

Development and validation of a synthetic model for stratified disease prevention for breast cancer

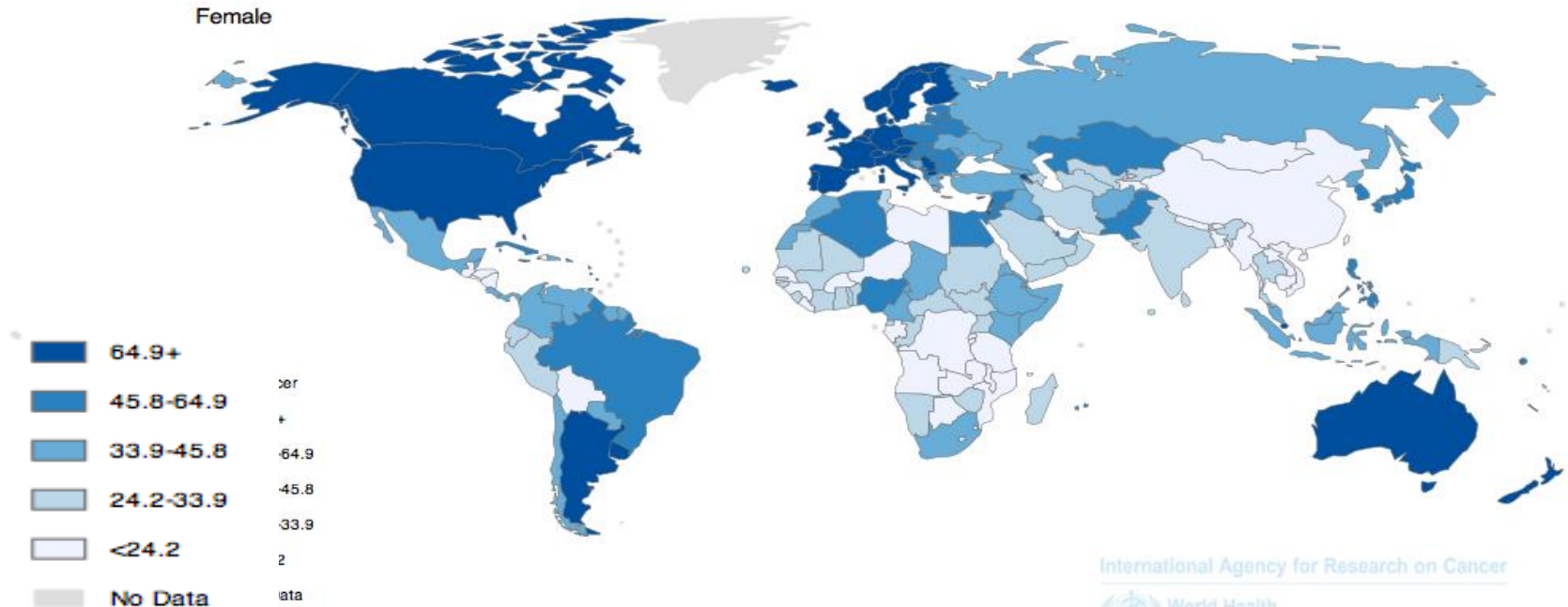
Montserrat Garcia-Closas, M.D. Dr.P.H.

Deputy Director

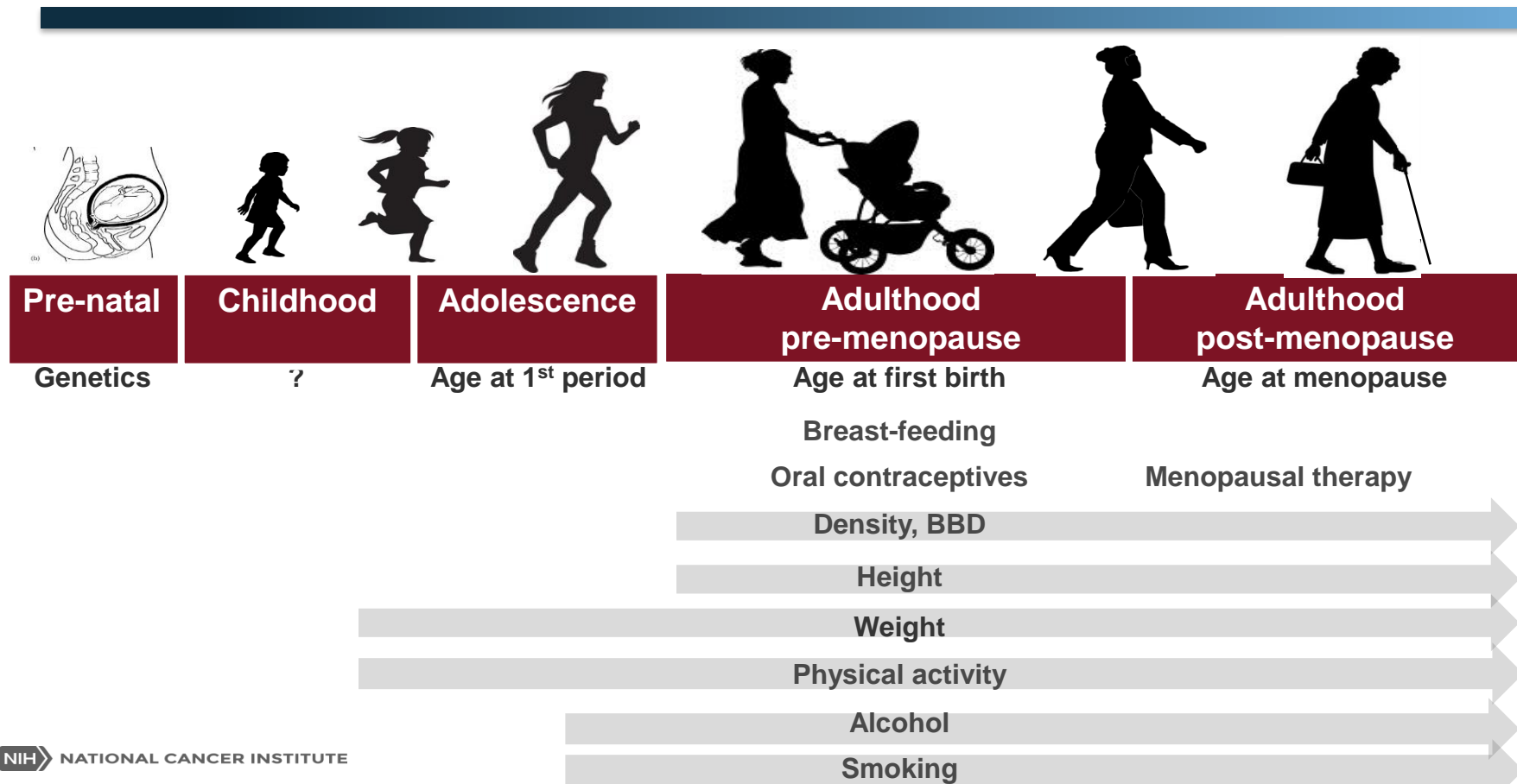
Division of Cancer Epidemiology and Genetics

Breast cancer: a global problem

Annual incidence of breast cancer per 100,000 women



Multiple factors affect breast cancer risk

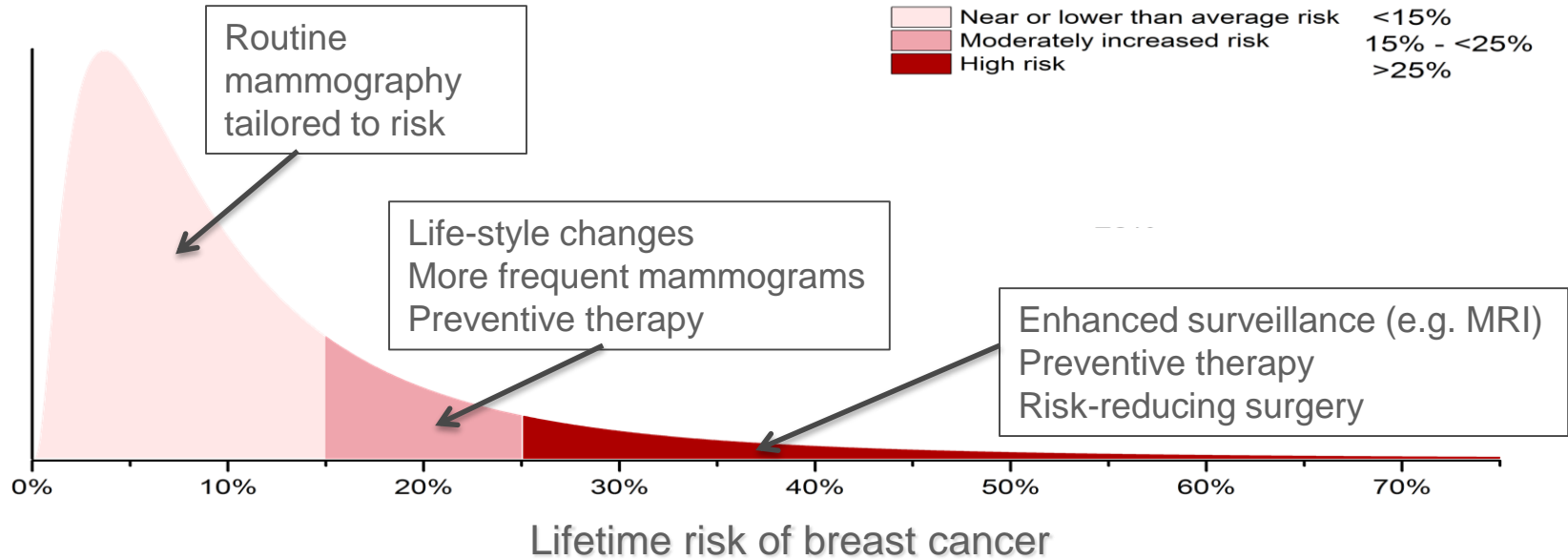


The challenge of primary prevention

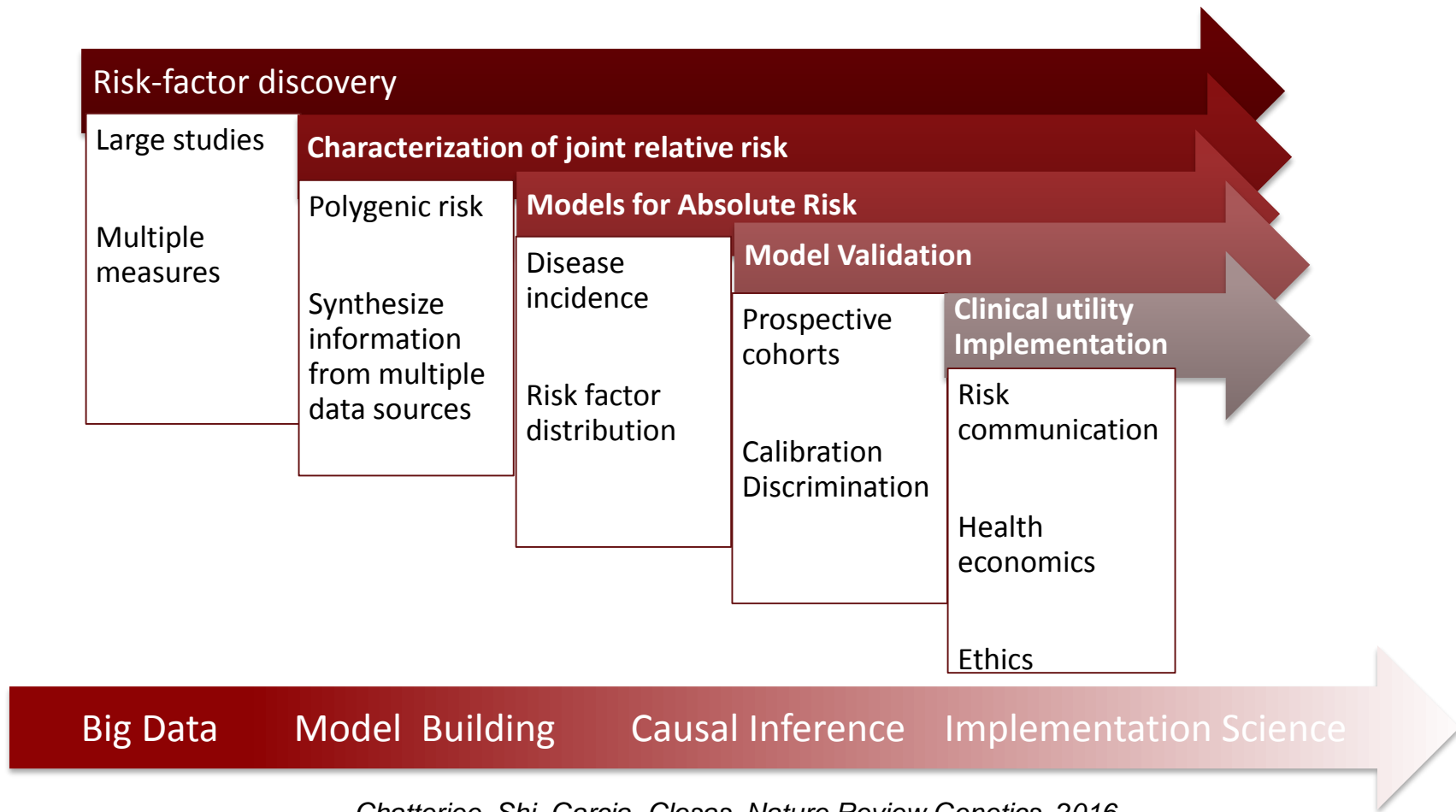
- No strong modifiable risk factors
- Changes at the population level are needed to have an impact on population rates, e.g. :
 - Reproductive patterns across countries
 - HRT rise and decline
- Population-wide changes are difficult to attain

Can precision prevention help?

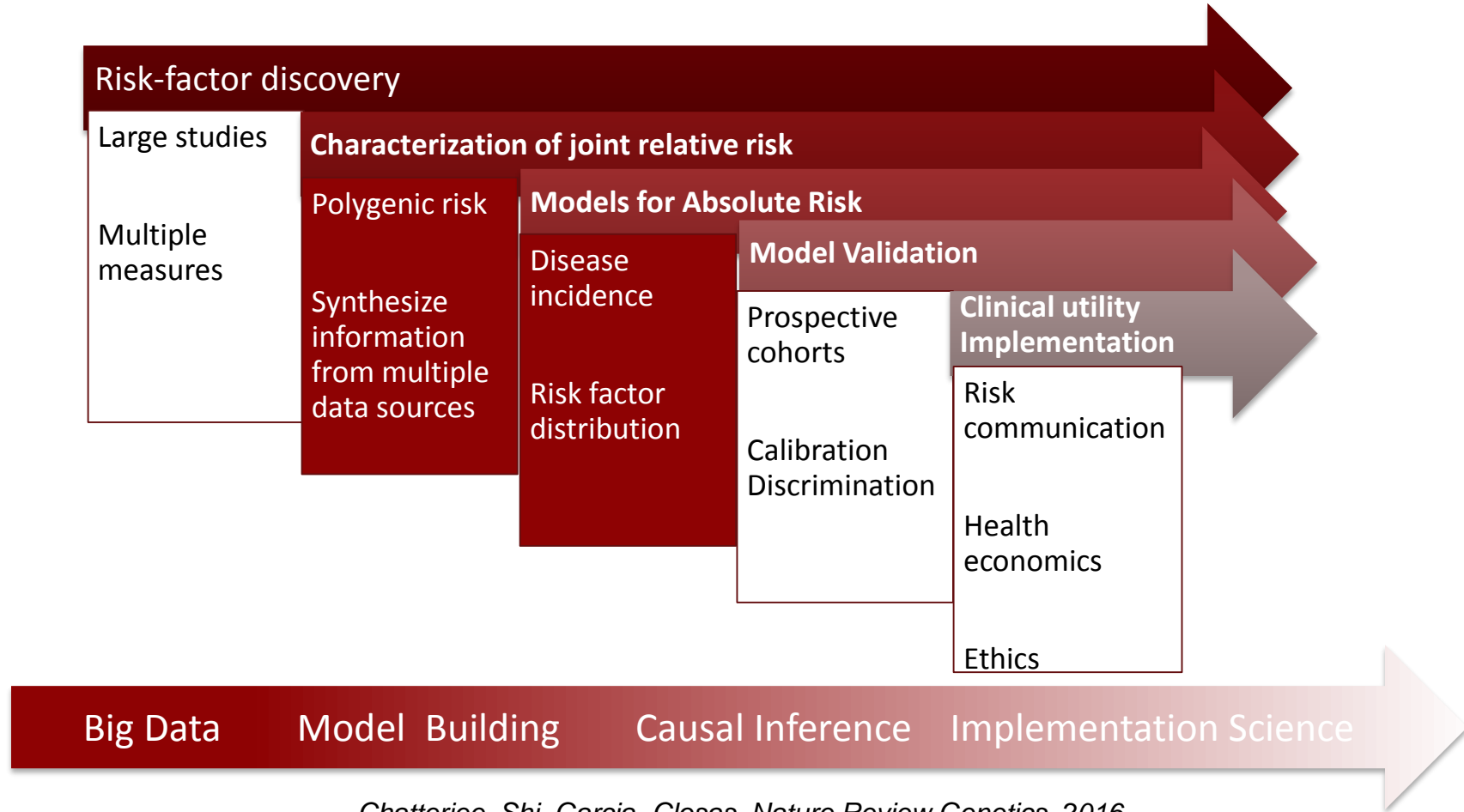
Stratification of the population into risk categories



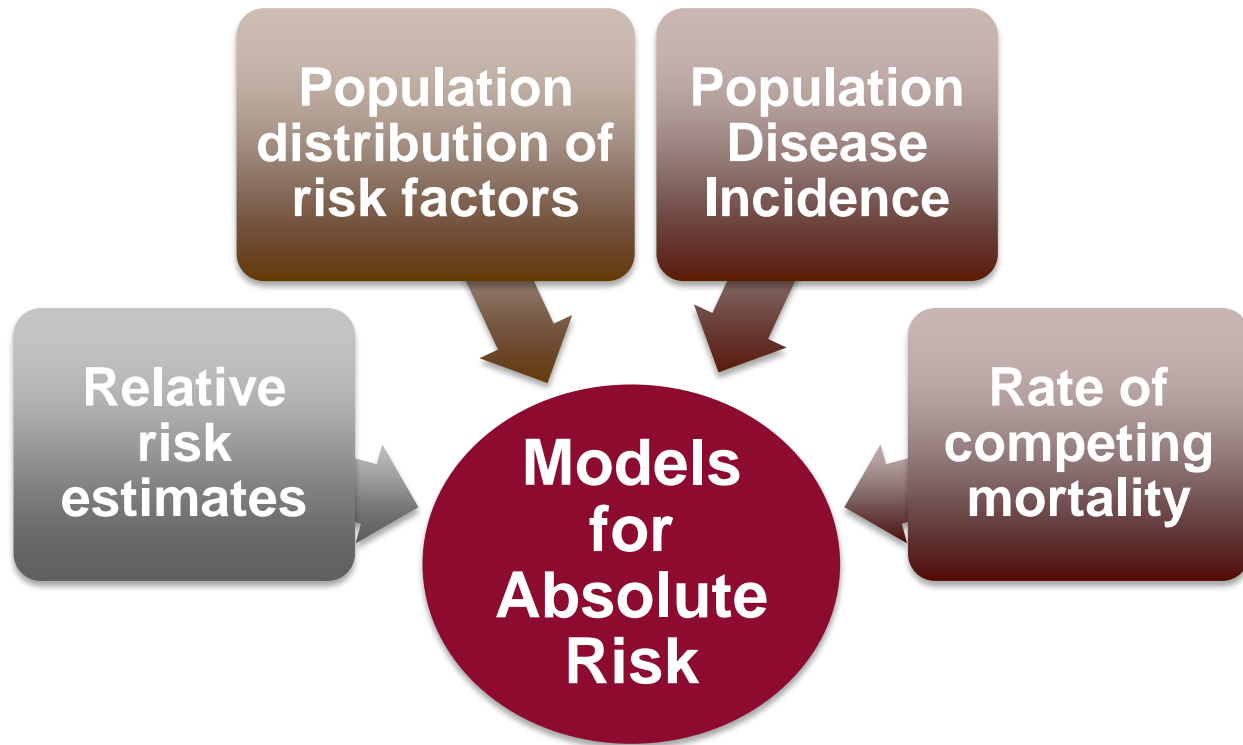
Precision Prevention: From Discovery to Practice



Precision Prevention: From Discovery to Practice



Individualized Coherent Absolute Risk Estimator (iCARE R package)



A synthetic breast cancer risk model, UK

Used for model calibration
and imputation of
missing data for
individual prediction

Distribution of risk
factors from Health
Survey for England,
Fertility Tables,
others

Breast cancer
incidence from
Office of National
Statistics, UK

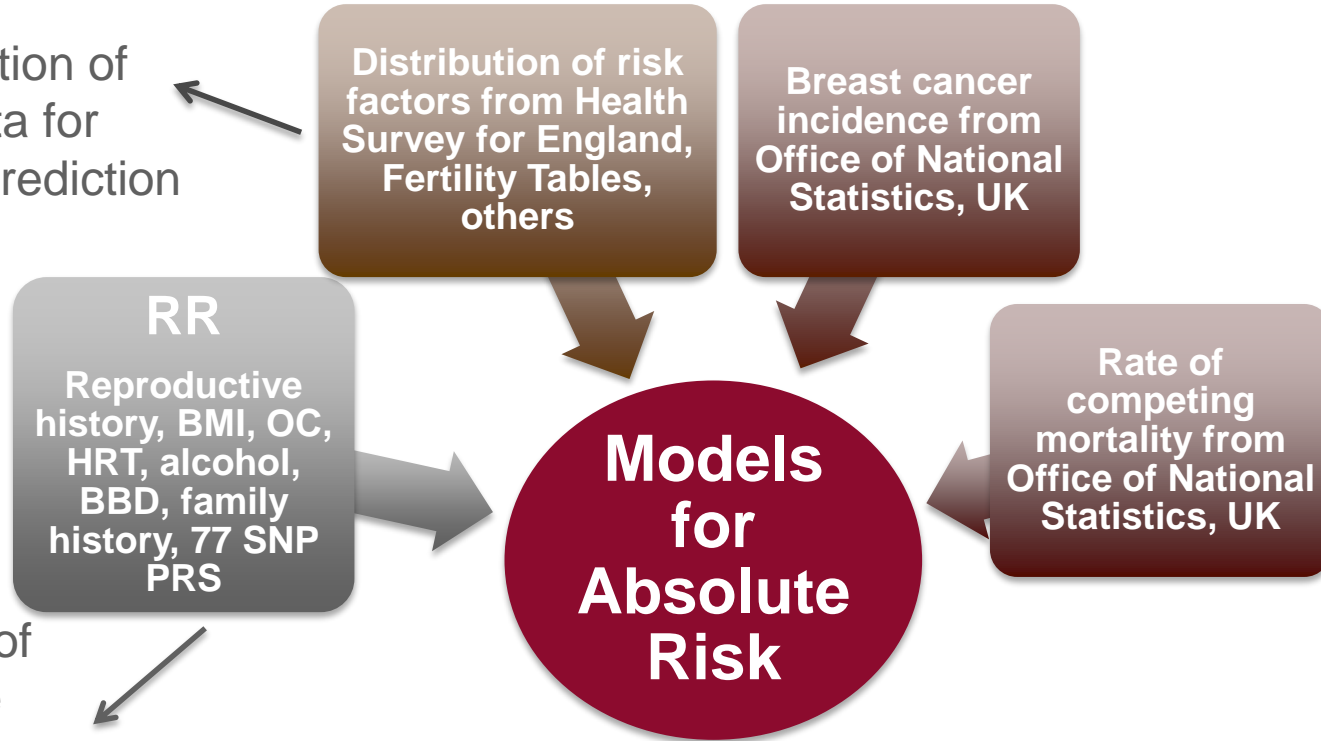
RR

Reproductive
history, BMI, OC,
HRT, alcohol,
BBD, family
history, 77 SNP
PRS

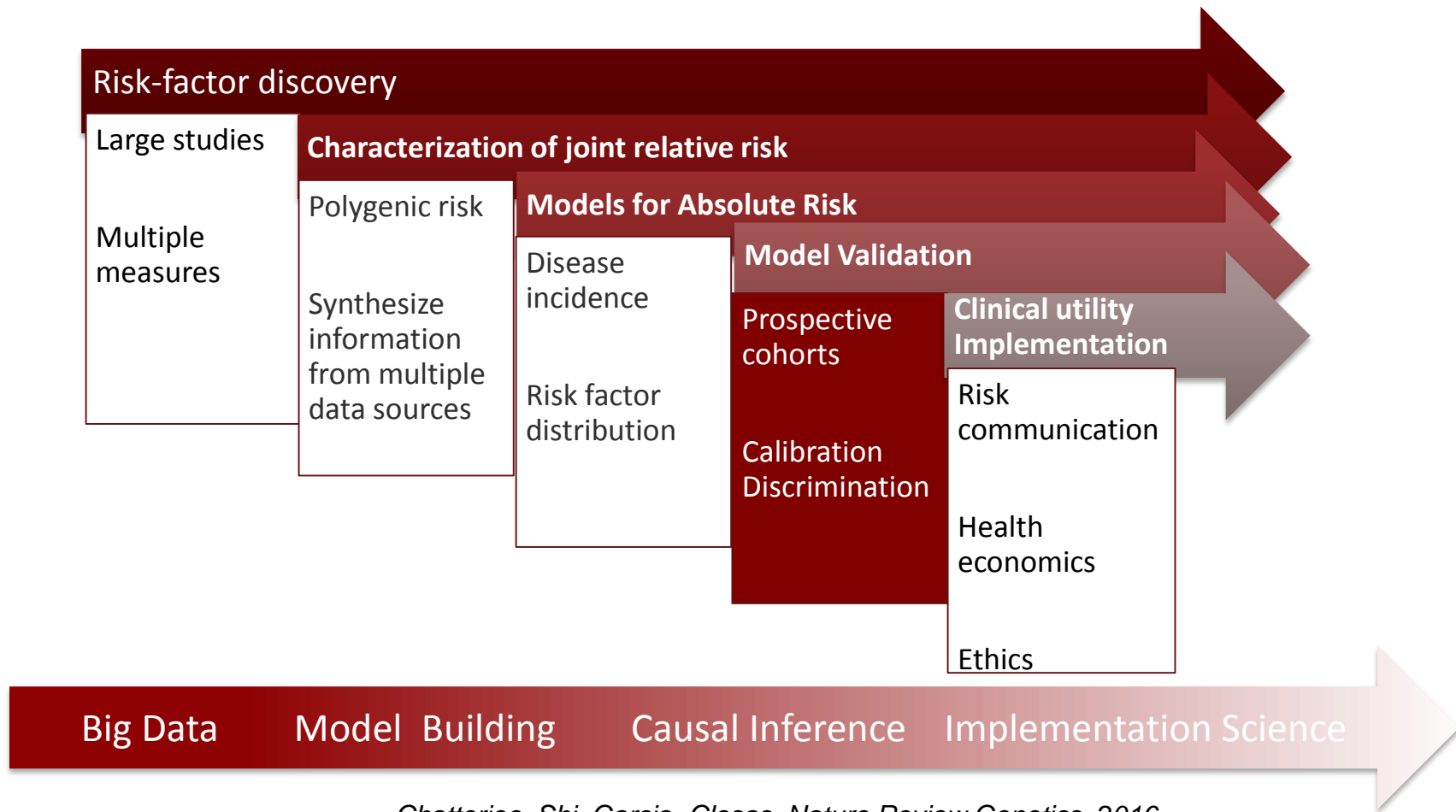
Rate of
competing
mortality from
Office of National
Statistics, UK

**Models
for
Absolute
Risk**

Assumption of
multiplicative
effects and
no G-E correlation



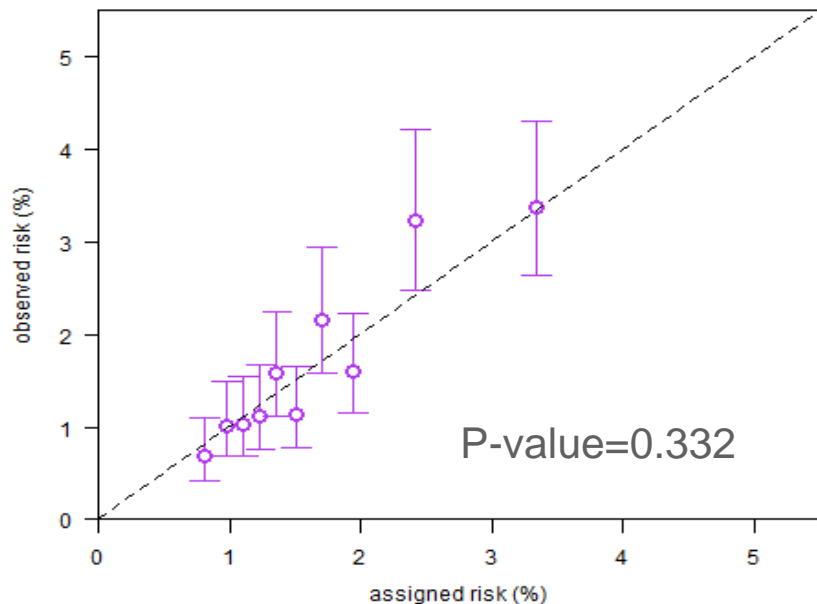
Precision Prevention: From Discovery to Practice



Generation Breast Cancer Cohort: calibration of synthetic breast cancer risk models (women >50 years old)

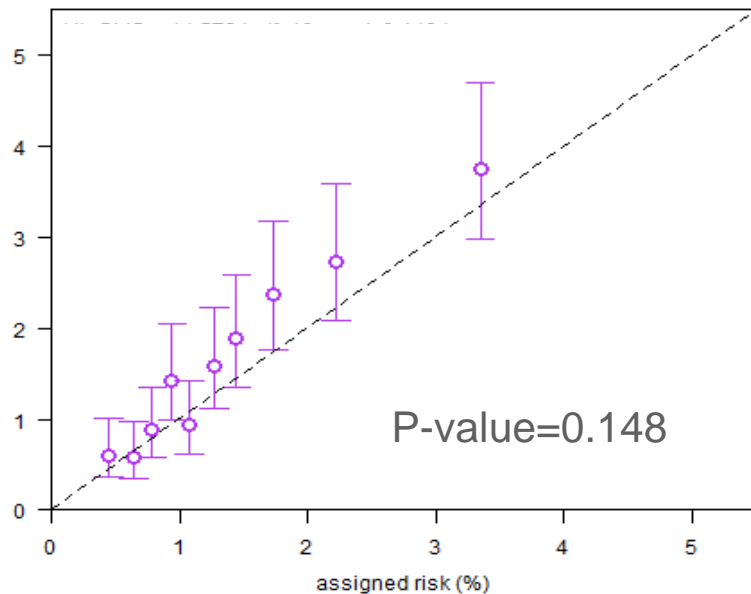
Model 1: Risk factors only

AUC = 64% (95%CI 60%-66%)

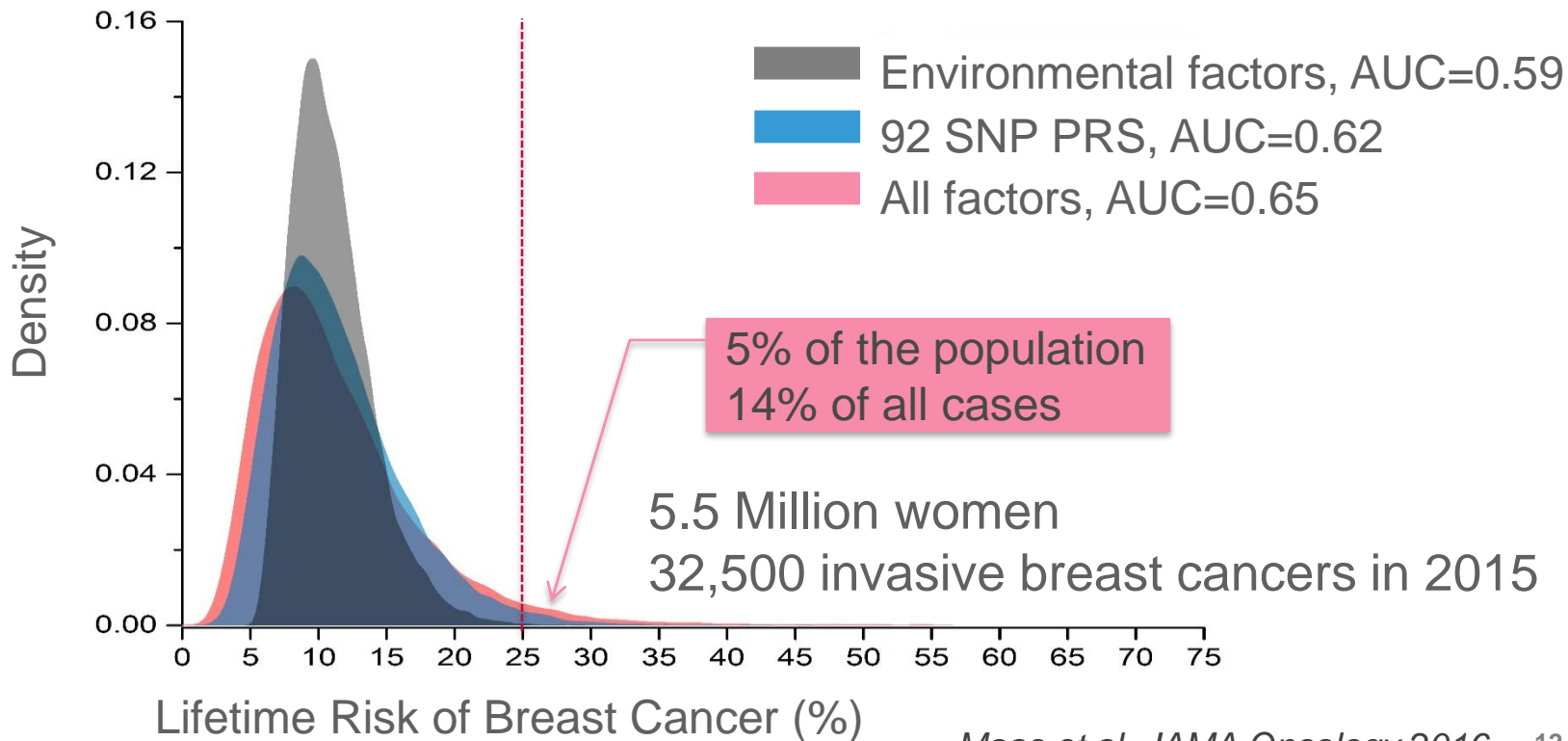


Model 2: Risk factors + 77 SNP PRS

AUC = 66% (95%CI 63%-69%)

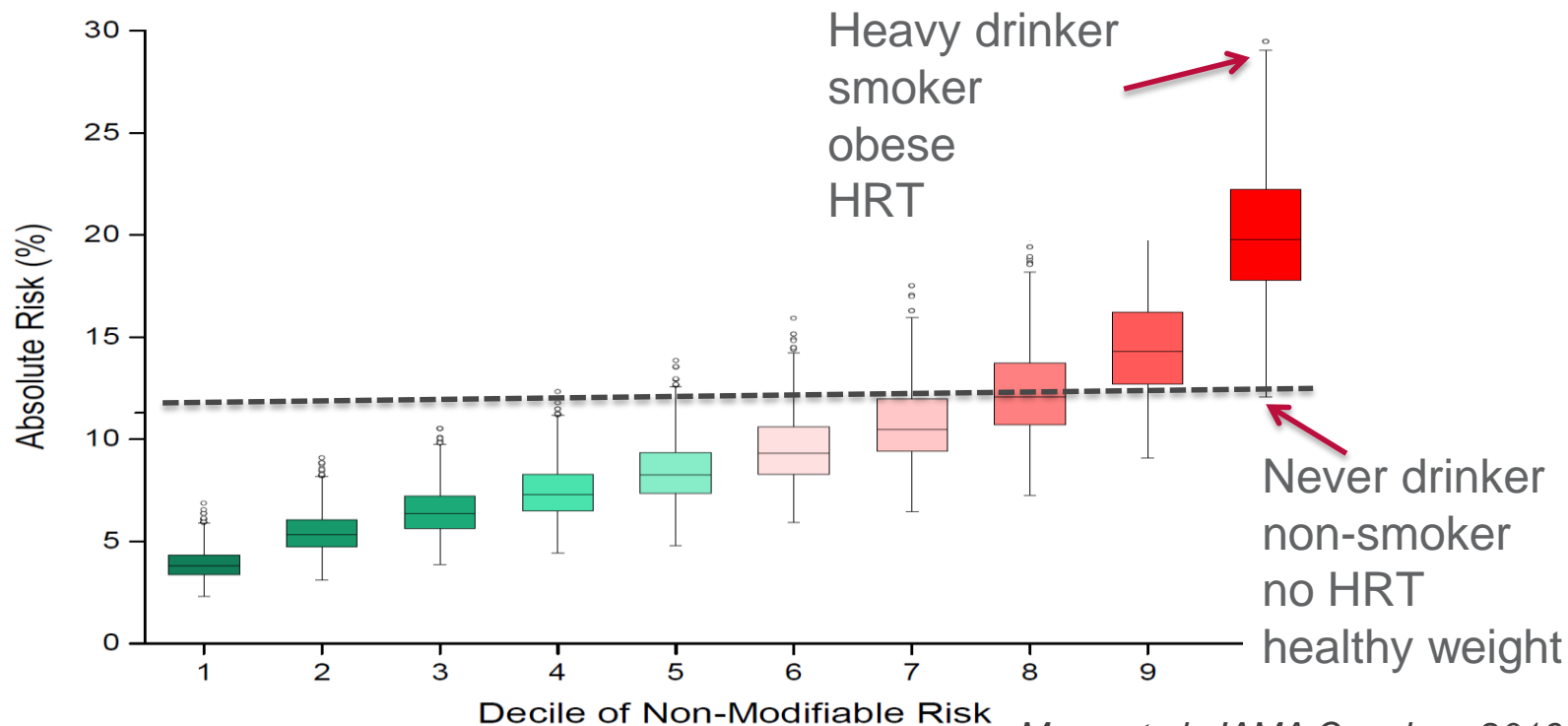


Projected lifetime risk of breast cancer, US Caucasian



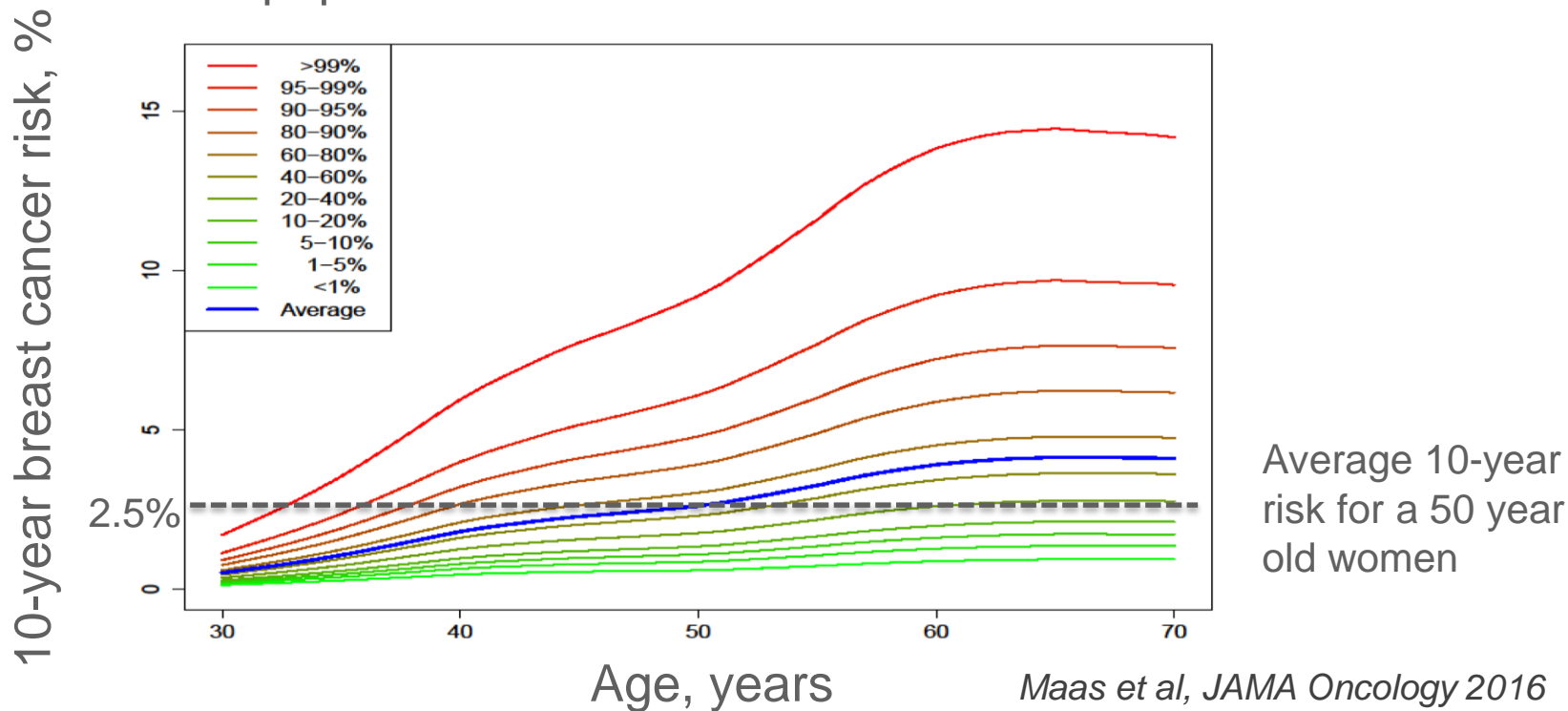
Changes in lifestyle may benefit women at higher non-modifiable risk most

Distribution of modifiable risk by deciles of non-modifiable risk



Women in different risk strata reach risk threshold at different ages

10-year risk of breast cancer by age for women in different risk strata in a population of US Caucasian women



Conclusions

- We have developed a flexible synthetic approach for risk model building (iCARE R package)
- A breast cancer model including risk factors and PRS is well calibrated in a UK population
- Current levels of risk stratification could have implications for precision prevention

Acknowledgments

DCEG, NCI, USA

Nilanjan Chatterjee (Hopkins)

Paige Maas (FaceBook)

Jianxin Shi

David Check

Amber Wilcox

Stephen Chanock

ICR, UK

Nick Orr

Mark Brook

Tony Swerdlow

Burak Gunsoy (GSK)

BCAC / DRIVE / PRESPECTIVE

Doug Easton, Antonis Antoniou, Paul

Pharoah, Nasim Mavaddat, Kyriaki

Michailidou (Cambrige)

Peter Kraft, David Hunter (Harvard)

Sara Lindström (U of Washington)

Jacques Simard (Laval University)

Marjanka Schmidt (NKI)

Jenny Chang-Claude (Heidelberg)

Per Hall (Karolinska)

Fergus Couch (Mayo Clinic)