



I pazienti guariti da tumore in Italia: le ricadute nella clinica

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Bolzano 20 marzo 2013

- **Personne con storia di cancro: 2.250.000 (4% dell'intera popolazione) donne (1.250.000) e anziani.**
- **Donne diagnosi più frequente (42%) è tumore della mammella.**
- **Uomini, il 22% dei casi prevalenti (quasi 220.000 italiani) tumore della prostata.**
- **1.300.000 italiani (2,2% della popolazione) sono lungo sopravvivenenti, hanno cioè avuto una diagnosi di tumore da più di 5 anni. Si tratta di persone spesso libere da malattia e da trattamenti antitumorali.**
- **Quasi 800.000 persone (l'1,5% della popolazione) sono vive dopo oltre 10 anni dalla diagnosi di tumore.**
- **Parallelamente quasi 200.000 uomini e donne hanno avuto una diagnosi di tumore prima dei 45 anni, significa circa lo 0,6% (1 ogni 160) di tutte le persone più giovani senza alcuna distinzione tra aree geografiche.**

- **Personne viventi con tumore: differenze geografiche rilevanti: il 5% in alcune aree del Nord, 2-3% al Sud. E' indubbio anche che la proporzione di persone con tumore sia più alta al Centro-Nord rispetto al Sud.**
- **E' stato inoltre stimato che circa 700.000 italiani, quasi un terzo di tutte le persone in vita dopo una diagnosi di tumore, possono ritenersi guarite. Ciò si basa sull'assunto che i pazienti siano guariti se raggiungono un'attesa di vita simile a quella delle persone non affette da tumore: evento che avviene per la maggior parte dei tumori dopo 10 o 15 anni dalla diagnosi.**
- **I pazienti pediatrici con tumore sono l'unico gruppo per cui esistono linee guida per seguire nel tempo l'evoluzione e le complicanze a lungo termine della malattia.**

Guariti o lungo sopravvivenenti

- Come si definisce un paziente guarito
- Quale è il limite temporale che definisce la guarigione: 5, 10, 20 anni, mai

Guariti o lungo sopravvivenenti

Guarigione:

- Medicina: scomparsa della malattia spontaneamente o dopo una terapia
- Oncologia: scomparsa della neoplasia (chirurgia, terapia adiuvante o neo-adiuvante) ma le micrometastasi?

EMT is an early process

- **EMT precede pancreatic tumor formation**
- **EMT acquisition of stem cell-like characteristics**
- **Cells having undergone EMT have tumor initiating properties**
- **Inflammation promotes EMT**

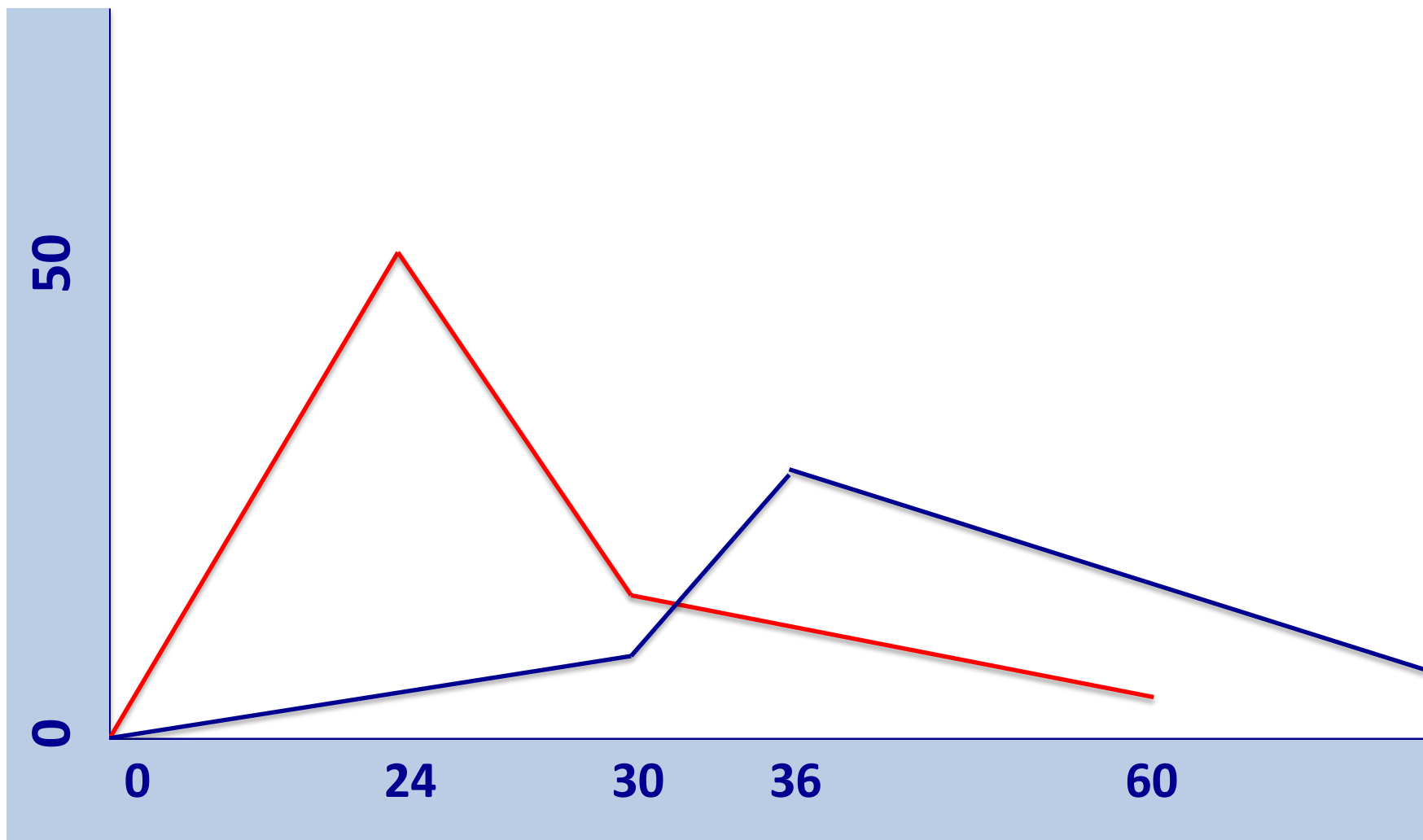
Guariti o lungo sopravvivenenti

- Quale è il limite temporale che definisce la guarigione: 5, 10, 20 anni, mai

Limite temporale di guarigione

- Carcinoma mammario
 - Triplo negativo 3 anni
 - Ormono positivo mai
- Carcinoma renale tempo indefinito, recidive a 15, 20 anni
- Carcinoma polmonare 2, 3 anni

Carcinoma colon e retto: differenze nel tempo di recidiva fra stadi II e III



Follow up

- Per quanto tempo?
Generalmente per 5 anni
- Con che cadenza e intensità?
 - Ricordare il colon stadio II o III
- Per trovare?
Una recidiva (fegato/colon)
- Il problema della tossicità tardive e dei secondi tumori

Practical Recommendations

- Several classes of chemotherapy agents commonly used are known to have myocardial dysfunction and HF as important consequences (anthracyclines, HER2-receptor antagonists, and antiangiogenic-based treatment).
- Cardiac biomarkers, particularly troponin I and BNP, are becoming useful in stratifying and identifying those patients undergoing cancer therapy at risk for cardiac dysfunction.
- Antihypertensive therapy is crucial to managing HTN during certain types of chemotherapy, and those agents known to prevent HF are preferred.
- Once a patient develops cardiac dysfunction related to chemotherapy, appropriate therapy for HF should be used.
- Early discontinuation of cardioprotective HF therapy is not recommended.

Late Cardiac Effects of Cancer Treatment

Daniel J. Lenihan and Daniela M. Cardinale

Table 2. Practical Screening Tools for Cardiovascular Disease in Cancer Survivors

Test	Timing Interval
Fasting lipid profile	Yearly, if abnormal
TSH (especially with neck irradiation)	Every several years, unless symptoms occur
Self-measurement of blood pressure	Several times per week in high-risk patients
Careful history and physical examination	At least yearly
Echocardiography (especially with any mediastinal irradiation or previous cardiotoxic chemotherapy)	Every 1-2 years in high-risk patients
Carotid ultrasound (particularly with mantle or neck irradiation)	Every 2 years in high-risk patients
Cardiac biomarkers (troponin, BNP)	Every 1-2 years in high-risk patients, unless symptoms occur
ECG	At least once every 2-3 years

Abbreviations: BNP, B-type natriuretic peptide level; TSH, thyroid-stimulating hormone.

Quali problematiche nei pazienti guariti o lungo sopravvissenti

- **Follow up**
 - Diagnosi di recidiva
 - Secondi tumori
 - Tossicità da trattamenti
- **Problematiche di vita**
 - Convivenza con esiti della malattia (stomie, ...)
 - Stili di vita
 - Ritorno al lavoro
 - Attività sportiva (agonistica)
 - Gravidanza/sterilità
 - Funzioni cognitive

Effect of Obesity on Prognosis After Early-Stage Breast Cancer

Marianne Ewertz, Maj-Britt Jensen, Katrín Á. Gunnarsdóttir, Inger Højris, Erik H. Jakobsen, Dorte Nielsen, Lars E. Stenbygaard, Ulla B. Tange, and Søren Coid

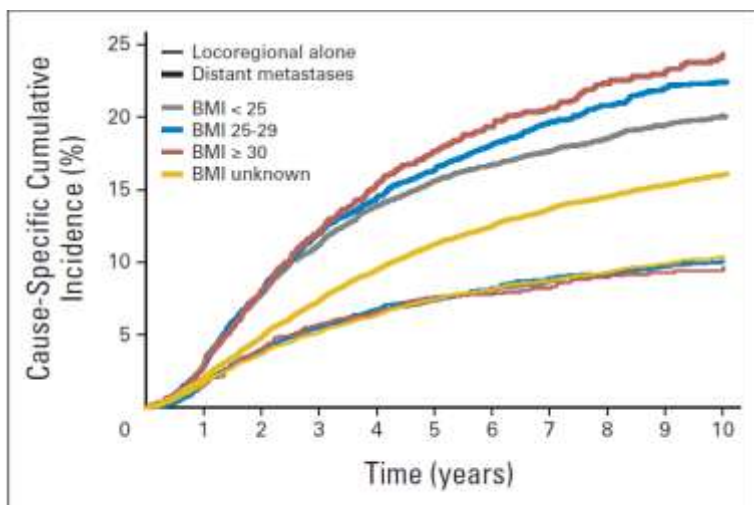


Fig 1. Cumulative incidence of first events (loco-regional recurrences and distant metastases) in relation to body mass index (BMI) among 53,816 patients with early-stage breast cancer in Denmark, 1977 to 2006.

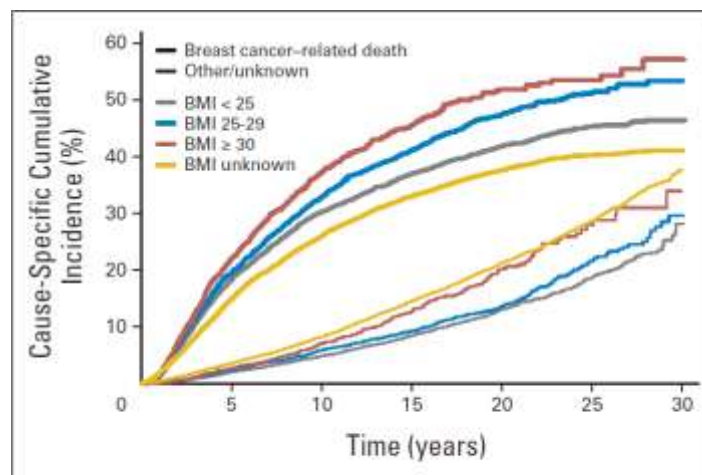
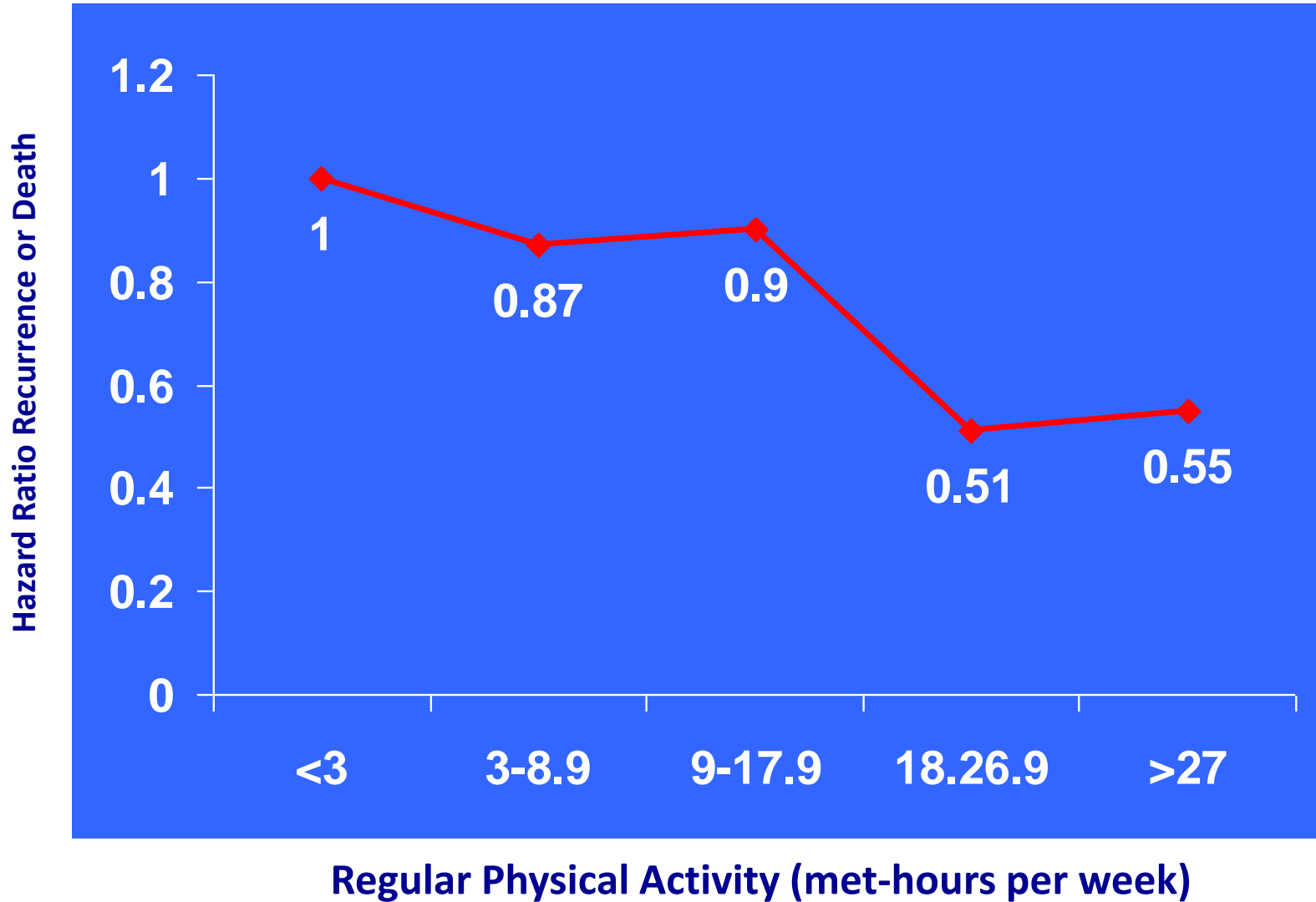


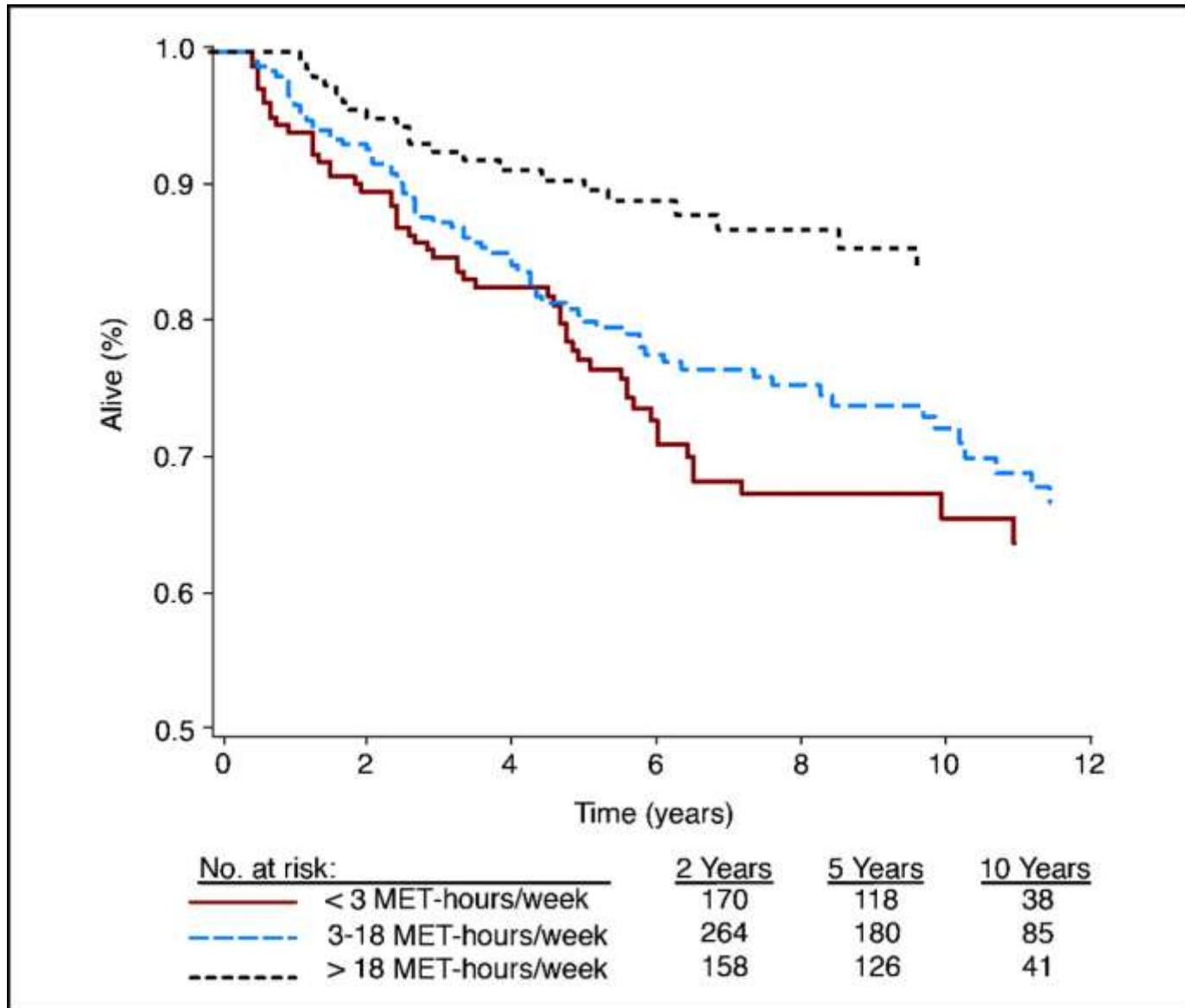
Fig 2. Risk of death as a result of breast cancer and other causes in relation to body mass index (BMI) among 53,816 patients with early-stage breast cancer in Denmark, 1977 to 2006.

**L'obesità è un fattore prognostico negativo indipendente.
Gli effetti positivi della terapia adiuvante sembrano perdersi più
rapidamente nelle pazienti obese.**

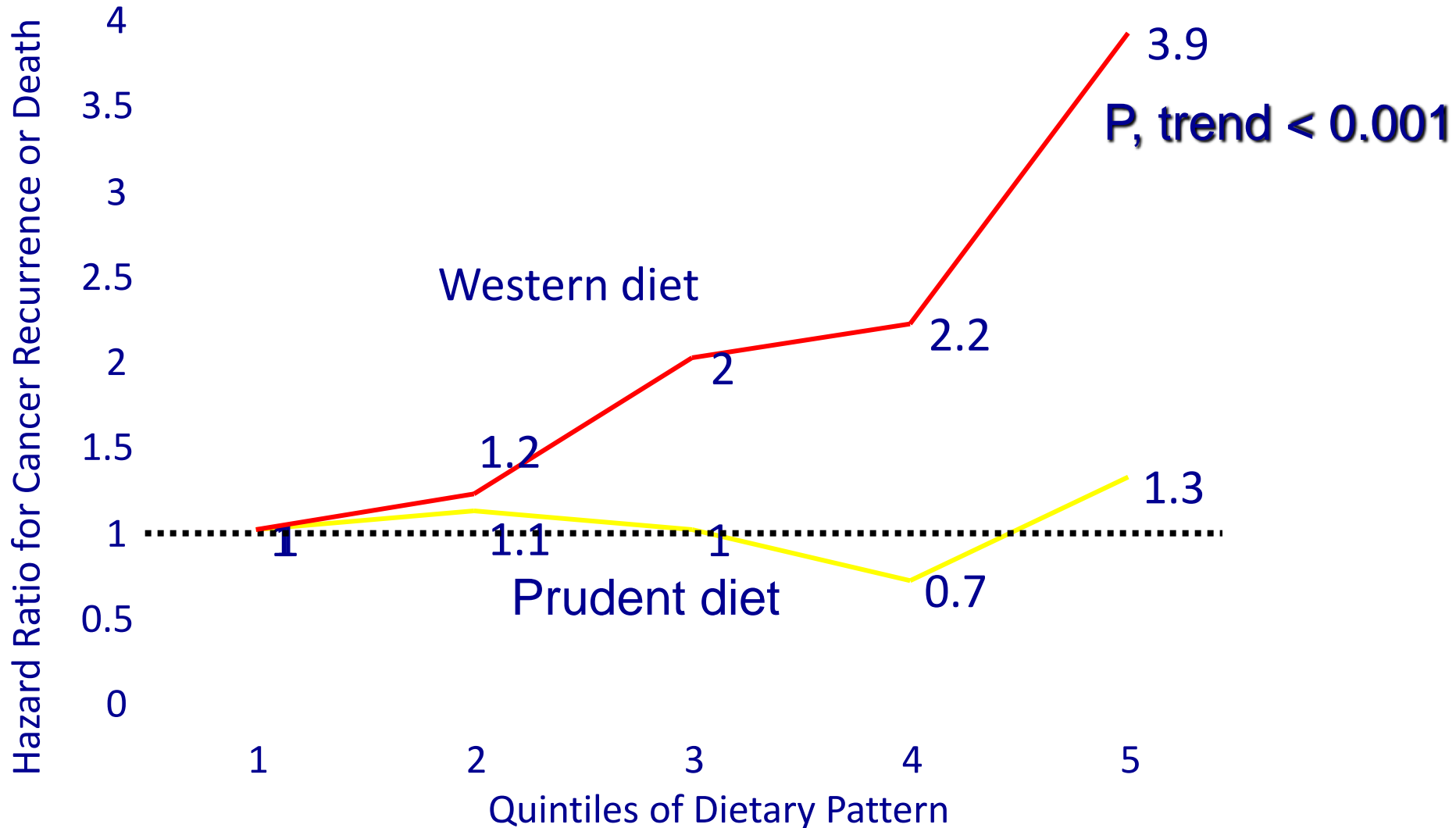
89803 and Exercise: Disease-Free Survival in Stage III Colon Cancer Survivors



NHS and Post-diagnosis Physical Activity



CALGB 89803: DFS By Dietary Pattern



Return to work after treatment for primary breast cancer over a 6-year period: results from a prospective study comparing patients with the general population

[Dorothee Noeres](#), [Tjoung-Won Park-Simon](#), [Jördis Grabow](#), [Stefanie Sperlich](#),
[Heike Koch-Gießelmann](#), [Jelena Jaunzeme](#), [Siegfried Geyer](#)

- **1 year after primary surgery, nearly three times as many cancer survivors had left their job.**
- **For breast cancer survivors, a lower level of education, part-time employment, the severity of work-related difficulties and participation in inpatient rehabilitation correlated significantly with the failure to return to work.**
- **Six years after surgery, the probability of returning to work was still only half as high among breast cancer survivors than among controls.**
- **The main predictor for not returning to work was found to be age; tumour stage and the severity of side effects of treatment also seemed to have an impact. Breast cancer survivorship increases the risk of dropping out of paid work.**

Table 1. Recommended Assessment of Treatment-Associated Female Reproductive and Sexual Function: Summary of COG Guidelines

Late Effect or Complication	Associated Therapies	Risk Factors	Assessment	Counseling and Additional Considerations
Hypogonadism Gonadotropin deficiency Delayed/arrested puberty Acute ovarian failure Premature menopause Infertility	Chemotherapy: · Alkylating agents · Heavy metals · Nonclassical alkylators Radiotherapy: · Cranial (≥ 40 Gy) · Cranial, orbital/eye · Ear/infratemporal · Nasopharyngeal · Waldeyer's ring · Ovarian (any dose) · Spine (lumbar, sacral, whole) · Flank/hemiabdomen below iliac crest · Whole abdomen/TLI/TBI · Inverted Y · Pelvic/iliac/vaginal/bladder Surgery · Oophorectomy	Host factors: · Older age at gonadal irradiation Treatment factors: · Higher cumulative doses or combinations of alkylators (busulfan > 600 mg/m ² , cyclophosphamide > 7.5 g/m ² or as conditioning for HSCT) · Prepubertal gonadal irradiation (≥ 10 Gy) · Pubertal gonadal irradiation (≥ 5 Gy) · Alkylators plus irradiation of: —Abdomen/pelvis —Lumbar or sacral spine —Neuroendocrine axis —TBI · Longer time since treatment Health behaviors: · Smoking	History (yearly): · Pubertal (onset, tempo) · Menstrual/pregnancy · Sexual function (vaginal dryness, libido) · Medications relevant to sexual function Physical examination (yearly until sexual maturity): · Tanner staging Screening: · LH, FSH, and estradiol (baseline at age 13 years and as clinically indicated by delayed puberty, irregular menses, primary or secondary amenorrhea, and/or clinical signs and symptoms of estrogen deficiency)	Referral: · Endocrinology/gynecology for delayed puberty, persistently abnormal hormone levels, or hypogonadism · Reproductive endocrinology for infertility evaluation and consultation on assisted reproduction or gestational surrogate · Consider oocyte cryopreservation for patients who wish to preserve fertility options Associated considerations: · Evaluation of bone mineral density in hypogonadal patients Counseling: · Counsel menstruating women at risk of early menopause about risk of delaying childbearing · Counsel all patients on need for contraception because alkylator-associated gonadal toxicity is extremely variable · Counsel regarding benefits of HRT in promoting pubertal progression and bone and cardiovascular health Resources: · American Society for Reproductive Medicine (www.asrm.org) · Fertile Hope (www.fertilehope.org)
Precocious puberty	Radiotherapy: · Cranial, orbital/eye · Ear/infratemporal · Nasopharyngeal · Waldeyer's ring	Host factor: · Younger age at treatment Treatment factor: · Radiation dose ≥ 18 Gy	Physical examination (yearly until sexual maturity): · Height/weight · Tanner staging	Referral: · Endocrine consultation for accelerated puberty (age < 8 years) Laboratory: · FSH, LH, and estradiol as clinically indicated by accelerated pubertal progression and growth Radiology: · X-ray for bone age in rapidly growing children · Consider pelvic ultrasound to rule out ovarian tumor Resource: · Magic Foundation (www.magicfoundation.org)
Uterine vascular insufficiency	Radiotherapy: · Spine (lumbar, sacral, whole) · Flank/hemiabdomen below iliac crest · Whole abdomen/TLI/TBI · Inverted Y · Pelvic/iliac · Vaginal/bladder	Host factor: · Women with Wilms tumor and associated Müllerian anomalies Treatment factors: · Higher pelvic radiation dose · Radiation dose ≥ 30 Gy	History (yearly and as clinically indicated): · Adverse pregnancy outcomes · Low-birth weight infant · Spontaneous abortions · Fetal malposition · Premature labor	Radiology · High-level ultrasound evaluation of genitourinary tract after pubertal development as clinically indicated in patients contemplating pregnancy
Sexual dysfunction Vaginal fibrosis/stenosis	Radiotherapy: · Flank/hemiabdomen below iliac crest · Whole abdomen/TLI · Inverted Y · Pelvic/iliac · Vaginal/bladder Hematopoietic cell transplantation: · GVHD Surgery: · Pelvic surgery (cystectomy) · Neurosurgery (spinal cord)	Host factors: · Chronic GVHD · Hypogonadism · Tumor adjacent to spinal cord or cauda equina · Vaginal tumor or pelvic tumor adjacent to vagina Treatment factors: · Prepubertal (≥ 25 Gy) · Postpubertal (≥ 50 Gy) · GVHD plus pelvic irradiation	History (yearly): · Psychosocial assessment · Altered or diminished sensation · Medication use · Dyspareunia · Vulvar pain · Postcoital bleeding · Difficulty with tampon insertion	Referral: · Gynecologic consultation for management · Psychological consultation for patients with emotional difficulties

Abbreviations: COG, Children's Oncology Group; FSH, follicle-stimulating hormone; GVHD, graft-versus-host disease; HRT, hormone-replacement therapy; HSCT, hematopoietic stem-cell transplantation; LH, luteinizing hormone; TBI, total body irradiation; TLI, total lymphoid irradiation.

Female Reproductive Health After Childhood, Adolescent, and Young Adult Cancers: Guidelines for the Assessment and Management of Female Reproductive Complications

Monika L. Metzger, Lillian R. Meacham, Briana Patterson, Jacqueline S. Casillas, Louis S. Constine, Nobuko Hijiya, Lisa B. Kenney, Marcia Leonard, Barbara A. Lockart, Wendy Likes, and Daniel M. Green

Cancer. 2013.

Birth rates among female cancer survivors: A population-based cohort study in Sweden.

[Hartman M](#), [Liu J](#), [Czene K](#), [Miao H](#), [Chia KS](#), [Salim A](#), [Verkooijen HM](#).

Saw Swee Hock School of Public Health, National University of Singapore, Singapore; Department of Surgery, Yong Loo Lin School of Medicine, National University Hospital, Singapore; Department of Medical Epidemiology and Biostatistics, Karolinska Institute, Stockholm, Sweden.

Cancer survivors are less likely to give birth compared with the background population.

Large variations in the likelihood to give birth after diagnosis were seen according to age at onset, cancer site, and parity status at diagnosis.

Long-term breast cancer survivors' symptoms and morbidity: differences by sexual orientation?

[Boehmer U](#), [Glickman M](#), [Winter M](#), [Clark MA](#).

- **Our finding that SMW respond more negatively to certain cancer treatments compared to heterosexual women suggests an opportunity to intervene with education and support for SMW breast cancer survivors for whom these life-saving treatments are necessary.**

IMPLICATIONS FOR CANCER SURVIVORS:

- **Because breast cancer survivors are at risk for multiple severe and persistent symptoms, assessing such symptoms is an important aspect of survivorship care.**
- **Cultural differences in perception of symptoms, communication issues, cultural barriers to reporting of symptoms, and different cultural norms about expressing pain or impairments have been established by studies.**
- **Knowledge about differences in impairment and symptoms by sexual orientation will help providers' efforts to provide high quality care to breast cancer survivors and may enhance cancer survivorship**

Table 2. Weighted Average Effect Sizes By Cognitive Domain

Domain	k	No. of Comparisons	Effect Size (g)	95% CI	P
Attention	16	21	-0.02	-0.12 to 0.08	.743
Executive functioning	14	19	-0.12	-0.23 to 0.00	.052
Information processing	6	11	-0.11	-0.25 to 0.03	.122
Motor speed	8	11	0.06	-0.37 to 0.49	.785
Verbal ability	12	15	-0.19	-0.30 to -0.07	.002
Verbal memory	17	23	-0.06	-0.18 to 0.06	.313
Visual memory	15	21	0.02	-0.09 to 0.13	.730
Visuospatial ability	8	9	-0.27	-0.45 to -0.08	.006

Meta-Analysis of Cognitive Functioning in Breast Cancer Survivors Previously Treated With Standard-Dose Chemotherapy

Heather S.L. Jim, Kristin M. Phillips, Sari Chait, Leigh Anne Faul, Mihaela A. Popa, Yun-Hsiang Lee, Mallory G. Hussin, Paul B. Jacobsen, and Brent J. Small

See accompanying editorial on page 3568; listen to podcast by Drs Dhillon and Vardy at www.jco.org/podcasts

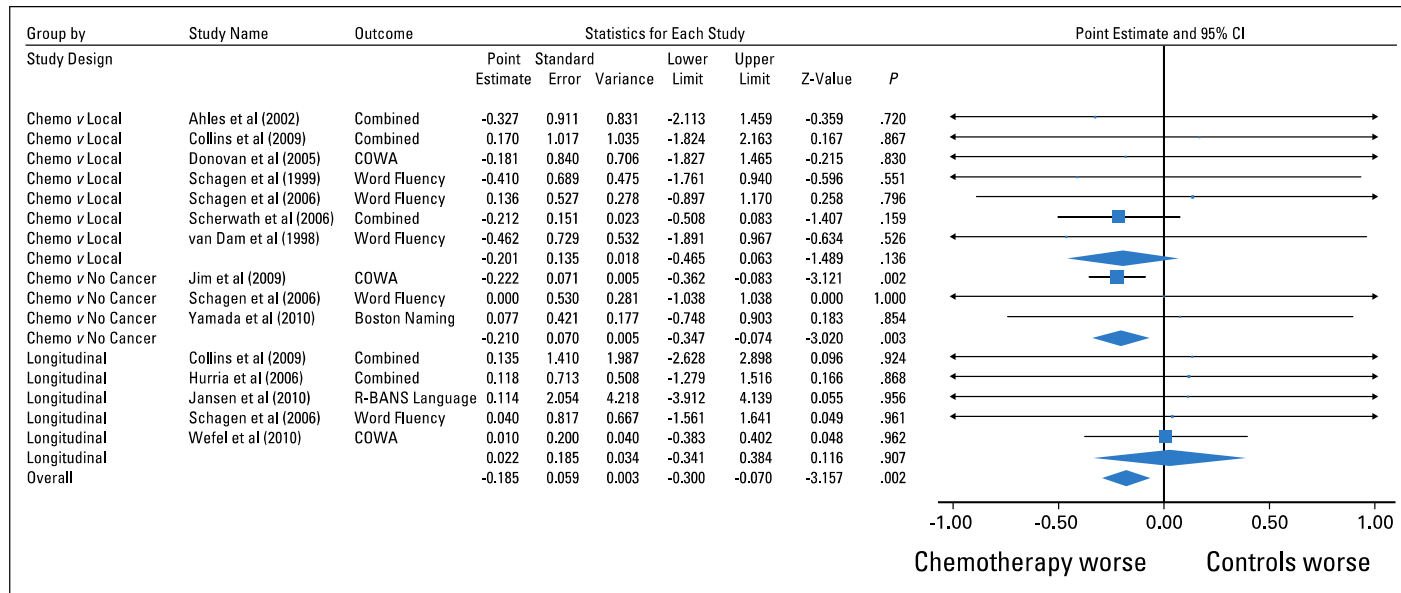


Fig 2. Forest plot of effect sizes (g) for studies assessing verbal ability. Chemo, chemotherapy; COWA, Controlled Oral Word Association; R-BANS, Repeatable Battery of Adult Neuropsychological Status.

Il problema clinico, il problema organizzativo

Dove

- I pazienti acuti l'ospedale
- Il paziente cronico il territorio
- Il paziente guarito ????????????

Chi

- L'oncologo
- Il medico di medicina generale
- Altri ?????