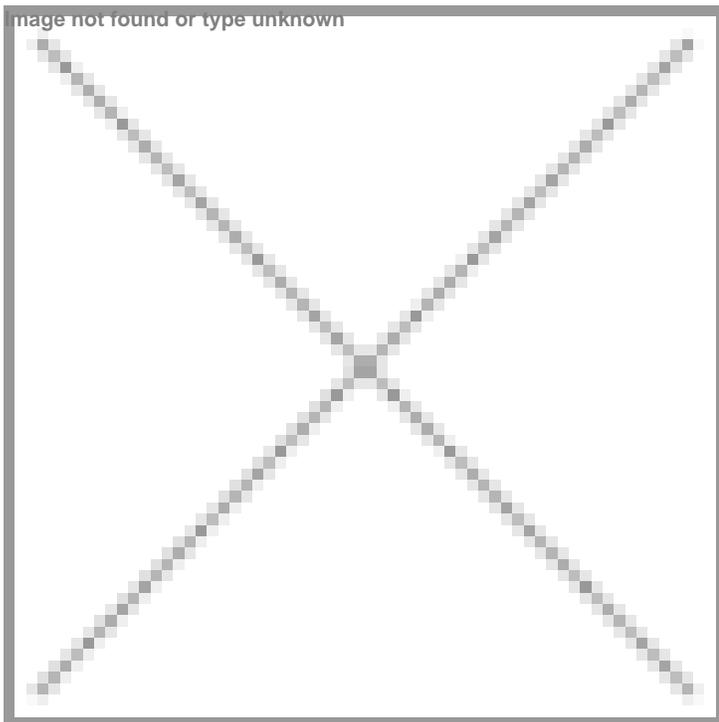


## Why Do Some Breast Cancer Treatments Stop Working? Science Is Finding New Answers!

16 April 2025 | Views | By Dr Anindita Chakrabarty, Associate Professor, Department of Life Sciences, Shiv Nadar University, Delhi-NCR

### Drug resistance contributing to about 90% of cancer deaths



Cancer remains one of the world's most formidable health challenges, with nearly 10 million cancer-related deaths each year globally, accounting for a significant percentage of non-communicable diseases. Among these, breast cancer is particularly significant.

According to the World Health Organization (WHO), breast cancer is the most common cancer among women, responsible for more than half a million deaths annually, with an estimated 2.3 million new cases diagnosed in 2020 alone (WHO, 2022).

Breast cancer affects a broad range of people, but its risk factors are well established. These include gender, age, family history, and lifestyle choices such as alcohol consumption and tobacco use. The WHO notes that women in high-income countries tend to be diagnosed more frequently, with better survival rates compared to women in low-income countries. In high-income nations, the five-year survival rate is approximately 80%, while in countries like India and South Africa, it drops to 66% and 40%, respectively (WHO, 2022).

In response to these disparities, the WHO launched the Global Breast Cancer Initiative in 2021 to improve diagnosis, treatment, and outcomes for women, particularly in low-resource settings. The initiative aims to reduce deaths through early detection and improved treatment strategies.

Even with advances in early detection and treatments such as surgery, radiation, and medication, drug resistance remains a major challenge, especially in advanced breast cancer.

### **The Challenge of Drug Resistance**

Drug resistance contributes to about 90% of cancer deaths (International Journal of Molecular Sciences, 2020). While initial treatments can be effective, breast cancer cells often adapt and resist treatment, leading to relapse. A key reason is heterogeneity within tumours, cells vary genetically, so some survive treatment and continue to grow. This makes resistance hard to predict or prevent.

Standard approaches to treating advanced breast cancer follow subtype-specific therapies—targeting hormone receptor-positive, HER2-positive, and triple-negative breast cancers. These can be effective initially but often fail as the cancer adapts. Despite knowing this, many oncologists still rely on these methods for advanced cases.

### **A New Era: Evolutionary Approaches to Cancer Treatment**

Researchers are now turning to evolutionary biology to develop adaptive treatment strategies. Like species evolving to survive, cancer cells evolve to resist therapies. Understanding this evolution is helping scientists design treatments that adapt to the tumour's changes over time. Unlike traditional methods that aim to kill all cancer cells at once, adaptive therapies seek to manage cancer more sustainably, avoiding the rise of highly resistant cells.

Mathematical models are guiding these strategies. Clinical trials are underway for adaptive therapies in late-stage breast cancer, especially triple-negative breast cancer (TNBC), one of the most aggressive subtypes, with a five-year survival rate of 77% (National Cancer Institute, 2021). These trials aim to test evolution-based treatments that can respond to the cancer's resistance patterns.

### **Rethinking Treatment: Adaptive and Evolution-Based Therapies**

In our research, we focus on understanding drug resistance in aggressive breast cancers and exploring ways to restore sensitivity to treatment. We're developing models to track how resistance traits evolve and testing approaches to prevent resistance from establishing.

One strategy involves a two-phase approach: an aggressive "first strike" followed by a secondary treatment targeting resistant cells. Another exploits the costs of resistance, making it harder for resistant cells to thrive. We're also studying cooperative behaviour among cancer cells to disrupt survival advantages.

These approaches aim for long-term control while reducing toxicity. Rather than trying to eliminate all cancer cells, the goal is to manage cancer as a chronic condition, like hypertension or diabetes.

We're currently testing these strategies on advanced breast cancer samples with clinical partners. If successful, evolution-guided therapy could reshape cancer care, offering a more sustainable, personalized way to manage advanced cancer and improve survival.

Breast cancer may not be curable for all, but adaptive treatments offer hope. As we better understand cancer's complexities, these strategies could help patients live longer, healthier lives with cancer managed, not just fought.

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