The Latest in Longevity Medicine: Predictive Genomics

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What is Longevity Medicine?

- The term is a real.
- 158,000,000 results on Google (10/8/23)
- National Academy of Medicine held a conference, *2023 Healthy Longevity Global Innovator Summit*, in Sept 2023.
- The therapeutic race is on between genetic changes, pharmaceuticals and natural compounds.
  - Genetic changes can increase lifespan 4x in the roundworm .
  - TAME trial (Targeting Aging by Metformin)
- Only single interventions studied so far.

What is Longevity Medicine?

- Longevity medicine is advanced personalised preventive medicine powered by deep biomarkers of aging and longevity, and is a fast-emerging field. The field encompasses the likewise rapidly evolving areas of biogerontology, geroscience, and precision, preventive, and functional medicine.

- Longevity medicine: upskilling the physicians of tomorrow

The Lancet, Healthy Longevity, VOLUME 2, ISSUE 4, E187-E188, APRIL 2021
https://www.thelancet.com/journals/lanhl/article/PIIS2666-7568(21)00024-6/fulltext#%20

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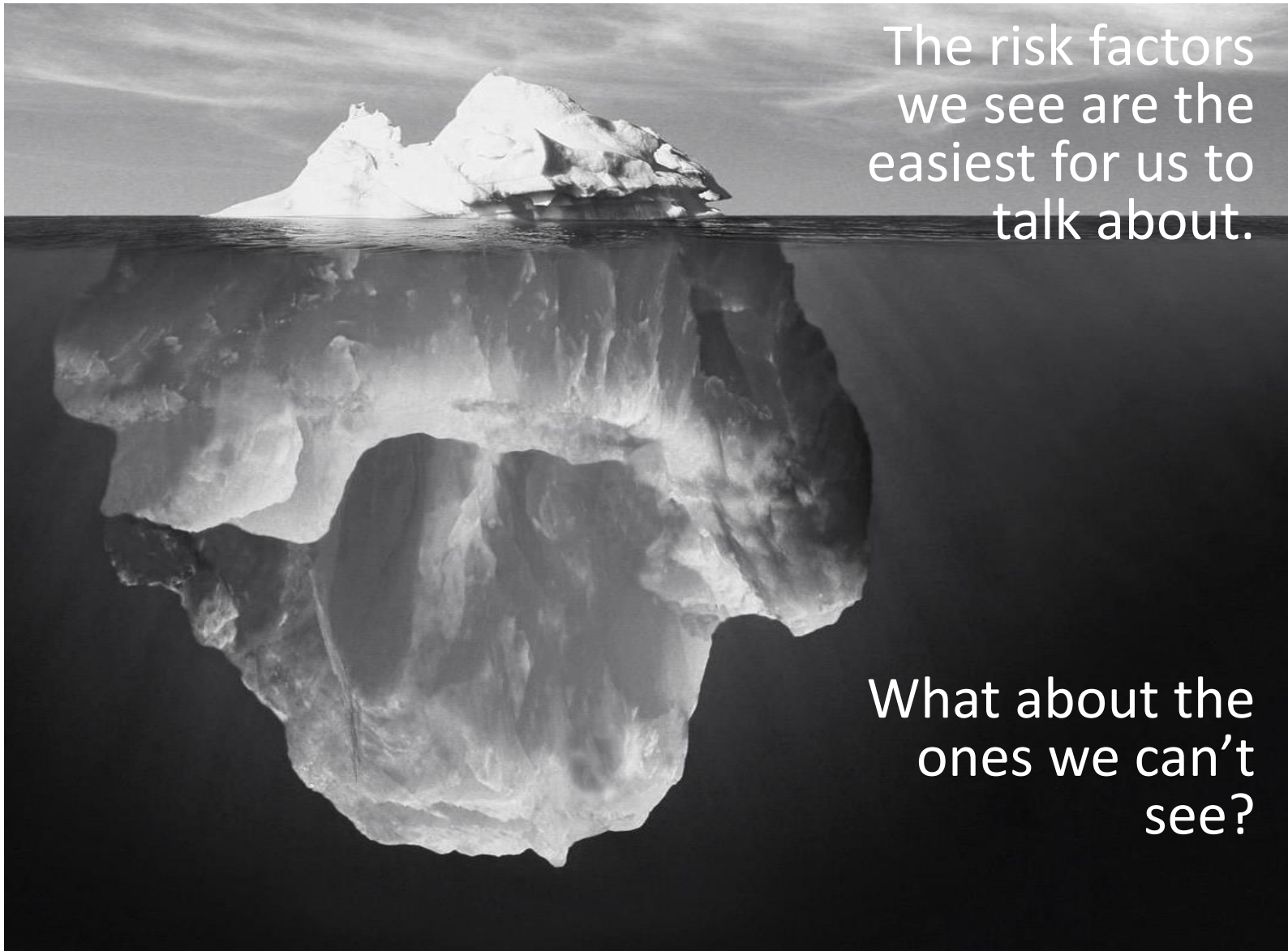
What is Predictive Genomics?

- The new precision (personalized) medicine, where genome sequencing and data analysis are essential components. It allows tailored diagnosis and treatment according to the information from the patient's own genome and specific environmental factors. P4 (predictive, preventive, personalized and participatory) medicine is introducing new concepts, challenges and opportunities.

- Carrasco-Ramiro F, Peiró-Pastor R, Aguado B. Human genomics projects and precision medicine. Gene Ther. 2017 Sep;24(9):551-561. doi: 10.1038/gt.2017.77.

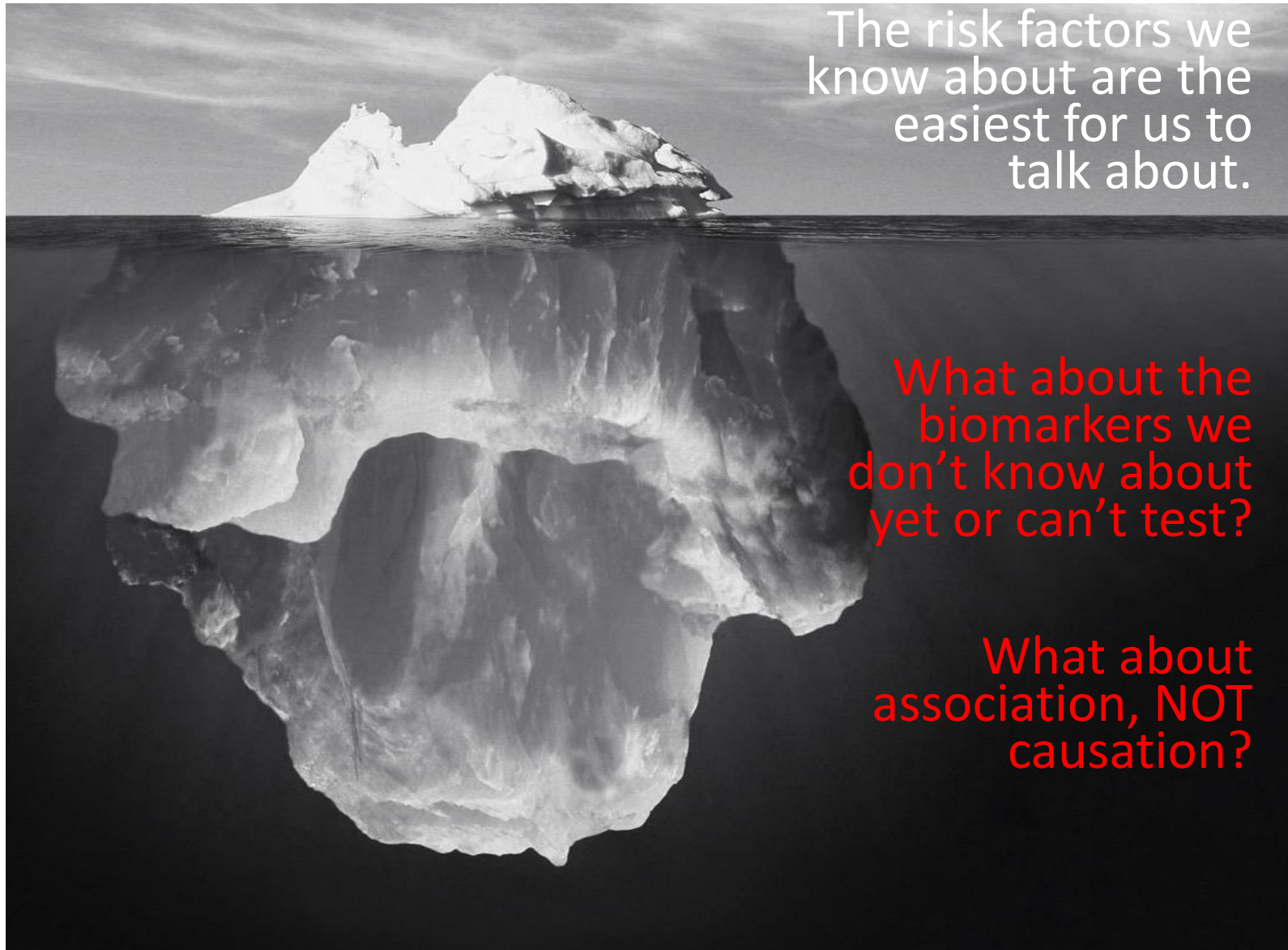
Predictive genomics allows us to look beneath the surface



Fr example, breast density for breast cancer.

Or newer biomarkers, like DNA Methylation.

But….



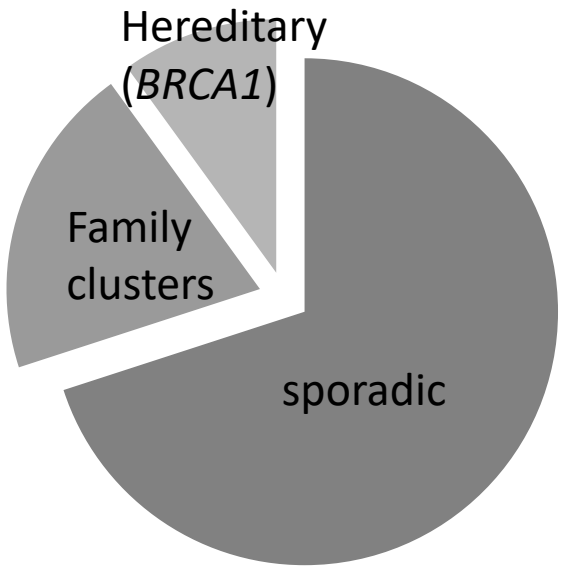
The Human Genome:

- 23 pairs of chromosomes
- Three billion nucleotides (base pairs)
- 20-25,000 genes

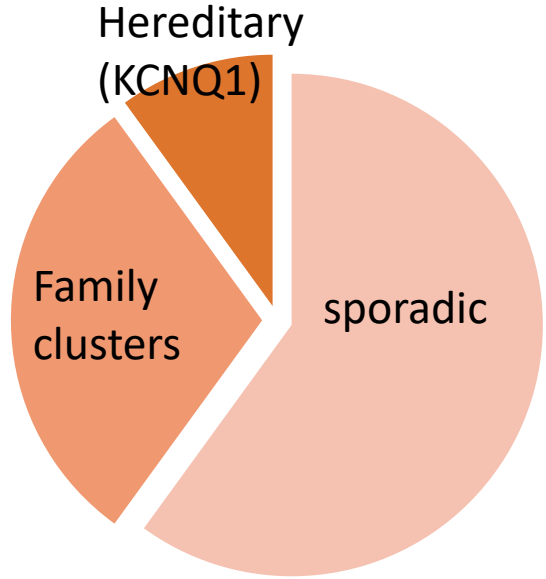
Clinical Genetics 101

- Hereditary
- Familial
- Sporadic

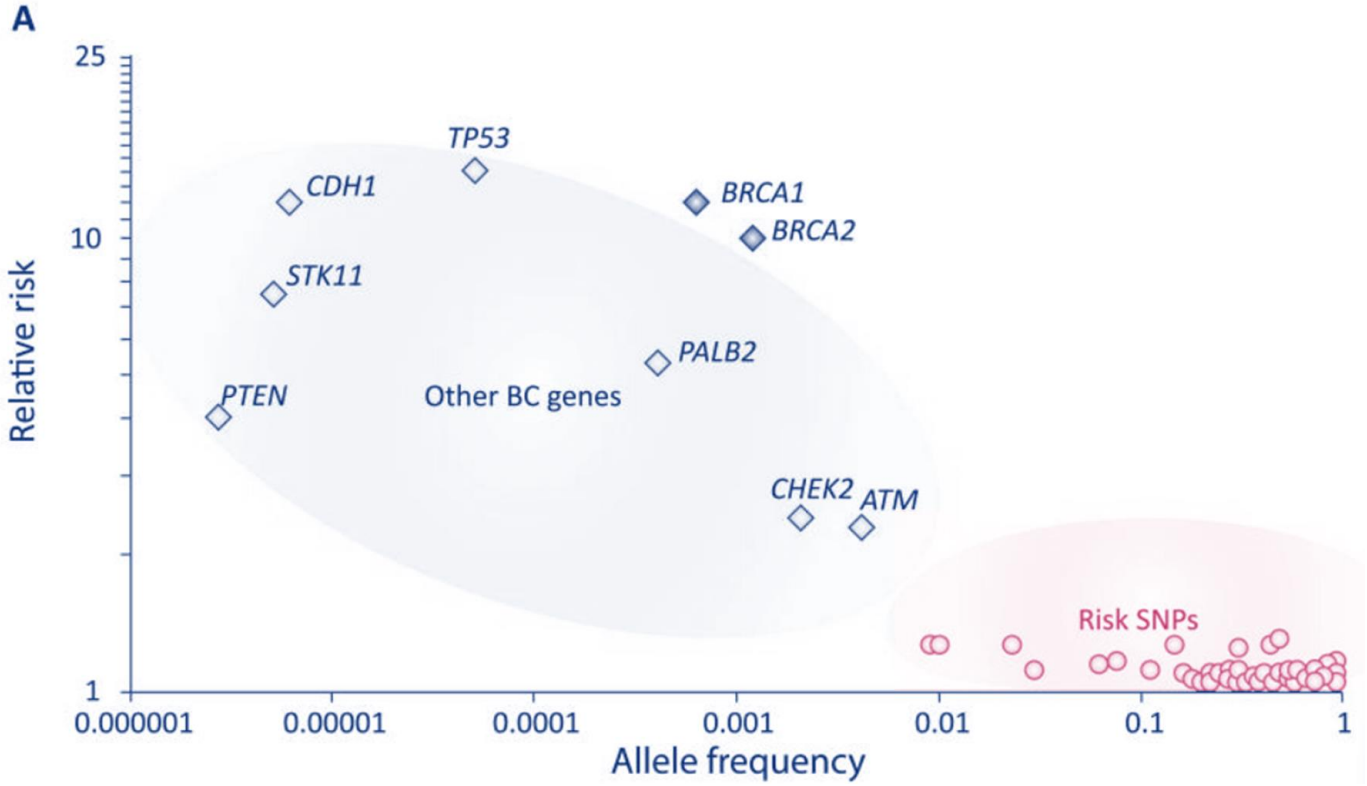
Cancers



Cardiovascular

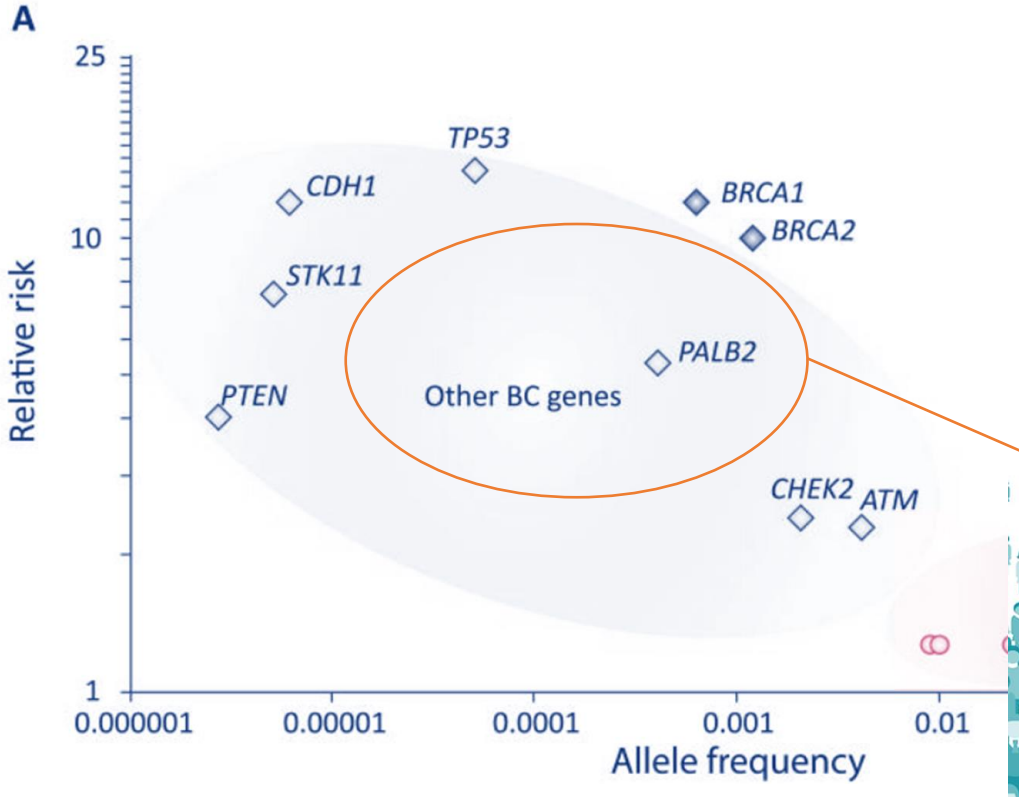


Clinical Genetics 101



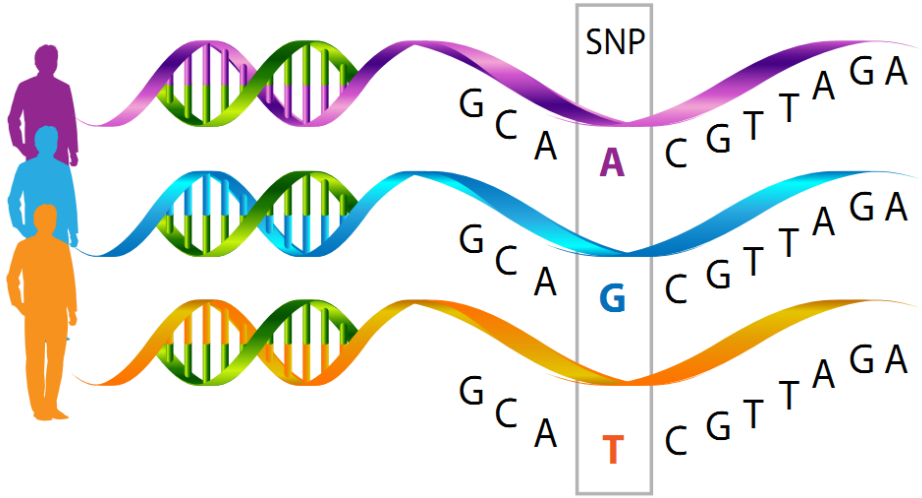
- High, moderate and low penetrance

Clinical Genetics 101



- Low penetrance SNP originally derived from genome wide association studies

Low penetrance risk alleles = SNP



- SNP = Single Nucleotide Polymorphisms
- All of us have 99.9% DNA in common. Some of the 0.1% differences in our DNA are due to SNP
- Predictive genomics has exploited these SNP by using ones that appear more often in adults who develop disease (like breast cancer) compared to those who don't

Putting SNP's together helps us calculate genetic risk

- What is polygenic Risk?
- What is a Polygenic Risk Score (PRS)?
- How does that differ from BRCA?

1 in 200+ adults will carry a pathogenic variant (*ex: BRCA1*)

High Penetrance
Low Prevalence

1 in 8

- women develop breast cancer
- men develop prostate cancer

Every adult has a disease-specific polygenic risk score

Polygenic Risk Scores

High Prevalence
Low Penetrance

Each SNP alone only as a small association with the disease…

…but in combination, the SNPs can have a measurable association with disease.

PRS: Each of us has a different combination of SNP risk alleles

PRS: Each of us has a different combination of SNP risk alleles

Patient

“Baseline” risk

SNP

Single Nucleotide Polymorphisms

Predictive genomics alone:

Predictive genomics alone:

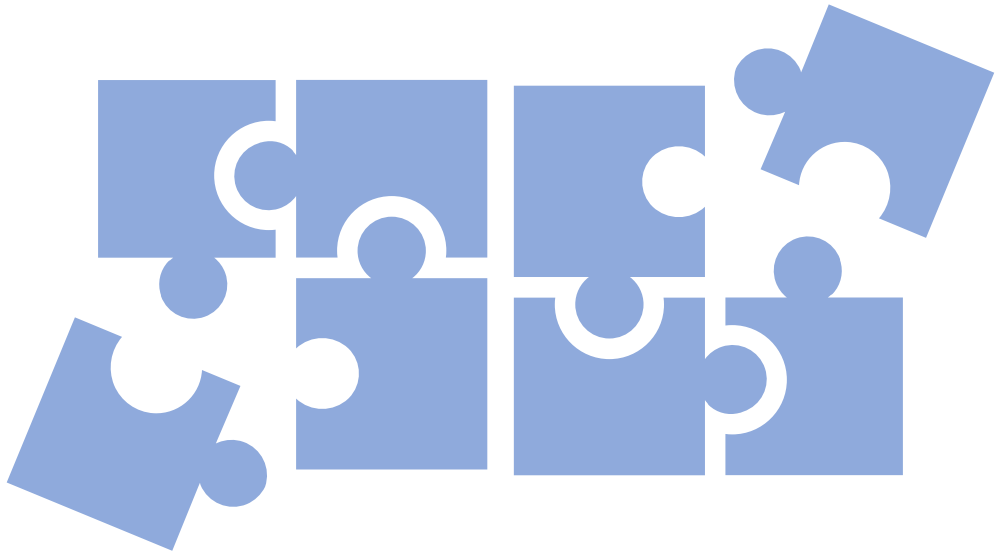
- Genome-wide association studies have shown unequivocally that common complex disorders have a polygenic architecture
- Researchers can identify genetic variants associated with diseases.
- These variants can be combined into a polygenic risk score to capture part of an individual's risk of diseases.
- Much of the research is on CVD, type 2 diabetes, breast, prostate cancers, Alzheimer's disease atrial fibrillation and inflammatory bowel disease

- Lewis CM, Vassos E. Polygenic risk scores: from research tools to clinical instruments. Genome Med. 2020 May 18;12(1):44. doi: 10.1186/s13073-020-00742-5. PMID: 32423490; PMCID: PMC7236300.

Many companies are in the commercial space

- So much so that The Guardian published a piece, **”Will genome sequencing bring precision medicine for all?”**
  - The health secretary wants to introduce genetic screening to the NHS
  - The commercial space is clear: there are three main phases in the advancement of personalised medicine. First, improved diagnosis, then improved treatment as a result of better diagnosis. And the third stage, he says, will be much earlier detection and prevention.
    - https://www.theguardian.com/science/2019/sep/28/genome-sequencing-precision-medicine-bespoke-healthcare-nhs

What if we could integrate the power of predictive genomics with clinical (phenotypic) factors?



- Might they be more powerful **together**?

CVD

Integrated Polygenic Tool Substantially Enhances Coronary Artery Disease Prediction

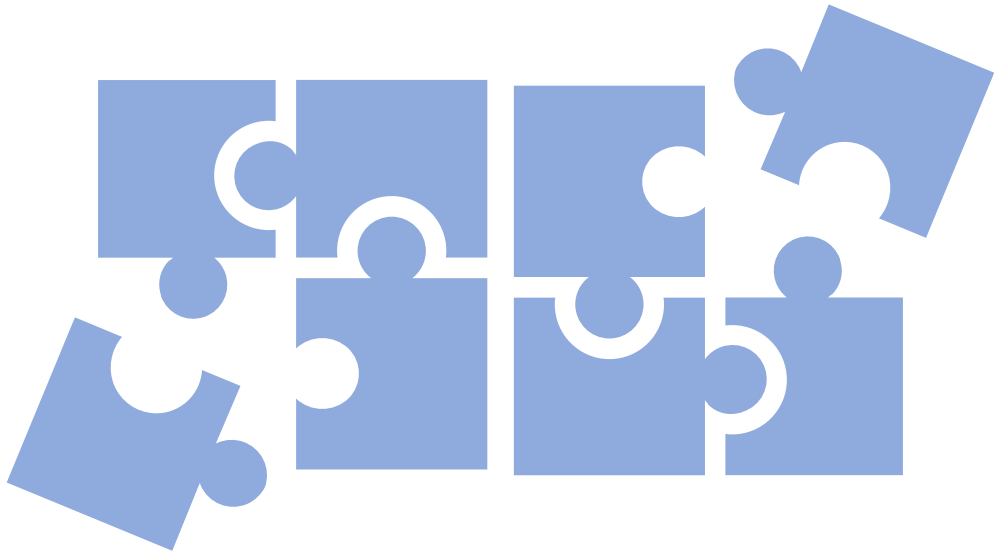
- Can genetic data can be used to improve standard cardiovascular disease risk calculators?
- We developed our own polygenic risk score for CAD and developed an integrated risk tool (IRT) that combined our polygenic risk score with established risk tools.

- *Circ Genom Precis Med.* 2021;14:e003304. DOI: 10.1161/CIRCGEN.120.003304

Integrated Polygenic Tool Substantially Enhances Coronary Artery Disease Prediction

- The addition of our PRS to PCE (pooled cohort equations)would up-classify 7% of people to a level of cardiovascular risk that warrants statin prevention
- **CONCLUSIONS:** An IRT that **includes** polygenic risk outperforms current risk stratification tools and offers greater opportunity for early interventions.
  - *Circ Genom Precis Med.* 2021;14:e003304. DOI: 10.1161/CIRCGEN.120.003304

What if we could integrate the power of predictive genomics with clinical (phenotypic) factors?



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Colon Cancer

Colorectal cancer risk stratification is crucial to improve screening and risk-reducing recommendations, and consequently do better than a one-size-fits-all screening regimen.

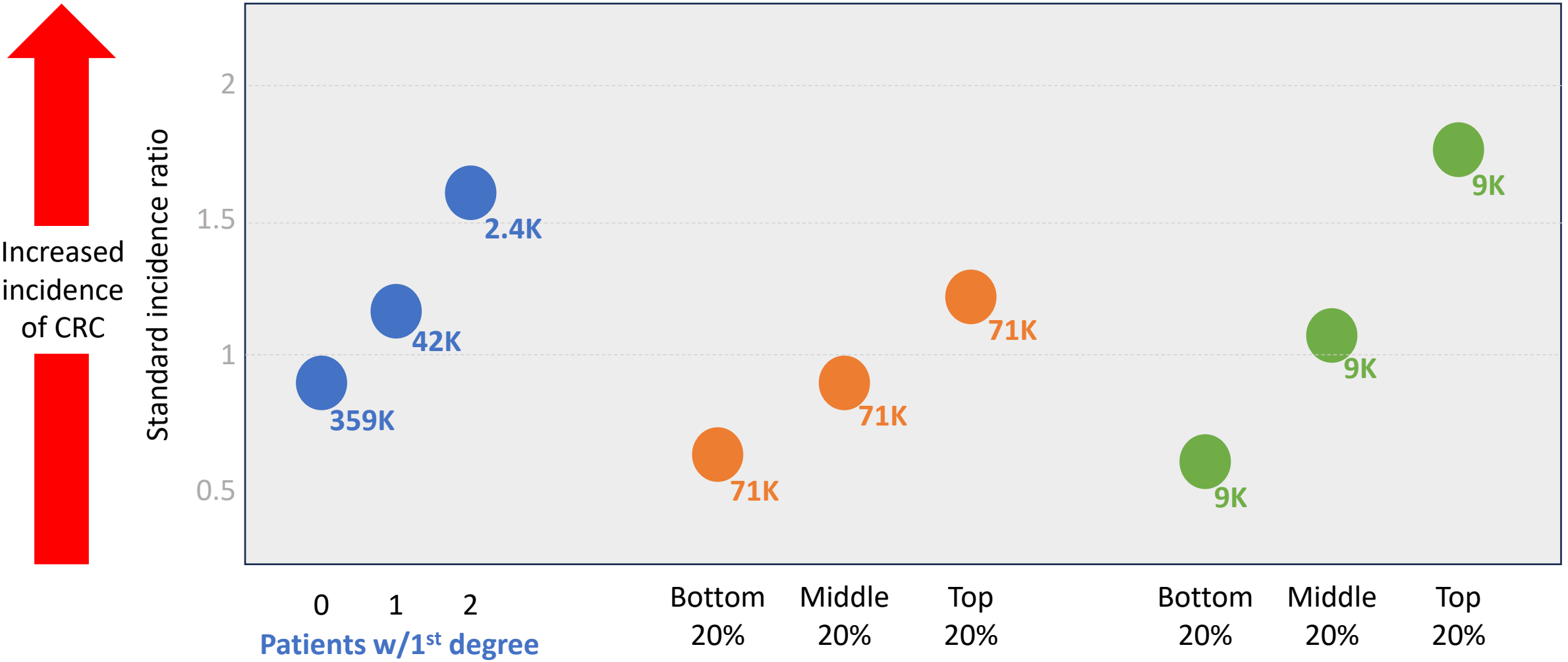
We investigated adding a polygenic risk score (45 SNP's) to a family history model to quantify how it improves risk stratification

Gafni A, Dite GS, Spaeth Tuff E, Allman R, Hopper JL (2021) Ability of known colorectal cancer susceptibility SNPs to predict colorectal cancer risk: A cohort study within the UK Biobank. PLoS ONE 16(9): e0251469. https://doi.org/10.1371/journal.pone.0251469

For both 10-year and full lifetime risk, the combined model had a wider risk distribution compared with family history alone, resulting in improved risk stratification of nearly 2-fold between the top and bottom risk quintiles of the full lifetime risk model. I

Importantly, the combined model can identify people who do not have family history of colorectal cancer but have a predicted risk that is equivalent to having at least one affected first-degree relative.

Gafni A, Dite GS, Spaeth Tuff E, Allman R, Hopper JL (2021) Ability of known colorectal cancer susceptibility SNPs to predict colorectal cancer risk: A cohort study within the UK Biobank. PLoS ONE 16(9): e0251469. https://doi.org/10.1371/journal.pone.0251469



Adapted from Gafni et al PlosOne 2021

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- The combined full lifetime risk model significantly improves discriminatory accuracy compared with a simple family history model

- Therefore, a combined polygenic risk score and first-degree family history model could be used to improve risk stratified population screening programs.

Gafni A, Dite GS, Spaeth Tuff E, Allman R, Hopper JL (2021) Ability of known colorectal cancer susceptibility SNPs to predict colorectal cancer risk: A cohort study within the UK Biobank. PLoS ONE 16(9): e0251469. https://doi.org/10.1371/journal.pone.0251469

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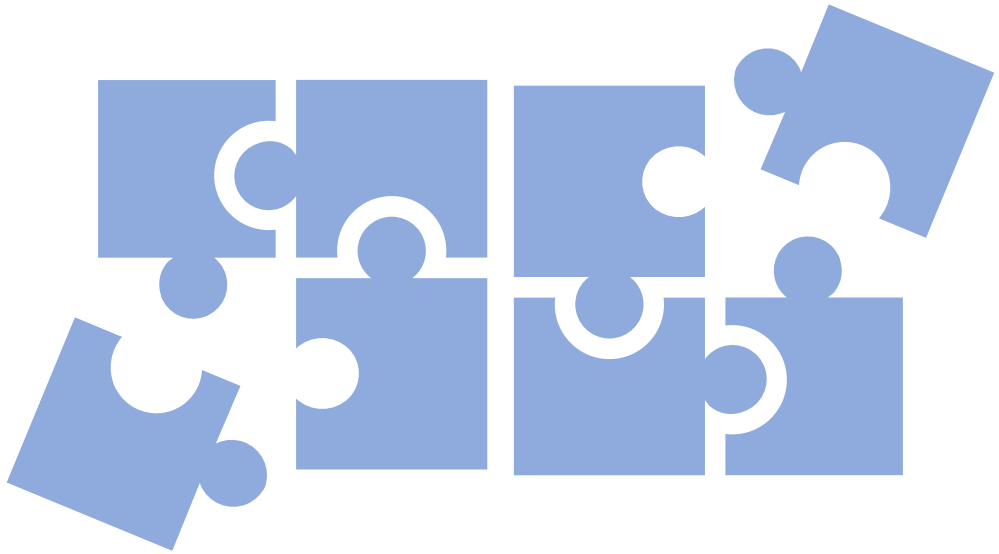

- Might they be more powerful **together**?

Prostate Cancer

- Accurate prostate cancer risk assessment will enable identification of men who are at increased risk of the disease
- Current screening options include the DRE and the PSA test
- Risk factors for prostate cancer include age, family history, and ethnicity. Familial risk confers a two- to threefold increased risk based on a first-degree family history of prostate cancer and represents 10%–20% of cases.
- Twin studies have suggested that heritable factors explain 42% of prostate cancer risk.
- Interestingly, there remains a genetic susceptibility in the form of low-penetrance single-nucleotide polymorphisms (SNPs) that explain a large portion of risk.

Dite, G. S., Spaeth, E., Murphy, N. M., & Allman, R. (2023). Development and validation of a simple prostate cancer risk prediction model based on age, family history, and polygenic risk. *Prostate*, *83*(10), 962-969. https://doi.org/10.1002/pros.24537

- The model can identify the top 10% of men who are at 2.8 times population risk and the next highest 10% of men at 1.5 times population risk
- At the other end, it can identify men who are at a very low risk
- Accurate knowledge of risk can inform decision-making when clinicians and patients discuss the risks and benefits of prostate cancer screening.
- Polygenic risk-tailored screening for prostate cancer is cost-effective and would result in a 30%–56% reduction in overdiagnosis.

Dite, G. S., Spaeth, E., Murphy, N. M., & Allman, R. (2023). Development and validation of a simple prostate cancer risk prediction model based on age, family history, and polygenic risk. *Prostate*, *83*(10), 962-969. https://doi.org/10.1002/pros.24537

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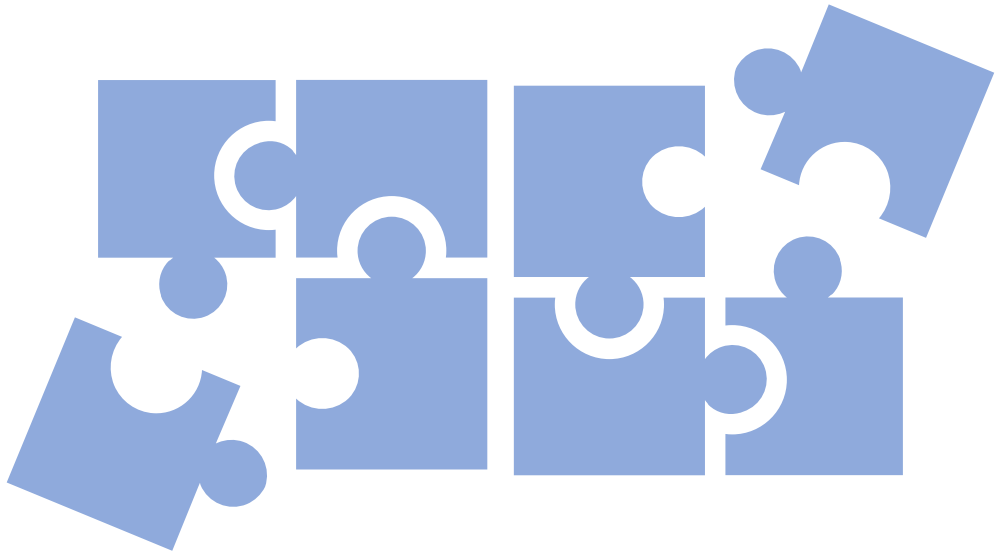


- Might they be more powerful **together**?

Ovarian Cancer

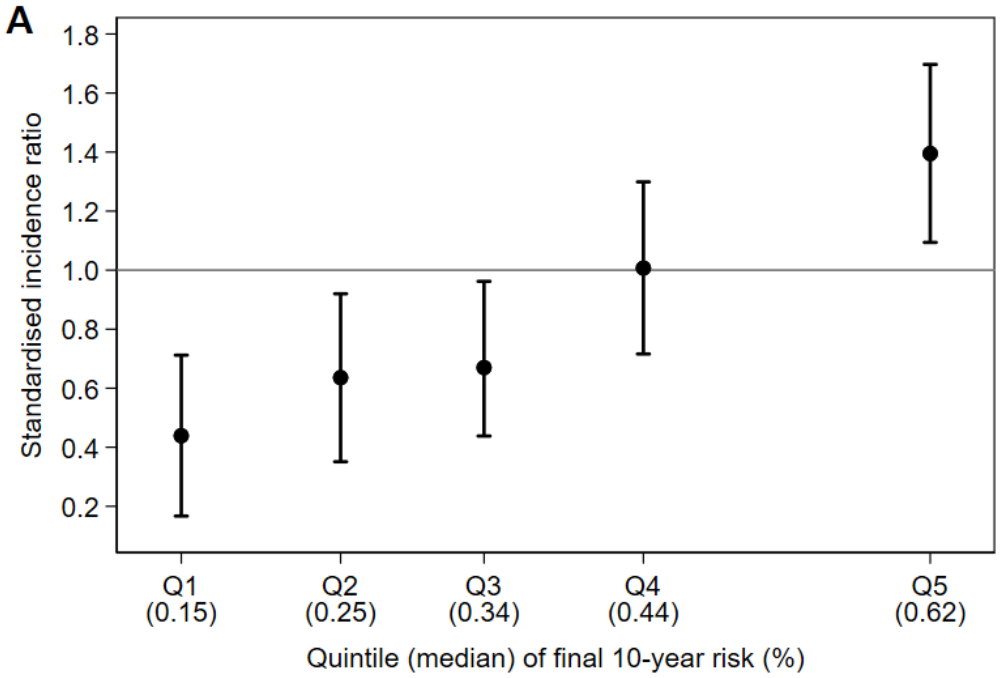
A combined clinical and genetic model for predicting risk of ovarian cancer

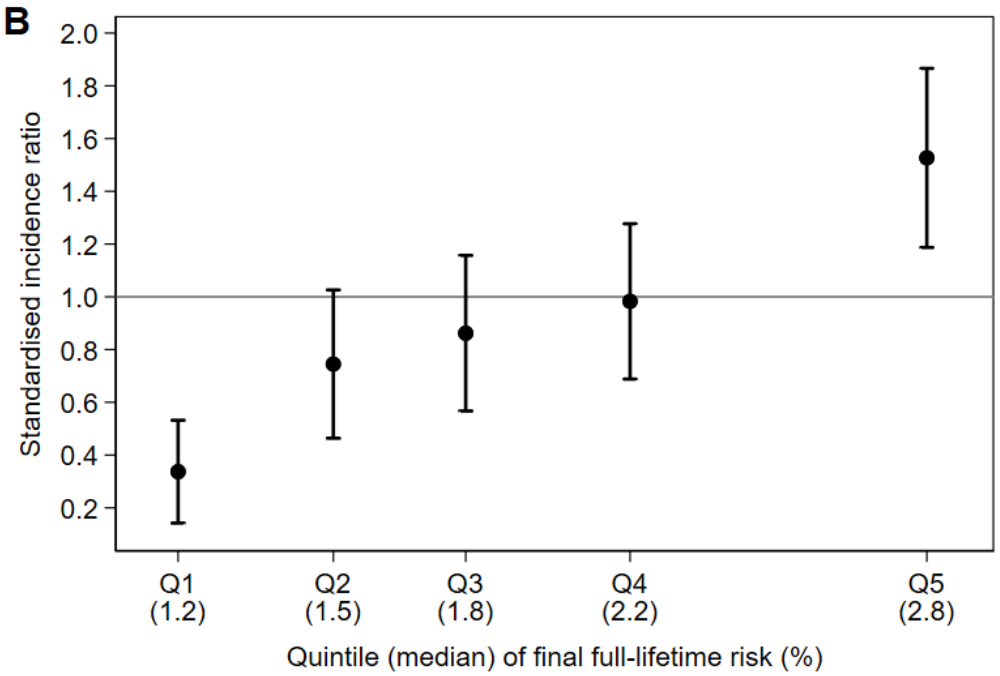
- Women with a family history of ovarian cancer or gene variants are at high risk of the disease, but very few women have these risk factors.
- GWAS studies have identified common genetic variants associated with ovarian cancer to construct PRS.
- We assessed whether a combined polygenic and clinical risk score could predict risk of ovarian cancer in population-based women who would otherwise be considered as being at average risk.
- Clinical factors: being menopausal, ever taking hormone replacement therapy, ever taking hormonal birth control and ever having had a full-term pregnancy.

Dite et al. European Journal of Cancer Prevention: October 25, 2022 - Volume - Issue - 10.1097

A combined clinical and genetic model for predicting risk of ovarian cancer

- A combined risk score incorporating a PRS and a clinical risk score has improved discrimination of ovarian cancer over 10 yrs.





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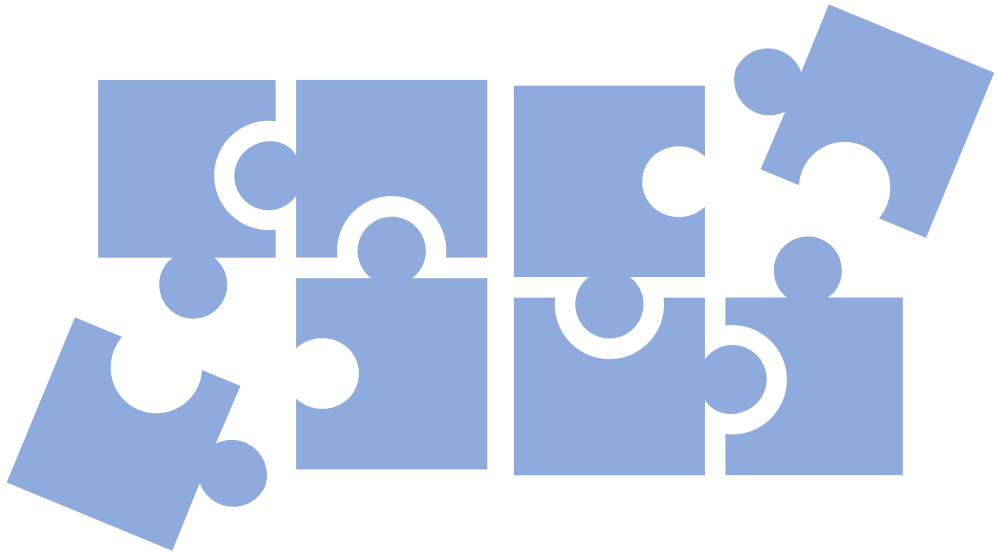


- Might they be more powerful **together**?

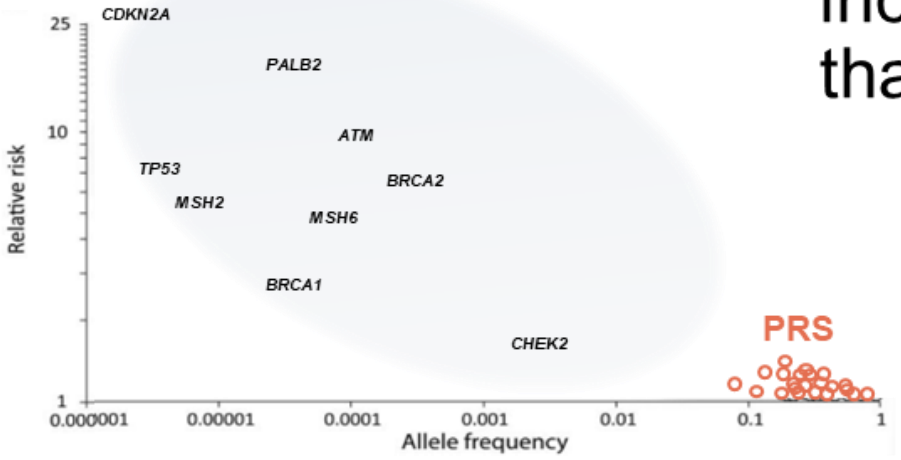
Pancreatic Cancer

Predicting 10-Year Risk of Pancreatic Cancer Using a Combined Genetic and Clinical Model

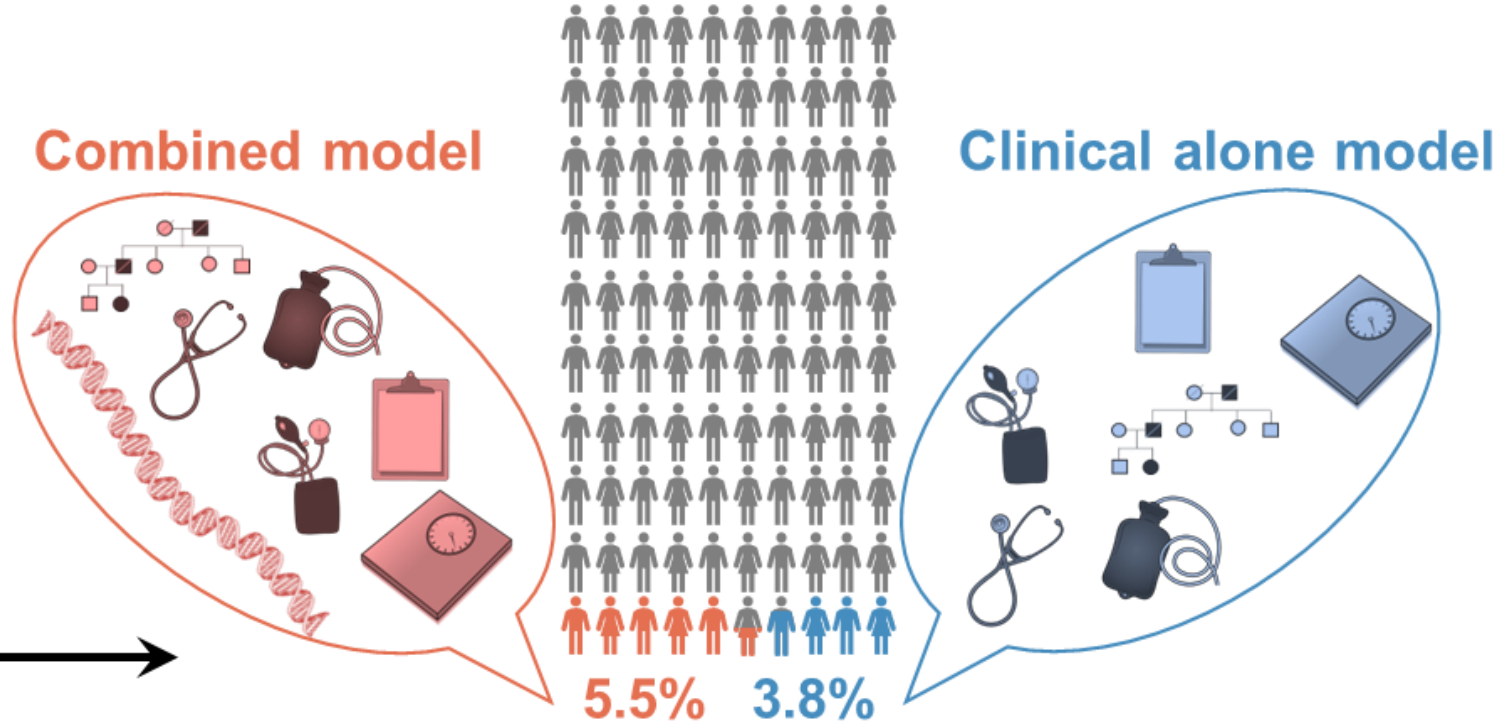
- Population screening is impractical because pancreatic cancer is rare with a lifetime risk of 1.7%.
- Accurate risk stratification in the general population could enable health care providers to focus early detection strategies to at-risk individuals. We already do this in BRCA+ patients (risk 5-10%).
- Clinical variables:
  - Smoking
  - T2 DM >3 yrs
  - FH (not in study)
  - ETOH (>3/d)
  - BMI
  - ABO Blood type (AO < AA < BO < BB < AB

Dite, Gillian S., et al. "Predicting 10-year risk of pancreatic cancer using a combined genetic and clinical model." *Gastro Hep Advances* (2023).

45% more *general population adults* identified at increased risk* of pancreatic cancer using a model that combines polygenic risk with clinical risk factors.



Adults that are ***not carriers*** of high/moderate cancer susceptibility variants can benefit from polygenic risk-integrated risk assessment.



*defined as >4-fold population average

Dite, Gillian S., et al. "Predicting 10-year risk of pancreatic cancer using a combined genetic and clinical model." *Gastro Hep Advances* (2023).

A risk-stratification tool, paired in a step-wise manner with existing or emerging pancreatic cancer screening techniques could lead to clinically significant downstaging of pancreatic cancer diagnoses.

Dite, Gillian S., et al. "Predicting 10-year risk of pancreatic cancer using a combined genetic and clinical model." *Gastro Hep Advances* (2023).

Integrative Healthcare SYMPOSIUM

This is important because identifying at-risk adults at early stage diagnosis where surgical resection is still possible is associated with increased survival rates.

Dite, Gillian S., et al. "Predicting 10-year risk of pancreatic cancer using a combined genetic and clinical model." *Gastro Hep Advances* (2023).

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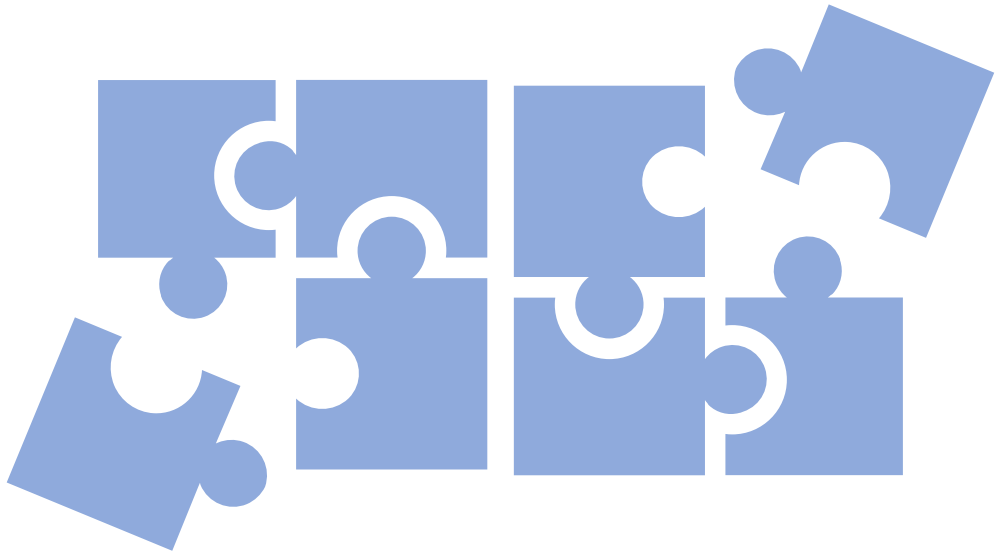

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Breast Cancer

Breast cancer genetics and risk assessment: an overview for the clinician

- Breast cancer is the most common cancer in women in the world.
- Prevention of breast cancer is therefore a public health imperative everywhere.
- Prevention starts with identification of individuals at high risk.
- Identification of high-risk women starts with identification of those who carry genetic mutations associated with an elevated risk of breast cancer.
- Once high-risk women are identified then early detection and risk reduction efforts can be instituted.

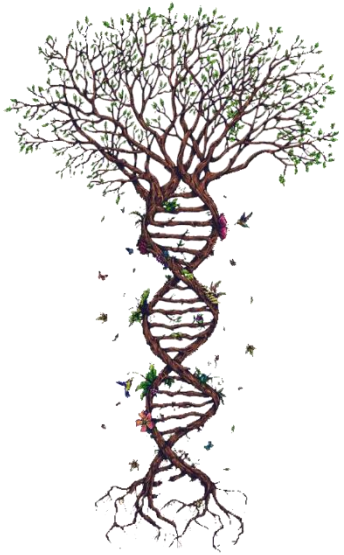
L. Larkin (2023): Breast cancer genetics and risk assessment: an overview for the clinician, Climacteric, DOI: 10.1080/13697137.2023.2184254

Breast Cancer Risk Assessment: The Basics of Genetic Risk Assessment

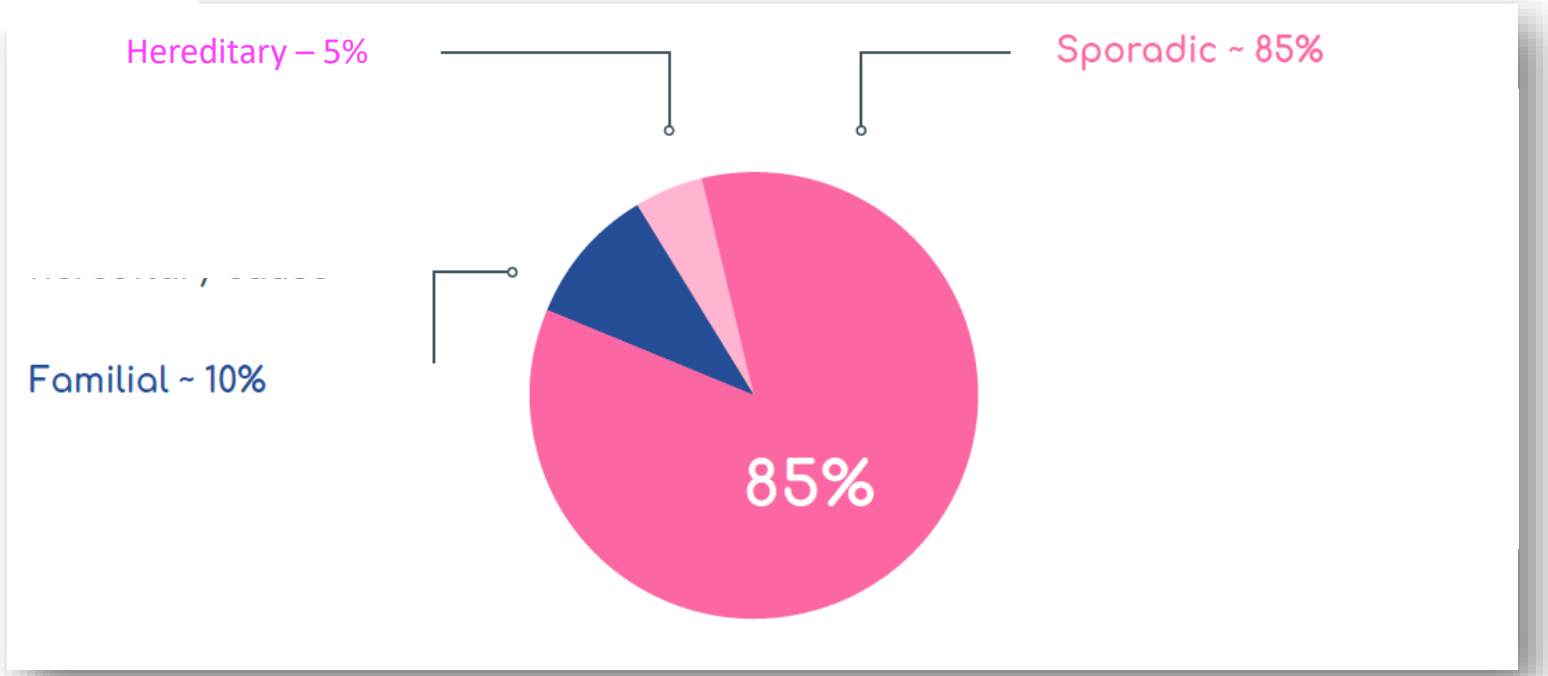
Sporadic vs Hereditary Breast Cancer

Sporadic = appearing or happening at irregular intervals in time; occasional

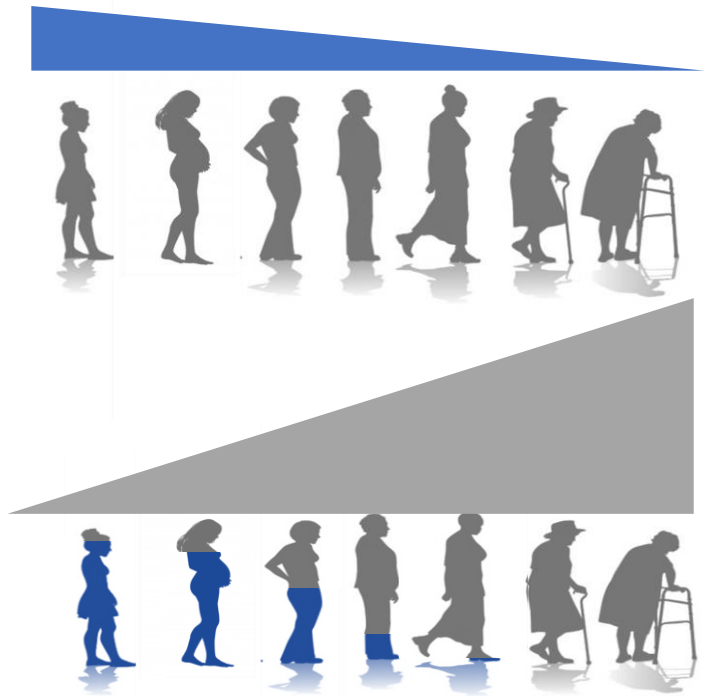
Hereditary = genetic event passed on from parents to their offspring



Most women who develop breast cancer have **little or no** family history of the disease



Hereditary/familial risk of breast cancer is less common, but develops earlier



The majority of women develop sporadic breast cancer, and it develops later: avg age at dx is 60

SEER 21 2014–2018, All Races, Females

1 in 400+ women will carry a *BRCA1* pathogenic variant

Toward more personalized breast cancer risk assessment: The polygenic risk score

- Oct 2023
- Healthcare providers are uncertain about how best to assess and manage breast cancer risk.
- Patients who carry gene mutations have more complex risk management choices, but only some are aware of their status.
- This article helps clinicians stratify breast cancer risk and discusses a newer genomic test, the polygenic risk score, that may enable more personalized risk management and decision-making.

•Sarkis-Tannous, Daad MPAS, PA-C; Sukol, Roxanne B. MD, MS; Sullivan, Erika MPAS, PA-C. Toward more personalized breast cancer risk assessment: The polygenic risk score. JAAPA 36(10):p 37-40, October 2023. | DOI: 10.1097/01.JAA.0000977692.63075.f3

Polygenic risk scores and breast cancer risk prediction

- Polygenic Risk Scores (PRS) are a major component of accurate breast cancer risk prediction.
- They have the potential to improve screening and prevention strategies.
- The personalized risk assessment of PRS identify women at higher risk of breast cancer development and enables the implementation of stratified screening and prevention approaches.

•Roberts E, Howell S, Evans DG. Polygenic risk scores and breast cancer risk prediction. Breast. 2023 Feb;67:71-77. doi: 10.1016/j.breast.2023.01.003. Epub 2023 Jan 10. PMID: 36646003; PMCID: PMC9982311.

Polygenic risk scores and breast cancer risk prediction

- PRS represent a significant advance in breast cancer risk prediction and their further development will undoubtedly enhance personalization.

•Roberts E, Howell S, Evans DG. Polygenic risk scores and breast cancer risk prediction. Breast. 2023 Feb;67:71-77. doi: 10.1016/j.breast.2023.01.003. Epub 2023 Jan 10. PMID: 36646003; PMCID: PMC9982311.

Identifying women with increased risk of breast cancer and implementing risk-reducing strategies and supplemental imaging

- Some women have a higher lifetime risk of BC because of genetic and lifestyle factors
- Because BC risk is variable, screening and prevention strategies should be individualized.
- Health care professionals need to be able to assess risk profiles, identify high-risk women, and individualize screening and prevention strategies

Breast Cancer (2022) 29:19–29 https://doi.org/10.1007/s12282-021-01298-x

Polygenic Risk Scores (PRS) Matter

What about lifestyle risks for breast cancer?

Do they matter?

Breast Cancer Risk Assessment: The Basics of Lifestyle Risk Assessment

The literature Supports:

- Dense Breasts
- Obesity
- Elevated Blood sugar, Insulin, Diabetes
- Inflammation
- Elevated Estrogen at Menopause
- Poor Estrogen Detoxification
- Lack of Exercise
- Diet (red meat, animal fat, dairy, non- organic, alcohol)
- EDC’s

What about combining lifestyle risk with polygenic risk in Breast Cancer?

1 in 5 women will have combination of common genetic markers and clinical factors that puts her at elevated risk of breast cancer

Based on remaining lifetime risk >20%; Allman et al 2023

Breast Cancer Risk Assessment: The Basics of combining Polygenic and Lifestyle Risk Assessment

Scientific Support for PRS Combined with Lifestyle

Identifying women with increased risk of breast cancer and implementing risk-reducing strategies and supplemental imaging

- Some women have a higher lifetime risk of BC because of genetic and lifestyle factors
- Screening and prevention strategies should be individualized after considering patient-specific risk factors
- We propose a stepwise approach to managing BC risk:
  1. Recognizing risk factors;
  2. Using a validated screening tool to assess the lifetime risk of BC

Vegunta Set al., Breast Cancer. 2022 Jan;29(1):19-29. doi: 10.1007/s12282-021-01298-x PMID: 34665436.

Validation of a breast cancer risk prediction model based on the key risk factors: family history, mammographic density and polygenic risk

- Mammographic density, polygenic risk and clinical factors as a breast cancer risk prediction model (BRISK) was compared to clinical models (Gail and IBIS) and PRS with more clinical factors.

- BRISK performs better than two commonly used clinical risk models and no worse compared to a similar model with more risk factors.

Breast Cancer Research and Treatment https://doi.org/10.1007/s10549-022-06834-7. Feb, 2023

At what age is risk assessment beneficial?

Initially and at any point in time when a woman has had a change in clinical risk factors

At what age is risk assessment beneficial?

Pre-screening age (30 – 50 years)
A woman who has not yet had a mammogram

Menopause
Nearly 80% of breast cancers are diagnosed post-menopause[1]

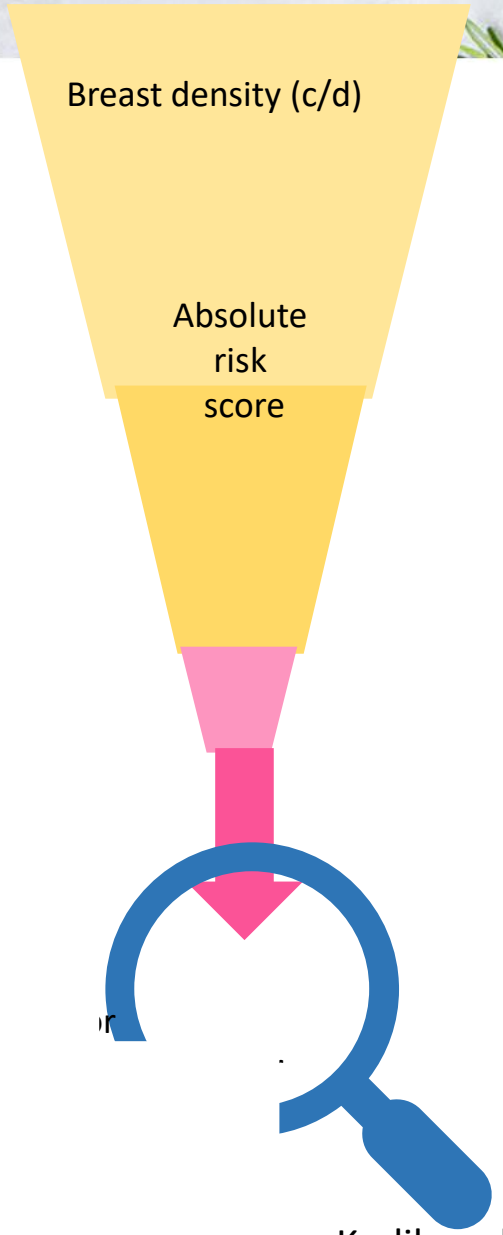
AGE

35 45 55 65 75

When high breast density is determined[2]

- A woman who has dense breast tissue, as identified by mammogram, is at higher risk of breast cancer
- **Nearly half of all women have heterogeneously or extremely dense breast tissue (BI-RADS C or D, respectively)**

1. National Breast Cancer Foundation Australia. Breast Cancer Stats. Available at: https://nbcf.org.au/about-breast-cancer/breast-cancer-stats/. Accessed March 2022.
2. Cancer Australia, 2018. Risk factors for breast cancer: A review of the evidence, Cancer Australia, Surry Hills, NSW.



Out of 600,000+ women:
47% of women had dense breasts but 60% of women with advanced breast cancers had dense breasts.

"**breast density notification** should be combined with **breast cancer risk** so women at **highest risk** for advanced cancer **are targeted** for supplemental imaging discussions"
(Kerlikowski *et al* 2019)

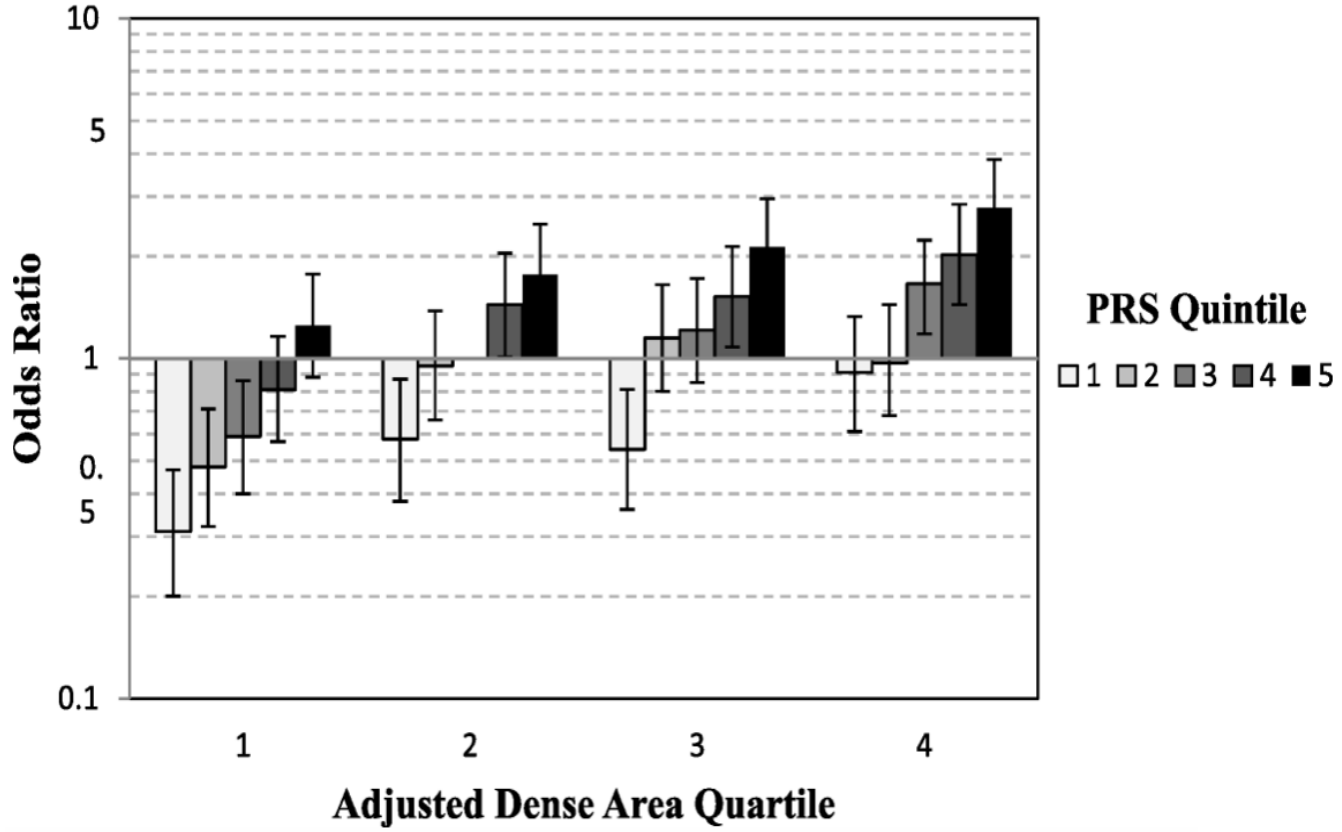
Kerlikowski et al Jama Int Med 2019; https://www.ncbi.nlm.nih.gov/pubmed/31260054

Independent risk factors can be added together

Polygenic risk

Breast density

Multiplicative capacity of breast density and polygenic risk score (PRS)[2]



Vachon CM *et al. Breast Cancer Res* 2019;21(1):68. 3. Internal validation data.

Examples of clinical models combined with polygenic risk scores to improve risk prediction for Breast Cancer

- IBIS (Tyrer-Cuzick)
- Gail
- Boadicea (Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm)
- BCSC (Breast Cancer Surveillance Consortium)
- Other

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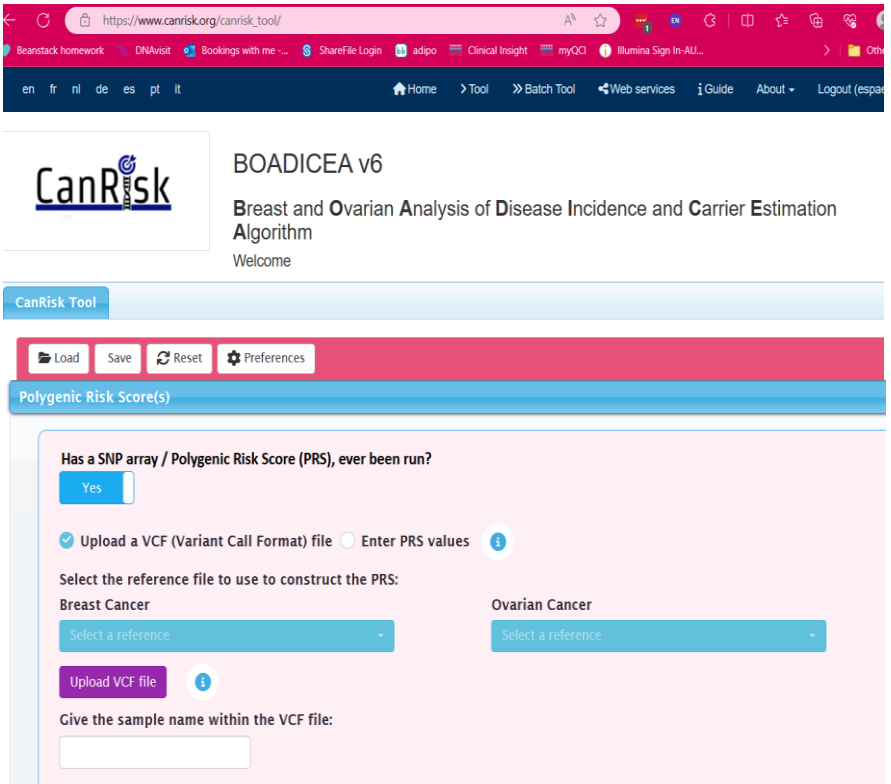
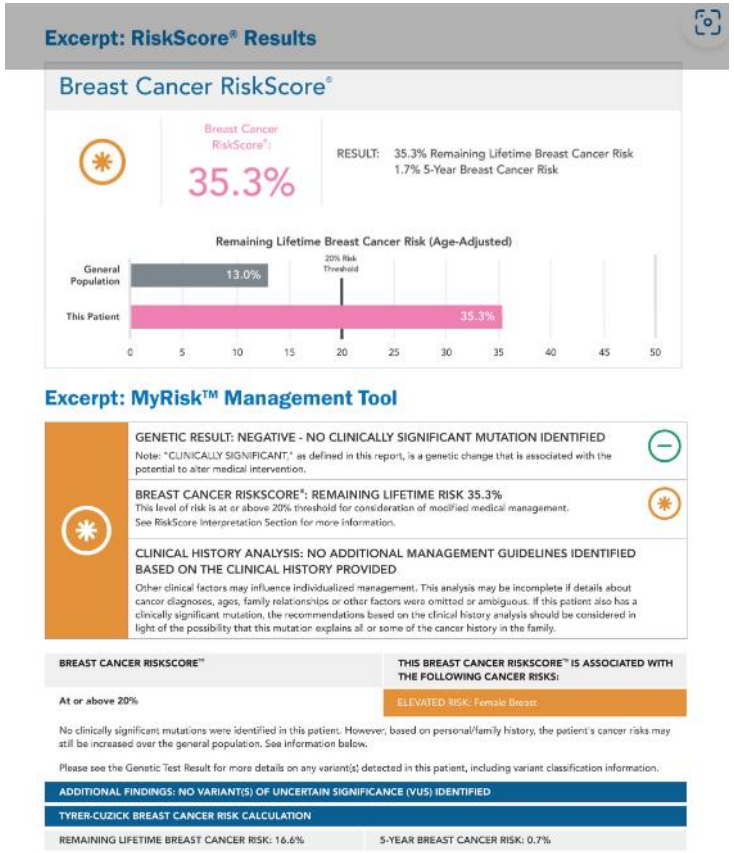
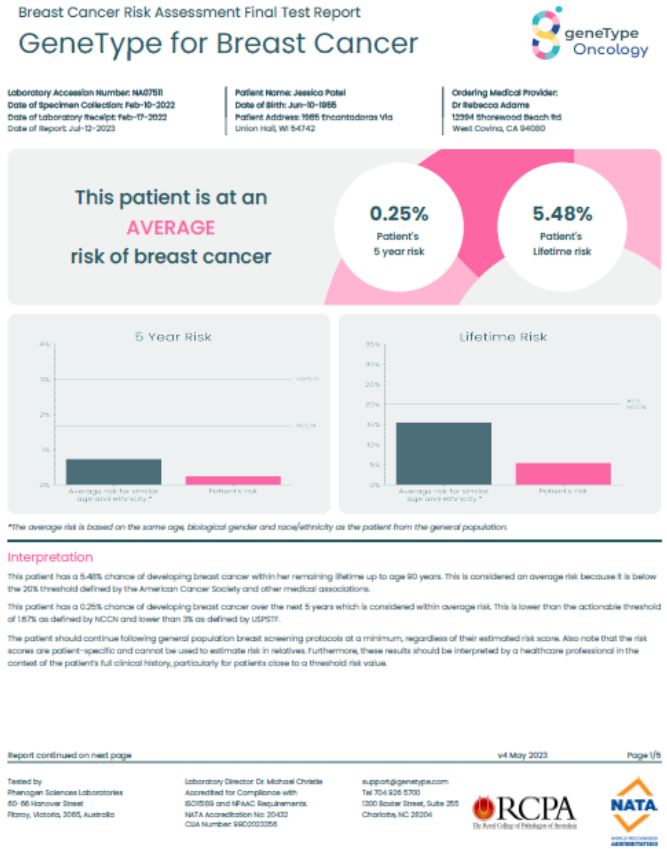
Clinical models are available that have an integrated PRS capability







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Changing Risk:

Breast Cancer Research and Treatment (2023) 198:335–347
https://doi.org/10.1007/s10549-022-06834-7

EPIDEMIOLOGY

Validation of a breast cancer risk prediction model based on the key risk factors: family history, mammographic density and polygenic risk

Richard Allman[1] · Yi Mu[2] · Gillian S. Dite[1] · Erika Spaeth[3] · John L. Hopper[4] · Bernard A. Rosner[2]

Received: 16 June 2022 / Accepted: 2 December 2022 / Published online: 7 February 2023

Abstract

Purpose We compared a simple breast cancer risk prediction model, BRISK (which includes mammographic density, polygenic risk and clinical factors), against a similar model with more risk factors (simplified Rosner) and against two commonly used clinical models (Gail and IBIS).

Methods Using nested case–control data from the Nurses' Health Study, we compared the models' association, discrimination and calibration. Classification performance was compared between Gail and BRISK for 5-year risks and between IBIS and BRISK for remaining lifetime risk.

Results The odds ratio per standard deviation was 1.43 (95% CI 1.32, 1.55) for BRISK 5-year risk, 1.07 (95% CI 0.99, 1.14) for Gail 5-year risk, 1.72 (95% CI 1.59, 1.87) for simplified Rosner 10-year risk, 1.51 (95% CI 1.41, 1.62) for BRISK remaining lifetime risk and 1.26 (95% CI 1.16, 1.36) for IBIS remaining lifetime risk. The area under the receiver operating characteristic curve (AUC) was improved for BRISK over Gail for 5-year risk ($AUC = 0.636$ versus 0.511, $P < 0.0001$) and for BRISK over IBIS for remaining lifetime risk ($AUC = 0.647$ versus 0.571, $P < 0.0001$). BRISK was well calibrated for the estimation of both 5-year risk (expected/observed $[E/O] = 1.03$; 95% CI 0.73, 1.46) and remaining lifetime risk ($E/O = 1.01$; 95% CI 0.86, 1.17). The Gail 5-year risk ($E/O = 0.85$; 95% CI 0.58, 1.24) and IBIS remaining lifetime risk ($E/O = 0.73$; 95% CI 0.60, 0.87) were not well calibrated, with both under-estimating risk. BRISK improves classification of risk compared to Gail 5-year risk ($NRI = 0.31$; standard error $[SE] = 0.031$) and IBIS remaining lifetime risk ($NRI = 0.287$; $SE = 0.035$).

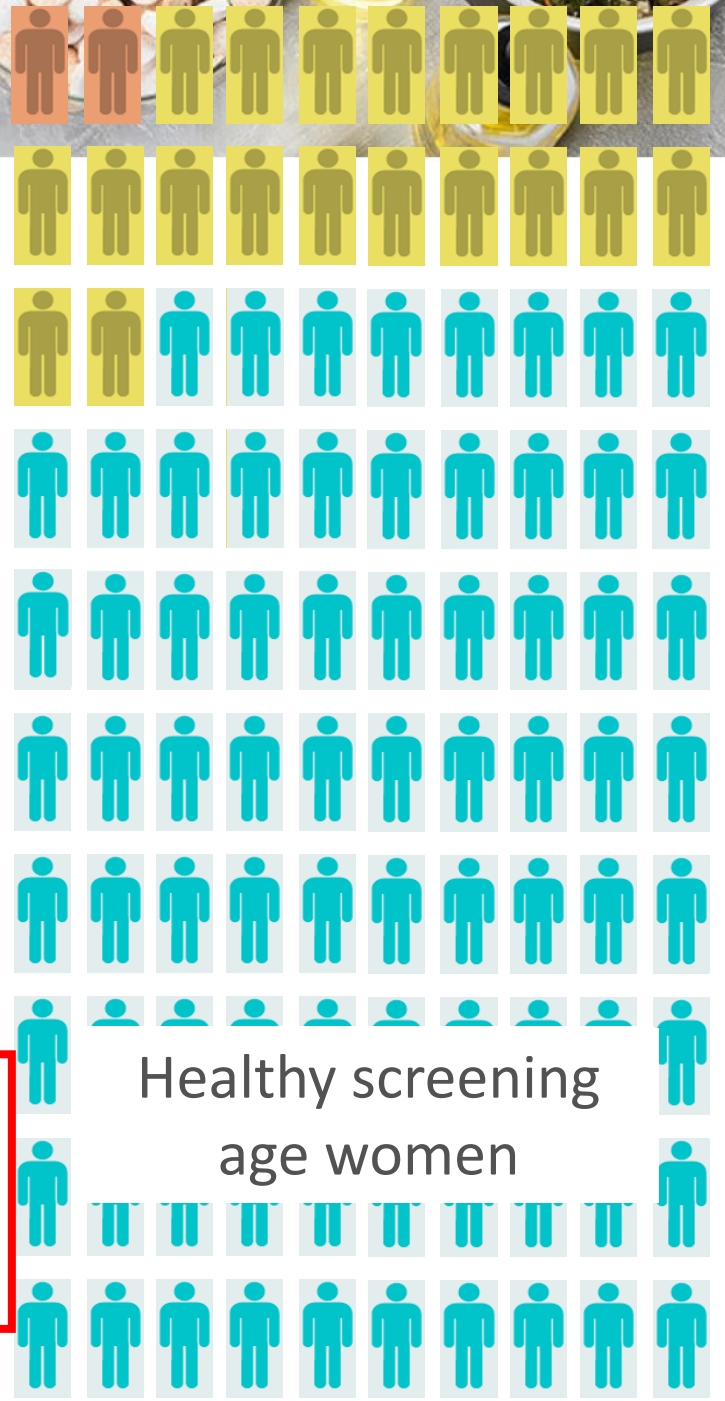
Conclusion BRISK performs better than two commonly used clinical risk models and no worse compared to a similar model with more risk factors.

9x

Integrated model

IBISv7

	IBISv7	Integrated model
% cases >20%	4.1%	**41.3%**
% controls >20%	2.5%	**22.4%**



Healthy screening age women

Which patients are eligible for risk assessment and who may benefit most?

The ideal Criteria:

- Age 30 years and older
- No previous breast cancer (or ductal carcinoma in situ [DCIS]) diagnosis
- No *BRCA1/BRCA2* mutations

- Pre-mammogram
  - Is she eligible to start sooner?
- Dense breasts
  - ~50% of women have dense breast tissue[1]
- Menopausal
  - Should she re/consider hormone replacement therapy?

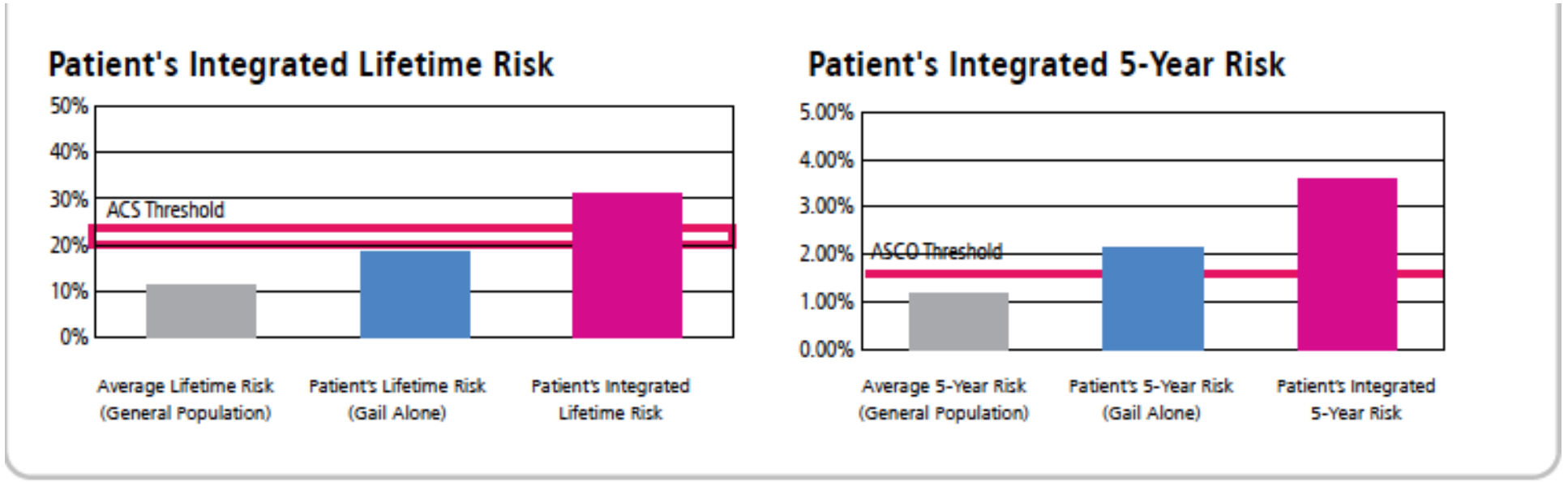
- Cases

51 yo female, LMP 6 mo ago, wants Bio-Identical HRT for Hot Flashes:

No FH, PMH Neg, PE WNL

SELF		NON-HEREDITARY BREAST CANCER
Y	N	Have you ever been diagnosed with any breast cancer or ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS)?
Y	N	Did you start your menstrual period before age 12?
Y	N	Did you have your first child AFTER 30 years of age?
Y	N	Have you ever been told you have DENSE BREASTS?
Y	N	Have you been tested for BRCA?
Y	N	Have you ever taken estrogen for hormone replacement therapy (HRT)?
Y	N	Have you ever had a (positive or negative) breast biopsy?

NO HRT!!


Patient's Integrated Lifetime Risk
50%
40%
30%
20%
10%
0%
ACS Threshold
Average Lifetime Risk (General Population)
Patient's Lifetime Risk (Gail Alone)
Patient's Integrated Lifetime Risk
Patient's Integrated 5-Year Risk
5.00%
4.00%
3.00%
2.00%
1.00%
0.00%
ASCO Threshold
Average 5-Year Risk (General Population)
Patient's 5-Year Risk (Gail Alone)
Patient's Integrated 5-Year Risk

60 yo for routine annual. No concerns. Ashkenazi Jewish.

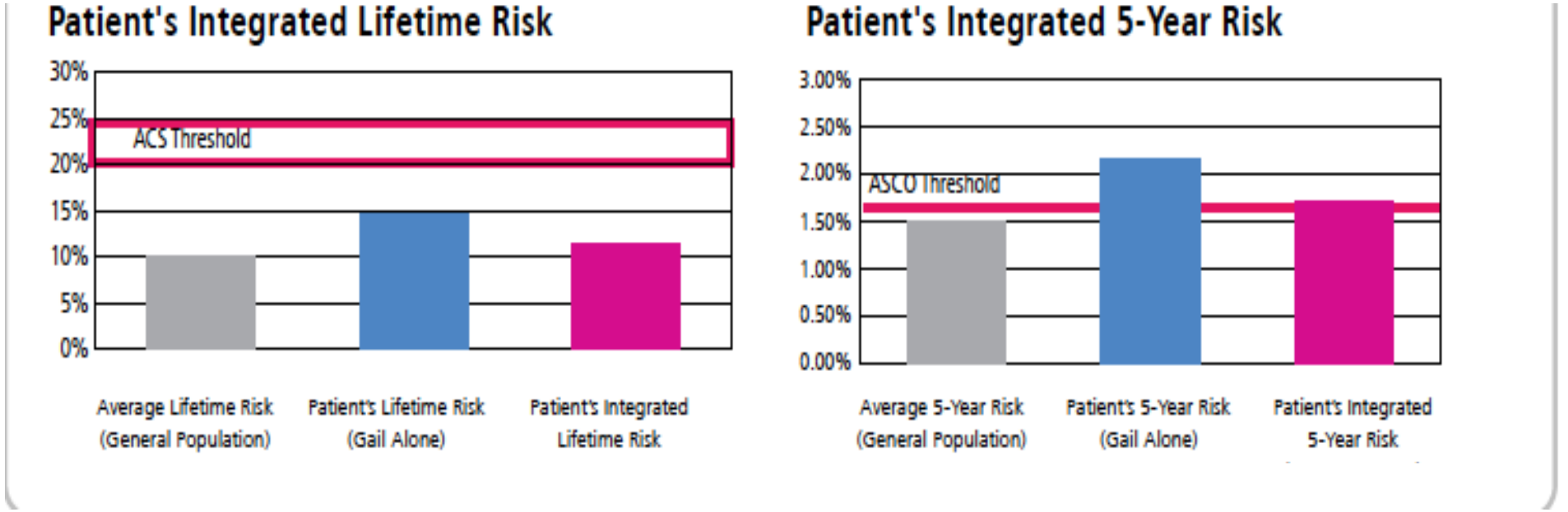
BRCA Testing Indicated

BRCA Neg… When reviewing results…..

Instruction: Circle "Y" to below statements that apply to YOU and/or YOUR FAMILY on both your **mother's and father's** sides; list the diagnosed person's relationship to you (eg; self, paternal aunt, maternal uncle, paternal grandmother) and the age at diagnosis. Each statement should be answered individually, so you may list the same cancer more than once.

BREAST AND OVARIAN CANCER	RELATIONSHIP	AGE AT DIAGNOSIS
(Y) N -Breast cancer before age 50	sister	46
Y N -Ovarian cancer		
Y N -2 Primary, unrelated breast cancer in same person or same side of family		
Y N -Both breast & ovarian cancer (in an individual or family)		
Y N -Pancreatic cancer w/ breast or ovarian cancer in same person or same side of family		
Y N -Ashkenazi Jewish ancestry w/ breast, ovarian or pancreatic in same person or same side of family		

PATIENT REASSURED!!



Should we really estimate breast cancer risk for all our patients?

The Endocrine Society says YES

Endocrine Society HRT Decision Tree

Evaluate breast cancer risk – for those with high to moderate risk, consider other options.

Stuenkel CA, Davis SR, Gompel A, et al. Treatment of Symptoms of the Menopause: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2015;100(11):3975-4011. doi:10.1210/jc.2015-2236

And the public is aware of this recommendation..

Breast Cancer Drugs Urged for Healthy High-Risk Women in NYT

The United States Preventive Services Task Force recommended that, for healthy women ages 40 to 70, doctors help assess the odds of breast cancer

Grady D. Breast Cancer Drugs Urged for Healthy High-Risk Women. The New York Times. https://www.nytimes.com/2013/04/16/health/breast-cancer-drugs-urged-for-healthy-high-risk-women.html. Published April 15, 2013.

Using integrated genomic models enables new screening paradigms

Population level Risk stratification

Liquid biopsy assays

↑ positive predictive value

Multi-Cancer early detection

Reducing Breast Cancer Incidence and Mortality: Rethinking an Approach to Risk Assessment and Prevention

- Breast cancer prevention strategies continue to evolve with advances in research resulting in newer polygenic profiles to improve breast cancer prediction.
- Ongoing studies are exploring the impact of single-nucleotide polymorphisms to estimate the polygenic breast cancer risk and revolutionize personalized risk assessment.
- We have previously shown that after being informed about their personalized risk on the basis of polygenic risk score, women at increased risk for breast cancer were more likely to use endocrine preventive medication.
- Future trials may demonstrate that polygenic risk scores may not only im- prove adherence to pharmacologic risk-reduction strategies but potentially improve compliance with a risk-free, low-cost intervention that saves lives, a low-fat diet.

Pruthi S, et al., JCO Oncol Pract. 2021 Dec;17(12):717-719. doi: 10.1200/OP.21.00551. Epub 2021 Sep 7. PMID: 34491812

What is Longevity Medicine?

- Equipping health-care providers with tools of obtaining and utilising an individualised precision dataset of each patient not only reduces the risks of the patient developing diseases, but mitigates and even eliminate diseases, and customizes optimal preventive and therapeutic approaches.

  - Longevity medicine: upskilling the physicians of tomorrow

  The Lancet, Healthy Longevity, VOLUME 2, ISSUE 4, E187-E188, APRIL 2021
  https://www.thelancet.com/journals/lanhl/article/PIIS2666-7568(21)00024-6/fulltext#%20

What is Longevity Medicine?

- The notion of longevity and healthy aging as a major priority for healthcare will undoubtedly substantially impact primary, secondary, and tertiary prevention.

- Longevity medicine: upskilling the physicians of tomorrow

The Lancet, Healthy Longevity, VOLUME 2, ISSUE 4, E187-E188, APRIL 2021
https://www.thelancet.com/journals/lanhl/article/PIIS2666-7568(21)00024-6/fulltext#%20

In Conclusion…

- Predictive genetic testing for complex diseases: a public health perspective (2014)
  - C. Marzuillo et al., Predictive genetic testing for complex diseases: a public health perspective, *QJM: An International Journal of Medicine*, Volume 107, Issue 2, February 2014, Pages 93–97

- The time is now ripe for the introduction of a range of genetic tests into healthcare practice

Breast cancer genetics and risk assessment: an overview for the clinician (2023)

"It is only through identification of high-risk women that we can prevent breast cancer, not just screen for it."

L. Larkin (2023): Breast cancer genetics and risk assessment: an overview for the clinician, Climacteric, DOI: 10.1080/13697137.2023.2184254

"It is only through identification of high-risk patients that we can prevent most complex chronic disease, not just screen for it."

JME, Personal Communication, 2024

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Thank You

Integrative Healthcare SYMPOSIUM

Saturday 12:30pm – 1:30pm

The Latest in Longevity Medicine: Predictive Genomics

Please scan this QR code on you mobile

or tablet device to access the session feedback survey

The Latest in Longevity Medicine: Predictive Genomics