

How to reduce the number needed to treat in prostate cancer screening

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Overview

- Why discuss the NNT in PC screening?
- NNT or NND ?
- What determines the NND
- The role of Active Surveillance



Why discuss the NNT?

- Publication of ERSPC in 2009 in NEJM

The number NNT in prostate cancer screening is of crucial importance since it is assumed that all men that are being diagnosed with prostate cancer will be treated actively with all known (considerable) side effects.

- PSA based screening reduced the rate of death from PC by 20% !!



1410 and breast cancer screening

- Relative risk of breast cancer death in the range of: 0.68-1.02 (mean 0.83; 10 trials)
- A meta-analysis of randomized controlled trials found that the **number needed to invite to screen** for 10 years to avoid or delay one death from breast cancer was **1,904** for women in their 40s, **1,339** for women in their 50s, and **377** for women in their 60s.

<http://www.cancer.gov/cancertopics/pdq/screening/breast/healthprofessional/page5>
Nelson HD, Tyne K, Naik A, et al. Screening for breast cancer: an update for the U.S. Preventive Services Task Force. Ann Intern Med 151 (10): 727-37, W237-42, 2009

48 and breast cancer screening

- For every one patient who avoids death from breast cancer approximately **10 to 20** women are **treated in excess of clinical situation**, typically receiving surgery, radiation, and chemotherapy.
- Some work needs to be done!!

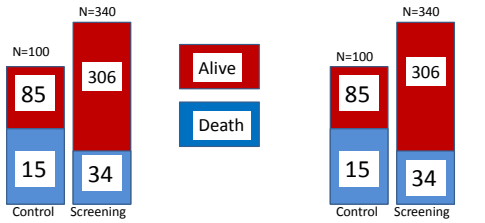
Esserman L, et al. Rethinking breast and prostate cancer screening. JAMA. 2009. 302(15): 1685-1692
Kalager M, et al. Effect of Screening Mammography on Breast-Cancer Mortality in Norway. N Engl J Med. 2010. 363:1203-1210

NNT or NND

(number needed to diagnose/manage)

- The NNT is the average number of patients who need to be treated to prevent one additional bad outcome.
- In the case of a prostate cancer screening trial with prostate cancer specific mortality as the main endpoint the NNT represents the number of patients that need to be treated for one man not dying of prostate cancer **compared with the clinical (control) situation**.
- The NND is defined as the inverse of the **absolute risk reduction** (risk difference) **times the excess incidence** that occurs through screening.

Absolute or Relative risk reduction

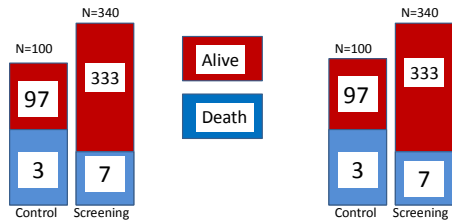


Absolute risk reduction:
15% - 10% = 5%

Relative risk reduction:
(15% - 10%) / 15% = 33%

$NND = 1/0.05 * 3.4 = 68$

Low rate of events affects NND!

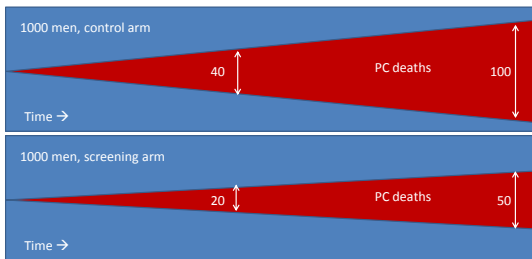


Absolute risk reduction:
3% - 2% = 1%

Relative risk reduction:
(3% - 2%) / 3% = 33%

$NND = 1/0.01 * 3.4 = 340$

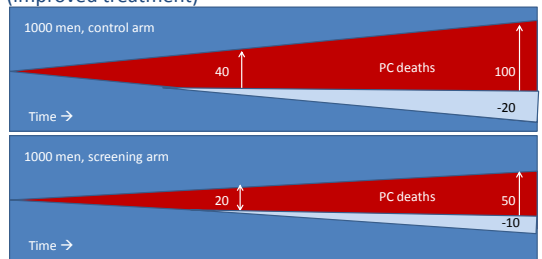
Time dependent



$RR = 4-2/4 = 50\%$
 $AR = 4-2 = 20\%$
 $NND = 1/0.2 * 3.4 = 17$

$RR = 10-5/10 = 50\%$
 $AR = 10-5 = 50\%$
 $NND = 1/0.5 * 3.4 = 7$

Affected by co-interventions (improved treatment)



$RR = 8-4/10 = 50\%$
 $AR = 8-4 = 40\%$
 $NND = 1/0.4 * 3.4 = 9$

To lower the NND:

A higher absolute risk reduction

A lower excess incidence

- An **effective** screening algorithm that **selectively** identifies men at **high risk** of having a potentially **life threatening** prostate cancer.



Active Surveillance reduces NND?

- The number NND in prostate cancer screening is of crucial importance since it is assumed that all men that are being diagnosed with prostate cancer will be treated actively with all known (considerable) side effects.
- However not all men confronted with a diagnosis of prostate cancer need (immediate) active treatment.
- AS will **NOT** decrease NND but it can decrease the harm of this currently existing drawback of PSA based prostate cancer screening.



Active Surveillance: the challenge

- The option of active surveillance can delay and even circumvent active treatment.
- **Current PRIAS data:**
- Treatment free survival: 73% (2 –year)
- Percentage Gleason score upgrading at one year repeat biopsy: 21.5%
- Percentage Gleason score upgrading from last biopsy to RP: 31%
- **An acceptable and safe AS protocol**