genetica

Humangenetisches Labor & genetische Beratungsstelle

Human Breast Cancer: Genetic Testing and Counselling

Molecular Diagnostics 2021, Symposium
Zürich, 31. Mai 2021

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Medizinische Genetik FMH u. FAMH
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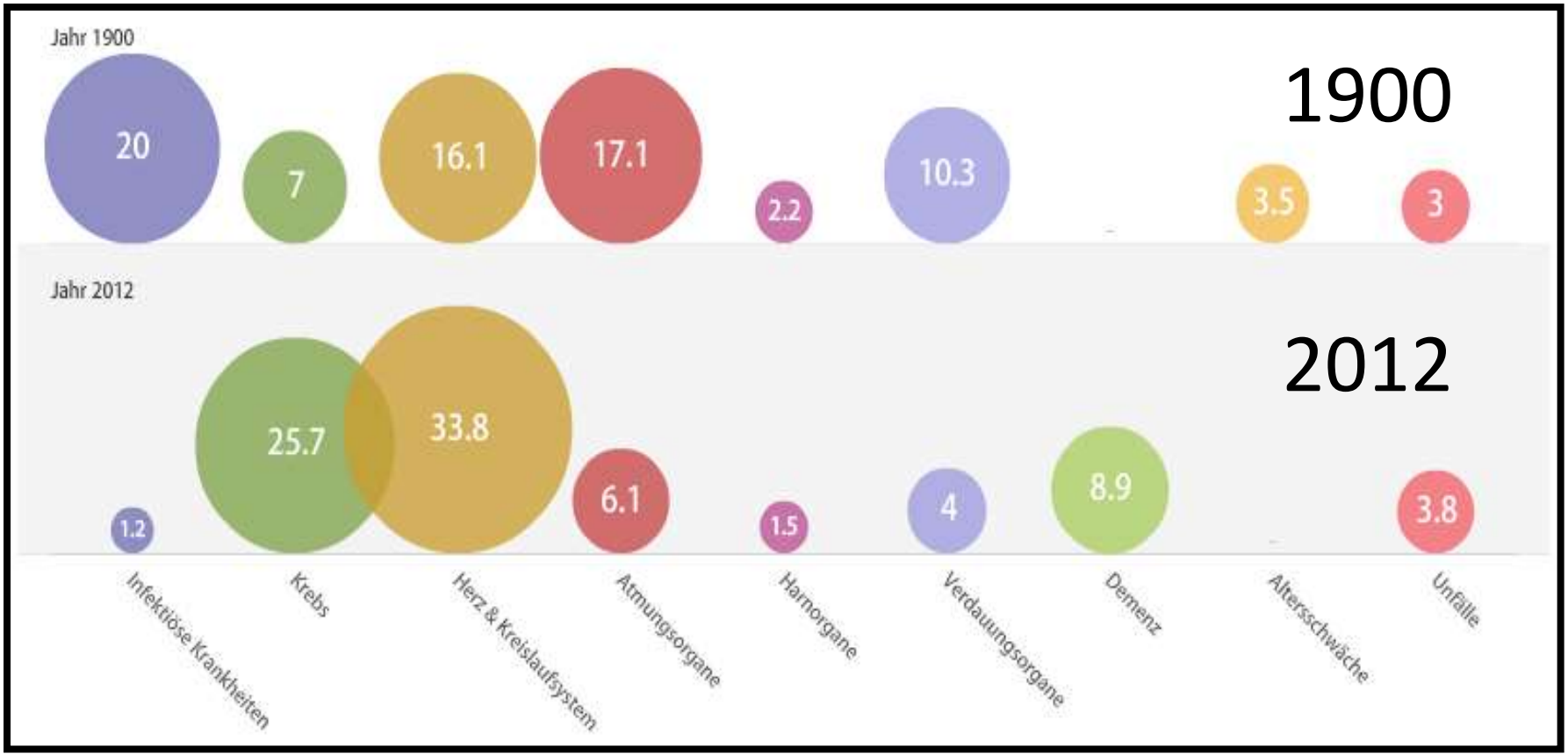
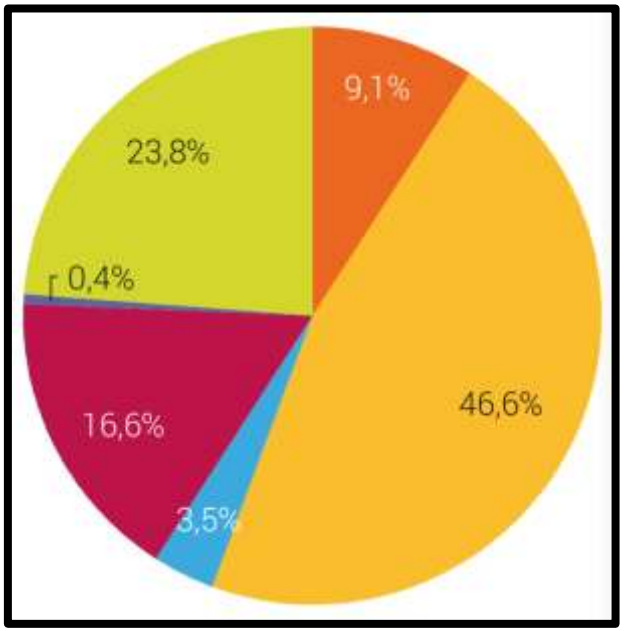
Causes of death in Switzerland

Infectious diseases Cancer

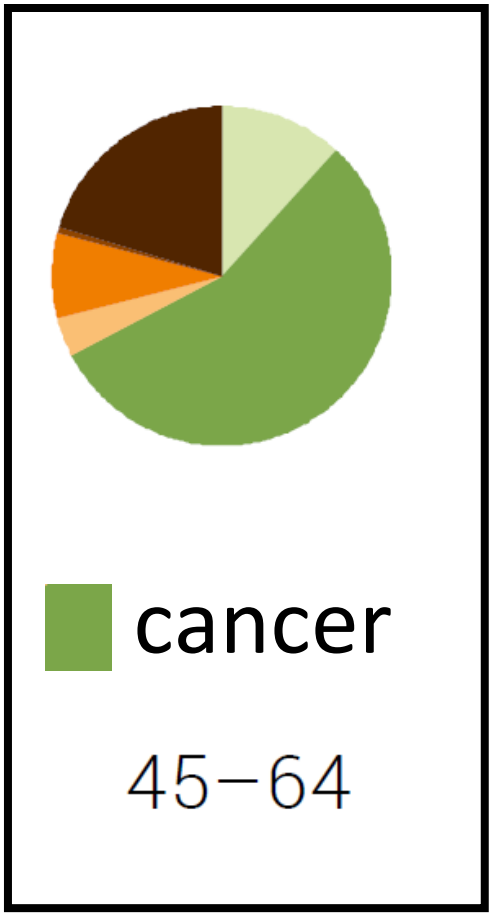


blog.derbund.ch, Bundesamt für Statistik (BfS)

- Years of potential life lost <75 years, women 2017



cancer



www.bfs.admin.ch
www.nicer.org

Breast cancer

>1‘300 women die of breast cancer

9.2% of all years of potential life lost
(all infectious diseases: 1.3%)

https://www.obsan.admin.ch/de/indikatoren/verlorene-potenzielle-lebensjahre (2018 – women, below 75 years)

www.bfs.admin.ch
www.nicer.org

First scientific report of hereditary breast cancer

	Née en	A eu sa fille en	Est morte en	A eu sa fille à l'âge de	A encore vécu	Est morte à l'âge de
1re génération. Mme Z.	1728	1763	1788	35 ans.	25 ans.	60 ans.
2e génération. Mme C.	1763	1780	1814	17 ans.	34 ans.	51 ans.
3e génération. Mme M.	1780	1805	1854	25 ans.	12 ans.	37 ans.
4e génération. Mme N.	1805		1859			49 ans.

- P. P. Broca, Traite des Tumeurs (P. Asselin, Paris, 1866).
- King MC. Science. 2014 Mar 28;343(6178):1462-5.

Heritability of breast cancer

	heritability (%)
Thyroidea	53
Breast	**25**
Colon	13
Lung	8
Leukemia	1

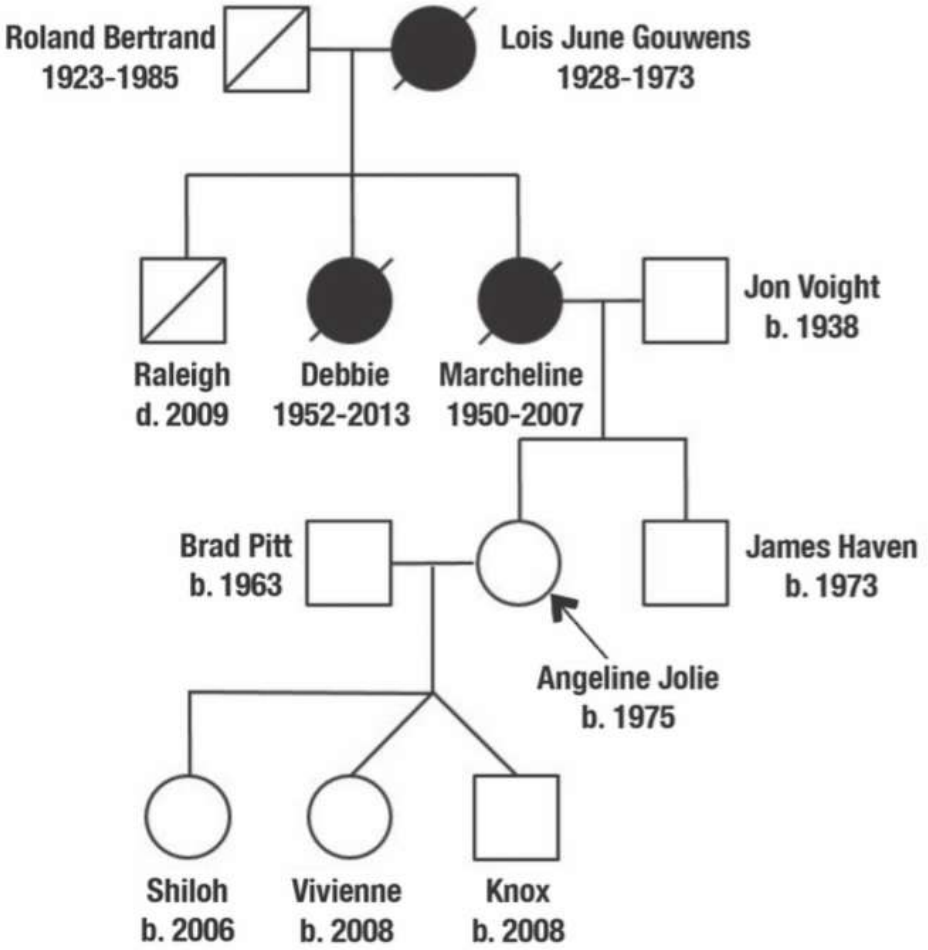
(700‘000 Tumoren; 9.6 Millionen Personen)

Czene et al., Int J Cancer. 2002;99(2):260-6
Swedish Family-Cancer Database

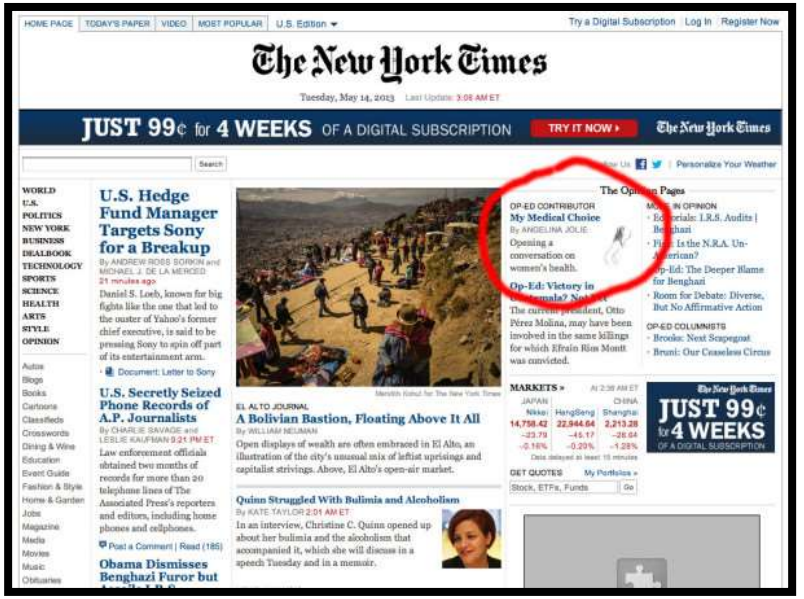
BRCA1: 1994 / *BRCA2*: 1995

Miki Y et al. A strong candidate for the breast and ovarian cancer susceptibility gene BRCA1. Science. 1994 Oct 7;266(5182):66-71.

Wooster, R et al. Identification of the breast cancer susceptibility gene BRCA2. Nature 378, 789–792 (1995)



Angelina Jolie: **May 14, 2013**

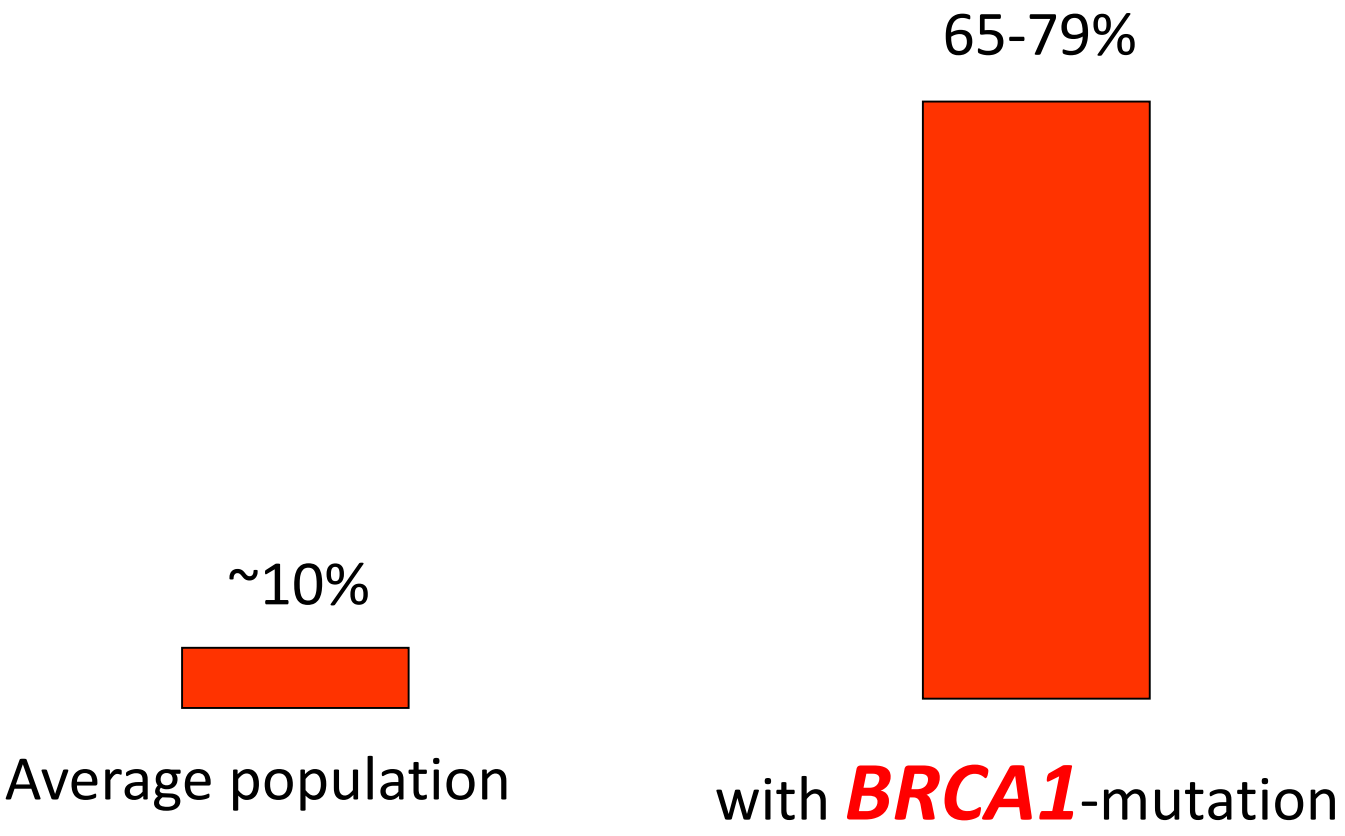


https://www.mygenecounsel.com/celebrities-share-their-breast-cancer-stories/

- For any woman reading this, I hope it helps you to know you have options. I want to encourage every woman, especially if you have a family history of breast or ovarian cancer, to seek out the information and medical experts who can help you through this aspect of your life, and to make your own informed choices.

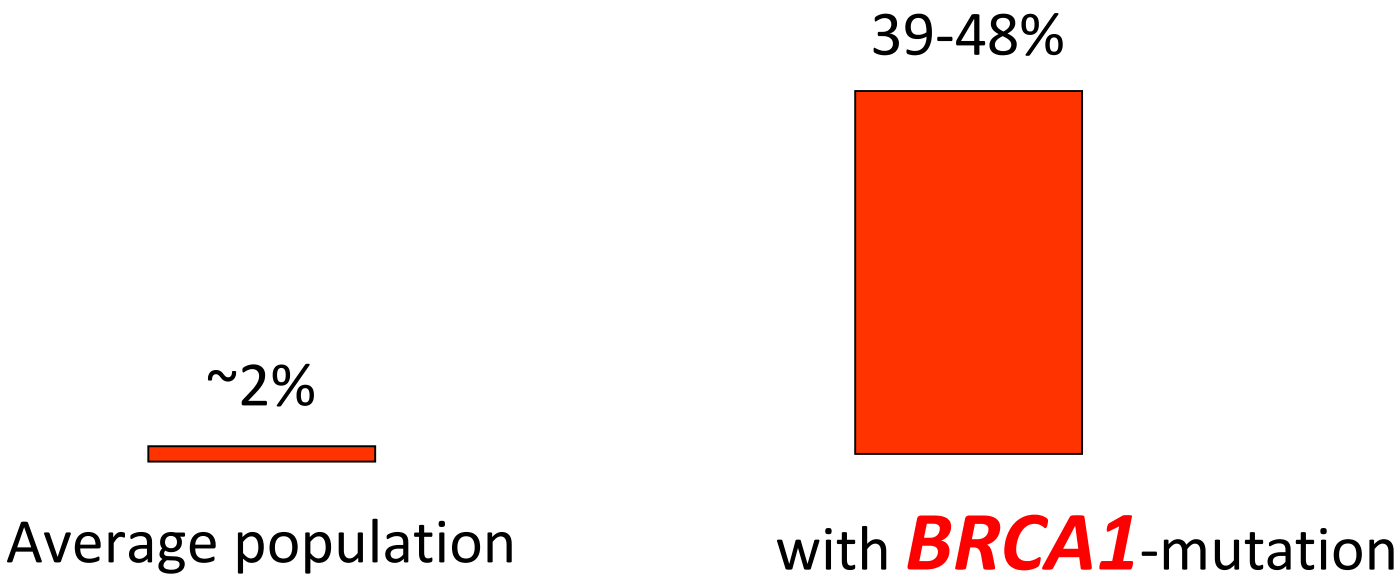
https://www.nytimes.com/2013/05/14/opinion/my-medical-choice.html

Risk for female breast cancer before the age of 80 years



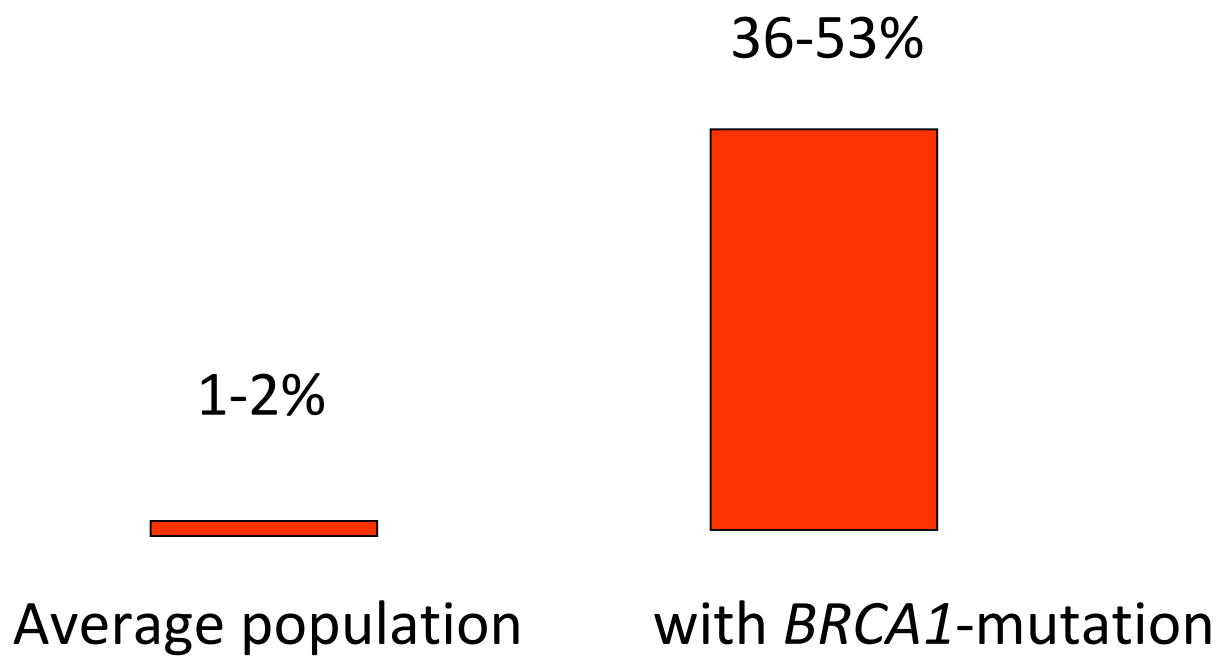
Kuchenbaecker KB, JAMA. 2017 Jun 20;317(23):2402-2416.

Breast cancer risk < 50 years

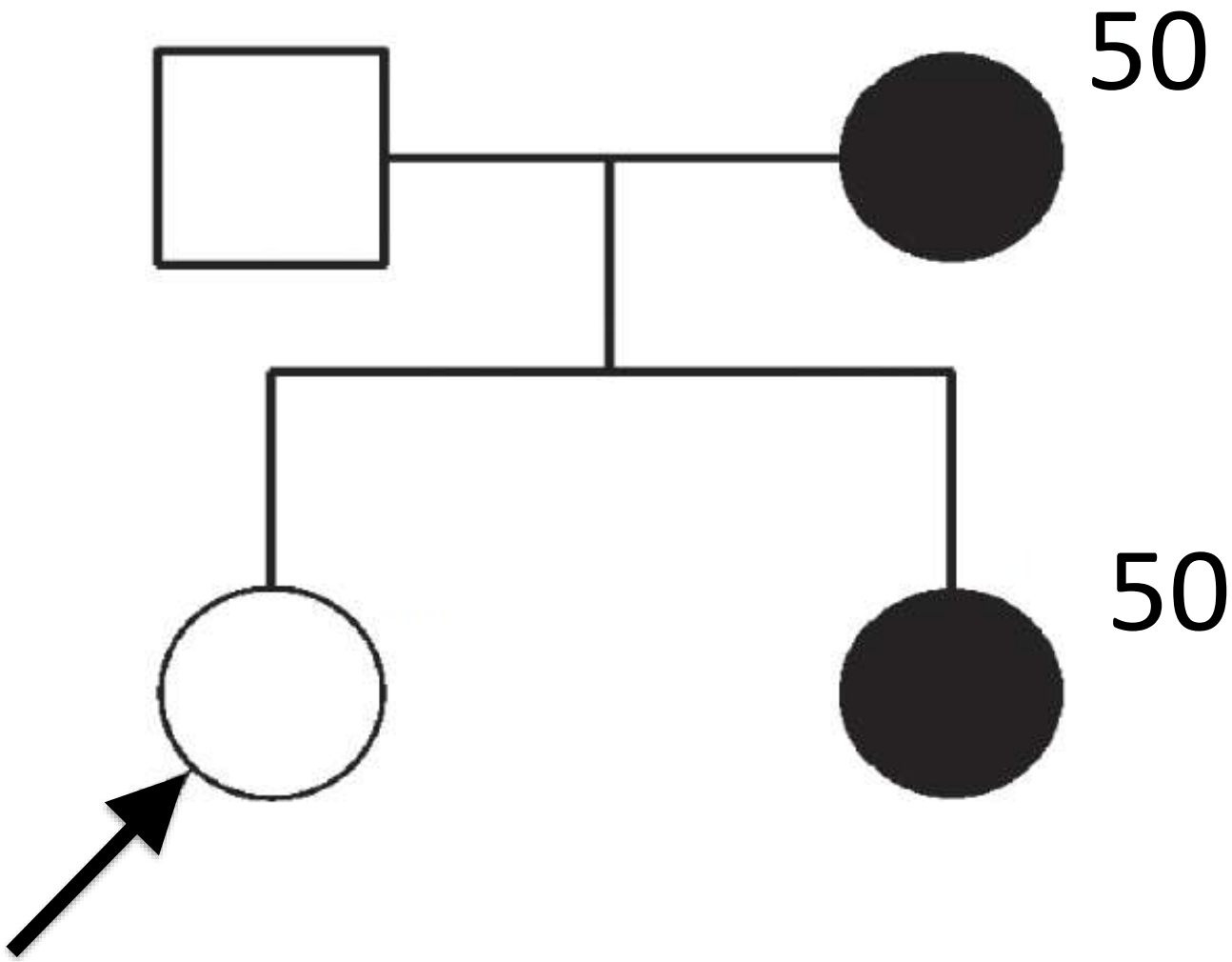


Kuchenbaecker KB, JAMA. 2017 Jun 20;317(23):2402-2416.

Risk for ovarian cancer before the age of 80 years



Kuchenbaecker KB, JAMA. 2017 Jun 20;317(23):2402-2416.


50
50

BRCA1/2 mutation prevalence in families

≥3x breast cancer >50 J.	3.7%
1x breast cancer ≤35 J.	13.7%
2x breast cancer ≤50 J.	17.5%
1x bilateral breast cancer ≤50 J.	22.7%
≥3x breast cancer ≤50 J.	30.4%
≥2x ovarian cancer	41.9%

Based on 21‘401 families

Kast K, Journal of Medical Genetics 2016;53:465-471.

Inclusion criteria for *BRCA1/2* testing

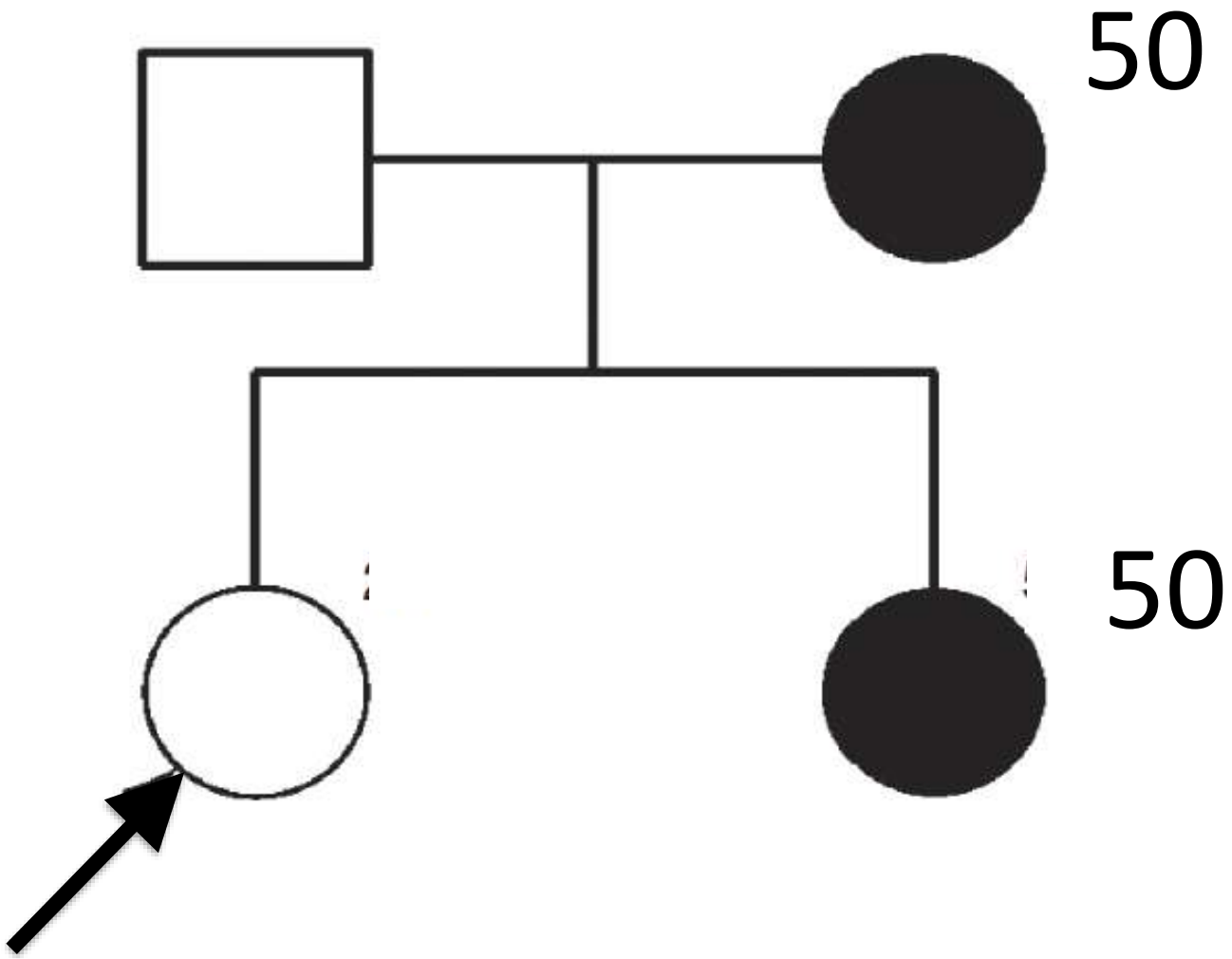
Swiss guidelines for counseling and testing for genetic predisposition to breast and ovarian cancer

Pierre O. Chappuis[1], Barbara Bolliger[2*], Nicole Bürki[3*], Katharina Buser[4*], Karl Heinimann[5*], Christian Monnerat[6*], Rudolf Morant[7*], Olivia Pagani[8*], Lucien Perey[9*], Manuela Rabaglio[10*], Sheila Unger[11*]; on behalf of the Swiss Group for Clinical Cancer Research (SAKK) Network for Cancer Predisposition Testing and Counseling

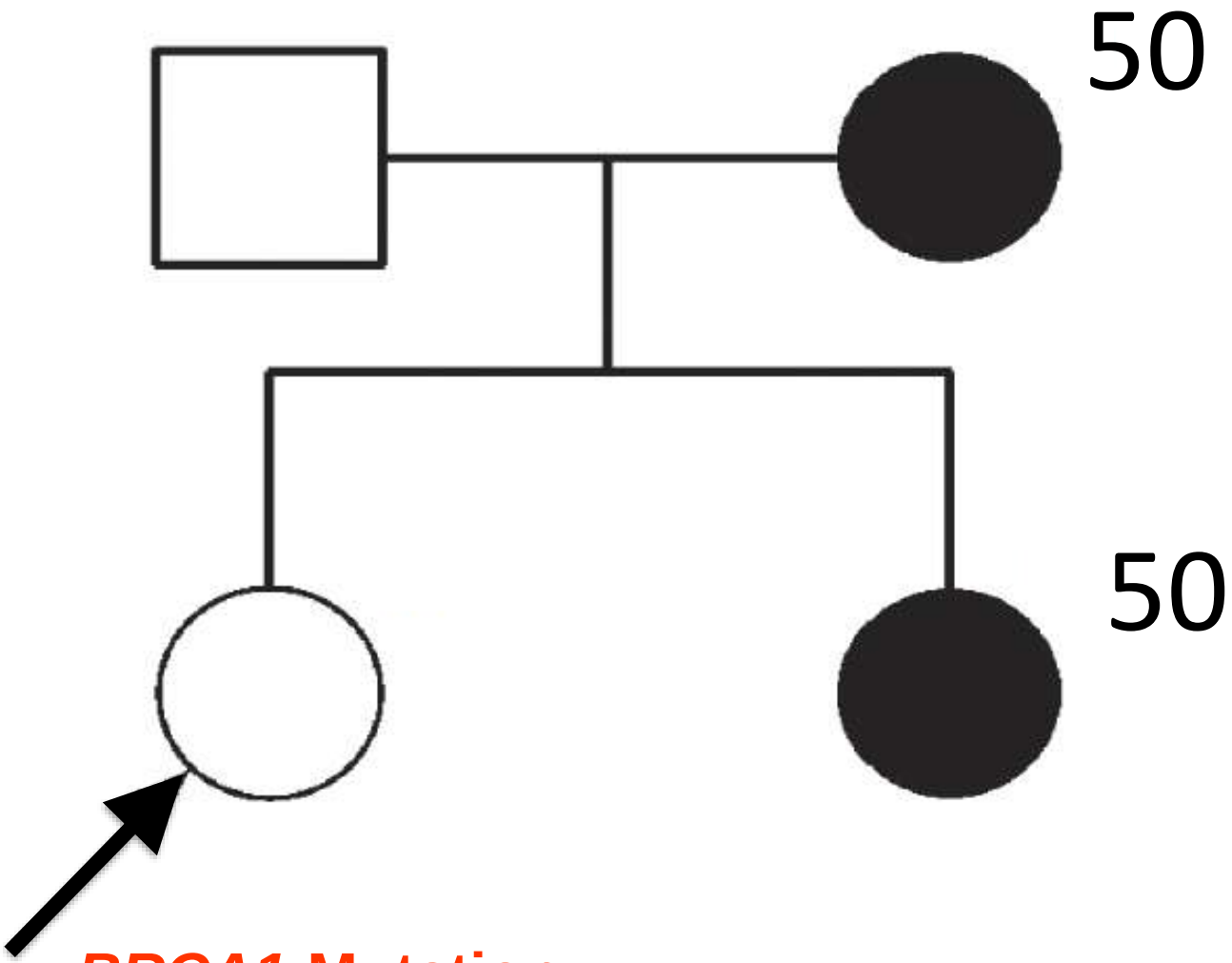
„Age at diagnosis ≤ 50 years, ... or with only 1 close relative with breast cancer ≤ 50 years“

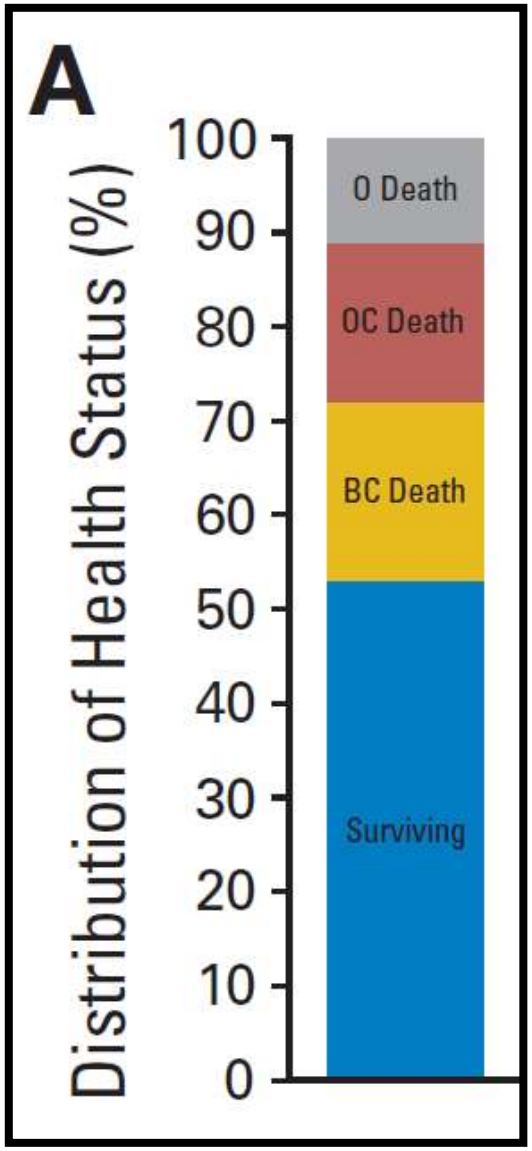
https://www.sakk.ch/sites/default/files/2018-11/Swiss_guidelines_for_counseling_and_testing_for_genetic_predisposition_to_breast_and_ovarian_cancer.pdf

BRCA1-Mutation



***BRCA1*-Mutation**

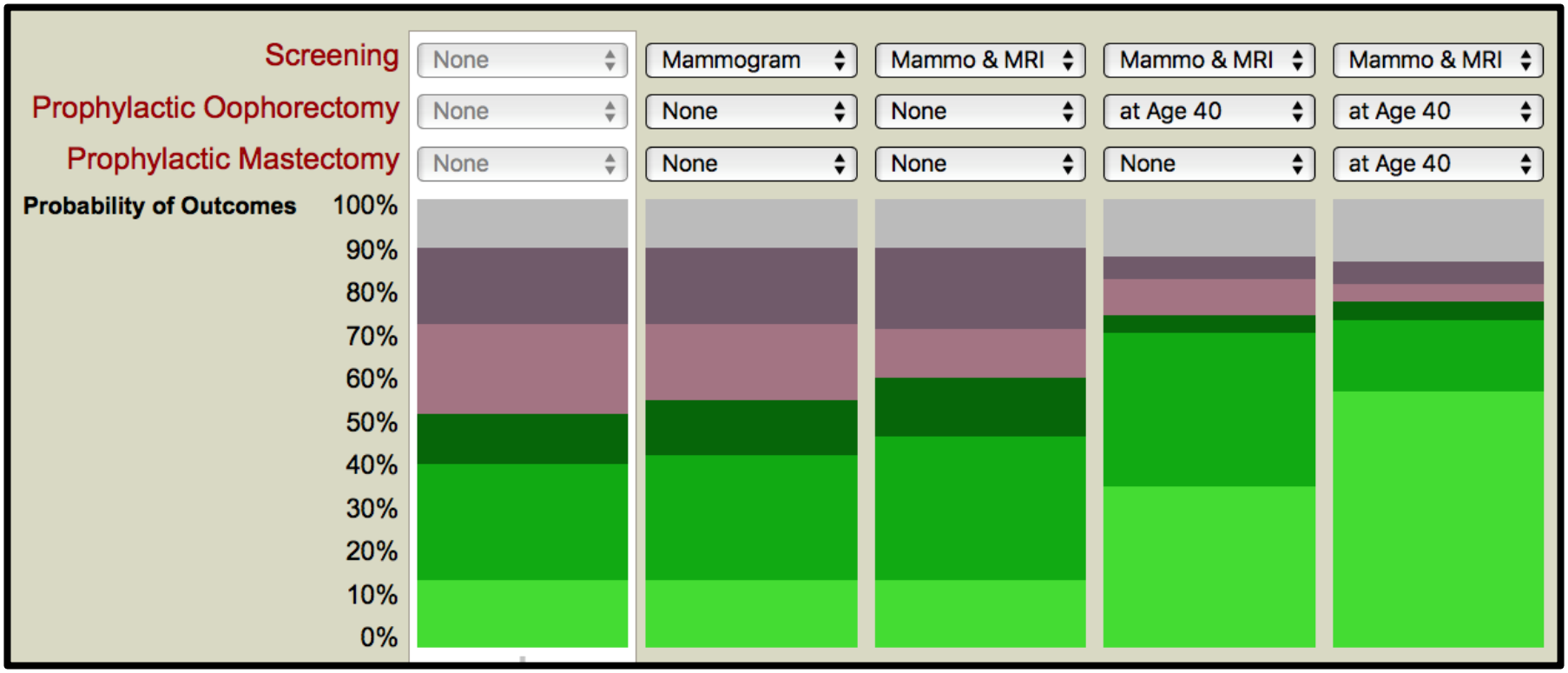




Survival probability in 25-year-old women with mutations in BRCA1 by age 70

Kurian AW et al., J Clin Oncol. 2010 Jan 10;28(2):222-31

Survival probability after different risk-reducing strategies



http://brcatool.stanford.edu/brca.html

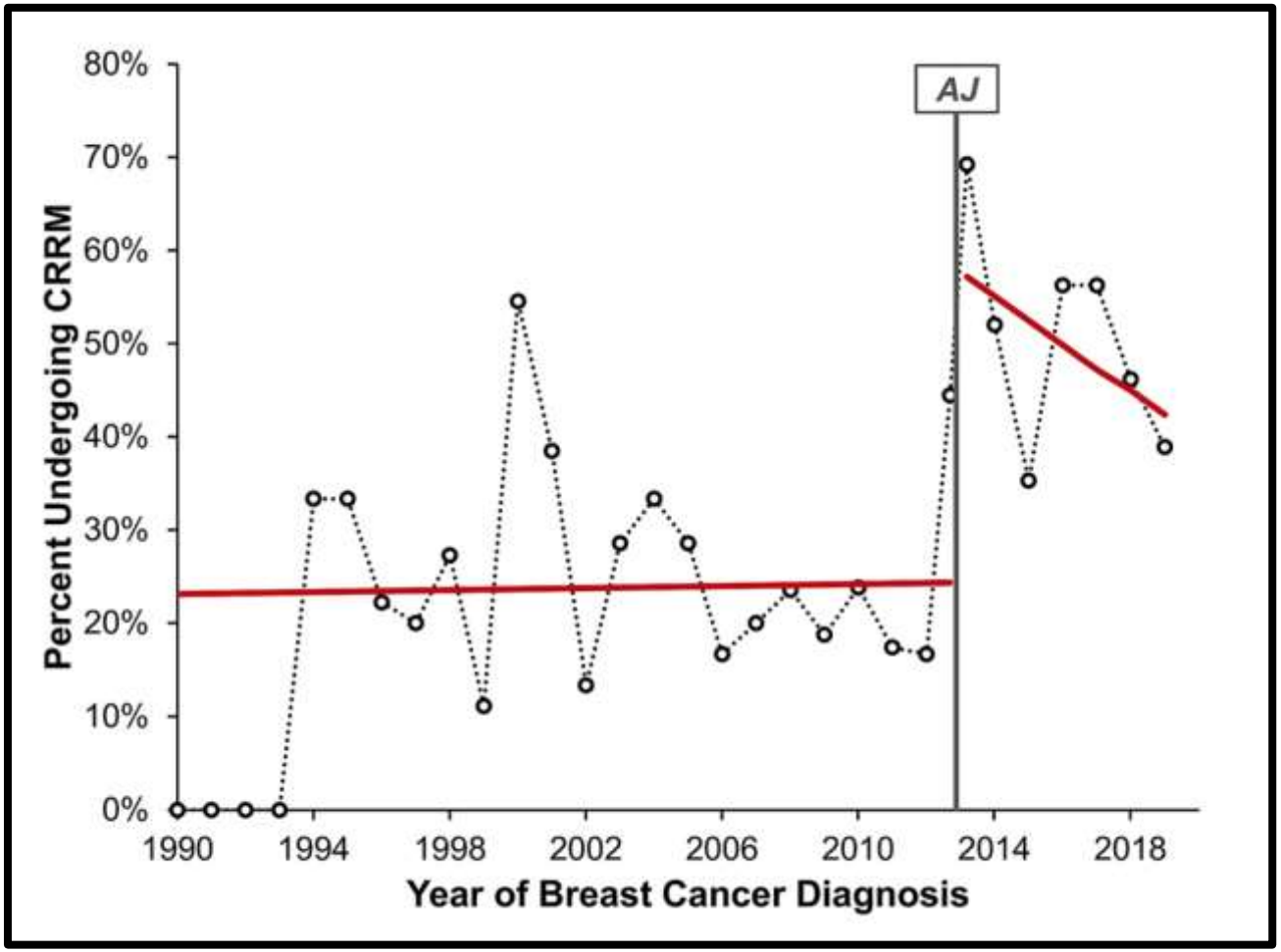
Referenzdokument „Überwachungsprotokoll“

zu Artikel 12d Absatz 1 Buchstabe d der Krankenpflege-Leistungsverordnung (KLV) – Stand 01/2021

BRCA1/2 Mutation: MRI 25 – 69, yearly

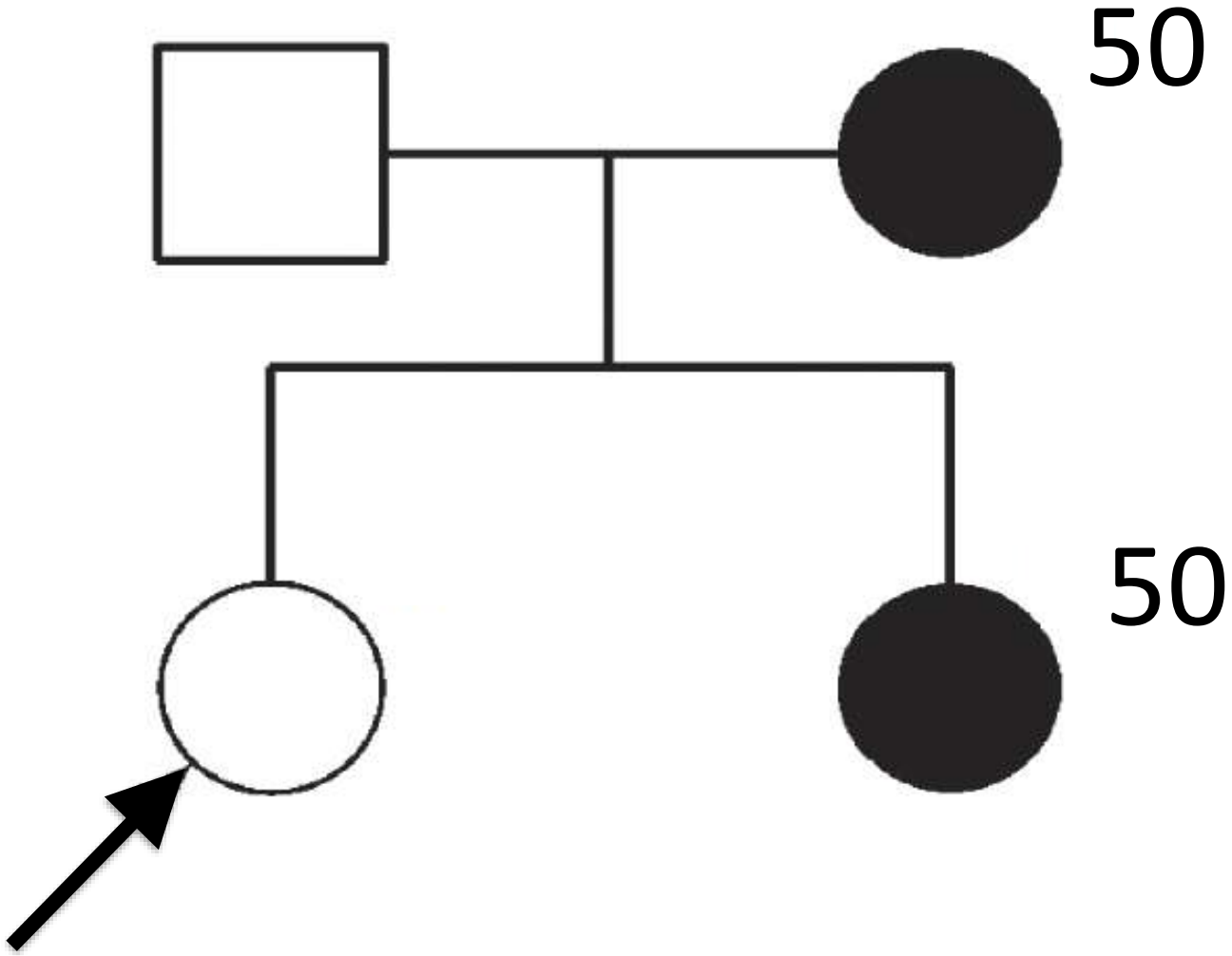
(until 12/2020: only age 30-49)

Angelina Jolie effect:
Contralateral risk-reducing mastectomy



Basu NN et al., Sci Rep. 2021 Feb 2;11(1):2847.

No *BRCA1/2*-Mutation detected



Age of onset of first relative (yr)			
		50–59	
Age of onset of second relative (yr)			
Age (yr)	50–59	60–69	70–79
29	.009	.006	.005
39	.030	.022	.016
49	.075	.056	.042
59	.138	.105	.081
69	.200	.157	.124
79	.245	.195	.158

Claus EB et al., Cancer. 1994 Feb 1;73(3):643-51.

Referenzdokument „Überwachungsprotokoll“

zu Artikel 12d Absatz 1 Buchstabe d der Krankenpflege-Leistungsverordnung (KLV) – Stand 01/2021

Lifetime risk 17-29%:

- Mammography 40-59, yearly
- Mammography 60-75, every 2 years

Lifetime risk ≥ 30%:

- MRI 30-59, yearly*
- MRI 60-69, every 2 years*

*if high breast density (ACR C or D)

High-risk breast cancer surveillance with MRI
German consortium for HBOC

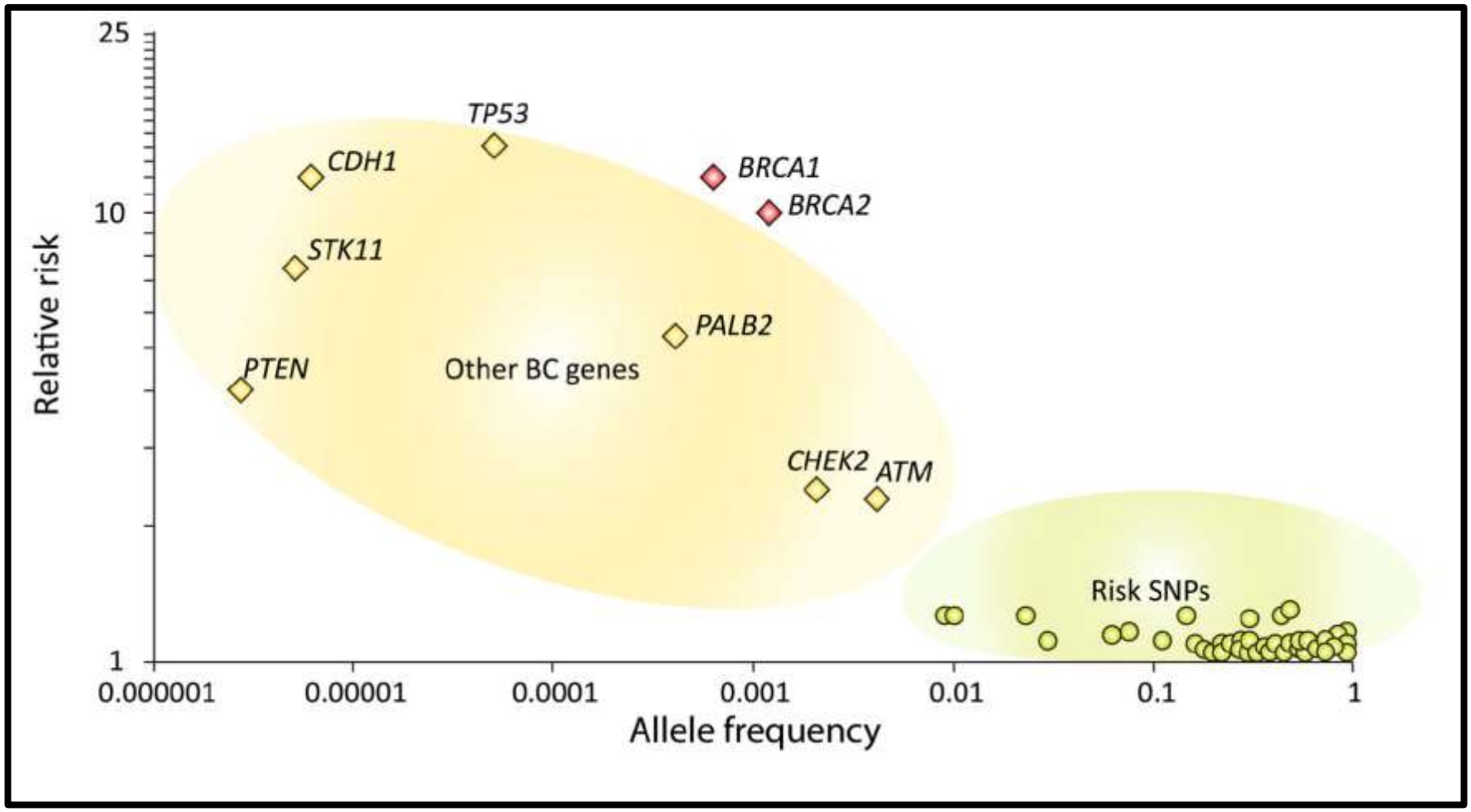
30-39 years	*Detection rate*	*PPV*
BRCA1 carriers	4.32 %	29.4 %
„high risk“	0.29 %	2.8 %

Bick U. Breast Cancer Res Treat. 2019 May 175(1):217-228.

***BRCA1, BRCA2*, ATM, BRIP1, CDH1, CHEK2, EPCAM, MLH1, MSH2, MSH6, PALB2, PMS2, PTEN, RAD51C, RAD51D, STK11, TP53, ……..**

https://www.konsortium-familiaerer-brustkrebs.de/betreuungskonzept/molekulare-diagnostik/truriskr-genpanel-analyse/

Risk penetrance profile for genetic susceptibility factors for breast cancer

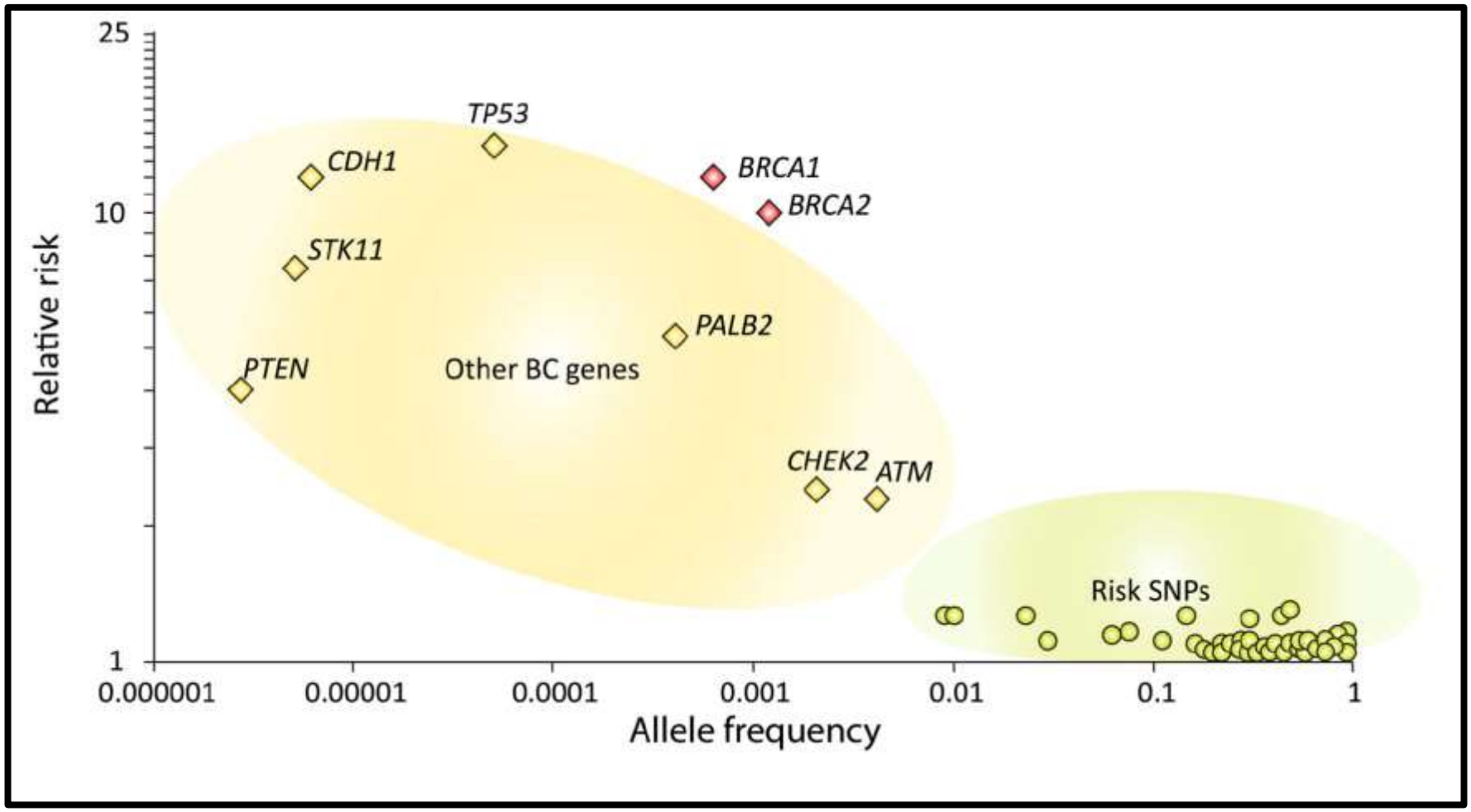


Turnbull C et al., Nat Genet. 2018 Sep;50(9):1212-1218.

Cancer	Opportunities for targeted intervention		
	Screening (7)	Chemoprevention (8)	Surgical prophylaxis (9)
Breast	+++	+	+++
Colorectal	++++	+++	++
Prostate	+	-	-
Lung	+	-	-
Ovarian	+	-	+++
Renal	+	-	-
Gastric	+	-	+
Pancreas	+	-	-
Oesophagus	+	-	-
Melanoma	++	-	-
Uterus	+	-	++++
Testicular	+	-	-

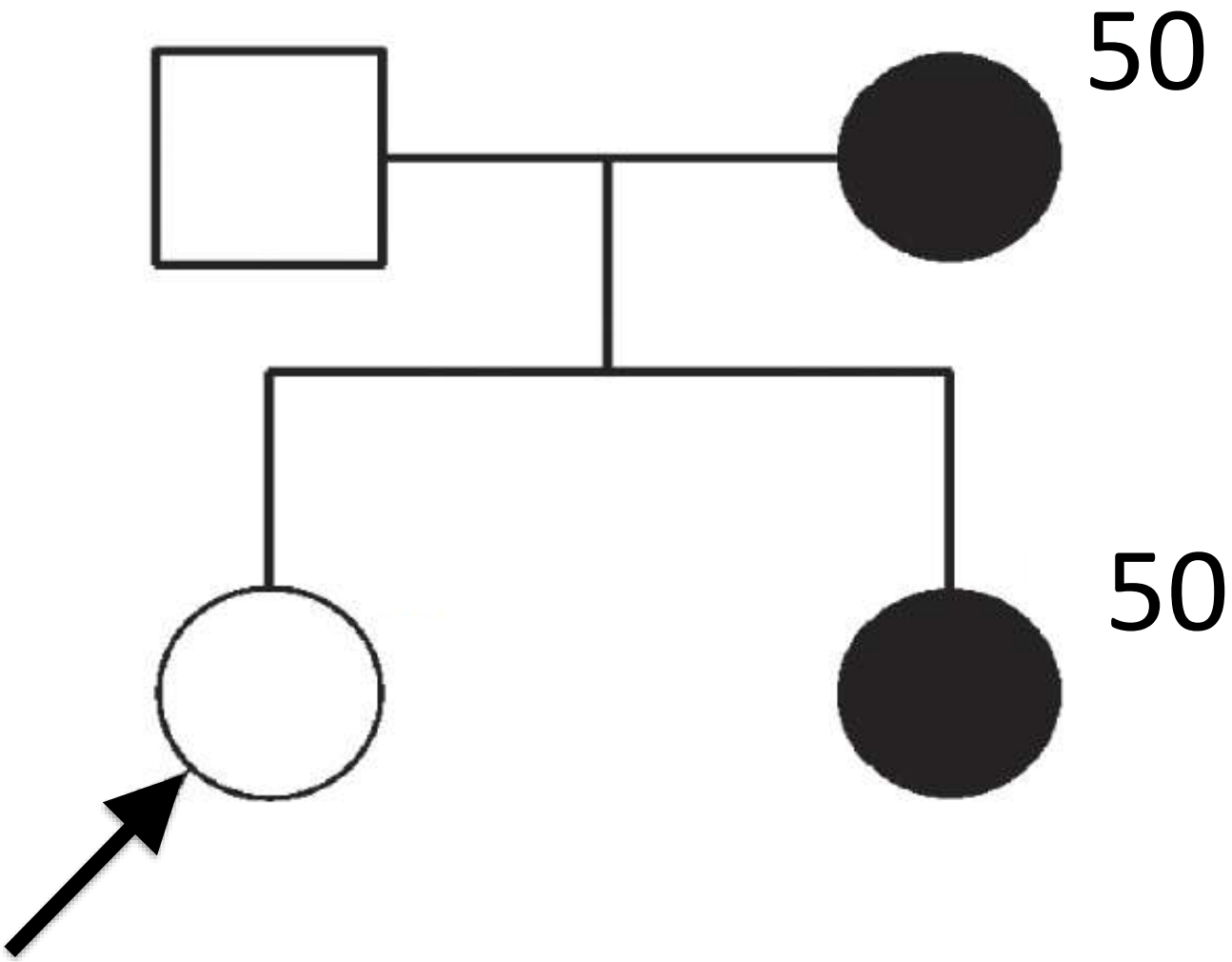
Turnbull C et al., Nat Genet. 2018 Sep;50(9):1212-1218.

Risk penetrance profile for genetic susceptibility factors for breast cancer

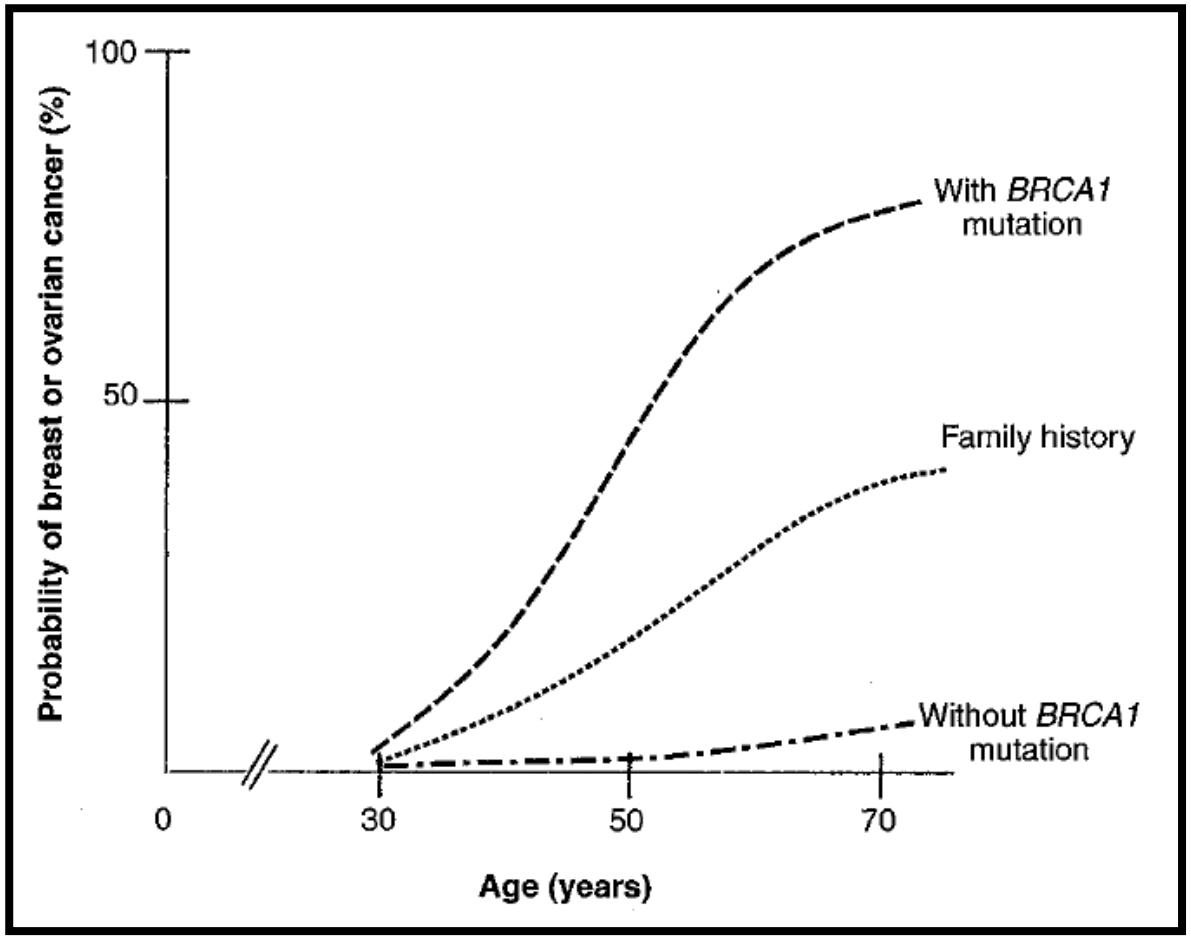


Turnbull C et al., Nat Genet. 2018 Sep;50(9):1212-1218.

BRCA1-Mutation

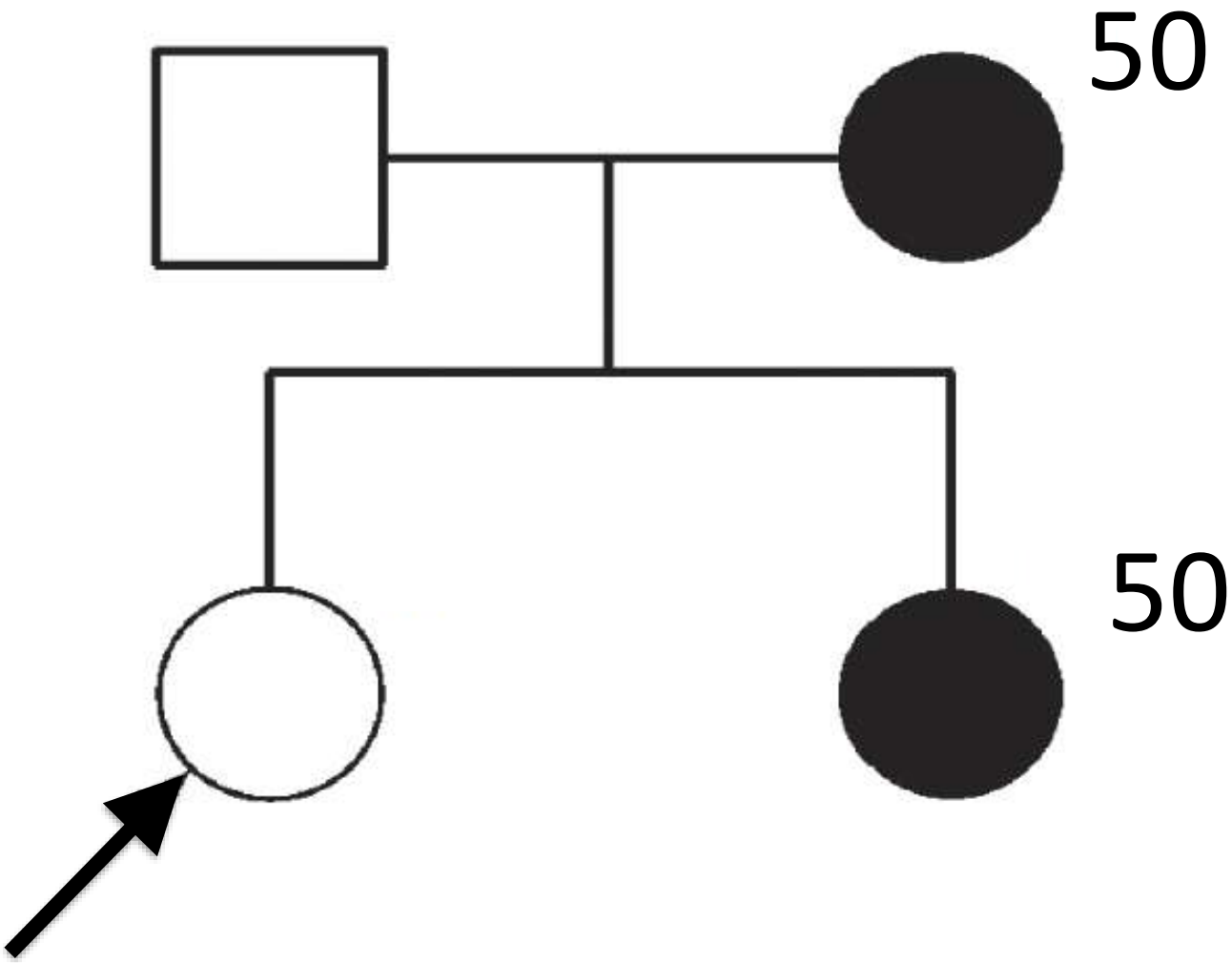


BRCA1-Mutation detected or not detected



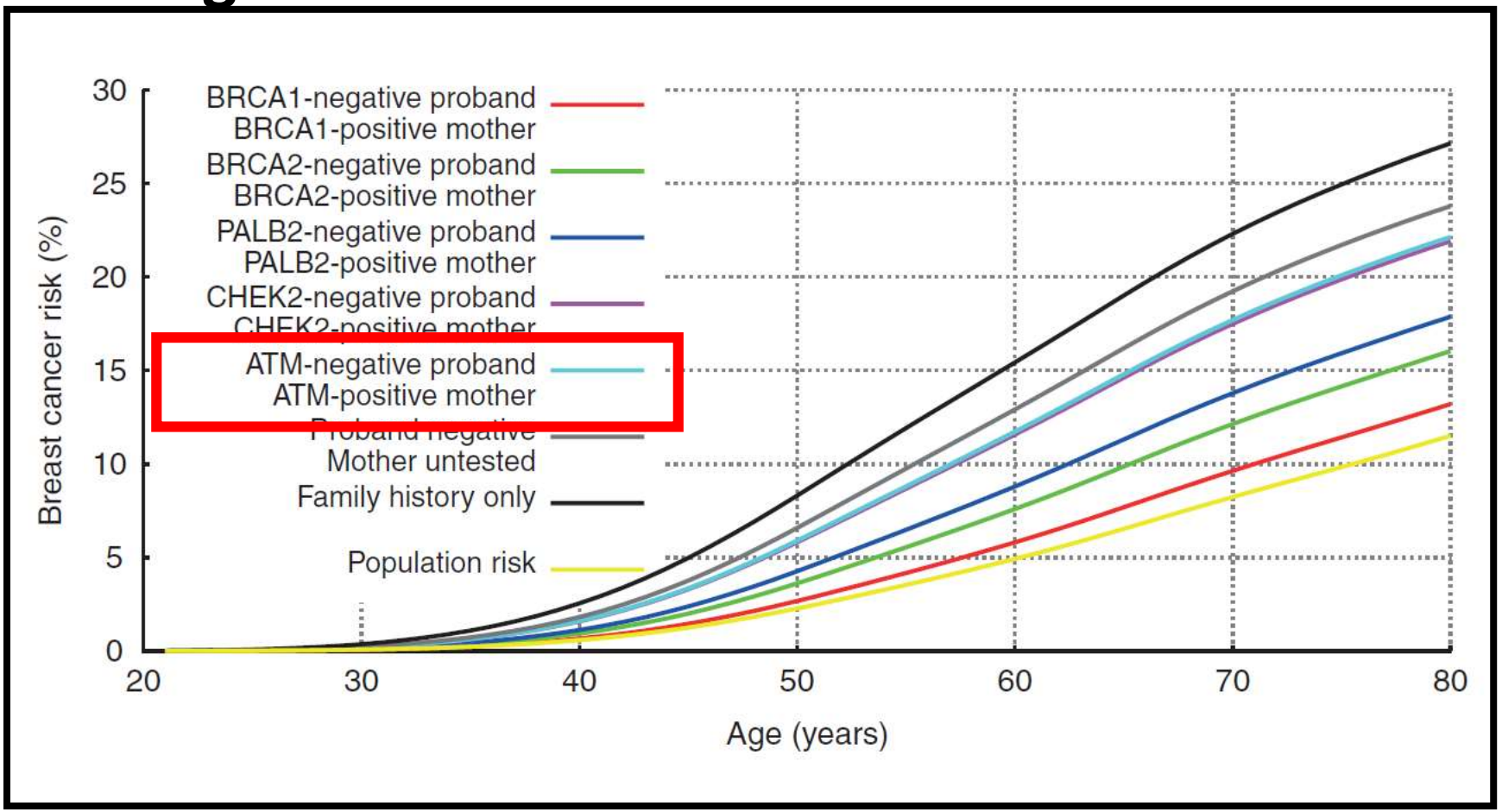
Ponder B. Science. 1997 Nov7;278(5340):1050-4.

ATM-mutation



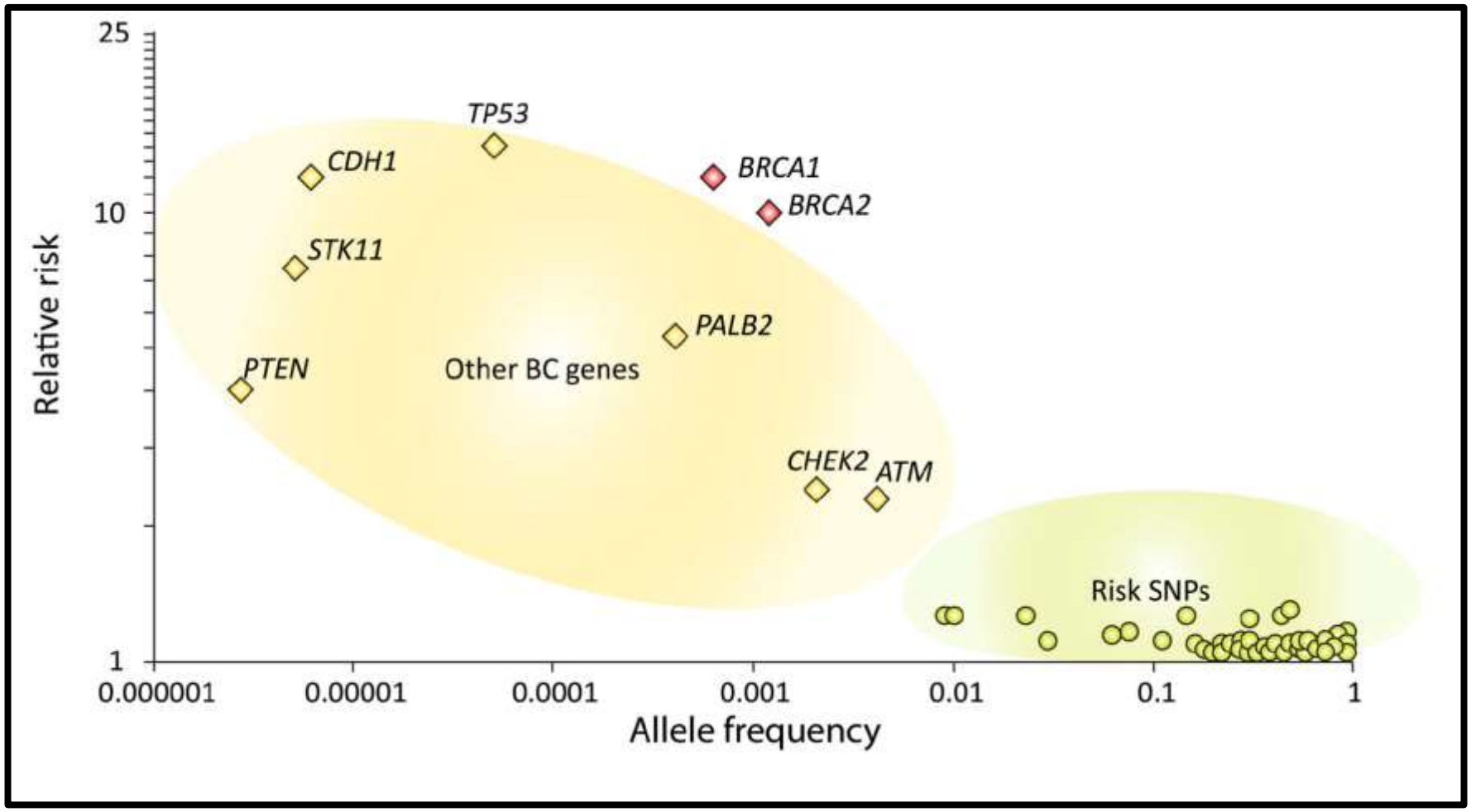
ATM-mutation not detected

BOADICEA breast cancer risk for negative testing



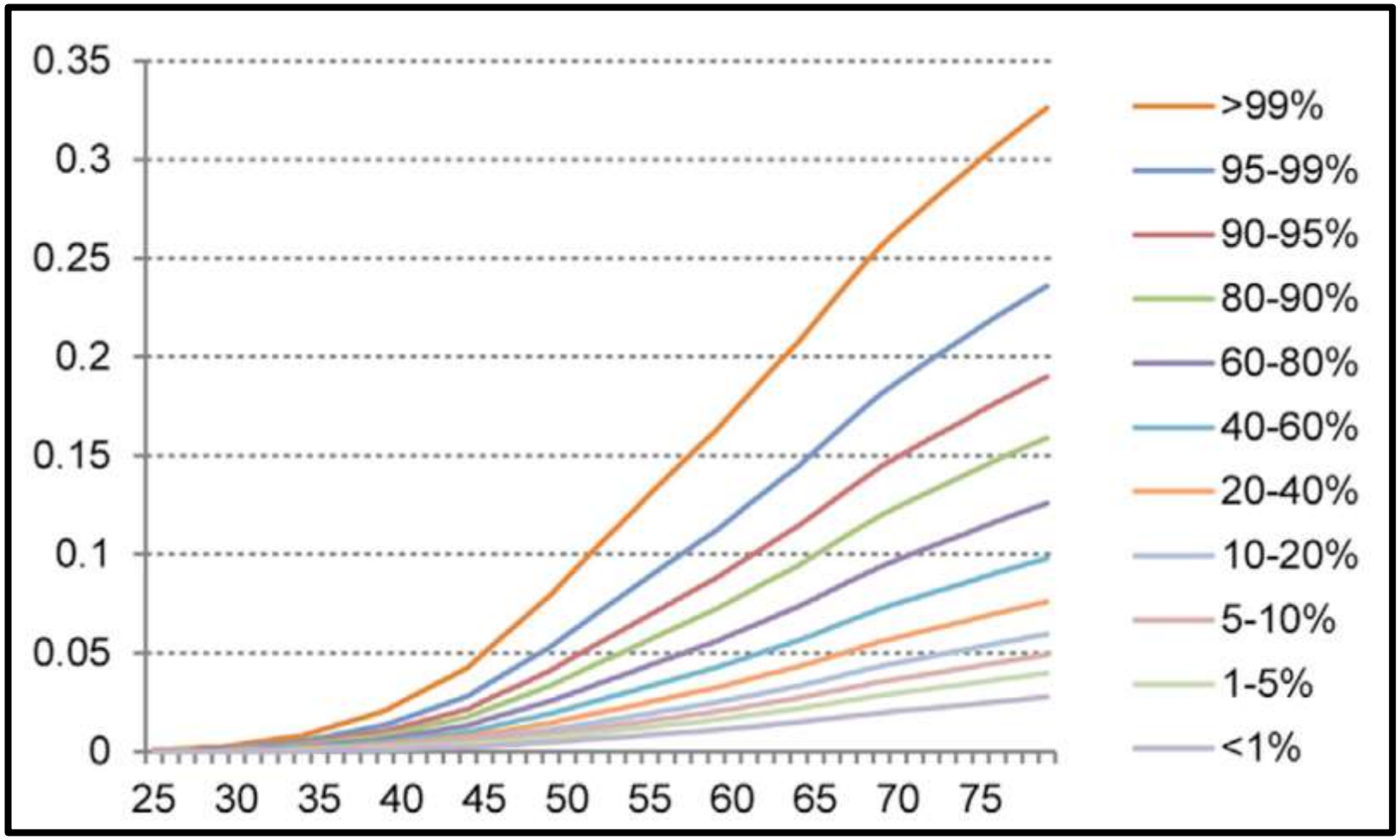
Lee AJ et al., Genet Med. 2016 Dec;18(12):1190-1198

Risk penetrance profile for genetic susceptibility factors for breast cancer

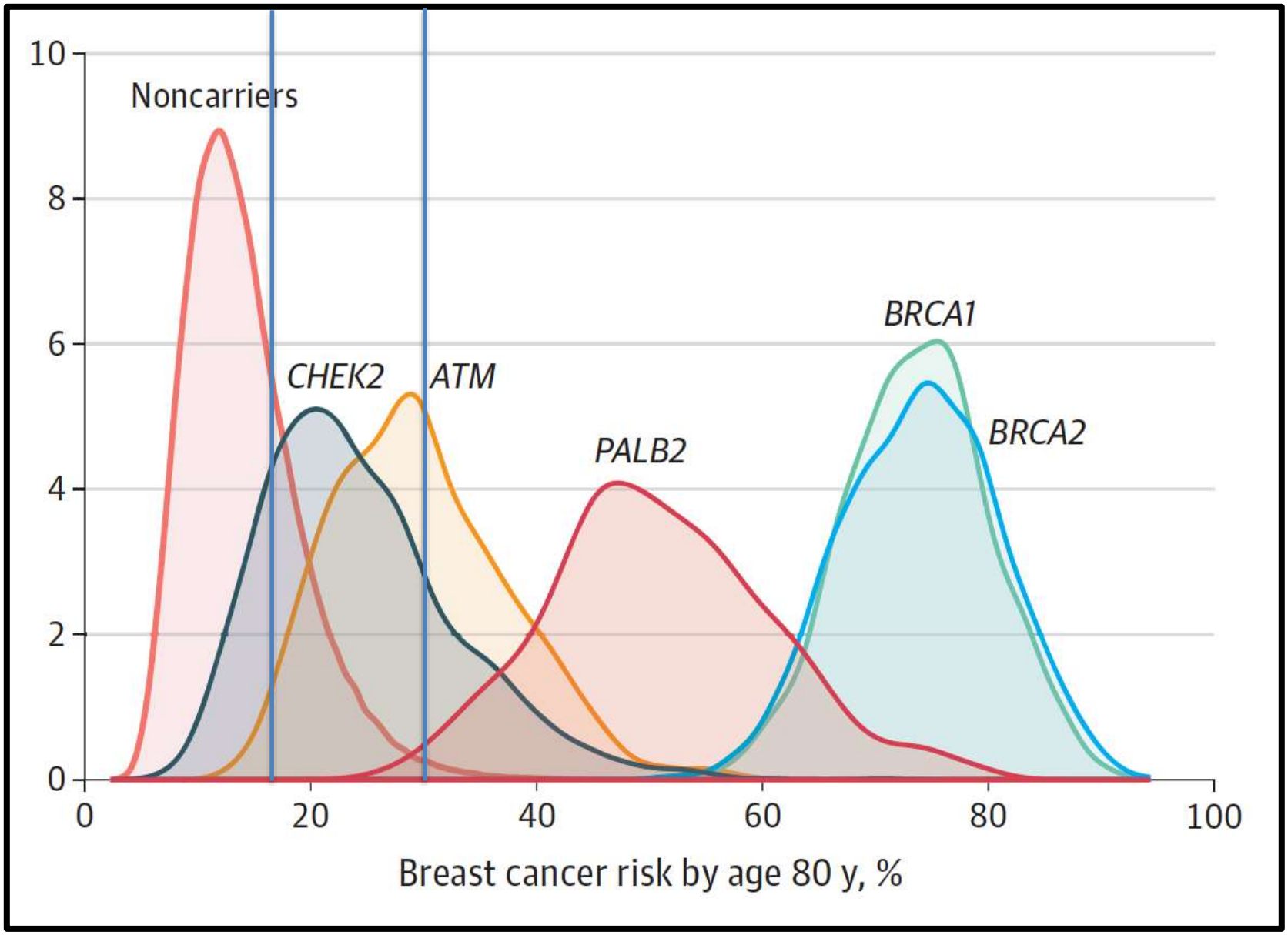


Turnbull C et al., Nat Genet. 2018 Sep;50(9):1212-1218.

Risk of developing breast cancer by percentiles of the 313 SNP polygenic risk scores

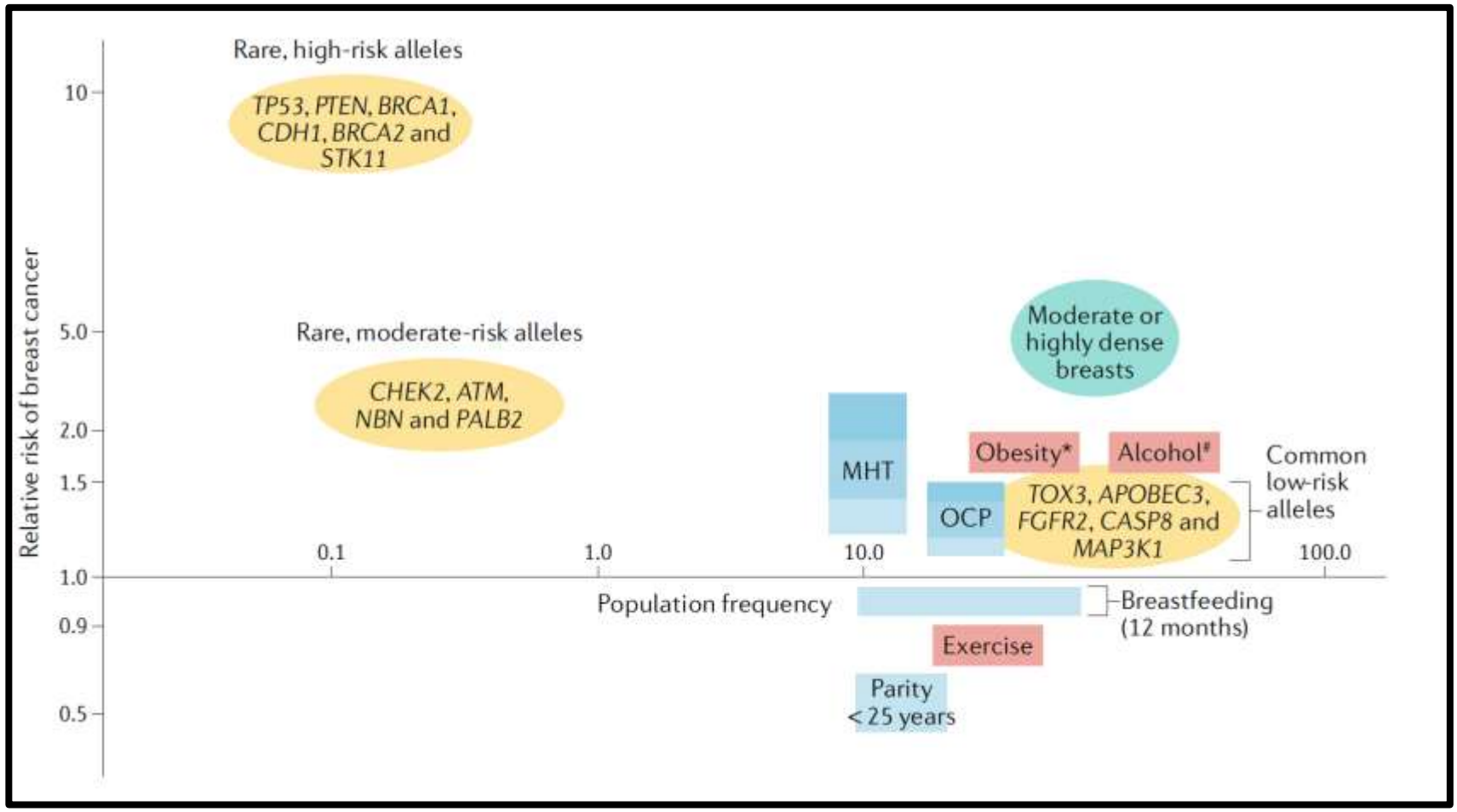


Mavaddat N et al., Am J Hum Genet. 2019 Jan 3;104(1):21-34.



Gallagher S. JAMA Netw Open. 2020 Jul 1;3(7)

Breast cancer risk modifiers and population frequency



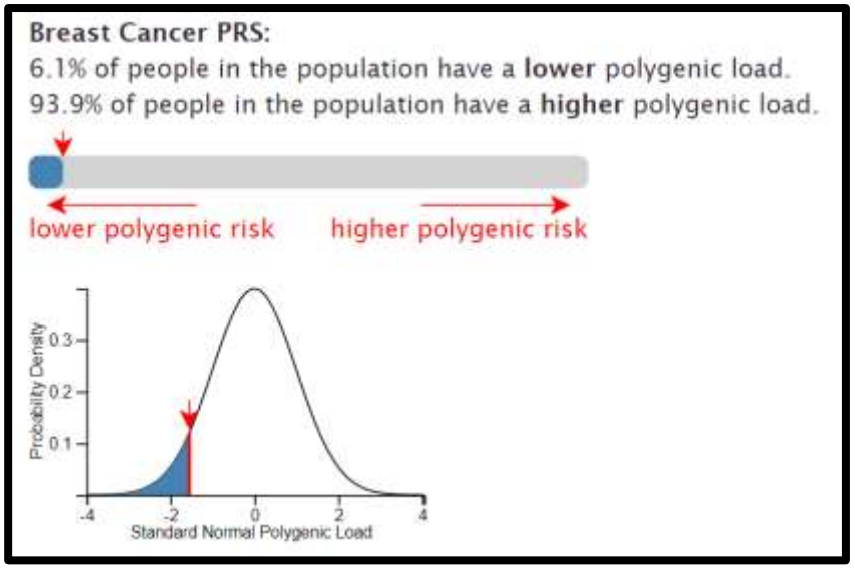
Britt KL, Cuzick J. Nat Rev Cancer. 2020 Aug;20(8):417-436.

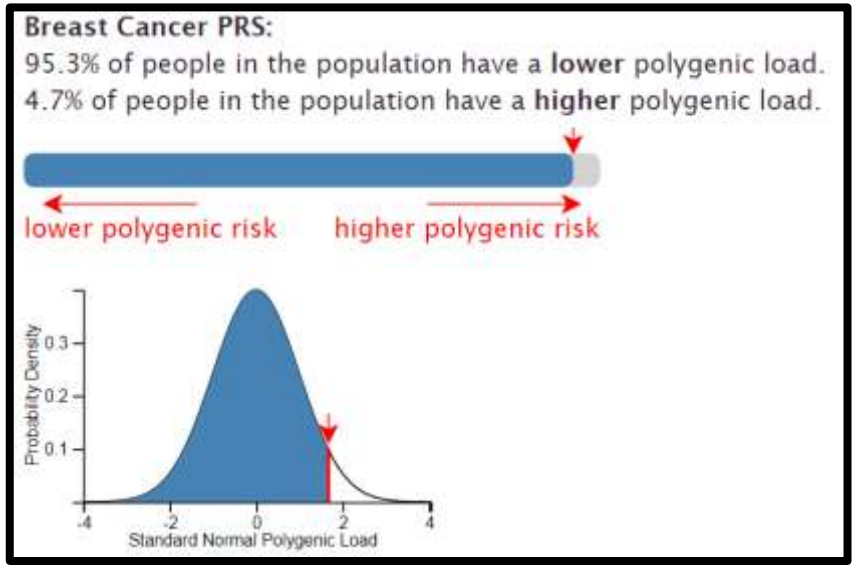
https://www.canrisk.org

Lee A et al., Genet Med. 2019 Aug;21(8):1708-1718.

Carver T et al., Cancer Epidemiol Biomarkers Prev. 2021;30(3):469-473.

- Proband asymptomatic
- Mother breast cancer 50y; sister breast cancer 50y.
- No mutation known in family





Breast cancer risk 13.8% Breast cancer risk 32.2%

https://www.canrisk.org

A personalised approach based on the individual breast cancer risk will result in a more effective breast cancer screening and as a consequence to a reduction of the mortality due to breast cancer

https://cordis.europa.eu/project/id/755394

https://www.mypebs.eu

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www.genetica-ag.ch

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