II SESSIONE:

LA BIOPSIA DEL LINFONODO SENTINELLA: PRIMA O DOPO LA CHEMIOTERAPIA NEOADIUVANTE?

Moderatori: Diana Crivellari, Alberto Massocco

Ore 15,00-15,15	Lo studio SENTINA - Laura Orlando
Ore 15,15-15,30	Commento sulla metodologia - Giovanni L. Pappagallo
Ore 15,30-15,45	Quale impatto sulla pratica clinica? - Nicla La Verde
Ore 15,45-16,00	Discussione

La Qualità Tedesca

È un’auto tedesca
È una modella tedesca

Sentinel-lymph-node biopsy in patients with breast cancer before and after neoadjuvant chemotherapy (SENTINA): a prospective, multicentre cohort study

Thorsten Kuehn, Ingo Bauerfeind, Tanja Fehm, Barbara Fleige, Maik Hausschild, Gisela Helms, Annette Lebeau, Cornelia Liedtke, Gunter von Minckwitz, Valentina Nekljudova, Sabine Schmatloch, Peter Schrenk, Annette Staebler, Michael Untch

Summary

Background The optimum timing of sentinel-lymph-node biopsy for breast cancer patients treated with neoadjuvant chemotherapy is uncertain. The SENTINA (SENTInel NeoAdjuvant) study was designed to evaluate a specific algorithm for timing of a standardised sentinel-lymph-node biopsy procedure in patients who undergo neoadjuvant chemotherapy.

Methods SENTINA is a four-arm, prospective, multicentre cohort study undertaken at 103 institutions in Germany and Austria. Women with breast cancer who were scheduled for neoadjuvant chemotherapy were enrolled into the study. Patients with clinically node-negative disease (cN0) underwent sentinel-lymph-node biopsy before neoadjuvant chemotherapy (arm A). If the sentinel node was positive (pN1), a second sentinel-lymph-node biopsy procedure was done after neoadjuvant chemotherapy (arm B). Women with clinically node-positive disease (cN+) received neoadjuvant chemotherapy. Those who converted to clinically node-negative disease after chemotherapy (ycN0; arm C) were treated with sentinel-lymph-node biopsy and axillary dissection. Only patients whose clinical nodal status remained positive (ycN1) underwent axillary dissection without sentinel-lymph-node biopsy (arm D). The primary endpoint was accuracy (false-negative rate) of sentinel-lymph-node biopsy after neoadjuvant chemotherapy for patients who converted from cN1 to ycN0 disease during neoadjuvant chemotherapy (arm C). Secondary endpoints included comparison of the detection rate of sentinel-lymph-node biopsy before and after neoadjuvant chemotherapy, and also the false-negative rate and detection rate of sentinel-lymph-node biopsy after removal of the sentinel lymph node. Analyses were done according to treatment received (per protocol).

Findings Of 1737 patients who received treatment, 1022 women underwent sentinel-lymph-node biopsy before neoadjuvant chemotherapy (arms A and B), with a detection rate of 99·1% (95% CI 98·3–99·6; 1013 of 1022). In patients who converted after neoadjuvant chemotherapy from cN+ to ycN0 (arm C), the detection rate was 80·1% (95% CI 76·6–83·2; 474 of 592) and false-negative rate was 14·2% (95% CI 9·9–19·4; 32 of 226). The false-negative rate was 24·3% (17 of 70) for women who had one node removed and 18·5% (10 of 54) for those who had two sentinel nodes removed (arm C). In patients who had a second sentinel-lymph-node biopsy procedure after neoadjuvant chemotherapy (arm B), the detection rate was 60·8% (95% CI 55·6–65·9; 219 of 360) and the false-negative rate was 51·6% (95% CI 38·7–64·2; 33 of 64).

Interpretation Sentinel-lymph-node biopsy is a reliable diagnostic method before neoadjuvant chemotherapy. After systemic treatment or early sentinel-lymph-node biopsy, the procedure has a lower detection rate and a higher false-negative rate compared with sentinel-lymph-node biopsy done before neoadjuvant chemotherapy. These limitations should be considered if biopsy is planned after neoadjuvant chemotherapy.

Funding Brustkrebs Deutschland, German Society for Senology, German Breast Group.

Introduction

Axillary-lymph-node status is one of the strongest prognostic factors for patients with breast cancer and it guides adjuvant local and systemic treatment decisions. In recent years, sentinel-lymph-node biopsy has replaced full axillary-lymph-node dissection as a staging procedure for patients who undergo primary surgery and have clinically negative lymph nodes. Sentinel-lymph-node biopsy provides an accurate assessment of histological nodal status and is associated with less acute and chronic morbidity than axillary-lymph-node dissection.[1–3] Neoadjuvant chemotherapy is established for treatment of locally advanced disease and is being used increasingly for early-stage breast cancer.[4] This therapeutic approach provides in-vivo chemosensitivity testing and prognostic information. Patients with an unfavourable tumour-to-breast ratio can be downstaged to allow less radical surgery and to increase the rate of breast-conserving treatment.[5,6]

Timing of sentinel-lymph-node biopsy in the neoadjuvant setting is controversial. Reliable data for the detection rate, accuracy (the false-negative rate), and the number of regional relapses are available for when biopsy is done before systemic adjuvant treatment in

Lancet Oncol 2013; 14: 609–18
Published Online May 15, 2013 http://dx.doi.org/10.1016/S1470-2045(13)70166-9

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È uno studio tedesco

Sentinel-lymph-node biopsy in patients with breast cancer before and after neoadjuvant chemotherapy (SENTINA): a prospective, multicentre cohort study

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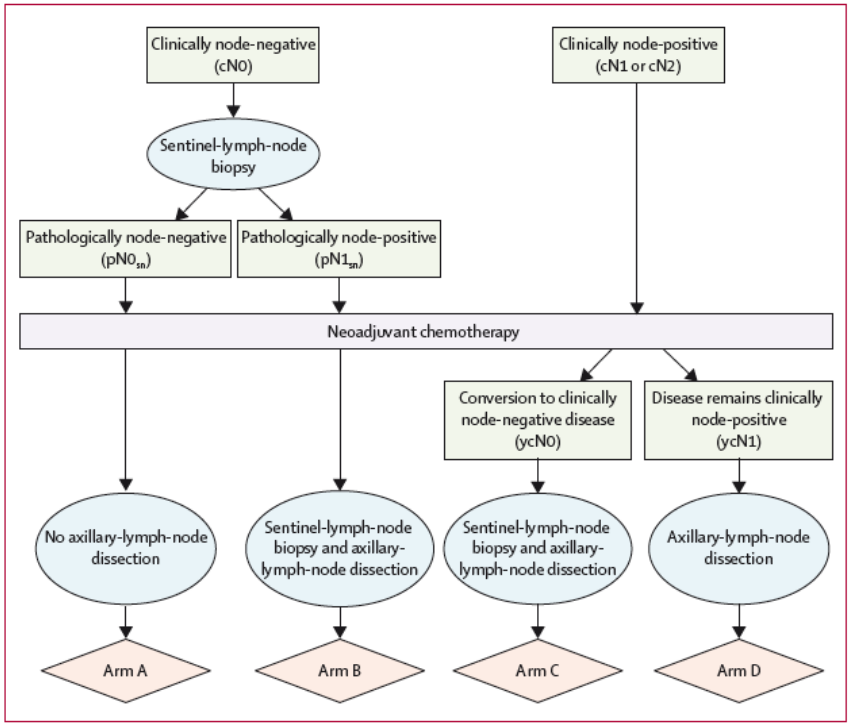
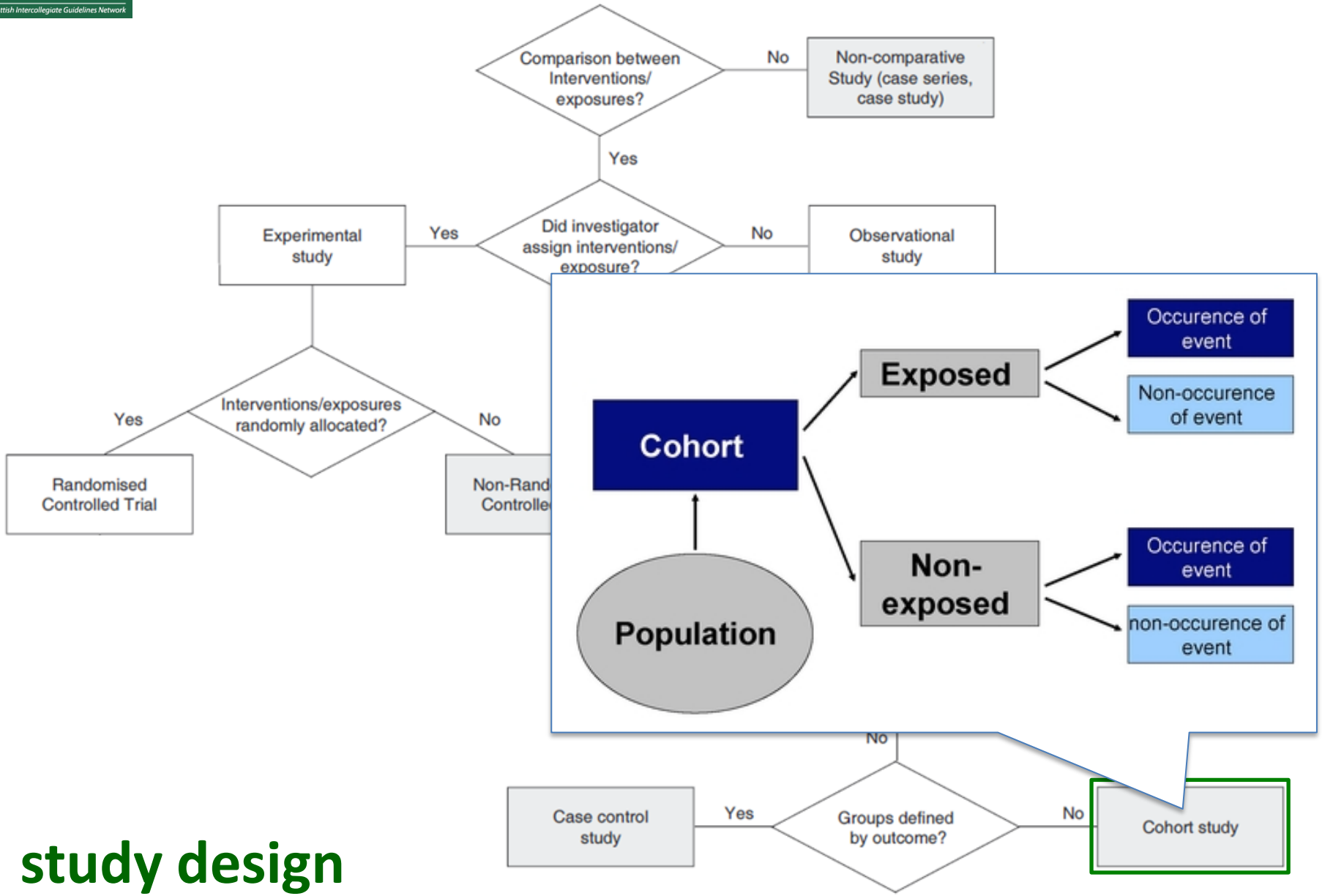
Lancet Oncol **2013; 14: 609–18**



The SENTINA study is a four-arm, prospective, multicentre cohort study undertaken at 103 centres in Germany and Austria.

study design



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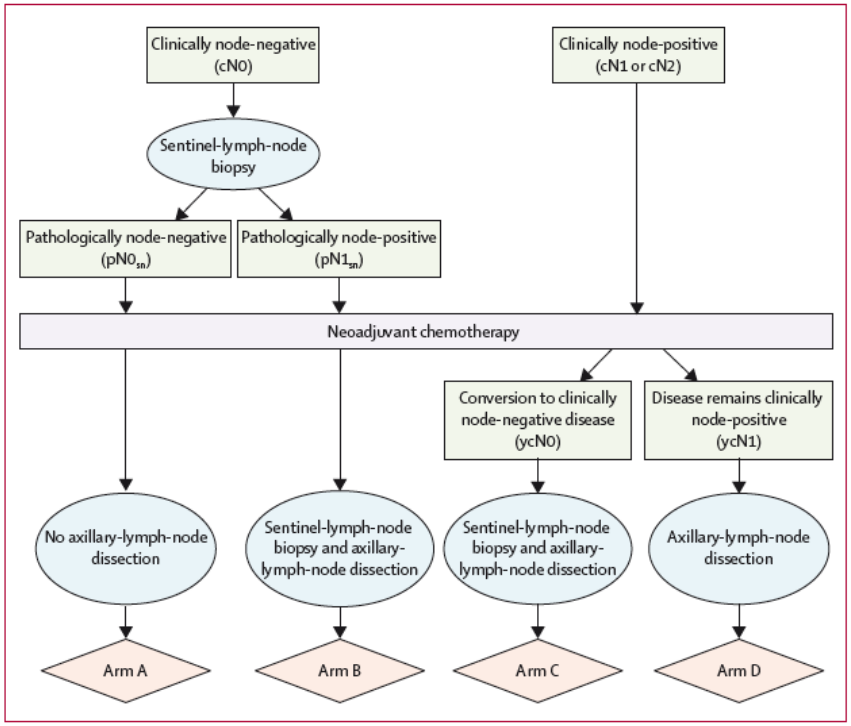

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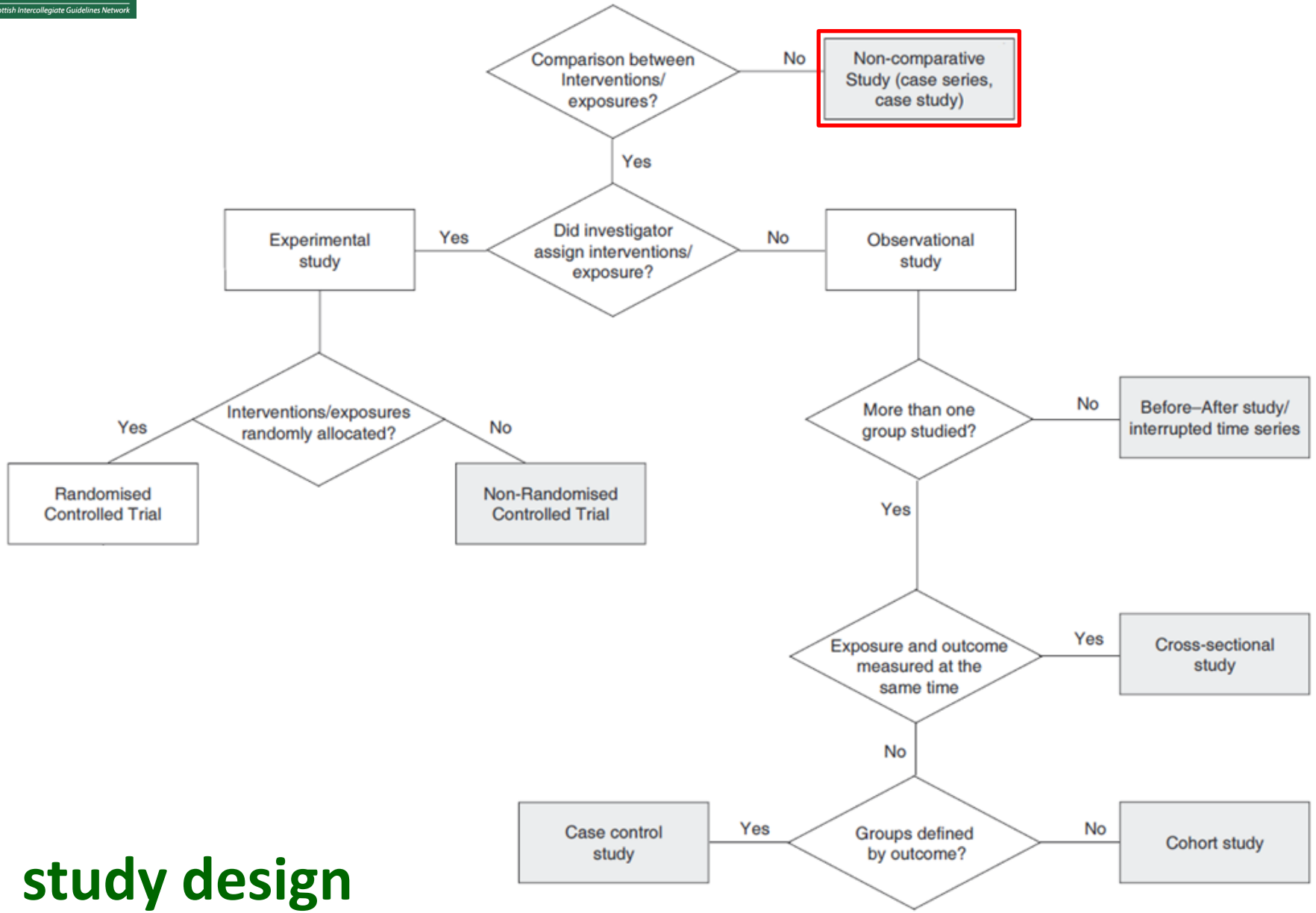

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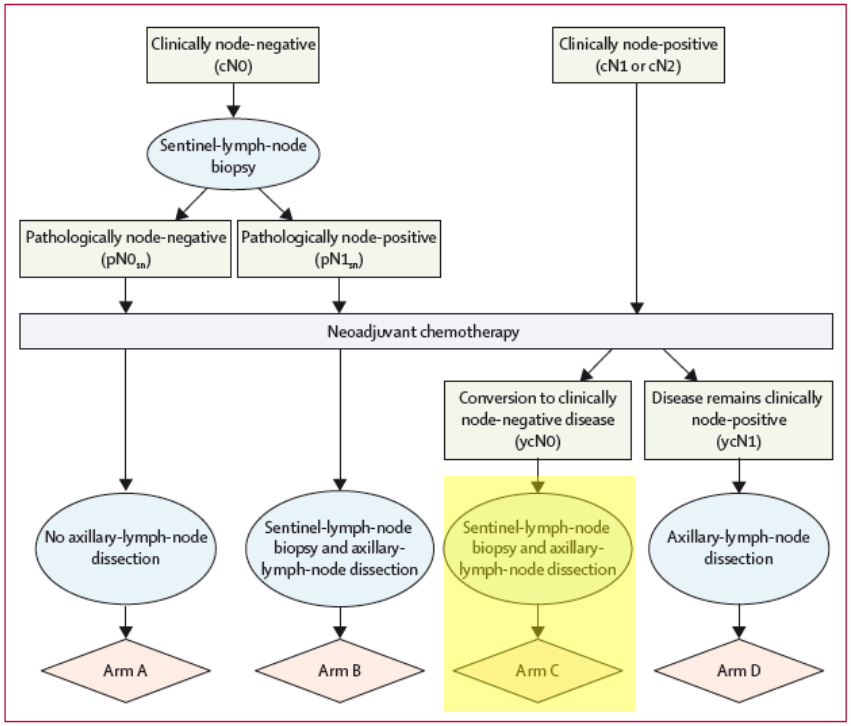

The primary outcome of our study was accuracy of sentinel-lymph-node biopsy (measured as the false-negative rate) in patients in arm C.

Sentinel-lymph-node biopsy in patients with breast cancer before and after neoadjuvant chemotherapy (SENTINA): a prospective, multicentre cohort study

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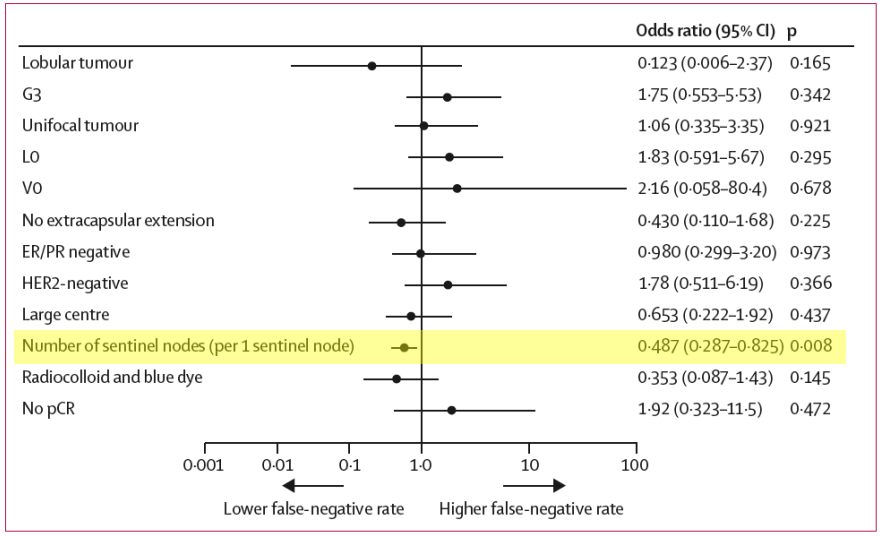
Statistical analysis

Using data from the German multicentre validation trial for sentinel-lymph-node biopsy in primary surgery,[25] we assumed a false-negative rate of 7% in arms B and C and calculated the sample size to exclude 10% in each of these arms, with a one-sided 95% CI. In every arm, we needed at least 196 patients with positive nodal status (calculated with nQuery Advisor, version 6.02). Based on findings of a pilot study, we expected that 13% of the entire study population would have a positive axillary status after neoadjuvant chemotherapy in arm B and 14% in arm C, resulting in a total number of 1508 patients for the study. Analyses were per protocol. We used Pearson χ^2 tests to compare rates across groups, with exact Pearson 95% CIs for the false-negative rate and detection rate. Also, we used Wilcoxon and Kruskul-Wallis testing to compare the number of detected sentinel lymph nodes between two groups and three groups, respectively. We did multivariate logistic regression in arm C to find factors that affected the detection rate and false-negative rate. We did analyses with SAS 9.2, under SAS Enterprise Guide 4.3.

	Arm B (n=64)	Arm C (n=226)
Overall false-negative rate (n/N; 95% CI)	51·6% (33/64; 38·7–64·2)	14·2% (32/226; 9·9–19·4)
False-negative rate, according to number of sentinel nodes removed		
1	66·7% (16/24)	24·3% (17/70)
2	53·8% (7/13)	18·5% (10/54)
3	50·0% (5/10)	7·3% (3/41)
4	50·0% (3/6)	0·0% (0/28)
5	18·2% (2/11)	6·1% (2/33)
False-negative rate, according to detection technique		
Radiocolloid alone	46·2% (18/39)	16·0% (23/144)
Radiocolloid and blue dye	60·9% (14/25)	8·6% (6/70)

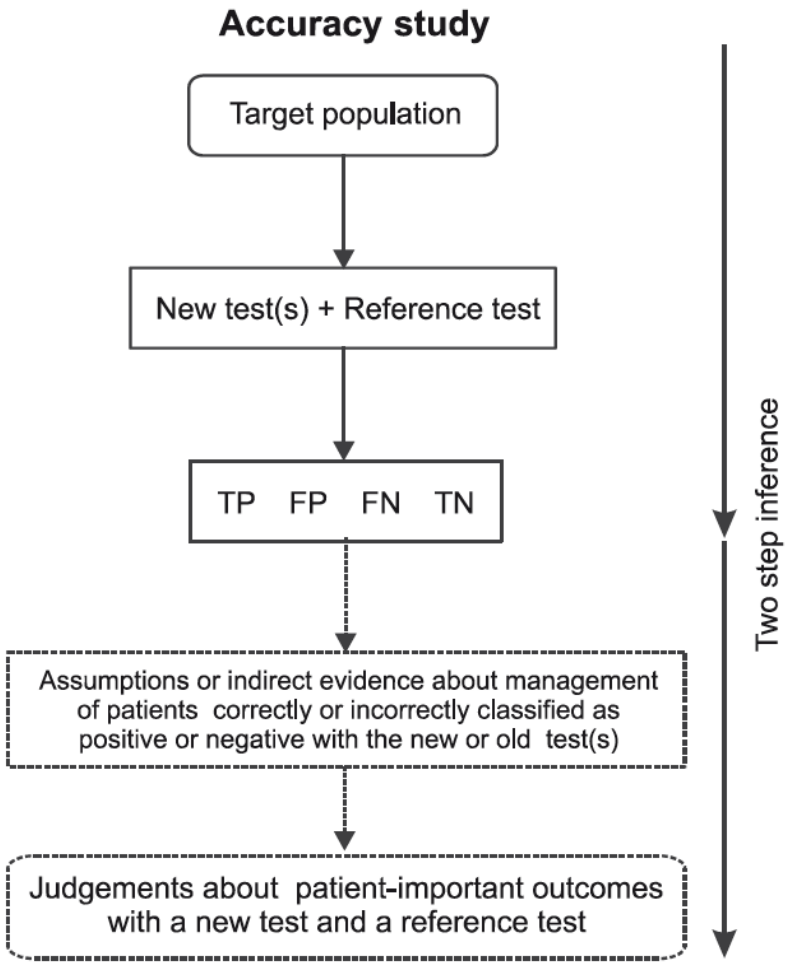
Data are rate (number of patients), unless otherwise stated.



Grading quality of evidence and strength of recommendations in clinical practice guidelines: Part 2 of 3. The GRADE approach to grading quality of evidence about diagnostic tests and strategies

J. L. Brożek[1,2], E. A. Akl[3], R. Jaeschke[4], D. M. Lang[5], P. Bossuyt[6], P. Glasziou[7], M. Helfand[8], E. Ueffing[9], P. Alonso-Coello[10,11], J. Meerpohl[12,13], B. Phillips[14], A. R. Horvath[15], J. Bousquet[16], G. H. Guyatt[4,17], H. J. Schünemann[3,17] for the GRADE Working Group

Allergy 2009: 64: 1109–1116



Usually, when clinicians face the decision to use or not to use a test, they consider its accuracy. They reason that the more sensitive and specific the test, the more likely they are to use it. But...

- What if performing the test will not induce any change in the manage-ment?
- Would the results of the test then make any difference even if it was very accurate?
- If recommendations to use diagnostic tests are based on test accuracy alone, are clinicians providing best care or a disservice to their patients when they follow these recommendations?

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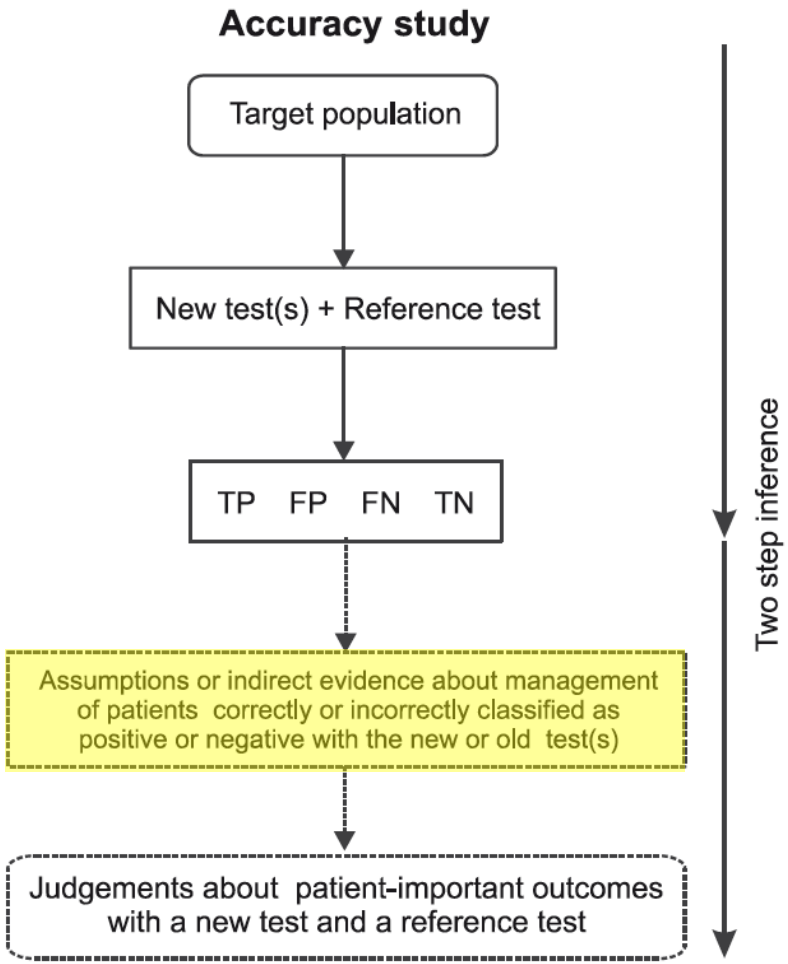

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Lancet Oncol 2013; 14: 609–18

A specific difficulty is the clinical rating of a particular false-negative rate after neoadjuvant chemotherapy.

Whether inaccurate sentinel-lymph-node biopsy translates into an increased recurrence rate is unclear.

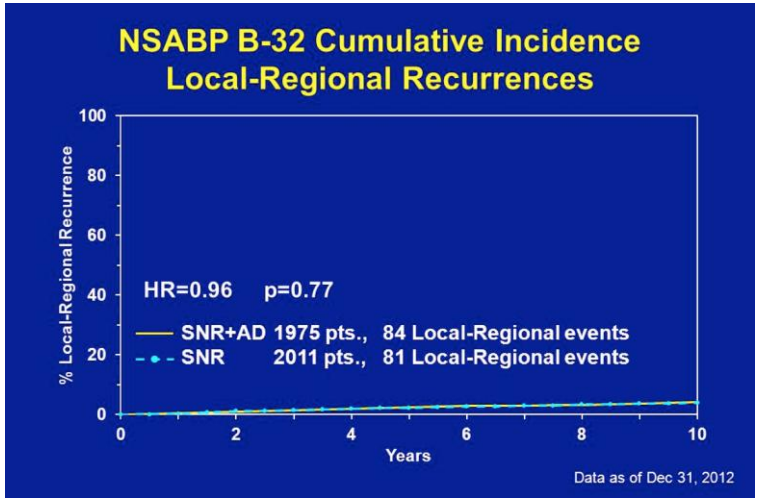
The NSABP-B32 trial included patients with only one resected sentinel node, who had a false-negative rate of 17·7%. The unfavourable accuracy in this subgroup did not translate into a clinically relevant regional recurrence rate.

Technical outcomes of sentinel-lymph-node resection and conventional axillary-lymph-node dissection in patients with clinically node-negative breast cancer: results from the NSABP B-32 randomised phase III trial

David N Krag, Stewart J Anderson, Thomas B Julian, Ann M Brown, Seth P Harlow, Takamaru Ashikaga, Donald L Weaver, Barbara J Miller, Lynne M Jalovec, Thomas G Frazier, R Dirk Noyes, André Robidoux, Hugh M C Scarth, Denise M Mammolito, David R McCready, Eleftherios P Mamounas, Joseph P Costantino, Norman Wolmark, for the National Surgical Adjuvant Breast and Bowel Project (NSABP)

Lancet Oncol 2007; 8: 881–88

The clinical significance of leaving ALND disease unresected will be tested by comparing the survival of patients in groups 1 and 2.



On the other hand, whether false-negative rates before and after neoadjuvant chemotherapy can be directly compared and whether the clinical outcome is similar is also unclear.

Assessing the value of diagnostic tests: a framework for designing and evaluating trials

The value of a diagnostic test is not simply measured by its accuracy, but depends on how it affects patient health. This article presents a framework for the design and interpretation of studies that evaluate the health consequences of new diagnostic tests

Lavinia Ferrante di Ruffano *research fellow*[1], Christopher J Hyde *professor of public health and clinical epidemiology*[2], Kirsten J McCaffery *associate professor and principal research fellow*[3], Patrick M M Bossuyt *professor of clinical epidemiology*[4], Jonathan J Deeks *professor of biostatistics*[1]

BMJ 2012;344:e686 doi: 10.1136/bmj.e686 (Published 21 February 2012)

Test accuracy, diagnostic yield, therapeutic yield, and treatment efficacy

More accurate tests will improve patient outcomes if the reductions in false positive or false negative results lead to more people receiving appropriate diagnoses (diagnostic yield) and appropriate treatment (therapeutic yield). The degree to which appropriate treatment can improve patient outcomes depends on its efficacy (treatment efficacy).

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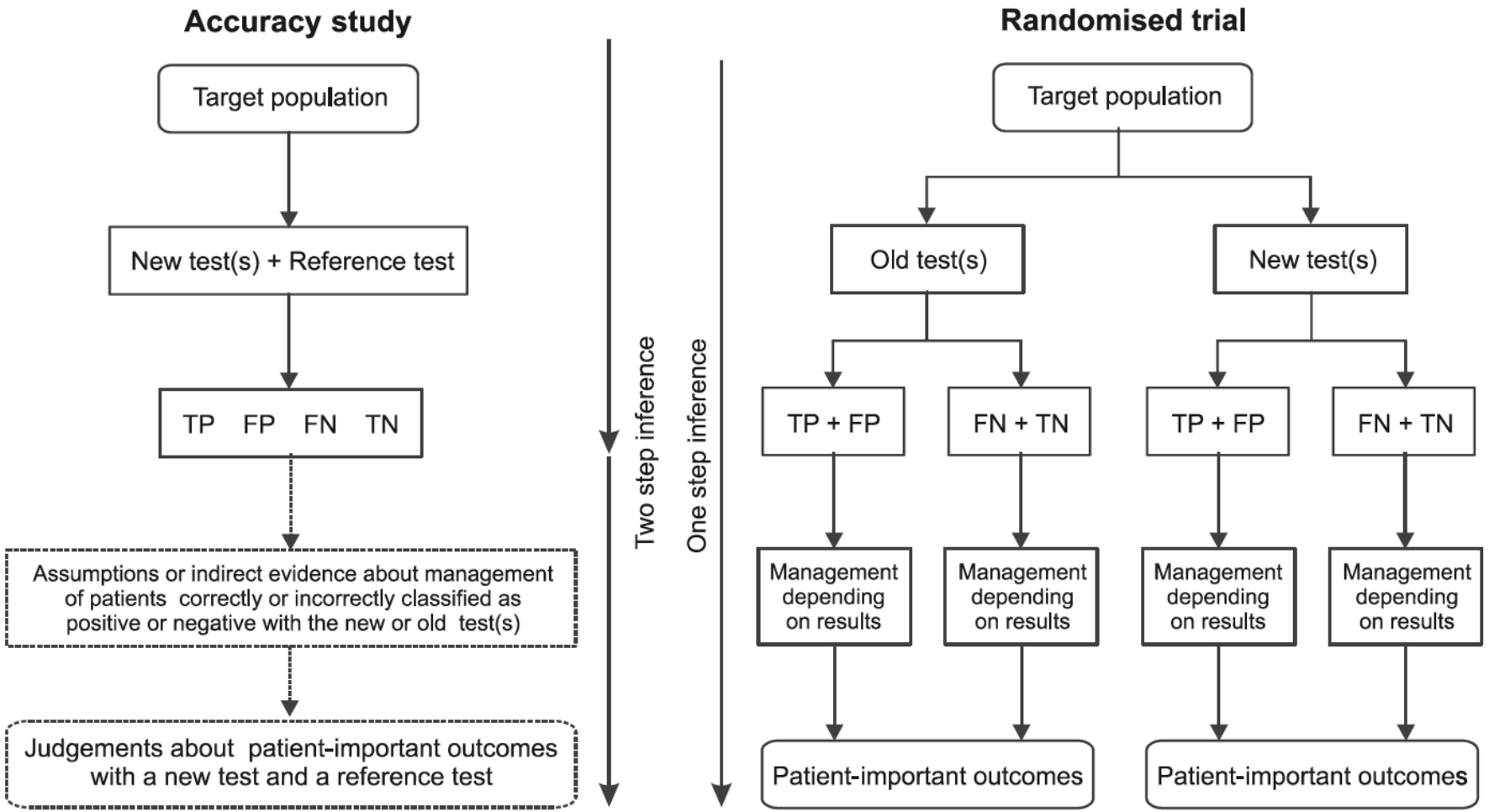

Hexaminolevulinate Guided Fluorescence Cystoscopy Reduces Recurrence in Patients With Nonmuscle Invasive Bladder Cancer

Arnulf Stenzl,* Maximilian Burger,*,† Yves Fradet, Lance A. Mynderse,‡ Mark S. Soloway,† J. Alfred Witjes,§ Martin Kriegmair, Alexander Karl,§ Yu Shen and H. Barton Grossman‖,¶

THE JOURNAL OF UROLOGY® Vol. 184, 1907-1914, November 2010

Table 2.

Ta-T1 additional detection rate: 16.4%

	with sta… tumor type)	With at Least 1 Lesion of Each Type Detected Only With Fluorescence (%)
Pts with Ta or T1 tumors	286 (78.4)	47 (16.4) (95% CI 12.3–21.2)
Pts with Ta tumors	262 (71.8)	41 (15.6)
Pts with T1 tumors	63 (17.3)	8 (12.7)
Pts with CIS	41 (11.2)	19 (46.3)

Note that patients may have more than 1…

Cis additional detection rate: 46.3%

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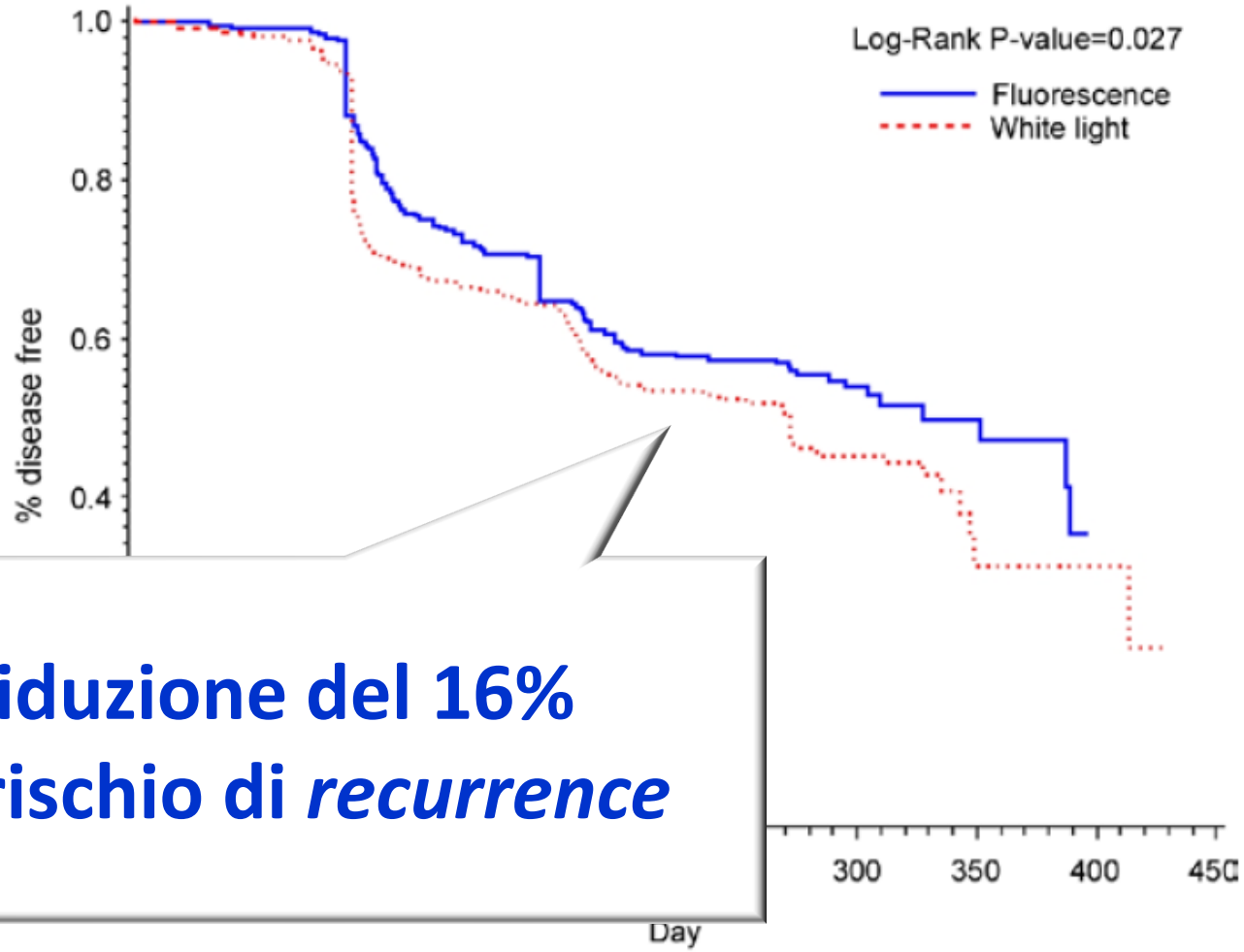

Riduzione del 16%
del rischio di *recurrence*

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Allergy 2009: 64: 1109–1116

Clinicians should always bear in mind that, whatever the test accuracy, application of any diagnostic test is of value only if it results in improved outcomes that are important for patients.

II SESSIONE:

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