Long-term recurrence risks after use of endocrine therapy for only 5 years

Relevance of breast tumour characteristics

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ER+ Breast Cancer: Endocrine therapy duration

- 5 years of adjuvant endocrine therapy (ET) substantially reduces long-term recurrence risk*

- Continuing ET past year 5 yields an additional risk reduction, but additional side-effects*

- To help decide who should continue ET, we need to know the prognosis if no further ET is given

* **References:** EBCTCG (tamoxifen) *Lancet* 2011;378:771, EBCTCG (AI) *Lancet* 2015;386:1341, MA.17 (AI) *NEJM* 2003;349:1793, ASCO 2016 Abs. LBA1, ATLAS *Lancet* 2013;381:805, aTTom *JCO* 2013;31;18(supp 5)

Methods: Study of prognostic factors

- Data from 91 trials on each individual with ER+ disease allocated only 5 years of ET*
- Analyse just the 46,000 women (n=46K) who were still alive and disease-free at year 5

* ET was 3/4 Tam and 1/4 AI (or partly AI); analyses are only of T1 or T2 tumours (diameter ≤20 or 21-50 mm) with <10 nodes (N0-N9) & age <80 after 5 years ET

Endpoints

- Any breast cancer event (distant, local or contralateral), ignoring unrelated deaths
- Distant recurrence (as defined by each trial), ignoring local or contralateral events

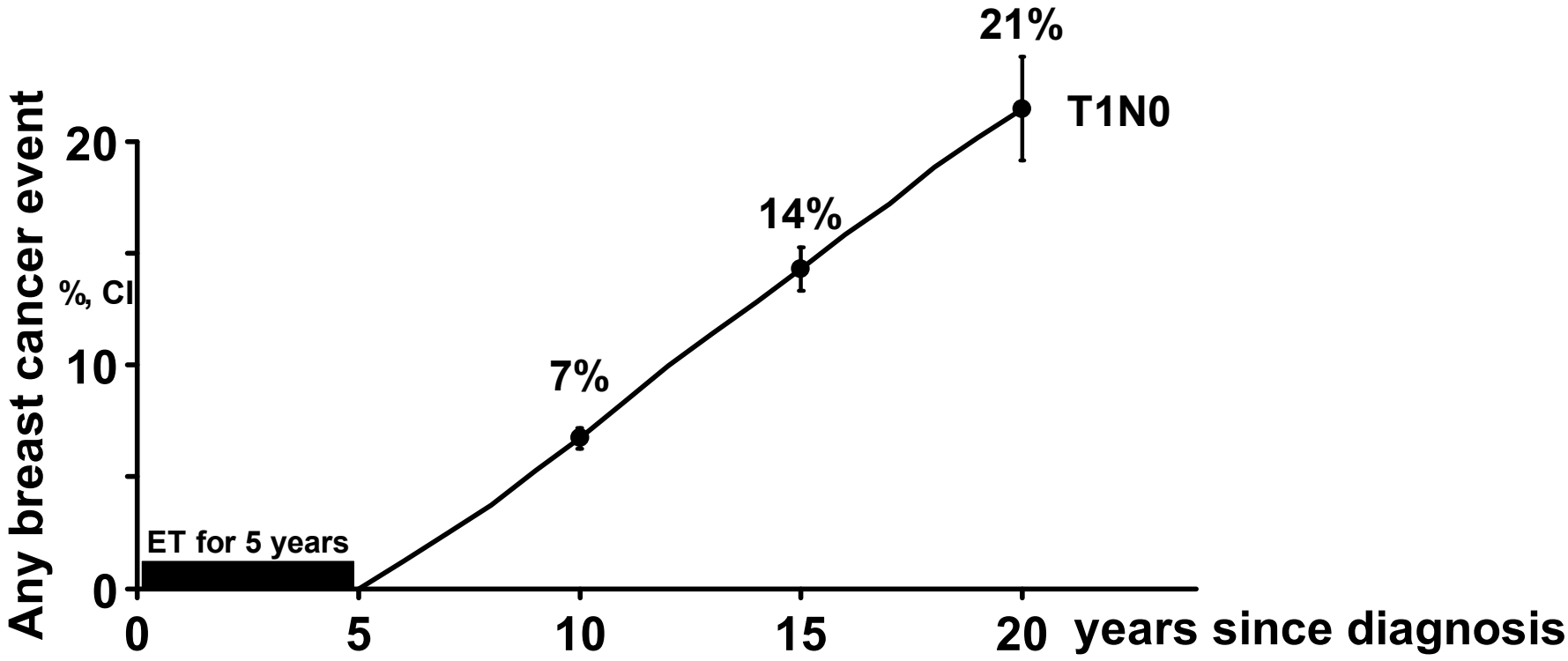
Analyses: Cox regressions (adjusted for T and N stage) and Kaplan-Meier graphs (% risk and 95% CI, with the distant recurrence rate in years 15-20 taken as the rate from years 10-20, ie, no. of events/person-years)

Main findings: Long-term risks

- Even after 5 years of ET, recurrences continue steadily, at least to year 20
- Absolute recurrence risk in years 5-20 is appreciable, even for T1N0 disease

Lowest-stage (T1N0) disease: Risk of ANY breast cancer event

21% risk, years 5-20 (14% DISTANT recurrence + 7% only local or contralateral)

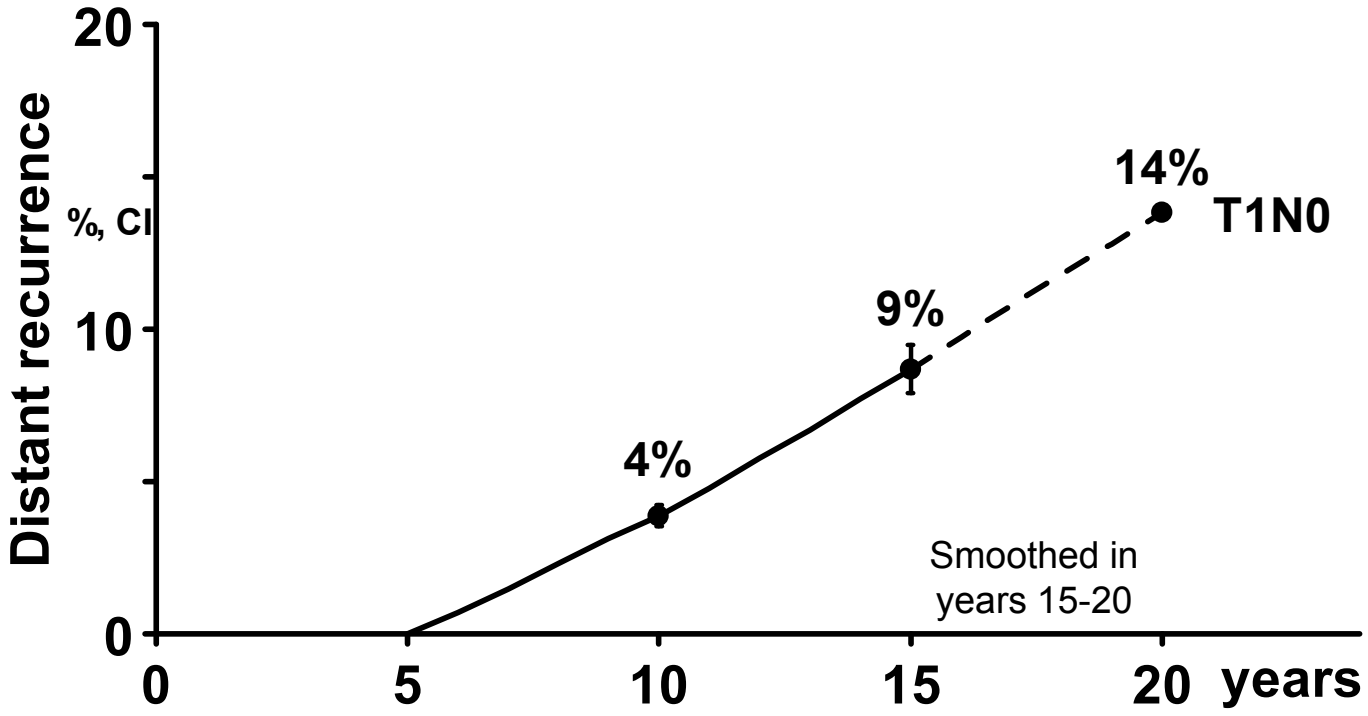


Annual event rate (and no. of events), by 5-year time period

T1N0 (n=16K): **1.4%** (807) **1.7%** (309) **1.8%** (54)

Lowest-stage (T1N0) disease: Risk of DISTANT recurrence

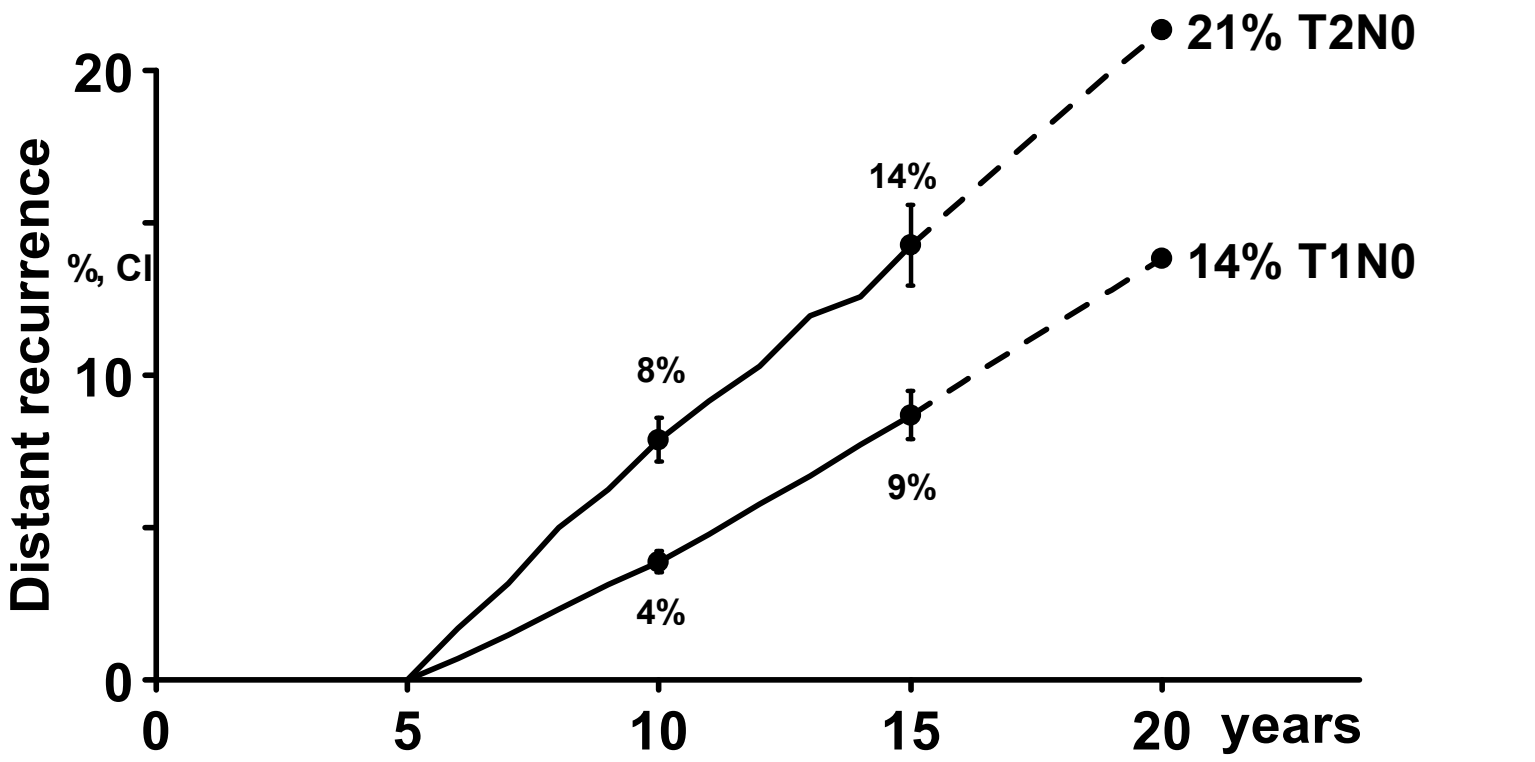
14% risk in years 5-20 (ie, about 1% per year)



Annual distant recurrence rate (and no. of events)

T1N0 (n=16K): **0.8%** (465) **1.0%** (191) **1.2%** (40)

Node-negative (N0) disease: Effect of tumour size



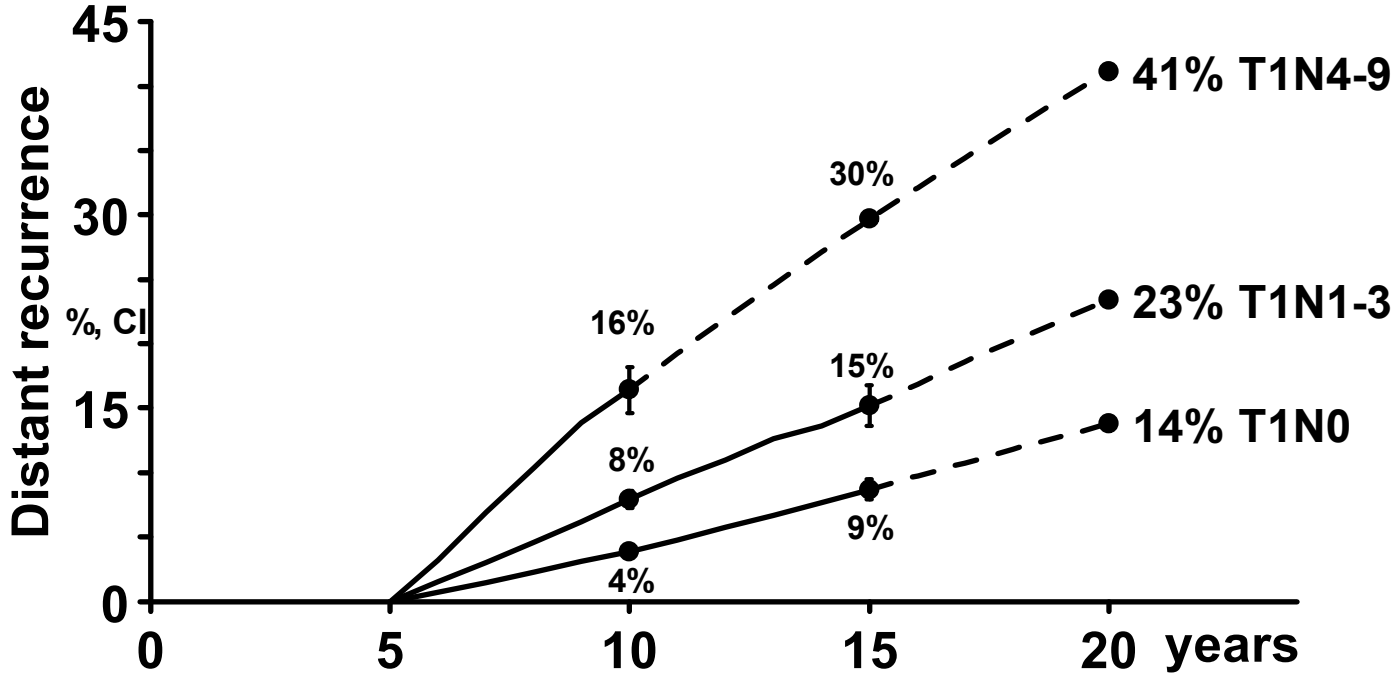
Annual distant recurrence rate (and no. of events)

T2N0 (n=8K): **1.7%** (451) **1.4%** (131) **1.7%** (29)

T1N0 (n=16K): **0.8%** (465) **1.0%** (191) **1.2%** (40)

Small tumours (T1 disease): Effect of nodal status

(Half got chemotherapy if N+, 1/6 if T1N0)

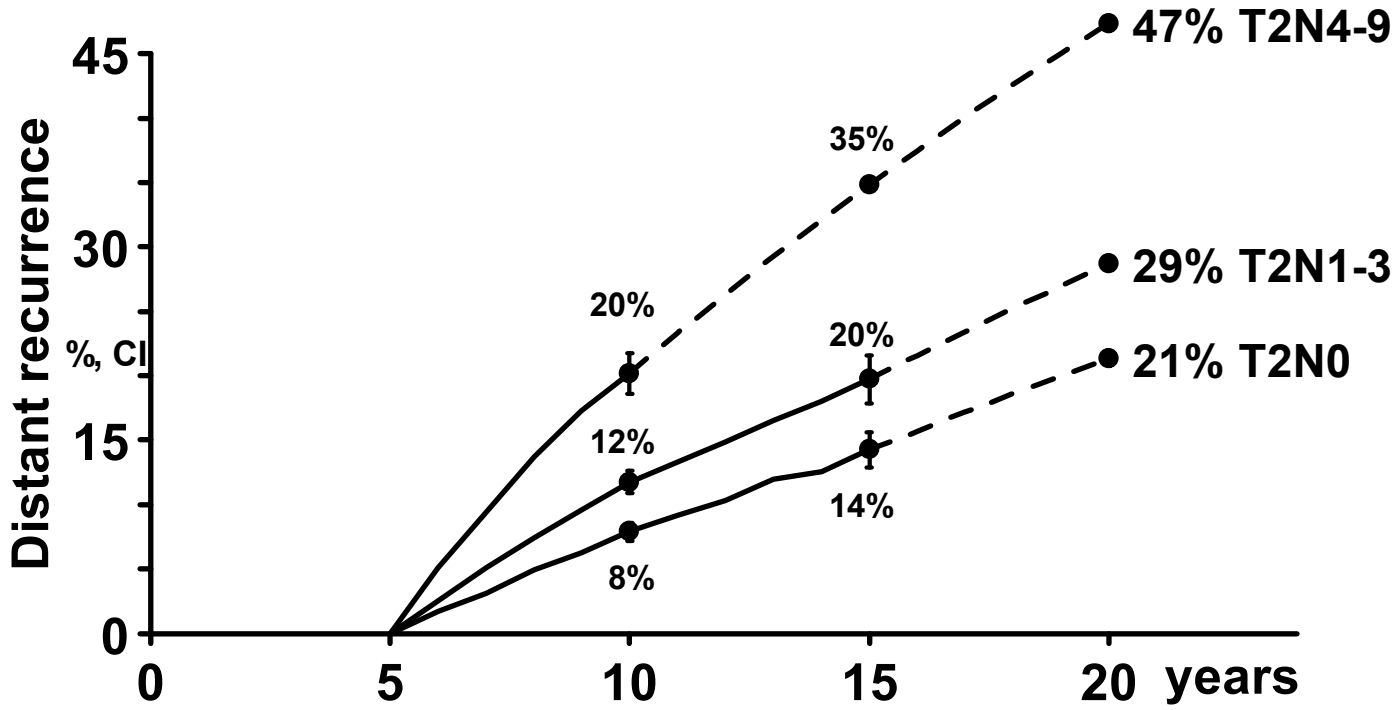


Annual distant recurrence rate (and no. of events)

T1N4-9 (n=2K):	**3.6%** (293)	**2.9%** (54)	**2.5%** (5)
T1N1-3 (n=9K):	**1.6%** (504)	**1.7%** (123)	**1.8%** (16)
T1N0 (n=16K):	**0.8%** (465)	**1.0%** (191)	**1.2%** (40)

Larger tumours (T2 disease): Effect of nodal status

(Half got chemotherapy if N+, 1/3 if T2N0)

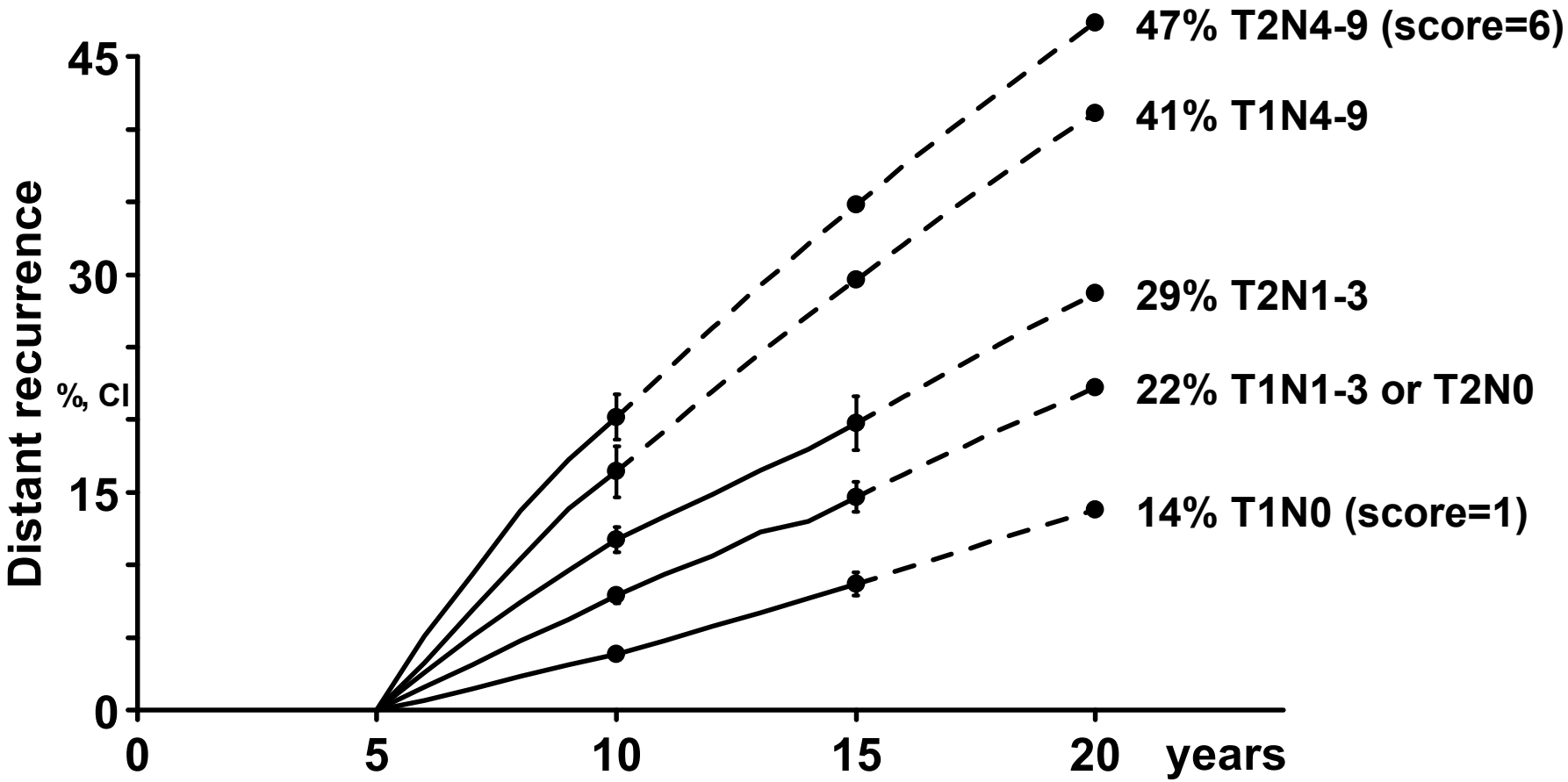


Annual distant recurrence rate (and no. of events)

T2N4-9 (n=3K):	**4.6%** (544)	**3.3%** (79)	**2.2%** (6)
T2N1-3 (n=8K):	**2.5%** (680)	**1.9%** (108)	**1.9%** (14)
T2N0 (n=8K):	**1.7%** (451)	**1.4%** (131)	**1.7%** (29)

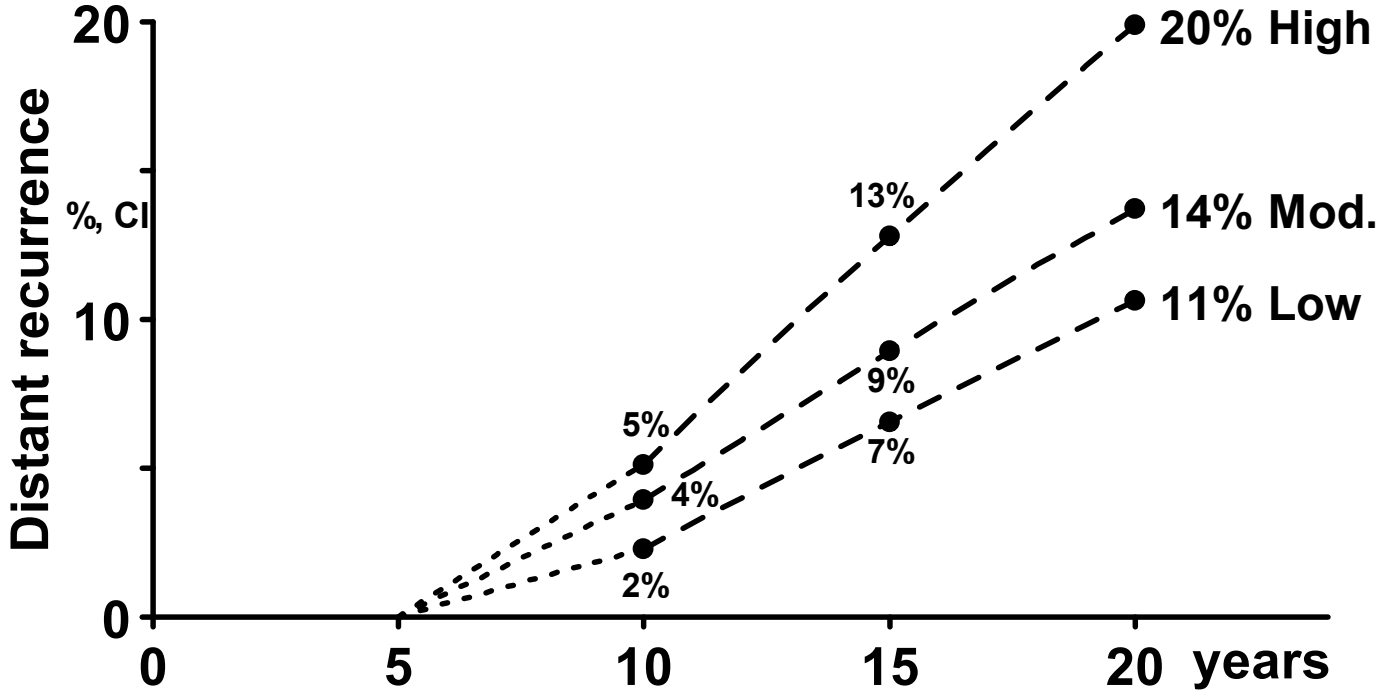
Effect of additive “T+N score” (range 1-6)

Score: 1/ 2 for T1/ T2, plus 0/ 1/ 4 for N0/ N1-3/ N4-9



Lowest-stage (T1N0) disease: Effect of tumour grade

Plot of smoothed rates for years 5-10, and for years 10-20

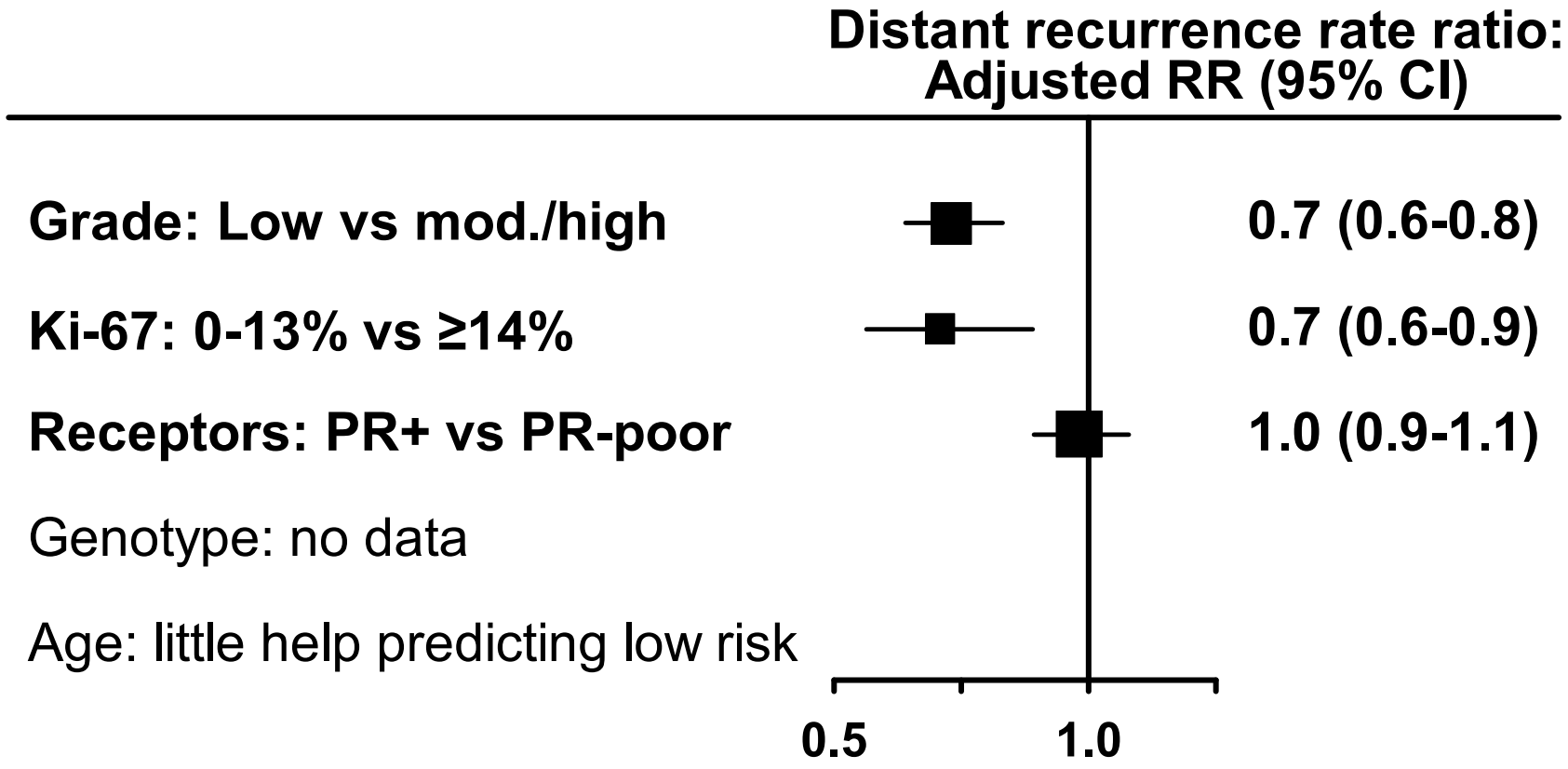


Annual distant recurrence rate (and no. of events)

High (n=2K):	**1.1%** (75)	**1.5%** (30)	**2.7%** (6)
Mod. (n=6K):	**0.8%** (168)	**1.0%** (57)	**1.1%** (6)
Low (n=3K):	**0.5%** (47)	**0.9%** (23)	**0.6%** (2)

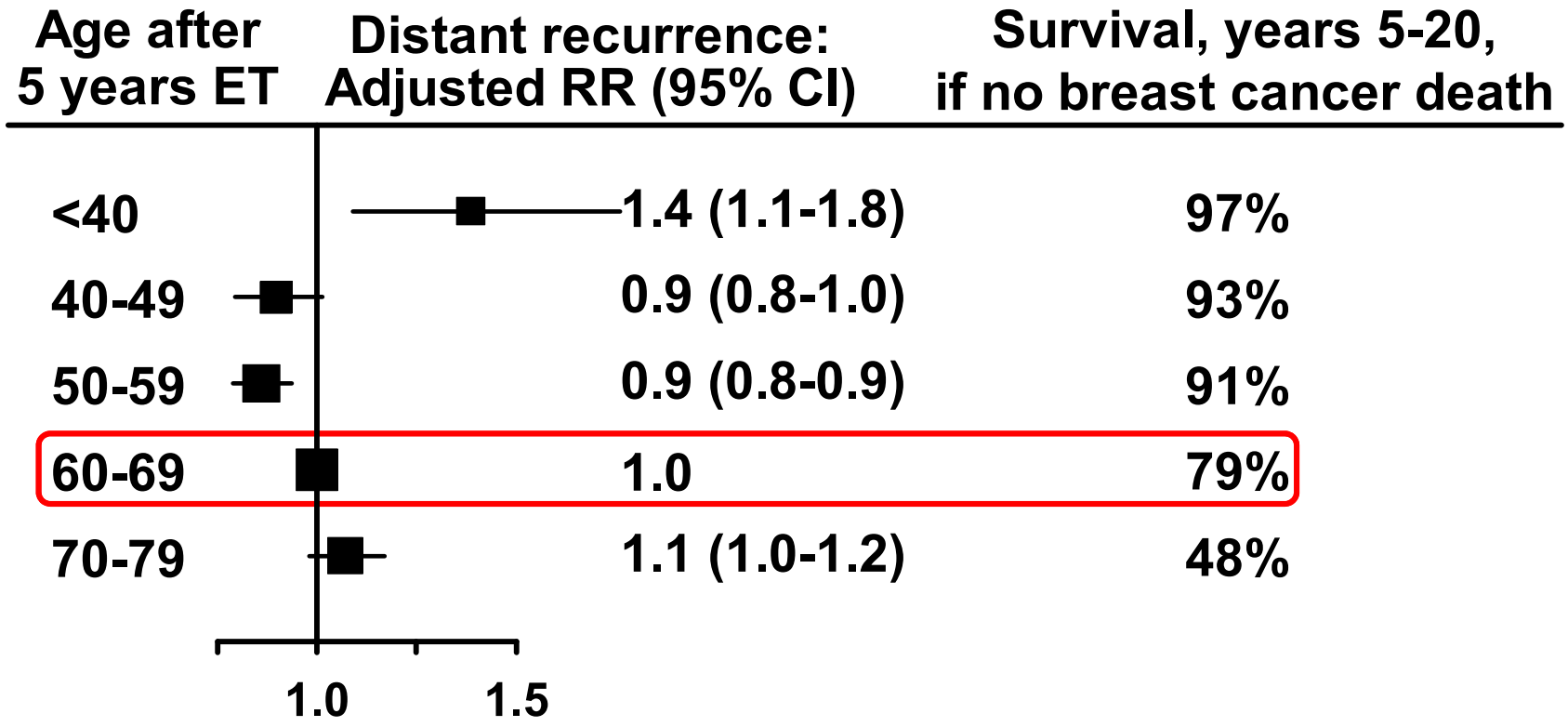
All women: Additional predictors of lower risk in years 5-20

Any (T1/2, N0-9) ER+ disease, adjusted for T and N status



By age: (1) Dist. recurrence; (2) Survival if no breast ca. death

Any (T1/2, N0-9) ER+ disease, adjusted for T and N status



Summary: Need 20-year perspective on ER+ disease

- About 80% would survive to beyond age 80 years, if there were no risk of death from breast cancer
- But, if endocrine therapy stops after only 5 years, then distant recurrences will continue steadily in years 5-20
- Without further ET, distant recurrence risk in years 5-20 is ~14% for T1N0, and much greater for T2N0 or N+ disease

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670 trialists who shared their data

60,000 women in 91 trials

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