I have no financial relationship(s) with commercial interests to disclose.

SAN ANTONIO BREAST CANCER SYMPOSIUM®

Increasing the dose intensity of adjuvant chemotherapy : an EBCTCG meta-analysis

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Early Breast Cancer Trialists' Collaborative Group

All authors declare no relevant conflict of interest

Background

- Adjuvant chemotherapy with anthracycline and taxane-based combinations for early breast cancer reduces the risk of breast cancer mortality by about one third*
- Cytokinetic modelling suggests that increasing the dose intensity of cytotoxic chemotherapy may enhance efficacy

*EBCTCG, Lancet 2012

Three ways to increase dose intensity (ie, the drug dose in mg/m^2 per week)*

1. Use higher doses of drugs in each cycle
2. Reduce the interval between treatment cycles
3. Give drugs sequentially rather than concurrently

* Norton L. Sem Oncol 1997

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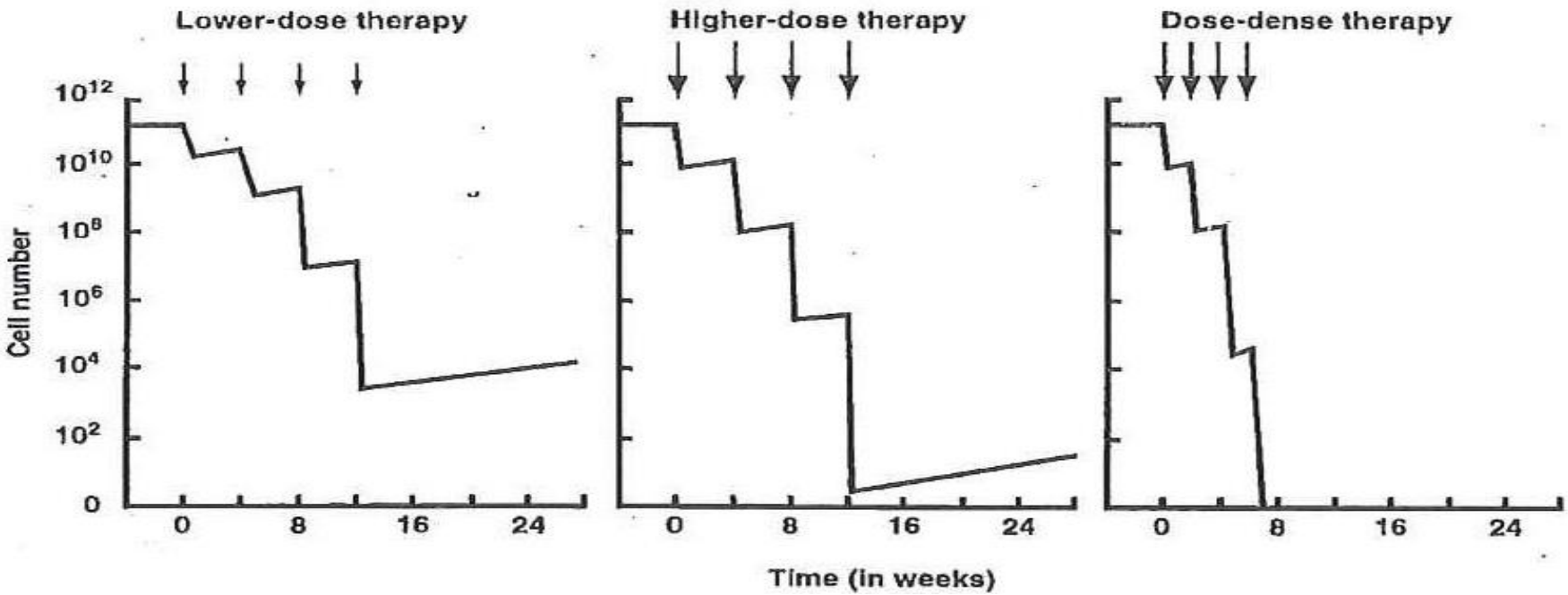
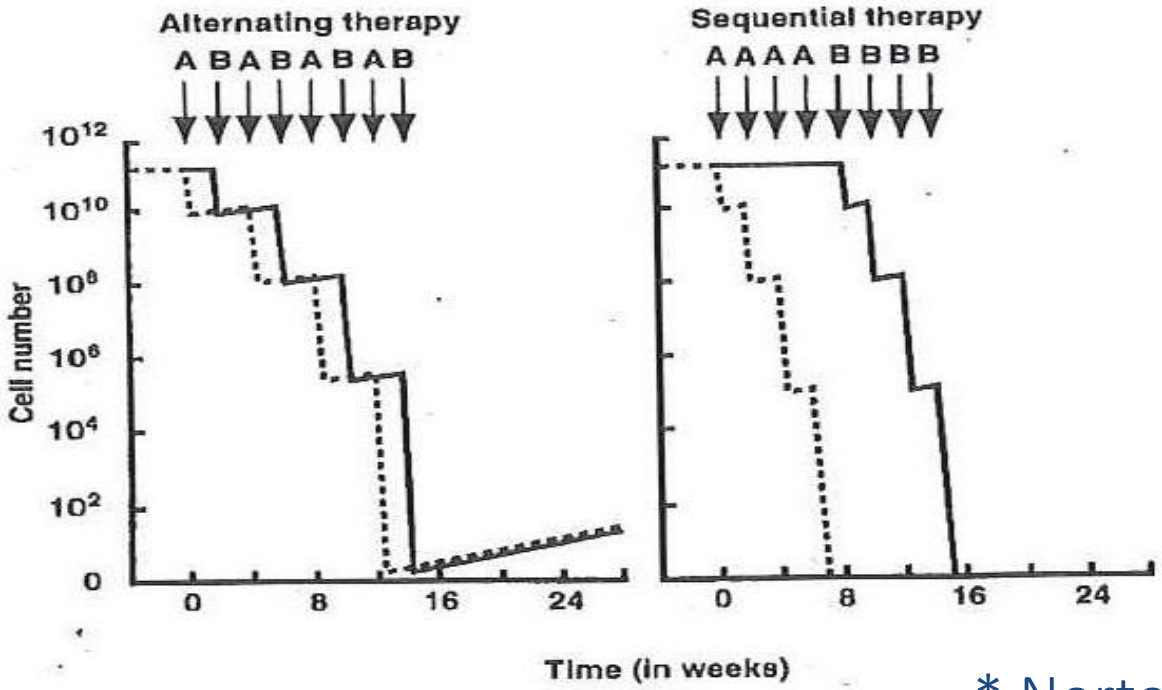
Models of tumour cytoreduction and regrowth following conventional, dose-escalated and dose-dense chemotherapy*



* Norton L. Sem Oncol 1997

Models of tumour cytoreduction and regrowth following alternating and sequential dose-dense chemotherapy*



Broken lines indicate cells sensitive to treatment A; solid lines cells sensitive to treatment B

* Norton L. Sem Oncol 1997

Three ways to increase dose intensity (ie, the drug dose in mg/m^2 per week)*

1. **Use higher doses of drugs in each cycle**
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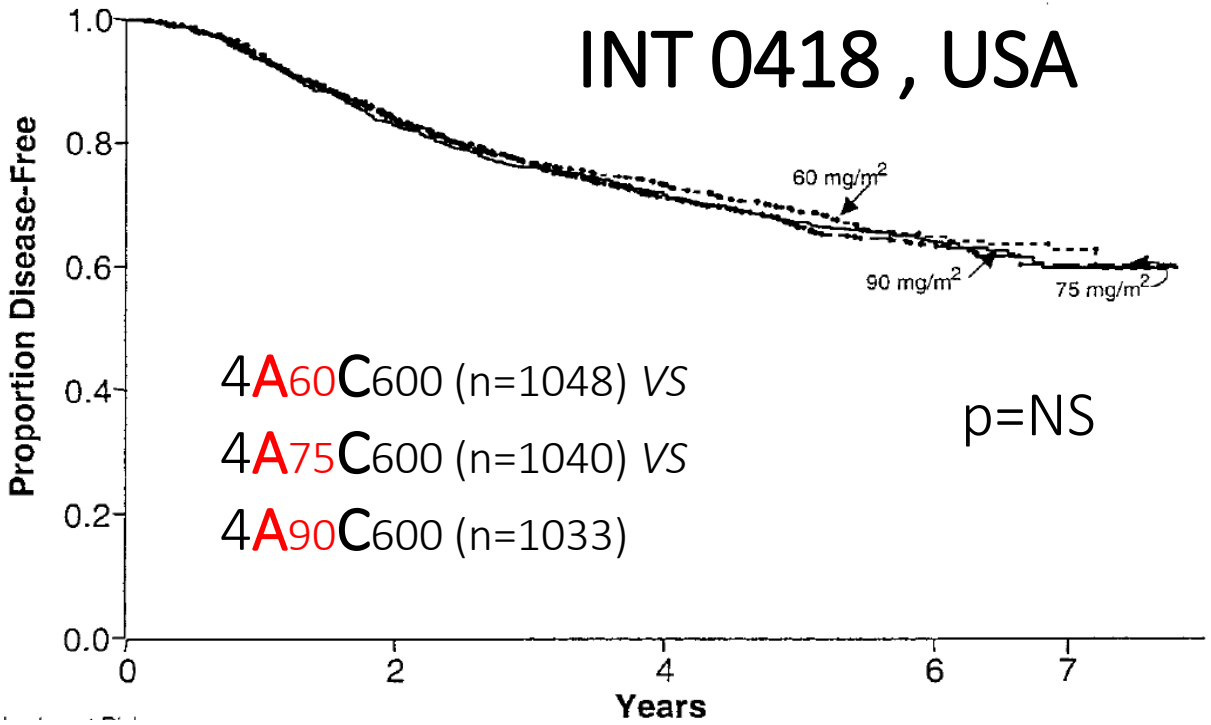
* Norton L. Sem Oncol 1997

Anthracyclines : no apparent benefit from escalation beyond standard dose



4A60C600 (n=1048) *VS*

4A75C600 (n=1040) *VS*

4A90C600 (n=1033)

p=NS

Henderson IC, et al. *J Clin Oncol* 2003; 21:976-983

Three ways to increase dose intensity (ie, the drug dose in mg/m^2 per week)*

1. Use higher doses of drugs in each cycle
2. **Reduce the interval between treatment cycles ("dose-dense" chemotherapy)**
3. **Give drugs sequentially rather than concurrently**

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Dose intensity trials

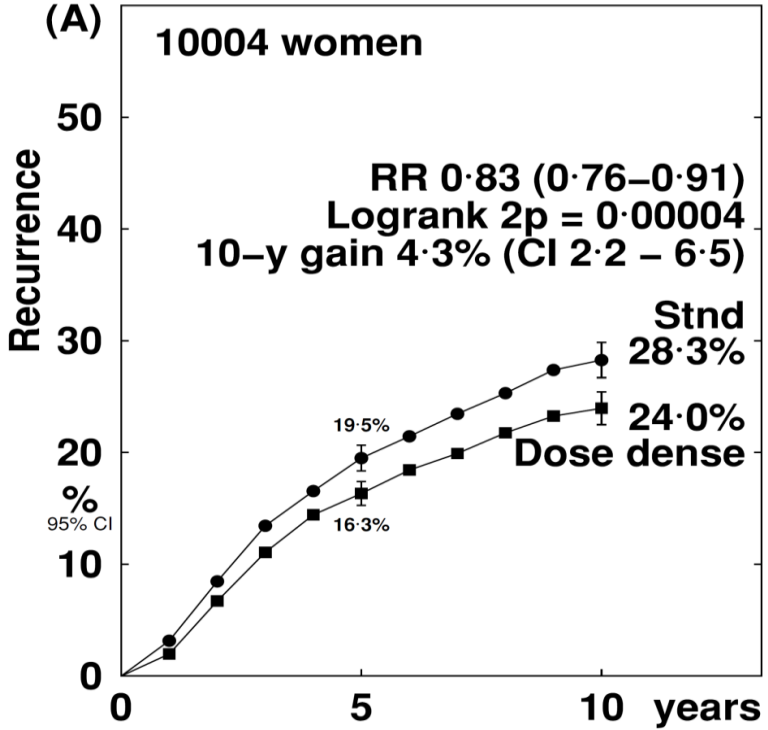
1. Dose-dense (2-weekly) vs Standard (3-weekly)
   a. Same chemotherapy drugs and doses: 7 trials, n=10,004
   b. Some differences in chemotherapy: 5 trials, n=5,508
2. Sequential (3-weekly) vs Concurrent (3-weekly)
   a. Same drugs in each group: 5 trials, n=9,644
   b. Some differences in drugs used: 1 trial, n=1,384
3. Sequential (2-weekly) vs Concurrent (3-weekly)
   a. Some differences in drugs used: 6 trials, n=6,532

Methods

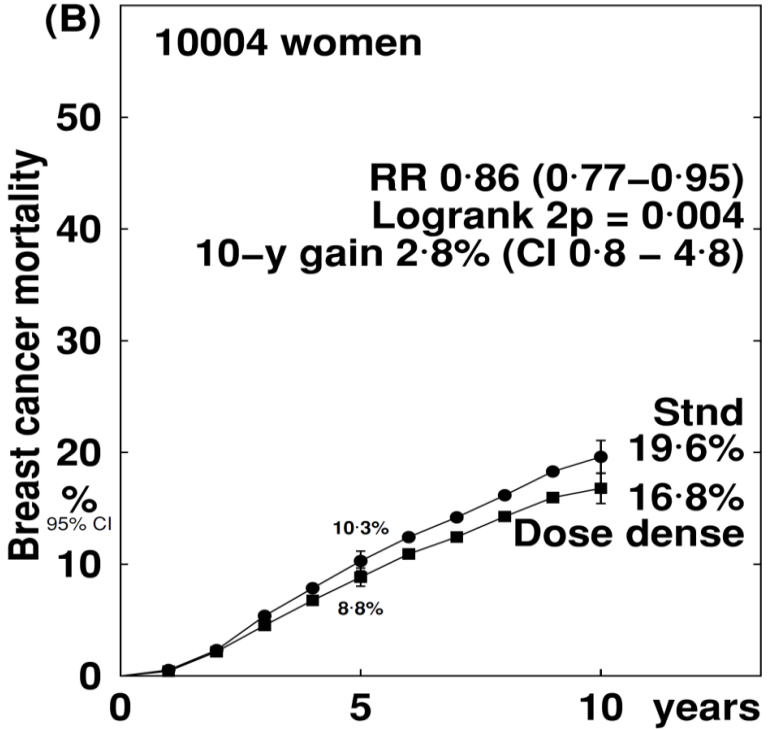
- Individual patient data were provided for 25 trials that included 94% of women randomised in the 31 relevant trials (34,122 / 36,292)
- Primary outcomes were recurrence and breast cancer mortality analysed by standard logrank methods

2-weekly (dose dense) *vs* the same chemotherapy given 3-weekly

Any Recurrence



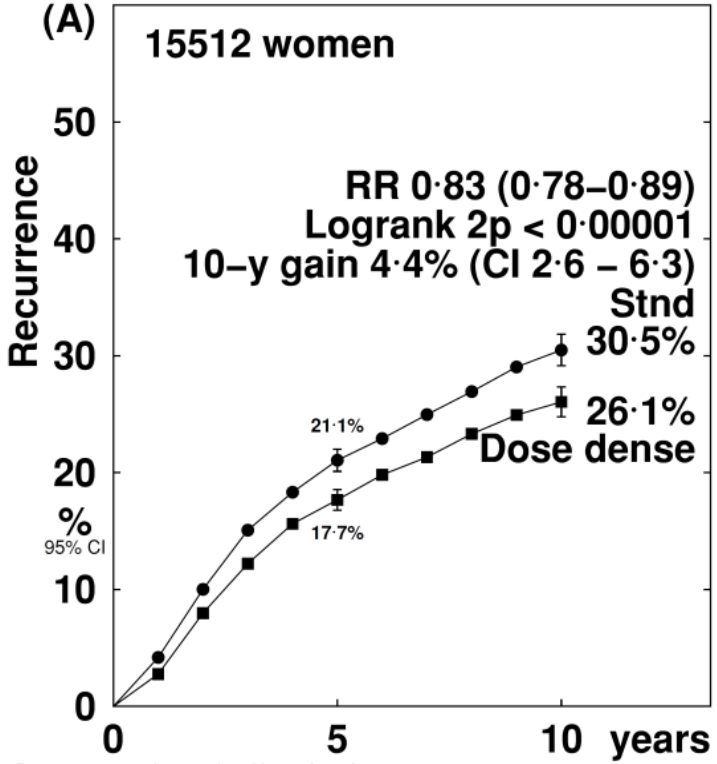
Breast Cancer Mortality



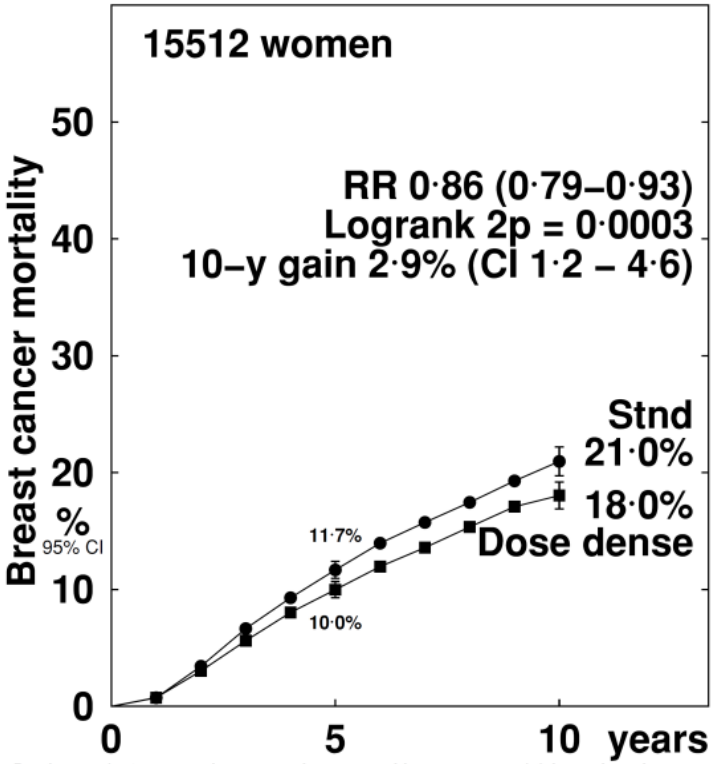
2-weekly vs 3-weekly chemotherapy: all trials

(including the 5 trials where chemotherapy differed between arms)

Any Recurrence

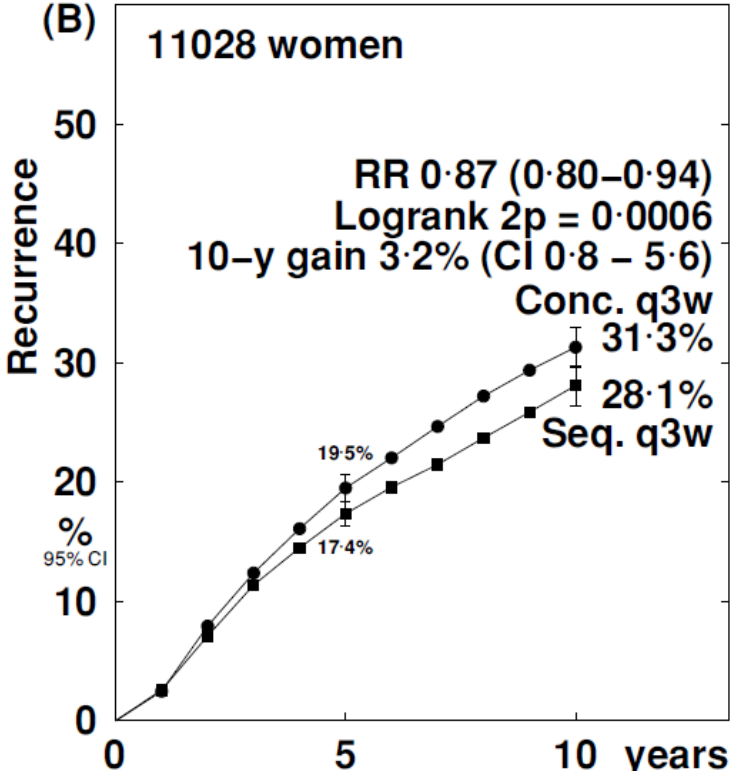


Breast Cancer Mortality

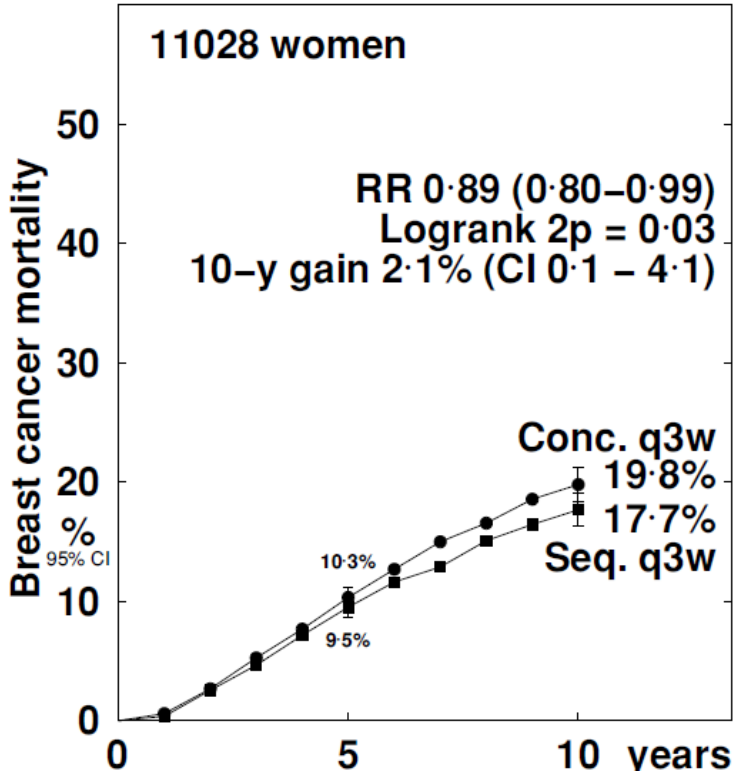


Sequential (3-weekly) vs Concurrent (3-weekly) chemotherapy

Any Recurrence

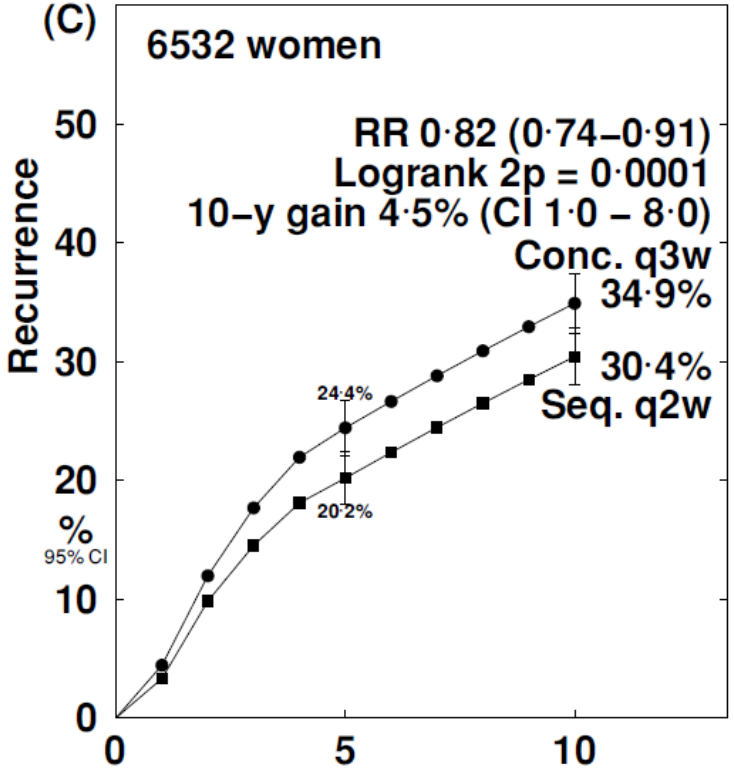


Breast Cancer Mortality

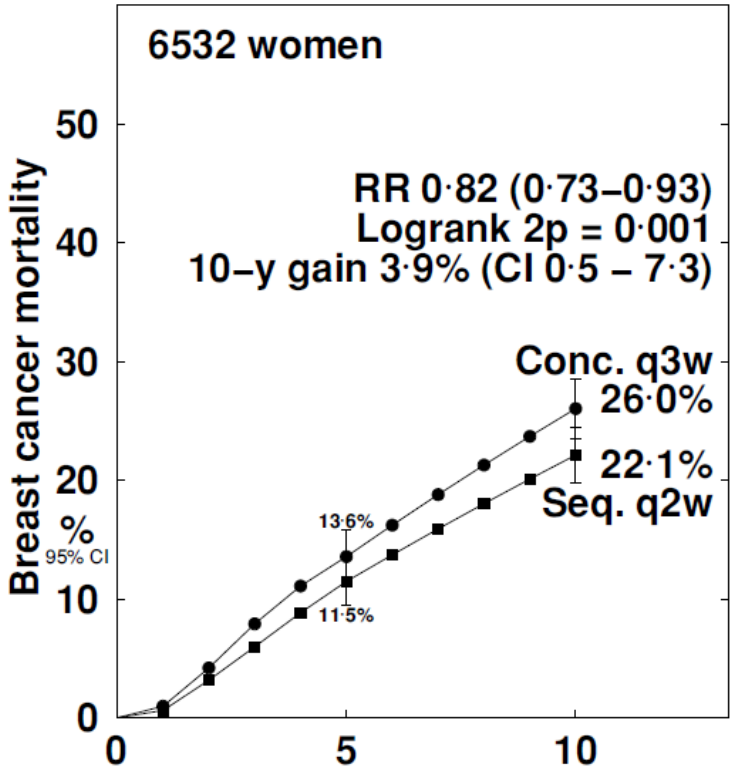


Sequential (2-weekly) vs Concurrent (3-weekly) chemotherapy

Any Recurrence

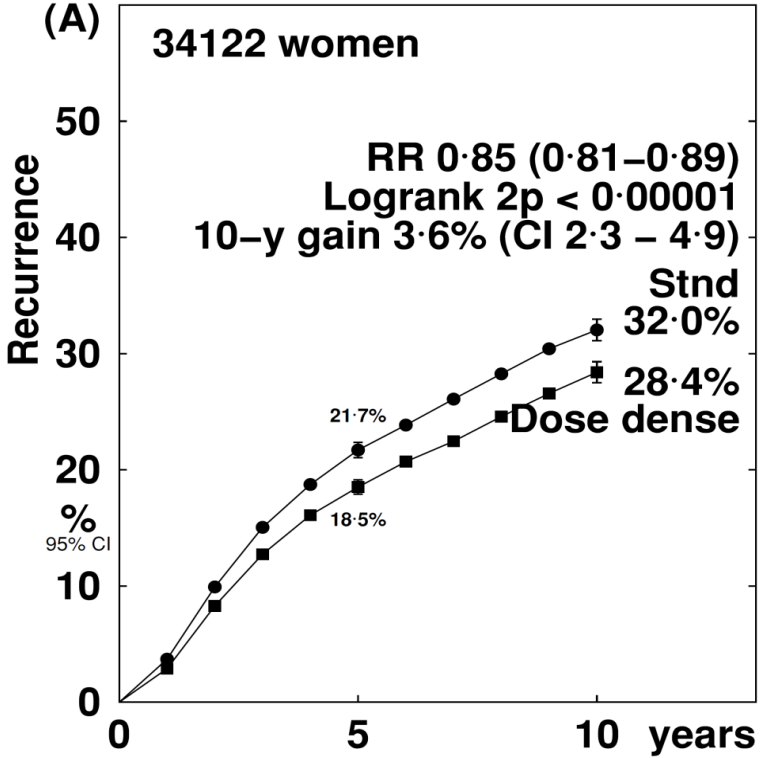


Breast Cancer Mortality

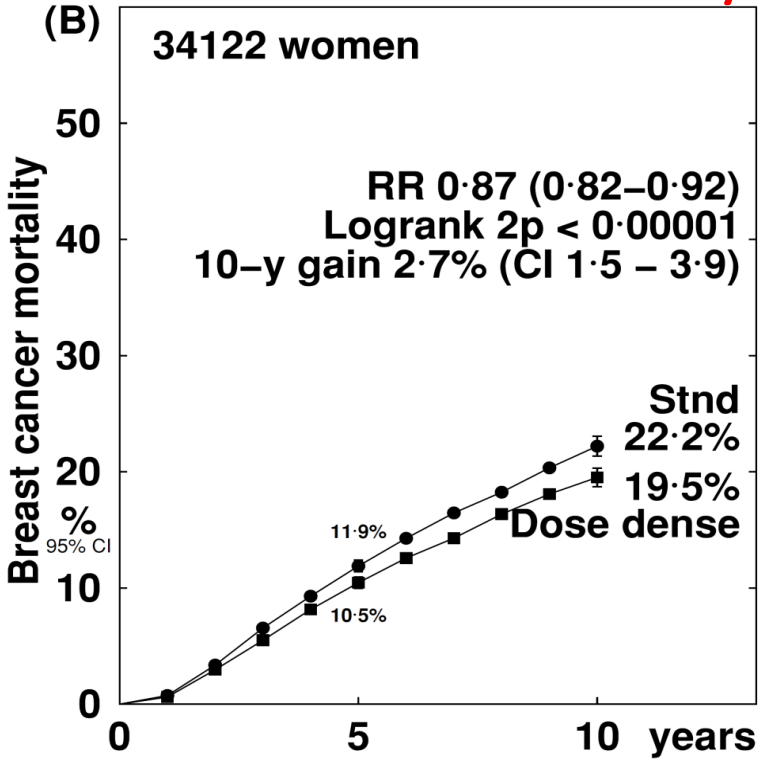


Pooled analysis of all 25 dose-dense and sequential trials

Recurrence

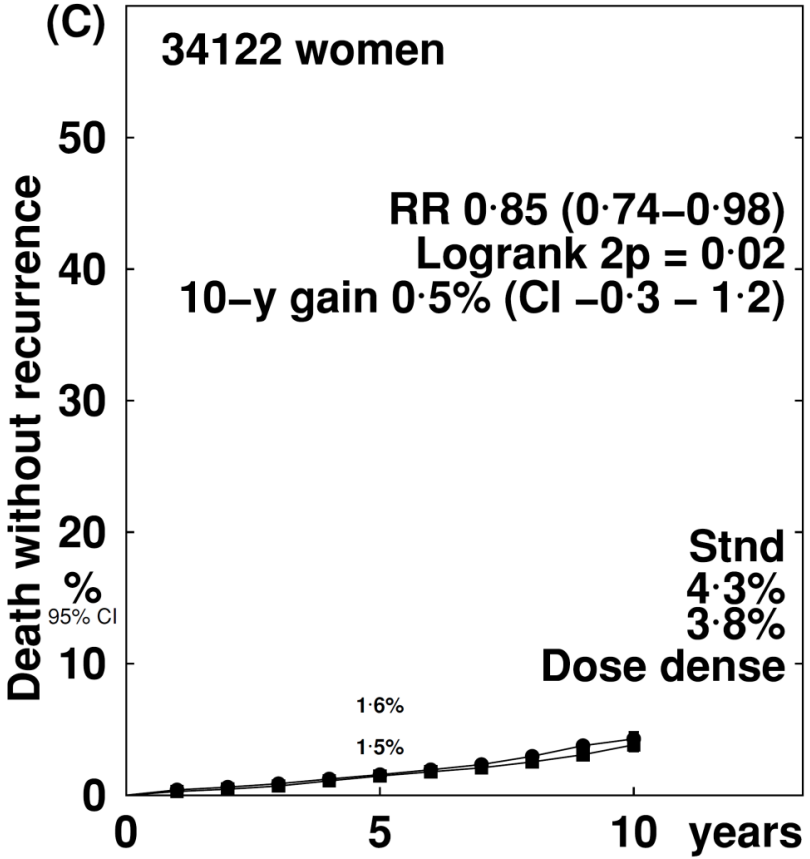


Breast Cancer Mortality

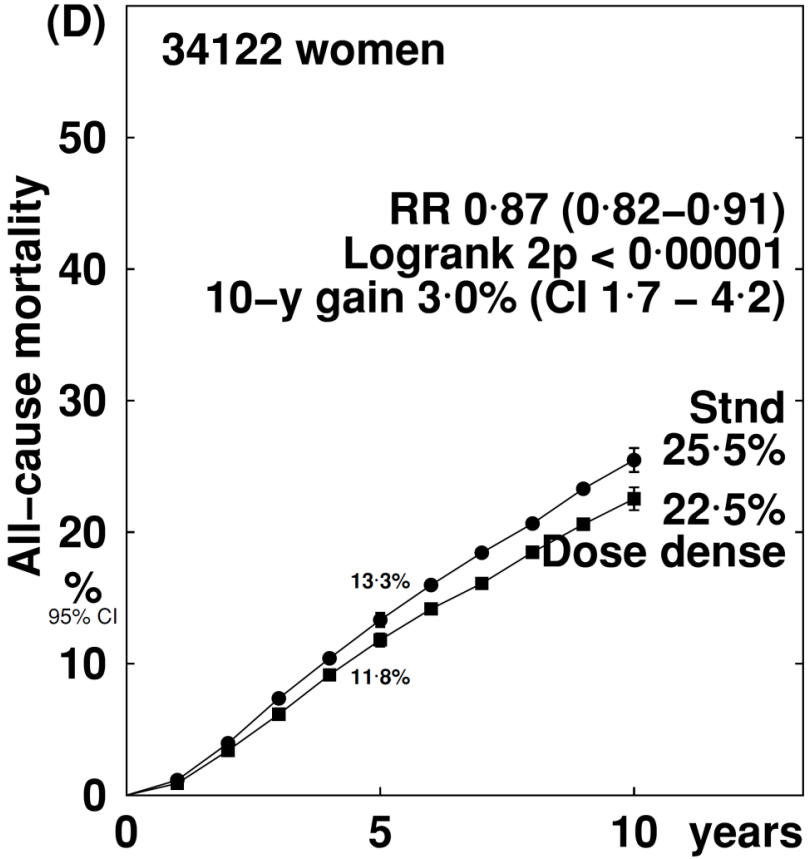


Pooled Analysis

Death without recurrence

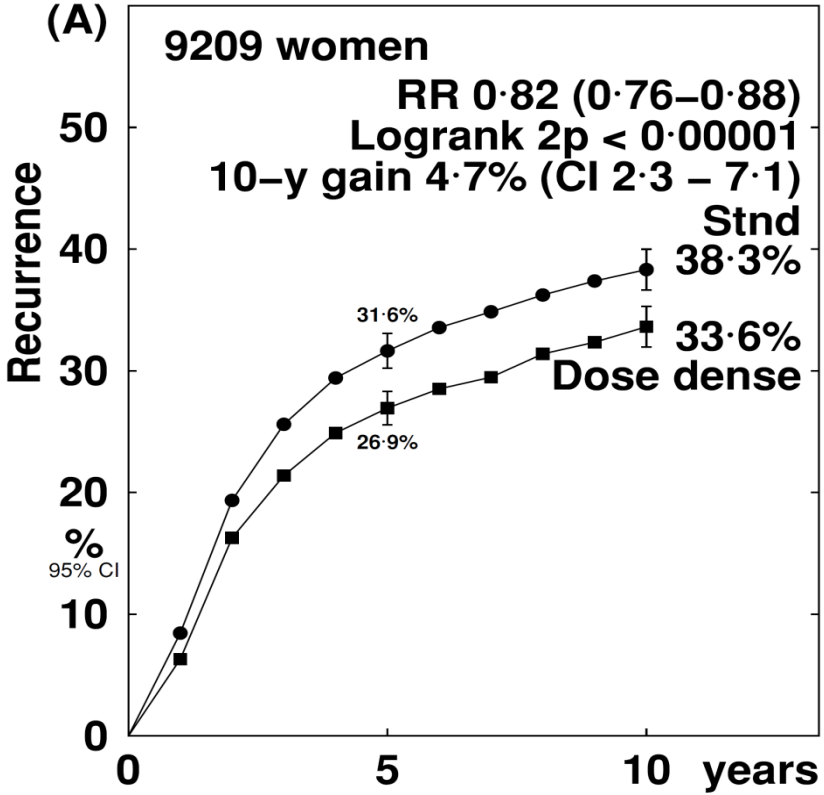


All cause mortality

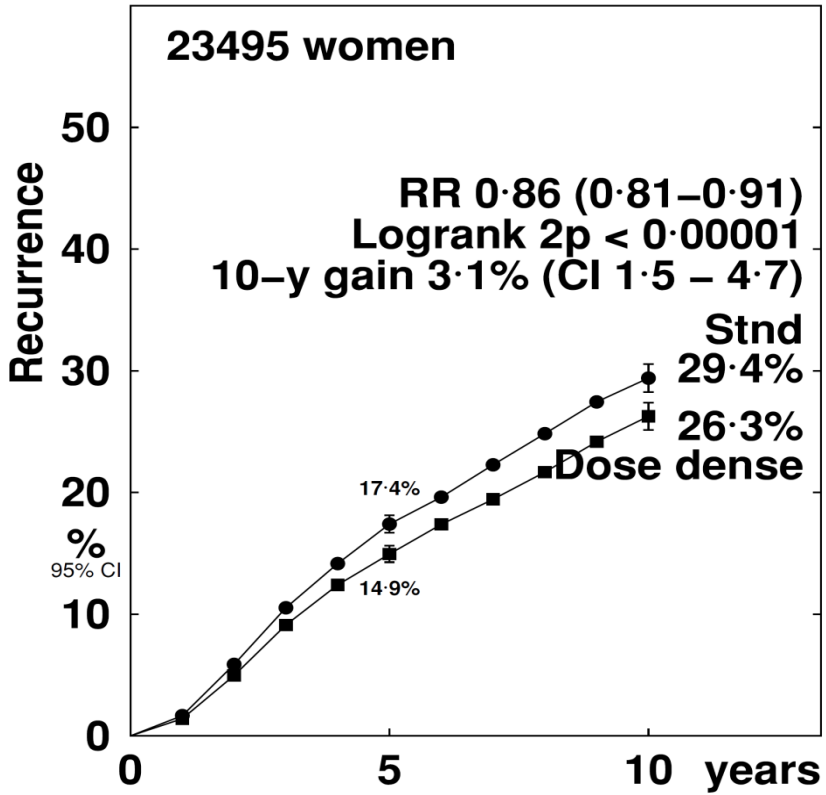


Pooled Analysis: recurrence by ER status

ER- Negative



ER - Positive



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Conclusions

- Shortening the interval between cycles and sequential administration of anthracycline and taxane chemotherapy reduces recurrence and death from breast cancer
- Reductions in recurrence of about 15% were similar in ER-positive and ER-negative disease and did not differ significantly by any other tumour or patient characteristic
- No increase seen in death without recurrence (overall or during chemotherapy)

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34,000 women in 25 trials

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