



Brystkreft: historie, epidemiologi, etiologi og patologi

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Historien



Edwin Smiths papyrus

- Edwin Smith (1822 – 1906) amerikansk egyptolog. Kjøpte papyrusdokumentet i 1862.
- Det er en kopi av en del av en egyptisk lærebok i traumatologi og som daterer seg tilbake til 3000 år f.Kr.
- Her finner man en beskrivelse av 8 tumores eller ulcera i bryst. Disse ble forsøkt fjernet ved kauterisering ved hjelp av et instrument man kalte en «ilddrill». Men selv da var man innforstått med at dette ikke var noen god behandling. Men det var det man hadde.



Edwin Smiths papyrus case 39



Diagnosis: Thou shouldst say concerning him: "One having tumors with prominent head in his breast, (and) they produce cysts of pus.

An ailment which I will treat with the fire-drill. "

Brystkreftens historie

- Brystkreft beskrives i alle historiske epoker. Dette skyldes sikkert at brystkreft – spesielt i de senere stadier av sykdommen – presenterer seg som en synlig tumor til forskjell fra maligne tilstander i viscera.
- Brystkreftsykdommen var tabubelagt og blir sjeldent nevnt utenfor de medisinske lærebøker. Å snakke åpent om sykdommen, er en særdeles nylig foreteelse.

Brystkraft i kunsten



Rafael

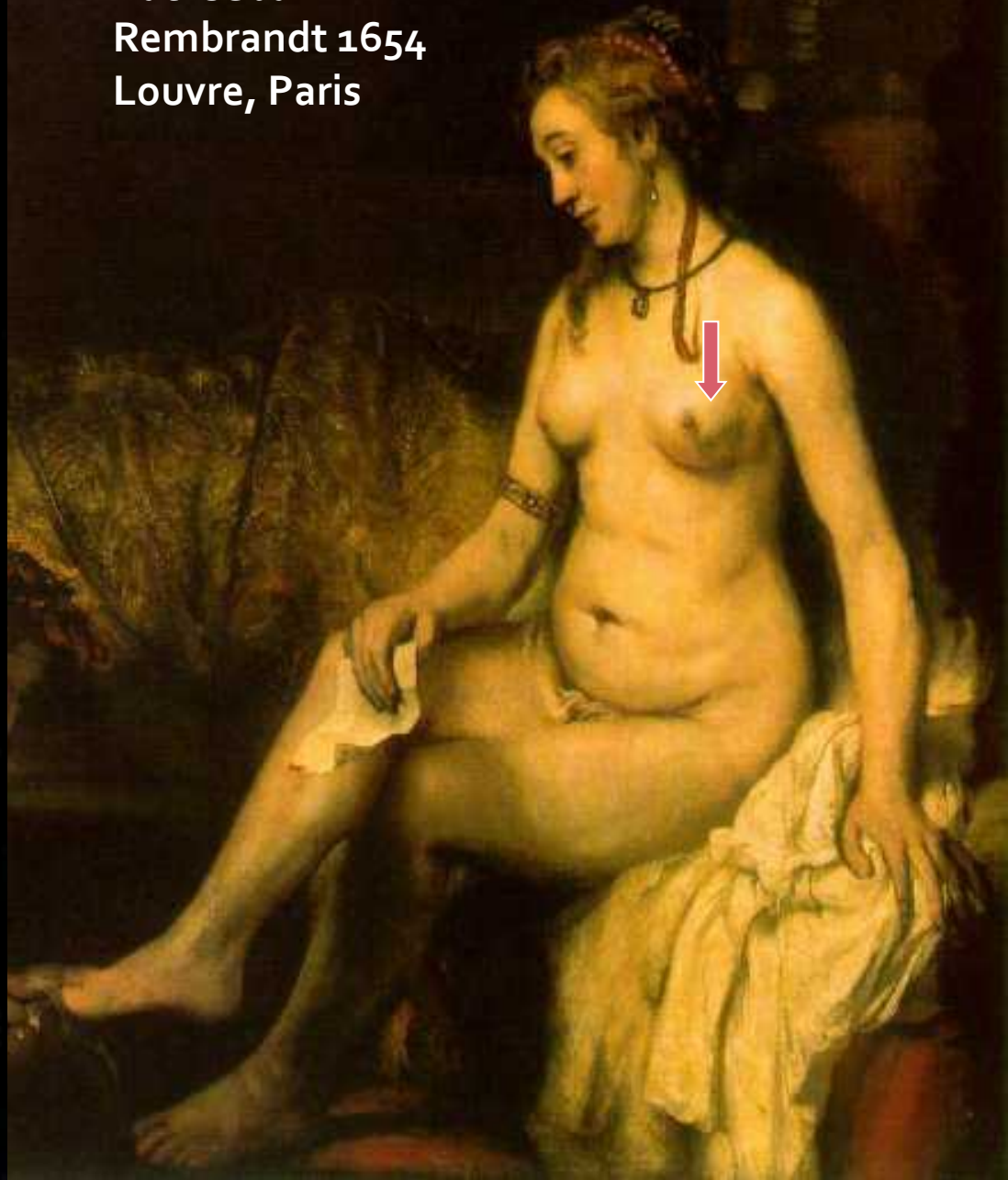


Rembrandt

La Fornarina
Rafael 1520
Galleria Barberini



Bathseba
Rembrandt 1654
Louvre, Paris



"Natt" 1524
Michelangelo
Medici-kapellet
i Firenze

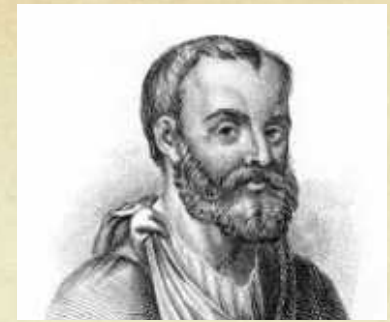


Madonna frir Milano fra pesten



Giovanni Battista Crespi (1573 – 1632)
called **Il Cerano**,

Historien



- Galen mente at brystkreft ble forårsaket av for mye svart galle. Han tok til orde for at enkelte svulster var mer aggressive enn andre. På den tiden var brystkreft en systemsykdom og kirurgi var ikke aktuelt.
- Galens lære kastet sine lange skygger over medisinen fram til 1600-tallet.
- I 1680, utfordret den franske legen Francois de la Boë Sylvius Galens teorier om for mye svart galle som årsak til kreft. Han mente det var en kjemisk prosess som omdannet lymfevæske fra å være sur til å være etsende/gjennomtrengende.



Historien



“Jeg mener at kreft utvikler seg når nerve og kjertelvev blander seg med lymfekar.
(1730 – årene)

Claude-Deshais Gendron
1663 - 1750

Historien



Bernardino Ramazzini
1633 - 1714

“ Min hypotese er at den høye forekomst av brystkreft hos nonner skyldes mangel på sex. Uten regulær seksuell aktivitet vil de reproduktive organer forfalle og kreft utvikles.” (1713)

Observasjonen av at nonner hadde mer brystkreft, står seg også i dag, men det er ikke selve mangelen på sex som det nå forklares med, men at nonner ikke drar nytte av svangerskaps beskyttende effekt.

Historien



” Jeg mener at kvinner som har regulær seksuell aktivitet, men som likevel utvikler kreft, praktiserer en form for kraftfull sex. Dette kan i sin tur føre til lymfeblokade som igjen kan føre til kreft.”

Friedrich Hoffman fra Preussen
1660 - 1742

Mammakirurgi anno 1679





Henri François Le Dran
(1685 – 1770)

I 1757 foreslo den franske legen Henri Francois Le Dran å behandle brystkreft ved å fjerne tumor kirurgisk så lenge man også fjernet infiserte lymfeknuter i armhulen. Dette førte etter hvert til utviklingen av radikal mastektomi og meget ekstensiv fjernelse av brystet.



Claude-Nicolas Le Cat
(1700 - 1768)

Claude-Nicolas Le Cat delte dette synspunktet og hevdet at kirurgi var den *eneste* måten å behandle brystkreft på.



New Yorkeren **William Stewart Halsted**, (1852 – 1922) gjorde radikal mastektomi til gullstandard. I 1898 presenterte han 76 mastektomikasuistikker for American Surgical Association.

Halsteds operasjons forble den vanligste operasjonsmåten for brystkreft til siste tredel av det 20. århundret. Foruten å fjerne hele brystet, skar kirurgen bort hele pectoralismuskulaturen som dekket brystveggen.

De mindre musklene ble også fjernet for at kirurgen skulle få lettere tilgang til armhulen (aksillen) og kunne ta ut lymfeknuter og omkringliggende fettvev.



Brystbevarende operasjoner

- Bernhard Fisher utfordret "more is better" dogmet. Fisher startet brystbevarende operasjoner i 1973 og gjennomførte randomiserte studier hvor han sammenlignet mastektomi med lumpektomi og lumpektomi pluss strålebehandling og fant at lumpektomi pluss stråling var like bra som mastektomi. Men det tok tid å overbevise kollegene om riktigheten og viktigheten av dette
- Veronesi i Italia gjorde mye av det samme, men valgte kvadrantektomi i stedet for lumpektomi. Også han fant at begrenset kirurgi med strålebehandling var like godt som mastektomi.





ON THE TREATMENT OF INOPERABLE
CASES OF CARCINOMA OF THE MAMMA:
SUGGESTIONS FOR A NEW METHOD
OF TREATMENT, WITH ILLUSTRATIVE CASES.¹

BY GEORGE THOMAS BEATSON, M.D. EDIN.,
SURGEON TO THE GLASGOW CANCER HOSPITAL; ASSISTANT SURGEON,
GLASGOW WESTERN INFIRMARY; AND EXAMINER IN SURGERY
TO THE UNIVERSITY OF EDINBURGH.

I HAVE no doubt it has fallen to the lot of nearly every medical man to have been consulted from time to time by patients suffering from carcinoma so widely spread or so situated that it has been quite apparent that nothing in the way of operative measures could be recommended. Such cases naturally excite our sympathy, but they also bring home to us the fact that once a case of cancer has passed beyond the reach of the surgeon's knife our curative measures are practically *nil*, and "that whether the case advance with giant strides or with slow and measured steps the result is equally sure and fatal." Of late, owing to my

REMARKS ON OOPHORECTOMY IN THE TREATMENT OF CANCER OF THE BREAST.

By STANLEY BOYD, M.B., F.R.C.S.,
Surgeon to Charing Cross Hospital.

In a paper published in the BRITISH MEDICAL JOURNAL of October 2nd, 1897, I gave notes of 5 cases of cancer of the breast in which I had performed the operation of double oophorectomy. The notes were brought down to August, 1897, so I am now able to add the results of more than a year's further observation.

In 2 (Nos. 3 and 4) of the 5 cases the ovaries were removed after the menopause; no obvious effect was produced upon the cancer, and one of these patients (No. 3) was dead before my paper was written. The other (No. 4, Fig. 1) had derived no



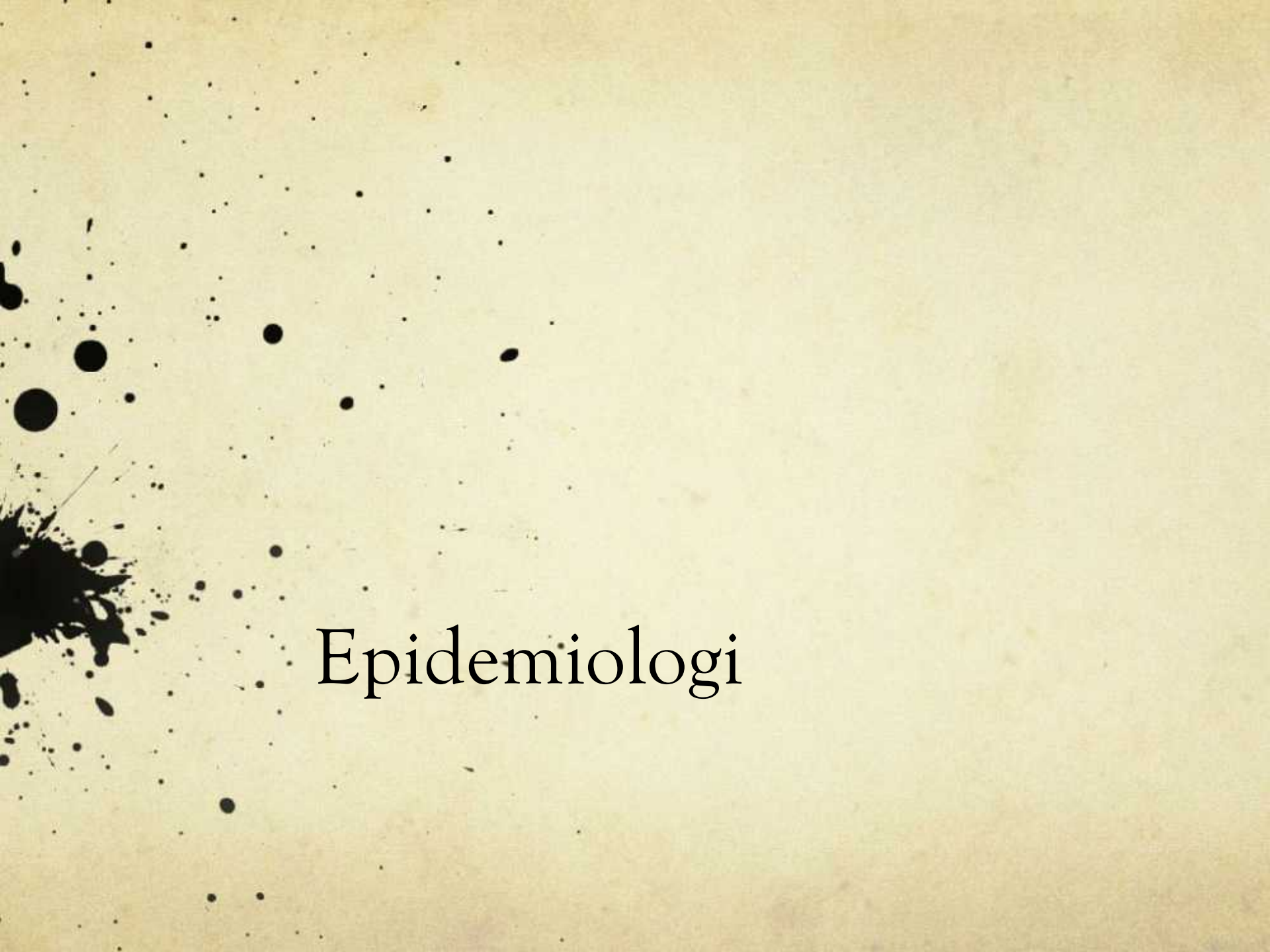
July that "the lump" (in pectoral) had "gone down very much," so that sometimes she could "scarcely feel it at all." I could find no nodule in the pectoral, but the muscle did not feel quite normal about its former site, and the deep parts were not quite so plainly felt through it on the left as on the right. I think there is slight fulness of the left pectoral region, but am not certain. The supraclavicular fulness is about the same as in March. The depression over the heart seems to be quite free from growth, and no subcutaneous or other secondary nodules can be found.

I do not think that all sign of cancer has yet disappeared in this case. I believe that the early continuous disappearance of cancer following upon the oophorectomy was due to the removal of the ovaries, but I feel that there is room for doubt as to the cause of the late variations of the pectoral nodule.

CASE II.—In this case (Fig. 2) the most rapid and satisfactory disappearance of cancer nodules and infiltrations occurred during the first six months.



Av 54 pasienter hadde 19 (35,2 %) nytte av det oophorectomi



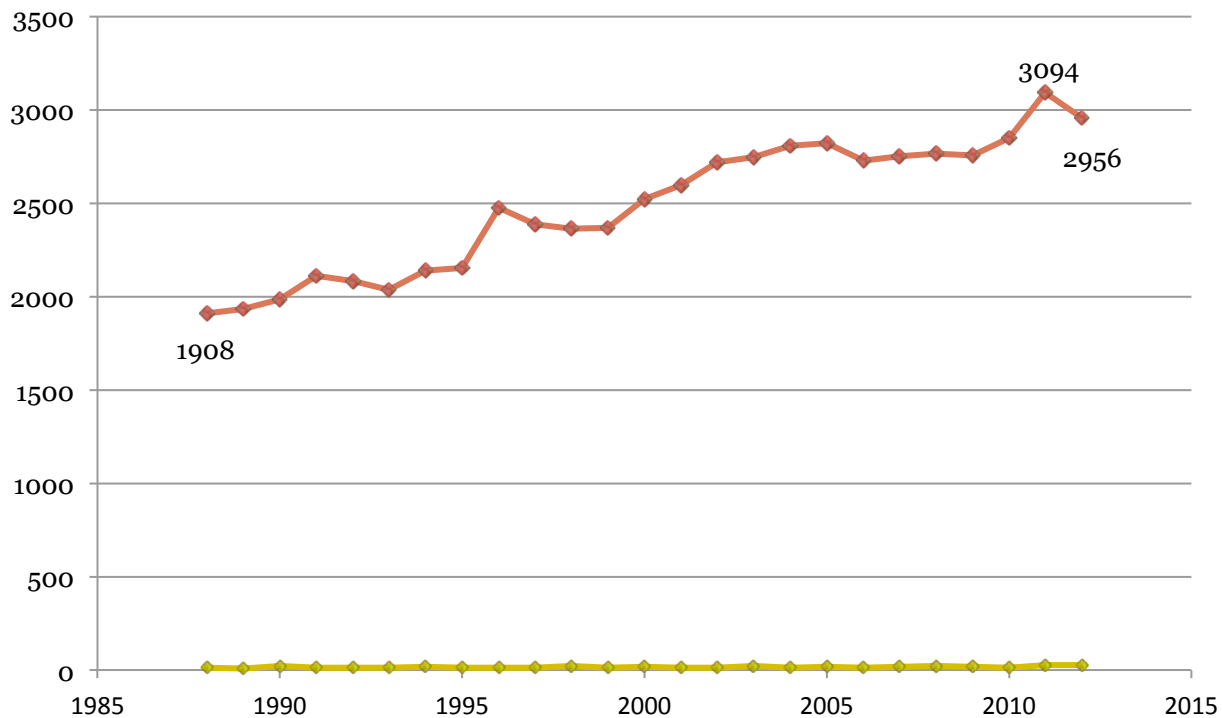
Epidemiologi

Cancer in Norway 2012

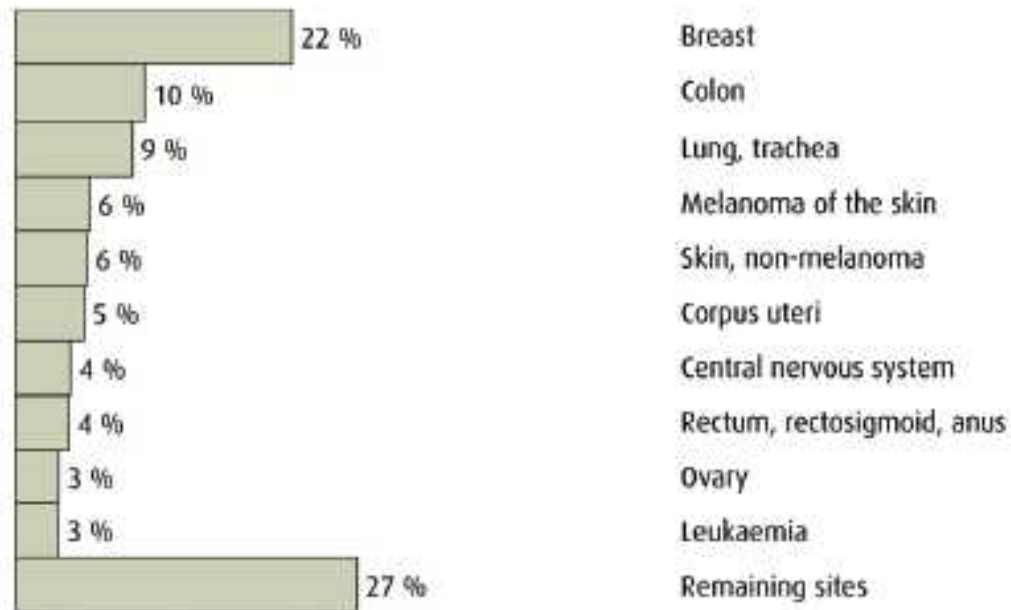
Cancer incidence, mortality,
survival and prevalence in Norway



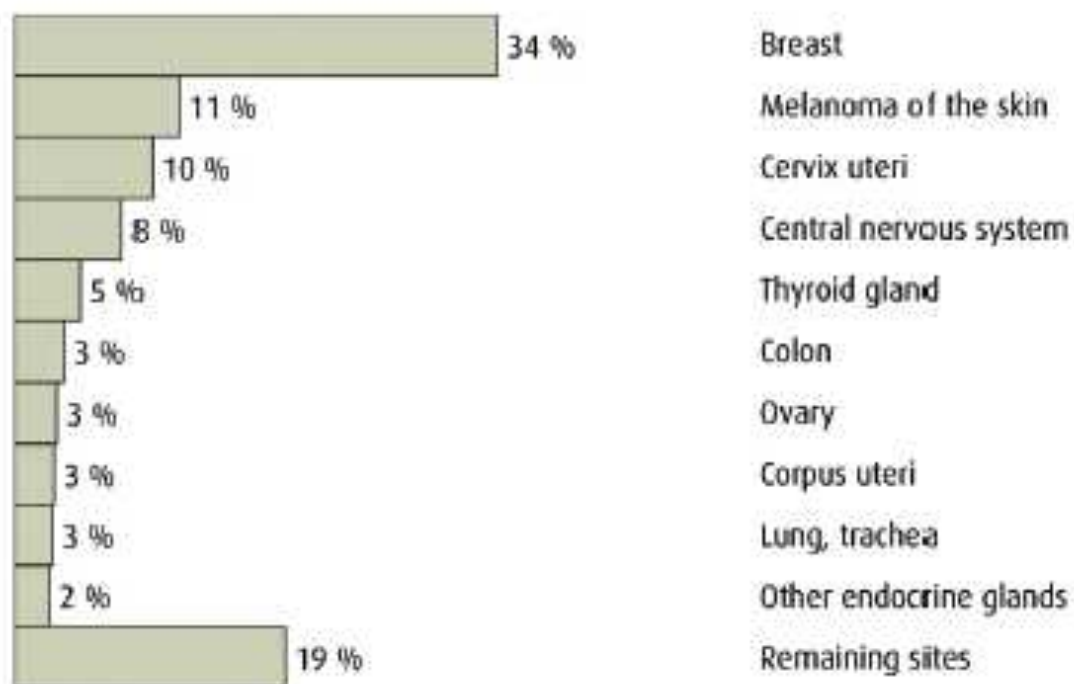
Brystkreft i Norge



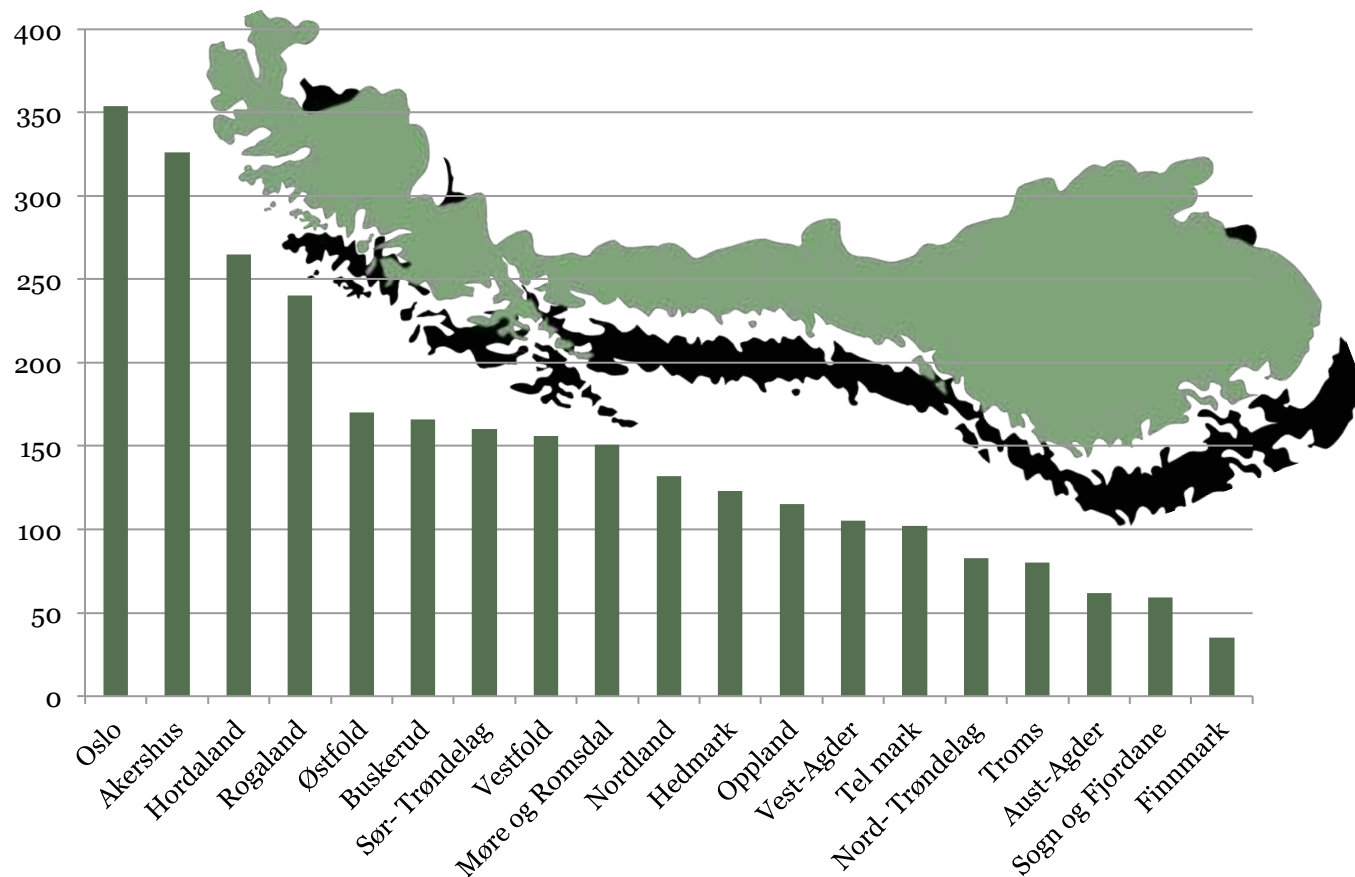
FEMALE all ages (66 541 cases)



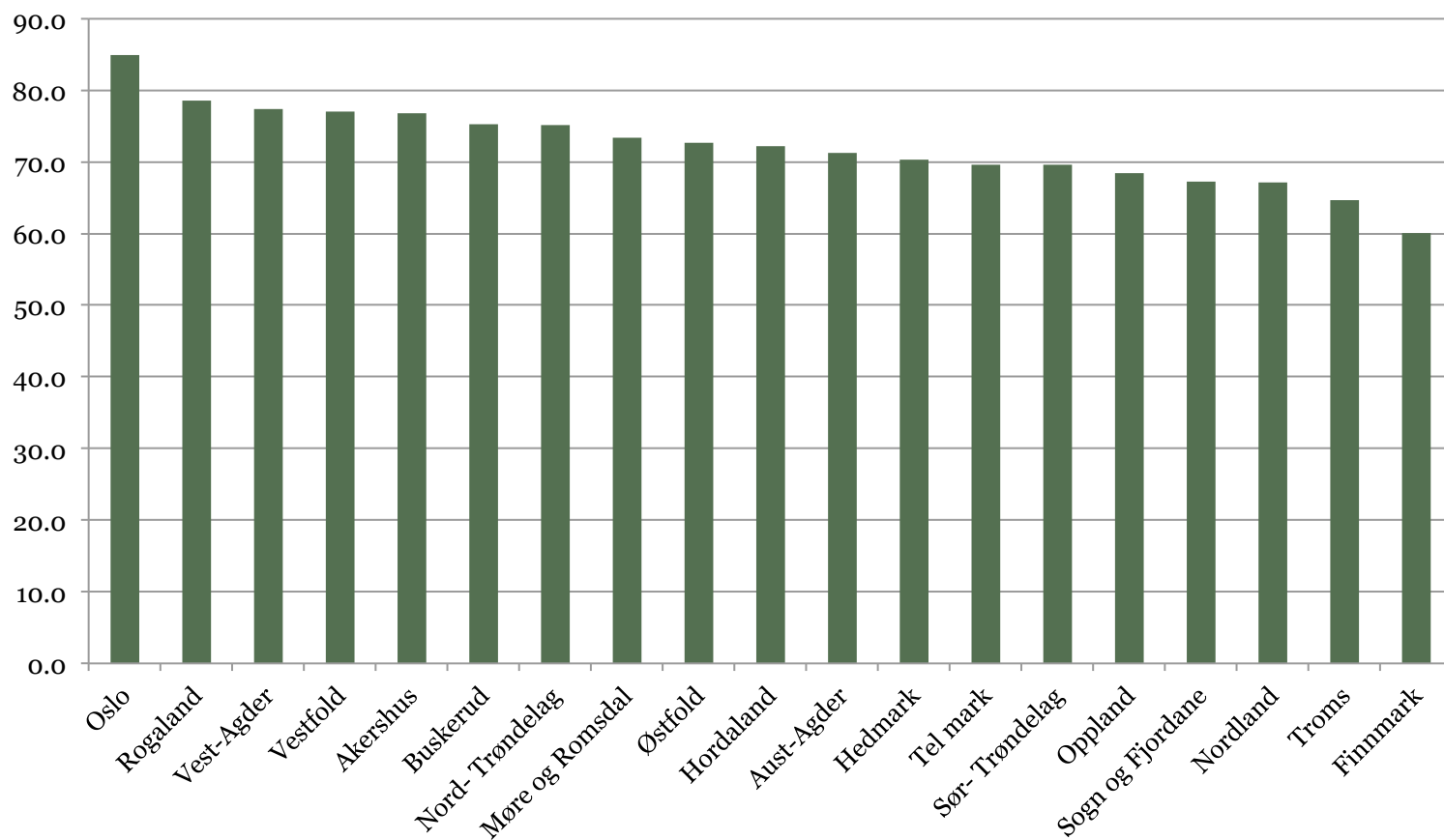
FEMALE 25-49 years (9 016 cases)



Antall per fylke 2008 - 2012

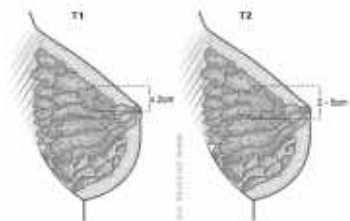


Insidens per fylke 2008 - 2012

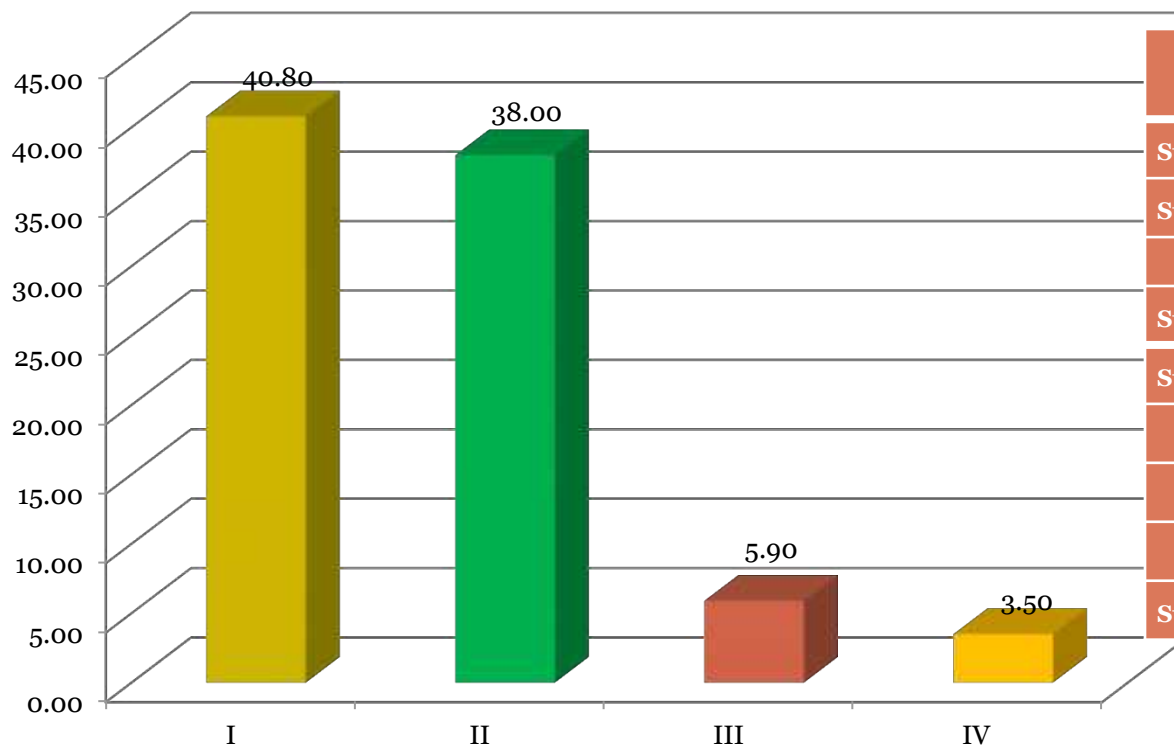
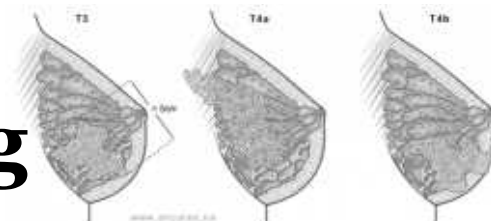


Prosentvis nye cancere diagnostisert hos kvinner under 50 år (2008 – 2012)

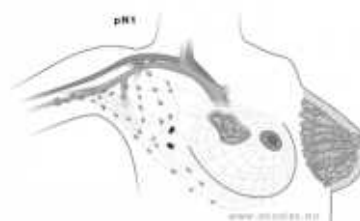
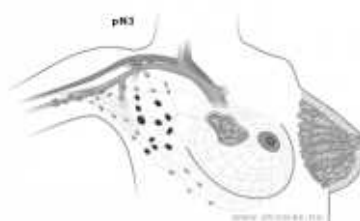
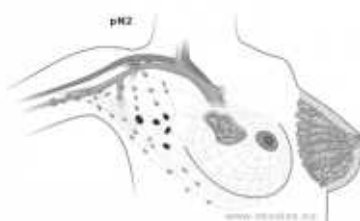
< 50 år	21.2 %
< 45 år	11.0 %
< 40 år	4.7 %
< 35 år	1.7 %
< 30 år	0.5 %



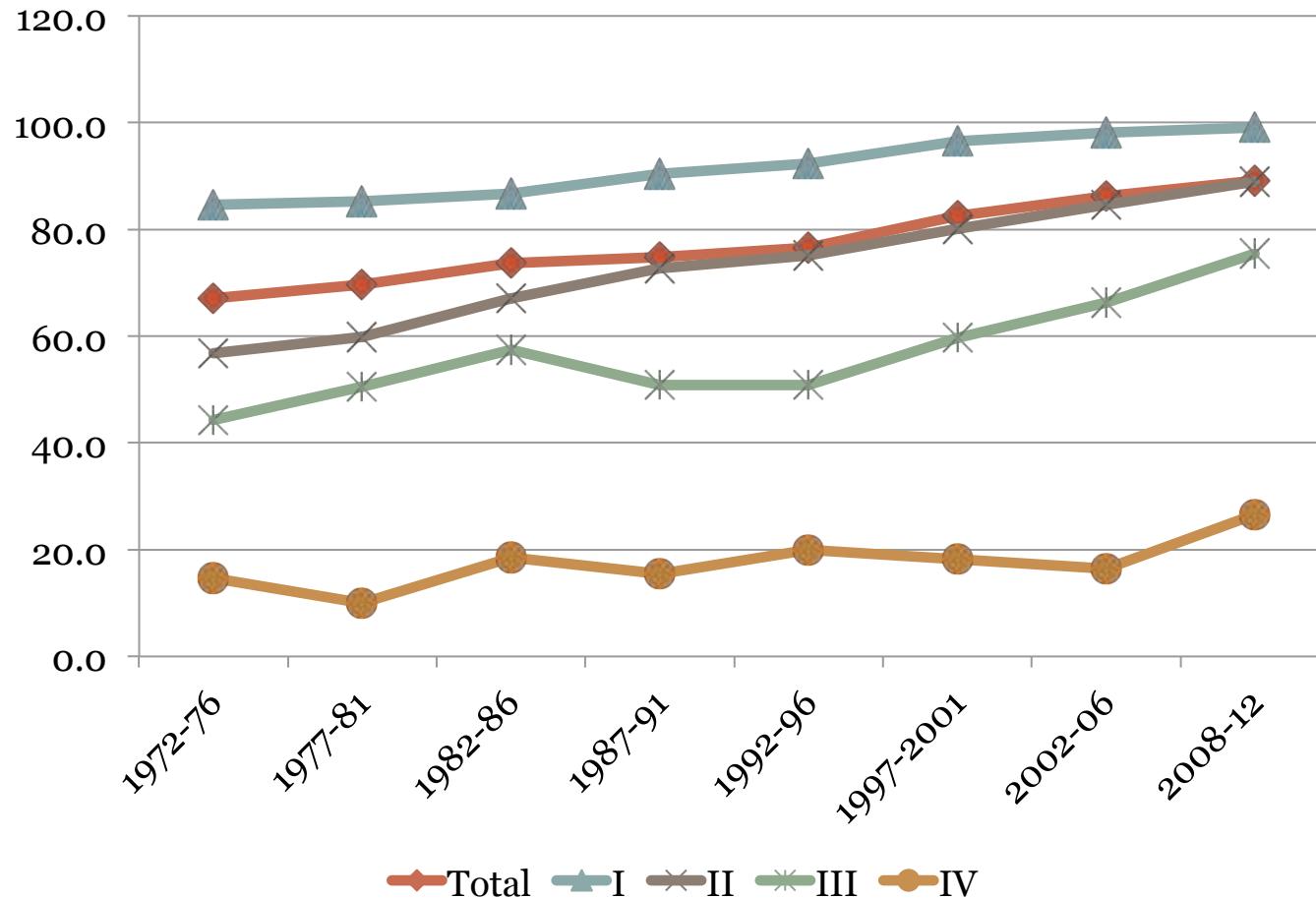
Stadieinndeling



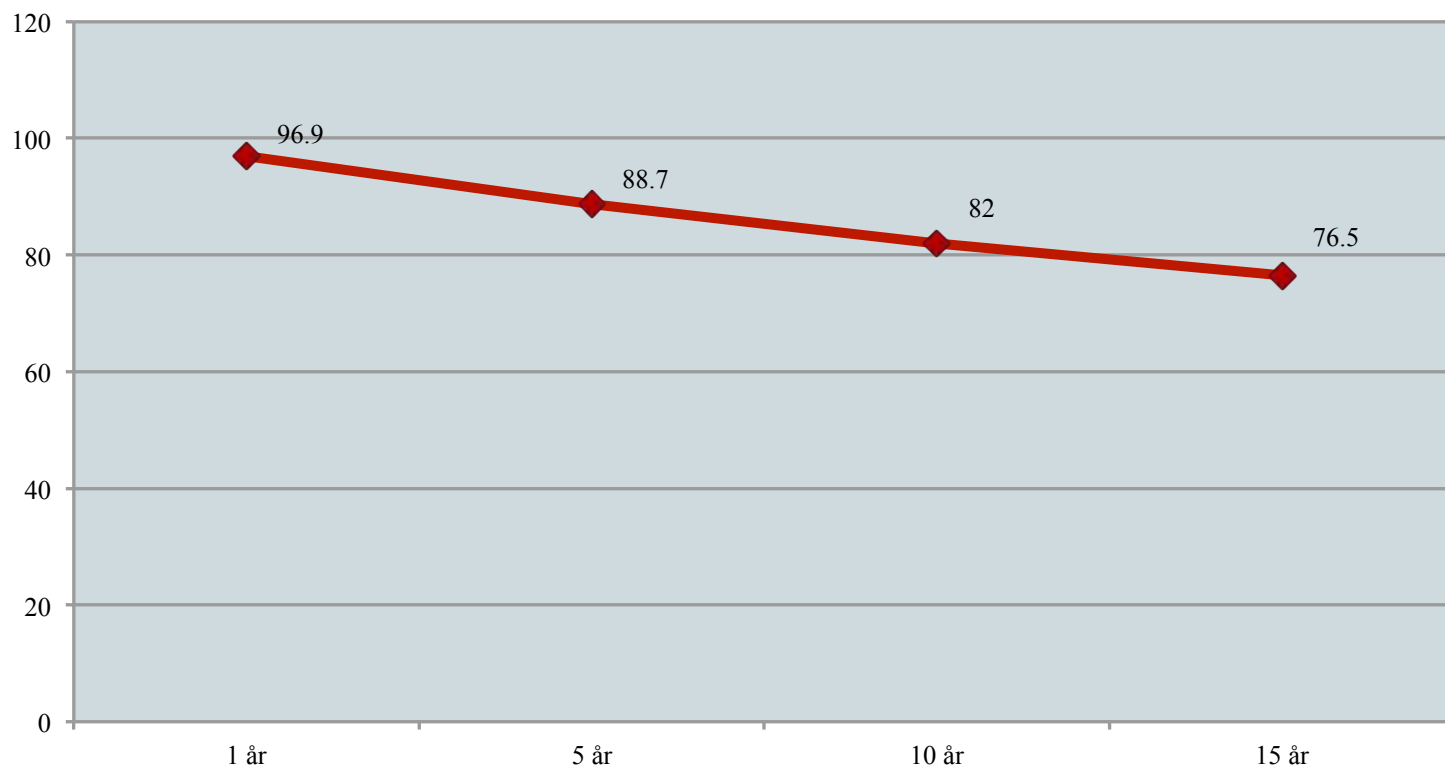
Primært operabel kreftsykdom	
Stadium I	T1NoMo
Stadium II	T0-2N1Mo
	T2NoMo
Stadium II	T3NoMo
Stadium III	T0-2N2Mo
	T3N1-2Mo
	T4No-2Mo
Stadium IV	T0-4N3Mo
	T1-4No-3M1



5-års overlevelse i henhold til stadium



Overlevelse opp til 15 år

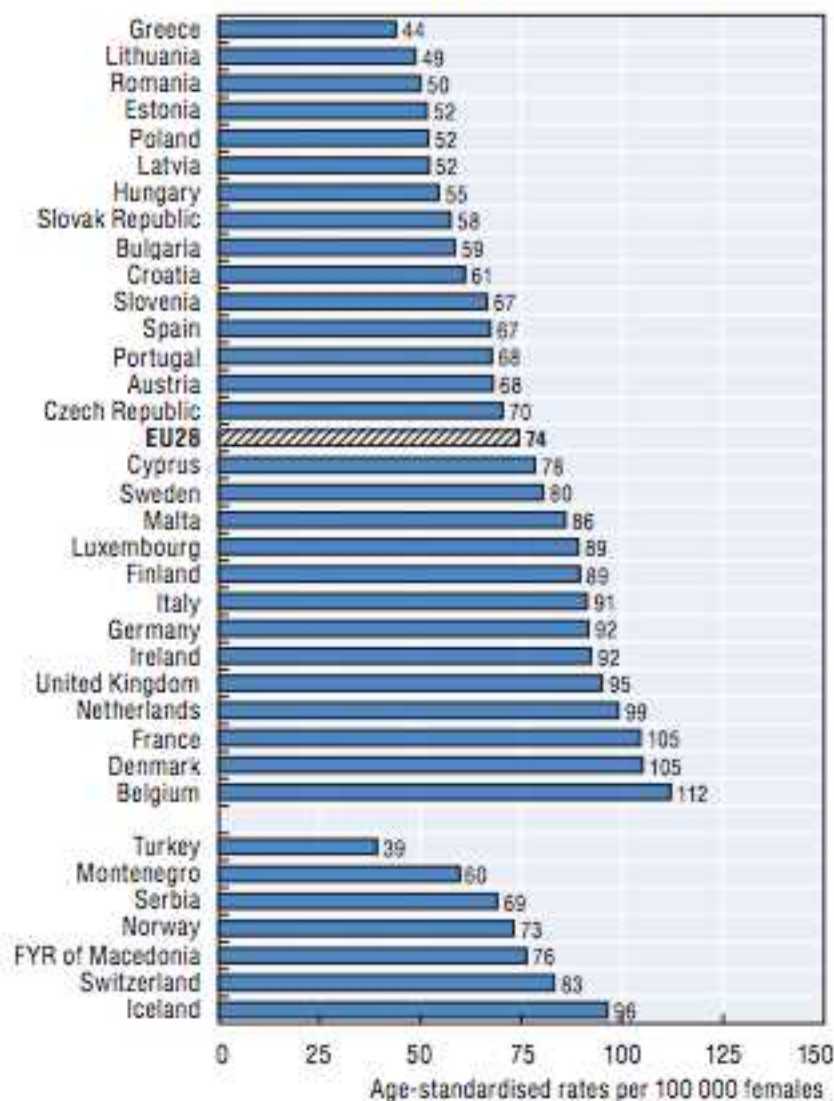




Health at a Glance: Europe 2014

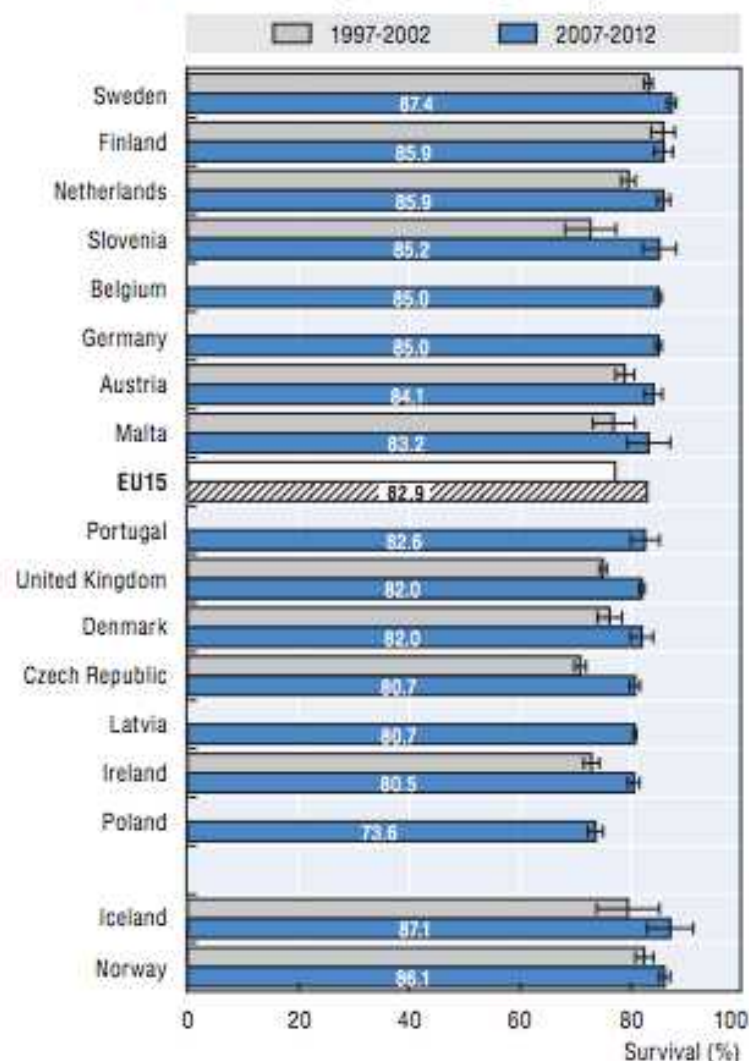


1.13.2. Breast cancer incidence rates, women, 2012

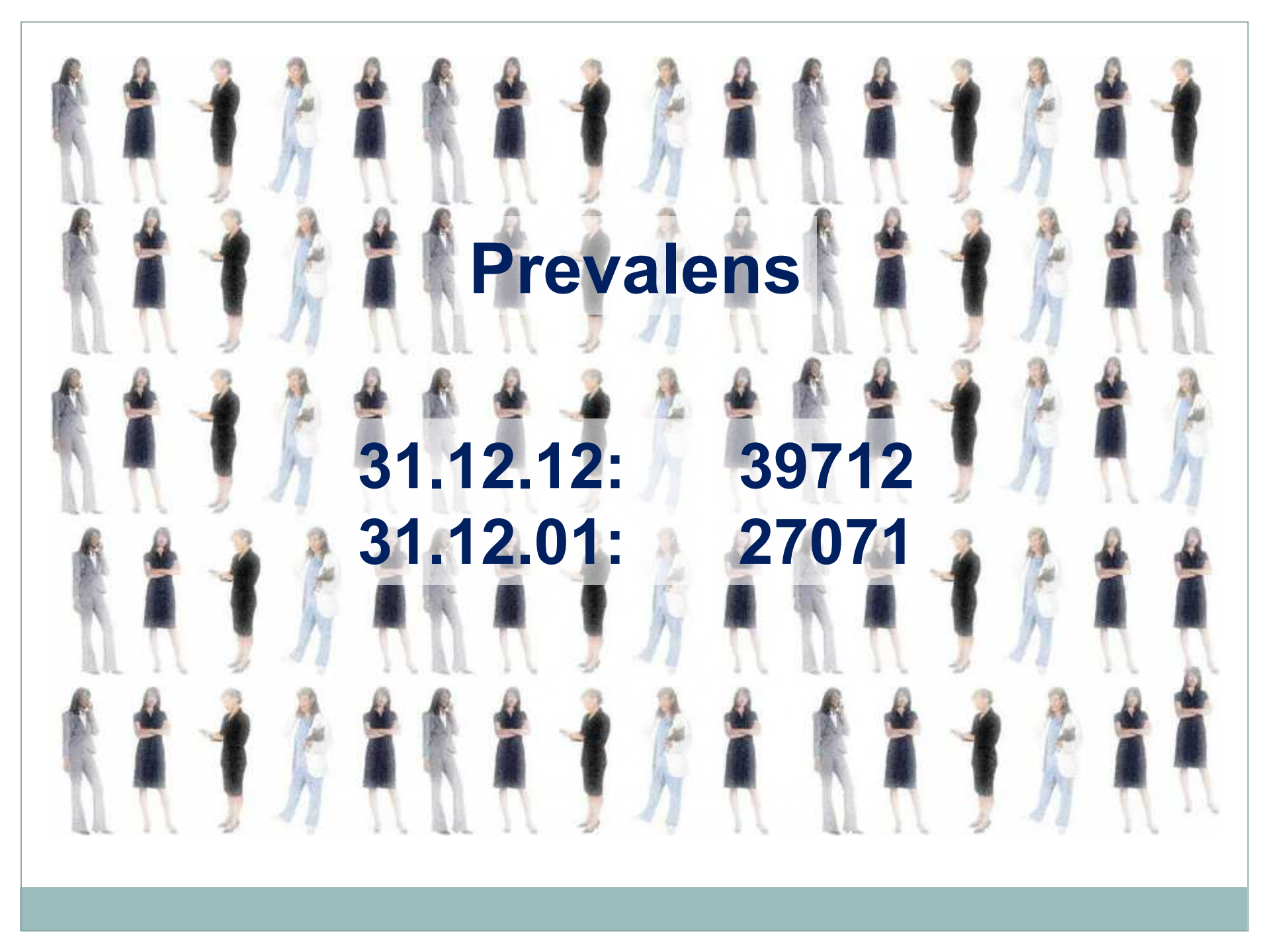


Source: International Agency for Research on Cancer (IARC), GLOBOCAN 2012.

4.7.2. Breast cancer five-year relative survival, 1997-2002 and 2007-12 (or nearest period)



Note: The 95% confidence intervals are represented by H.
Source: OECD Health Statistics 2014, <http://dx.doi.org/10.1787/health-data-en>.



Prevalens

31.12.12:

39712

31.12.01:

27071

An aerial photograph of the city of Bodo, Norway. The foreground shows a harbor filled with numerous sailboats and yachts. A large, multi-story building with a blue and orange facade is situated on the waterfront. A teal arrow points to a small boat in the harbor. The background is a dense residential area with many houses and buildings, surrounded by green hills.

BODØ

38 973



ETIOLOGI

VIKTIGSTE RISIKOFAKTOR FOR Å FÅ BRYSTKREFT



Alder



Hva er en kvinnes risiko for å utvikle brystkreft etter hvert som hun blir eldre?

Estimert risiko Storbritannia (2008)	
Ved 30	1 av 2,000
Ved 40	1 av 215
Ved 50	1 av 50
Ved 60	1 av 22
Ved 70	1 av 13
Livstidsrisiko	1 in 8

Sasieni et al. Br J Cancer. 2011, 26;105(3):460-5

Faktorer som påvirker risikoen for brystkreft



Alder for første menstruasjon (menarche)

- Ca. 4 % redusert risiko per år senere menarche
 - ✦ Gjennomsnittlig alder ved menarche for norske jenter er nå 12.5 år (Ca. 1850 var den 16 -17 år)
 - ✦ For eliteidrettsutøvere er alderen 13.1 år
- Ca. 4.5% økt risiko per år tidligere menarche





Barnefødsler m.m.



Redusert risiko

Tidlig graviditet (20 – 25 år)

Flere graviditeter før 30 år (7% reduksjon per fødsel)

Tvillingfødsler 15 % reduksjon sammenlignet med enkeltfødsler

Kvinner som har født har 30 % lavere risiko enn de som ikke har født

Amming (Ca. 4 % reduksjon per år med amming)

Spontane eller induserte aborter endrer ikke på risiko

Fjernelse av eggstokkene <35 år

Økt risiko

Høy alder ved første svangerskap (>30 år)

Sen menopause (3 % per år)

Hormonbehandling av klimakterielle plager (HRT)

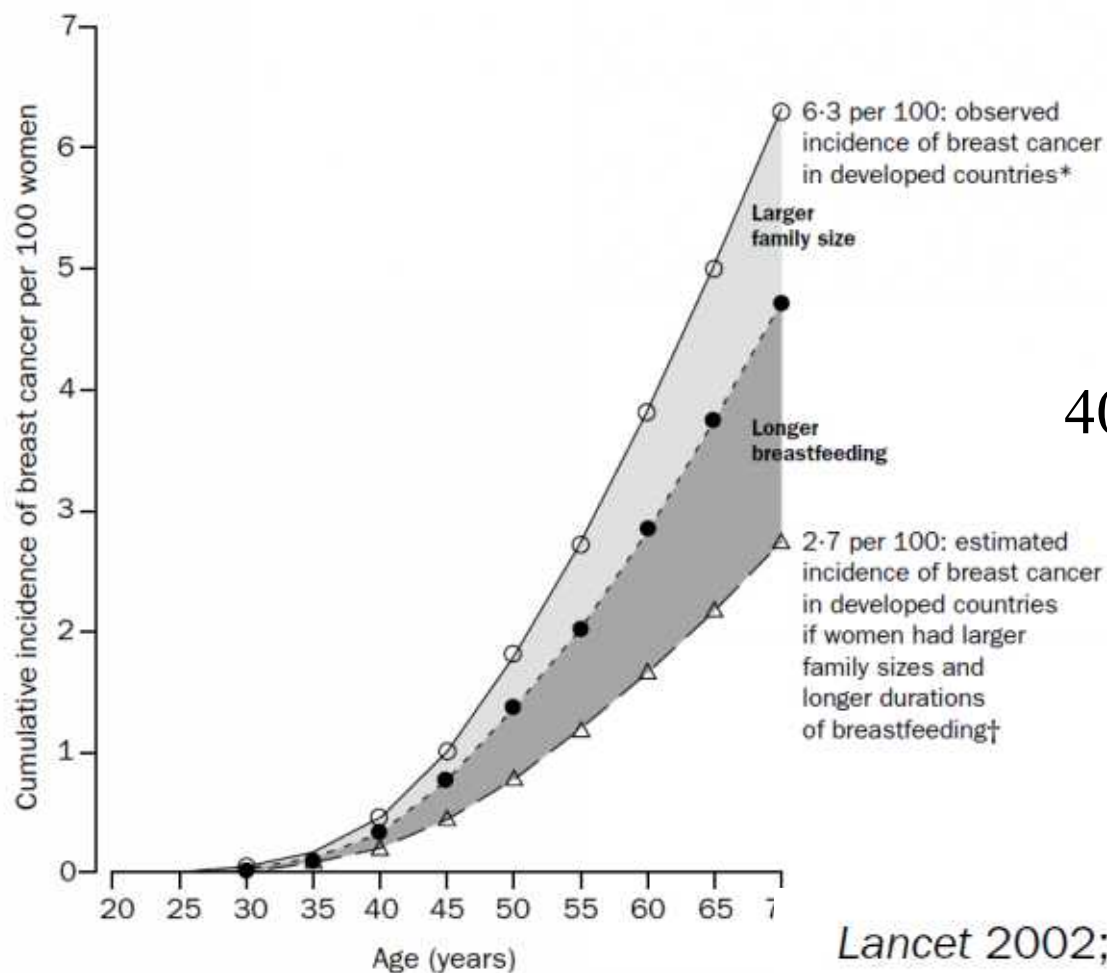
Østrogen (2.3 % per år)

Østrogen og progesteron (5 – 20 % per år)

Tett brystvev

Tidligere brystkreft: 2-3 ganger så høy risiko på å få kreft i det andre brystet eller på et annet sted i samme bryst

Estimated cumulative incidence of breast cancer in developed countries if women had family sizes and breastfeeding patterns typical of developing countries



40 % ↓

Lancet 2002; **360**: 187–95

P-piller

Bruk av p-piller	Relativ risiko (konfidensintervall)
Aldri brukt	1,0
Bruker	1.24 (1.15-1.33)
1-4 år etter å ha sluttet	1.16 (1.08-1.23)
5-9 år etter å ha sluttet	1.07 (1.02-1.13)
10+ år etter å ha sluttet	1.01 (0.96-1.05)



Fysisk aktivitet



25.000 kvinner - 20 - 54 år - møtte frem til helseundersøkelse i Oppland, Sogn og Fjordane og Finnmark i 1977 og 1983.

I en oppfølgingsperiode på gjennomsnittlig 14 år etter helseundersøkelsen fikk 351 av kvinnene brystkreft.

Ukentlig aktivitet på 4 timer reduserte brystkrefttrisikoen med hele 40 prosent.



Inger Thune et al. New England Journal of Medicine. 336(18):1269-75, 1997

The New England Journal of Medicine

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PHYSICAL ACTIVITY AND THE RISK OF BREAST CANCER

INGER THUNE, M.D., TORMOD BRENN, M.Sc., EILIV LUND, M.D., Ph.D., AND MARIA GAARD, M.D.

ABSTRACT

Background Because physical activity may affect hormonal concentrations and energy balance, we decided to investigate whether everyday exercise is related to the risk of breast cancer.

Methods During 1974 to 1978 and 1977 to 1983, a total of 25,624 women, 20 to 54 years of age at entry, enrolled in health surveys and answered questionnaires about leisure-time and work activity.

Results During a median follow-up of 13.7 years, we identified 351 cases of invasive breast cancer among the 25,624 women in the cohort. Greater leisure-time activity was associated with a reduced risk of breast cancer, after adjustments for age, body-mass index (the weight in kilograms divided by the square of the height in meters), height, parity, and county of residence (relative risk, 0.63; 95 percent confidence interval, 0.42 to 0.95), among women who exercised regularly, as compared with sedentary women (P for trend = 0.04). In regularly exercising women, the reduction in risk was greater in premenopausal women than in postmenopausal women, and greater in younger women (<45 years at study entry) than in older women (≥ 45 years) (relative risk, 0.38; 95 percent confidence interval, 0.19 to 0.79). In stratified analyses the risk of breast cancer was lowest in lean women (body-mass index, <22.8) who exercised at least four hours per week (relative risk, 0.28; 95 percent confidence interval, 0.11 to 0.70). The risk was also reduced with higher levels of activity at work, and again there was a more pronounced effect among premenopausal than postmenopausal women.

Conclusions Physical activity during leisure time and at work is associated with a reduced risk of breast cancer. (N Engl J Med 1997;336:1269-75.)

©1997, Massachusetts Medical Society.

gen and progesterone, thereby inhibiting carcinogenesis in the breast.¹²⁻²² Energy balance might also influence the risk of breast cancer. Caloric restriction in rodents reduces the proliferative activity of the mammary glands²³ and inhibits carcinogenesis.^{24,25} However, the effect of energy balance, as indicated by energy intake, body-mass index (the weight in kilograms divided by the square of the height in meters), and energy expenditure, on the risk of breast cancer has not been examined thoroughly in humans.

In this study we evaluated the influence of physical activity, both at work and during leisure time, on the risk of breast cancer in a cohort of 25,624 premenopausal and postmenopausal women. Data on parity, dietary factors, and body-mass index allowed adjustment for potentially confounding factors, and reassessment of physical activity after three to five years gave an indication of the effect of sustained physical activity on the risk of breast cancer.

METHODS

Study Population

From 1974 to 1978, the National Health Screening Service invited people in three counties in Norway (Oppland, Sogn og Fjordane, and Finnmark) to participate in a survey of risk factors for cardiovascular disease. All women who were 35 to 49 years of age and a random sample of 10 percent of those who were 20 to 34 years of age were invited. In four municipalities in Finnmark all women who were 20 to 34 years of age were invited. A comprehensive description of these populations has been published previously.²⁶ A total of 31,556 women were invited to participate, and 28,621 (91 percent) actually did.

All women in this survey as well as a random sample of women who were 20 to 39 years of age were invited to participate in a second survey three to five years later (1977 to 1983). Of these 34,378 women, 31,209 (91 percent) participated.²⁷ This second survey was used as the base line, because no information on parity and dietary factors was collected during the first survey.

Each woman received a written invitation to participate, to-

Manglende fysisk aktivitet



- Mer enn 3 % av brystkrefttilfellene i Storbritannia i 2010 var forbundet med inadekvat fysisk aktivitet (<150 minutter med moderat fysisk aktivitet per uke)

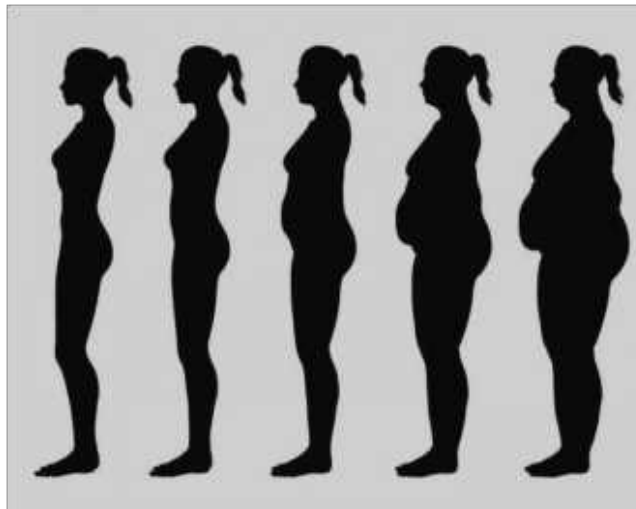


*D M Parkin ,British Journal of Cancer (2011) **105**, S38–S41.*

Body Mass Index

Relativ risiko (95%CI) for brystkreft etter BMI-kategori og menopausal status

BMI	Pre-menopausal	Post-menopausal*
<22.5	0.96 (0.85 to 1.08)	0.85 (0.80 to 0.91)
22.5-24.9 (referansegruppe)	1.00 (0.90 to 1.11)	1.00 (0.95 to 1.06)
25-27.4	0.93 (0.82 to 1.05)	1.10 (1.04 to 1.16)
27.5-29.5	0.99 (0.84 to 1.16)	1.21 (1.13 to 1.29)
≥ 30	0.79 (0.68 to 0.92)	1.29 (1.22 to 1.36)
* Aldri brukt HRT		



Faktorer som øker risikoen for brystkreft



- Overvekt etter klimakteriet (1 % økning/kg)
- Kroppshøyde (1% per cm)



Gjennomsnittsvekt Norge 2012: 72 kg



Gjennomsnittshøyde Norge 2012: 168 cm

Alkohol



- 7 - 12 % økning per drink (10 g)/dag
- 6 % av brystkrefttilfellene i Storbritannia skyldes alkohol



Parkin DM. Cancers attributable to consumption of alcohol in the UK in 2010. Br J Cancer 2011; 105 (S2):S14-S18.

Terapeutisk stråling



- Bestråling av brystkjertelvev (Hodgkins lymfom)



Radioaktiv stråling.



- Data fra Hiroshima viser økt risiko for alle som var yngre enn 40 år da de ble eksponert?



- Det har vært rapportert økt risiko blant flyvertinner i Finland, Danmark og England, men ikke i Norge, men når man korrigerer for kjente faktorer, forsvinner den økte risiko



Utdannelse og ekteskap



- Generelt hadde kvinner med universitets-utdanning 15 % høyere risiko for å dø av brystkreft enn kvinner med ungdomsskole.



- Gifte kvinner hadde lavere brystkreft-dødelighet enn ikke-gifte kvinner.



○ Strand et al. Eur J Cancer. 2007 Feb 27

Kosthold



Den som spiser pølsemat og kjøttmat hele dagen,
han blir så doven og så lat og veldig tykk i magen.

Men den som spiser gulerøtter, knekkebrød og
peppernøtter, tyttebær og bjørnebær og kålrot og persille
han blir så på vekt i magen,
glad og lystig hele dagen
og så lett i bena at han ikke kan stå stille.



Grønnsaksspisesang
Torbjørn Egner

- Diett i lavrisikoområder

- Cerealer og stivelse
- Grønnsaker

- P
- S

worldwide
breast cancer



Diet and breast cancer: A review of the prospective observational studies



- **Conclusions, Recommendations, and Future Directions**
 - Among the prospective epidemiologic studies conducted on diet and breast cancer to date there is no association that is consistent, strong, and statistically significant, except for regular alcohol consumption, overweight, and weight gain.

Karin B. Michels, ScD, PhD^{1 2 *}, Anshu P. Mohllajee, MPH^{1 2}, Edith Roset-Bahmanyar, MD, MPH¹, Gregory P. Beehler, MA³, Kirsten B. Moysich, PhD³

Cancer: Volume 109, pp 2712-2749, 2007

FOOD, NUTRITION, PHYSICAL ACTIVITY AND BREAST CANCER (PREMENOPAUSE) 2010

	DECREASES RISK	INCREASES RISK
Convincing	Lactation	Alcoholic drinks
Probable	Body fatness	Adult attained height ¹ Greater birth weight
Limited - suggestive	Physical activity ²	
Limited - no conclusion	Dietary fibre; vegetables and fruits; soya and soya products; meat; fish; milk and dairy products; total fat; folate; vitamin D; calcium; glycaemic index; dietary patterns; adult weight gain; abdominal fatness	
Substantial effect on risk unlikely	None identified	

1 Adult attained height is unlikely directly to modify the risk of cancer. It is a marker for genetic, environmental, hormonal, and also nutritional factors affecting growth during the period from preconception to completion of linear growth (see chapter 6.2.13 – Second Expert Report).

2 Physical activity of all types: occupational, household, transport and recreational.



American Institute for
Cancer Research

FOOD, NUTRITION, PHYSICAL ACTIVITY AND BREAST CANCER (POSTMENOPAUSE) 2010

	DECREASES RISK	INCREASES RISK
Convincing	Lactation	Alcoholic drinks Body fatness Adult attained height ¹
Probable	Physical activity ²	Abdominal fatness Adult weight gain
Limited - suggestive		Total fat
Limited - no conclusion	Dietary fibre; vegetables and fruits; soya and soya products; meat; fish; milk and dairy products; folate; vitamin D; calcium; selenium; glycaemic index; dietary patterns; birth weight; energy intake	
Substantial effect on risk unlikely	None identified	

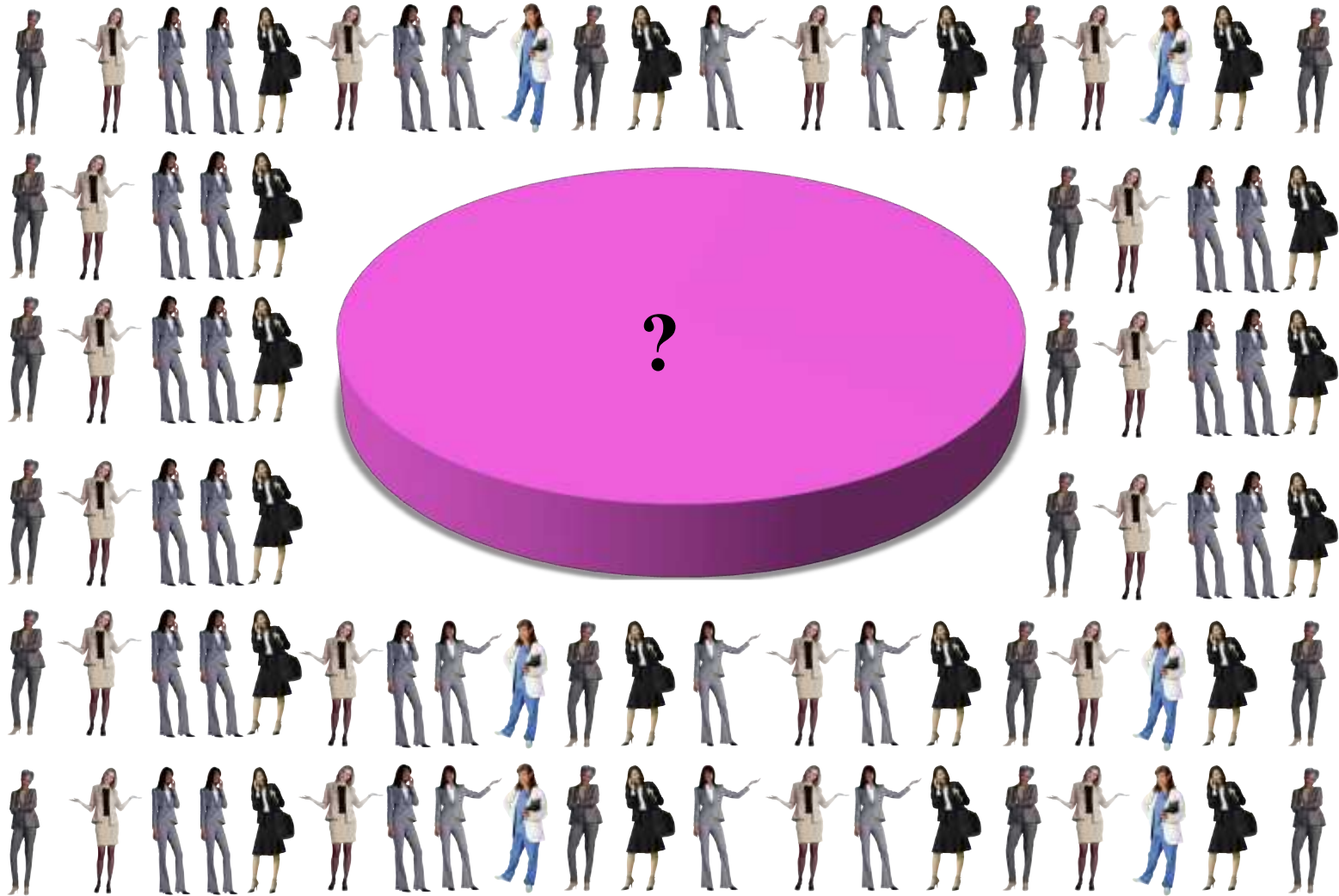
¹ Adult attained height is unlikely directly to modify the risk of cancer. It is a marker for genetic, environmental, hormonal, and also nutritional factors affecting growth during the period from preconception to completion of linear growth (see chapter 6.2.13 – Second Expert Report).

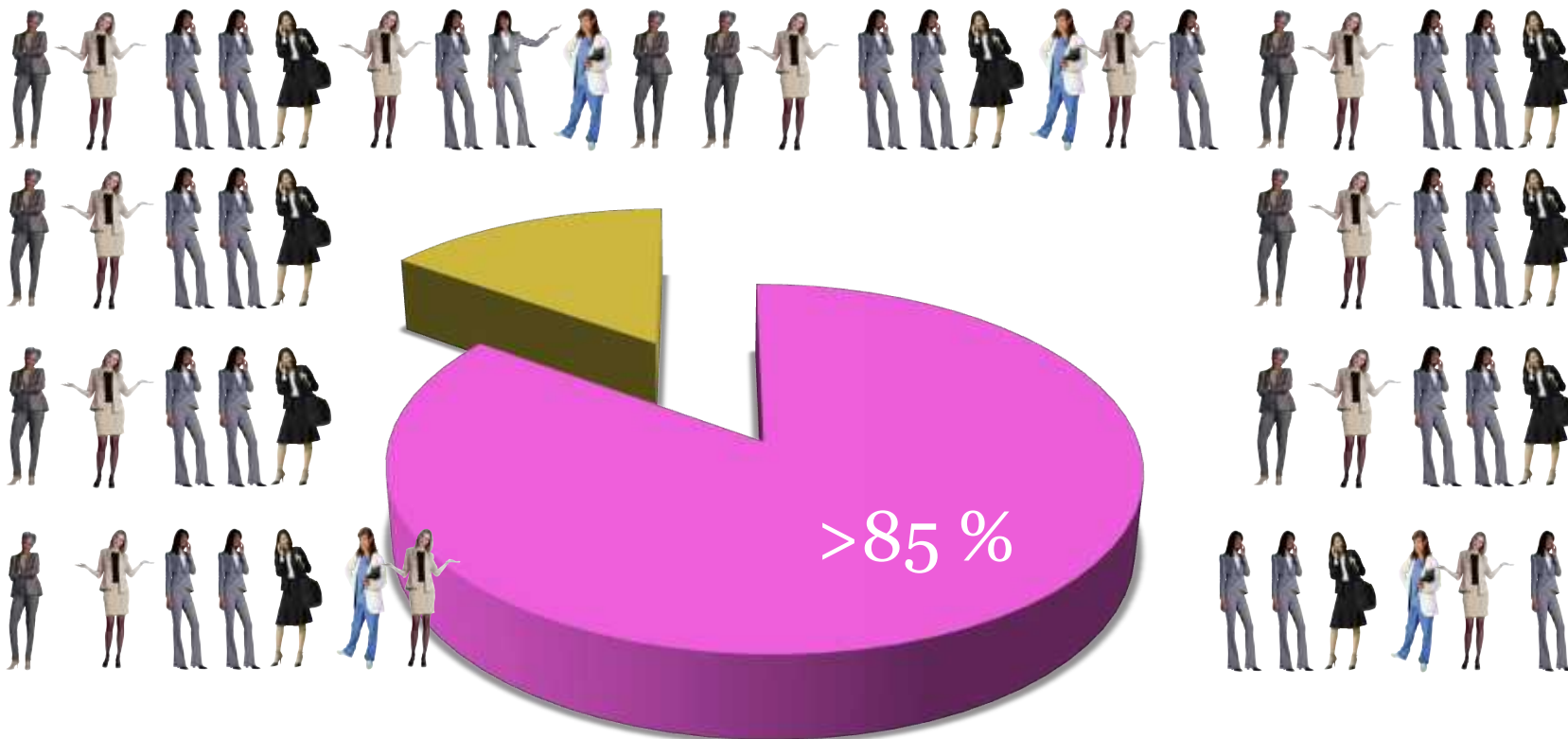
² Physical activity of all types: occupational, household, transport and recreational.



American Institute for
Cancer Research

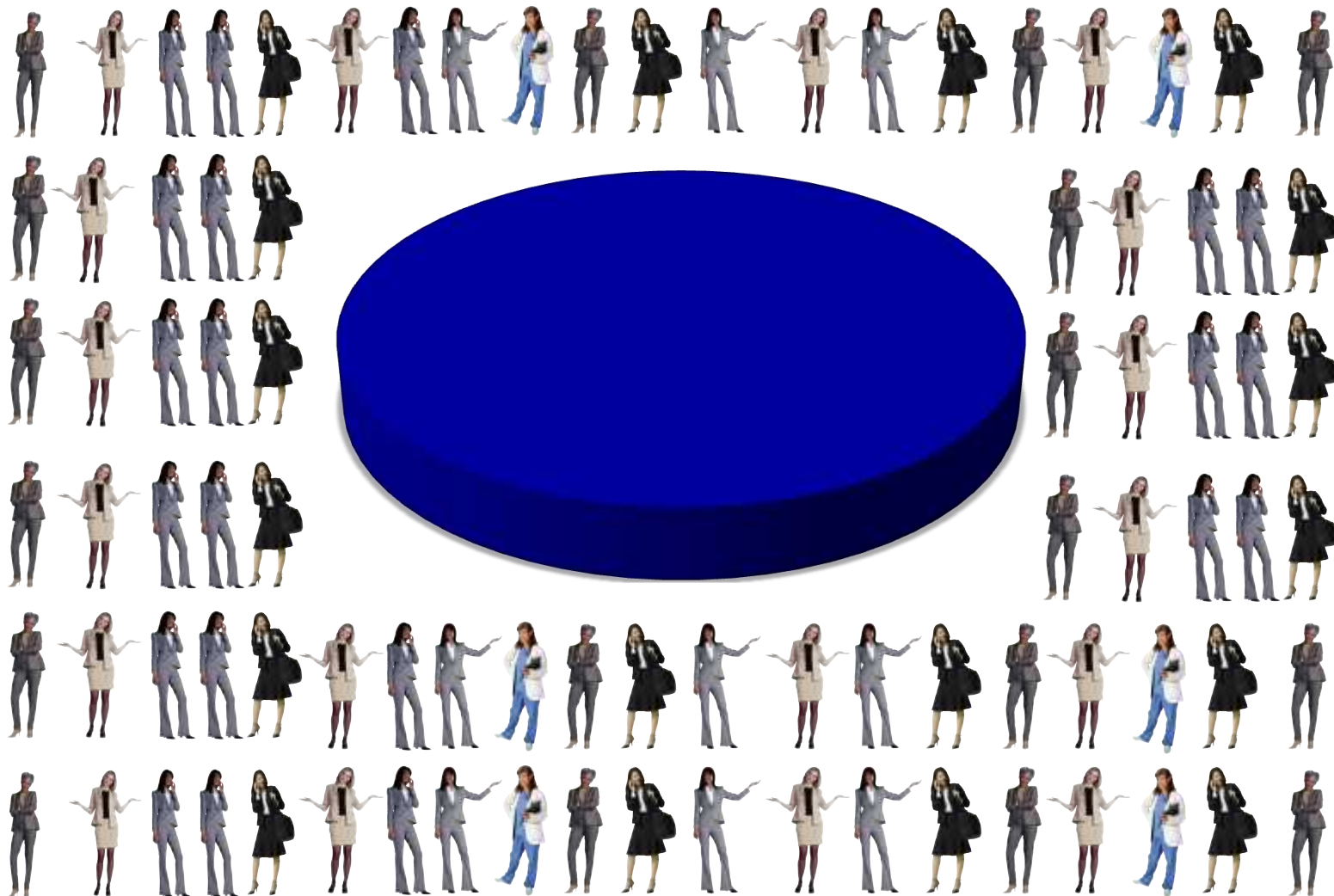
Familiehistorie

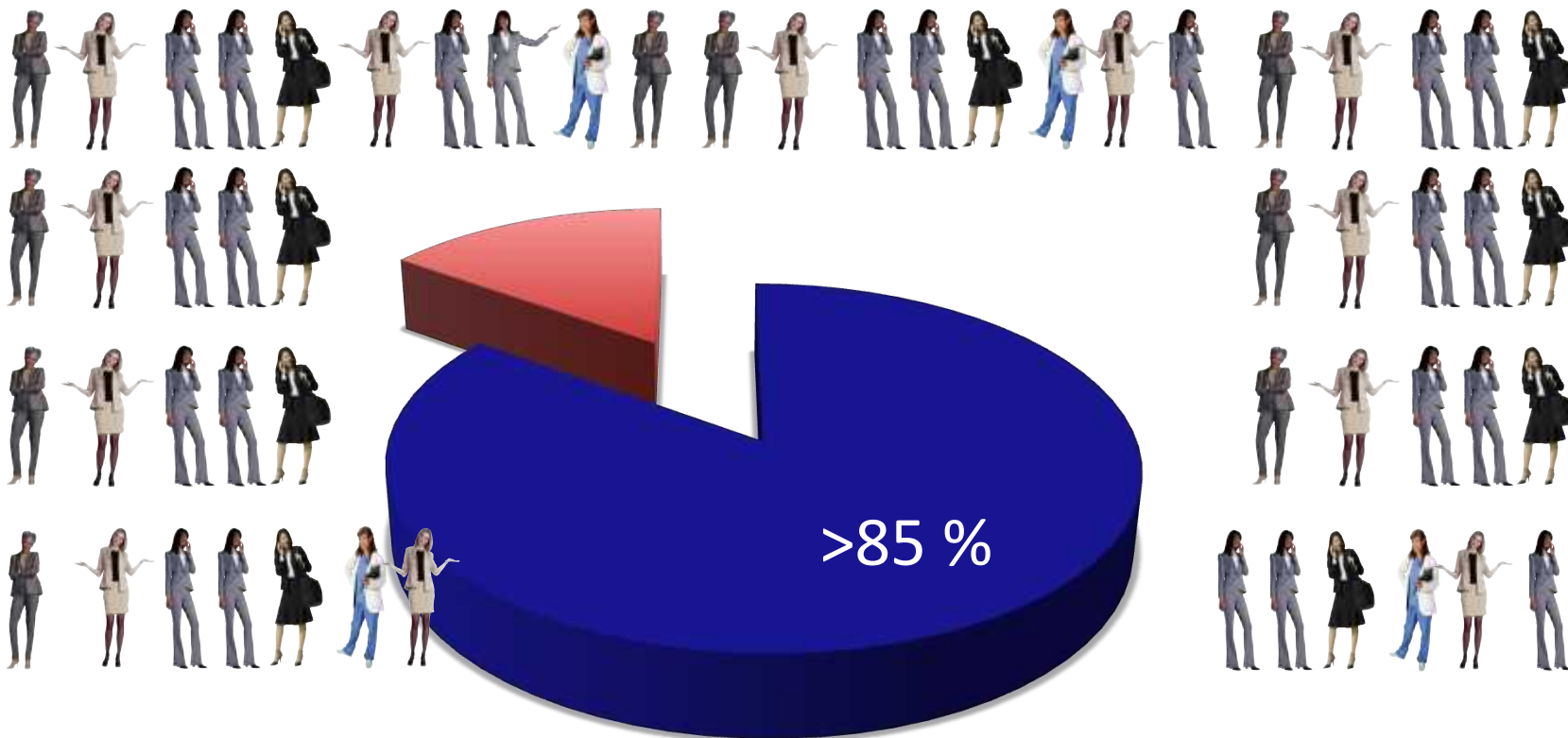




Mer enn 85% av kvinner med brystkreft har INGEN familiehistorie

Kvinner med nær slektning med brystkreft





- Kvinner med nær slektning med brystkreft, men som ikke får brystkreft selv

BRCA1 og 2



- Har en risiko på ca.45 % (BRCA2) – 55 - 65 % (BRCA1) til å utvikle brystkreft innen fylte 70 år
- Har en risiko på 11 - 17 % (BRCA2) til 39 % (BRCA1) til å utvikle ovarialcancer innen fylte 70 år.
- 1 av 450 kvinner er bærer av en feil i ett av disse genene (prevalens 0.11 – 0.12 %)
- Er årsak til 2 % av alle brystkrefttilfeller
- Er årsak til 20 % av tilfellene der hvor det foreligger familiær risiko



PATOLOGI

4 Diagnostisering og utredning

4.6.3 Patologidiagnostikk av betydning for behandlingsvalg ved invasiv brystkreft

Anbefalinger

Den patologisk-anatomiske undersøkelsen bør inneholde informasjon om:

- Tumors lokalisasjon (eventuelt multifokalitet)
- Tumors største mål (i millimeter) eventuelt tumorområdets utbredelse ved diffus vekst (typisk lobulære karsinomer). Det bør angis om det foreligger et eller flere tumorfoci
- Histologisk type
- Histologisk gradering
- Utbredelse, lokalisasjon og grad av DCIS, også som komponent i et invasivt karsinom
- Tumors relasjon til reseksjonskanter (angitt i mm), eventuelt til hud og til brystvegg
- Antall lymfeknuter med metastaser og totalt antall undersøkte lymfeknuter
- Størrelse på den største påviste lymfeknutemetastase
- Perinodal tumorinfiltrasjon inkludert beskrivelse av om den er makroskopisk eller kun mikroskopisk og beskrivelse av eventuell øyer av tumorceller i fettvev
- Hormonreseptoranalyse basert på immunhistokjemi eller - cytologi
- HER2 status
- Ki67 status

2012 WHO Classification of tumors of the Breast

• Epithelial Tumors

- Microinvasive carcinoma

• Invasive breast carcinoma

- Invasive carcinoma of no special type (NST)
 - Pleomorphic carcinoma
 - Carcinoma with osteoclast-like stromal giant cells
 - Carcinoma with choriocarcinomatous features
 - Carcinoma with melanotic features
- Invasive lobular carcinoma
 - Classic lobular carcinoma
 - Solid lobular carcinoma
 - Alveolar lobular carcinoma
 - Pleomorphic lobular carcinoma
 - Tubulolobular carcinoma
 - Mixed lobular carcinoma
- Tubular carcinoma
- Cribriform carcinoma
- Mucinous carcinoma
- Carcinoma with medullary features
 - Medullary carcinoma
 - Atypical medullary carcinoma
 - Invasive carcinoma NST with medullary features
- Carcinoma with apocrine differentiation
- Carcinoma with signet-ring differentiation
- Invasive micropapillary carcinoma
- Metaplastic carcinoma of no special type
 - Low-grade adenosquamous carcinoma
 - Fibromatosis-like metaplastic carcinoma
 - Squamous cells carcinoma
 - Spindle cell carcinoma
 - Metaplastic carcinoma with mesenchymal differentiation
 - Chondroid differentiation
 - Osseous differentiation
 - Other types of mesenchymal differentiation
 - Mixed metaplastic carcinoma
 - Myoepithelial carcinoma
- Rare types
 - Carcinoma with neuroendocrine features
 - Neuroendocrine tumor, well differentiated
 - Neuroendocrine carcinoma, poorly differentiated (small cell carcinoma)
 - Carcinoma with neuroendocrine differentiation
 - Secretory carcinoma
 - Invasive papillary carcinoma
 - Acinic cell carcinoma
 - Mucoepidermoid carcinoma
 - Polymorphous carcinoma
 - Oncocytic carcinoma
 - Lipid-rich carcinoma
 - Glycogen-rich clear cell carcinoma
 - Sebaceous carcinoma
 - Salivary gland/skin adnexal type tumors
 - Cylindroma
 - Clear cell hidradenoma

• Mesenchymal Tumors

- Nodular fasciitis
- Myofibroblastoma
- Desmoids-type fibromatosis
- Inflammatory myofibroblastic tumor
- Benign vascular lesions
 - Haemangioma
 - Angiomatosis
 - Atypical vascular lesions
- Pseudoangiomatous stromal hyperplasia
- Granular cell tumor
- Benign peripheral nerve-sheath tumors
 - Neurofibroma
 - Schwannoma
- Lipoma
 - Angiolipoma
- Liposarcoma
- Angiosarcoma
- Rhabdomyosarcoma
- Osteosarcoma
- Leiomyoma
- Leiomyosarcoma

• Fibroepithelial Tumors

- Fibroadenoma
- Phyllodes tumor
 - Benign
 - Borderline
 - Malignant
 - Periductal stromal tumor, low grade
- Hamartoma

• Tumors of the nipple

- Nipple adenoma
- Syringomatous adenoma
- Paget disease of the nipple

• Malignant lymphoma

- Diffuse large B cell lymphoma
- Burkitt lymphoma
- T cell lymphoma
 - Anaplastic large cell lymphoma, ALK negative
- Extranodal marginal-zone B cell lymphoma of MALT-type
- Follicular lymphoma

• Metastatic tumors

• Tumors of the male breast

- Gynaecomastia
- Carcinoma
 - Invasive carcinoma
 - In situ carcinoma

• Clinical Patterns

- Inflammatory carcinoma
- Bilateral breast carcinoma

• Epithelial-myoepithelial tumors

- Pleomorphic adenoma
- Adenomyoepithelioma
 - Adenomyoepithelioma with carcinoma
- Adenoid cystic carcinoma

• Precursor lesions

- Ductal carcinoma in situ
- Lobular neoplasia
 - Lobular carcinoma in situ
 - Classic lobular carcinoma in situ
 - Pleomorphic lobular carcinoma in situ
 - Atypical lobular hyperplasia

• Intraductal proliferative lesions

- Usual ductal hyperplasia
- Columnar cell lesions including flat epithelial atypia
- Atypical ductal hyperplasia

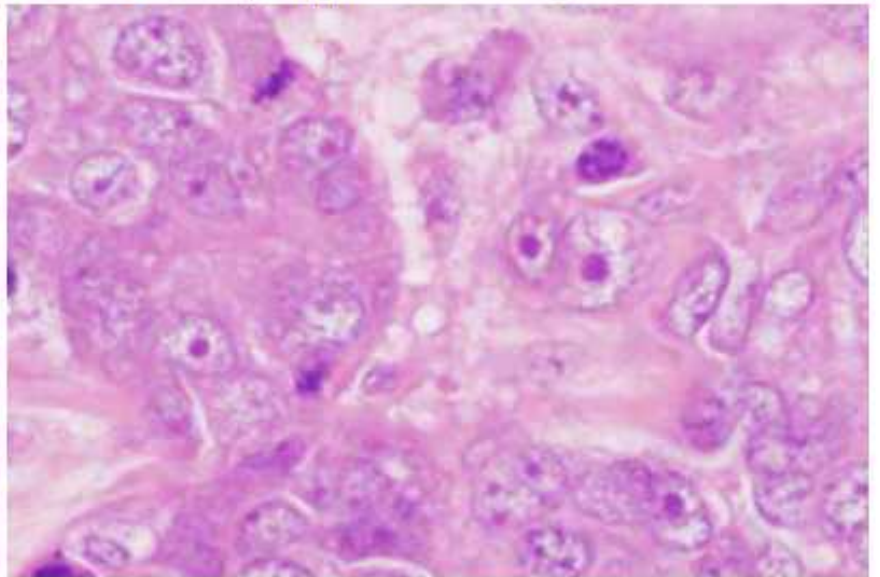
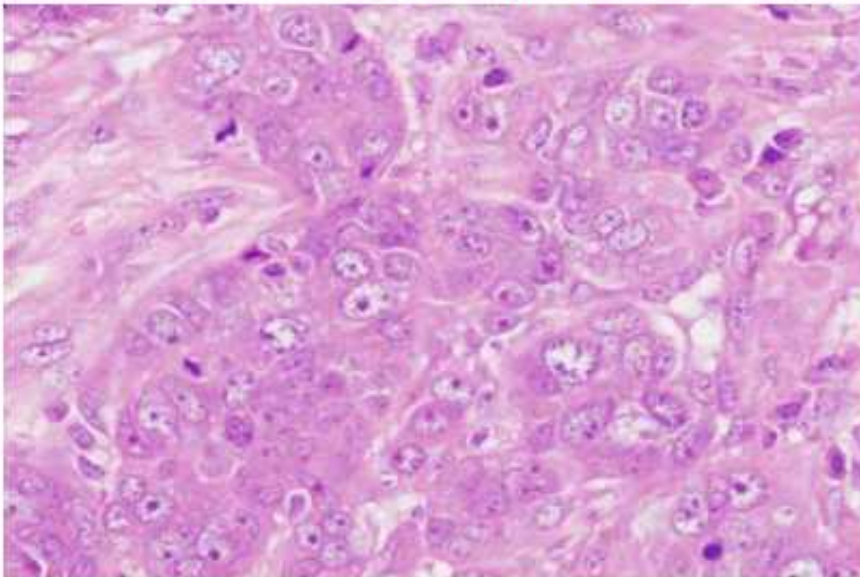
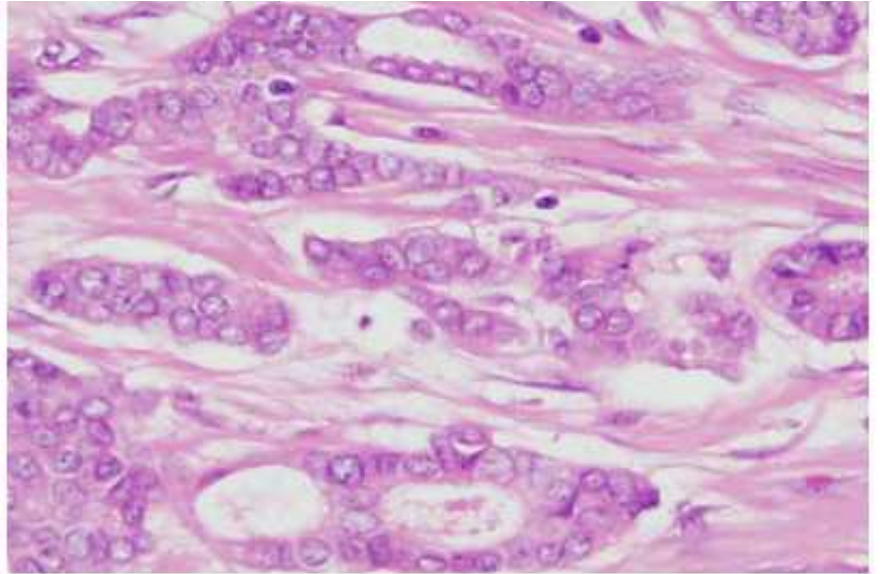
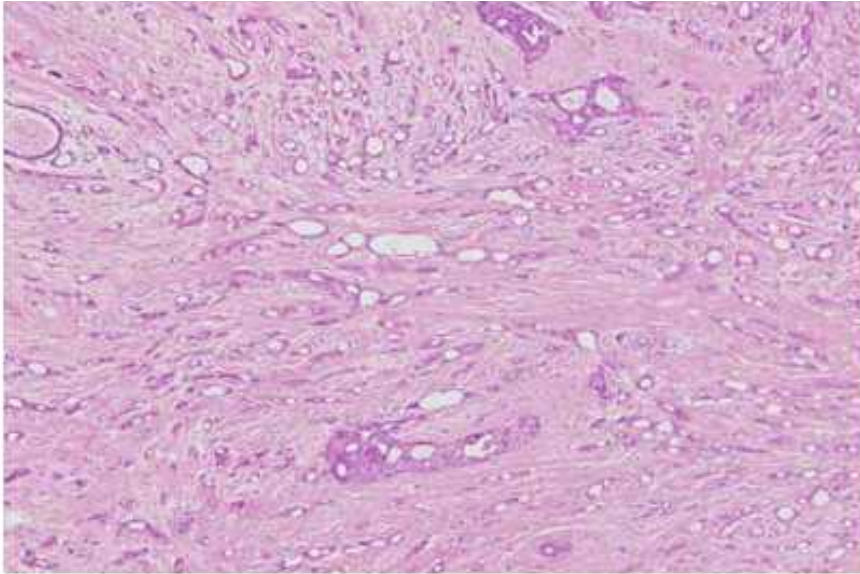
• Papillary lesions

- Intraductal papilloma
 - Intraductal papilloma with atypical hyperplasia
 - Intraductal papilloma with ductal carcinoma in situ
 - Intraductal papilloma with lobular carcinoma in situ
- Intraductal papillary carcinoma
- Encapsulated papillary carcinoma
 - Encapsulated papillary carcinoma with invasion
- Solid papillary carcinoma
 - In situ
 - Invasive

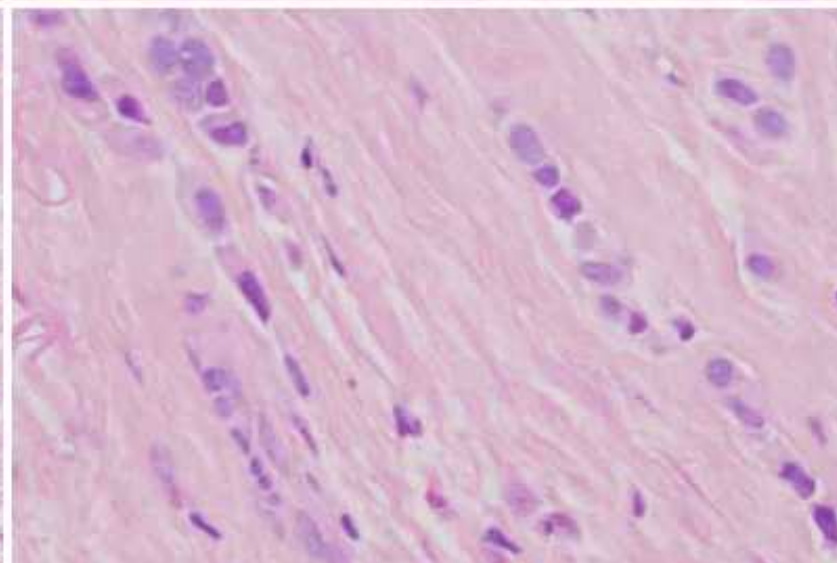
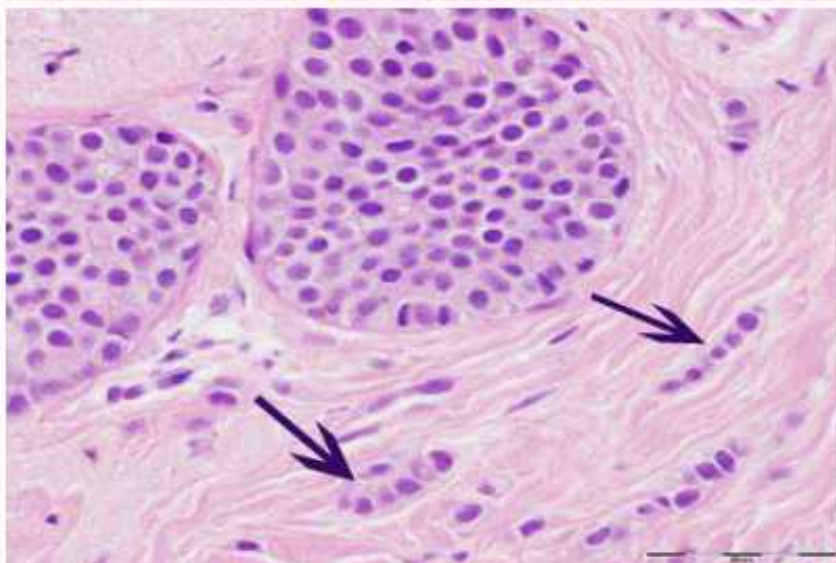
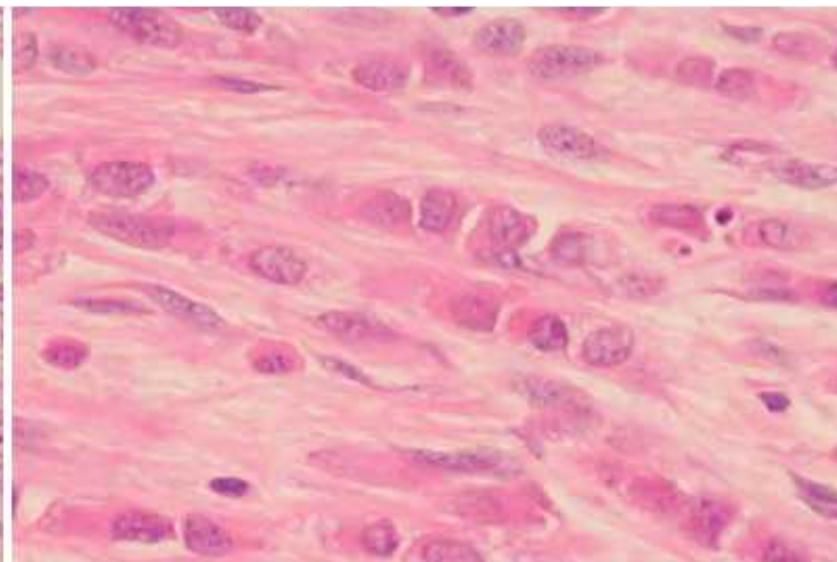
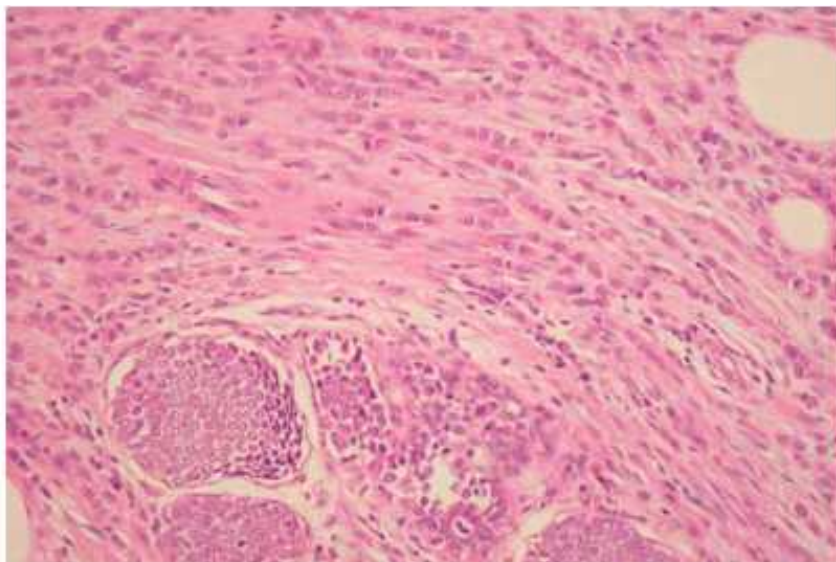
• Benign epithelial proliferations

- Sclerosing adenosis
- Apocrine adenosis
- Microglandular adenosis
- Radial scar/complex sclerosing lesion
- Adenomas
 - Tubular adenoma
 - Lactating adenoma
 - Apocrine adenoma
 - Ductal adenoma

Infiltrierende duktalt carcinom 70 - 80 %

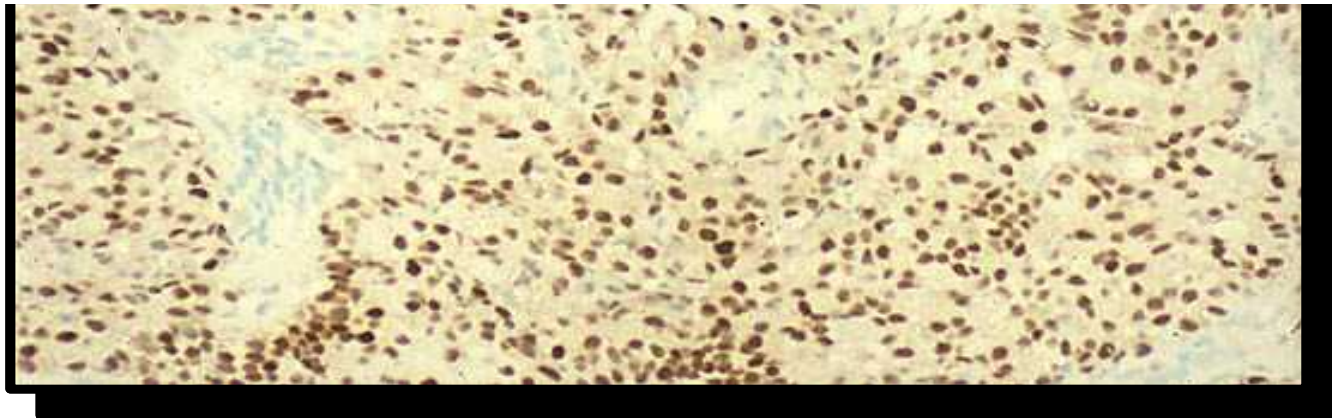


Infiltrerende lobulært carcinom 10 - 20 %



Hormonreseptorer

- Brystkreft er ofte følsom for hormonell behandling som påvirker østrogennivå eller østrogenvirkning –
 - Nivået av østrogenreseptorer og progesteronreseptorer har betydning for hvor stor nytte en kan forvente av hormonbehandling og om det er indikasjon for kjemoterapi



DNA: amplifisert HER-2 onkogen – FISH/ CISH/SISH

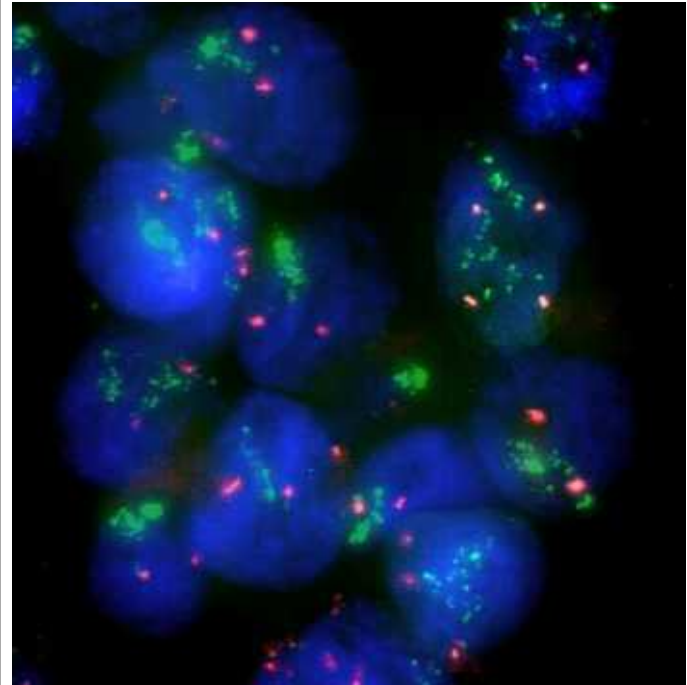
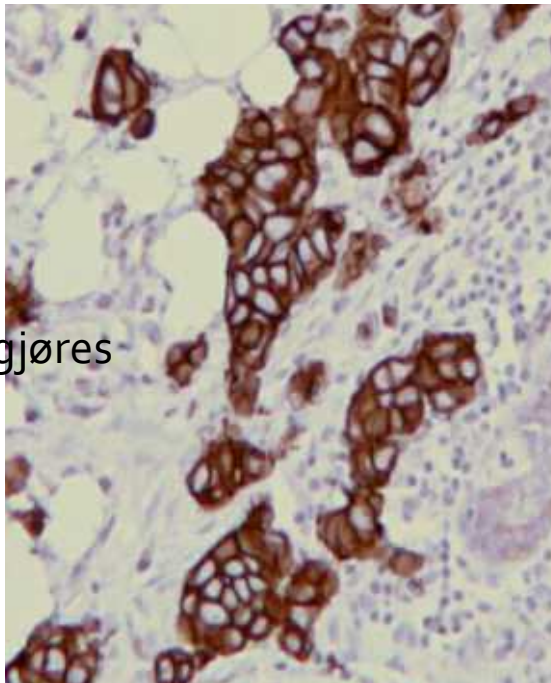
- Betydning for bruk av Herceptin
- Effekt av høyere antracyclindose (FEC100)

HER-2 Protein : IHC

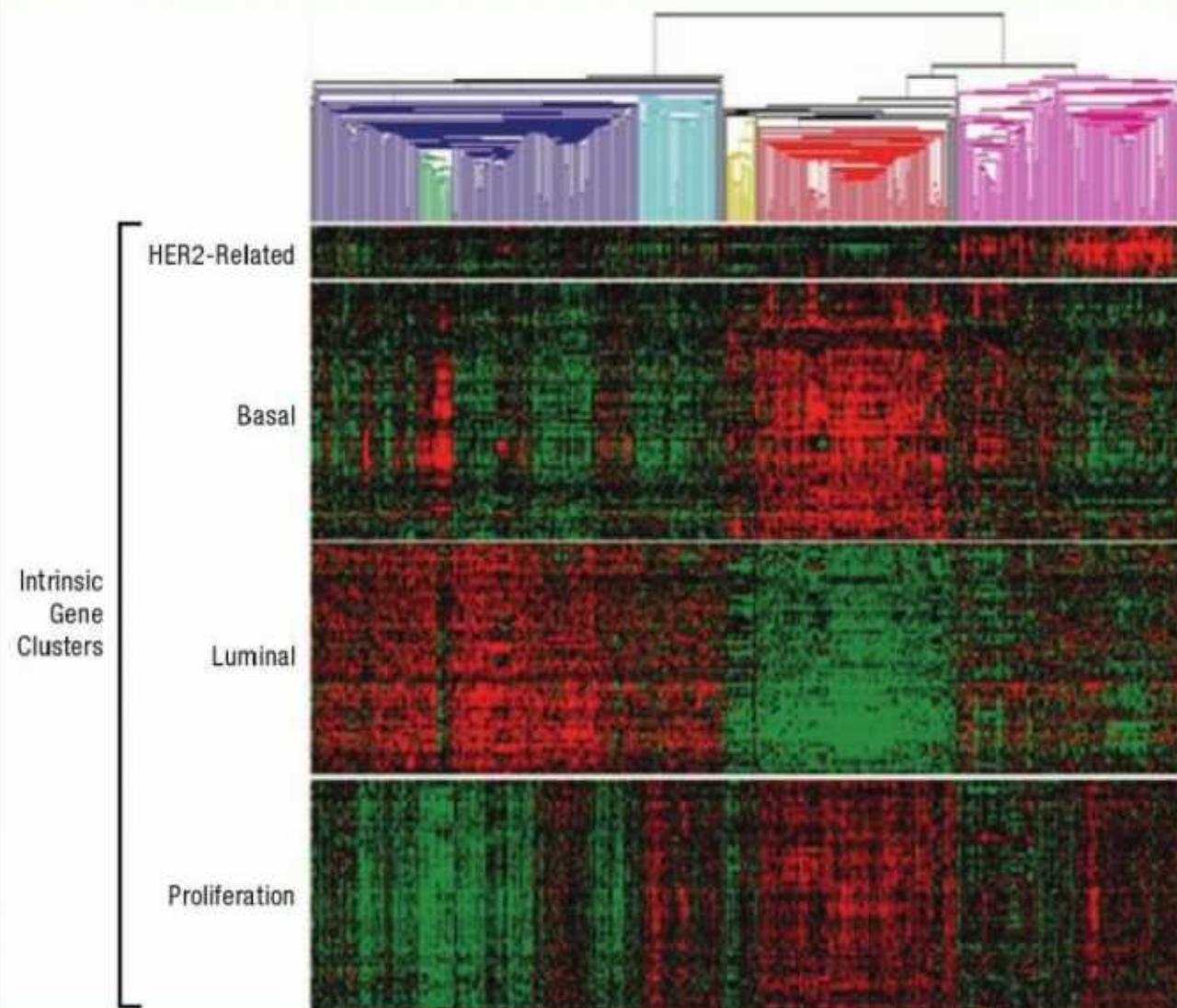
0
+ } = neg

++ FISH må gjøres

+++ = pos



- = neg
+ = pos



Source: Clin Breast Cancer © 2010 CIG Media, LP

Figure 1.

Semi-Unsupervised Gene Expression Array Analysis of a Cohort of Breast Cancers Identifies Several Intrinsic Subtypes

Shown are luminal A (outlined in dark blue), luminal B (pale blue), HER2-enriched (pink), basal-like (red), claudin-low (yellow), and normal-like (green) tumors. Heat map courtesy of CM Perou.