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Aromatase inhibitors versus tamoxifen in pre-menopausal women with ER+ early stage breast cancer treated with ovarian suppression: A patient level meta-analysis of 7,030 women in four randomised trials

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Background

- Tamoxifen reduces 15-year breast cancer mortality by one third in ER+ disease (EBCTCG Lancet 2011)
- Aromatase inhibitors (AIs) are even more effective than tamoxifen in post-menopausal women (EBCTCG Lancet 2015)
- AIs may benefit pre-menopausal women treated with ovarian suppression (OFS)

Methods

- Meta-analysis of individual patient data for 4 trials of pre-menopausal women with early stage breast cancer treated with OFS, randomised to AI or tamoxifen

- Primary outcomes were recurrence and cause specific mortality analysed by standard EBCTCG* methods

- $2p<0.05$ for primary outcomes
- $2p<0.01$ for subgroup analyses

*EBCTCG 1990

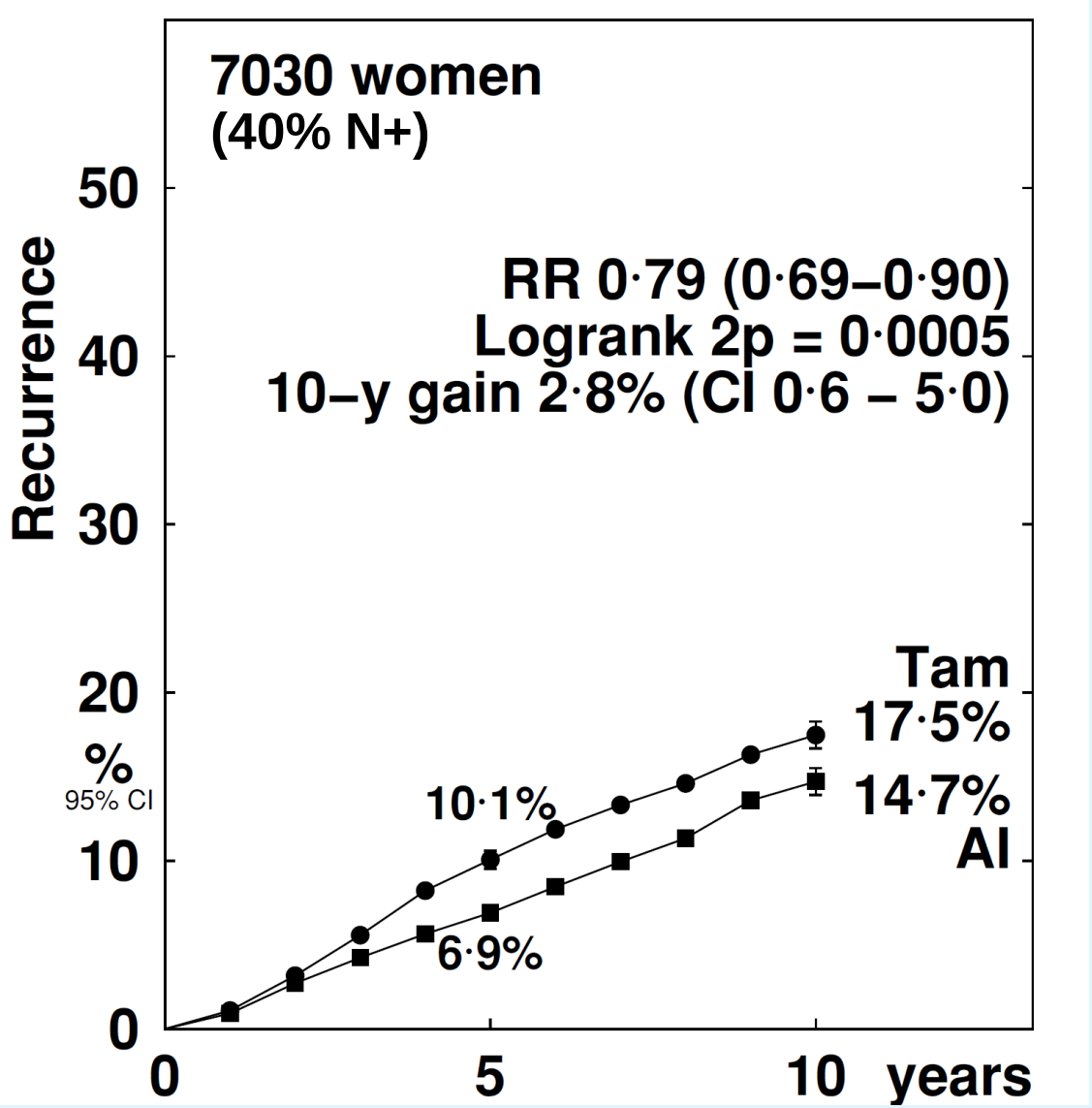
Trials

Trial	Year started	Comparison	N	Median FU
ABCSG 12	1999	Goserelin: (anastrozole vs tamoxifen) ± zoledronic acid x 3yrs	1694	8.0yrs
TEXT	2003	Triptorelin: (exemestane vs tamoxifen) x 5yrs	2635	9.1yrs
SOFT	2003	Triptorelin: (exemestane vs tamoxifen) x 5yrs	1998	7.9yrs
HOBOE	2004	Triptorelin: (letrozole vs tamoxifen) x 5yrs	703	5.3yrs
Total			7030	8.0yrs

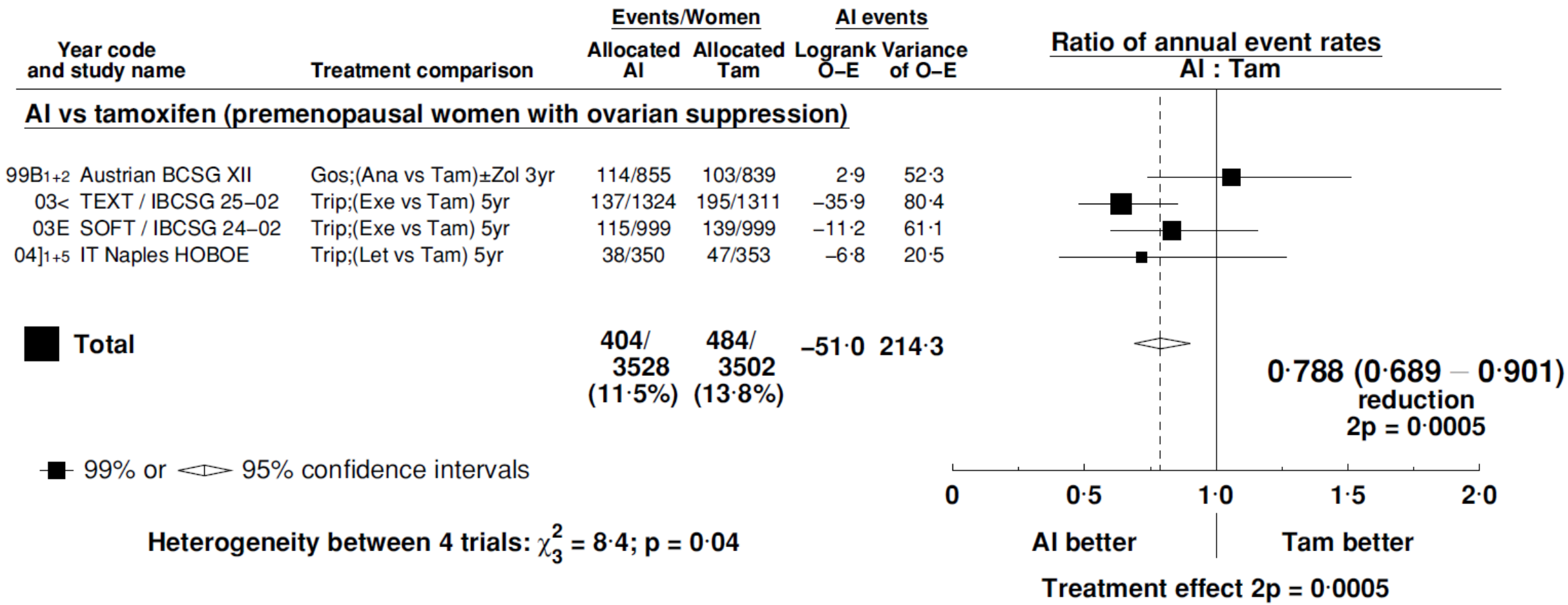
Chemotherapy by trial

- ABCSG 12: only neo-adjuvant allowed (5%)
- TEXT: optional, concurrently with OFS (60%)
- SOFT: before randomisation but patient had to remain pre-menopausal after completion (54%)
- HOBOE: before randomisation (63%)

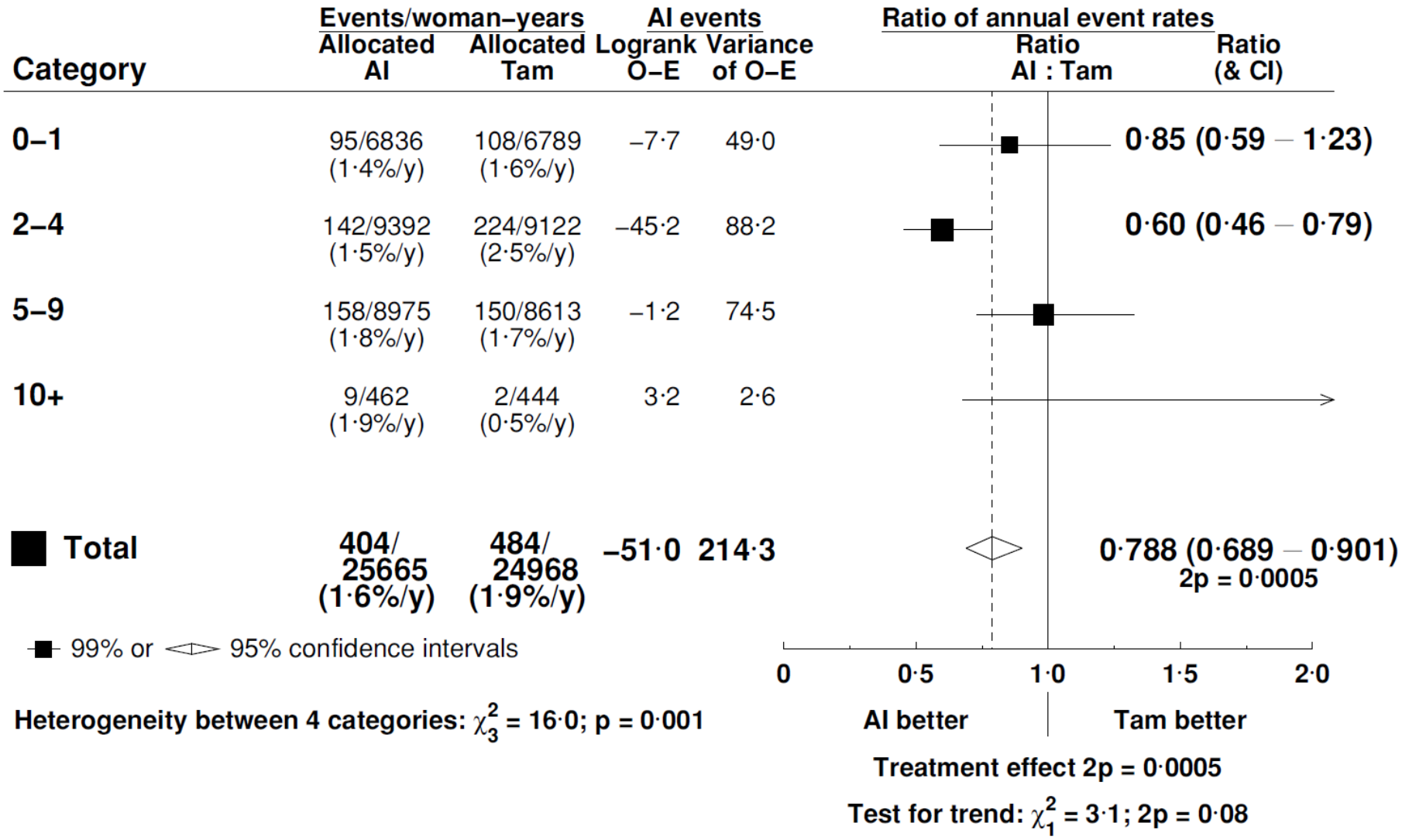
Recurrence



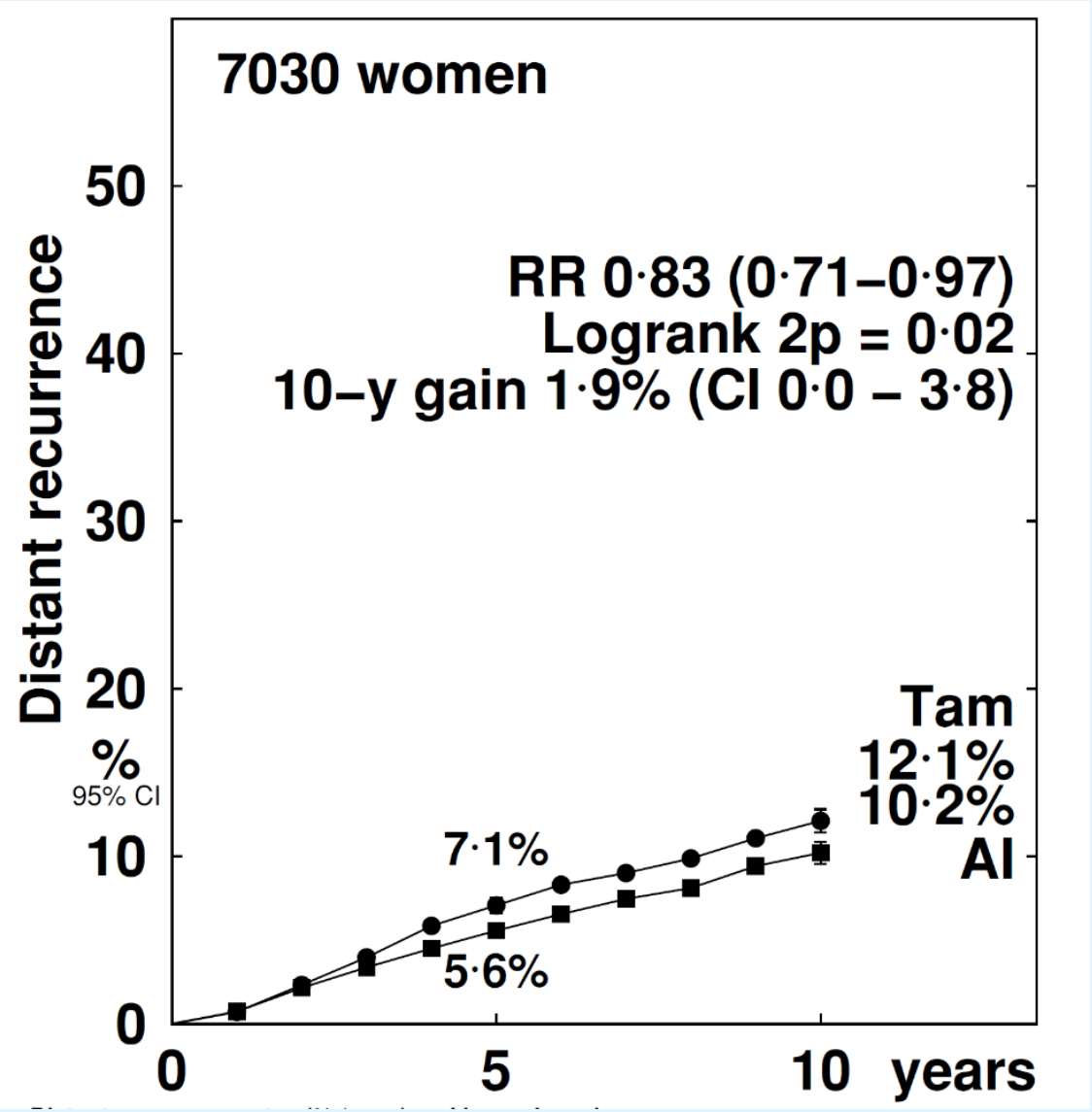
Recurrence



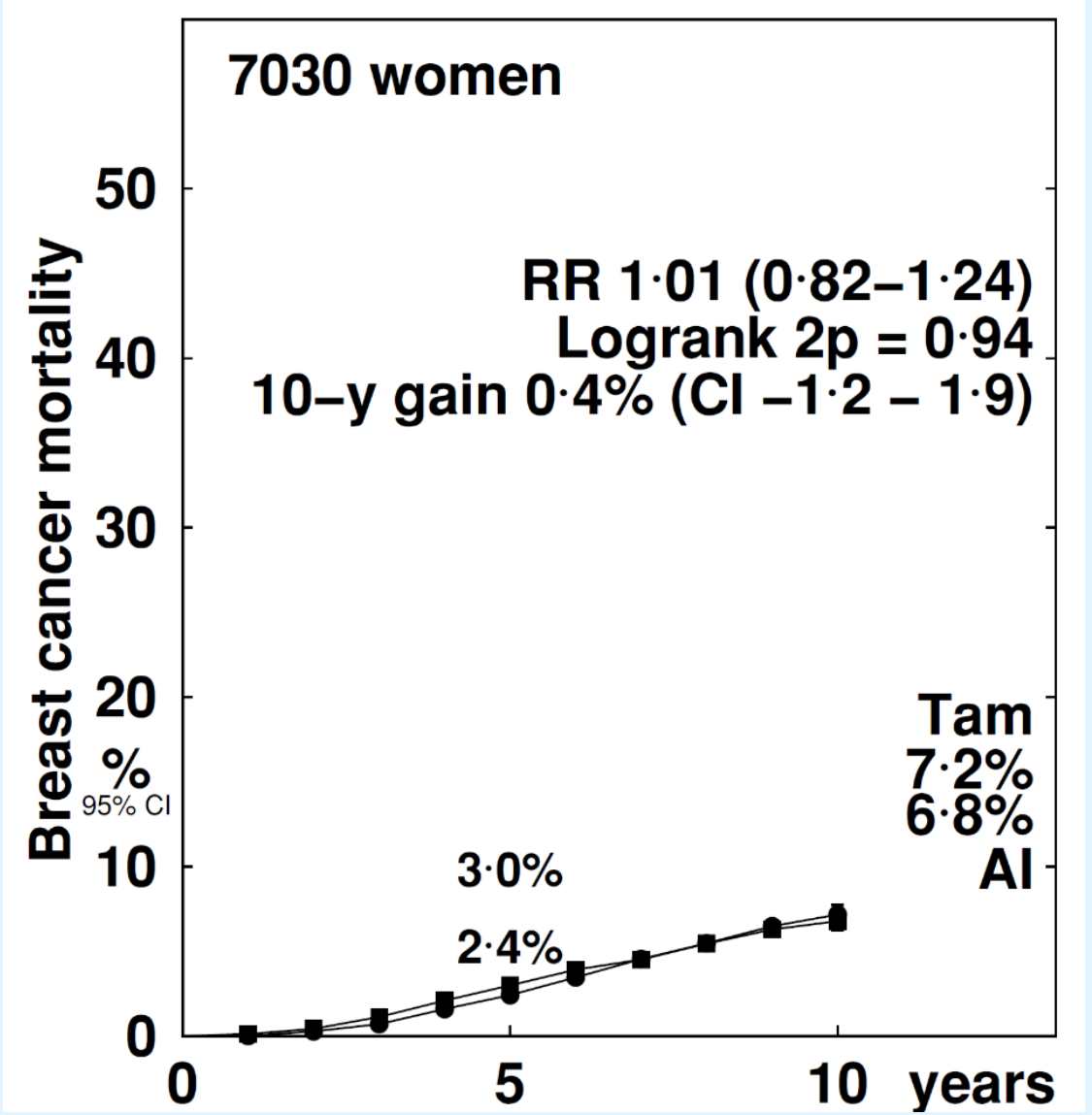
Recurrence by follow up period



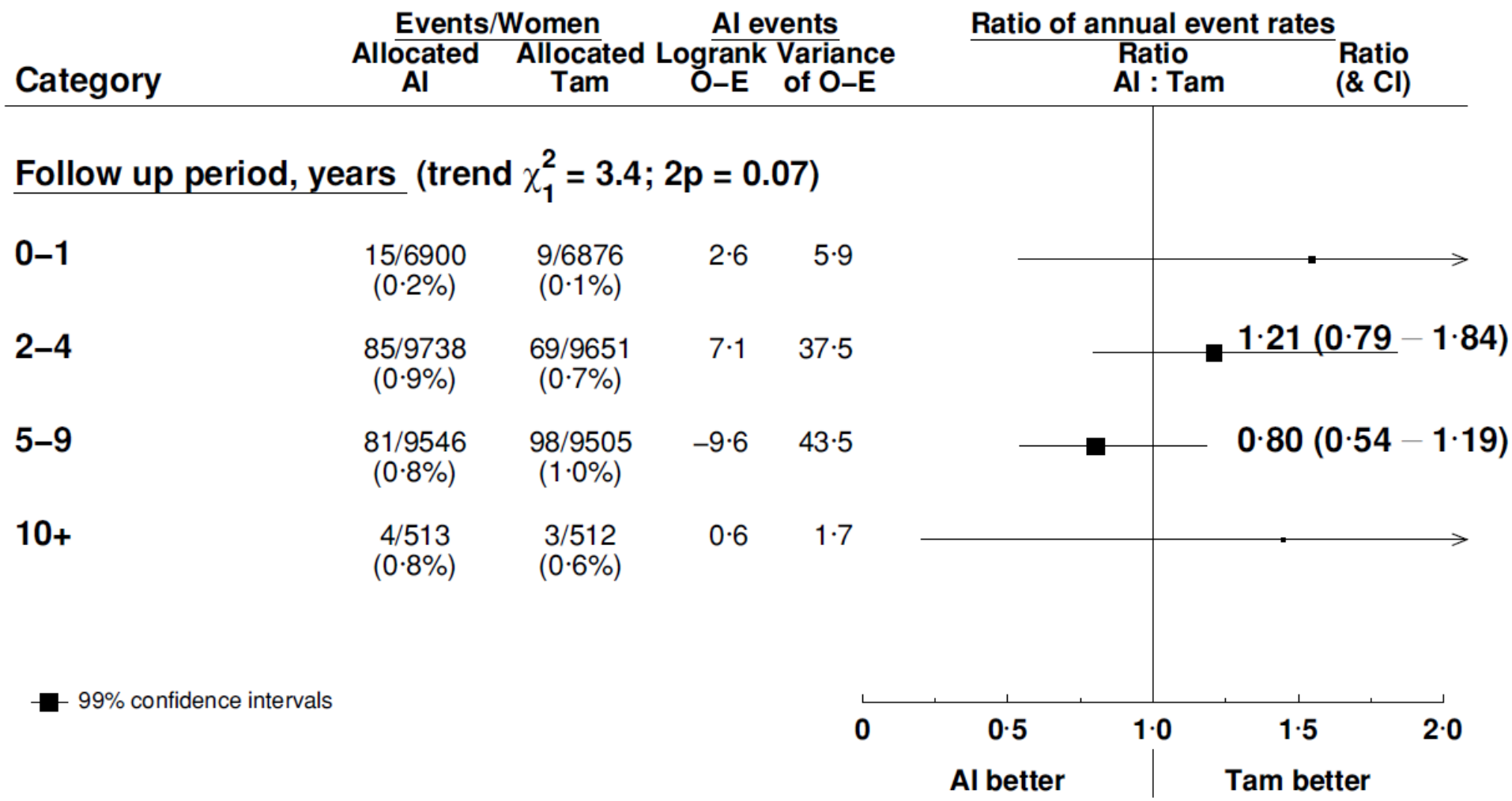
Distant recurrence



BC mortality



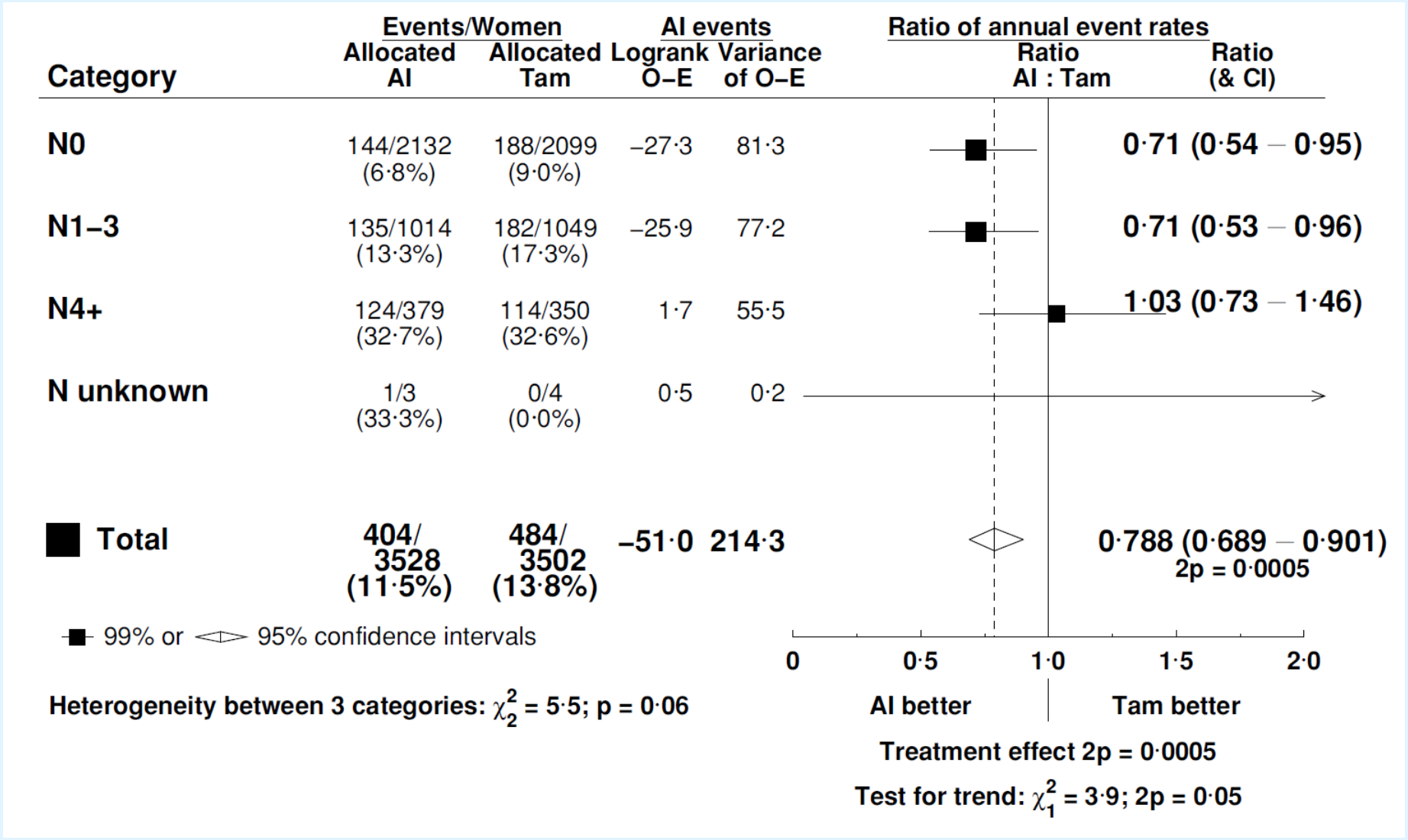
Breast cancer mortality by follow up period



Subgroup analyses by any recurrence

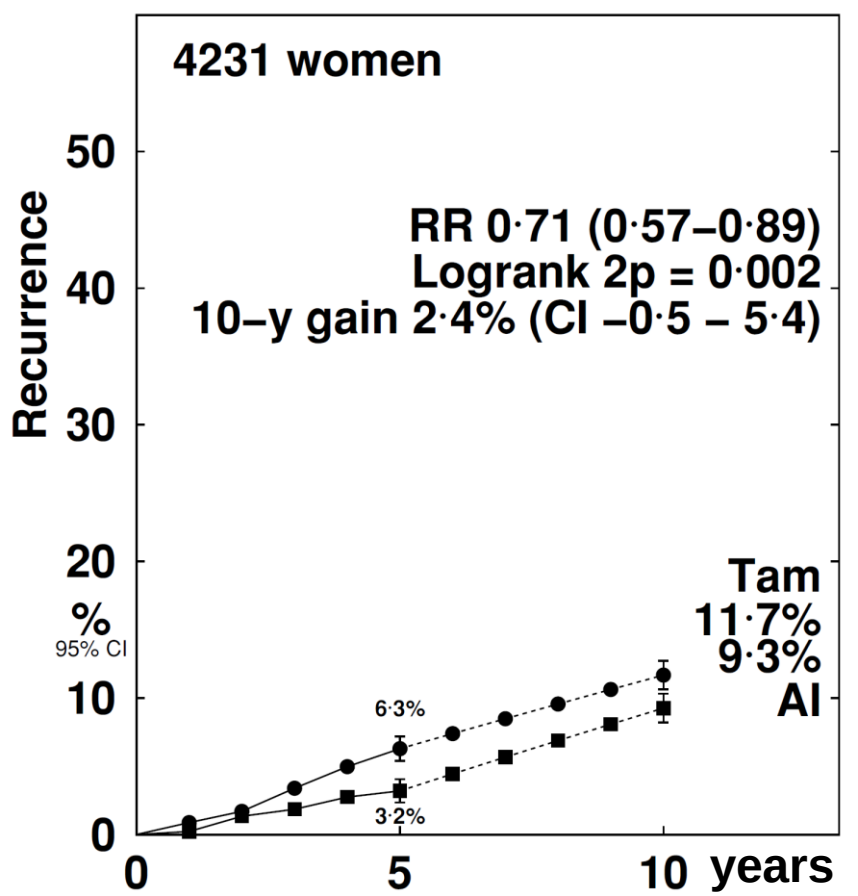
- 13 analyses investigating possible variability (so $p<0.01$ for significance)
- Proportional reduction in recurrence did not vary by age, BMI, tumour size, tumour grade, histological subtype, or presence/absence of chemotherapy

Recurrence by nodal status

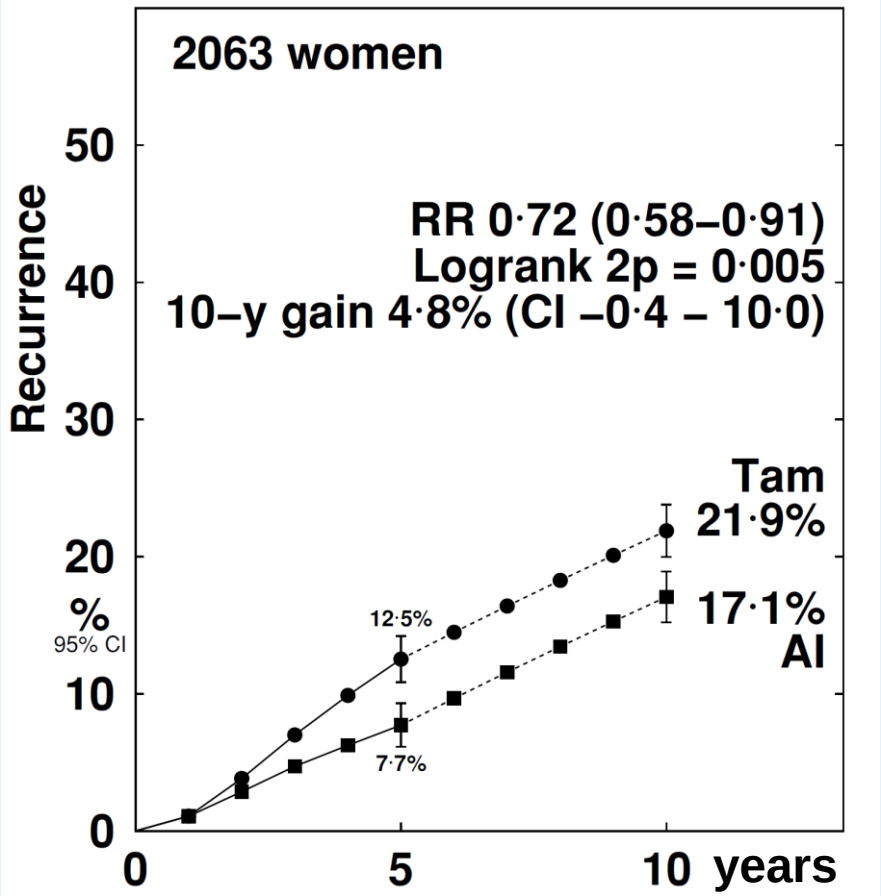


Recurrence by nodal status*

N0

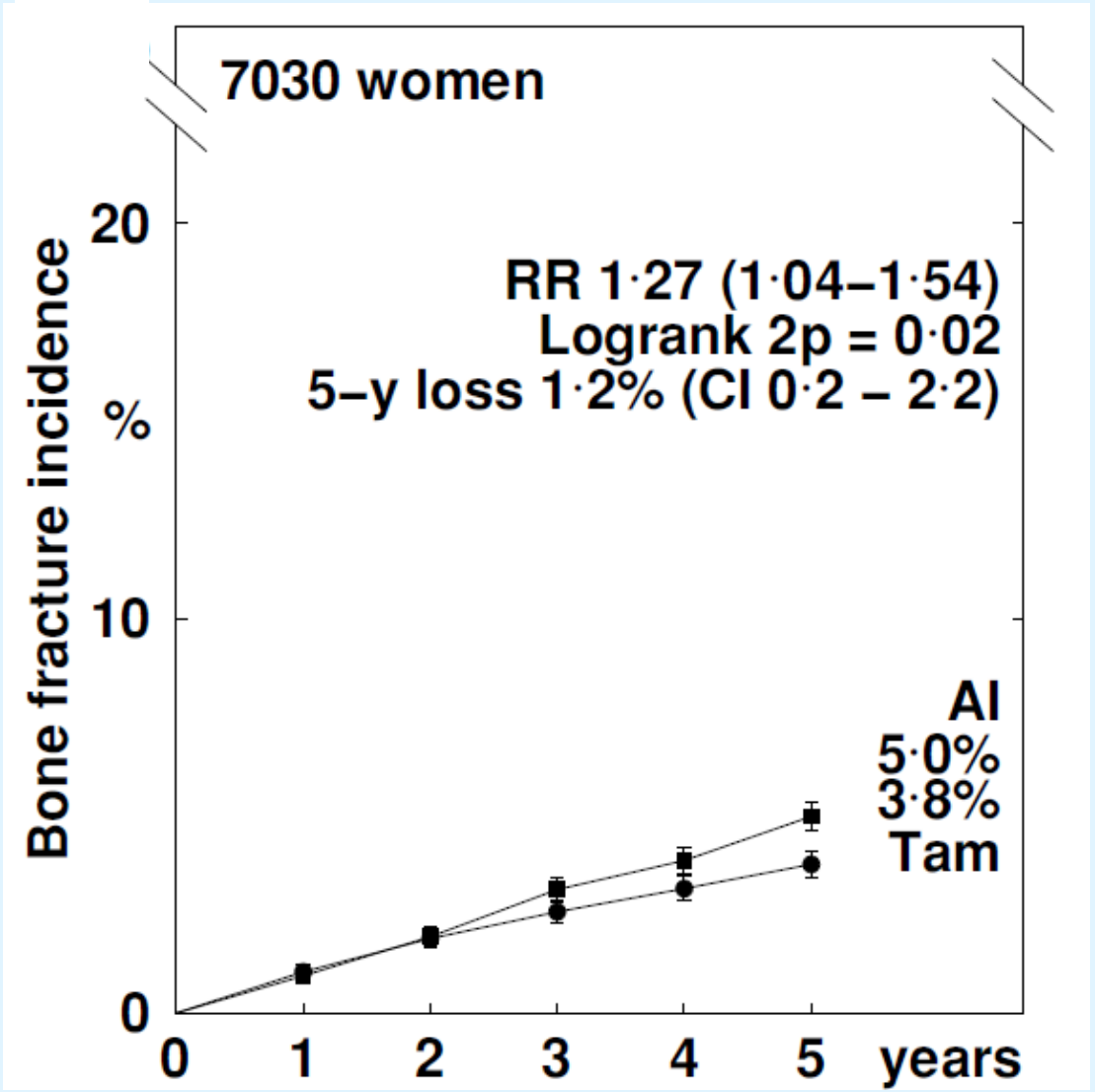


N1-3

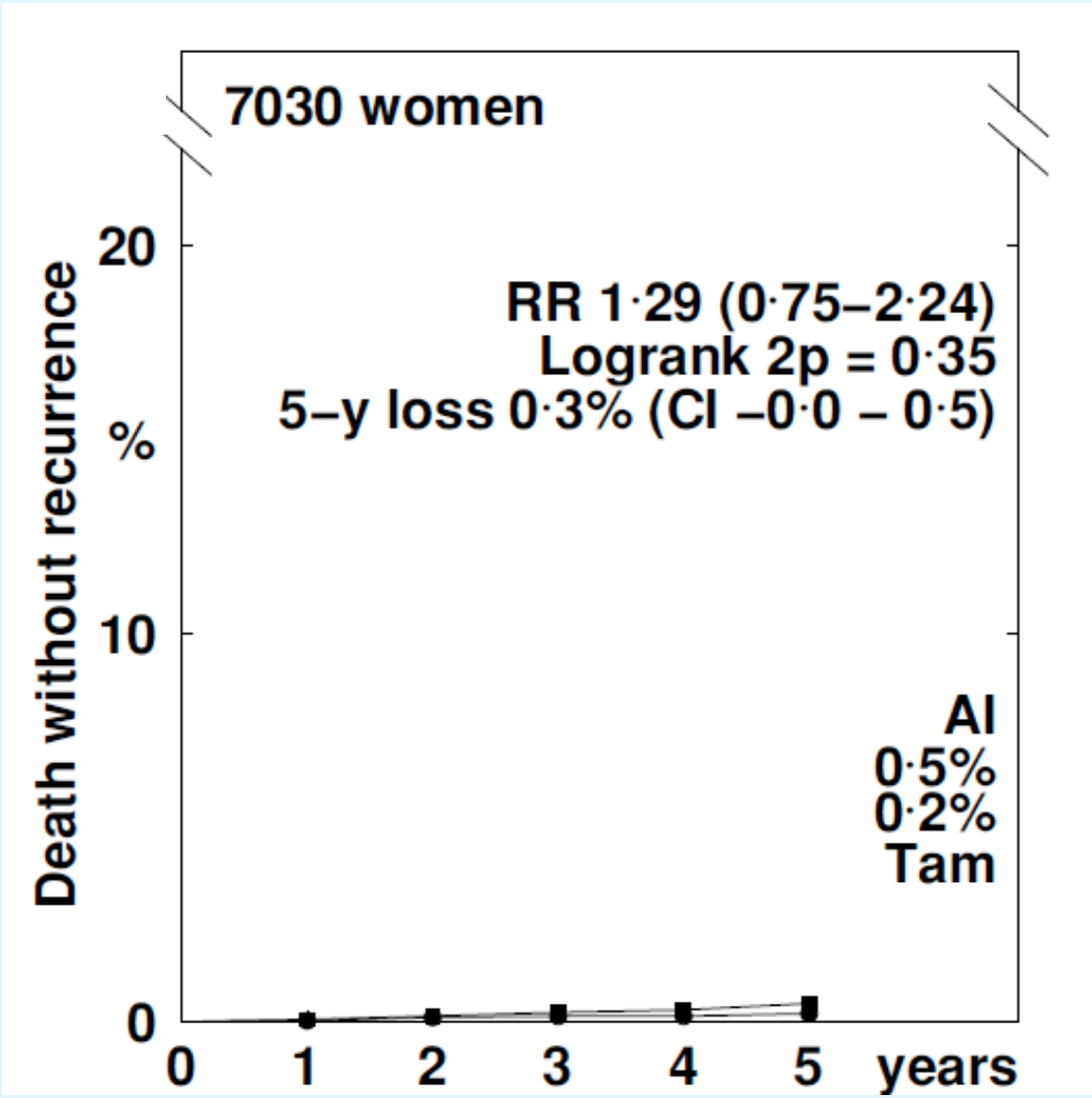


*Smoothed from 5 years

Bone fractures



Non-breast cancer death



Conclusions

- Using AI rather than tamoxifen, in pre-menopausal women receiving OFS, reduces the risk of breast cancer recurrence by ~21%
- Reduction in distant recurrence (17%) but no effect on breast cancer mortality or overall survival – longer FU needed
- No increase in non-breast cancer deaths
- More fractures in women receiving AI

Acknowledgements

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7,030 women in 4 trials

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