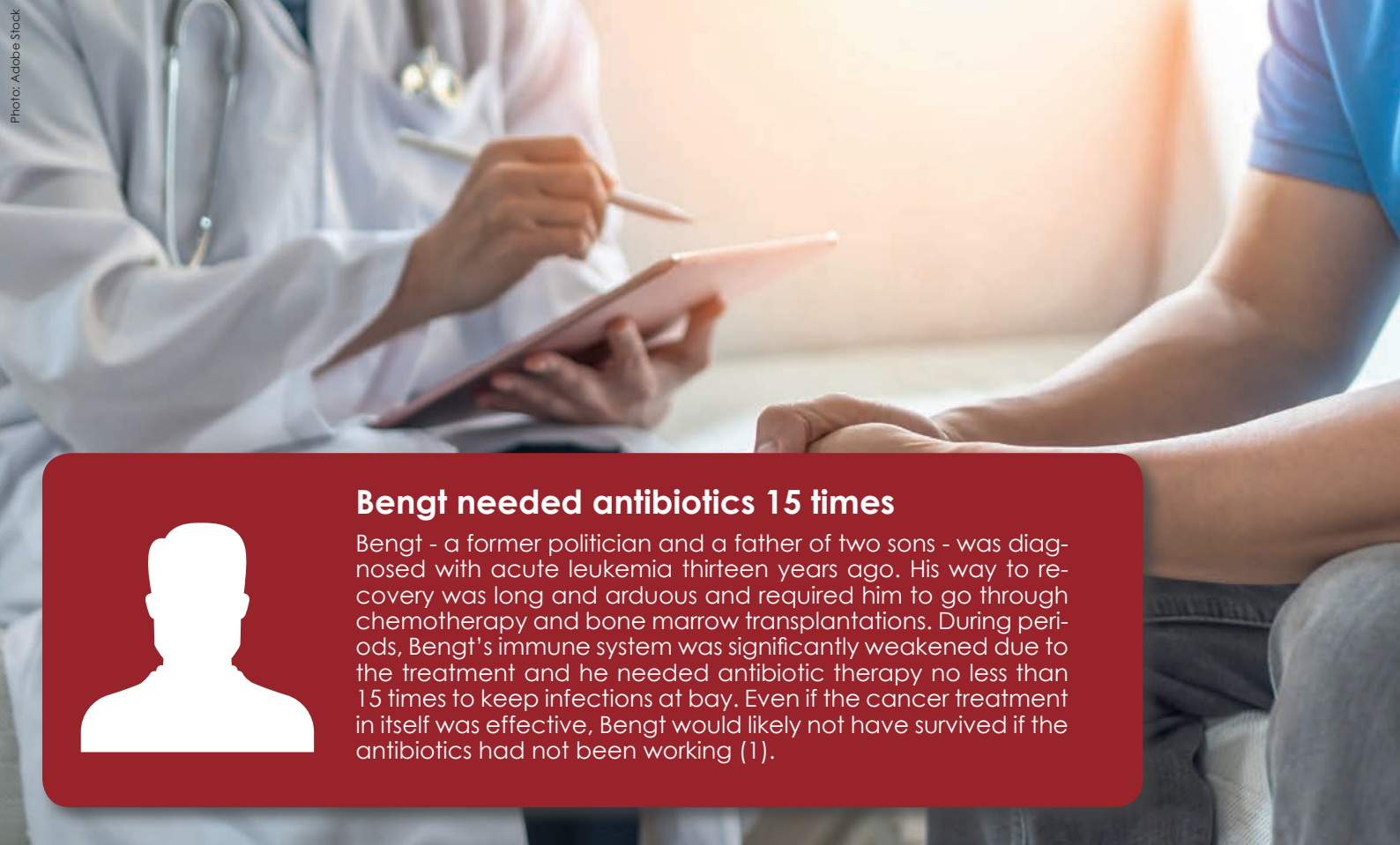


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## Bengt needed antibiotics 15 times



Bengt - a former politician and a father of two sons - was diagnosed with acute leukemia thirteen years ago. His way to recovery was long and arduous and required him to go through chemotherapy and bone marrow transplantations. During periods, Bengt's immune system was significantly weakened due to the treatment and he needed antibiotic therapy no less than 15 times to keep infections at bay. Even if the cancer treatment in itself was effective, Bengt would likely not have survived if the antibiotics had not been working (1).

## Effective antibiotics enable successful cancer treatment

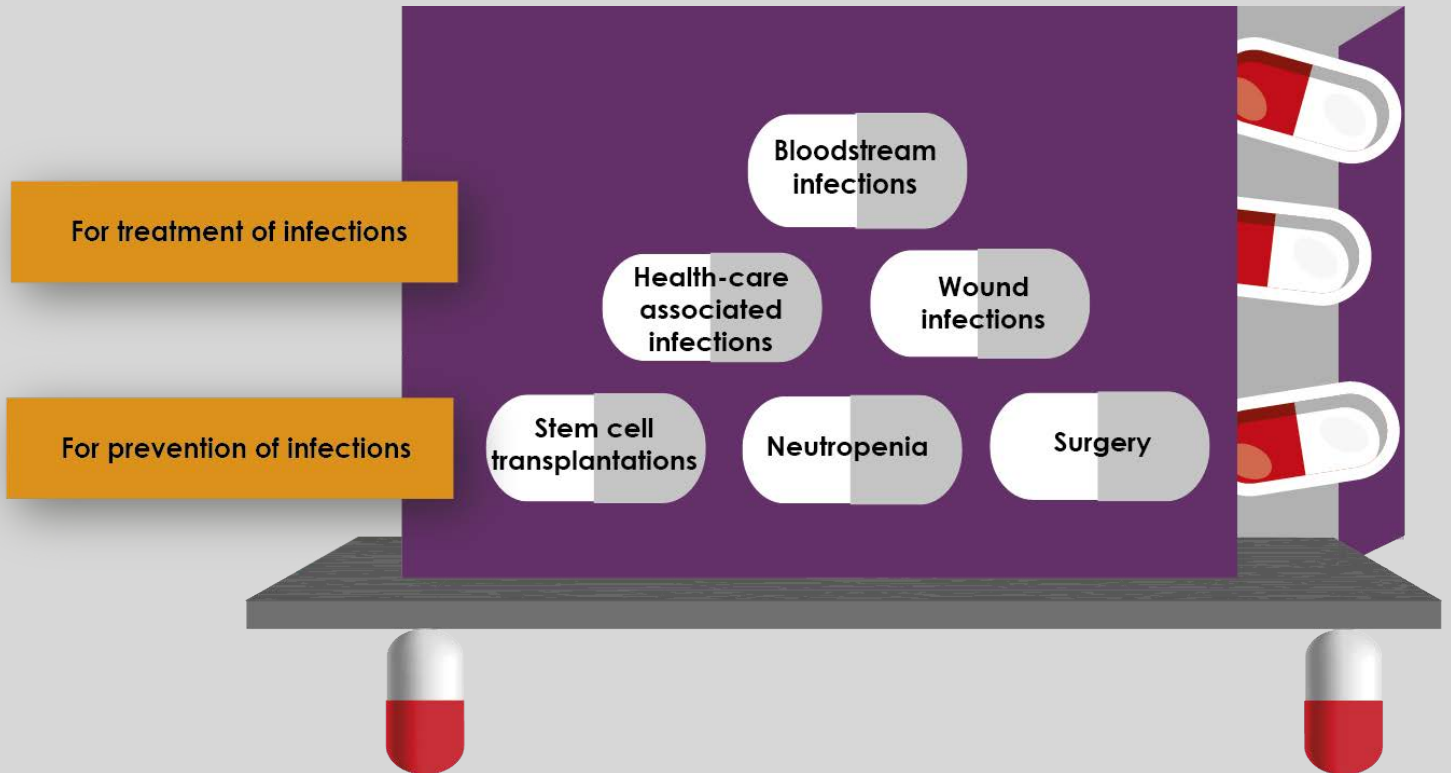
Effective antibiotics are a prerequisite for the continued success of modern cancer treatment as they are used both to prevent and treat bacterial infections. However, with bacteria becoming increasingly resistant to antibiotics, their continued effect can no longer be taken for granted.

Here is why cancer societies should get engaged on addressing antibiotic resistance:

- Infections are one of the most common complications faced by cancer patients.
- Antibiotics are crucial for safe cancer surgery.
- Multidrug-resistant infections are more common in patients treated for cancer than other patients.

# The antibiotic pyramid of cancer care

Cancer patients rely on effective antibiotics



Antibiotics are pillars for the care and treatment of cancer patients and are used to both prevent (prophylactic use) and treat (therapeutic use) infections.



***Patients treated for cancer are at high risk for serious infections that increase suffering and delay essential cancer treatment.***

***Effective antibiotic treatment is therefore lifesaving.***

***Antibiotic resistance threatens modern cancer care and may have devastating consequences for already vulnerable patients.***

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## Infections are one of the most common complications faced by cancer patients

Cancer and cancer treatment increase the risk of infection. Cancer patients often become neutropenic, which means the concentration of immune cells in the blood becomes too low. This makes it harder for the body to eliminate disease-causing intruders and patients therefore get infected more easily. Neutropenia is particularly common in patients with blood cancers, but it may also be directly caused by chemotherapy.

Patients with profoundly weakened immune systems may get antibiotics to prevent infections. Preventive use of certain antibiotics (prophylaxis) have been found to reduce the likelihood of bloodstream infections (2). Nevertheless, infections remain one of the most common complications cancer patients experience.

- Severe infection and sepsis are among the most frequent reasons cancer patients are admitted to intensive care units (3,4)
- It has been estimated that close to one in ten cancer deaths is due to severe sepsis (5) – not the cancer itself.

When cancer patients get bacterial infections, they rely on effective antibiotics for recovery. Antibiotic treatment of bloodstream infections, which may lead to sepsis, is usually started before the disease-causing bacterium is known. Rising levels of antibiotic resistance therefore increases the risk of treating seriously ill patients with ineffective medicines.

- One study found that 70% of cancer patients who initially received ineffective antibiotic treatment for bloodstream infections died within a month, compared to less than 20% of those who received appropriate antibiotics. Both inappropriate treatment and resistant bacteria were associated with bad outcomes, as was progression or relapse of the cancer itself (6).



## Antibiotics are crucial for safe cancer surgery

Diagnosis and treatment of cancer often requires invasive surgery for the removal of tumors. In fact, close to all patients with for example testis cancer, thyroid cancer and skin melanoma have surgery. This is also the case for the vast majority of patients that are diagnosed with early stage colorectal cancer or breast cancer (7). Since surgical site infections are rather common, irrespective of whether or not the surgery is cancer-related, preventive use of antibiotics is generally common practice (8). With other words, increased resistance to these antibiotics would mean that surgical-site infections became more prevalent. Up to about 50% of bacteria causing surgical-site infections in the USA may already be resistant to antibiotics routinely used as prophylaxis (9).

## Multidrug-resistant infections are more common in patients treated for cancer than other patients

Multidrug-resistant infections are typically defined as infections caused by bacteria that are resistant to at least three different classes of antibiotics, which makes them much more difficult to treat. Cancer patients are more likely than other patients to be infected by multidrug-resistant bacteria (8), partly because of frequent health care visits, prolonged hospitalizations and use of medical devices and antibiotics, which can make bacteria in the patients' microbiome resistant (8,11).



### George contracted a resistant infection following a surgery

When George had surgery for colorectal cancer, he was infected with a resistant bacterium. Over the course of 1,5 year, George was admitted to hospital no less than twenty-two times for treatment with intravenous antibiotics. Unfortunately, the resistant infection prevailed and George died in early 2018 (10).



***Addressing antibiotic resistance is critical in improving cancer care outcomes globally and is a priority for UICC.***

***We need to raise awareness and mobilize action towards change.***

***Furthermore, the lack of access in low resource settings and the excessive irrational use of antibiotics need to be addressed.***

***The time to address this issue is now.***

Dr. Cary Adams  
Chief Executive Officer  
Union for International  
Cancer Control (UICC)

In fact, a large proportion of infections in cancer patients are caused by bacteria normally residing in or on the patient's own body. A small study from India showed that almost three quarters of patients with blood cancers had bacteria resistant to carbapenem, a last-resort antibiotic, in their gut (12). However, the full picture of how often cancer patients are affected by resistant bacteria is still missing, due to lack of data. Single studies can however provide a snap shot of the current situation:

- 95 % of polled oncologists in the United Kingdom worry about increasing drug resistance and its consequences on future cancer care (13).
- More than half of Italian health-care centers reported caring for stem cell transplanted patients infected by a carbapenem-resistant bacterium. (14).
- A study from an intensive care unit of a Brazilian cancer hospital reported that more than 60% of patients with certain extensively resistant bloodstream infections died before they received effective treatment. Receiving appropriate therapy within 48 hours was strongly correlated with improved survival (15).

While the risk of *getting* cancer generally is higher in richer countries with a higher human development index (HDI), the risk of *dying* from cancer is higher in countries with a low HDI (17). In fact, 70% of all cancer-related deaths occur in low- and middle-income countries (LMICs) (18). People living in LMICs are also the most affected by antibiotic resistance, and are less equipped to financially tackle the increased costs associated with both advanced cancer care and treatment of resistant infections. At the same time, lack of access to antibiotics continue to cause more deaths than resistance in many LMICs (19,20). While global overuse and misuse of antibiotics is a major driver of antibiotic resistance, it is important that any interventions to reduce inappropriate use does not jeopardize access for those in need. In fact, in some places antibiotic use needs to increase.





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## Lack of access to medicines – a barrier to universal health coverage and health equity

High prices are a key barrier to access to a wide range of medicines – including cancer drugs – in both high-, middle- and low-income countries. One in three respondents of an international survey ranked making cancer treatment and services more affordable as the most important measure governments could take on cancer (21).

According to the WHO and the World Bank, at least half of the world's population cannot obtain essential health services and many people are being pushed into poverty because they must pay for health care out of their own pockets (22). Access to antibiotics – like access to any other medicine – should be driven by medical need and guidelines, and not by financial considerations. Restricting access by applying high prices is therefore not an appropriate tool to reduce global overuse of antibiotics.



### **Meredith was successfully treated for cancer but died from a resistant infection**

Meredith was diagnosed with acute myeloid leukemia and underwent several chemotherapy courses and successful bone marrow transplantation. However, a localized infection under her arm turned out impossible to treat even with a last resort antibiotic. The infection spread to her lungs and ultimately into her bloodstream which caused septic shock. Meredith died just before she was supposed to start University (16).



## The rising threat of antibiotic resistance

Antibiotic resistance is an urgent problem, which is already causing tremendous suffering around the world. Conservative global estimates suggest that antibiotic resistance claims at least 750.000 lives annually (23). Every third minute, a newborn dies due to sepsis caused by resistant bacteria, adding up to an estimated 214.000 deaths per year (20). In the European Union, about 670.000 cases of antibiotic resistant infections occur annually, which results in the death of about 33.000 individuals (24). Similarly in the United States, over 35.000 persons die each year because of untreatable infections (25).

## A need to act on antibiotic resistance now

Antibiotic resistance threatens the present and future of modern cancer treatment but the global and governmental response to tackle it is far from commensurate with the scale and urgency of the problem. If the global arsenal of antibiotics loses its effect, it does not matter how advanced or effective new cancer treatments are - mortality rates would go up.

## What can cancer societies do?

Cancer societies have an important role to play by advocating broadly for:

- Development of truly new and affordable antibiotics
- Political engagement on antibiotic resistance
- Universal access to cancer care and effective antibiotics - which can only be achieved through general health systems strengthening



## To keep antibiotics effective we need:

- **Increased political attention** that is commensurate with the actual scale of the problem with antibiotic resistance.
- **To stop wasting this precious resource!** The OECD estimates that up to 50% of antibiotic use for humans in OECD countries is unnecessary (26). As all use drives resistance, all unnecessary use must be avoided. There is no good reason why these countries which all have well-functioning health systems are not addressing this with urgency.
- **Development of new antibiotics.** All classes of antibiotics currently on the market were discovered before late 1980s. The current R&D model is broken. A publicly lead model, which does not rely on high sales or high prices of new antibiotics, needs to be created.
- **Global rules-based governance** to collectively manage antibiotics across sectors in a sustainable manner, to ensure that everyone in need has affordable access to effective antibiotics including in LMICs where the need is the greatest.

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