

# The strengths of partnerships in addressing AMR for better cancer care outcomes

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## Helge's story

- Helge was 21 years when he was diagnosed with Leukaemia.
- Over a 5-year period, he endured several chemotherapy cycles, a stem cell transplant and a lung transplant to survive.
- Due to the stem cell transplant, he was in isolation and dependent on antibiotics, without which he would never have been able to receive the necessary treatments that saved his life.
- It was a combination of the cancer treatments and the antibiotics that saved his life.
- He is doing well today and is a strong advocate for addressing antimicrobial resistance.

Source- Norwegian Cancer Society

## Matilda's story (name changed)

- Matilda is nine years old and is living with cancer. She was initially treated with a chemotherapy protocol but relapsed and is now getting more aggressive chemotherapy at the hospital. Matilda is a happy child and surrounded by her family and friends.
- She is now on antibiotics for an ongoing fever.
- Unfortunately, within a short time, her heart rate starts to increase, and the residents get called. She starts to look progressively unwell and within 12 hours her blood pressure drops, she has trouble breathing and is taken to the intensive care unit (ICU), intubated and put on a ventilator. Twelve hours later despite everything the ICU doctors and nurses try to do she dies.
- The blood culture that was taken at the start of the whole episode shows that it was a gram-negative bacterium (*klebsiella pneumoniae*) resistant to most antibiotics including the ones she was taking.

One in six deaths is due to cancer (1) and this number will increase. In order to ensure higher rates of survival and a better quality of life, effective cancer control must include raising awareness, effective prevention strategies, early detection, access to effective treatments and palliative care. Ensuring access to timely and appropriate cancer treatment includes access to antimicrobials to address infections. These are a crucial element in the arsenal of cancer

treatment modalities.

Infections in cancer patients are a common occurrence, making the use of antibiotics can be lifesaving in the treatment of these patients (2). As many as 1 in 5 cancer patients undergoing treatment will need antibiotics at some point (frequently multiple times) during their treatment (3).

Cancer patients are at a higher risk of infections due to the lowering of immune defences resulting from their treatment, in

particular radiation therapy, chemotherapy (4). Infections may also be related to an immunosuppressed state due to changes in the immune system caused by some haematologic malignancies (5). In the case of solid tumours many factors contribute to an increased risk of infection, including obstructions caused by the tumour itself and the disruption of natural barriers such as skin and mucosal membranes (6). Furthermore, surgery, catheters and other devices used in treatment often increase the risk of infections (7). Sepsis and Pneumonia are among the most common causes for admission to intensive care units for cancer patients. It is estimated that 8.5% of cancer deaths are due to severe sepsis (8).

### **AMR and its impact on cancer care outcomes**

Antimicrobial resistance is a global public health problem, especially as antimicrobial treatment options are becoming limited. Antimicrobial resistance (AMR) happens when microorganisms (such as bacteria, fungi, viruses and parasites) change and are still able to grow, even when they are exposed to antimicrobial medicines that are meant to kill or limit their growth (such as antibiotics, antifungals, antivirals, antimalarials and anthelmintics). As a result, the medicines become ineffective and infections persist, increasing the risk of spread to others. Currently, an estimated 750,000 people die every year from drug-resistant infections (9).

Although multi-country studies to provide comparable data on a global level is lacking, several in-country hospital surveillance studies suggest an increase in AMR in cancer patients. For example, a study in India showed that 73% of patients with blood cancers were colonized with carbapenem-resistant bacteria in the gut (10). A 2017 study in Ethiopia, showed that bacterial infections in cancer patients was 19.4%, and that multi-drug resistance was not uncommon (11). These studies indicate that key advances in medicines, including the newer targeted therapies for cancer patients, could be undermined by the increasing threat of AMR.

To address the impact AMR has on negative cancer care outcomes, a series of actions have to be put in place to ensure that cancer patients have access to the right treatment at the right time. For this to happen, we need to build strong and effective partnerships.

### **Better addressing AMR for improved cancer care outcomes through partnerships**

The critical need to address AMR to improve cancer care outcomes is finally starting to get the attention it deserves. However, the current global response is still far from reaching the scale and urgency required to address the problem of AMR effectively. For this reason, the Union for International Cancer Control (UICC), which is one of the oldest and largest

nongovernmental organizations dedicated to cancer control, has prioritized AMR and is committed to addressing this issue within the cancer community and beyond.

Three priorities for UICC have been identified, which need to be addressed simultaneously. These are (i) evidence generation that effectively mobilizes policymakers, (ii) raising awareness and increasing knowledge within the cancer community and (iii) uniting the cancer and infectious diseases communities towards a joint goal in supporting access to affordable medicines and responsible use of antibiotics (neither overuse nor misuse).

In 2020, UICC and the Wellcome Trust participated in the London Global Cancer Week (LGCW), an annual event (12) that provided the ideal platform to bring together experts from the fields of cancer and AMR to discuss what action needs to be taken. The objective was to raise awareness on AMR and ensure its prioritization in the global cancer agenda. At this event, the UK Government's Special Envoy on AMR, the Norwegian Cancer Society, the International Society for Paediatric Oncology (SIOP), the Wellcome Trust and others called for increased collaboration to raise awareness and ultimately ensure strategies are in place to control AMR, including access to and rational use of treatments.

### **Partnerships to improve and disseminate data on AMR and cancer care**

Review of the existing evidence shows a lack of data on the impact of AMR on treatment outcomes for cancer patients. A recent report commissioned by the Wellcome Trust found that cancer patients who developed drug-resistant infections had a greater risk of dying and were more likely to need additional medical support. But the report also mentioned that this evidence was weak and more systematic research is needed to quantify the impact of AMR on cancer care outcomes (13). It is important that clinicians and policymakers know which negative outcomes including mortality in cancer care are due to AMR and how often these occur (14). This data is needed not only to help shape a more comprehensive response at the political level and clinical level, but to also increase awareness at grassroot and patient levels (15).

Many initiatives and partnerships are aimed at addressing AMR, such as the UK's Fleming Fund which supports low- and middle-income countries (LMICs) with building laboratory and surveillance capacity to ensure quality data (16). The Fund has provided training and laboratory equipment to a number of countries to strengthen national AMR surveillance systems (17). In 2015, the World Health Organization (WHO) launched the Global Antimicrobial Resistance and Use Surveillance System (GLASS) to improve knowledge through surveillance and research. It is the first global collaborative effort to standardize AMR surveillance. However, Dr. Abdul Ghafur,

an infectious disease specialist from Apollo Hospitals in India, pointed out at the LGCW event that many countries have yet to implement systems to feed national data into GLASS. High quality data is needed to back up advocacy efforts and convince policymakers that this issue needs action now.

Other smaller initiatives between governments, private foundations and the pharmaceutical industry have also been established towards this end.

Such data collection should also be used to capture the impact of AMR on cancer care in order to understand the depth of the issue and reinforce anecdotal evidence from cancer patients and oncologists who deal with AMR on a frequent basis, with real-world data.

A Longitude Prize survey among 100 oncologists from across the United Kingdom, showed that 95% worry about increasing drug resistance and how it will impact cancer care. In addition, more than 7 out of 10 believe that drug-resistant infections will make some cancer treatments obsolete within 10 years (18).

### **Partnerships in raising the profile of AMR and cancer**

Research collaborations to improve data collection and surveillance, showcasing the evidence-based data through effective communication, needs to be combined with raising awareness among the public and policymakers. Currently, knowledge and awareness within the cancer community of how drug resistant infections affect cancer care outcomes are low. It is urgent that the cancer community, oncology professionals, cancer advocates, programme managers, patient groups and other stakeholders working in the field of cancer understand and address the factors that contribute to the development and spread of AMR (19).

This is a multi-sectoral issue and in order to bring about policy change through tailored strategies and guidelines, the infectious diseases community and cancer community should come together. In this regard, addressing AMR is a priority for UICC and a task force of experts was convened in 2019 to support evidence generation, identify research gaps in knowledge of cancer and AMR, share best practices, and ultimately engage the cancer community to work together and bring about policy change. Since AMR has become a UICC priority, UICC and the UICC-led task force on AMR and cancer care have been very active in raising awareness on AMR among the cancer community and beyond, through various platforms, including LGCW and the Cancer Control series.

### **Partnerships for ensuring access to antimicrobials**

Antimicrobials are a key and indispensable part of cancer treatment. However, access to treatments for infections is not always a reality. Medicines to treat infections are not available in many parts of the world. Of the 25 antibiotics developed

between 1999 and 2014, only 12 had registered sales in more than 10 countries (20). Shortages and lack of access to older antibiotics in many countries is also a chronic problem, and the reasons for this includes fragile – sometimes single-source – supply chains, regulatory challenges and the lack of commercial incentives to manufacture, register and distribute these medicines. Ensuring access to these existing treatments need to be addressed urgently.

In addition, recent years have seen huge advances in cancer care, including the new targeted therapies and immunotherapy for cancer treatment. Similar prioritization of R&D for newer therapies to address infectious pathogens, which undermine the effectiveness of both old and new cancer treatments, is urgently needed.

A number of initiatives do exist that specifically support new medicines and R&D such as the UK's Global AMR Innovation Fund (GAMRIF), R&D-funders like CARB-X, non-profit drug developers such as GARDP and the industry-funded AMR Action Fund. New approaches to R&D investment and more collaborative approaches are needed. Several legislative proposals in Europe and the United States (various subscription models and the PASTEUR and DISARM acts) have been put forward to try to incentivize R&D for new therapies. There is, however, considerable concern that these initiatives will not take a global nor an end-to-end approach that could ensure sustainable access for all. These proposals and other novel collaborative mechanisms should be expanded to ensure equitable and affordable access in LMICs and HICs alike, so that cancer patients everywhere receive the medicines they need.

While the current global COVID-19 pandemic has shown the importance of multi-sectoral cooperation, with active participation of relevant stakeholders i.e. governments, civil society, research institutions and industry, the crucial importance of government leadership should however not be understated. As the WHO's newly established "Council on the Economics of Health for All" stated in its recent publication on the governance of health innovation for the common good: "The development of multiple coronavirus disease 2019 (COVID-19) vaccines in less than a year shows how much can be accomplished when human ingenuity and solid medical research and development capabilities are given extensive public support. It further notes however that "...this experience also demonstrates that unless innovation is governed for the common good, many people remain excluded from its benefits, limiting the positive impact of health interventions, and creating unacceptable inequities that potentially exacerbate the health needs that it is supposed to address".

There is an urgent need for key players to come together and explore innovative ways to fund R&D for new antibiotics, increase collaborative networks and ensure there is a

sustainable supply of medicines and diagnostics (existing and new) for cancer patients, especially in LMICs.

Against this background a more in-depth discussion on access to antimicrobials for cancer patients will take place during the forthcoming 3rd LGCW in November 2021. The focus of this session will be access to medicines and diagnostics. Taking forward the messages from LGCW 2020, speakers at this session will elaborate on and provide insight into possible partnerships in ensuring equitable access to treatments globally. The session is once again a partnership between UICC, the Wellcome Trust, the Norwegian Cancer Society and will include UICC task force members, SIOP and ReAct along with insights from the industry. ■

### Research areas that need urgent attention and collaboration

- ➔ Strengthening surveillance capacity to ensure quality data on the impact of AMR.
- ➔ Evidence generation on the impact of AMR on cancer care outcomes.
- ➔ Evidence-based resources to increase knowledge and awareness on AMR across communities to influence policy change.
- ➔ Ensuring equitable access to novel therapies.

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