

A randomised controlled trial of post-operative radiotherapy following breast-conserving surgery in a minimum-risk population. Quality of life at 5 years in the PRIME trial

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Executive summary

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Executive summary

Background

Post-operative breast irradiation is the standard treatment following breast-conserving surgery and adjuvant endocrine therapy, irrespective of age. However, the differences between older and younger patients in response to treatment are poorly defined as, historically, patients >70 years are frequently excluded from trials.

The use of breast irradiation declines substantially with age, although just over half of cases of breast cancer occur in women aged ≥ 65 years. Current data suggest that the risk of local recurrence after conservation surgery and endocrine therapy may decline with age. At the same time, there are competing risks of death, particularly vascular, in older patients.

Objectives

To assess whether omission of post-operative radiotherapy (RT) in women with 'low-risk' axillary node-negative early breast cancer [tumour size of less than 5 cm (T0–2) although the eligibility criteria further reduce the eligible size to a maximum of 3 cm] treated by breast-conserving surgery and adjuvant endocrine therapy improves quality of life and is more cost-effective.

Design

A randomised controlled clinical trial, using a method of minimisation balanced by centre, grade of cancer, age, lymphovascular invasion and pre-operative endocrine therapy.

Setting

Breast cancer clinics in cancer centres in the UK.

Participants

Patients aged ≥ 65 years were eligible provided their breast cancers were considered to be at low risk of local recurrence, they were suitable for breast conservation surgery, they were receiving endocrine therapy and they were able and willing to give informed consent.

Interventions

The standard treatment of post-operative breast irradiation, or the omission of RT. This report is a follow-up report to one published by the *Health Technology Assessment* journal in 2007 [Prescott RJ, *et al.* A randomised controlled trial of post-operative radiotherapy following breast-conserving surgery in a minimum-risk older population. The PRIME trial. *Health Technol Assess* 2007;**11**(31)].

Main outcome measures

Quality of life was the primary outcome measure, together with anxiety and depression and cost-effectiveness. Secondary outcome measures were recurrence rates and survival, and treatment-related morbidity. The principal method of data collection was by questionnaire, completed at home with a research nurse on four occasions over 15 months, then by postal questionnaire at 3 and 5 years after surgery.

Results

The hypothesised improvement in overall quality of life with the omission of RT was not seen in the summary domains of the European Organisation for Research in the Treatment of Cancer (EORTC) scales. Some differences were apparent within subscales of the EORTC questionnaires, and insights into the impact of treatment were also provided by the qualitative data obtained by open-ended questions added by the trial team. Differences were most apparent shortly after the time of completion of RT. RT was then associated with increased breast symptoms and greater (self-reported) fatigue, but with lower levels of insomnia and endocrine side effects. These statistically significant differences in breast symptoms persisted for up to 5 years after RT [mean difference, RT was 5.27 units greater than no RT, 95% confidence interval (CI) of 1.46 to 9.07], with a similar, though non-significant, trend in insomnia. No significant difference was found in the overall quality of life measure, with the no RT group having 0.36 units greater quality of life than the RT group (95% CI -5.09 to 5.81).

Even at 3 and 5 years after surgery, patients from both treatment groups are still expressing concern about the recurrence of breast cancer, although by 5 years this has fallen to <10% of patients.

Treatment-related morbidities, such as radiation-induced toxicities, persist and even, in some cases, increase for up to at least 5 years.

A basic cost-effectiveness analysis of the 5-year data showed that the mean quality-adjusted life-years (QALYs) were lower for the no RT arm, but the difference was not statistically significant. The costs were lower for the no RT arm and the difference was statistically significant. This would suggest that the omission of RT is the dominant option. However, it is important to consider the joint uncertainty of the cost and effects differences. The cost-effectiveness acceptability curve showed that at the conventional threshold of £30,000 per QALY there is a 41.6% chance that the no RT option is cost-effective compared with the RT option.

Conclusions

Although there are no global differences in quality of life scores between the patients treated with and without RT, there are several dimensions that exhibit significant advantage to the omission of irradiation.

The omission of RT may not be cost-effective. Given the high levels of uncertainty surrounding the estimates, further analysis of the cost-effectiveness of omitting RT is required.

Breast RT is tolerated well by most older breast cancer patients without impairing their overall health-related quality of life (HRQoL). While HRQoL should always be taken into account when determining treatment, our results show that the addition of RT does not impair overall quality of life.

Implications for health care

As our conclusions remain, for the most part, the same as in our previous report, the implications for health care are also very similar:

1. Our evidence suggests that there are significant differences in some dimensions of quality of life, although there is no significant overall quality of life advantage in the omission of adjuvant RT.
2. Certain quality of life issues persist for patients over longer periods of time than previously thought, and may need to be taken into consideration when discussing treatment options with patients. Patients should be informed that radiation-induced toxicities may persist up to at least 5 years.
3. Older low-risk patients have significant concerns about recurrence of breast cancer, even following RT, although less so at 3 and 5 years.

Recommendations for further research

Primary recommendation for further research:

1. Further economic modelling on the longer-term costs and consequences of omitting RT.

Secondary recommendations

1. There are clear indications that there is a short-term economic benefit from the omission of RT in this group of patients. However, the evidence for the longer-term benefit requires longer follow-up to determine local recurrence rates with and without post-operative whole breast RT.
2. Investigate the application of novel methodologies (such as touch-screen technology) for capturing and grading comorbidity and quality of life at baseline and at clinical follow-up.
3. Investigate the influence of specific types and degrees of comorbid disease on quality of life.
4. Refine methodologies and develop software to integrate the prediction of recurrence rates from breast cancer with the competing effects of mortality from other diseases to improve clinical decision-making.
5. Develop a validated questionnaire/scale to assess the impact of access to health-care services for older patients.

Trial registration

This study is registered as ISRCTN14817328.

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Publication

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NIHR Health Technology Assessment programme

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