

A microscopic image of various cells, likely cancer cells, showing blue and green fluorescence. The cells are scattered across the frame, with some appearing more prominent than others. The background is dark, making the glowing cells stand out.

LONGITUDE PRIZE

EFFECTIVENESS OF CANCER TREATMENTS THREATENED BY RISING ANTIBIOTIC RESISTANCE

February 2020

RESEARCH METHODOLOGY

medeConnect Healthcare Insight surveyed 100 UK Oncologists from across the UK between 20 December 2019 and 3 February 2020. Their answers provide a snapshot of the threat that rising antibiotic resistance poses to the treatment of cancer.

There are approximately 900 clinical oncologists in the UK meaning this study represents one in nine clinical oncologists. In comparison, for a GP Omnibus survey, the target is 1,000 out of around 40,000 GPs.

medeConnect is the market research division of Doctors.net.uk. Doctors.net.uk is the largest website for doctors in the UK and around a quarter of UK doctors log on every day.

LONGITUDE PRIZE

The Longitude Prize is a £10 million prize fund with an £8 million payout that will reward a competitor that can develop a point-of-care diagnostic test that will conserve antibiotics for future generations. The test must be accurate, rapid, affordable and easy to use anywhere in the world. The Longitude Prize is run by Nesta Challenges, part of Nesta, the UK's innovation foundation, with funding from Innovate UK.

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Innovate UK



SCIENCE
MUSEUM

INTRODUCTION

Antibiotic resistance is one of the biggest threats to global health today. As more and more infections become harder to treat and the economic and environmental costs mount, there is a growing consensus that the many of the medical treatments we take for granted may soon be at risk.

Much has been done to raise awareness of the problem and, while significant progress has been made in addressing the threat, much remains to be done.

In this report, we highlight the danger antibiotic resistance poses to just one area of modern medicine – cancer treatment.

Our survey of 100 oncologists from around the UK revealed that 95 per cent are worried about the rise of drug-resistant bacteria and what it means for the future of cancer treatments and the care of their patients.

When asked how quickly they think drug-resistant infections will make some cancer treatments obsolete: 28 per cent oncologists say within the next five years; 39 per cent say within the next decade; 15 per cent in 20 years' time. 46 per cent of oncologists are worried that chemotherapy will soon be unviable.

Four in ten oncologists (41 per cent) have seen a rise in drug-resistant infections in the past 12 months and 5 per cent of their surgical patients already develop infections that are resistant to antibiotics. Extrapolated nationally, this could mean some **65,000 cancer patients** developing potentially life-threatening drug-resistant infections following operations in the next decade alone.

Antibiotic resistance can affect anyone, of any age, anywhere in the world and these figures should act as a wake-up call to us all.

FOREWORDS



Cancer patients rely on antibiotics for prevention and treatment of infections. This is one of the most common complications of their treatment. Multidrug-resistant bacteria pose a major global health problem and for cancer patients, the implications are significant.

As 'superbugs' proliferate, routine medical interventions that we take for granted, like chemotherapy and surgery, may be rendered unviable when effective antibiotics are no longer available. Worldwide, at least 700,000 people already die annually from drug-resistant infections. According to Jim O'Neill's Review on Antimicrobial Resistance (AMR), commissioned in July 2014, that number will reach ten million a year by 2050 and, without collective intervention, will cost more than \$100 trillion in lost economic output.

At the Longitude Prize, we are committed to accelerating the development of a point-of-care diagnostic test that will help conserve antibiotics.

Focusing simply on either the discovery of a new antibiotic or a reduction in the volume of antibiotics, though both valuable and important, will simply not be enough.

No new class of antibiotics has been discovered since the 1980s and the lack of market incentives for research and development has led the pharma industry to largely abandon projects developing new treatments. Even with significant subsidies for research and recent efforts by the UK and US to increase payments for new antibiotics, the market is still sluggish and recent antibiotic R&D biotech bankruptcies have rung alarm bells amongst the medical community.

To both preserve existing antibiotics and to ensure that new ones last longer, diagnostics are an essential place to focus in the battle against drug resistance. We need to be using antibiotics only when strictly necessary, with medical practitioners able to choose the right treatment from the outset; this means we need new innovative tests. Recent studies (like the CDC's Antibiotic Resistance Threats in the United States, 2019) confirm that sanitation, infection control, behaviour change and awareness are critical but can only go so far.

This research was carried out to shine a light on what the UK's oncologists think about the rise of antibiotic resistance and what it means, in their eyes, for patient care. It serves a dual purpose of raising awareness of the risks posed by superbugs to healthcare as we know it and, we hope, will encourage increased support for R&D and procurement for both antibiotics and diagnostics.

The warning signs are loud and clear. At the same time, cancer treatment is improving and people are living for longer, superbugs are on the increase and putting patients at risk. A key finding from this new study shows that out of some of the most common types of cancer – kidney, skin and bladder – the proportion of specialists across the UK who have seen a rise in drug-resistant infections amongst their patients in the past 12 months alone is significant (78 per cent, 69 per cent and 63 per cent respectively).

Daniel Berman is the Global Health Director at Nesta Challenges



I am pleased to welcome this new research. Infections are the leading cause of death in cancer patients in India.

Oncology patients are the most obvious victims of the superbug crisis. With no immunity of their own, these patients are heavily dependent on antimicrobial agents, to tide over the highly vulnerable period following chemotherapy.

The human gut is full of bacteria and fungi. Chemotherapy disrupts the protective mucosal barrier; opening the floodgate and facilitating the entry of these bugs to the bloodstream. In countries with high AMR rates, even healthy volunteers in the community may carry highly drug-resistant bugs in their gut. The carriage rate is many times higher in oncology patients.

My colleagues and I in India have been sounding the alarm over the threat of untreatable infections to our cancer patients for a long time. The AMR crisis has made the management of infections in oncology patients a nightmare.

In India, bloodstream infections caused by superbugs have become the leading cause of illness and death in our leukaemia patients. We have seen first-hand the additional suffering resistance causes cancer patients. Antibiotics are essential to prevent and treat infections in people being treated for cancer. Without effective antibiotics at hand, cancer treatment is nearly impossible.

As economic and political momentum lags behind, we need a dramatic shift in public awareness of the risks they face - only by mass mobilisation of the public can we drive change from the ground up. This study provides us with timely and crucial insight into what is developing in the UK and, I hope, will do much to mobilise people to action.

We need new antibiotics, antifungal agents and rapid effective diagnostics to overcome the crisis. Sincere and co-ordinated efforts by experts, organisations and countries could mobilise political will to tackle AMR at global level.

Dr. Abdul Ghafur is a member of the Longitude Prize Advisory Panel. He is a consultant and Adjunct Professor in infectious diseases and clinical microbiology at the Apollo Hospitals, Chennai, India. He is also the primary author and coordinator of the Chennai Declaration, a document and initiative to tackle the challenge of antimicrobial resistance from an Indian perspective.

PART 1

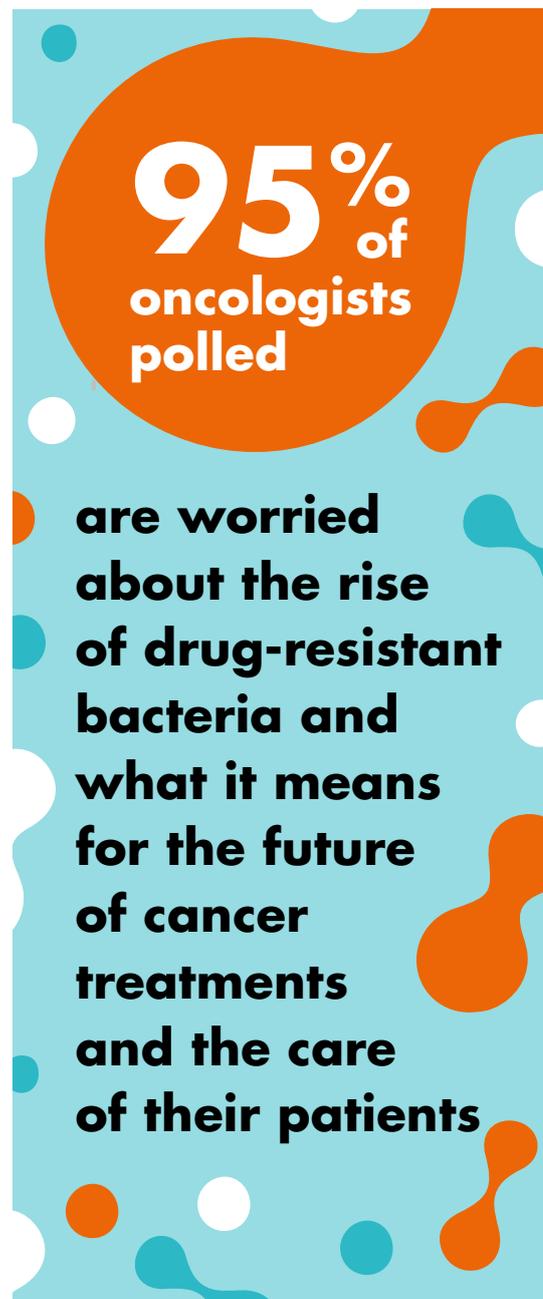
IS THIS THE DEFINING DECADE FOR CANCER CARE?

Cancer care and antibiotics go hand-in-hand. Chemotherapy, for instance, suppresses the immune system, leaving patients vulnerable to infections – particularly in the first two weeks after completing treatment. To protect patients, doctors often prescribe antibiotics immediately after finishing chemo. Major surgery, meanwhile, puts a great strain on the body. It leaves wounds which can harbour infection and lowers the immune response for weeks or months afterwards, leaving patients more vulnerable to infections.

Overall, an estimated one in five cancer patients will need antibiotics during their treatment (Norwegian Cancer Society, [Kreftforeningen](#)). Indeed, some types of cancer, such as multiple myeloma and acute leukaemia, cannot be treated without antibiotics. [Research published in *The Lancet*](#) warned as early as 2015 that more than a quarter of infections after chemotherapy are caused by organisms already resistant to antibiotics.

This new research shows that 95 per cent of the oncologists polled are worried about the rise of drug-resistant bacteria and what it means for the future of cancer treatments and the care of their patients. Given the crucial role of antibiotics in cancer care, it is understandable that doctors are increasingly concerned that, as antibiotics become less effective, many common cancer treatments could become too risky or impossible to give.

39 per cent fear that drug-resistant infections will make some cancer treatments obsolete by 2030 – just ten years from now; making this the defining decade for modern cancer care. This view is further reinforced by the insight that 86 per cent of oncologists agree that the rise of drug resistance is putting their patients at risk of serious harm; more than four in ten (46 per cent) oncologists are already worried that chemotherapy will soon be unviable.



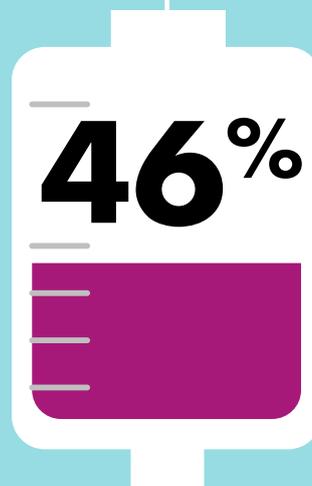
Nationally, we have discovered that doctors in the West Midlands and South West are the most concerned about what antibiotic resistance means for their work (89 per cent and 63 per cent respectively).

From the moment Alexander Fleming's penicillin was first prescribed in the 1940s, bacteria have been developing strategies to outsmart antibiotics. Superbugs are displays of evolution in action: as drugs are created and prescribed to treat infections, the microbes they kill begin to develop resistance to them, ensuring their survival.

We cannot change the rules of biology to stop new superbugs appearing – but we can slow their development. Key to this, is reducing the misuse and over-prescription of antibiotics – and to do this we need fast, accurate and affordable diagnostic tests. These will reveal if an illness is caused by bacteria, rather than a virus that can't be treated with antibiotics.

They might also identify the type of bacteria – and even which antibiotics are still likely to be still effective against it. This will reduce the number of antibiotics being prescribed unnecessarily – one of the main causes of antibiotic resistance. It will also ensure more people get the right treatment at the right time – saving lives and improving health. The development of such tests will have a major impact on one of the biggest problems facing the world today and define the future of cancer treatment.

More than four in ten oncologists are already worried that chemotherapy will soon be unviable



PART 2

THE RACE AGAINST TIME

Oncologists treating three of the most common types of cancer have seen an increase in the number of drug-resistant infections amongst their patients in just 12 months

Kidney cancer 78%

Skin cancer 69%

Bladder cancer 63%

The overuse of antibiotics and the lack of tests that give real-time results are contributing to rising resistance levels. A recent study of GP databases in England found that between 8.8 per cent and 23 per cent of all antibiotic prescriptions between 2013 and 2015 were inappropriate (*Journal of Antimicrobial Chemotherapy*, 2018). In the US, the figure is as high as 30 per cent.

Antibiotic resistance is rising to dangerously high levels globally and public health officials across the world now rightly talk of AMR as a “catastrophic threat” (Dame Sally Davies, former Chief Medical Officer for England and the UK’s special envoy on antimicrobial resistance). After all, superbugs can affect anyone – and they are proliferating fast.

The proportion of oncologists treating three of the most common types of cancer that have seen an increase in drug-resistant infections in their patients in just 12 months is significant: kidney cancer (78 per cent of oncologists), skin cancer (69 per cent of oncologists) and bladder cancer (63 per cent of oncologists). We also know that three of the most prevalent drug-resistant bacteria witnessed in cancer treatment in the UK are *Staphylococcus* (21 per cent), *E. coli* (15 per cent) and enterococci (14 per cent).

'MRSA' - methicillin-resistant *Staphylococcus aureus* - is, arguably, the most well-known strain of drug-resistant *Staphylococcus*. Although infections of MRSA often go into decline following increased preventative measures, the treatment of this infection remains difficult, requiring stronger, more expensive drugs.

PART 3

ONCOLOGISTS DEMAND ACTION

What is particularly worrying is that one in five cancer patients will be hospitalised due to an infection during the course of their treatment (NCBI, 2015).

Delays in diagnosing infections can be particularly serious. Oncologists are well aware of this but, without better diagnostic tests that return results in minutes rather than days (as is the case now), they struggle to identify the right antibiotic for any given infection.

Revealingly, 90 per cent of oncologists polled agree with the statement that a rapid diagnostic tool would significantly improve how bacterial infections are diagnosed. In all, 60 per cent of doctors agree that labs take too long to accurately diagnose bacterial infections in their patients, especially when treating kidney (78 per cent), prostate (72 per cent) and bladder (70 per cent) cancer.

It should therefore come as no surprise then to learn that 70 per cent of the oncologists polled are calling for better resources to protect their patients from superbugs.

Ultimately, if we are to effectively combat the antibiotic-resistant bacteria that exist today and reduce the development of new superbugs, we must provide better tools to doctors so that they can prescribe the right antibiotic in the first instance.

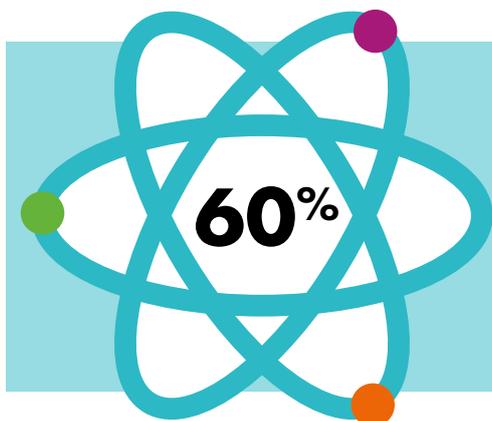
“Two months ago, one of my breast cancer patients who was having chemotherapy was rushed to hospital at 6 o’clock in the evening. Her levels of infection-fighting white blood cells were less than half of what they should have been and she had septicaemia (blood poisoning). She was given IV antibiotics and discharged 72 hours later with antibiotics to take at home.

Two chemotherapy cycles further on, her white cell count plummeted and she was admitted again to be treated for another infection, caused by a different microorganism.

In chemotherapy patients, very small numbers of bacteria can cause infections that can kill very rapidly.

This patient has now finished her chemo and is doing extremely well but without antibiotics, she wouldn’t have survived.”

Professor Karol Sikora is a consultant oncologist and dean of medicine at the University of Buckingham



of doctors agree that labs take too long to accurately diagnose bacterial infections in their patients

PART 4

SURGERY RISKS: 65,000 CANCER PATIENTS AT RISK OF CONTRACTING SUPERBUGS

No matter how small, each operation carries a chance of infection, both during surgery and during wound healing. When coupled with the immuno-suppressing treatments commonly used in cancer treatment, patients face a much greater risk of developing an infection than the general population.

The oncologists involved in our research say that approximately that 5 per cent of their surgical patients develop a drug-resistant infection. We have used publicly available data to estimate what this could mean over the next decade.

Research has found that more than a third of cancer patients (36 per cent) require surgery (*The Lancet Infectious Diseases*, 2015) and *Macmillan* statistics show that there are 360,000 new cancer cases in the UK a year – suggesting 129,000 patients have surgery each year. Keep in mind, some patients will require several operations over a period of time, and their risk of infection will increase with each.

Our research suggests that 6,480 (5 per cent) of those 129,000 cancer patients will go on to develop potentially life-threatening drug-resistant infections. That means, between now and 2030, 64,800 cancer patients could develop drug-resistant infections following surgery – and that is only if the current infection rate stays static. Every indication shows that this rate is rising, putting even more patients at risk each year.

For those 64,800 patients, not having surgery is not an option.

129,000



cancer
patients

Of those 129,000 cancer patients, 6,480 will go on to develop potentially life-threatening drug-resistant infections. That means, between now and 2030, 64,800 cancer patients that could develop drug-resistant infections following surgery – and that is only if the current drug-resistant infection rates stay static

PART 5

BREAST CANCER AND SUPERBUGS

There is no cancer that will be untouched by the rise of superbugs. In fact, any disease treated with surgery or immuno-suppressing therapies will have the same issues. From our research, we know that 68 per cent of breast cancer doctors believe that drug-resistant infections will make some cancer treatments obsolete in the next decade.

Breast cancer is the most common cancer among women globally and the leading cause of cancer death in females ([Future Medicine](#), 2019) and one in eight British women will be diagnosed with it in their lifetime ([NHS](#), 2011).

When treating breast cancer, most patients will undergo surgery, whether a total mastectomy (removal of the whole breast) or a lumpectomy (removal of the cancerous lump) and will likely receive systemic antibiotic treatment either before or after surgery.

In our study, looking across all cancers, 36 per cent of patients required surgery in the last 12 months. Breast cancer has one of the highest incidences of surgery with half of patients having an operation as part of their treatment.

Depending on how far breast cancer has progressed before it is diagnosed, the five-year survival rate is between 80 per cent (for stage one or two) to 15 per cent (stage four) ([CRUK](#)). Great strides have been made in treating breast cancer and in raising awareness of condition and a woman diagnosed today is twice as likely to survive as one 40 years ago. The rise of drug-resistant bacteria, however, threatens some of these gains.

In the UK, more than half (59 per cent) of oncologists who specialise in breast cancer have seen an increase in drug-resistant infections in their patients in the last 12 months. They estimate that a quarter (25 per cent) of their patients develop a bacterial infection during their treatment. They also told us that 6 per cent of those having surgery contracted infections resistant to antibiotics following their operation.

“The development of sepsis, a potentially life-threatening complication of an infection, in chemotherapy patients can be so devastating that we must start them on IV antibiotics straightaway. We can’t wait two days or more for the results of the microbiology tests to come back.

If the patient doesn’t respond to these antibiotics, or if the tests flag up a bacterium that needs a different treatment, we’ll change them. We might have to try several different antibiotics and so many patients end up having multiple courses, which encourages the development of antibiotic resistance.

We needed faster, more precise tests which would identify not only which infection a patient has but which antibiotics will be effective.”

Professor Kefah Mokbel is a consultant breast cancer surgeon and chairman of the multidisciplinary breast cancer programme at the London Breast Institute

CONCLUSION

It is clear from our survey that oncologists are concerned about growing levels of resistance to antibiotics in their patients and are demanding changes.

Investment in cancer – from research to treatment is high – and survival rates have doubled in the last 40 years. Today, half of people with cancer in England and Wales are still alive at least ten years after diagnosis ([CRUK](#)). We must not let the rise of antibiotic resistant infections undermine the investment in cancer care or erode these hard-won improvements in survival.

Antibiotics are a key part of cancer treatment – many patients simply have to take them – and we owe it to them to better manage our use of the drugs.

Central to this stewardship is the development of affordable, easy-to-use tests that will rapidly and accurately diagnose bacterial infections. Innovators, researchers and laboratories around the world are already working on this but a redoubling support of governments, public health officials and R&D financiers is vital in accelerating this research, as well getting any new tests ready for market and fast-tracking them into doctors' surgeries and onto hospital wards.

Such diagnostics are fundamental to reducing the over-prescription of antibiotics and will lead to a sea-change in the handling of the AMR crisis. They will ensure more patients are given the right treatment at the right time, improving recovery and, in many cases, saving lives. Earlier, more appropriate treatment will also save on costs by cutting hospital admissions and reducing lengths of stays.

Of course, diagnostics are not a panacea. There is no 'silver bullet' solution. AMR must be tackled on multiple fronts, in a collaborative and cross-sector manner. Accelerating the production of a rapid point-of-care diagnostic is key while we wait for a new antibiotic to be developed (an essential part of the long-term solution). At the same time, we need to see these measures supported by strong clinical guidelines and improved infection control and prevention methods.

Cancer patients are among the millions who will benefit from better AMR management and, as our report makes clear, there is no time to be lost.

Oncologists around Britain are demanding action and we need to listen to them – and act accordingly, now.

APPENDIX

HEADLINE RESULTS PER QUESTION

Q1 – Approximately what percentage of your patients develop a bacterial infection during cancer treatment?

- Over a quarter of doctors (26 per cent) state that between 26 per cent to 50 per cent of their cancer treatment patients develop a bacterial infection during cancer treatment.
- One in twenty doctors say that more than half of their cancer treatment patients develop a bacterial infection during cancer treatment.

Q2 – Have you seen an increase in drug-resistant infections in your patients in the last 12 months?

41 per cent of UK oncologists have seen an increase in drug-resistant infections over the past 12 months.

Q3 – Approximately what percentage of your cancer patients required surgery as part of their cancer treatment in the last 12 months?

Almost a quarter of doctors (23 per cent) said that over half (51+ per cent) of their patients required surgery as part of their cancer treatment. Half (50 per cent) said that between 11 per cent and 50 per cent of their patients required surgery.

Q4 – And of your cancer patients who required surgery, what percentage developed a drug-resistant infection following this surgery?

Half of oncologists said that between 1 per cent and 10 per cent of their patients developed a drug-resistant infection. An additional 11 per cent of the doctors said that 11 per cent and upwards of their patients developed a drug-resistant infection following surgery.

Q5 – Which type of drug-resistant bacterial infection do you see most commonly in your patients?

- Staphylococcus – 21 per cent of respondents
- E. coli – 15 per cent of respondents
- Pseudomonas – 14 per cent of respondents
- Enterococci - 14 per cent of respondents

Q6 – How worried are you about drug-resistant bacteria and the future treatment of your patients?

95 per cent (Q6) of doctors are worried by drug-resistant bacteria and future treatment of cancer patients.

Q7a – When asked about drug-resistant infections and cancer treatments:

46 per cent agree that drug-resistant infections will make some cancer treatments obsolete.

Q7b – When asked about chemotherapy:

46 per cent believe that drug-resistant infections will make chemotherapy unviable.

Q7c – When asked about the rise of drug-resistant infections:

84 per cent stated that drug-resistant infections are putting patients at greater-risk of serious harm

Q7d – When asked about the future effectiveness of cancer treatments as drug-resistant infections increase:

56 per cent agreed that they do worry about the future effectiveness of cancer treatment as drug-resistant infections increase.

Q7e – When asked if doctors need better support and resources:

70 per cent agreed that they need better support and resources to protect their patients from the risk of contracting a drug-resistant infection during their treatment.

Q7f – When asked about accurately diagnosing an infection:

60 per cent (Q7) agree that labs take too long to accurately diagnose an infection in their patients.

Q7g – When asked about cutting antibiotic prescriptions:

54 per cent said that tackling AMR by only cutting antibiotic prescriptions will eventually put patients at risk.

Q7h – When asked about diagnostic tools for bacterial infections:

90 per cent say that rapid diagnostic tools would significantly improve how bacterial infections are diagnosed.

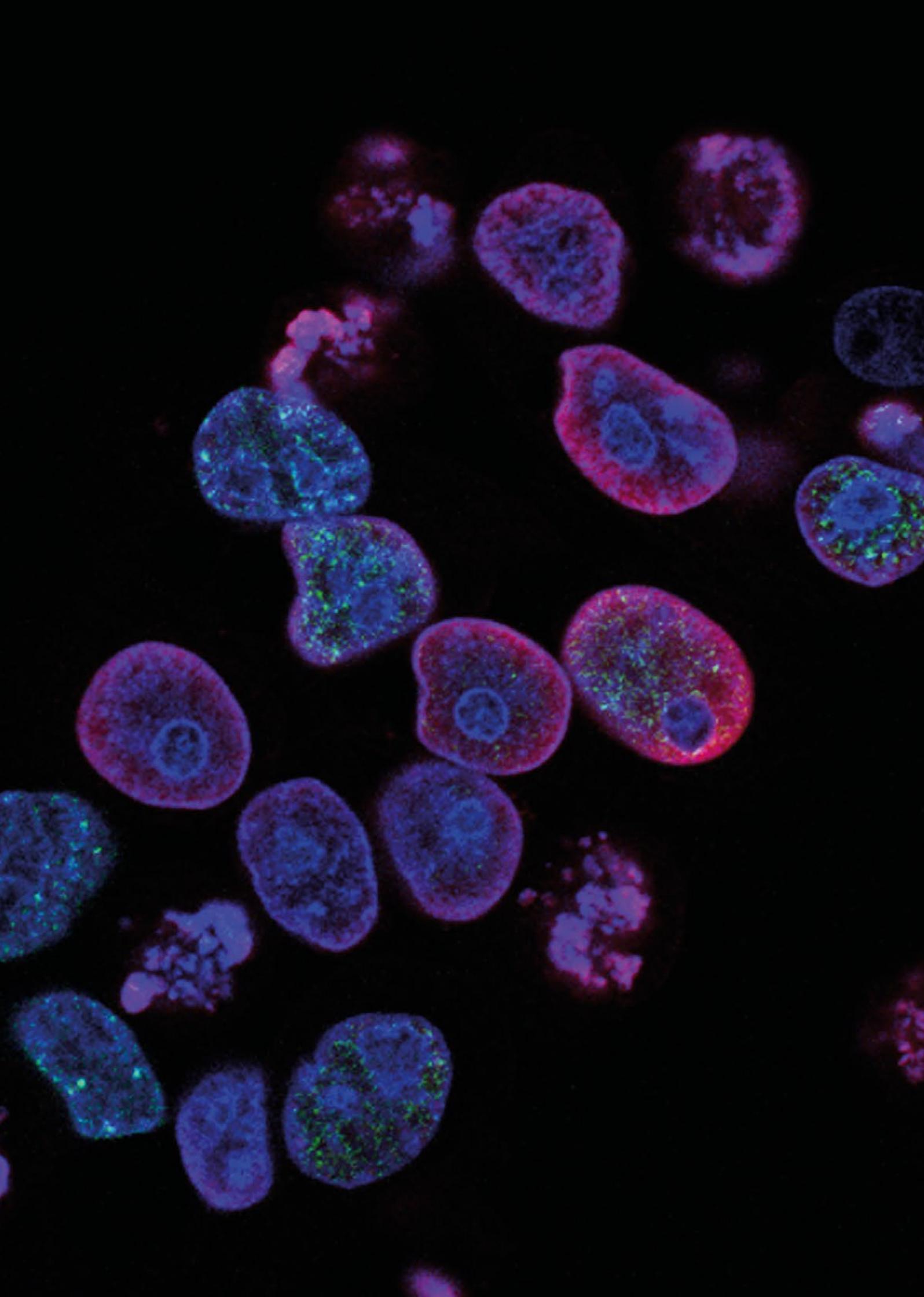
Q8 – How quickly do you think drug-resistant infections will make some cancer treatments obsolete?

72 per cent believe that drug-resistant infections will make some cancer treatments obsolete in 10 yrs.

Q9 – In terms of urgency in managing drug resistant bacteria, where do you think innovation would have the most long-term impact?

- To tackle the issue, 26 per cent of oncologists called for the development of rapid, point-of-care diagnostics that are able to distinguish between viral and bacterial infections, 10 per cent for the development of new antibiotics and 6 per cent for improved prevention and infection control.
- Reflecting the need for a multi-pronged approach, 55 per cent of respondents called for a combination of all three options.

Survey information: medeConnect Healthcare Insight surveyed 100 UK Oncologists from across the UK between 20th December 2019 and 3rd February 2020. Their answers provide a snapshot of the threat that rising antibiotic resistance poses to the treatment of cancer. medeConnect is the market research division of Doctors.net.uk. Doctors.net.uk is the largest website for doctors in the UK and around a quarter of UK doctors log on every day.



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