The risk of breast cancer from using hormone replacement therapy is double what was previously thought, according to a major piece of research, which confirms that HRT is a direct cause of the cancer.

The findings of the definitive study will cause concern among the 1 million women in the UK and millions more around the world who are using HRT. It finds that the longer women take it, the greater their risk, with the possibility that just one year is risk-free. It also finds that the risk does not go away as soon as women stop taking it, as had been previously assumed.

The UK’s drug licensing body suggested women who have used HRT in the past or use it now should be vigilant for signs of breast cancer in the light of the findings, while the Royal College of GPs urged them not to panic but to consult their doctor if they are concerned.

The research, published in the Lancet medical journal, says one in 50 women of average weight taking the most common form – combined daily oestrogen and progestogen – for five years will get breast cancer as a result.

That risk is twice what was thought, because it continues at some level for 10 or more years after women stop taking HRT. There are about 1 million women in the UK on HRT, 5 million in the rest of Europe and 6 million in the US.

The Medicines and Healthcare Products Regulatory Authority (MHRA) said women who are taking or have ever taken HRT should be vigilant and may want to talk to their doctor next time they have a routine appointment. They should ensure they go for breast screening.

“Women should be aware of this new information, so that it can be considered with the other risks and benefits of using HRT,” said Sarah Branch, the deputy director of the MHRA’s vigilance and risk management of medicines division.

“The menopause can have unpleasant side-effects and HRT products can be
effective in helping to ease the symptoms. No medicine is completely without risk, but it is important for women to be able to make an informed decision about the risks and benefits that are appropriate for them.”

The MHRA recommends women should only take hormone therapy at the lowest dose and for the shortest possible time that works for them. The study shows there may be no increased risk for the first year.

HRT has long been linked to breast cancer, and to a lesser extent to ovarian cancer as well. But the issue has been fraught with controversy, pitching supporters of HRT – including many gynaecologists – against the epidemiologists concerned about cancer risks.

The British Menopause Society and the Royal College of Obstetricians and Gynaecologists have strongly defended HRT, which is very effective in alleviating the hot flushes, night sweats and other debilitating symptoms of menopause that can make one in four women’s lives miserable. They have disputed past studies linking HRT to cancer and claimed hormones have other health benefits, including protecting women from heart attacks and strokes, for which the authors of the new study say there is no evidence. HRT does help protect brittle bones, say the authors, but only while women are taking it.

The British Menopause Society rejoiced at the recent guidelines from the National Institute for Health and Clinical Excellence (Nice), which its members helped write. Nice suggested the risks were small – although without quantifying how small. GPs have been urged to prescribe HRT to more women as a result.

“We really are concerned that many GPs have been saying it is not something you really have to worry about,” said Prof Valerie Beral from the University of Oxford, a co-author of the study. The scientists say the Nice guidelines should now be reconsidered.

Nice said it is aware of the new research. “We will be reflecting on this study’s findings and considering it in our final decision as to whether we will update our menopause guidelines, a decision on which we will publish in due course,” said a spokesperson.

Sir Richard Peto, professor of medical statistics and epidemiology at the Nuffield department of population health, University of Oxford, said they could now be certain that HRT is a cause of about 5% of breast cancers. The cancer
risk increases with the length of time women are on hormones and the cancers tend to be oestrogen receptor-positive, which means they are driven by oestrogen. Women who are given drugs that dry up their oestrogen supply – like tamoxifen – get high protection against the tumours returning.

“These are cause and effect relationships,” said Peto. “It is not just an association that exists, because the menopausal hormone therapy is causing the increase in breast cancer.

“The big problem is how to describe the one in 50 risk,” he said. They did not want to exaggerate it, nor did they want to play it down. “On current websites, [the risks] are misrepresented,” he said.

The paper, by the global Collaborative Group on Hormonal Factors in Breast Cancer, pulled together data from 58 studies around the world on more than 108,000 women who had developed breast cancer after taking menopausal hormone therapy (MHT) – they say “replacement” therapy or HRT is a misnomer and a marketing description.

In western countries, 6.3% of women of average weight will develop breast cancer over the 20 years from the age of 50 without any hormone therapy. The study found that rose to 8.3% among women taking the most common hormonal combination – oestrogen plus daily progestogen.

The odds were better (7.7%) for women who took progestogen only intermittently, maybe for 10 to 14 days a month. Those who took oestrogen only, because they did not need progestogen to protect from womb cancer after a hysterectomy, had a risk of 6.8%.

Women who are obese are at increased risk of breast cancer because their adipose (fat) tissue produces extra oestrogen after the menopause. The study found that taking HRT did not further increase their risk.

Baroness Delyth Morgan, the chief executive of Breast Cancer Care and Breast Cancer Now, said the longer-term effect of HRT might be an important consideration for women. “Taking HRT is a really personal decision, and it’s vital that everyone fully understands the benefits and risks, discusses them with their GP and is supported to make the decision that’s right for them,” she said. “Rather than causing concern, we hope [the findings] will help anyone considering HRT treatment to make an even more informed decision.”

Other scientists said the study was well conducted. Kevin McConway, emeritus
professor of applied statistics at The Open University, called it “a very careful, thorough, excellent piece of research”. Stephen Evans, professor of pharmacoepidemiology at the London School of Hygiene and Tropical Medicine, called it “a tour de force in what has been done and the way it has been done – the findings cannot be dismissed”.

But the Royal College of Obstetricians and Gynaecologists, in a joint statement with the British Menopause Society, said the findings were in line with the Nice guidelines that showed a “small increased risk”.

“Women and doctors should be reassured that the findings of this study do not add anything new in terms of the effects of hormone replacement therapy. Research shows that, for most women, HRT helps to manage menopausal symptoms and is safe,” said gynaecologist Prof Janice Rymer, the vice-president of the college.

“Women must be informed of the small increase in risk of breast cancer so they can weigh this up against the benefits that they may have from taking HRT. Every woman experiences the menopause differently and symptoms vary. These can be extremely debilitating and have a significant impact on a woman’s physical and psychological health, career, social life and relationships. Unfortunately, many women are still suffering in silence and are reluctant to seek advice and support due to concerns around the risks of breast cancer associated with HRT.”

The Royal College of GPs urged patients not to panic and to carry on taking their HRT, and GPs to carry on as normal “until clinical guidelines recommend otherwise. If a patient is concerned about her HRT prescription, she should discuss it with her GP at her next routine appointment.”