Outcome of patients with an ultralow risk 70-gene signature in the MINDACT trial

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NETHERLANDS CANCER INSTITUTE
ANTONI VAN LEEUWENHOEK

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European Organisation for Research and Treatment of Cancer

The future of cancer therapy

MINDACT

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Increase in the incidence and survival of breast cancer

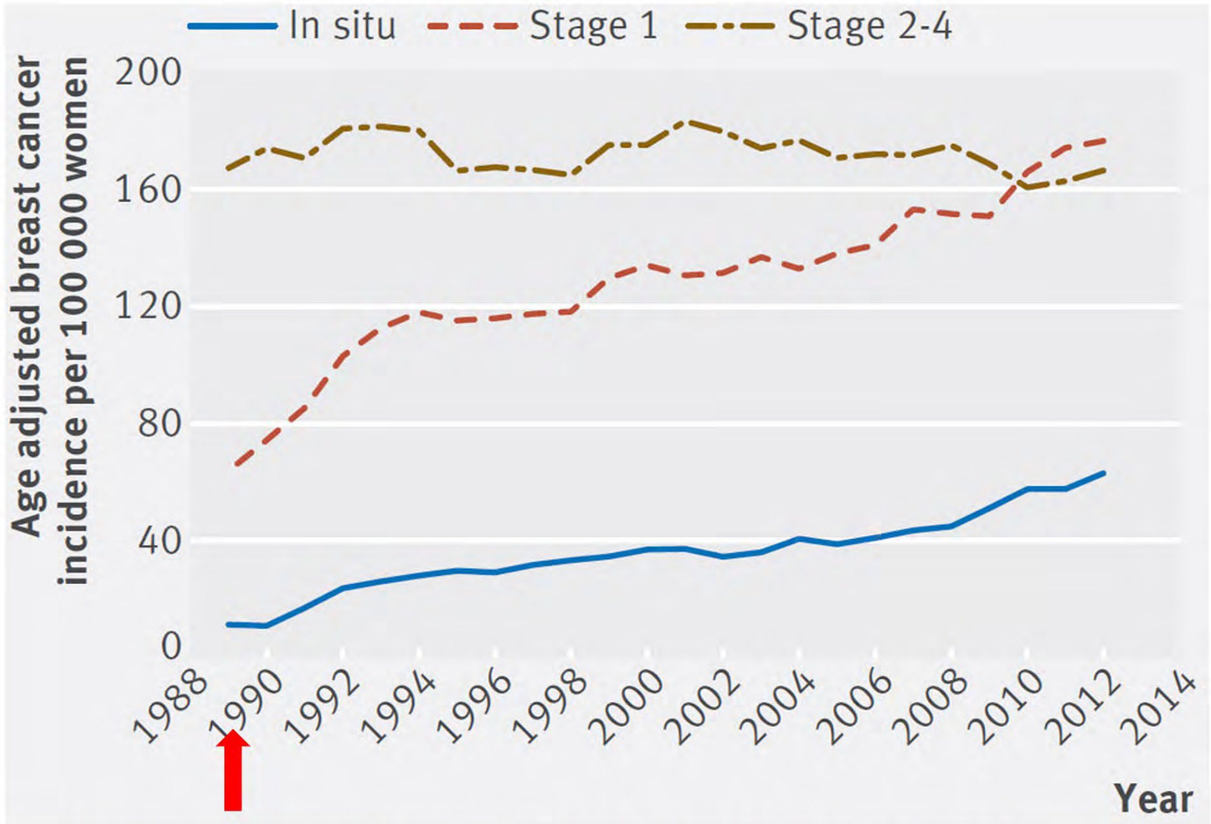

Figure: Trends in Breast Cancer Incidence by Stage in Women over 50 in the Netherlands, 1989-2012

Autier et al (2017).*BMJ*, *359*, j5224.

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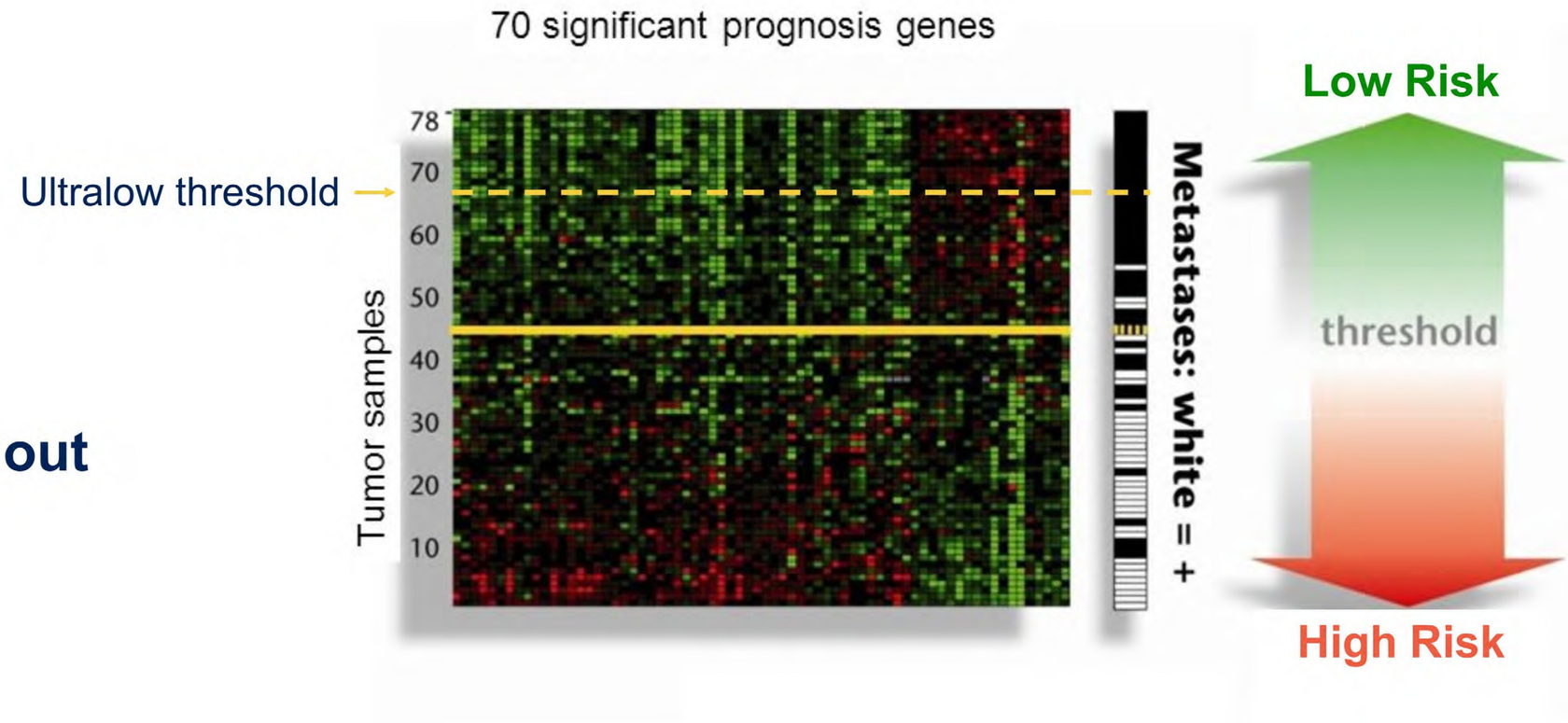
Gene signatures can identify patients at low risk of distant recurrence

- **70-gene signature**
- **Level 1 clinical utility**
- **Preserved outcome without chemotherapy**



Piccart (2021) Lancet Oncol.; 22:476–488.; van ’t Veer (2002) Nature, 415, pp. 530–6 ; Delahaye (2017) Breast Cancer Research and Treatment, 164 pp. 461–466.

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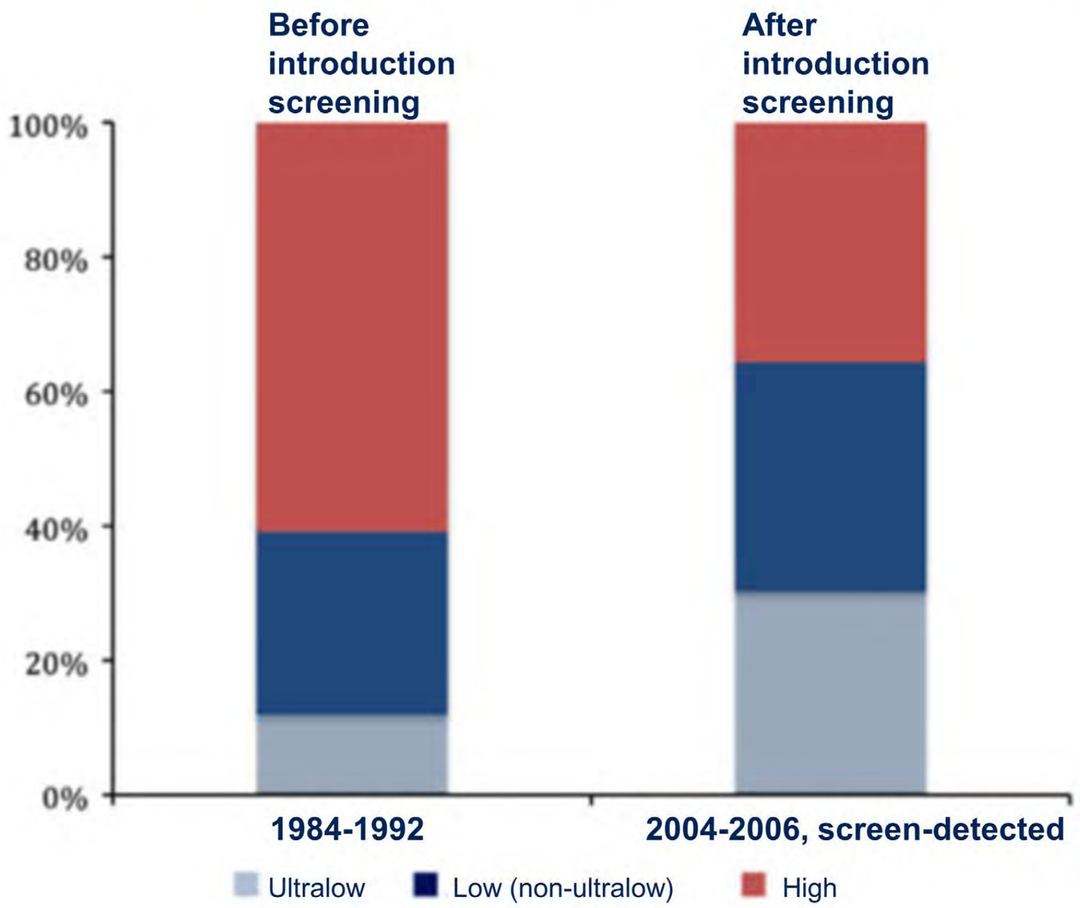
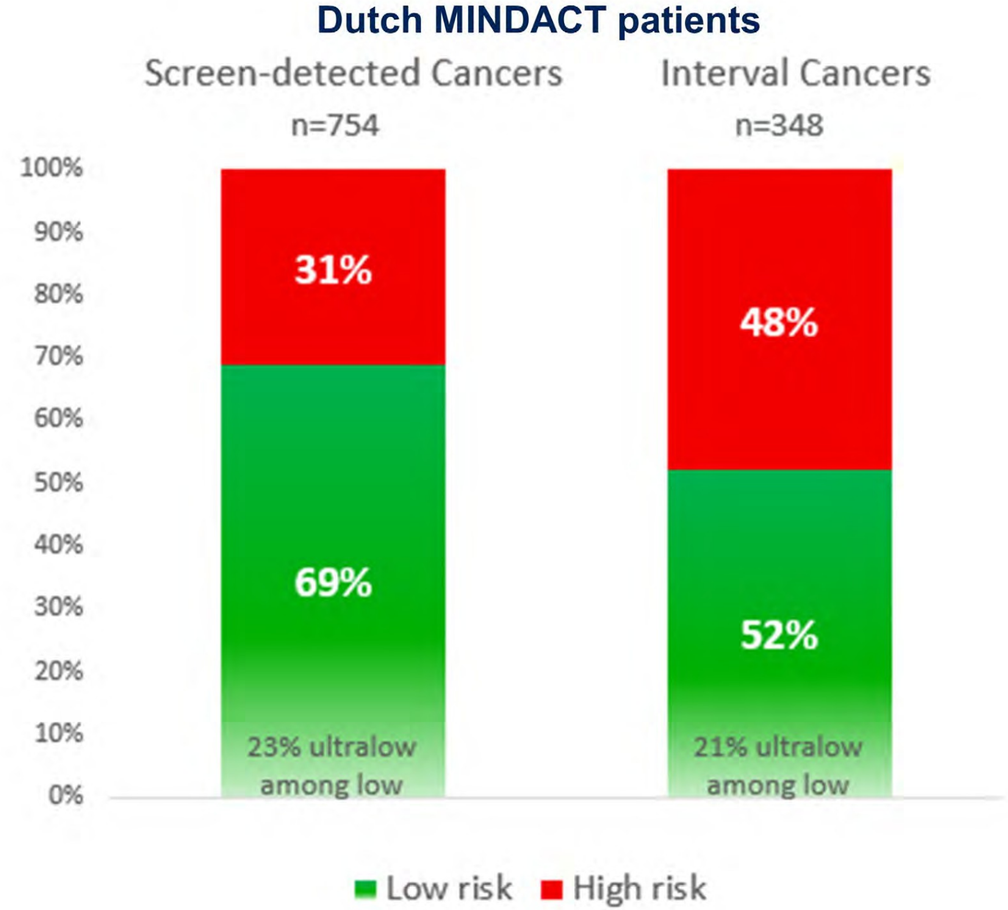
70-gene signature Low and Ultralow risk tumors overrepresented in screen-detected cancers





Esserman (2011).Breast Cancer Research and Treatment, 130, 725–734. ; Drukker (2014) Breast Cancer Research and Treatment, 144, 103–111.

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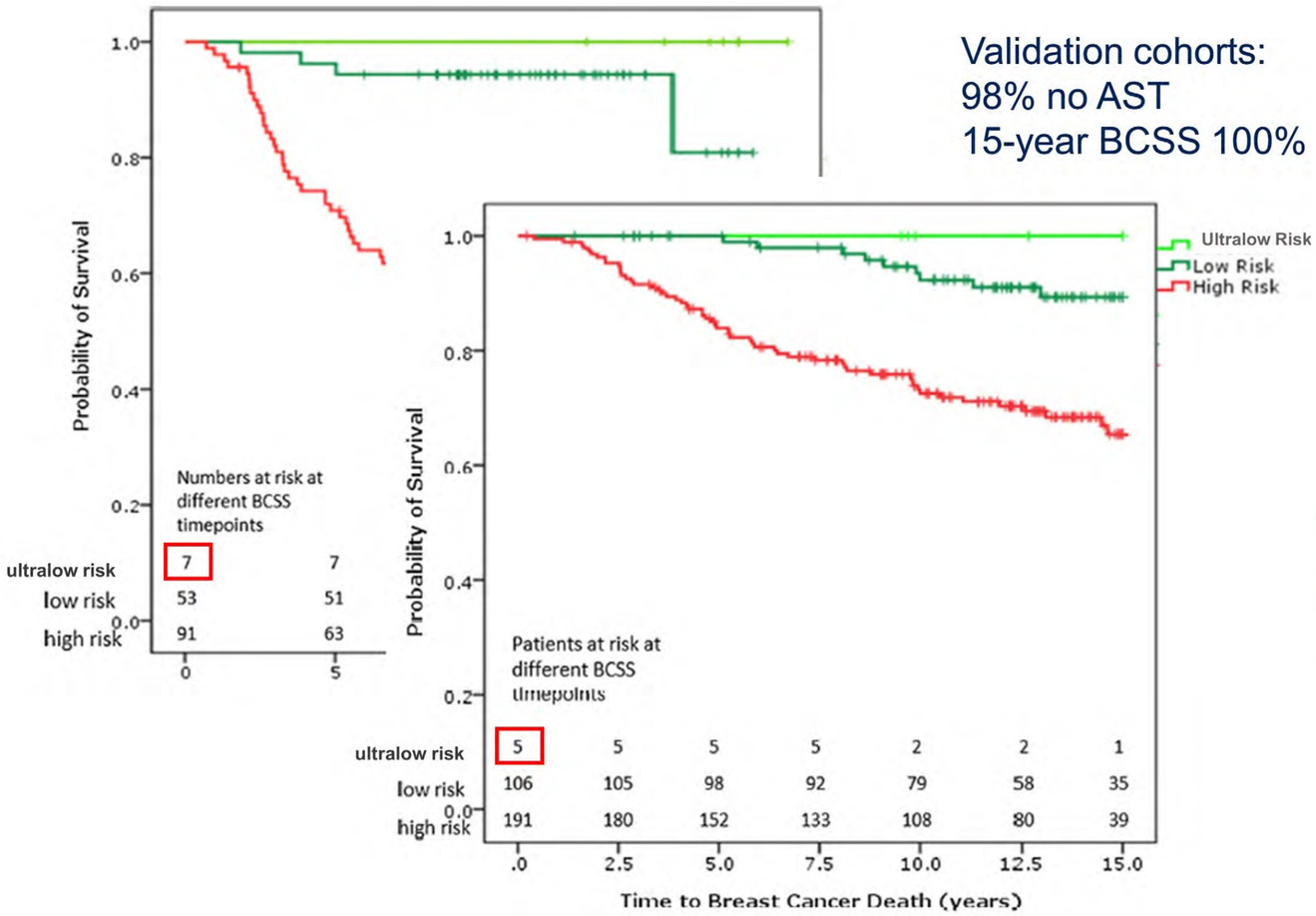
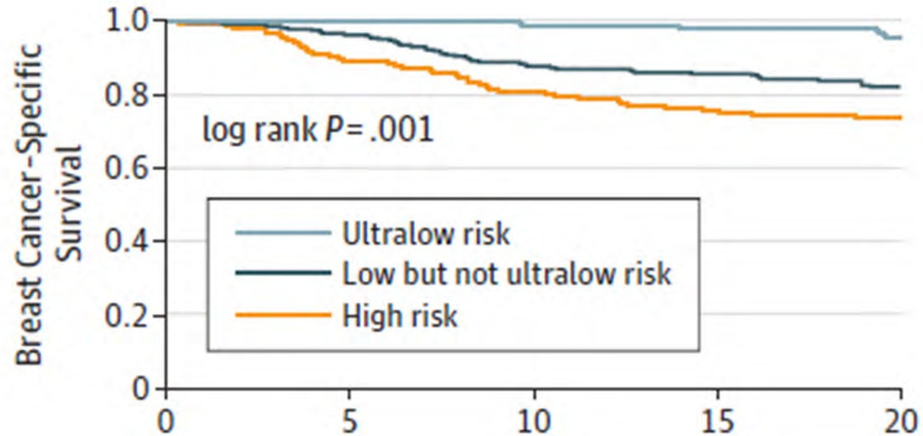
Ultralow risk patients have excellent survival in historic cohorts



Validation cohorts:
98% no AST
15-year BCSS 100%



No. at risk					
Ultralow risk	98	95	84	69	47
Low but not ultralow risk	279	253	208	169	116
High risk	275	227	183	150	121

STO-3, 1976-1990
LN0, <3cm, 339 received tamoxifen, 313 received no AST
20-year BCCS for ultralow risk patients:

- 97% for patients receiving tamoxifen
- 94% for patients receiving no AST

Delahaye (2017) Breast Cancer Research and Treatment, 164, pp. 461–466.; Esserman (2017) JAMA Oncology, 3, pp. 1503–1510.

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Assess survival outcome of MINDACT patients with an ultralow risk tumor biology

Can the identification of patients with an ultralow risk 70-gene signature help to avoid overtreatment in early-stage breast cancer?

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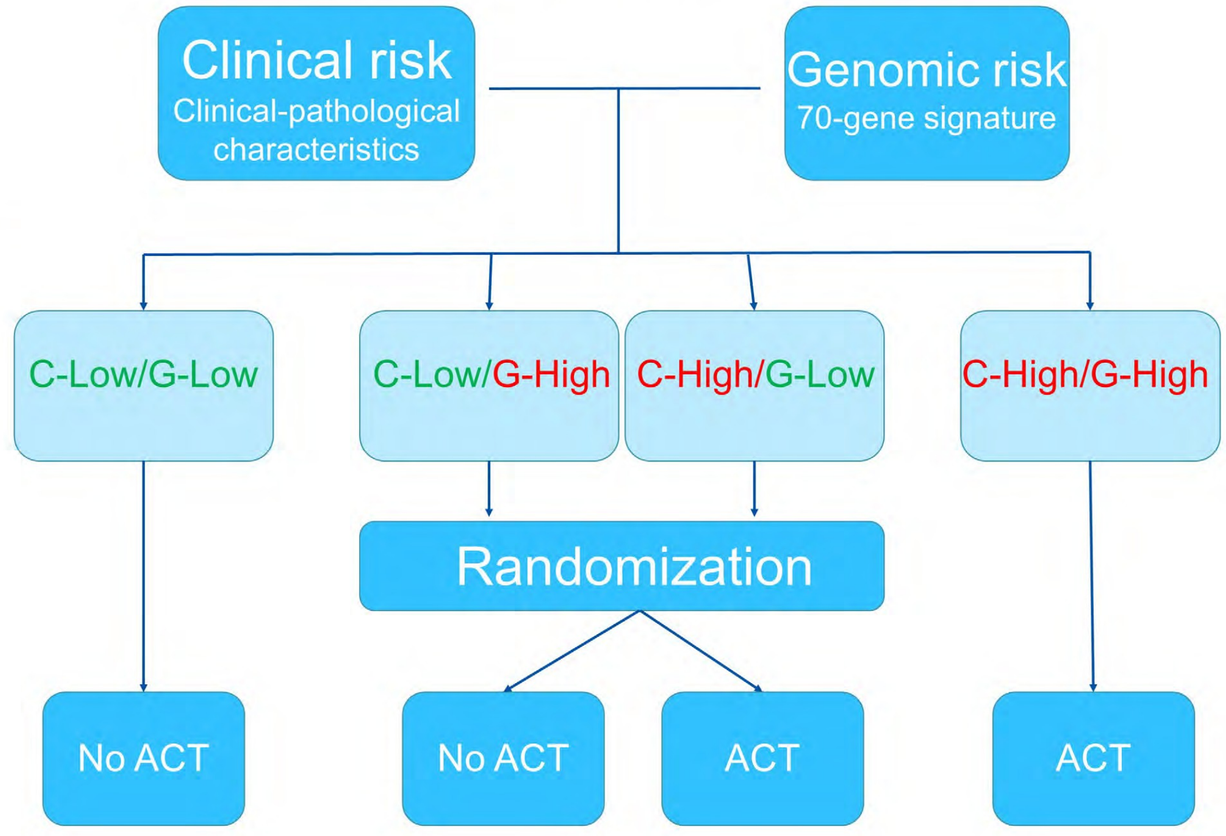
Inclusion criteria

- **Women aged 18-70**
- **Operable invasive breast cancer**
- **Tumor size max 5 cm**
- **0-3 positive lymph nodes**
- **No distant metastasis**

MINDACT trial design



Cardoso (2016) NEJM;375:717-729. ; Piccart (2021) Lancet Oncol. 2021; 22:476–488

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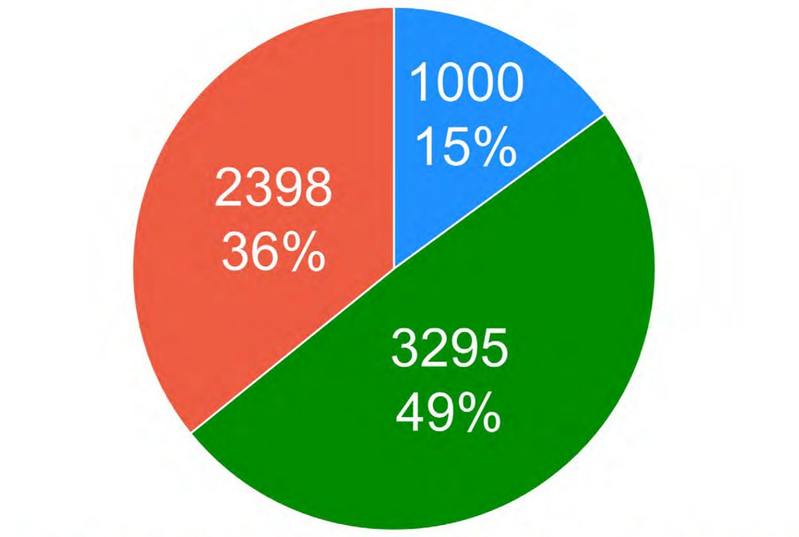
15% of MINDACT patients genomic ultralow risk

70-gene signature result



Total N=6693

- **HR+/HER2- subtype**
- ~95% of Low* and Ultralow risk patients
- 57% of High risk patients

- **Adjuvant systemic treatment**
- 76-85% endocrine therapy or no AST in Low and Ultralow risk
- 83% chemotherapy in High risk

*Low risk also referred to as Low not Ultralow

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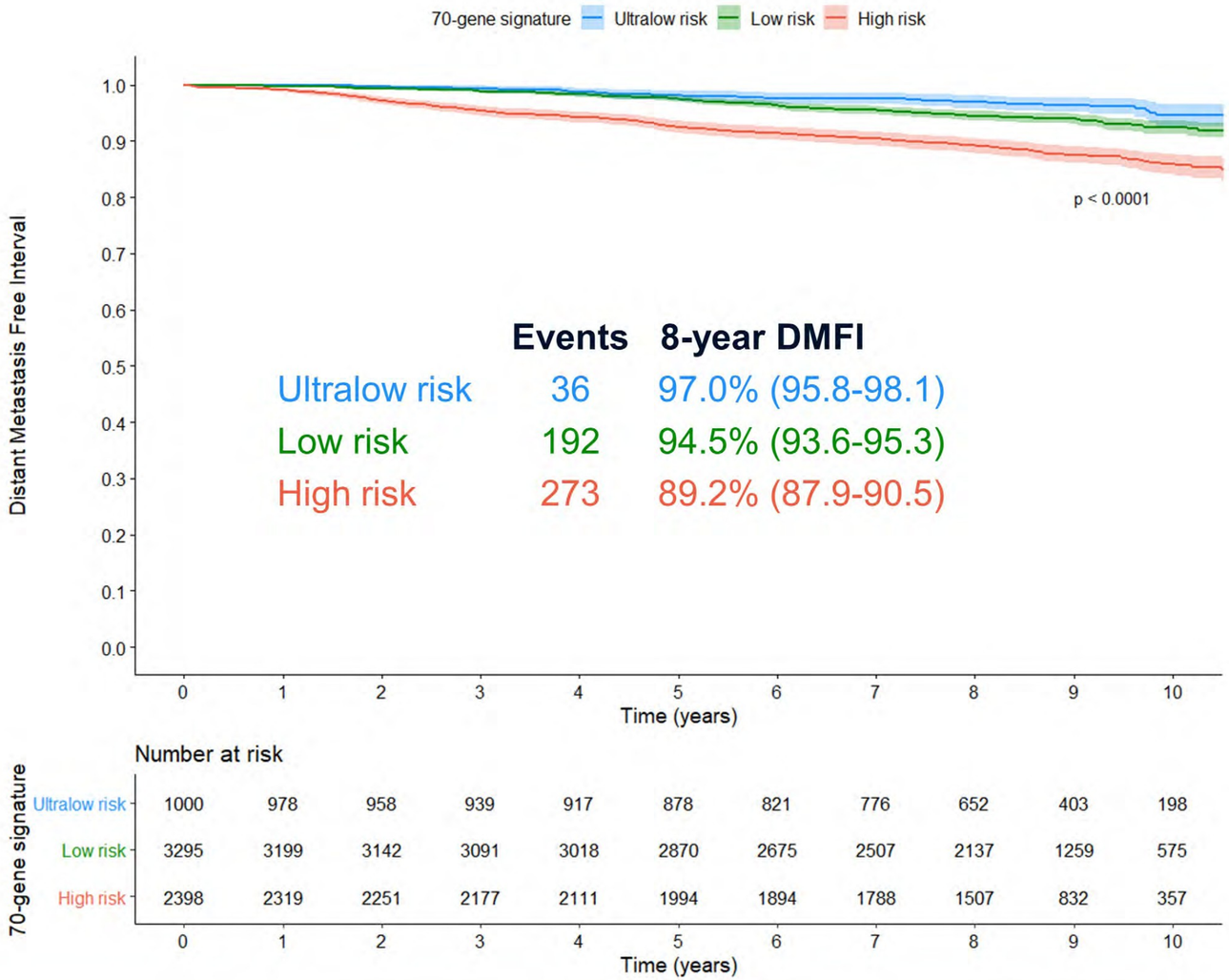
Excellent Distant Metastasis Free Interval rates for genomic Low and Ultralow risk patients



	Events	8-year DMFI
Ultralow risk	36	97.0% (95.8-98.1)
Low risk	192	94.5% (93.6-95.3)
High risk	273	89.2% (87.9-90.5)

Median follow-up: 8.7 years

Risk of distant metastasis or BC-death	
	Adj* HR (95% CI)
Ultralow risk vs low risk	0.65 (0.45-0.94)
High risk vs low risk	2.17 (1.68-2.80)

*Adjusted for clinical-pathological and treatment characteristics

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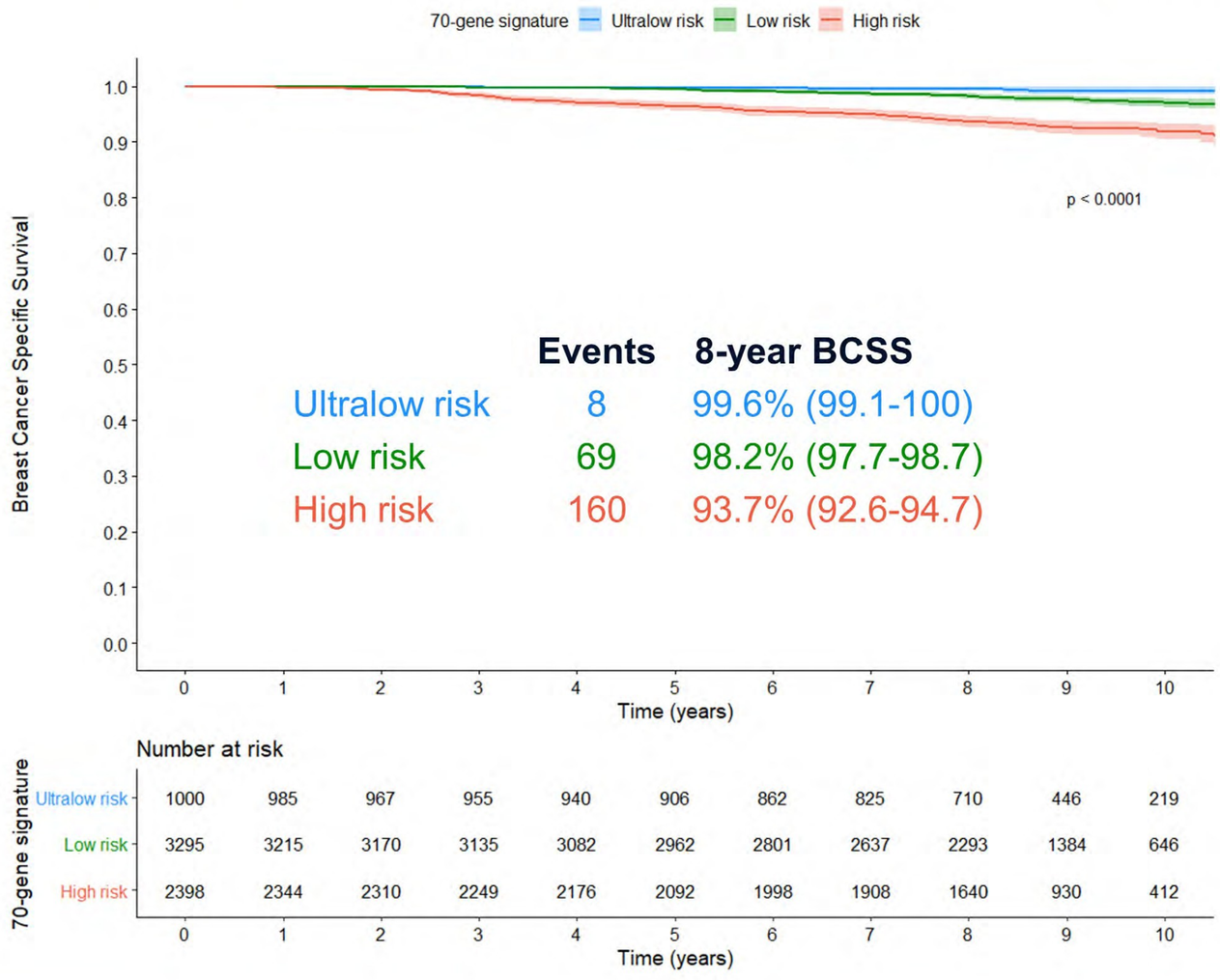
Excellent Breast Cancer Specific Survival rates for genomic Low and Ultralow risk patients



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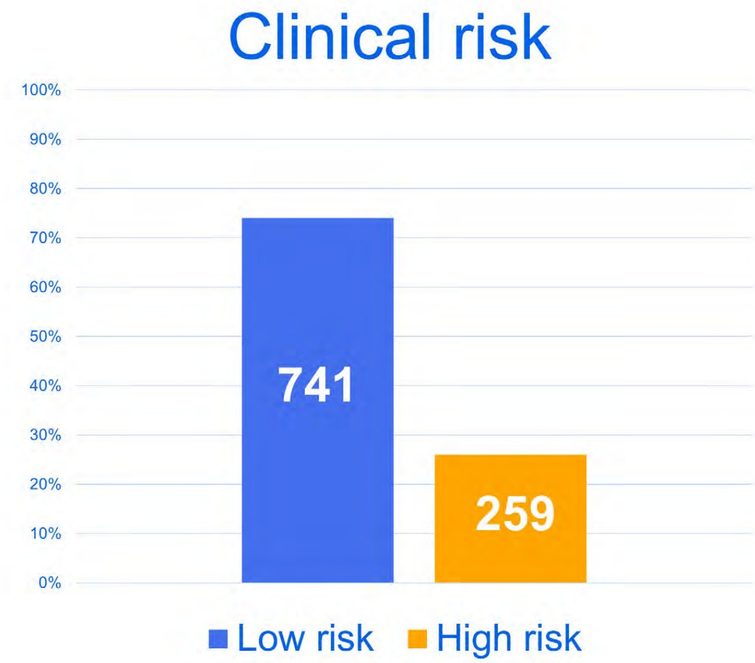
Characteristics 1000 genomic Ultralow risk patients

- 67% >50 years
- 80% lymph node negative
- 81% tumors ≤2 cm
- 96% Grade 1 or 2
- 97% HR+/HER2- subtype

- 16% no adjuvant systemic treatment
- 69% endocrine therapy
- 14% chemotherapy



Clinical High risk tumors
- Larger size
- Higher grade
- Lymph node positive

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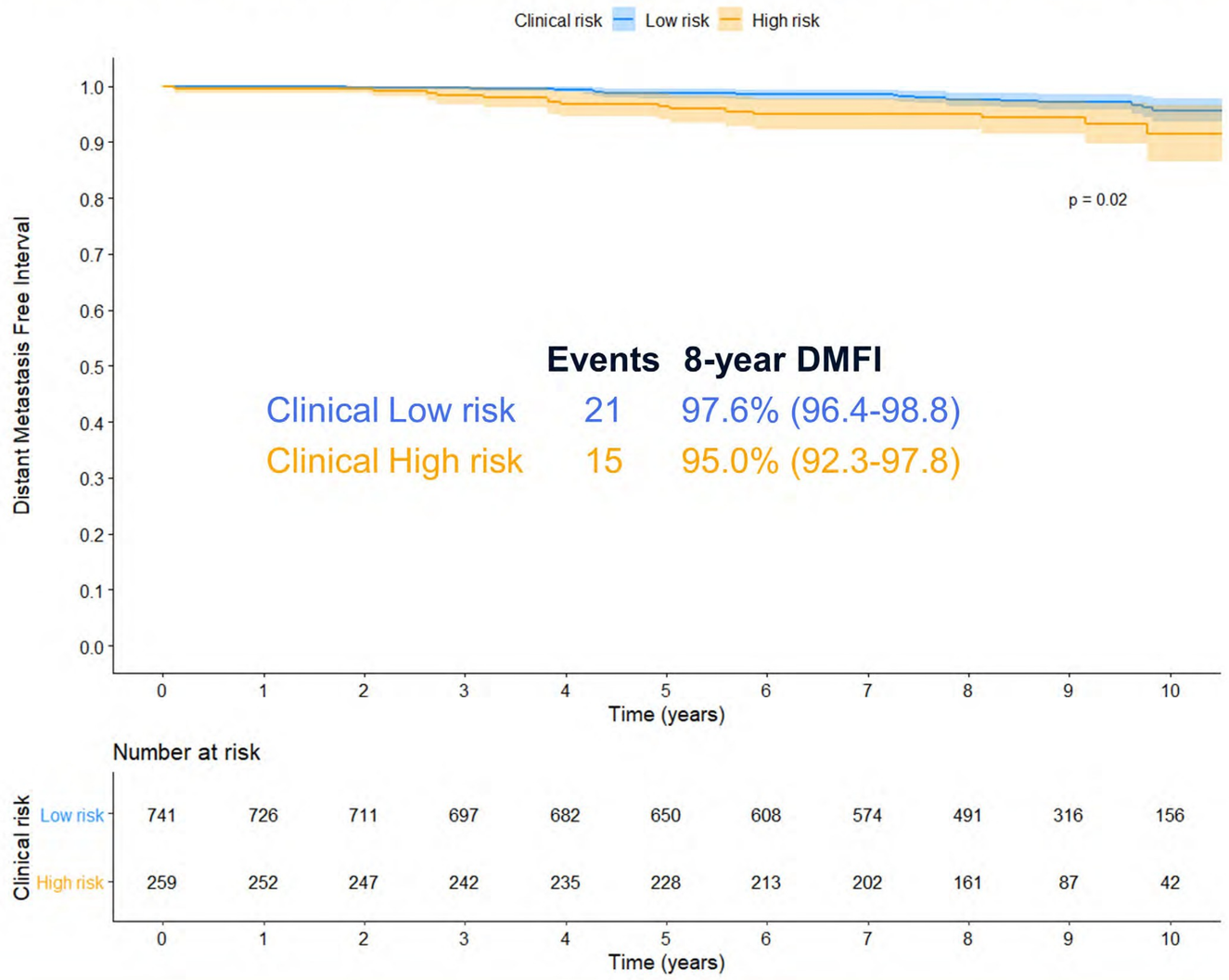
Small difference in Distant Metastasis Free Interval in genomic Ultralow risk patients by Clinical risk



	Events	8-year DMFI
Clinical Low risk	21	97.6% (96.4-98.8)
Clinical High risk	15	95.0% (92.3-97.8)

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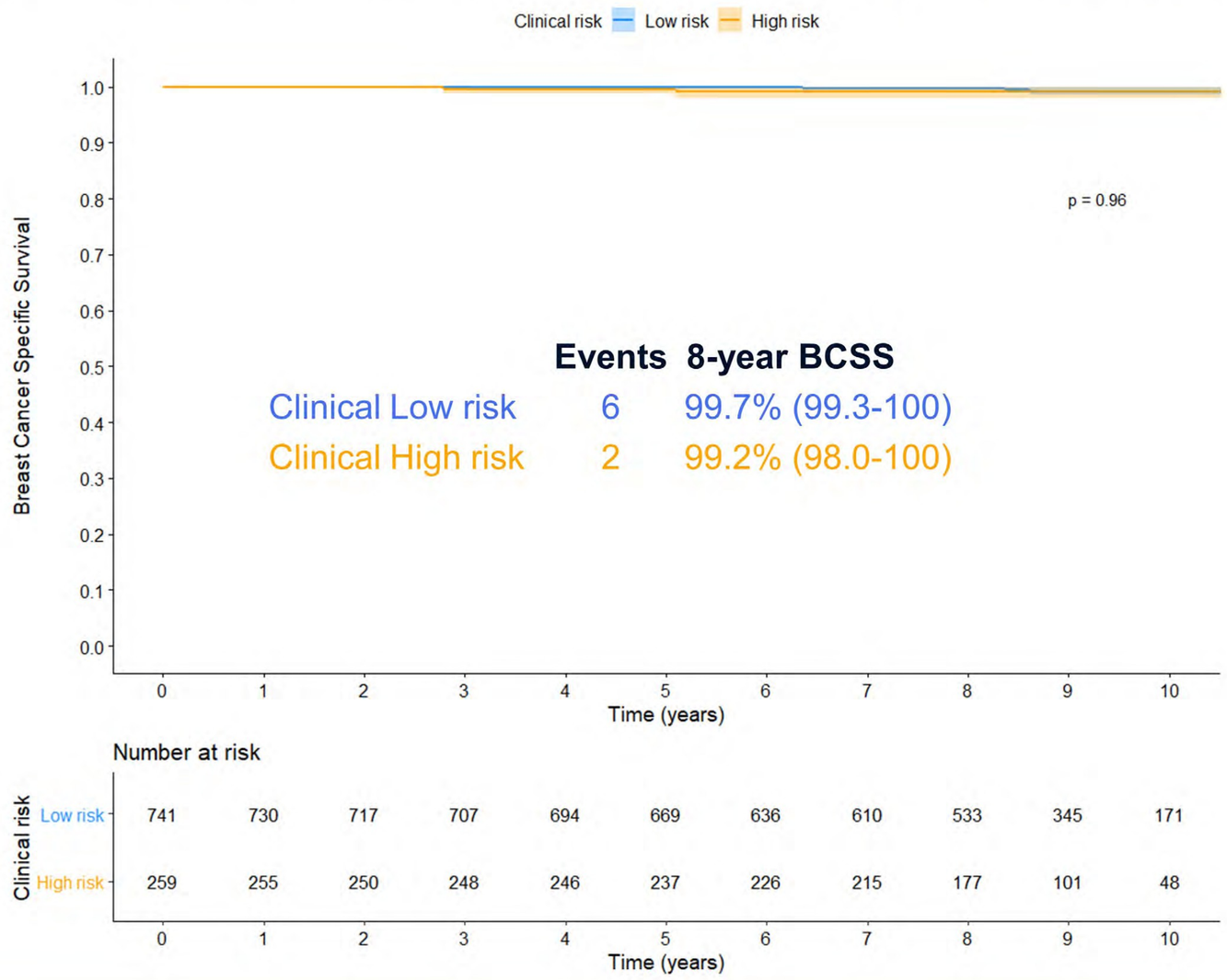
No difference in Breast Cancer Specific Survival in genomic Ultralow risk patients by Clinical risk



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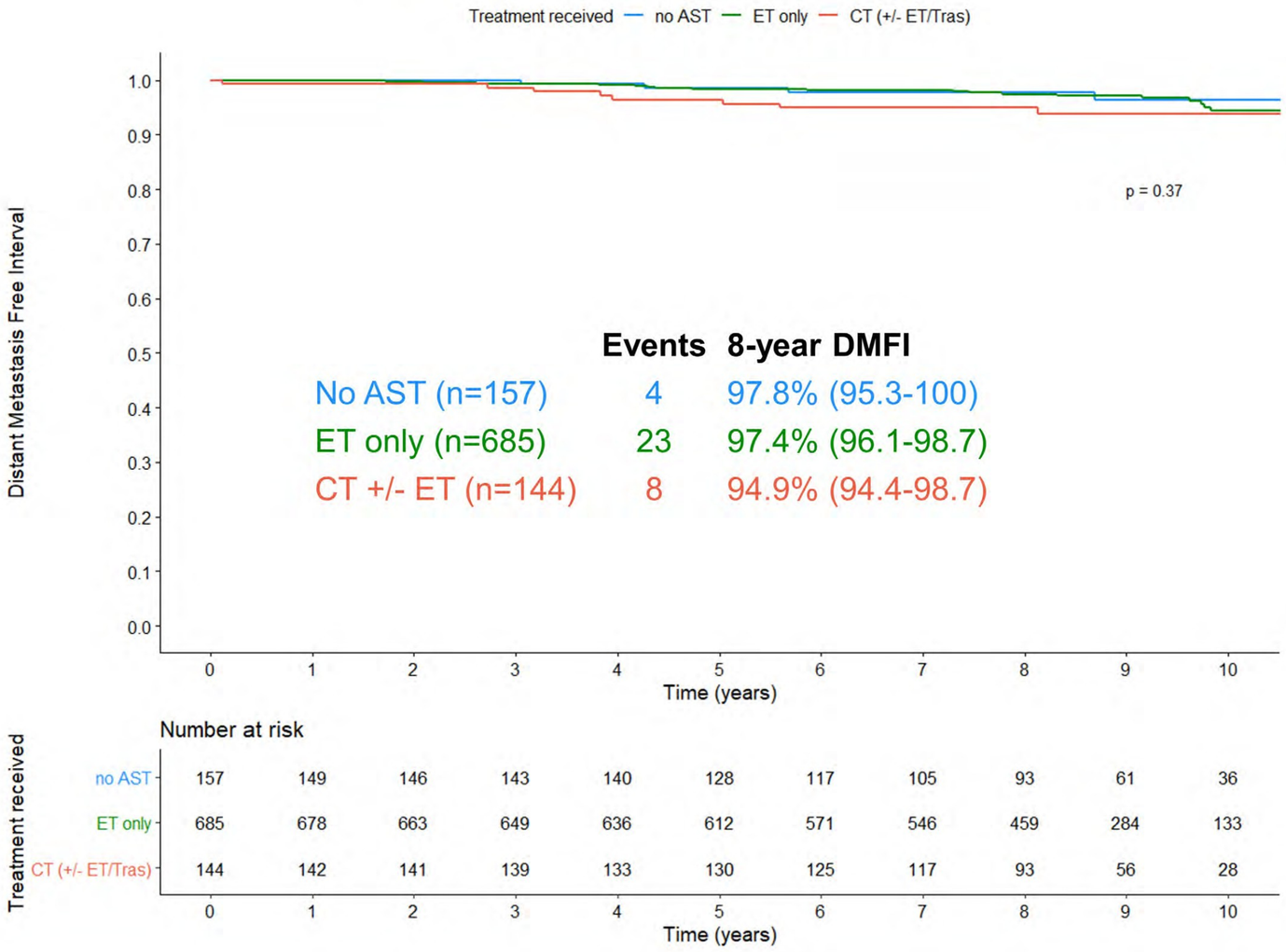
Excellent outcomes for genomic Ultralow risk patients receiving only endocrine therapy or no adjuvant systemic treatment



Risk of distant metastasis or BC-death (Ultralow risk patients only)	
	Adj* HR (95% CI)
CT vs no CT	0.98 (0.37-2.61)
ET vs no ET	0.59 (0.27-2.13)

*Adjusted for clinical-pathological characteristics

Note: 92% of patients receiving chemotherapy were Clinical High risk

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Conclusions

- 70-gene signature ultralow risk patients have excellent 8-year DMFI and BCSS
- Very few patients developed distant metastases
- Excellent DMFI rates for patients who received only endocrine therapy or no adjuvant systemic treatment
- Confirmation of previously published results in the largest cohort of ultralow risk patients to date

Delahaye (2017) Breast Cancer Research and Treatment, 164, pp. 461–466.; Esserman (2017) JAMA Oncology, 3, pp. 1503–1510. ; Pan (2017) NEJM; 377:1836–1846.

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Clinical implications

- The 70-gene signature MammaPrint can identify patients with an ultralow risk of distant recurrence

- Patients with ultralow risk tumors could be candidates for further de-escalation of treatment, further reducing overtreatment and the risk of side-effects

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Acknowledgements

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- All patients who participated in the MINDACT trial

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Questions?

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