Validation of breast cancer risk models in a German population-based study: the KORA cohort

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Introduction

Background

In Germany, women aged 50–75 are invited to mammographic screening for early breast cancer (BC) detection [1]. For high-risk women, risk-adapted screening starting at younger ages is increasingly implemented in clinical practice [2]. Validating risk-prediction models is the first step toward implementing them for risk-adapted screening.

Objective

External validation of breast cancer risk models , in a population-based German cohort to inform risk-adapted screening

Methods

The population-based German KORA cohort (four independent surveys, 1984–2001) was used to analyze 3,869 women (180 breast cancer cases), of whom 3,350 had polygenic risk scores (PRS), contributing 7,824 observations over up to 27 years.

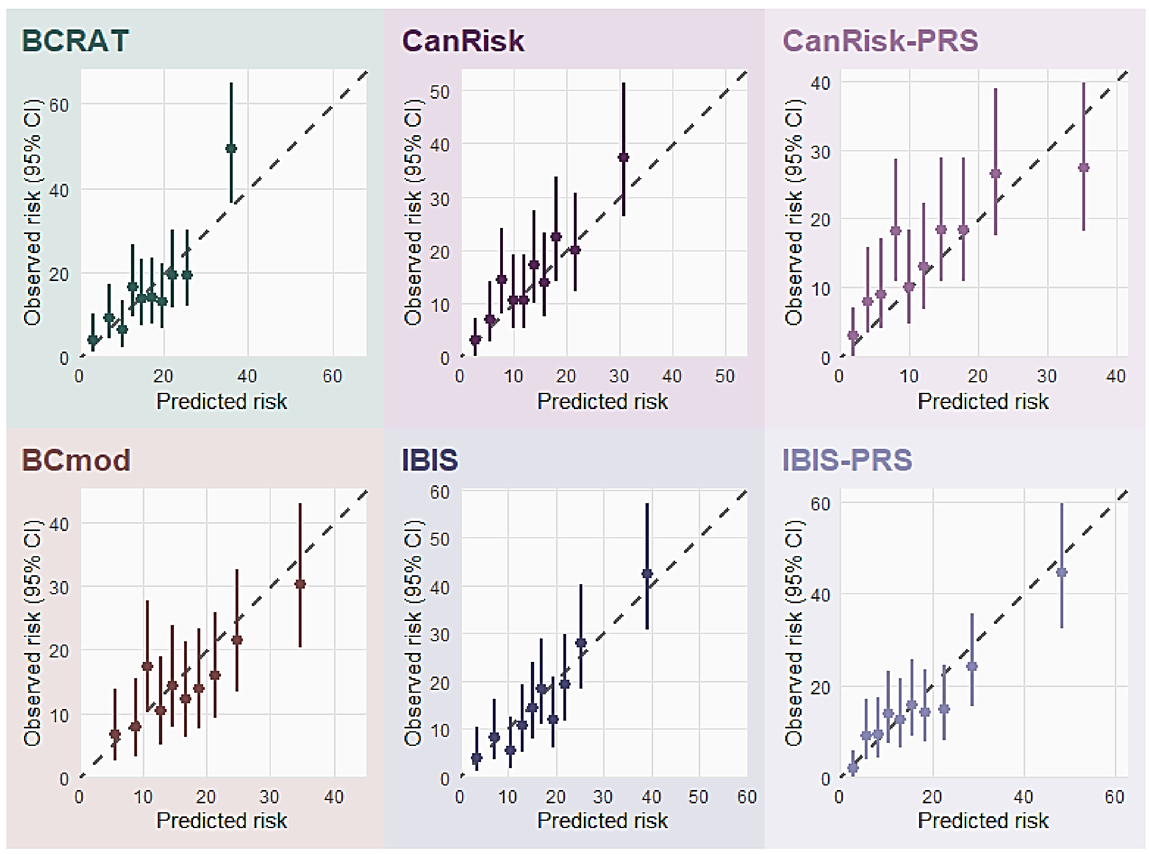
1. Missing predictors were multiply imputed.
2. Ten-year risk estimated using BCRAT [3], BCmod [4], CanRisk [5], and IBIS [6], including PRS-extended versions (CanRisk–PRS, IBIS–PRS).
3. Performance assessed by calibration (expected-to-observed [E/O] ratio) and discrimination (time-dependent area under the curve, AUC).
4. 95% confidence intervals (CI) accounted for repeated measurements and multiple imputation.
5. CanRisk–PRS used the provided standardized PRS. For IBIS–PRS: log relative risk (logRR) = log(1.6) × standardized PRS (zPRS).

Key Results

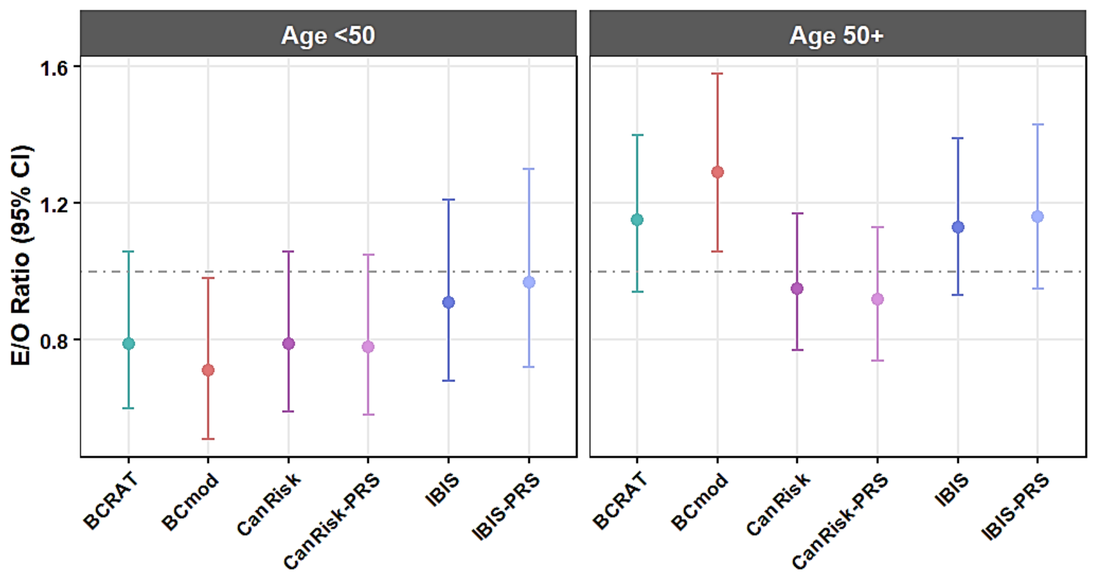
1 Overall Model Performance for 10-year Predictions

Model	E/O (95% CI)	AUC (95% CI)
BCRAT	1.03 (0.87–1.21)	0.63 (0.59–0.68)
BCmod	1.13 (0.95–1.34)	0.60 (0.55–0.65)
CanRisk	0.89 (0.75–1.06)	0.57 (0.53–0.62)
CanRisk–PRS	0.87 (0.73–1.03)	0.58 (0.53–0.68)
IBIS	1.06 (0.89–1.25)	0.63 (0.59–0.68)
IBIS–PRS	1.10 (0.93–1.30)	0.63 (0.58–0.67)

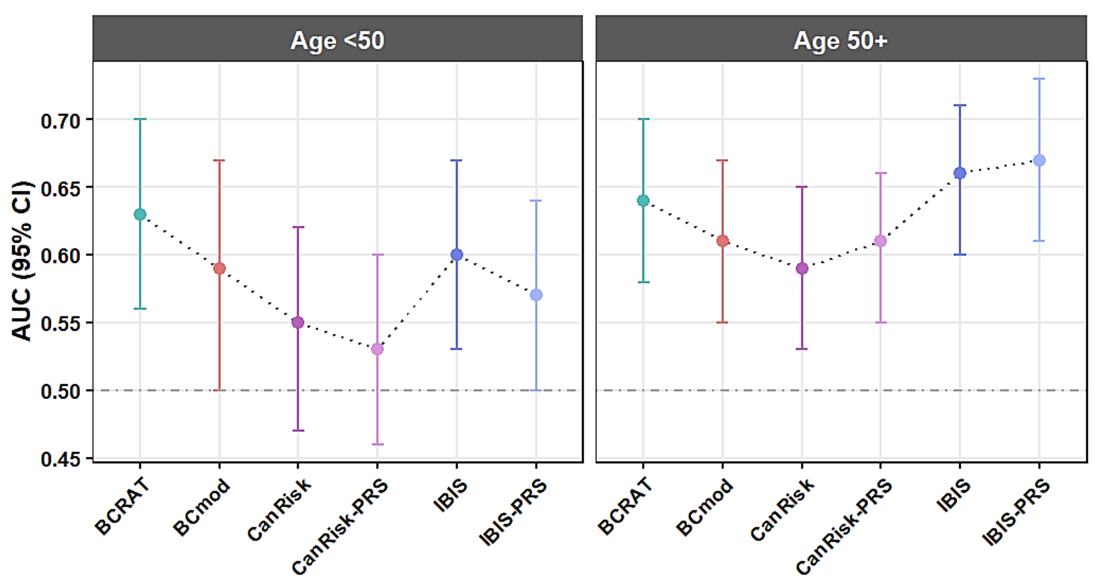
2 Calibration in Risk Deciles for 10-year Predictions



3 Model Performance by Age Groups



Horizontal dot-dash line indicates perfect calibration (E/O = 1)



Horizontal dot-dash line indicates no discrimination (AUC = 0.5)

Results and Conclusion

- BCRAT and IBIS were well calibrated for 10-year risk and showed the highest discrimination, supporting their potential use in risk-stratified screening.
- BCmod overestimated risk, particularly in women ≥50 years, while CanRisk showed lower discrimination, especially in women ≤50 years.
- Inclusion of PRS did not materially improve model performance in KORA cohort.

References

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