Although treatments for breast cancer have come a long way over the past few generations, researchers are still puzzling over some tough questions.

BY CHRIS WOOLSTON

QUESTION

Which cancers need to be treated?

WHY IT MATTERS

Treatment for breast cancer can be disfiguring, expensive and painful. Identifying the tumours that actually pose a threat can focus therapy where it is needed, while saving millions of women from potentially harmful interventions.

WHAT WE KNOW

Roughly 15–30% of tumours detected by screening are unlikely to cause trouble if left alone. Ductal carcinoma *in situ*, — a common cancer of the milk ducts — rarely turns invasive, but women with the disease often undergo surgery (see page \$114).

NEXT STEPS

Researchers are sorting through genetic and molecular biomarkers that could help to forecast the course of an individual tumour. Such predictions may never be 100% accurate, but a little more clarity could go a long way.

2

Who should be having mammograms, and how often?

Women face a cacophony of conflicting recommendations regarding screening. Should they be screened every year starting at age 40, every 2 years at age 50 or never? Although overscreening can create false alarms, under-screening could lead to preventable deaths.

Mammograms prevent about 4 cancer deaths for every 1,000 women screened regularly for 20 years. The benefits seem to be especially small for women in their 40s (see page S118).

Radiologists are working to improve the accuracy and clarity of breast imaging, and public health experts are developing evidence-based guidelines that can save lives while minimizing harm.

3

What are the possibilities, and limits, of immunotherapy?

Harnessing the immune system to fight breast cancer could be a winning strategy, a major disappointment or both. For certain women, immunotherapy could mean not just a treatment, but also a cure.

With more than 40 clinical trials underway, data continues to roll in (see page S105). So far, immunotherapy, including anti-cancer vaccines, alone or in combination with other therapies, seems to be especially promising for cases of 'triple-negative' breast cancer.

Each case of cancer is different, and so is each immune system. Matching the right treatment with the right patient could prove to be the defining challenge of the future.

4

What are the risk factors for the disease?

Knowing which women are susceptible to breast cancer — and why — could illuminate the root causes of the disease and lead to new approaches for prevention and treatment.

Some women are more likely to develop breast cancer because they carry a mutation in a *BRCA* gene (see S116), but even the risk for these women is shaped by exposure to hormones, which in turn are influenced by exercise, weight control and pregnancy.

Researchers are looking beyond *BRCA* for other gene mutations that could help to set breast cancer in motion. The genetic links probably will not be as strong, but finding them could still prove lifesaving.

Chris Woolston is a science writer based in Billings, Montana.