

PSI – tilpasset adjuverende behandling

Validering af den kliniske anvendelse af PSI-værktøjet til risiko-tilpasset behandlingsallokering



Outcomes based on risk-adapted adjuvant therapy in postmenopausal women with early breast cancer: a nationwide, prospective cohort study by the Danish Breast Cancer Group

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Summary

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Background Clinical prediction models are increasingly used to guide treatment in patients with early breast cancer. The Danish Breast Cancer Group (DBCG) has developed a prognostic standard mortality rate index (PSI) for prediction of excess mortality based on 5 years of endocrine therapy. In this study, we aimed to evaluate the clinical utility of the PSI.

Aug **2013-2018**; 25 027 women with breast cancer registered in DBCG

8921 eligible with PSI calculated based on

Ejlertsen B, Jensen MB, Mouridsen HT; Danish Breast Cancer Cooperative Group.

Excess mortality in postmenopausal high-risk women who only receive adjuvant endocrine therapy for estrogen receptor positive breast cancer.

Acta Oncol. 2014

Including: Age at surgery, nodal status, tumor size, histological type, grade, ER expression levels, lymphovascular invasion, and loco-regional therapy

6704 (75%) with **PSI 1** recommended endocrine therapy

1300 (15%) with **PSI 2** recommended chemotherapy plus endocrine therapy

745 (8%) with **PSI 3**

172 (2%) with **PSI 4**

April 2017 PAM50 PSI 2; 357 with PAM50 excluded

Baseline characteristics

	PSI 1	PSI 2	PSI 3	PSI 4
Age				
50–59	796 (12%)	667 (51%)	488 (66%)	145 (84%)
60–69	2813 (42%)	498 (38%)	238 (32%)	26 (15%)
70–79	2201 (33%)	121 (9%)	19 (3%)	1 (1%)
80–95	894 (13%)	14 (1%)	0	0
Med 67	69	59	57	54
# Positive lymph nodes				
0	5103 (76%)	749 (58%)	309 (41%)	36 (21%)
1	1223 (18%)	377 (29%)	254 (34%)	63 (37%)
2	287 (4%)	124 (10%)	120 (16%)	43 (25%)
3	91 (1%)	50 (4%)	62 (8%)	30 (17%)
Tumour size				
0–10 mm	1382 (21%)	213 (16%)	28 (4%)	1 (1%)
11–20 mm	3826 (57%)	652 (50%)	292 (39%)	39 (23%)
21–50 mm	1447 (22%)	404 (31%)	388 (52%)	110 (64%)
>50 mm	49 (1%)	31 (2%)	37 (5%)	22 (13%)

	PSI 1	PSI 2	PSI 3	PSI 4
Malignancy grade				
I	2117 (34%)	207 (16%)	57 (8%)	5 (3%)
II	3642 (59%)	791 (63%)	444 (60%)	65 (38%)
III	452 (7%)	257 (20%)	239 (32%)	101 (59%)
CCI				
0	4051 (60%)	847 (65%)	524 (70%)	125 (73%)
1	1206 (18%)	199 (15%)	98 (13%)	24 (14%)
2	642 (10%)	97 (7%)	57 (8%)	9 (5%)
≥3	805 (12%)	157 (12%)	66 (9%)	14 (8%)

Adjuvant systemic treatment

	PSI 1	PSI 2	PSI 3	PSI 4
Adjuvant therapy				
Completed	4358 (65%)	632 (49%)	426 (57%)	107 (62%)
Not completed	2346 (35%)	668 (51%)	319 (43%)	65 (38%)
Chemotherapy				
Completed	17 (<1%)	854 (66%)	618 (83%)	146 (85%)
Not completed	6687 (100%)	446 (34%)	127 (17%)	26 (15%)
Not initiated	6686 (100%)	400 (31%)	109 (15%)	20 (12%)
< 4 cycles	1	37 (3%)	13 (2%)	4 (2%)
Unknown	0	9 (1%)	5 (1%)	2 (1%)
Endocrine therapy				
Completed	4358 (65%)	905 (70%)	500 (67%)	120 (70%)
AI	4077 (61%)	804 (62%)	405 (54%)	91 (53%)
AI → TAM	198 (3%)	58 (4%)	46 (6%)	11 (6%)
Tamoxifen	61 (1%)	23 (2%)	26 (3%)	5 (3%)
TAM → AI	22 (<1%)	20 (2%)	23 (3%)	13 (8%)
Not completed	2346 (35%)	395 (30%)	245 (33%)	52 (30%)
1·0–4·5 years [‡]	1343 (20%)	268 (21%)	164 (22%)	38 (22%)
<1 year [‡]	674 (10%)	78 (6%)	58 (8%)	8 (5%)
Not initiated	254 (4%)	40 (3%)	17 (2%)	5 (3%)
Unknown	75 (1%)	9 (1%)	6 (1%)	1 (1%)

Adherence rate for endocrine treatment in the PSI 1 group was
85.5% (95% CI 84.7–86.4) after 1 year
67.8% (95% CI 66.6–69.0) after 4.5 years.

Adherence in the PSI 2-4 group was
90.3% (95% CI 89.1–91.5) after 1 year
72.3% (95% CI 70.5–74.3) after 4.5 years

Patients who completed therapy were younger.

Crude standard mortality ratio

0.89 (95% CI 0.85–0.95) for PSI 1*

1.71 (95% CI 1.47–1.97) for PSI 2

2.39 (95% CI 1.99–2.88) for PSI 3–4

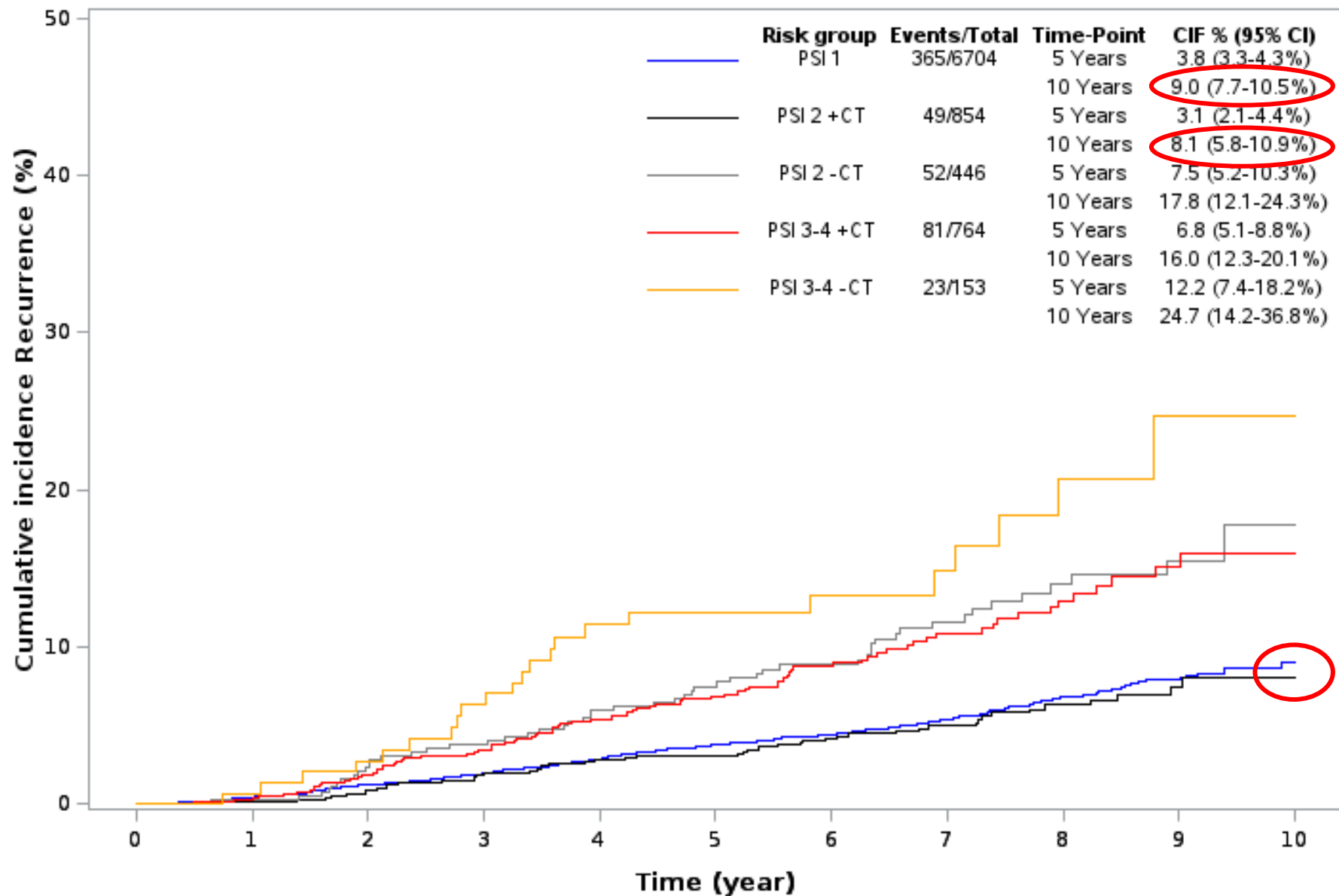
The cumulative incidence of recurrence at 5 years and 10 years

3.8% (95% CI 3.3–4.3) and **9.0% (95% CI 7.7–10.5)** for PSI 1

4.5% (95% CI 3.5–4.8) and **11.4% (95% CI 8.8–14.3)** for PSI 2

7.7% (95% CI 6.0–9.6) and **17.3% (95% CI 13.8–21.2)** for PSI 3–4

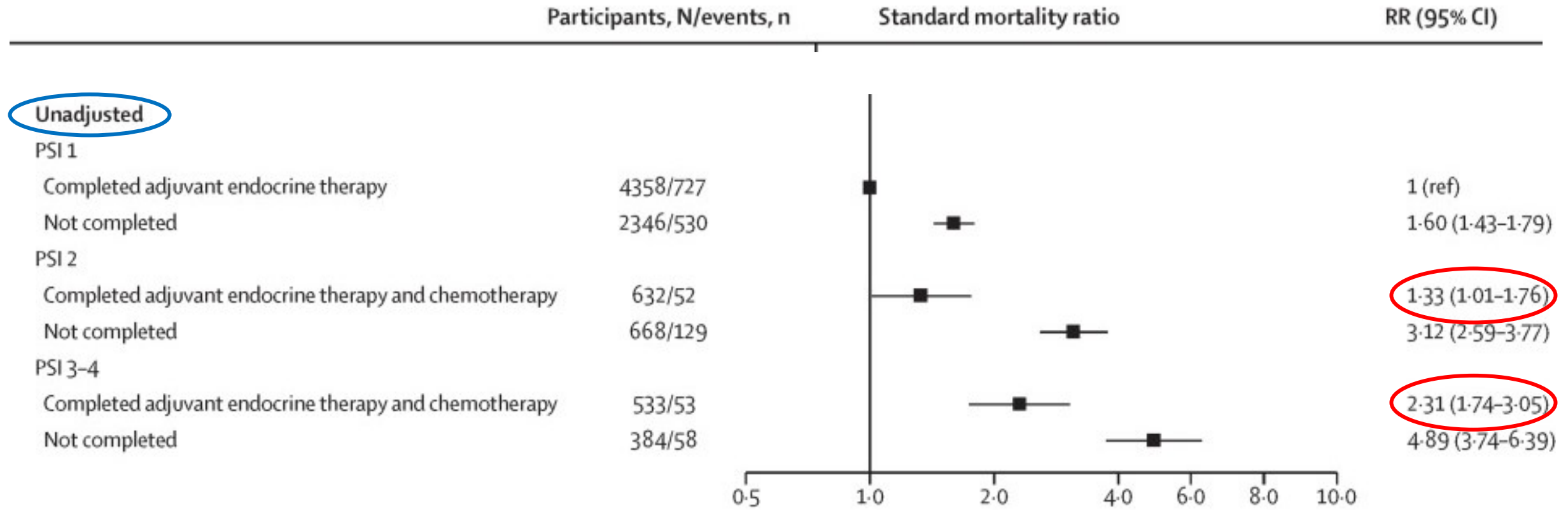
*Excl pt's with prev. malignancy, median age 69 (max 95), loc trt



	Patients-at-Risk										
	0	1	2	3	4	5	6	7	8	9	10
PSI 1	6704	6108	5412	3426	1552	103					
PSI 2 +CT	854	832	779	636	316	19					
PSI 2 -CT	446	394	343	257	120	9					
PSI 3-4 +CT	764	725	653	429	188	12					
PSI 3-4 -CT	153	132	104	65	26	1					

Estimates for assigned PSI and completed adjuvant treatment as a time-dependent factor using patients assigned PSI 1 and completed treatment as reference

RR estimates for standard mortality ratio



Konklusion

Hos patienter allokeret til PSI 1 er udeladelse af kemoterapi ikke forbundet med øget mortalitet samlet set, og et tydeligt bedre udfald blev observeret for patienter med gennemført endokrin terapi.

Blandt patienter allokeret til PSI 1 er

N=1601 (24%) N1 og

N=3220 (48%) N0 & (>20 mm eller høj grad)

Konklusion

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Ved gennemført adjuverende behandling var overdødelighed høj for patienter allokeret til PSI 3-4, hvilket potentielt taler for intensiveret behandling:

3EC → 3TAX ↑↑ 4EC & 4TAX

CDK4/6i

MU arbejder på opdatering af retningslinjer.

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For patienter allokeret til PSI 2 sås en betydelig overdødelighed samlet set, dog mere moderat for patienter med gennemført behandling

SMR 1.71 (95% CI 1.47;1.97)

RR PSI 2 vs PSI 1 completed therapy 1.33 (95% CI 1.01;1.76)

Lænkholm AV, et al. JCO 2018

PAM50 ... in a Danish Cohort of Postmenopausal Women Allocated to 5 Years of Endocrine Therapy

Recurrence: HR 1.92 (95% CI 1.47;2.49) Lum B vs Lum A

PSI 2 2018-2022, PAM50:

N=715 Lum A

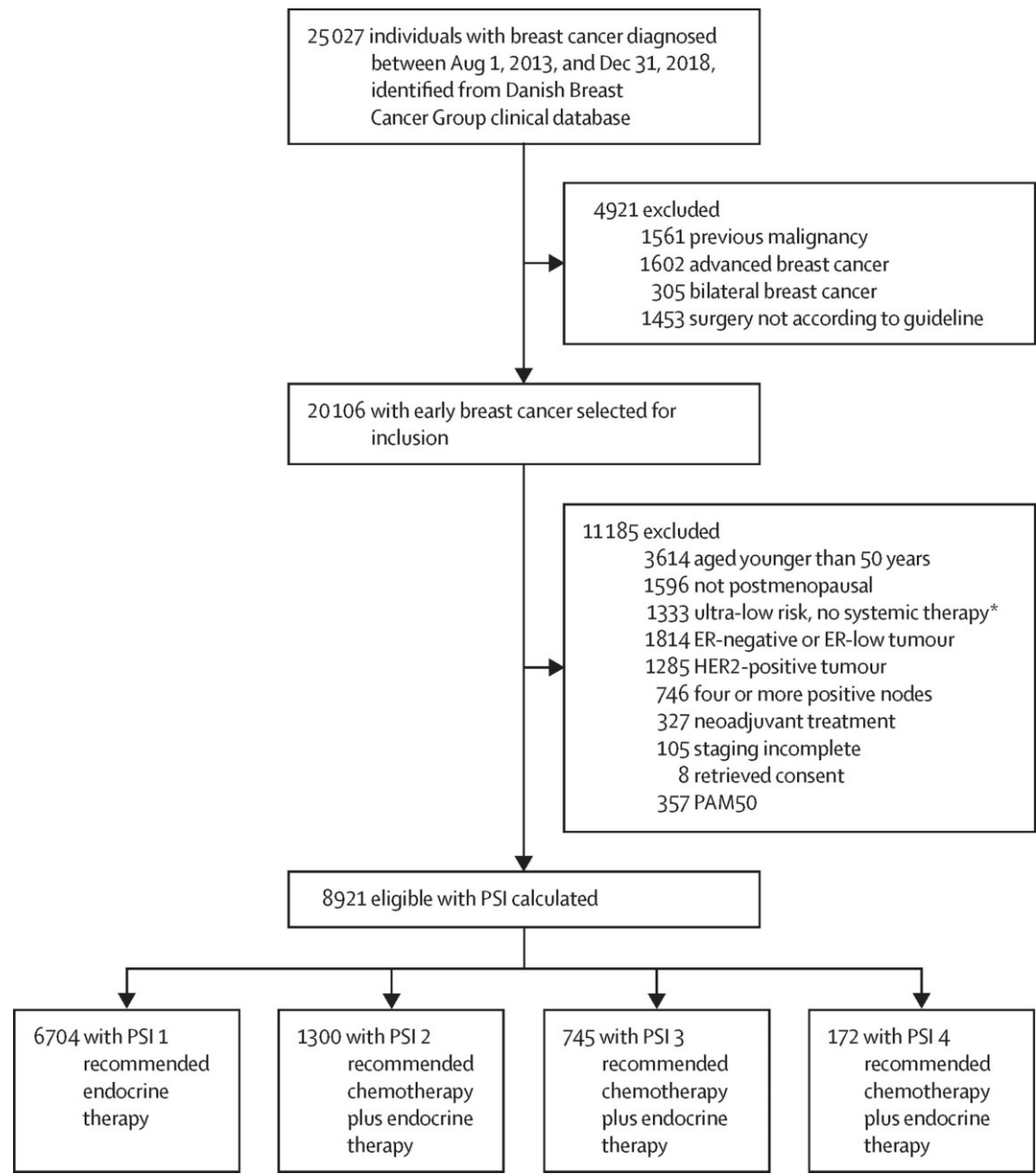
N=565 non-LumA

TBA

Fordeling af patienter med PSI allokering og mulighed for behandling med CDK4/6i

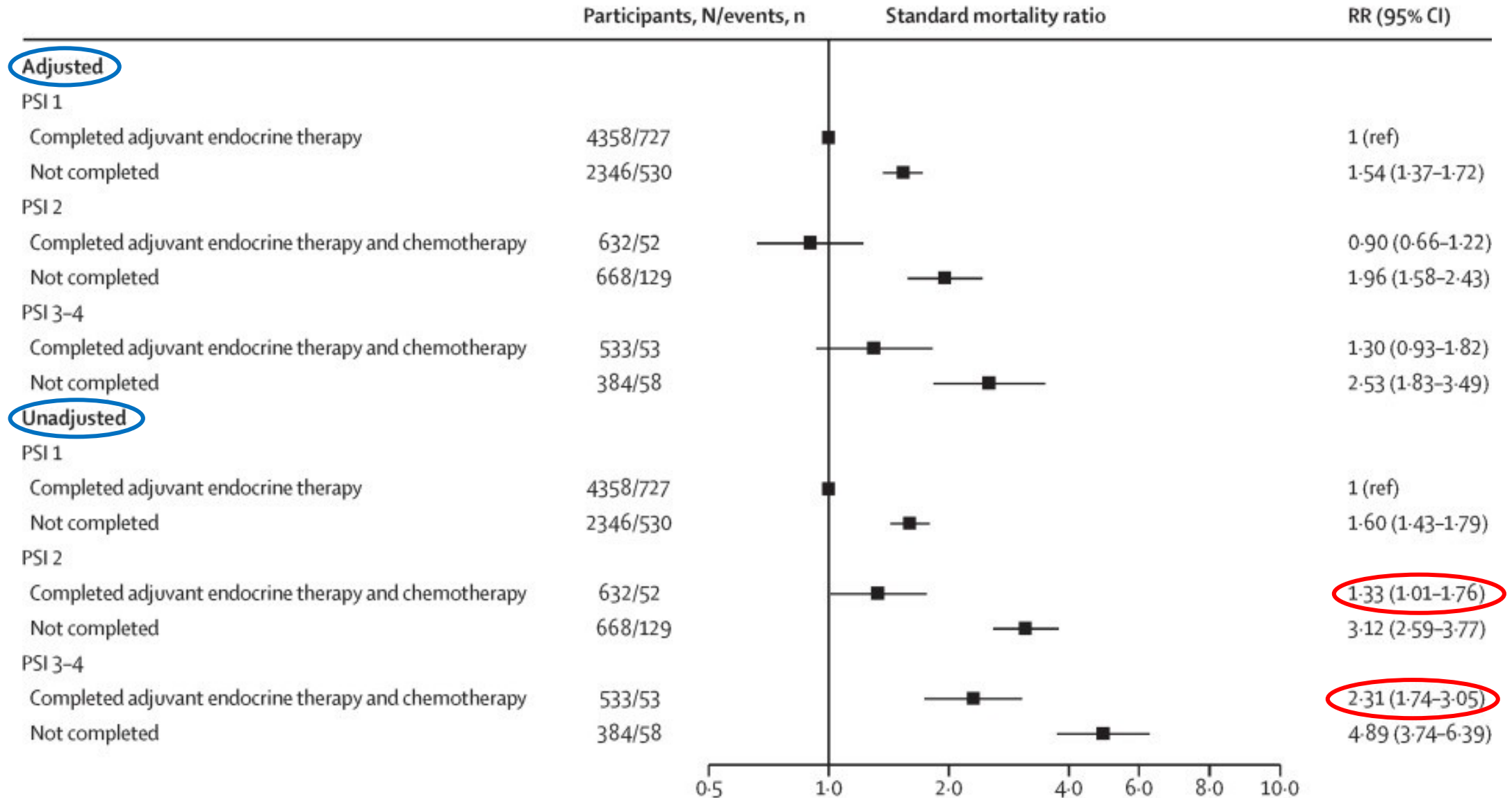
2024 PSI 1-4	Total N=2103	÷ CDK4/6i Studie- kriterier	+ CDK4/6i		? T2N0 IIA G2 Low/High? LumA/Ki67
			Godkendt MR	Ej godkendt	
PSI 1	1458 (69%)	1056			
PSI 2 Lum A	215 (10%)	91	100	259	167
PSI 2 non- LumA	236 (11%)	64	113	188	23
PSI 3-4	194 (9%)	42			





Estimates for assigned PSI and completed adjuvant treatment as a time-dependent factor using patients assigned PSI 1 and completed treatment as reference

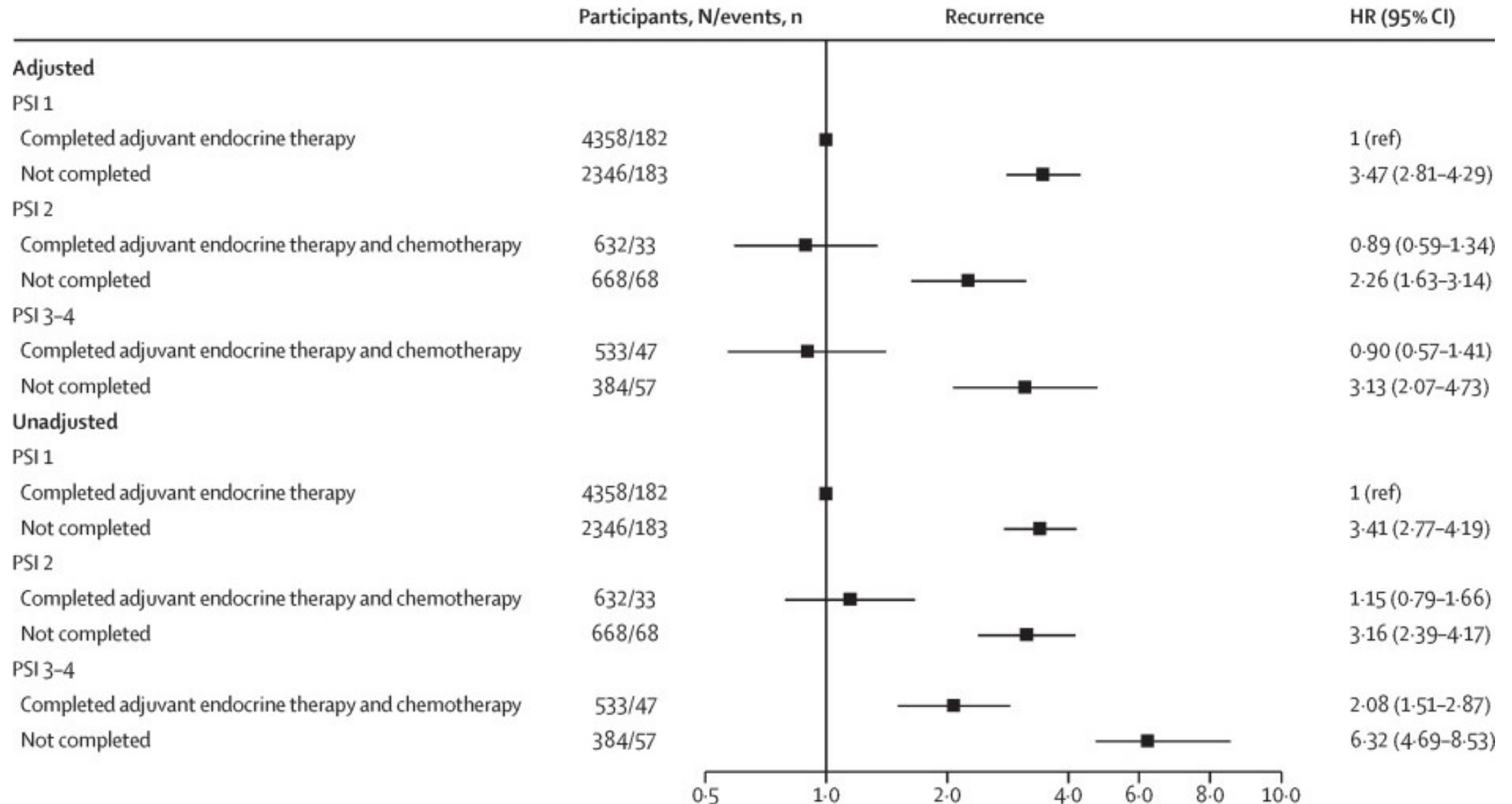
RR estimates for standard mortality ratio



Estimates for assigned PSI and completed adjuvant treatment as a time-dependent factor using patients assigned PSI 1 and completed treatment as reference

HR for recurrence from Fine–Gray subdistribution hazard model

B



Præmenopausale kvinder med ER-positiv, HER2-normal sygdom

Analyse af prognostiske faktorer med henblik på en behandlingsallokering

- DBCG har i perioden 2007-2020 **N=6360** præmenopausale kvinder med unilateral, ER $\geq 10\%$, HER2-normal sygdom allokeret til KT+ET eller ET alene
- LABC: 680 har N2-N3 sygdom, og yderligere 100 T3 sygdom; disse evalueres separat
- Helt unge patienter <40 på diagnosetidspunkt (N=595) evalueres særskilt
- Til udvikling af algoritmen er således **900** patienter allokeret til ET alene og **4080** til KT+ET

NATALEE Eligible Patients

