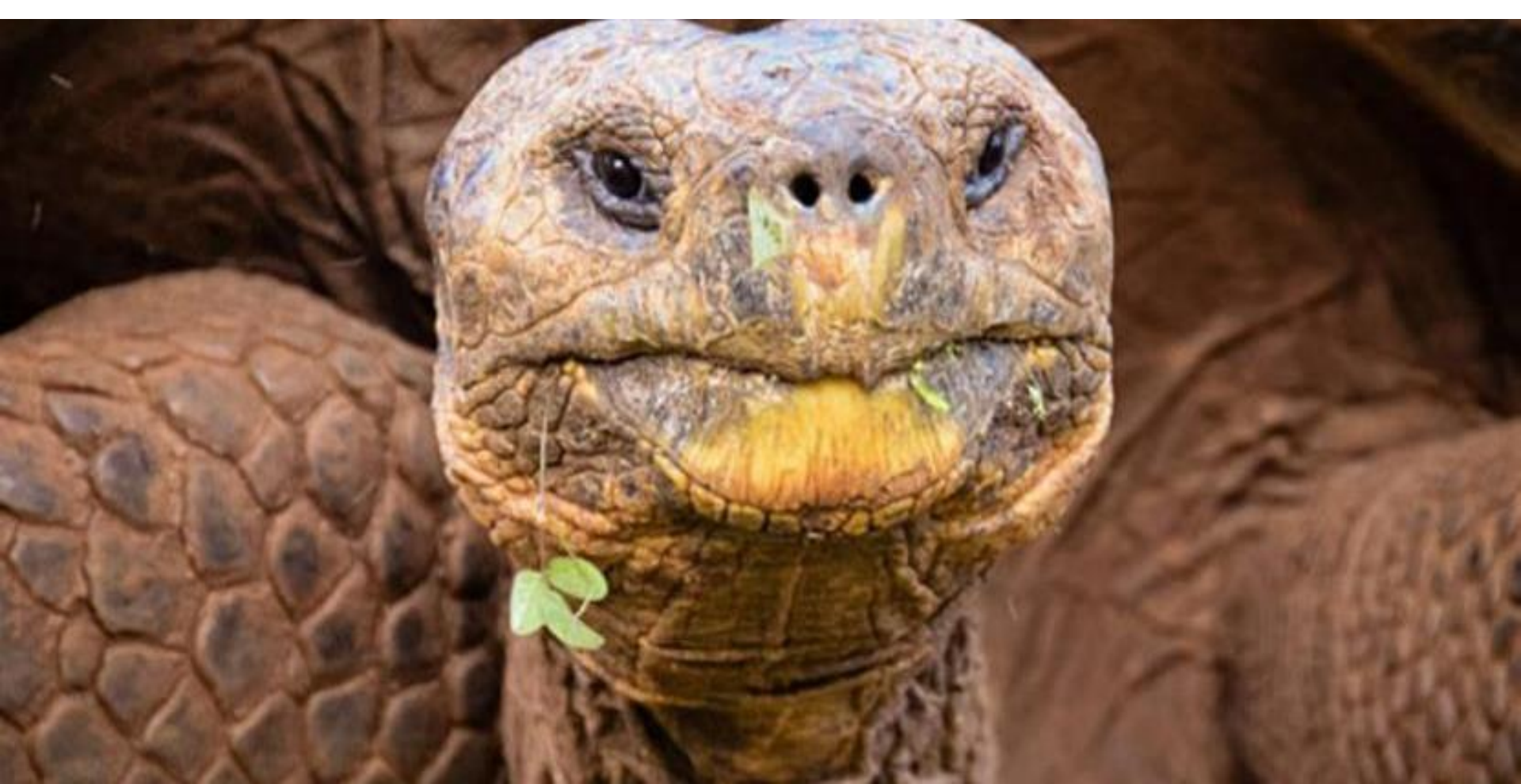


# Langzeitüberleben und Survivorship nach einer Krebsdiagnose

Ärztefortbildung #ComprehensiveCancerControl des BTZ, 19.12.2024

Dr. med. Flurina Saner



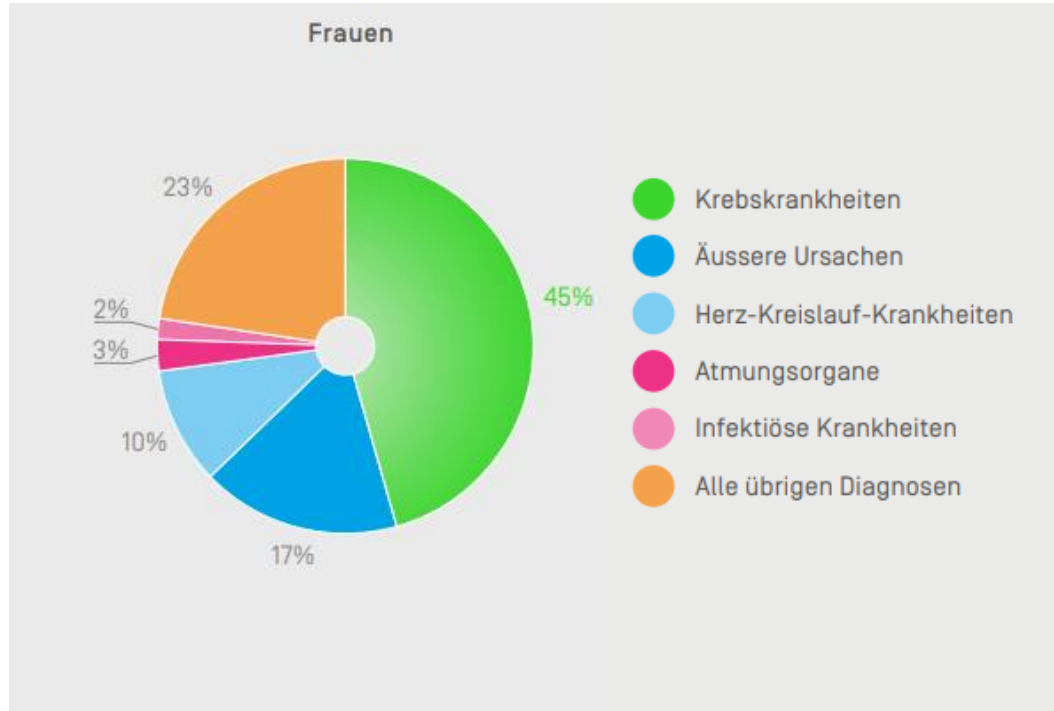


# Übersicht

- Definition Langzeitüberleben
- Determinanten für ein Langzeitüberleben
- Beeinflussbare Faktoren
- Lebensqualität von Langzeitüberlebenden
- Survivorship nach einer Krebsdiagnose

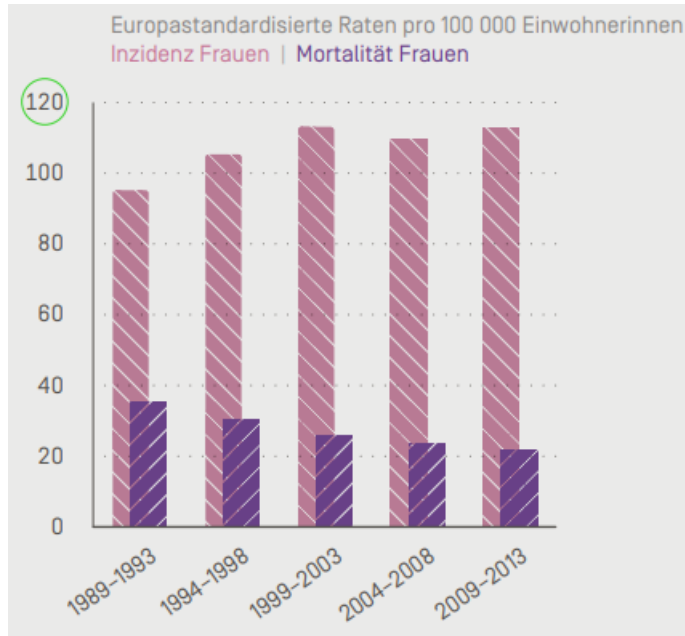


# Verlorene potentielle Lebensjahre

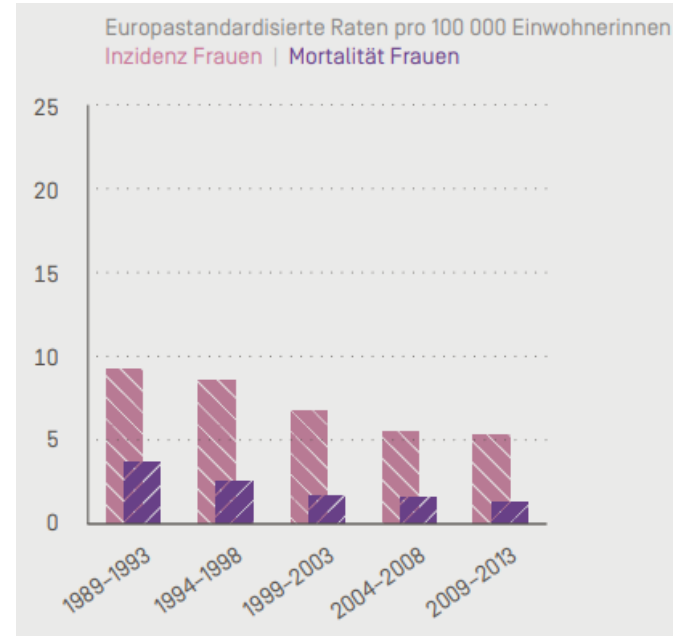


# Mortalität nach Karzinom

## Mammakarzinom



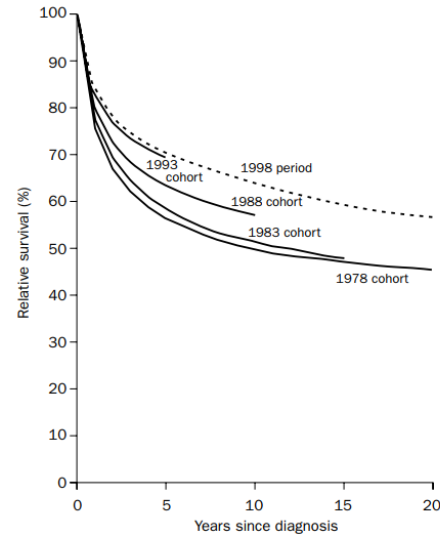
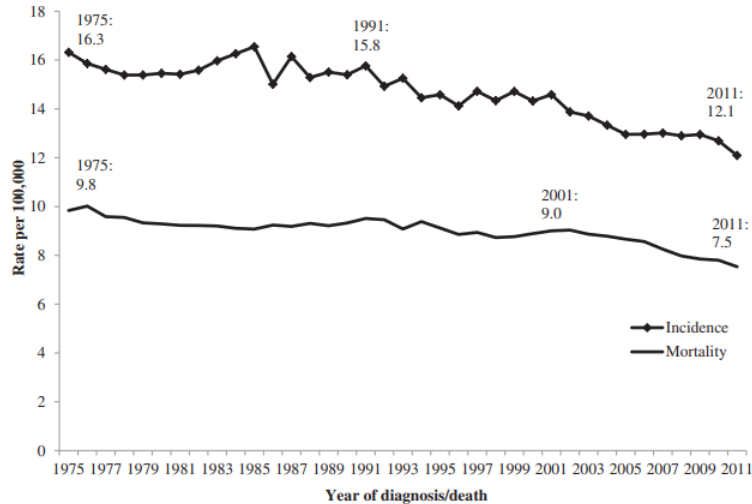
## Zervixkarzinom



Quelle: Krebsliga

# Mortalität

## Ovarialkarzinom



**20-year period-based and 5-year, 10-year, 15-year, and 20-year cohort-based relative survival curves**

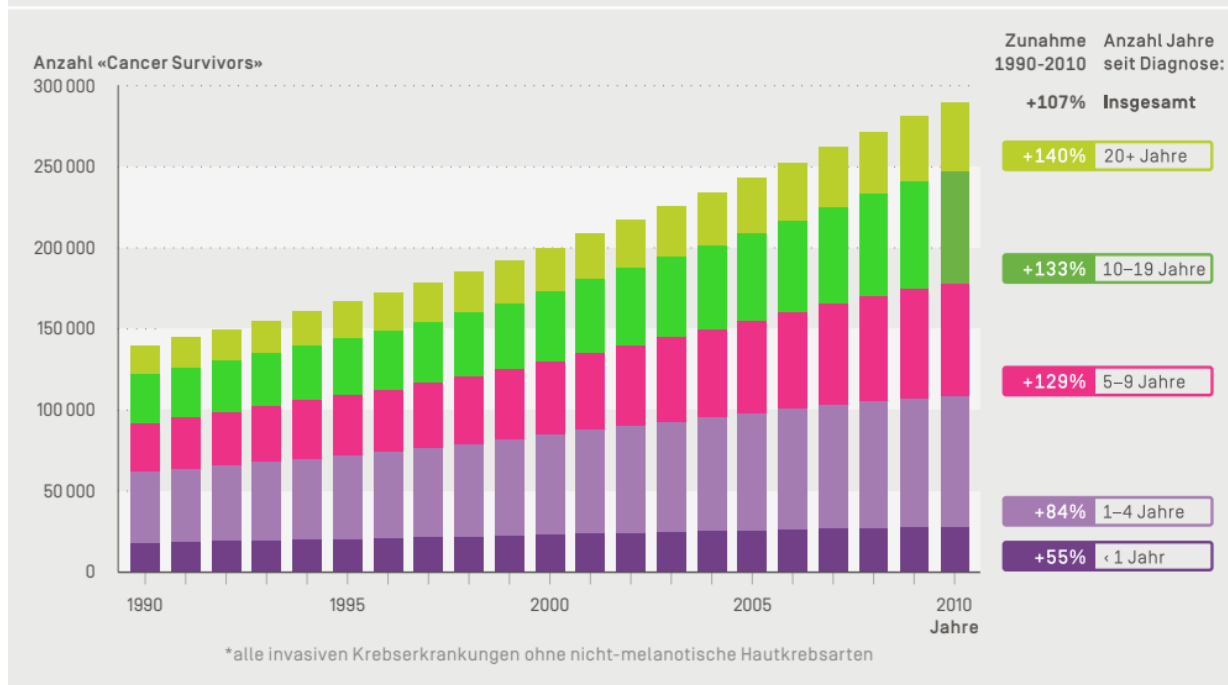
Most recent curves derived from SEER 1973-98 database,<sup>12</sup> including all ethnic groups, both sexes, and all cancer sites apart from lung and bronchus.

Sopik V. et al, Gynecologic Oncology, 2015

Brenner H., Lancet 2002

# Cancer Survivors

**Abb. 2** Geschätzte Anzahl der aktuell in der Schweiz lebenden Personen, bei denen jemals eine Krebsdiagnose\* gestellt wurde («Cancer Survivors»), Zeitperiode 1990–2010



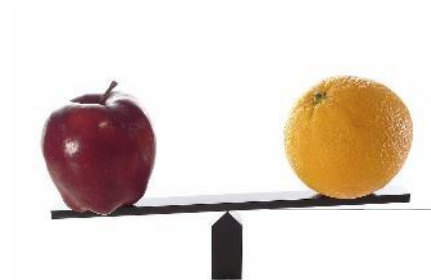
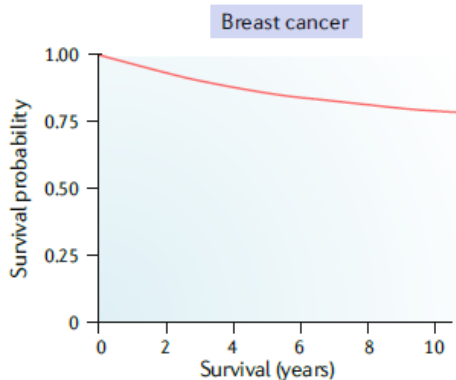
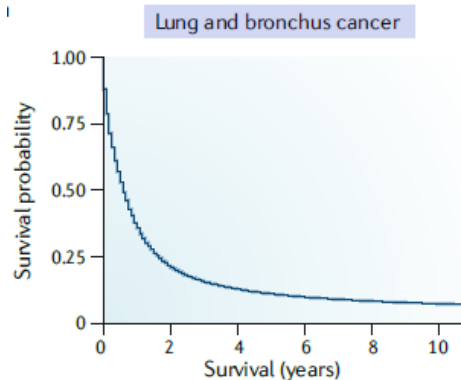
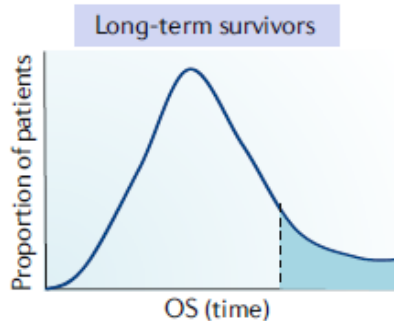
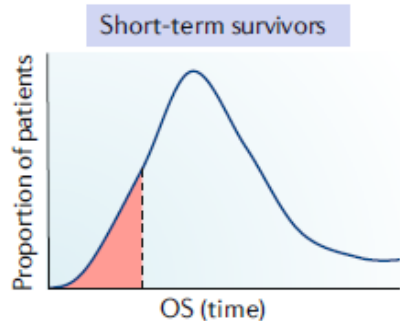
Herrmann et al., Cancer survivors in Switzerland: a rapidly growing population to care for; BMC Cancer 2013 Jun 14; 13: 267

# Survivorship – rascher Anstieg

- Zunahme der Krebs-Inzidenz
  - ungesunder Lifestyle
  - Schädliche Umgebung
  - Zunehmendes Alter der Bevölkerung
- Frühere Diagnostik
- Bessere Behandlung

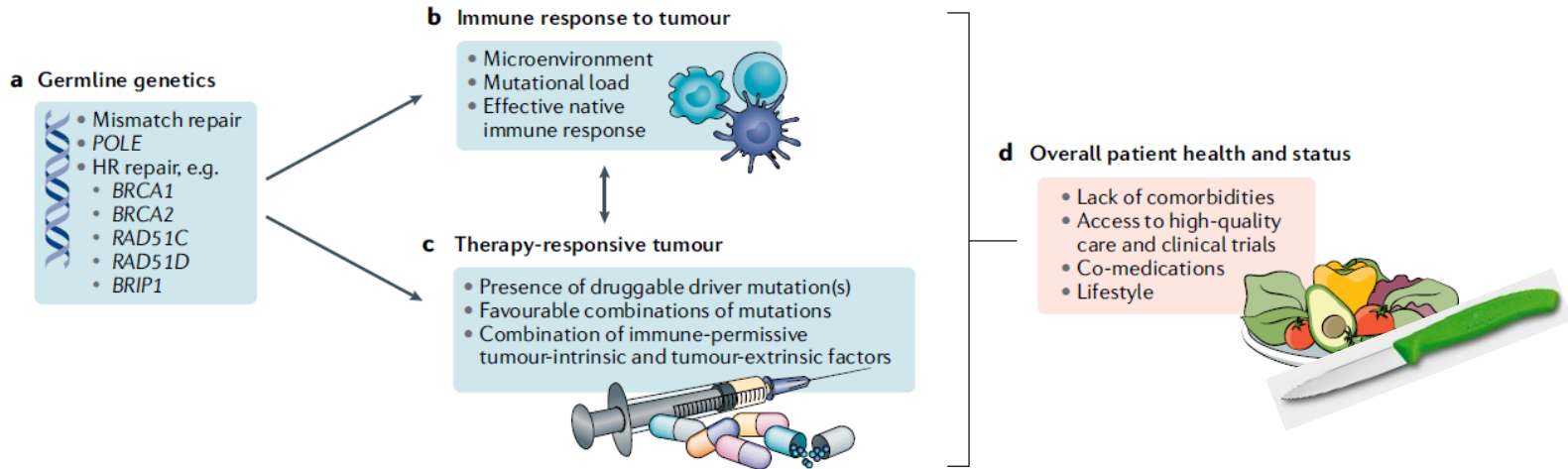


# Definitionen von Langzeitüberleben



Saner F. et al., Nature Cancer Reviews, 06/2019

# Determinanten für ein Langzeitüberleben



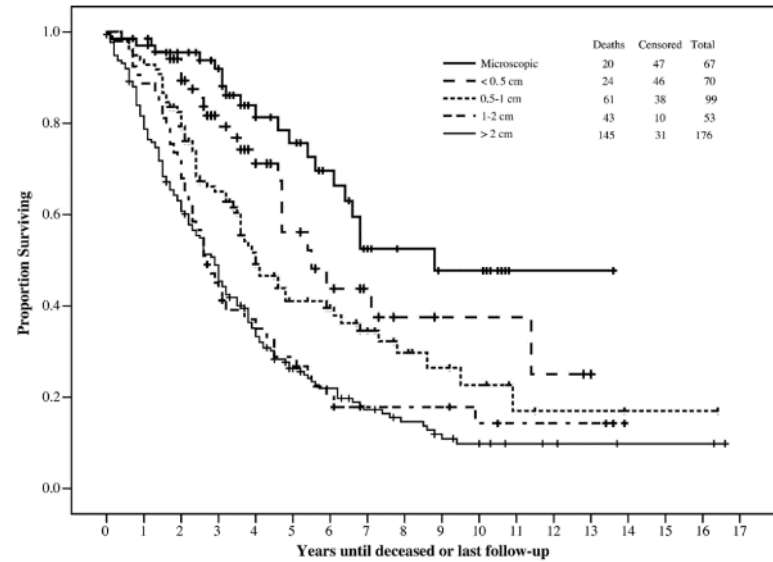
Saner F. et al., Nature Cancer Reviews, 06/2019



# Langzeitüberleben nach Ovarialkarzinom

Clinical factors associated with LTS in ovarian cancer:

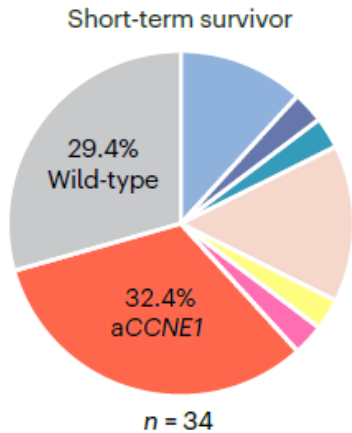
- Young age, early FIGO stage
- Type of insurance, comorbidities
- Smoking history
- low grade, non-serous histology
- absence of ascites
- less upper abdomen involvement
- surgical resection status



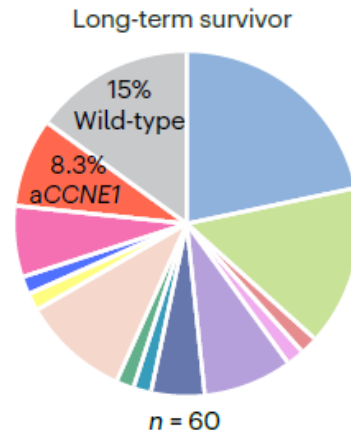
Hoppenot C, et al. Gynecol Oncol, 01/2018; Baum J, et al. Int J Gynecol Cancer, 01/2021; Chi D. et al, Gynecol Oncol 2006



# Langzeitüberleben nach Ovarialkarzinom



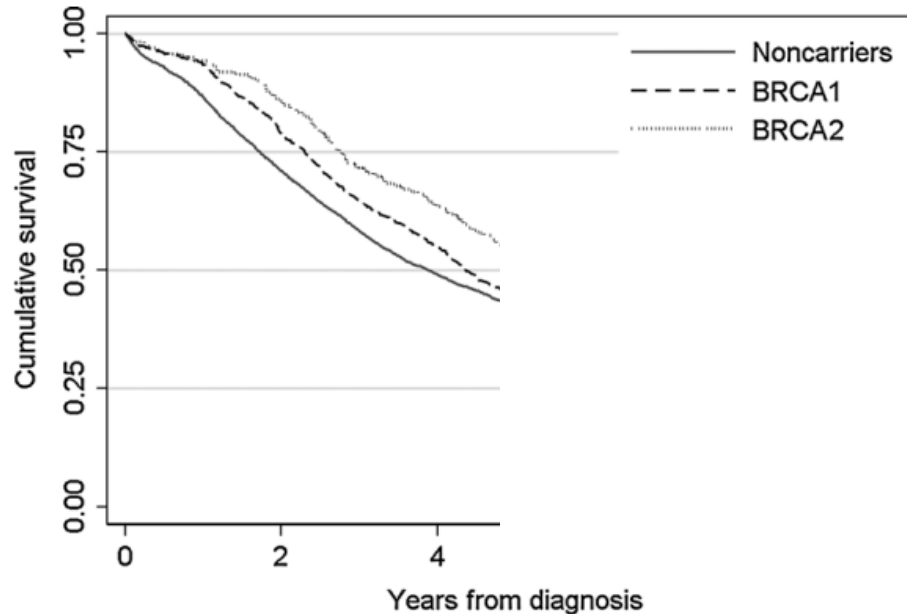
- 38.2% HR altered
- 11.8% gBRCA1
- 2.9% sBRCA2
- 2.9% sRAD51C
- 14.7% mBRCA1
- 2.9% mRAD51C
- 2.9% sCDK12



- 76.7% HR altered
- 21.7% gBRCA1
- 15% gBRCA2
- 1.7% gPALB2
- 1.7% gRAD51C
- 8.3% sBRCA1
- 5% sBRCA2
- 1.7% sRAD51C
- 1.7% sRAD51D
- 10% mBRCA1
- 1.7% mRAD51C
- 1.7% sPTEN
- 6.7% sCDK12

Garsed D. W. et al., Nature Genetics, 10/2022

# Langzeitüberleben nach Ovarialkarzinom



## 10-year OS:

30% noncarrier (95%CI 28-31%)

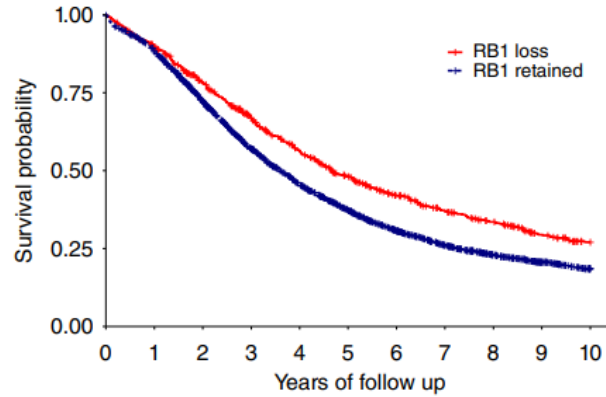
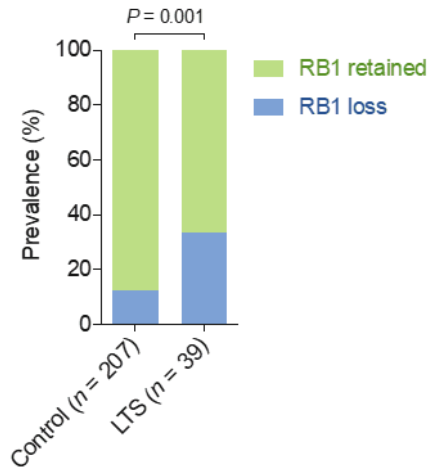
25% *gBRCA1* (95%CI 22-28%)

35% *gBRCA2* (95%CI 30-41%)

Candido-dos-Reis et al., Clinical Cancer Research 2015

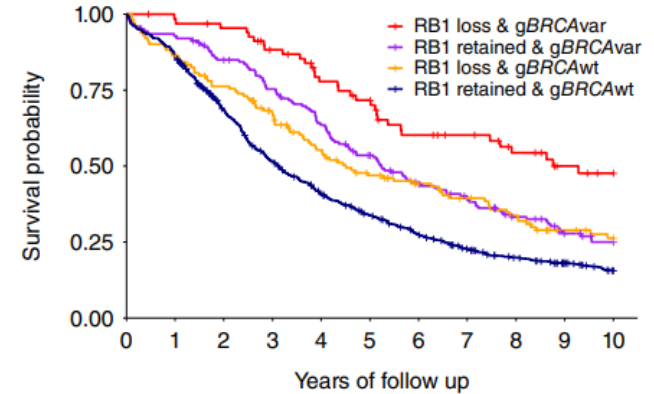


# Langzeitüberleben nach Ovarialkarzinom



Number at risk

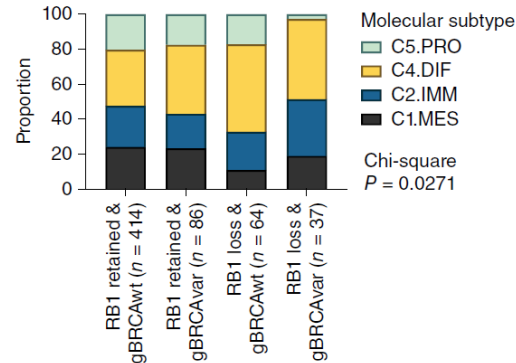
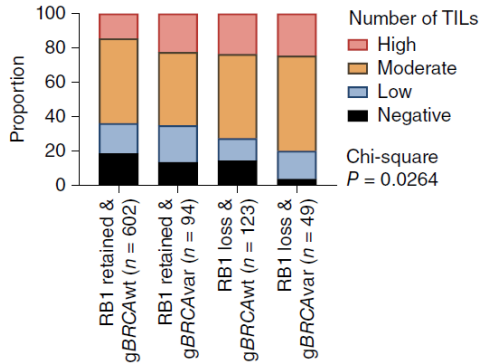
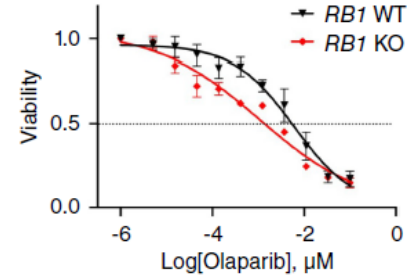
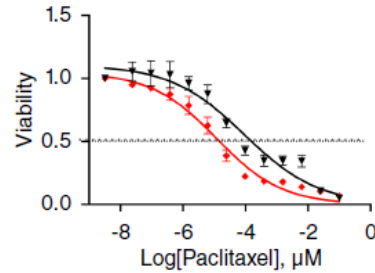
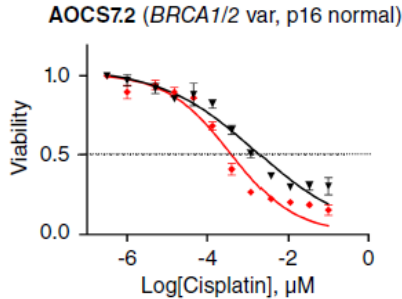
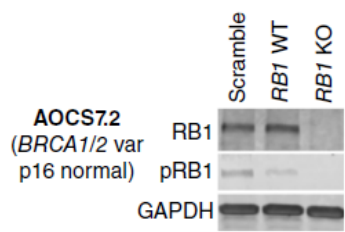
—	453	564	507	430	348	284	226	185	158	117	91
—	1802	2810	2418	1935	1521	1200	934	723	561	430	325



Number at risk

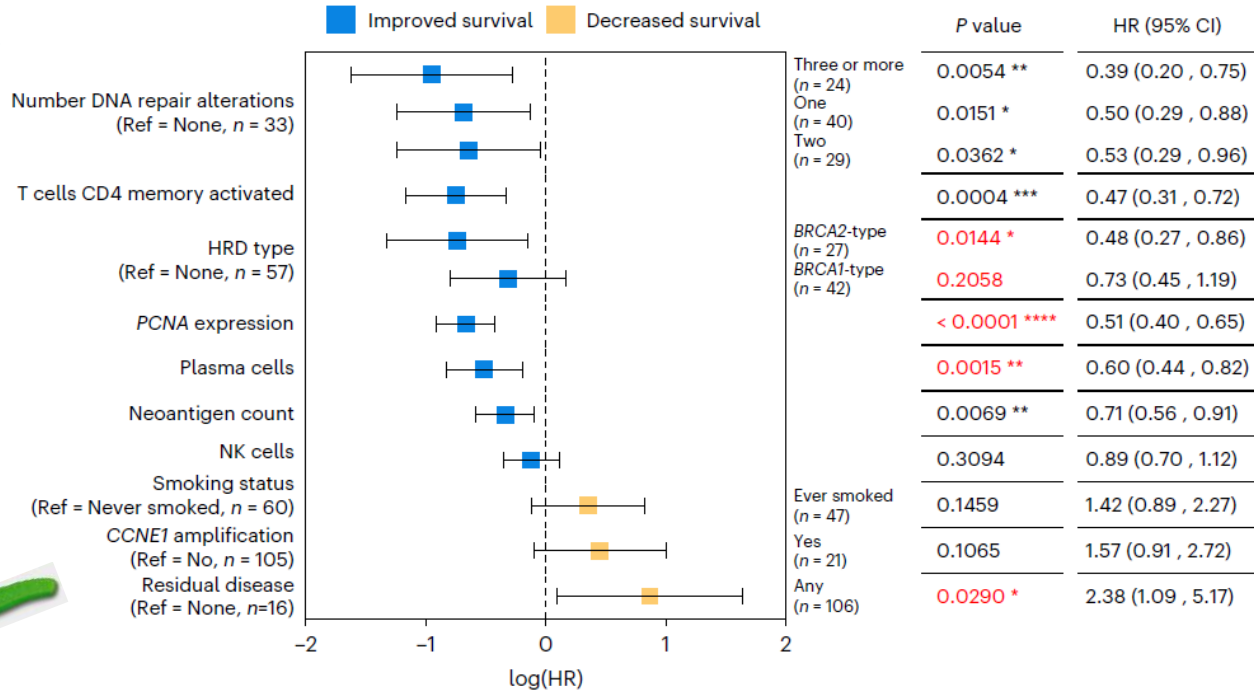
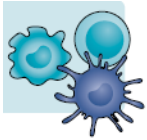
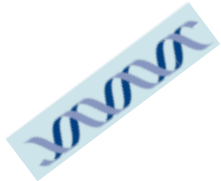
—	63	64	67	61	51	46	36	33	27	21	18
—	85	126	126	121	102	86	68	58	45	32	26
—	101	90	93	86	67	55	46	42	36	24	20
—	412	480	443	390	313	258	206	163	135	111	85

# Langzeitüberleben nach Ovarialkarzinom



Saner F. et al., Clinical Cancer Research, 2024

# Langzeitüberleben nach Ovarialkarzinom



Garsed D. W. et al., Nature Genetics, 10/2022



# Langzeitüberleben – beeinflussbare Faktoren

- Regelmässige physische Aktivität
- Gesunde Ernährung
- Gewichtsabnahme bei Adipositas
- Nikotinstopp
- Reduktion von Alkoholkonsum
- Versicherungsmodell: privat (USA)

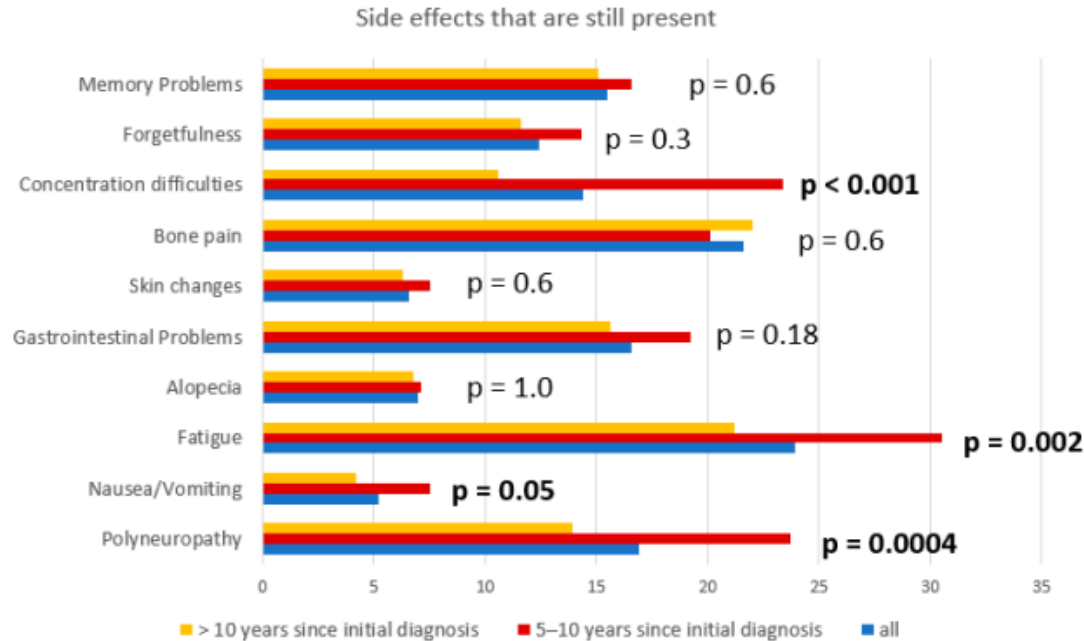
PA Quintile, HR (95% CI)	Recurrence, n=10, 685 (1,421 events)	Breast Cancer Mortality, n=11,282 <sup>b</sup> (971 events)	All-Cause Mortality, n=11,315 (1,468 events)
Meets PA Guidelines, HR (95% CI)	0.96 (0.86–1.06)	<b>0.75 (0.65–0.85)</b>	<b>0.73 (0.66–0.82)</b>

Reported comparisons of cancer incidence in bariatric and nonsurgical cohorts

First Author (yr)	Bariatric, n/N (%)	Nonsurgical, n/N (%)	HR or RR	95% CI	P value
Tsui [6] (2020)	1,448/71,000 (2.0)	7,685/323,197 (2.4)	HR: .87	.82–.92	<.0001
Christou [7] (2008)	21/1035 (2.0)	487/5746 (8.5)	RR: .22	.14–.35	.001
Schauer [8] (2019)	488/22,211 (2.2)	2,055/66,481 (3.1)	HR: .67	.6–.74	<.001
Aminian [13] (2022)	96/5053 (1.9)	780/25,265 (3.1)	HR: .68	.53–.87	.002

Referenzen im Abspann

# Lebensqualität von LTS

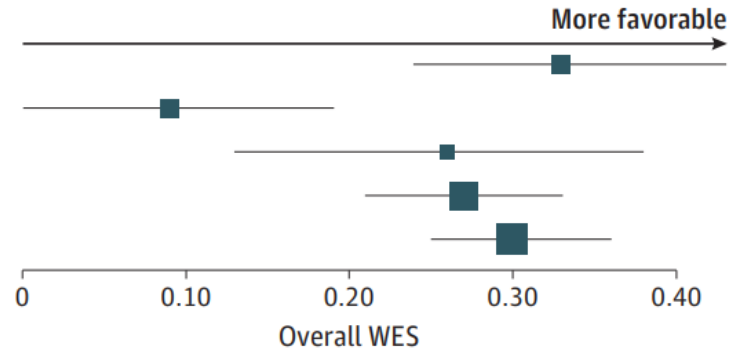


Woopen H. et al., Cancers, 11/2023

# Fatigue nach Karzinom

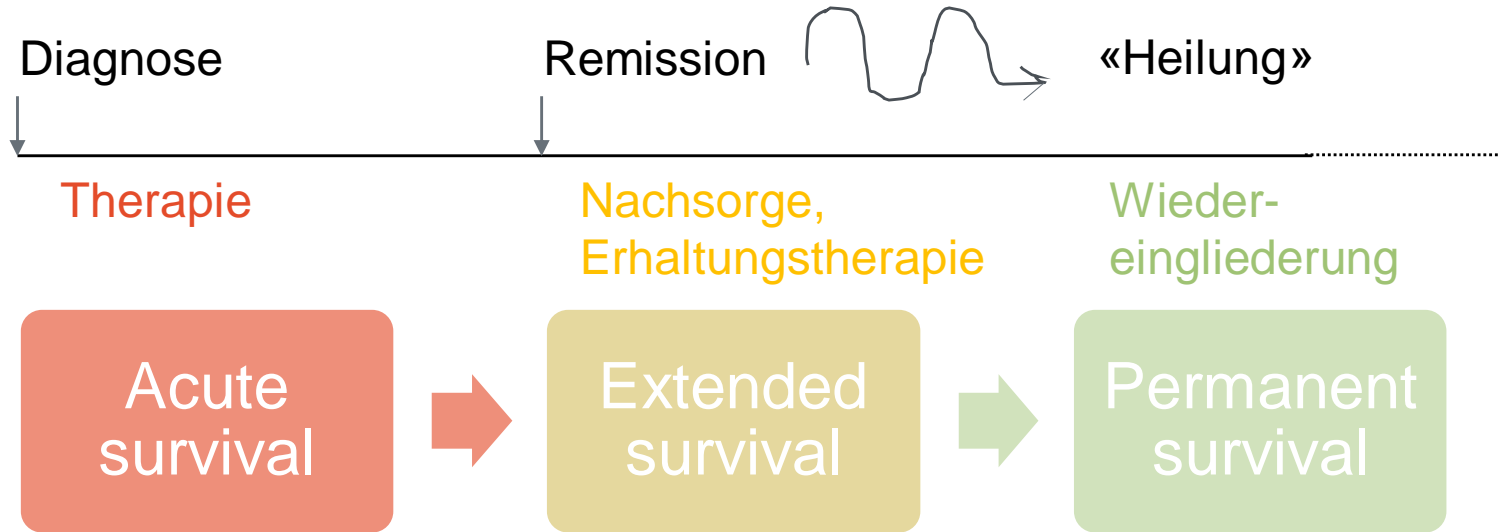
Figure 2. Forest Plot of Weighted Effect Sizes (WESs)

Intervention	No. of Effect Sizes	WES	SE	(95% CI)
All	127	0.33	0.05	(0.24-0.43)
Pharmaceutical	14	0.09	0.05	(0.00-0.19)
Exercise plus psychological	10	0.26	0.07	(0.13-0.38)
Psychological	34	0.27	0.05	(0.21-0.33)
Exercise	69	0.30	0.03	(0.25-0.36)



West S. et al, J Cancer Surviv, 2016

# Survivorship – verschiedene Phasen



Abgeleitet aus: Fitzhugh Mullan, NEJM, 1985

# Survivorship Care – 5 Grundpfeiler

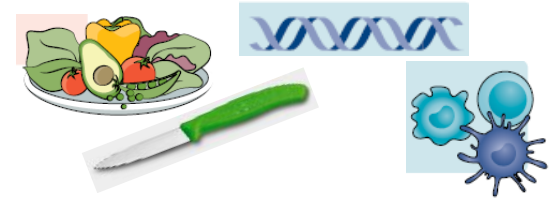
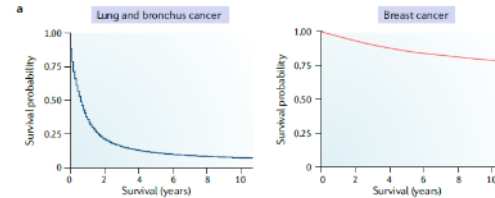


Ambulantes Präventions- und  
Rehabilitationsprogramm für Krebspatienten



# Zusammenfassung

- Definition Langzeitüberleben
- Determinanten für ein Langzeitüberleben
- Beeinflussbare Faktoren
- Lebensqualität von Langzeitüberlebenden
- Survivorship nach einer Krebsdiagnose





**Vielen Dank für Ihre Aufmerksamkeit!**

# Referenzen (weitere)

Beasley, J. M. et al. Meeting the physical activity guidelines and survival after breast cancer: findings from the after breast cancer pooling project. *Breast Cancer Res. Treat.* 131, 637–643 (2012).

Cannioto, R. A. et al. Recreational physical inactivity and mortality in women with invasive epithelial ovarian cancer: evidence from the Ovarian Cancer Association Consortium. *Br. J. Cancer* 115, 95–101 (2016).

Nagle, C. M. et al. Obesity and survival among women with ovarian cancer: results from the Ovarian Cancer Association Consortium. *Br. J. Cancer* 113, 817–826 (2015).

Eeles, R. A. et al. Adjuvant hormone therapy may improve survival in epithelial ovarian cancer: results of the AHT randomized trial. *J. Clin. Oncol.* 33, 4138–4144 (2015).

Praestegaard, C. et al. Cigarette smoking is associated with adverse survival among women with ovarian cancer: results from a pooled analysis of 19 studies. *Int. J. Cancer* 140, 2422–2435 (2017).

<https://www.wcrf.org/research-policy/evidence-for-our-recommendations/supplements/>

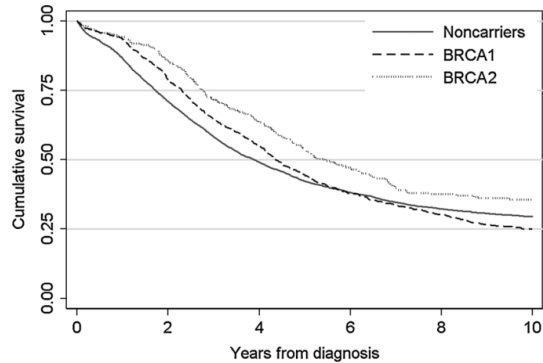
ESMO Consensus Statement Cancer Survivorship, *Annals of Oncology*, 2022



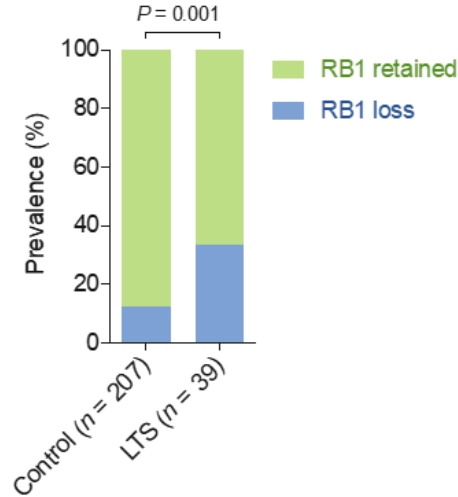


# Introduction

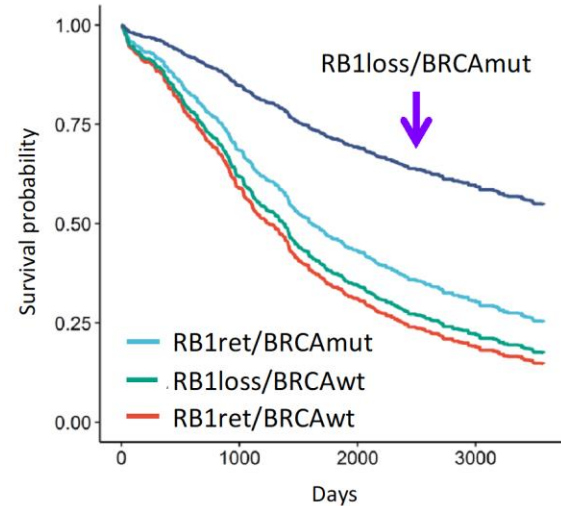
- Genomic determinants for LTS
  - HR deficiency



Number at risk	0	2	4	6	8	10
Noncarriers	1,924	2,914	2,295	1,657	1,120	812
Carriers						
BRCA1	404	676	499	323	198	118
BRCA2	162	278	239	152	86	58



Control (n = 207)  
LTS (n = 39)



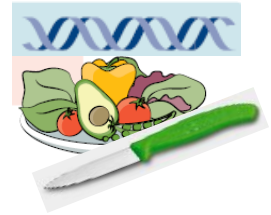
p = 0.0004

Ovarian Tumour Tissue Consortium OTTA (n=847).

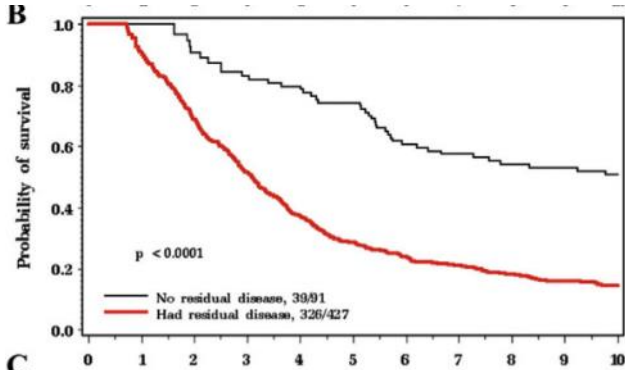
Candido-dos-Reis, et al. Clin Can Res, 11/2014

Garsed D, et al. Clin Can Res, 10/2017

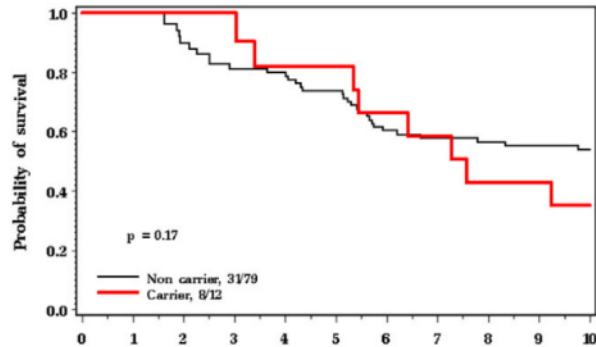
Saner FAM et al. unpublished



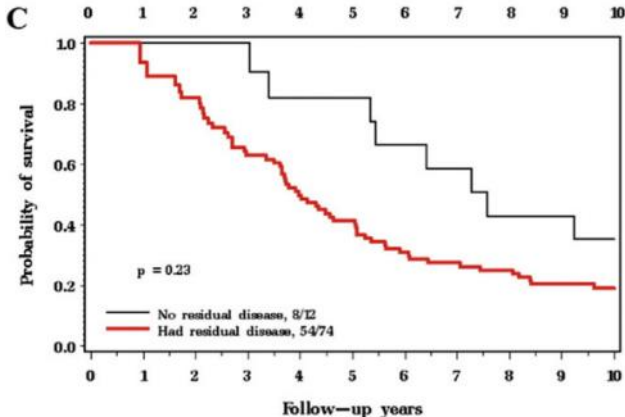
# Langzeitüberleben nach Ovarialkarzinom



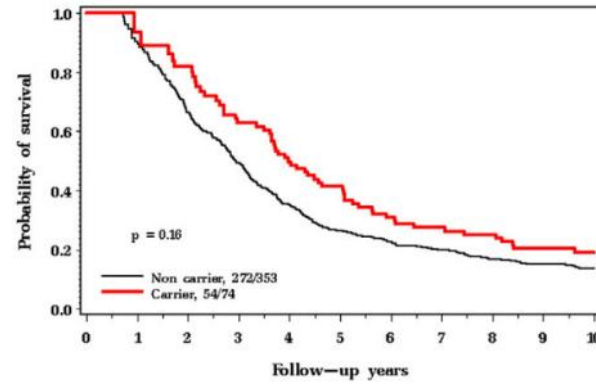
Non-carrier



No residual disease



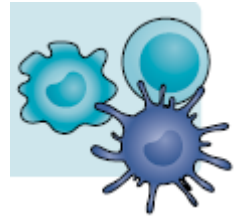
BRCA mutation carrier



With residual disease

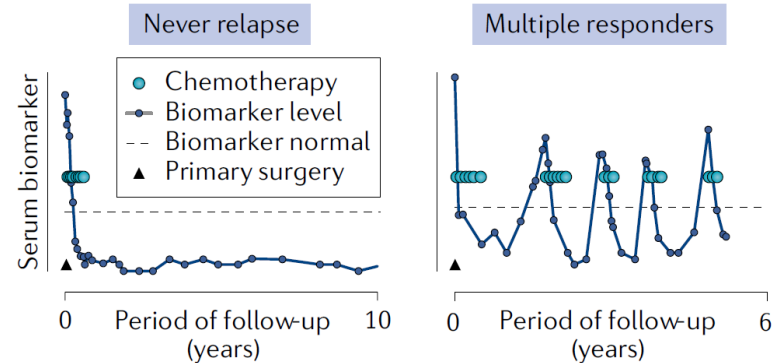
# Hypotheses

1. **Clinical and epidemiological** factors contribute to long-term survival in ovarian cancer.
2. **Genomic alterations** in DNA repair and homologous recombination pathway genes are associated with favourable treatment response and survival.
3. Tumor mutation burden can influence intratumoral **immune cell infiltration** and patient survival.



# Introduction

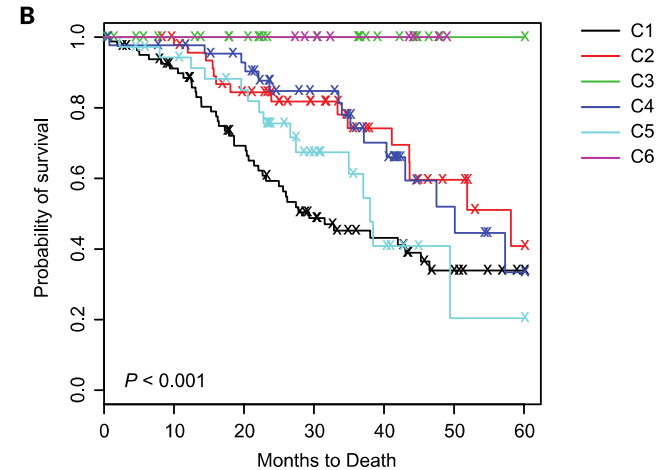
- Ovarian cancer: most lethal gynaecological malignancy
- High grade serous ovarian cancer (HGSC) accounts for ~105`000 deaths worldwide annually
- Studies on long-term survival in cancer are emerging globally
- Outliers in cancer treatment response:
  - Long-term survivors
  - Exceptional responders



Saner FAM et al., Nature Cancer Reviews, 06/2019

# Langzeitüberleben nach Ovarialkarzinom

- Clinical factors associated with LTS in ovarian cancer:
  - Young age, early FIGO stage, low grade, non-serous histology
  - absence of ascites, less upper abdomen involvement
  - surgical resection status
- Molecular determinants for LTS
  - Molecular subtype



Hoppenot C, et al. Gynecol Oncol, 01/2018; Baum J, et al. Int J Gynecol Cancer, 01/2021;  
Tothill R, et al. Clin Cancer Res, 2008

# Survivorship nach einer Krebsdiagnose

1. physical effects of cancer and chronic medical conditions
2. psychological effects of cancer
3. social, work and financial effects of cancer
4. surveillance for recurrences and second cancers
5. cancer prevention and overall health and well-being promotion

# Lebensqualität (QoL) von LTS

- QoL steigt insgesamt mit der Dauer seit Therapie
- >50% der LTS beschreiben noch Symptome
  - fatigue (44.3%), sexual dysfunction (35.7%), sleep disturbance (35.3%), neurologic symptoms (35.2%), urinary dysfunction (33.0%), bowel problems (31.2%), memory problems (30.8%), depression (26.4%), anxiety (19.3%) and lymphedema (17.6%)
  - Changes in sexuality (55%) including distortion of self-image (45%), dry vaginal mucosa (25%), fear of physical harm and dyspareunia (20%)



# Survivorship nach einer Krebsdiagnose



ESMO Patienteninformation Survivorship

# Survivorship nach einer Krebsdiagnose

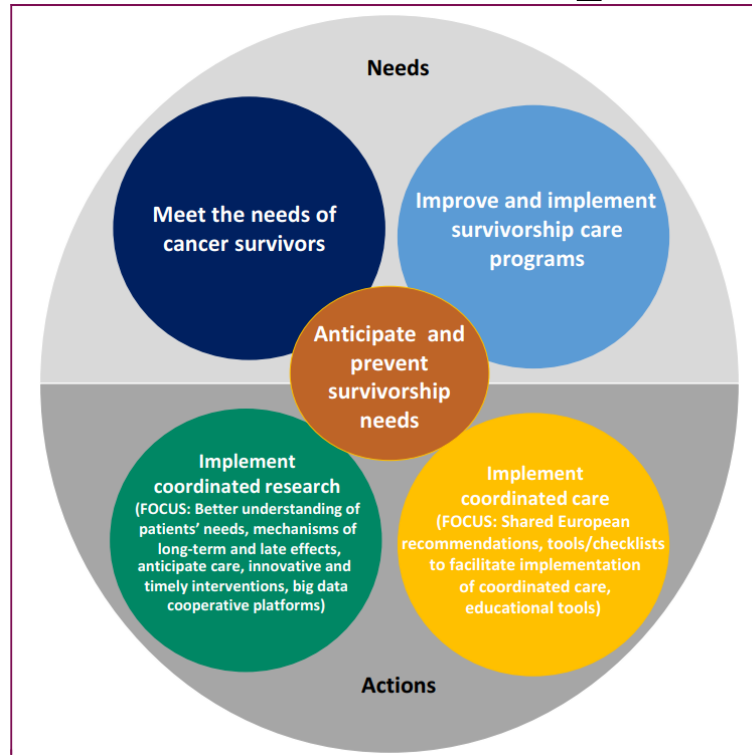


Figure 1. European Society for Medical Oncology (ESMO) and cancer survivorship: key priorities and strategies.

ESMO Consensus Statement Cancer Survivorship, Annals of Oncology, 2022