Twenty Years of *BRCA* Testing in Denmark: Treatment Patterns and Survival of Women with *BRCA*-associated Breast Cancer

Aleksandar Martinov Kostov, MD, PhD

Principal supervisor Associate Professor Anne-Vibeke Lænkholm

Assessment committee

(Chair) Professor Julie Gehl, University of Copenhagen

Professor Peer Christiansen, Aarhus University

Associate Professor Niklas Loman, Lund University, Sweden

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Clinical context

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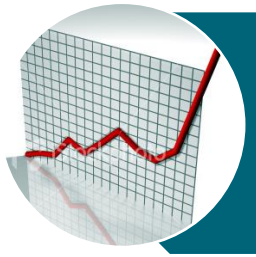
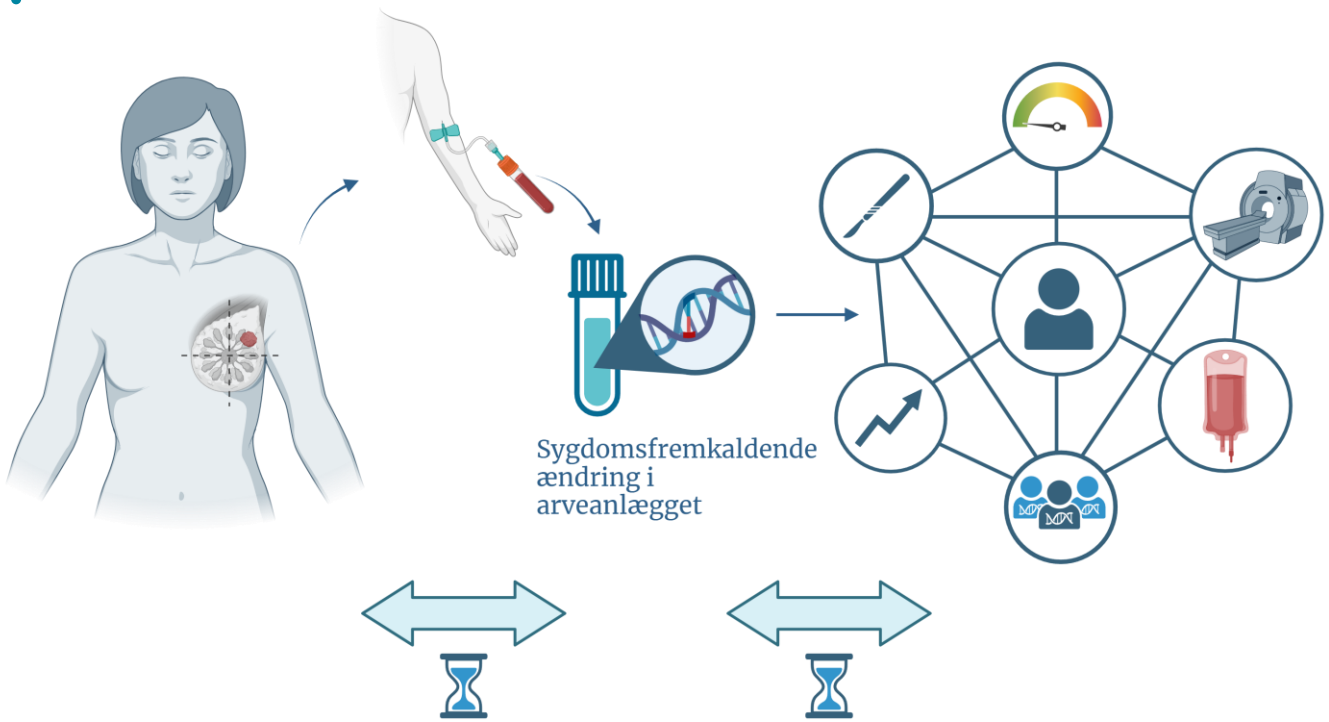


5000 women and 40 men are diagnosed with BC yearly –
Up to 1 out of 10 cases due to hereditary BC

Germline pathogenic and likely pathogenic variants in the
BRCA1 and *BRCA2-genes are the most common cause (BRCA-carriers)*
Increased risk of CBC (and OC) and worse prognosis?

Current recommendations for genetic testing focuse on family predisposition, early age onset of BC (<50 years) and ER-/HER2- BC. *BRCA2* carriers at risk of missing due to more frequently ER+ BC and higher age

Which BC patients undergo BRCA testing and when? How does the test timing and test result influence on the treatment and on survival after BC?

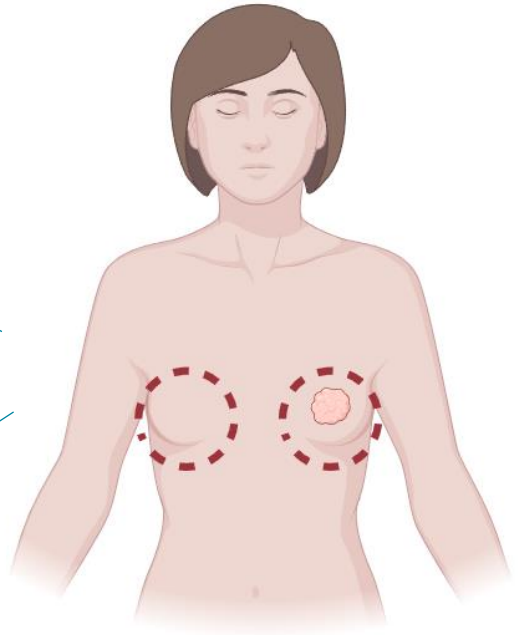


Knowledge of *BRCA* status at BC diagnosis guides surgical treatment decisions

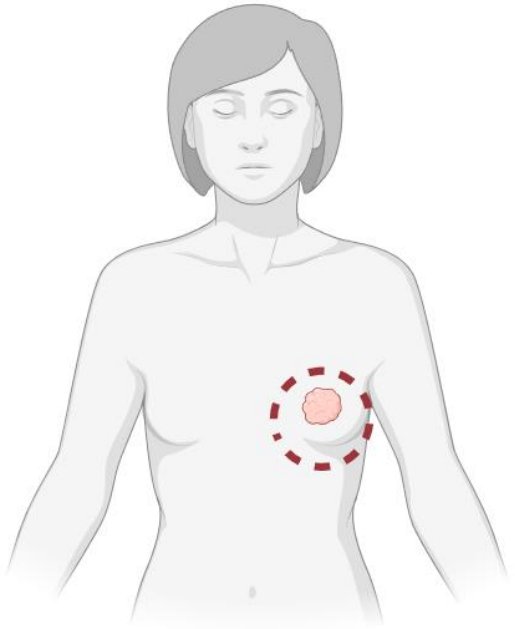
BRCA PV Carriers

Bilateral risk-reducing mastectomy (BRRM)

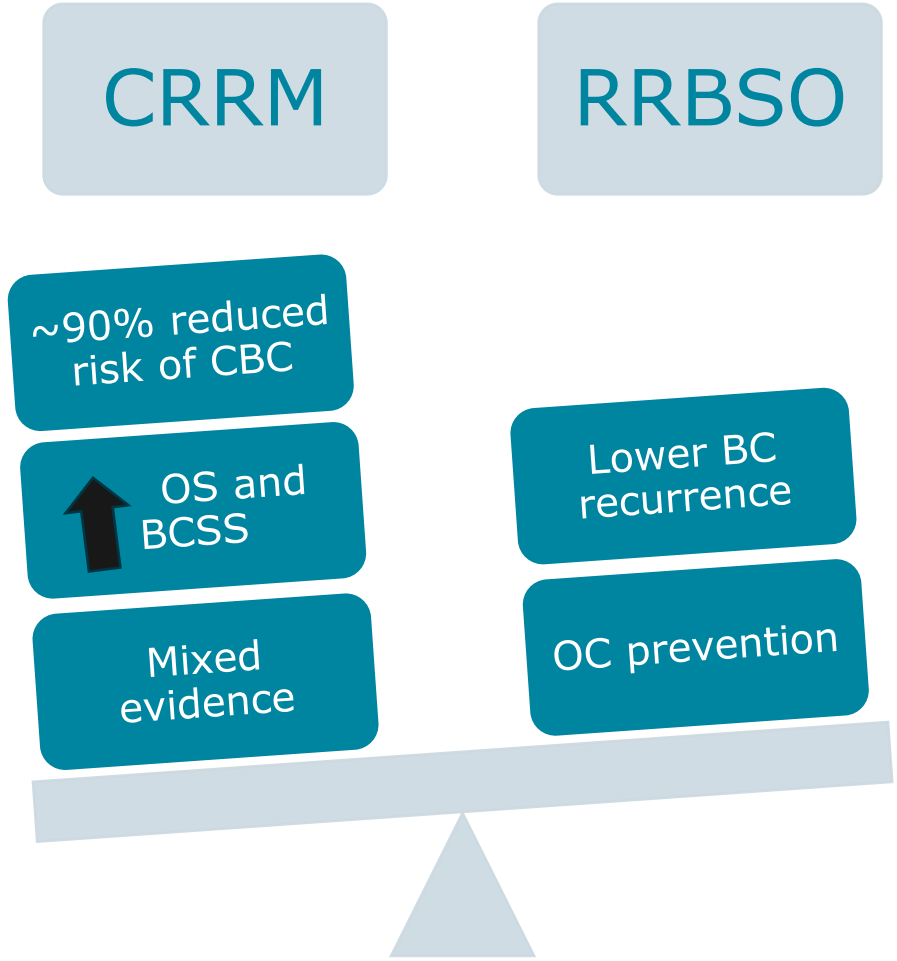
Contralateral risk-reducing mastectomy (CRRM)



BRCA Wild-Type Carriers



Risk-reducing surgery



Evans DGR, Ingham SL, Baildam A, et al. Contralateral mastectomy improves survival in women with BRCA1/2-associated breast cancer. Breast Cancer Res Treat. 2013;140(1):135-142. doi:10.1007/s10549-013-2583-1
Metcalfe K, Lynch HT, Foulkes WD, et al. Effect of Oophorectomy on Survival After Breast Cancer in BRCA1 and BRCA2 Mutation Carriers. JAMA Oncol. 2015;1(3):306-313. doi:10.1001/jamaoncol.2015.0658

Studies

Paper I

Kostov AM, Jensen, MB., Ejlertsen, B. et al. **Germline *BRCA* testing in Denmark following invasive breast cancer: Progress since 2000.**

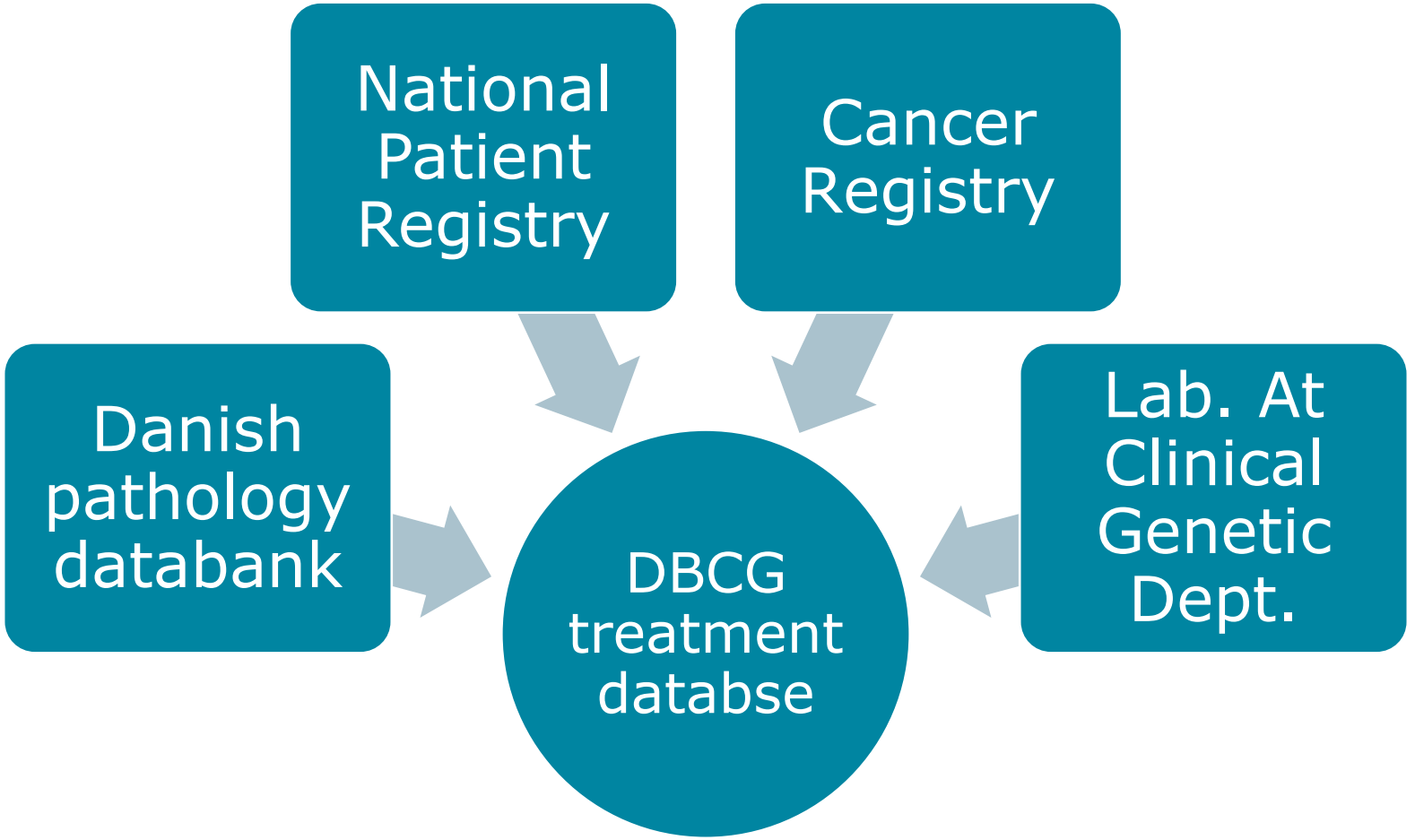
Acta Oncologica. 2025;64:147-155. doi:10.2340/1651-226X.2025.42418

Paper II

Kostov, A.M., Jensen, MB., Ejlertsen, B. et al. **Timely germline *BRCA* testing after invasive breast cancer promotes contralateral risk-reducing mastectomy and improves survival: an observational retrospective study.**

Breast Cancer Res Treat 212, 309–323 (2025). https://doi.org/10.1007/s10549-025-07726-21.

Data sources



Results of Study I

Included

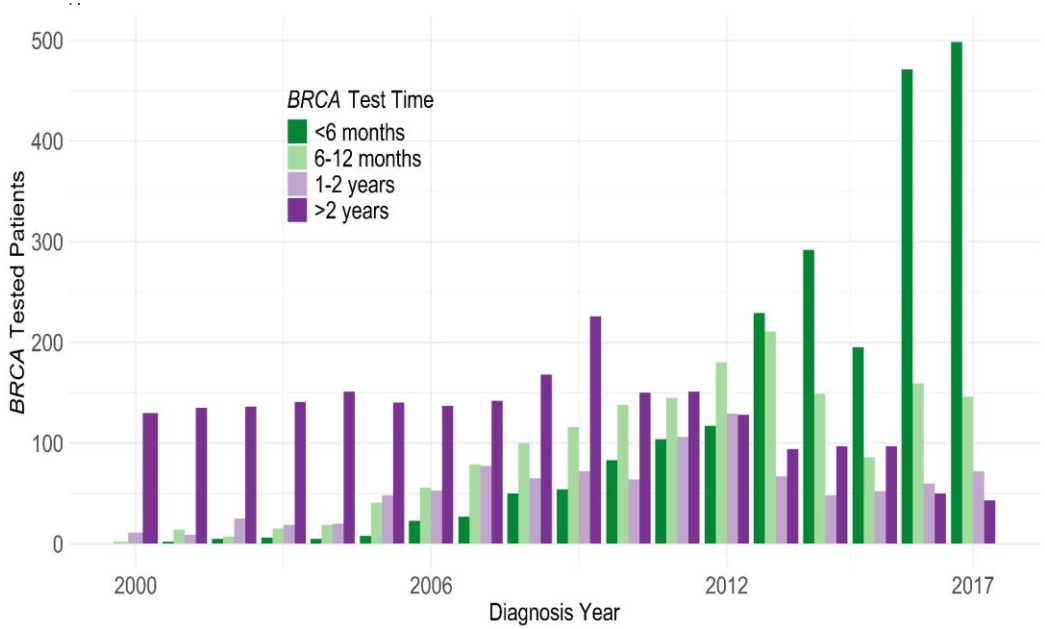
- 65,117 women – median age: 61 yrs

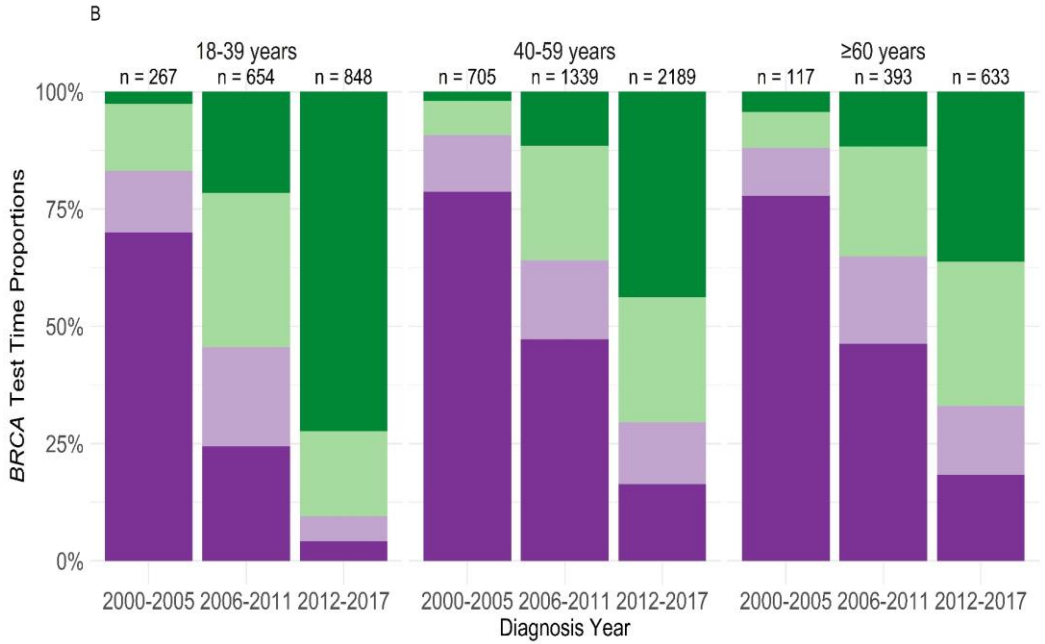
With *BRCA* test

- 9,125 (14%) – median age: 48 yrs
  - 173 (2%) before BC
  - 7,145 (78%) after BC, before 2nd event
  - 1,807 (20%) after 2nd event

***BRCA* PV carriers**

- 720 (10%) of 7,145 with test after BC and before 2nd event
  - 267 (15%) of patients aged 18-39
  - 378 (12%) of patients aged 40-59
  - 75 (7%) of patients aged 60 years and older





Increasing test rates over time

- From 10%(2000-2005) to 18%(2012-2017)
- Highest for young patients <40 years

  50%(2000-2005) to 88%(2012-2017)

More timely testing (<6 mths after BC)

- Zero patients in year 2000 vs 498 in 2017
- 70% (18-39 yrs) vs less than half in 40 yrs and older

Results of Study I

- **Logistic regression model**
- **Outcome *BRCA* test (Yes/No)**
  - Age, year of diagnosis, region of residency and receptor status (all p<0.0001)
  - **Higher odds for testing**
    - Age <40 years
    - ER-/HER2- BC

Table 3. Multivariate logistic regression models with interactions, where Odds ratio>1.0 favours BRCA testing.

Diagnosis year	2000–2005	2006–2011		2012–2017		*P*
Age at diagnosis[1]		Odds ratio	[95% CI]	Odds ratio	[95% CI]	<0.0001
18–39	Ref	2.75	[2.21–3.41]	4.78	[3.77–6.07]	
40–59	Ref	0.71	[0.65–0.78]	1.06	[0.97–1.16]	
≥60	Ref	0.79	[0.68–0.93]	0.96	[0.82–1.13]	
ER/HER2[2]		Odds ratio	[95% CI]	Odds ratio	[95% CI]	<0.0001
ER-/HER2-	Ref	1.48	[1.22–1.78]	3.63	[3.00–4.38]	
ER-/HER2+	Ref	1.28	[0.99–1.67]	1.83	[1.38–2.45]	
ER+/HER2-	Ref	0.71	[0.71–0.97]	0.87	[0.80–0.96]	
ER+/HER2+	Ref	0.93	[0.81–1.21]	1.25	[1.03–1.54]	
Unknown	Ref	2.16	[1.75–2.66]	1.79	[1.05–3.05]	

CI: confidence interval.

[1] Odds ratios for the interaction term of age at diagnosis and diagnosis year in multivariate LR model, adjusted for region of residency and receptor status; [2] Odds ratios for the interaction term of receptor status and diagnosis year in the multivariate LR model, adjusted for region of residency and age at diagnosis.

Results of Study II

Included

- 7,145 women – *BRCA test after BC*

720 (10%) BRCA PV carriers

- 403 *BRCA1* (56%) – one double carrier
- 317 *BRCA2* (44%)

Characteristics of *BRCA* PV

- Younger at diagnosis; median age 43 vs 47
- Ductal carcinomas, *BRCA1* often ER-/HER2-, *BRCA2* mostly ER+/HER2-
- Higher malignancy grade and larger tumors
- Mastectomy as primary surgery
- More chemo and less endocrine therapy

Results of Study II

👩‍⚕️ Timely *BRCA* Testing

- 30% (2,169 of 7,145) received *BRCA* results **within 6 months**
- Among timely tested:
  - **7%** *BRCA1* PV (n=154)
  - **4%** *BRCA2* PV (n=88)

🛡️ Risk-Reducing Surgery

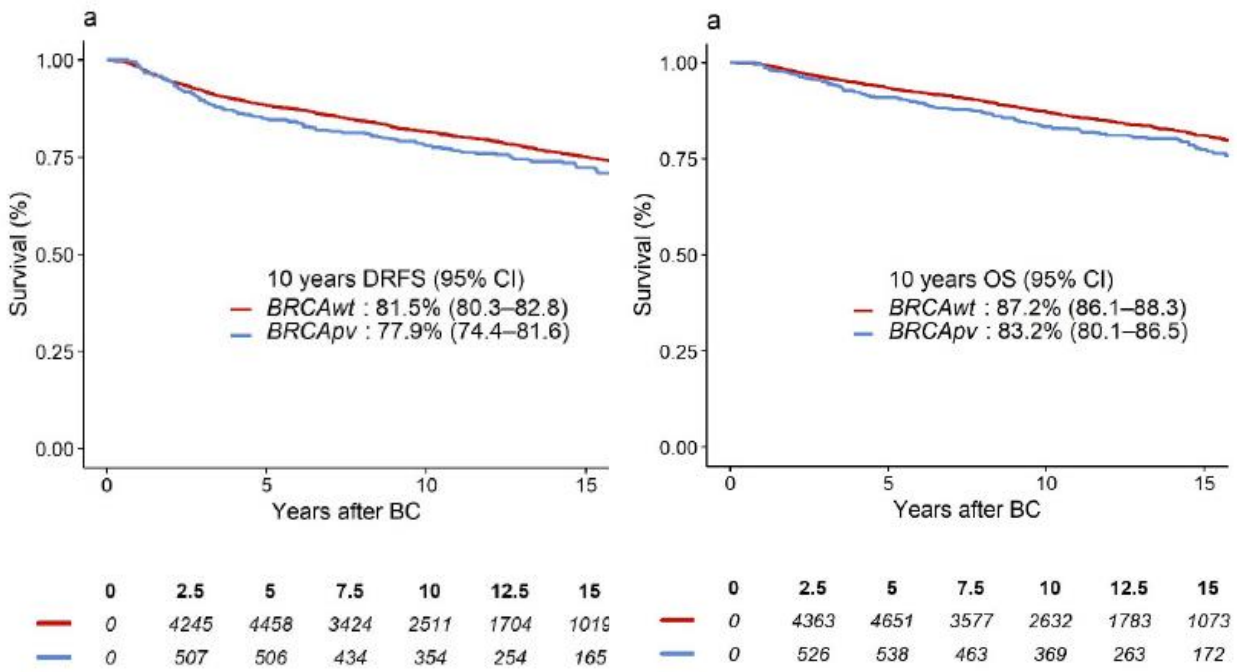
- **High uptake** in ***BRCA* PV** (90% vs. 26%)
- 🟦 **Higher CRRM uptake** in *BRCA1* vs *BRCA2* (66% vs. 52%, p<0.001)

  🟩 **Timely-tested** patients more often chose CRRM (75% vs. 52%, p = 0.004)
- Similar uptake of **RRBSO** (82%) in *BRCA1* and *BRCA2,* not influenced by the test timing

Survival after BC

- Median follow-up 10.8 years
- **DRFS**: 1104 events (785 (70%) events of distant recurrence as first event)
- **OS**: 841 events

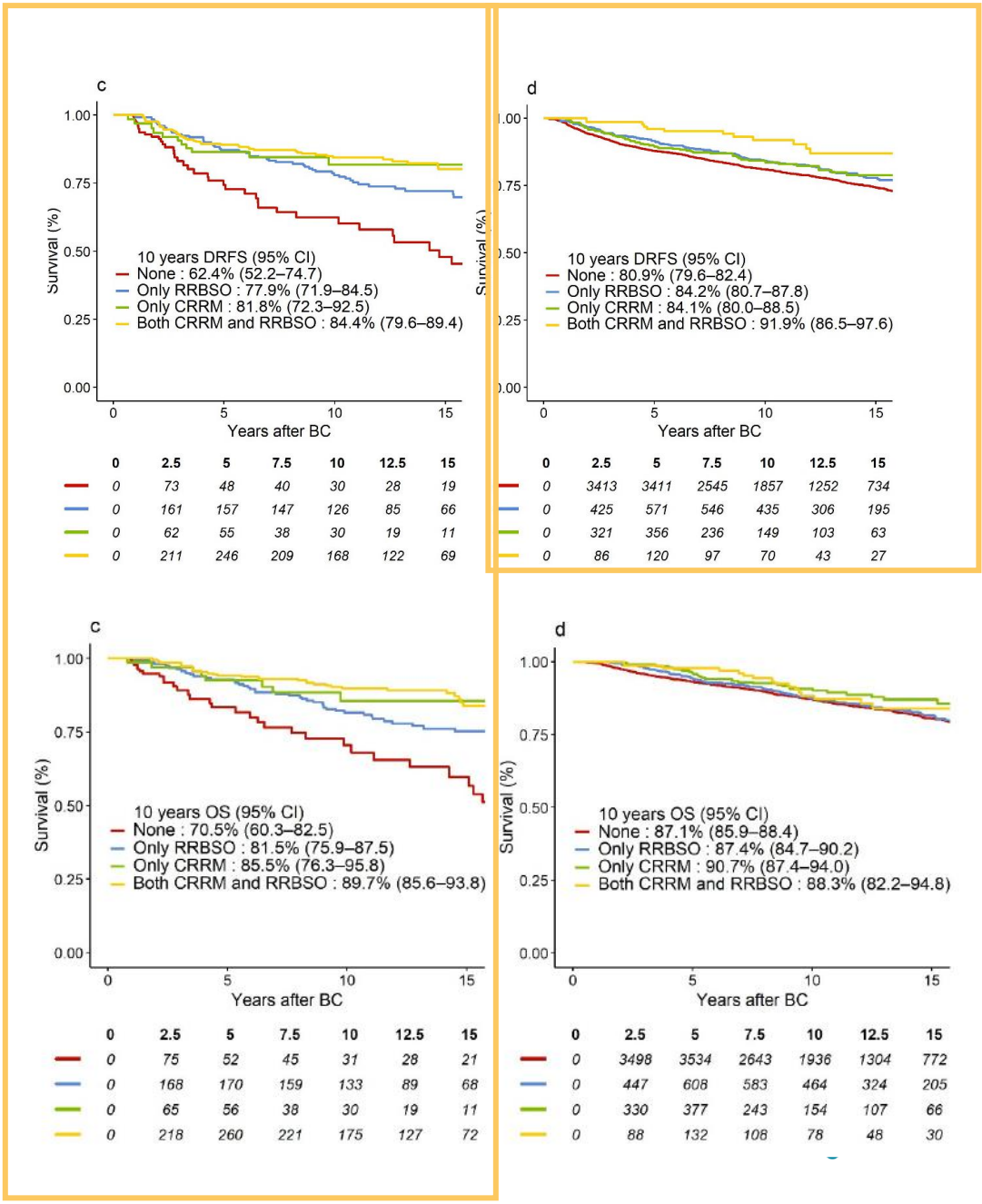
- Lower DRFS and OS for *BRCA* PV



Survival benefit of RRS

- Higher absolute 10-years survival after either CRRM or RRBSO or both for *BRCA* PV

- Improved 10-year DRFS for *BRCA* wt



CRRM and Survival outcomes

Adjusted for *BRCA* status, baseline clinical characteristics and treatment

CRRM	Yes vs. No	0.63 (0.51–0.78)	<0.001	
Interactions **CRRM**	*BRCA*wt	0.72 (0.56–0.93)		0.06
	BRCApv	0.49 (0.35–0.70)		
	BRCA1pv	0.38 (0.23–0.62)		0.12
	BRCA2pv	0.65 (0.40–1.04)		
	BRCAwt <50 years	0.66 (0.49–0.88)		0.14
	BRCAwt ≥50 years	0.98 (0.63–1.55)		
	BRCApv <50 years	0.47 (0.32–0.69)		0.58
	BRCApv ≥50 years	0.57 (0.31–1.05)		

RRBSO and Survival Outcomes

❌ **No significant association** with:

DRFS:

HR 0.89 [0.75 – 1.06] (p = 0.20)

OS:

HR 0.98 [0.82 – 1.18] (p = 0.84)

✅ **Significant Benefit in *BRCA* PV**

In ***BRCA* PV carriers aged ≥50**,

RRBSO was associated with:

- **>50% reduction in mortality**
- HR 0.44 [95% CI 0.26–0.75]

  heterogeneity p=0.01

BRCA PV and Survival after BC

❗ Significantly Elevated Risk of distant recurrence

📈 HR=1.31 [1.06 – 1.63] p=0.01

HR=1.53 [1.22 – 1.93] after 2 years

Applies to both ***BRCA1*** and ***BRCA2*** carriers

📉 Overall Survival

- HR 1.25 (95% CI 0.99–1.59)
- Not statistically significant (p = 0.07)

⚠️ Tumour Characteristics

- Larger tumours
- Higher malignancy grade
- More **triple-negative** subtype → All contribute to **worse prognosis**

Conclusions

Testing in DK

- ***BRCA* testing** for women with BC is well adopted in Denmark, however **older** patients and those living more distant to the University hospitals might be at risk of late *BRCA* testing
- **Test to all women <60 at BC is recommended**

⏱️ Timely *BRCA* Identification

increases CRRM uptake → survival **benefit**

- RRBSO less prominent survival effect

⚠️ *BRCA* PV and prognosis

- ❌ Not significantly linked to worse **overall survival (OS)**
  - **Not an independent factor**

❗ Other factors (age, CCI, tumour traits, treatment) have **greater impact**