

Managing Cancer Risk in the Genetics Clinic

Dr Jonathan N Berg

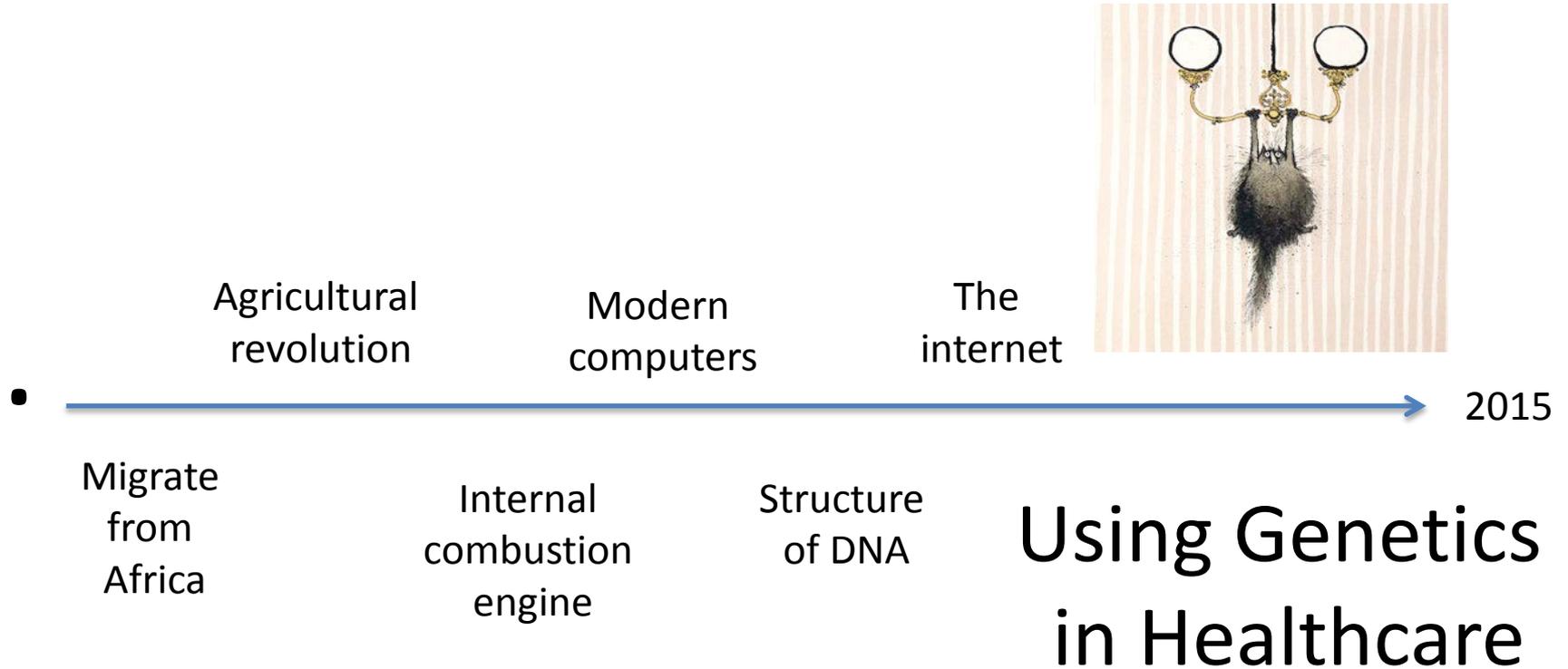


On hearing the word 'genetics'



**PANIC
WILDLY
AND
RUN
AWAY**

The timeline of human evolution



PCR
Invented

First gene
mapped

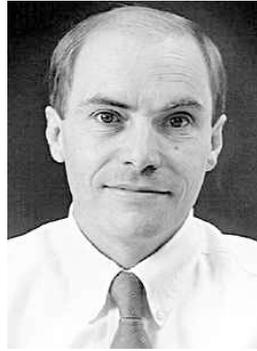
Genomewide
maps

First whole
Human
Genome
Sequence

Next
Generation
Sequencing

1985

2015

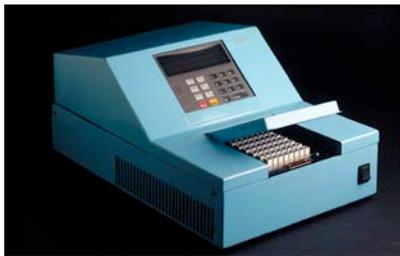


Why would
we need
Clinical Genetics ?

Clinical Genetics
a purely
observational specialty

Clinical Genetics
patient
management

Genome
enabled Medicine

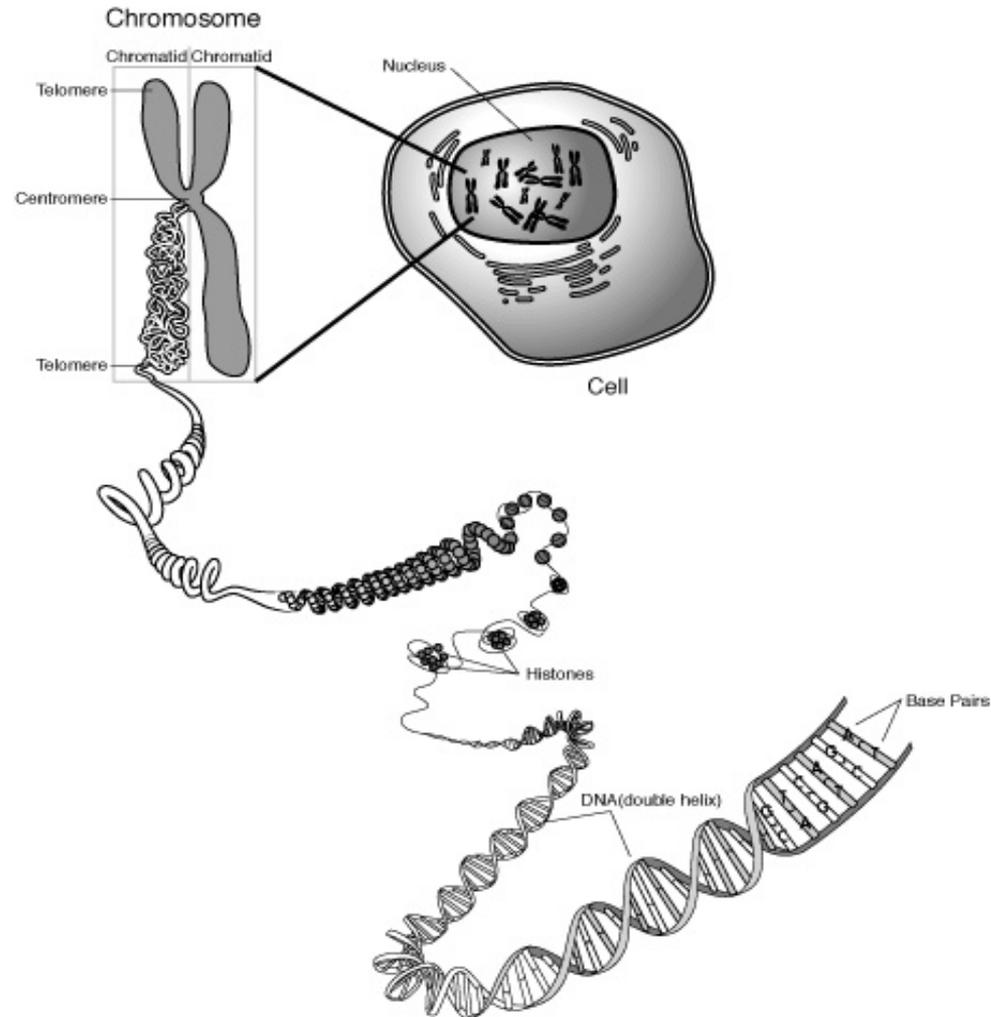


Clinical Genetics

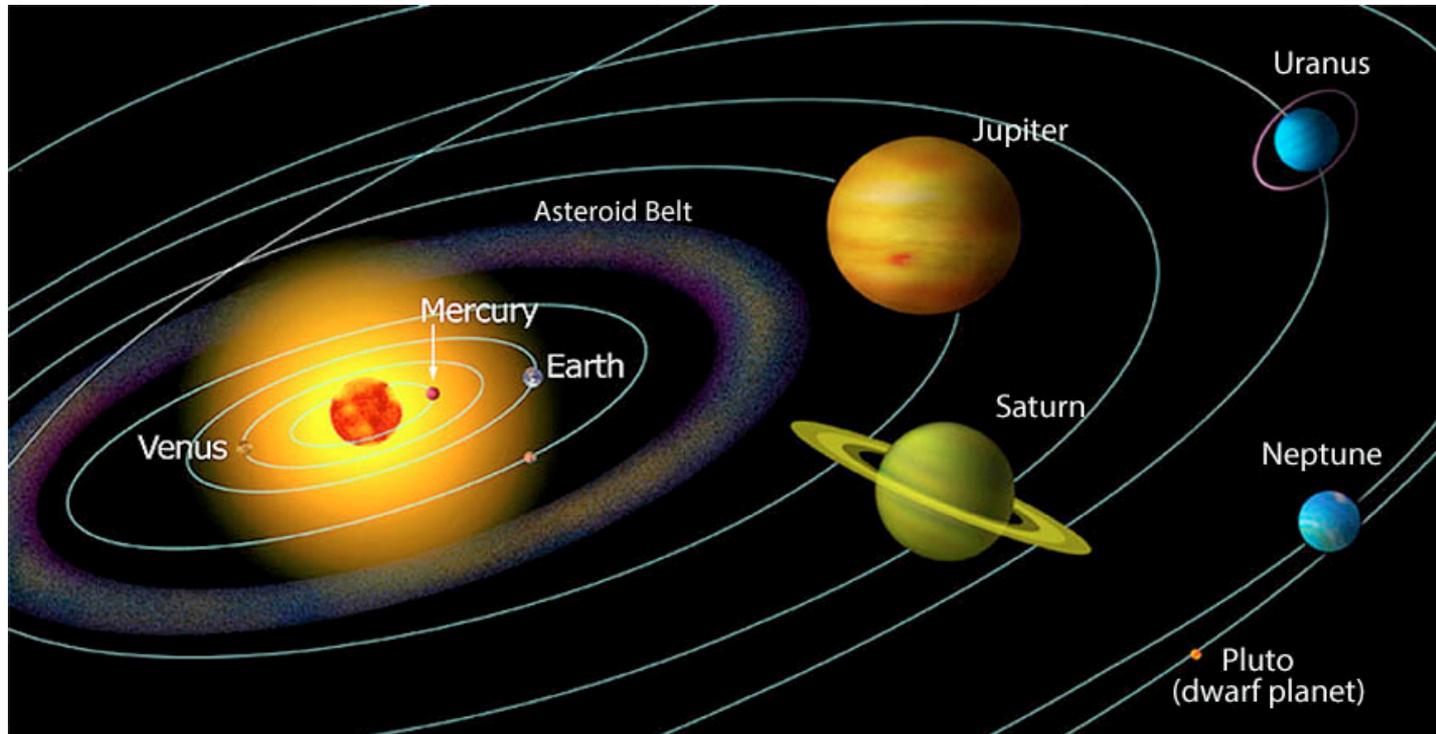
Useless

Useful

DNA and chromosomes



You have 18 light hours of DNA in your body



3,000,000,000 'letters' in the genome

Every person is different

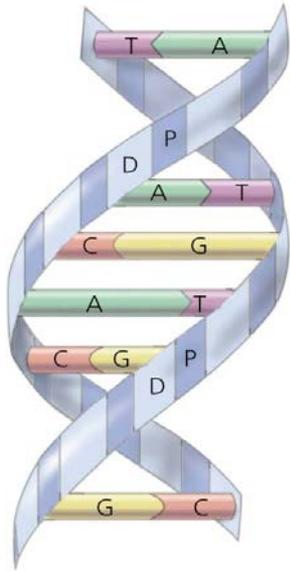
Polymorphisms

About 3,000,000 variations from the 'normal' sequence in each person. Some are risk factors for disease.

Mutations

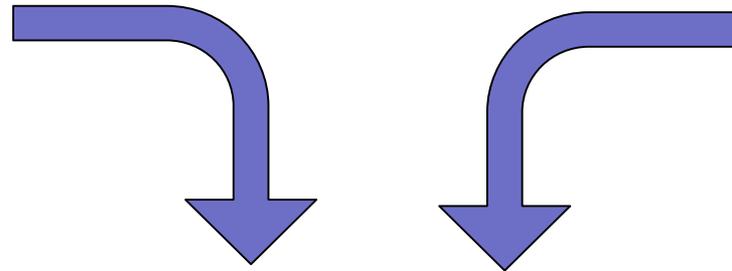
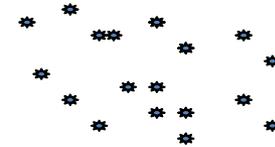
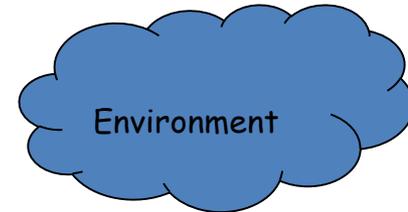
Rare variations in the genome that cause disease all by themselves.

Disease = genes + environment



Academy Artworks

Genes



Disease

What is the real question ?

A 30 year old woman comes to your clinic because her Mother died from breast cancer at the age of 47.



Inherited Risk of Cancer

Little bad genes

many polymorphisms of small effect

Big bad genes

A single genetic mutation or “fault” that causes a very high risk of breast cancer

Breast Cancer Risk

Little Bad Genes

- Polymorphisms



Genetic variations present in the population

More frequent in people affected with breast cancer

Size of effect is small

The general principle – more risk polymorphisms, greater likelihood of cancer



Higher risk

Lower risk

A single high penetrance mutation 'beats' other factors

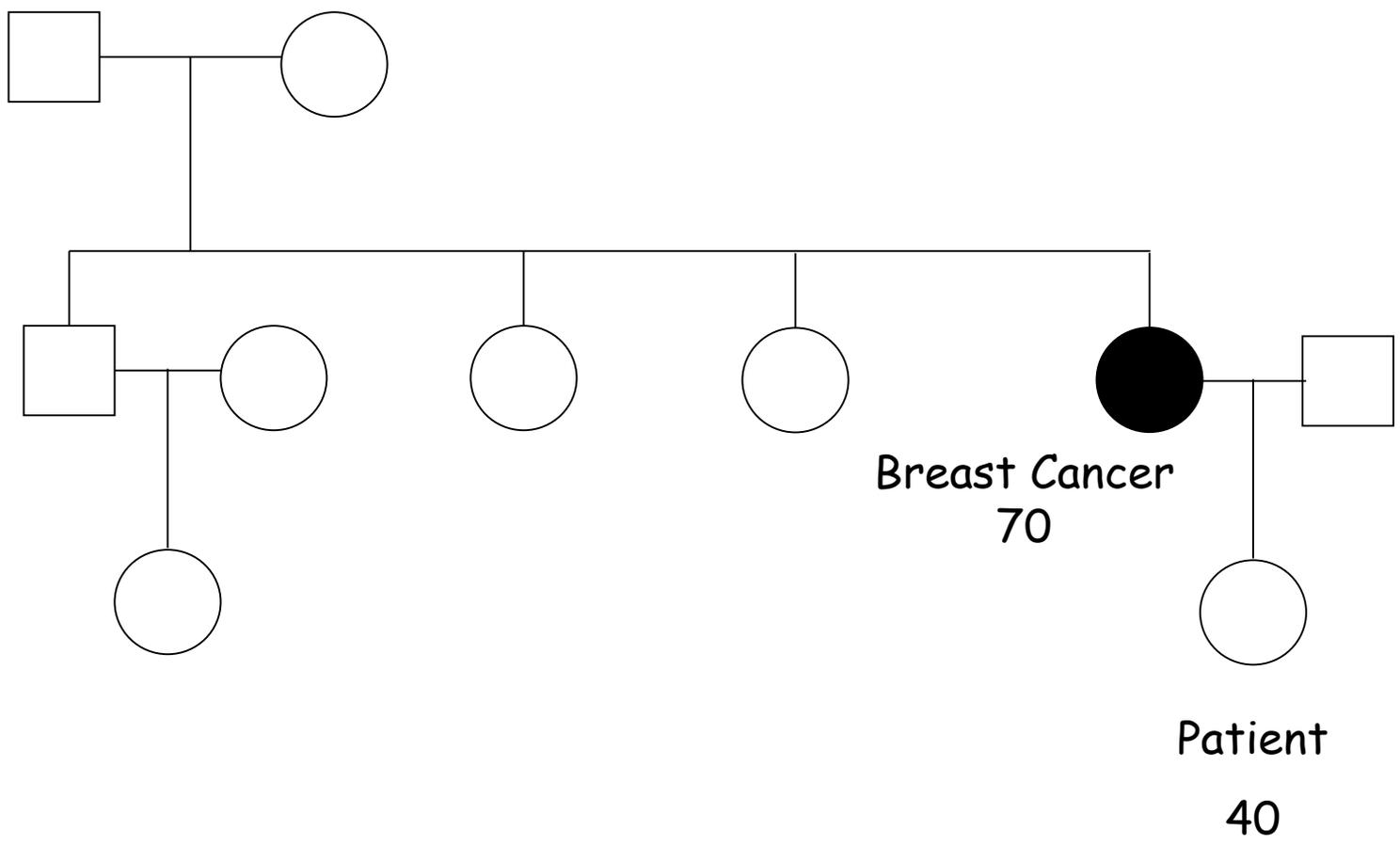


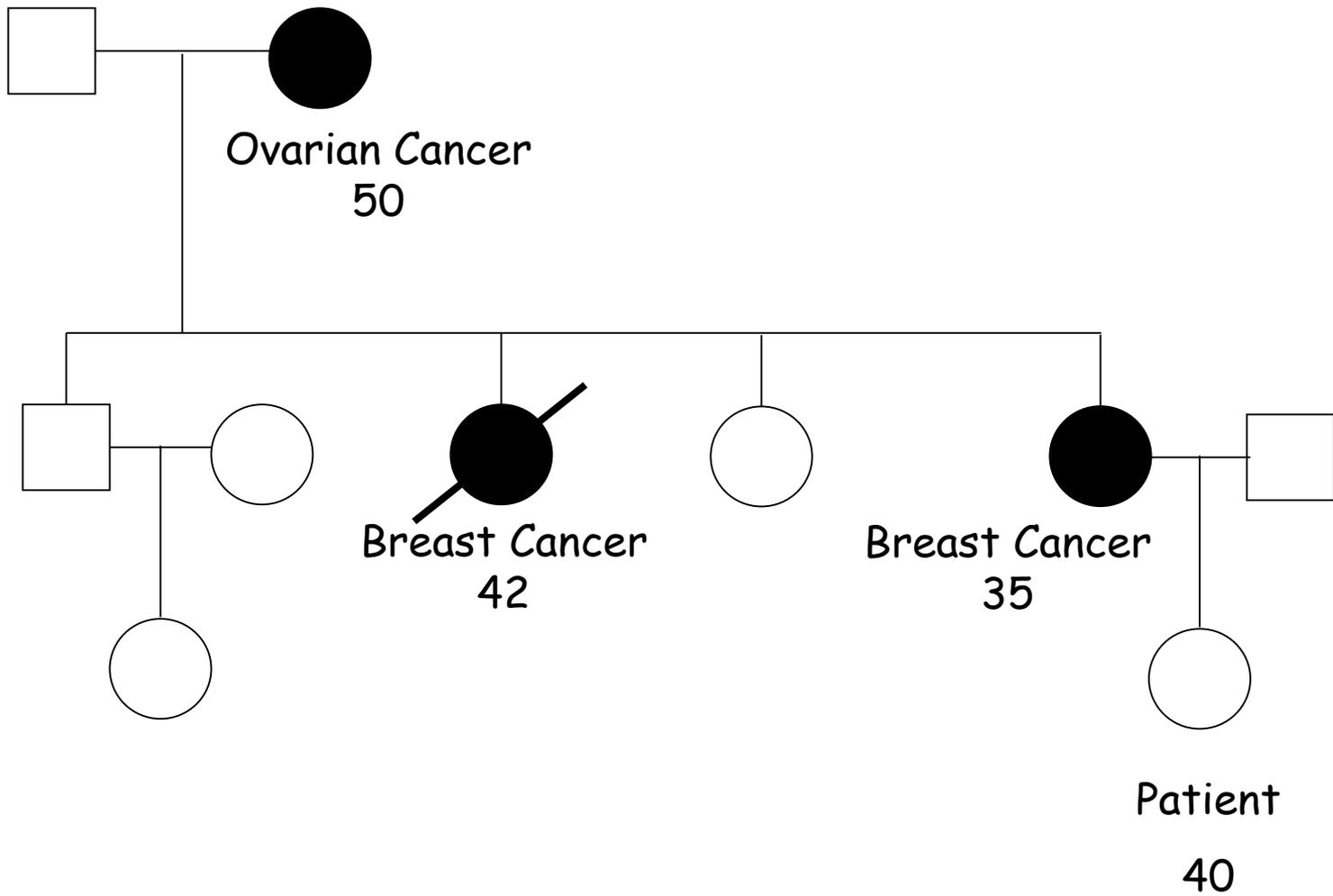
Older
TV



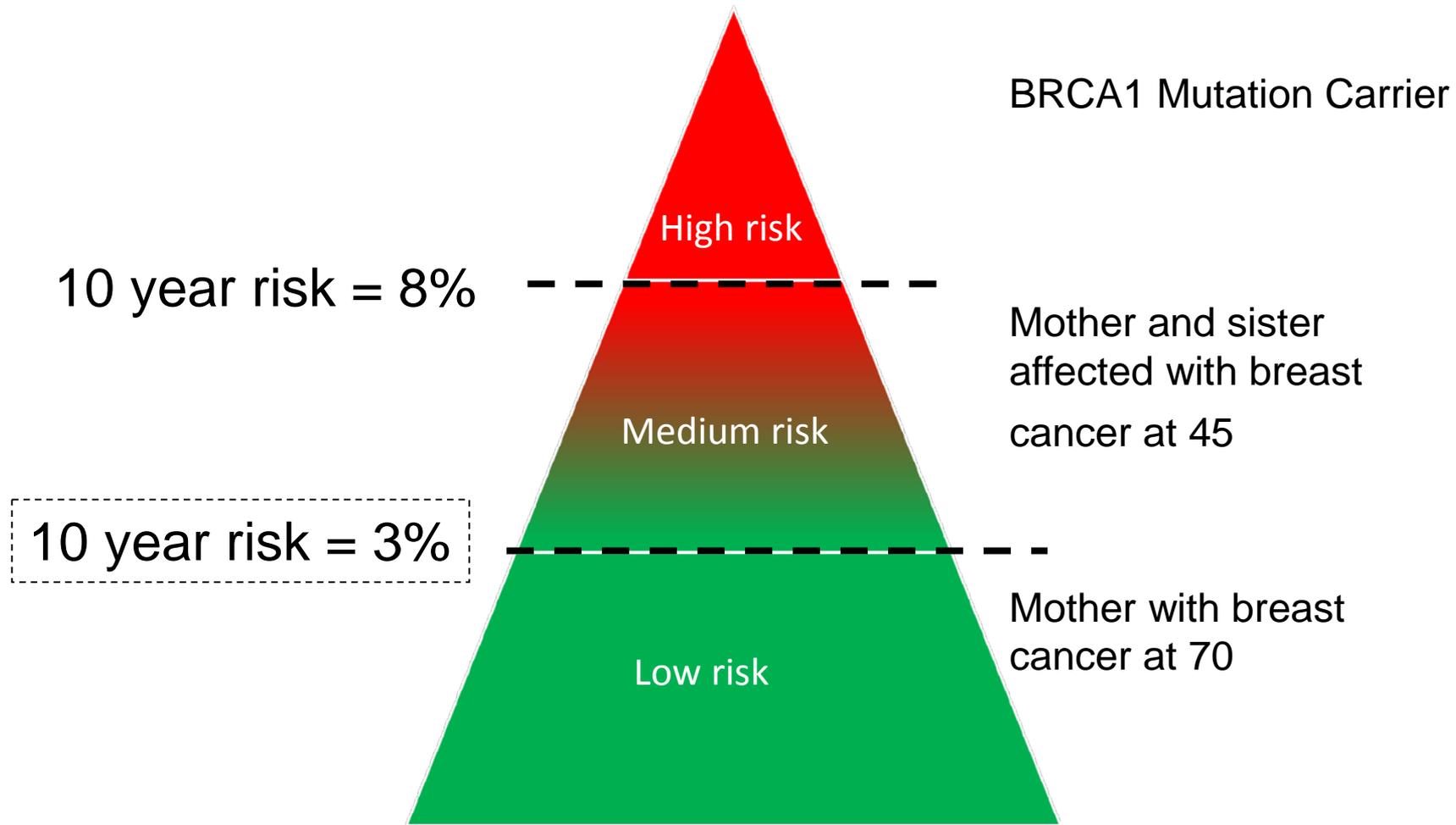
High risk

Low risk





Clinical Assessment of Breast Cancer Risk

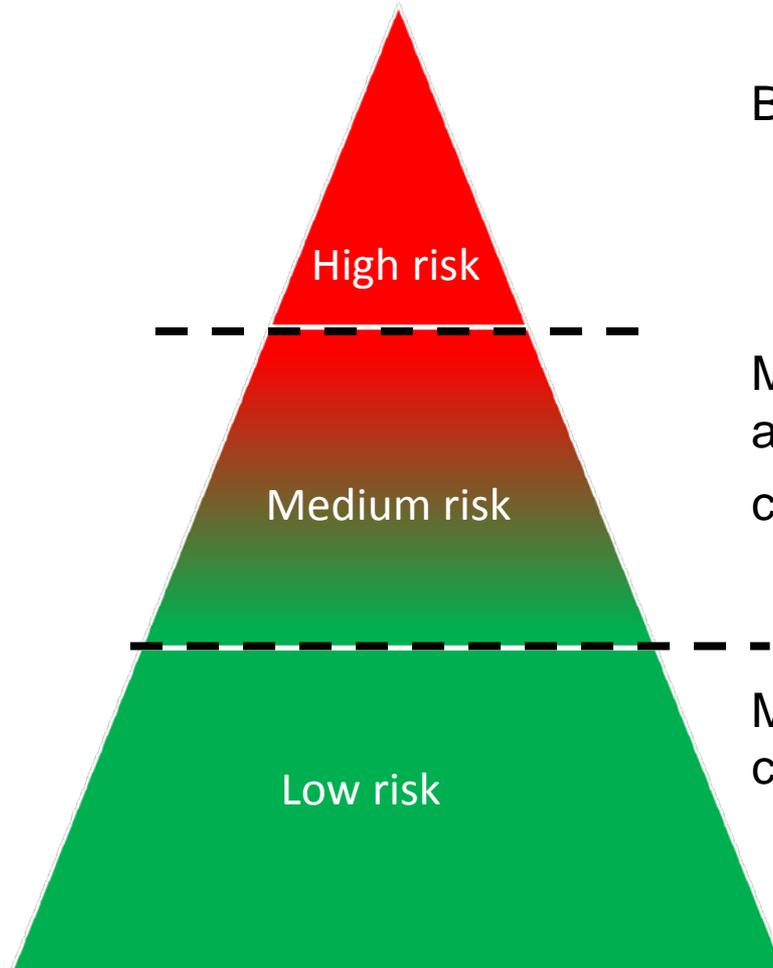


Clinical Assessment of Breast Cancer Risk

Single Mutation



Genes + Environment



BRCA1 Mutation Carrier

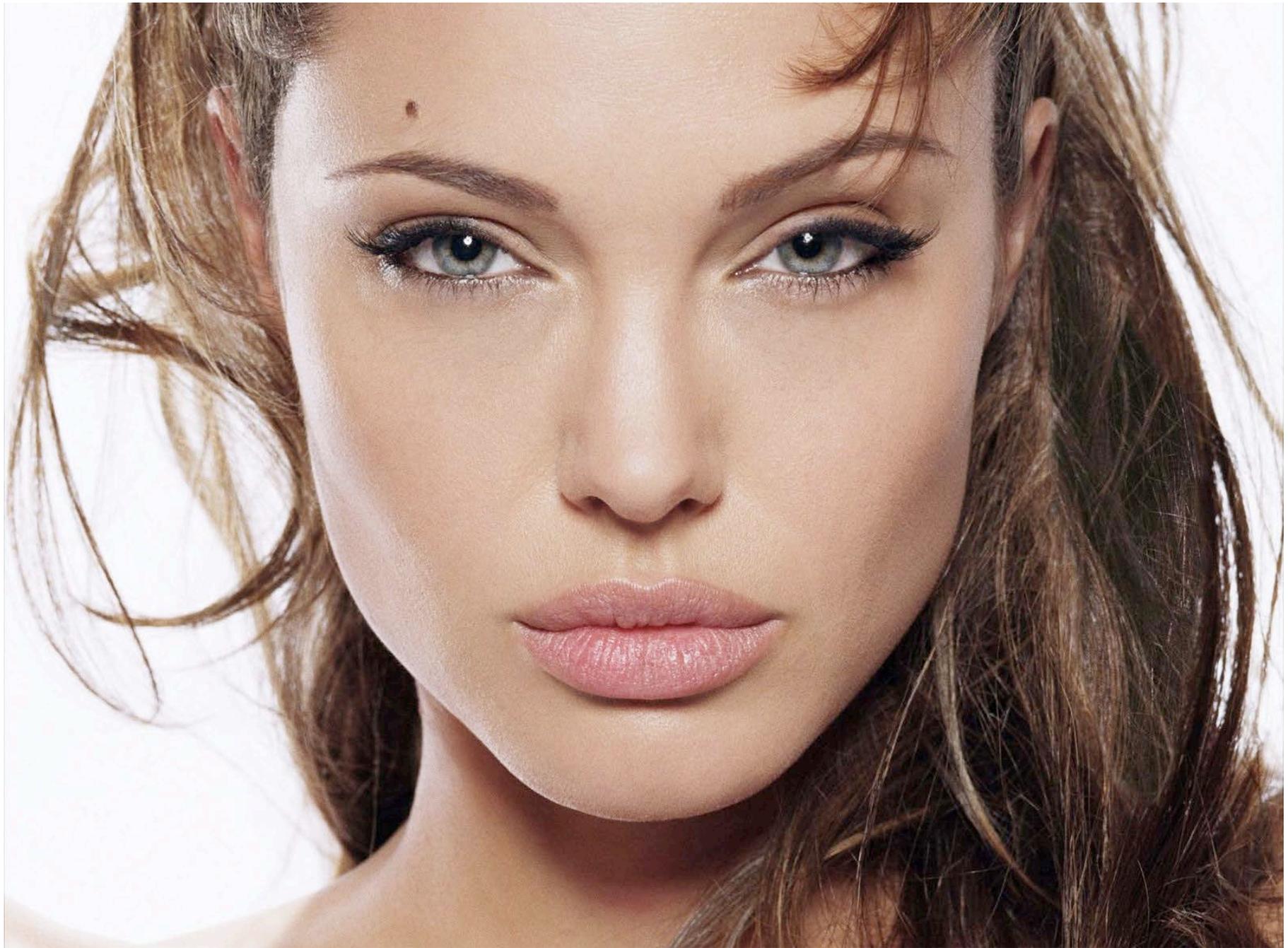
High risk

Mother and sister
affected with breast
cancer at 45

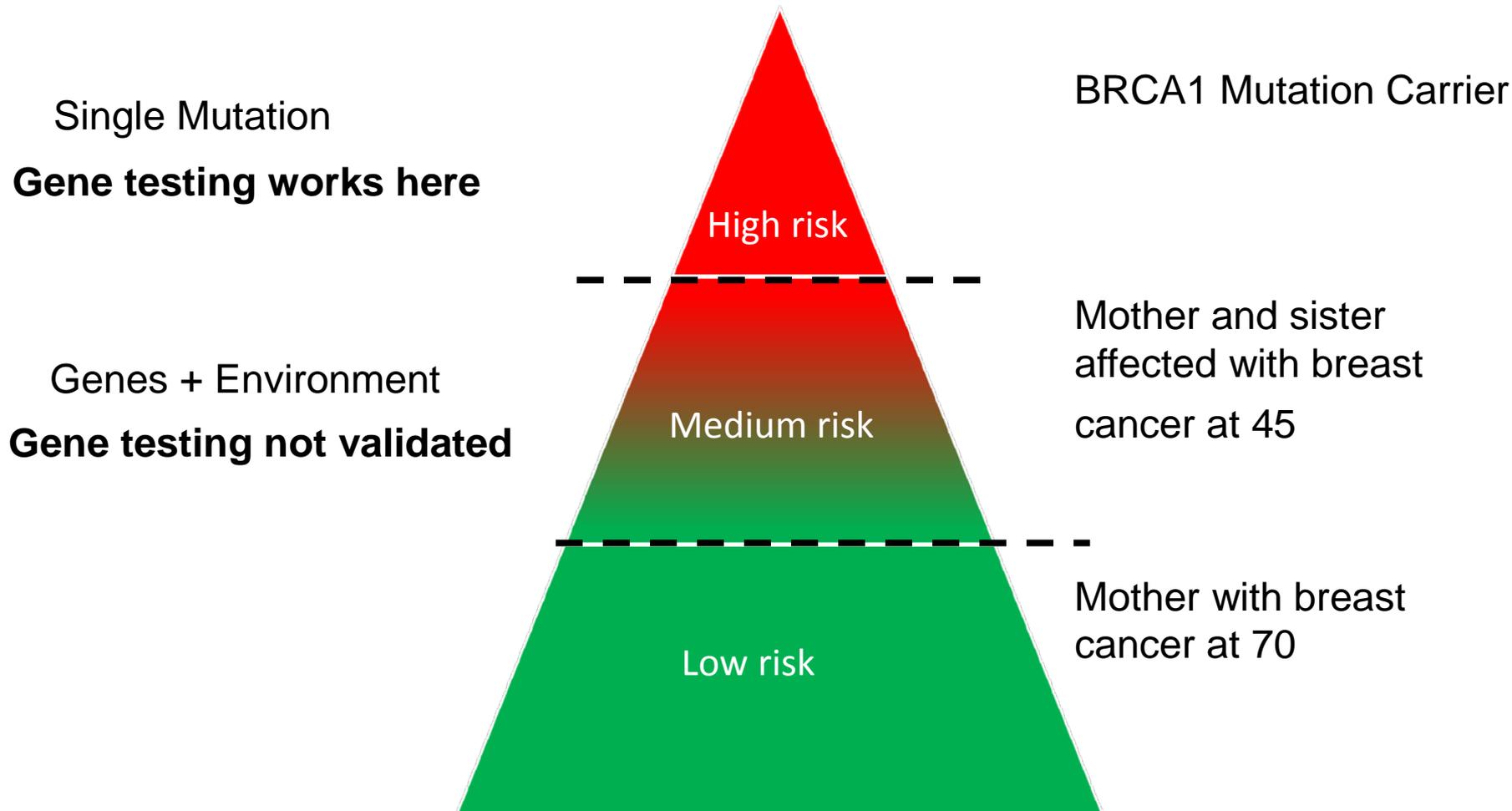
Medium risk

Mother with breast
cancer at 70

Low risk



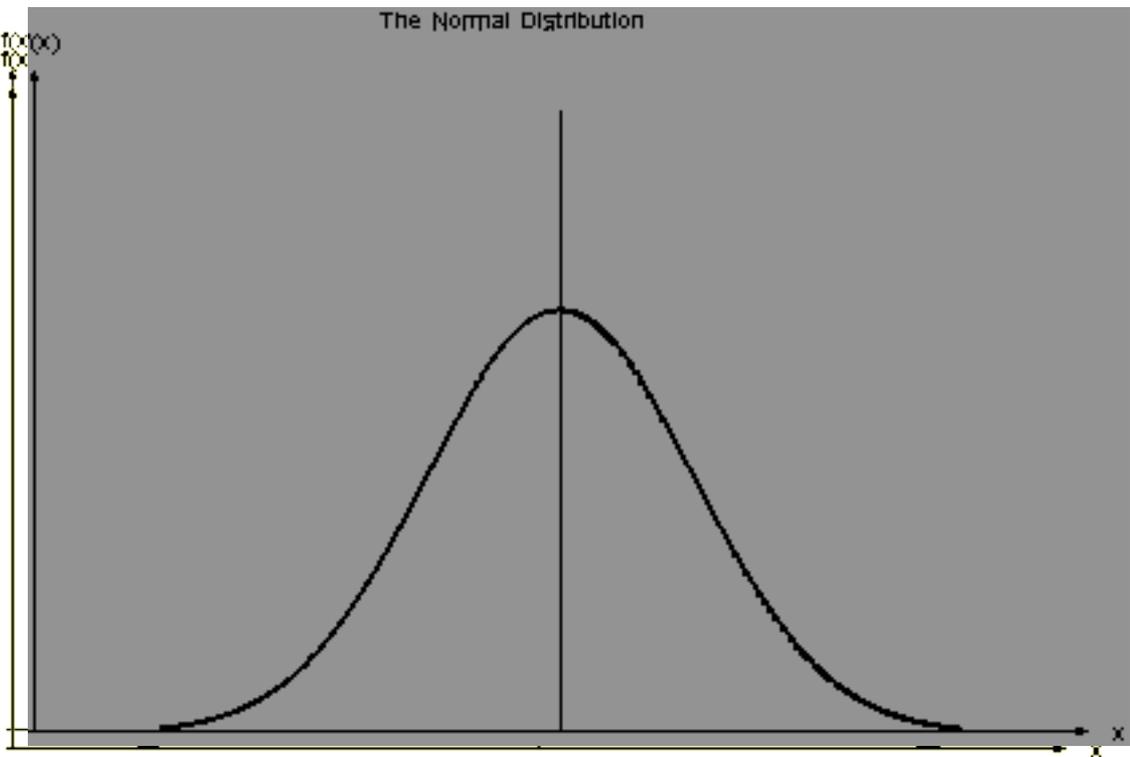
Clinical Assessment of Breast Cancer Risk





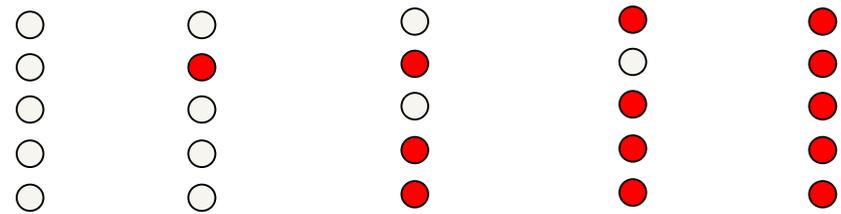
The Normal Distribution

Proportion of Population

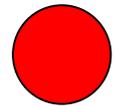


Risk of Disease

Different Risk Factors

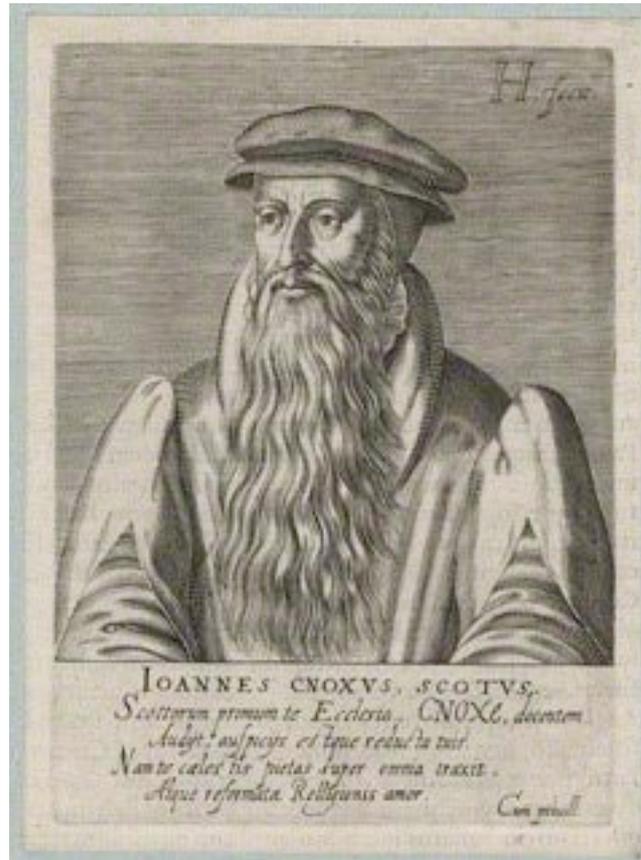


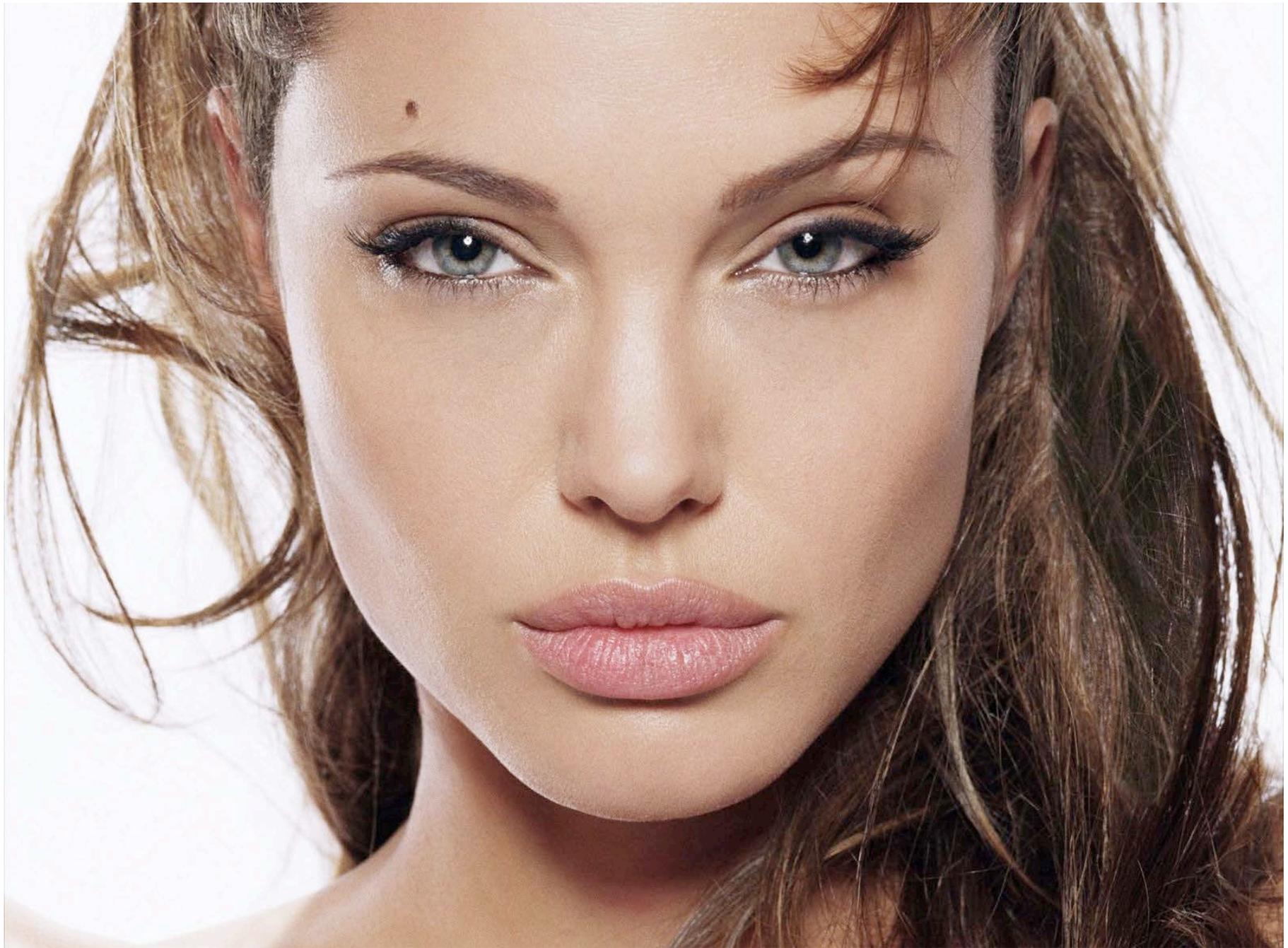
Gene 1
Gene 2
Obesity
HRT
Alcohol



BRCA1 Mutation

Genetic testing is not just about predestination





When we are dealing with small genetic effects

- Genetic testing doesn't help
- **Moderate Risk is more amenable to lifestyle changes**
- This is the majority of people with a family history of cancer (bowel or breast)

Are patients with a family history more amenable to lifestyle changes ?

Can we communicate the potential for reducing risk ?

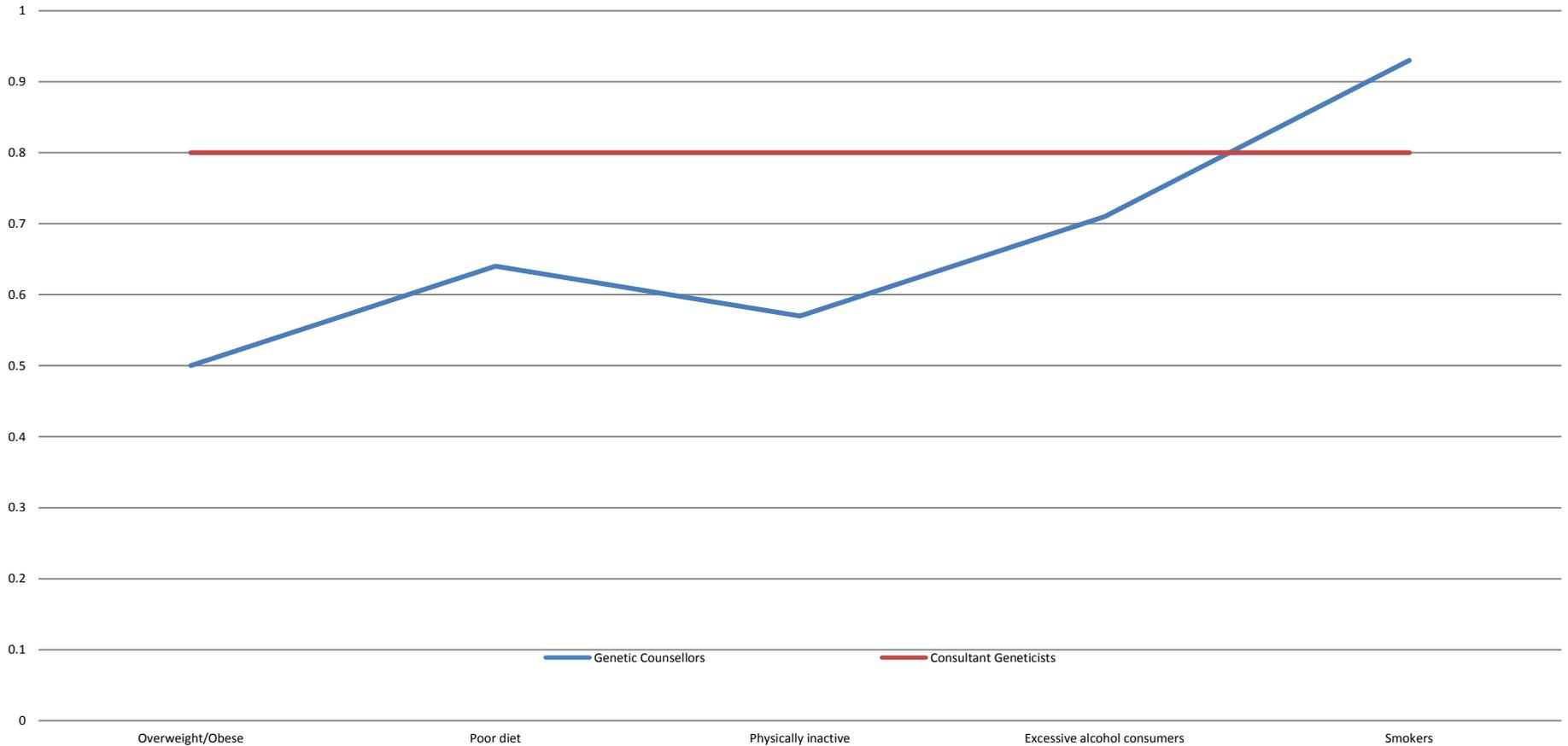
Do the same risk reductions apply where there is a family history ?

Are there effective interventions we can offer ?

Can this be implemented within the NHS ?

Willingness of genetics clinic staff to address health behaviours with certain types of individuals.

Rimbi et al. 2014



How well do our patients do now ?

A. Anderson, S. Caswell et al. submitted 2016

Recommendation	Met recommendations in this study if:	Breast Cancer Screening n =165		Colorectal Cancer Screening n =61		All ^a n =237	
		n	Achieving n (%)	n	Achieving n (%)	n	Achieving n (%)
Alcohol: Limit alcohol drinks to one per day for women, two per day for men	≤1 drink/per day for women, ≤2 drinks/day for men	165	72 (44)	61	22 (36)	236	100 (42)
Body fatness: Be as lean as possible within the normal range of body weight	BMI ≥ 18.5 and ≤ 25.0	156	75 (48)	59	24 (41)	225	102 (45)
Fibre: Eat mostly foods of plant based origin	DINE fibre score > 40	138	12 (9)	55	7 (12)	222	19 (9)
Physical Activity: Be physically active	IPAQ ≥ 30 min moderate 5 days	156	72 (45)	60	24 (40)	231	103 (45)
Processed meat: Avoid	Avoid	165	15 (9)	59	2 (3)	236	18 (8)
Red meat: Limit intake	<500g/week	158	134 (85)	60	47 (78)	228	191 (84)
Smoking: avoid	Non smoker	166	149 (90)	60	54 (90)	236	210 (89)
Mean score (0-7)		166	3.19 (±1.14)	61	2.95 (±1.0)	237	3.14 (±1.1)

Genetics and Cancer Risk

We can identify and effectively manage people at high risk gene mutations that cause cancer

Genetic testing doesn't help (yet) in the moderate risk group with genes of small effect

Lifestyle intervention is likely to be more useful in the moderate risk group

We need to work on developing interventions for this group

Better staff skills



Effective Intervention Programmes

