# Efficacy of 23-valent pneumococcal vaccine in preventing pneumonia and improving survival in nursing home residents: double blind, randomised and placebo controlled trial

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## STUDY QUESTION

Does the 23-valent pneumococcal polysaccharide vaccine prevent pneumonia and improve survival in nursing home residents?

## SUMMARY ANSWER

The 23-valent pneumococcal vaccine prevented pneumococcal pneumonia and reduced the mortality from this disease in nursing home residents.

## WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Previous studies have been inconclusive about the effect of this vaccine in nursing home residents and its uptake is low. In this study the vaccine prevented pneumococcal pneumonia and reduced the mortality from this disease in nursing home residents in Japan.

### Design

This was a double blind, randomised and placebo controlled trial.

### Participants and setting

Overall, 1006 nursing home residents were randomised; 502 were allocated to the 23-valent pneumococcal polysaccharide vaccine and 504 to placebo (sodium chloride).

### Primary outcome(s)

The primary end points were the incidence of all cause pneumonia and pneumococcal pneumonia. The follow-up time in the vaccine group was 1140 person years (mean 2.27 person years) and in the placebo group 1149 (2.28).

### Main results and the role of chance

During the follow-up period, one episode of pneumonia was diagnosed in 167 of the 1006 (16.6%) participants. All cause pneumonia developed in 63 (12.5%) participants in the vaccine group and 104 (20.6%) in the placebo group. Pneumococcal pneumonia was diagnosed in 14 (2.8%) in the vaccine group and 37 (7.3%) in the placebo group. The incidence per 1000 person years of all cause pneumonia (P=0.0006) and pneumococcal pneumonia (P=0.001) was significantly higher in the placebo group than the vaccine group. The reductions in the incidence of all cause pneumonia and pneumococcal pneumonia in the vaccine group were 63.8% and 44.8%, respectively. Survival curves showed a significantly increased cumulative proportion of participants without pneumococcal pneumonia (hazard ratio 0.368, 95% confidence interval 0.199 to 0.680, P=0.0009) and without all cause pneumonia (0.587, 0.429 to 0.802, P=0.0007) in the vaccine group compared with the placebo group. Death from pneumococcal pneumonia was significantly higher in the placebo group than the vaccine group (P<0.01). No deaths occurred among the 14 participants with pneumococcal pneumonia in the vaccine group, but 13 occurred among the 37 participants with pneumococcal pneumonia in the placebo group. Deaths from all causes (pneumonia, cerebrovascular disease, ischaemic cardiomyopathy, renal failure, senility, and others) occurred in 89 participants in the vaccine group and 80 in the placebo group. Death from all causes did not differ between the groups.

### Harms

No harms occurred during the study.

### Bias, confounding, and other reasons for caution

The sputum and urine specimens used to diagnose pneumococcal pneumonia were obtained from non-sterile sites. We also did not measure the antibody responses to vaccination so could not correlate this with clinical outcomes.

### Generalisability to other populations

Because of the increase in the elderly population, a progressive increase in the incidence of pneumonia can also be predicted in elderly people living in the community; future investigations should focus on the efficacy of the 23-valent pneumococcal vaccine in this population.

### Study funding/potential competing interests

This study was supported by a grant in aid from the Ministry of Education, Culture, Sports, Science and Technology of Japan. We have no competing interests.

### Trial registration

Japan Medical Association Center for Clinical Trials JMA-IIA00024.

**INCIDENCE OF PNEUMONIA IN NURSING HOME RESIDENTS**

| End point | Incidence (per 1000 person years) Vaccine group (n=502) | Placebo group (n=504) | % reduction in incidence (95% CI) | P value |
|---|---|---|---|---|
| Pneumococcal pneumonia | 12 | 32 | 63.8 (32.1 to 80.7) | 0.0015 |
| Non-pneumococcal pneumonia | 43 | 59 | 29.4 (−4.3 to 52.3) | 0.0805 |
| All cause pneumonia | 55 | 91 | 44.8 (22.4 to 60.8) | 0.0006 |

# Sex, health, and years of sexually active life gained due to good health: evidence from two US population based cross sectional surveys of ageing

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EDITORIAL by Goodson

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## STUDY QUESTION

What is the relation between health and several dimensions of sexuality, and on average, how many years of sexually active life are gained as a result of good health in midlife and later life?

## SUMMARY ANSWER

Sexual activity, a good quality sex life, and interest in sex were positively associated with self rated health in midlife and later life and were higher for men than for women, with the gender gap widening with age. Sexually active life expectancy (average remaining years of sexually active life) is higher for men, but men lose more years of sexually active life than women because of poor health.

## WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Partnership and sexual activity have been positively associated with health in midlife and later life. Regular sexual activity, a good quality sex life, and interest in sex are positively associated with health in midlife and later life, with the gender gap in sexual interest increasing with age.

### Participants and setting

Our study comprised two samples representative of the US population: the national survey of midlife development in the United States (MIDUS, 1995-6) and the national social life, health and aging project (NSHAP, 2005-6), with 3032 adults aged 25 to 74 years (1561 women, 1471 men) from the MIDUS cohort and 3005 adults ages 57 to 85 years (1550 women, 1455 men) from the NSHAP cohort.

### Design

This study used a cross sectional design.

### Primary outcome(s)

The main outcome measures were sexual activity, quality of sex life, interest in sex, and average remaining years of sexually active life, referred to as sexually active life expectancy.

### Main results and the role of chance

The survey response rates were 60.8% for MIDUS and 74.8% for NSHAP. Overall, men were more likely than women to be sexually active, to report a good quality sex life, and to be interested in sex, with gender differences increasing with age. Men and women reporting very good or excellent health were more likely to be sexually active compared with their peers in poor or fair health. Among sexually active people, good health was also strongly associated with regular sex (once or more a week) in men, with a good quality sex life among men and women in the MIDUS cohort, and with interest in sex. At age 55, men in very good or excellent health gained on average five to seven years of sexually active life, whereas women gained three to six years compared with their peers in poor or fair health.

**GENDER DIFFERENCES IN SEXUALLY ACTIVE LIFE EXPECTANCY AT AGE 55 IN MIDUS AND NSHAP**

| | Average remaining years of sexually active life (95% CI) | |
|---|---|---|
| Variables | Men | Women |
| MIDUS: | | |
| All | 14.9 (14.4 to 15.4) | 10.6 (10.0 to 11.2) |
| Self rated health: | | |
| Poor or fair | 11.5 (10.3 to 12.7) | 10.1 (8.9 to 11.3) |
| Very good or excellent | 16.9 (16.1 to 17.7) | 12.9 (11.9 to 13.9) |
| NSHAP*: | | |
| All | 15.3 (14.8 to 15.8) | 10.6 (10.0 to 11.2) |
| Self rated health: | | |
| Poor or fair | 11.2 (10.1 to 12.3) | 7.1 (6.0 to 8.2) |
| Very good or excellent | 18.0 (17.0 to 19.0) | 12.7 (11.5 to 13.9) |

MIDUS=national survey of midlife development in the United States; NSHAP=national social life, health and ageing project.
*Prevalence for age group 55-59 years was estimated using data for 57-59 age group.

### Bias, confounding, and other reasons for caution

This study relied on cross sectional data. Longitudinal data are needed to determine whether regular sexual activity, a good sex life, or high interest in sex promote health or whether good health promotes these positive sexual attributes. Measures of sexuality were comparable, but not identical, in NSHAP and MIDUS.

### Generalisability to other populations

The study findings are generalisable to the US population of middle aged and older people and were consistent with European studies where data were available. Generalisability to populations in developing or culturally distinct regions might be limited.

### Study funding/potential competing interests

This study was supported by US federal funding distributed directly and through grants to STL from the University of Chicago and Rutgers University. We have no competing interests. The funders had no role in the study design and the authors maintained full independence in generating this work.

# Impact of interval from breast conserving surgery to radiotherapy on local recurrence in older women with breast cancer: retrospective cohort analysis

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**response on bmj.com**

**"The ultimate reduction in delay can be achieved by delivering radiotherapy immediately after surgical excision using the Targit (targeted intraoperative radiotherapy) technique. This novel effect of radiotherapy has only recently been demonstrated: radiotherapy delivered to the tumour bed immediately after surgical excision using the Targit technique abrogates the tumour stimulating effect of surgical wound fluid"**
Jayant S Vaidya, senior lecturer and consultant surgeon, Research Department of Surgery, University College London, in a rapid response

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## STUDY QUESTION

Does the length of time between breast conserving surgery and the start of radiotherapy affect the risk of local recurrence in older women with breast cancer?

## SUMMARY ANSWER

An interval from surgery to radiotherapy of more than six weeks was associated with an increase in local recurrence. Each additional day to start of radiotherapy was associated with a slight increase in the risk of recurrence.

## WHAT IS KNOWN AND WHAT THIS PAPER ADDS

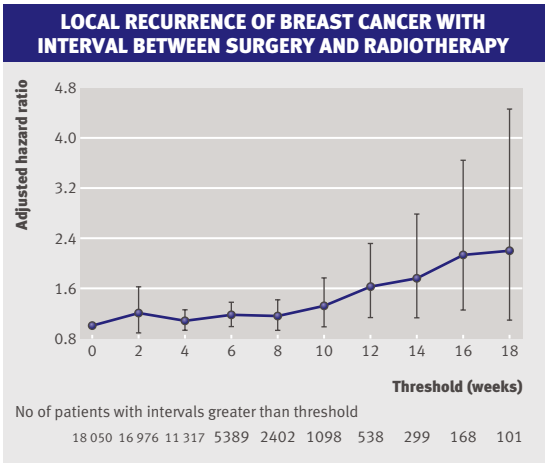
Previous studies regarding the effect of interval to radiotherapy in patients with breast cancer have had mixed results. Using a population based database we found an increase in the risk of local recurrence with longer interval to radiotherapy. Our results suggest that the relation between interval to radiation and local recurrence is continuous.

### Participants and setting

Retrospective cohort analysis of 18 050 women aged >65 with stage 0-II breast cancer who received breast conserving surgery and radiotherapy but not chemotherapy.

### Design, size, and duration

Patients and data for diagnoses during 1991-2002 were obtained from the Surveillance, Epidemiology, and End Results-Medicare linked database in the United States. We used Cox proportional hazards models to study the association between time to radiotherapy and local recurrence. Propensity score and instrumental variable analyses were used to confirm findings. Logistic regression was used to investigate factors associated with later start of radiotherapy.




### Main results and the role of chance

The median time from surgery to initiation of radiotherapy was 34 days, with 29.9% of women beginning treatment after six weeks. Just over 4% of the cohort experienced a local recurrence. After adjustment for clinical and sociodemographic factors, an interval over six weeks was associated with increased local recurrence (hazard ratio 1.19, 95% confidence interval 1.01 to 1.39, P=0.033). The longer the threshold interval studied, the greater the impact on risk of recurrence. When interval was modelled continuously, the effect was stronger (1.005 per day, 1.002 to 1.008, P=0.004). Propensity score and instrumental variable analysis confirmed these findings. Intervals over six weeks were associated with a 0.96% increase in recurrence at five years (P=0.026). Starting radiotherapy after six weeks was significantly associated with positive nodes, comorbidity, history of low income, Hispanic ethnicity, non-white race, later year of diagnosis, and residence outside the southern states of the US.

### Bias, confounding, and other reasons for caution

We used three different statistical methods to increase the certainty that our primary finding—association between recurrence and time to radiotherapy—is causal rather than the result of unmeasured and unaccounted for confounders. The consistency across the results from these methods provides strong support for the validity of our conclusions. We cannot, however, completely exclude the possibility that there might be additional factors associated with both time to initiation of radiotherapy and local recurrence, which our dataset did not enable us to study and that might confound our results.

### Generalisability to other populations

We did not measure the effect of interval to radiotherapy in younger women or patients who received chemotherapy. Our findings are probably generalisable to younger women because previous studies that have included them have yielded consistent results. In fact because younger age might be an independent risk factor for local recurrence after breast conserving surgery, the association between interval to radiotherapy and local recurrence could be even more pronounced in younger patients.

### Study funding/potential competing interests

Supported in part by a grant from the National Institutes of Health (1K07 CA118629) and from the American Society of Clinical Oncology.

# Educational inequalities in mortality over four decades in Norway: prospective study of middle aged men and women followed for cause specific mortality, 1960-2000

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**STUDY QUESTION** T
o what extent did educational inequalities in relation to mortality widen in Norway during 1960-2000 and what causes of death were the main drivers of this disparity?

**SUMMARY ANSWER**
Mortality fell in all educational groups in Norway during 1960-2000, but inequalities in mortality by education noticeably widened, particularly for men.

**WHAT IS KNOWN AND WHAT THIS PAPER ADDS**
Inequalities in mortality by educational level are widening in Western populations and the reasons for this are not clear. We found that the main drivers for widening inequalities in Norway were smoking related causes of death such as lung cancer and chronic lower respiratory tract diseases, as well as cardiovascular diseases for men.

### Participants and setting
The whole Norwegian population aged 45-64 years in 1960, 1970, 1980, and 1990 followed up over 10 years.

### Design, size, and duration
Prospective cohort study of educational inequalities in cause specific mortality: cancer of lung, trachea, or bronchus; other cancer, cardiovascular diseases; suicide; external causes; chronic lower respiratory tract diseases; or other causes. Absolute and relative indices of inequality were used to present differences in mortality by educational level (basic, secondary, and tertiary). The study included 359 547 deaths and 32 904 589 person years.

### Main results and the role of chance
Mortality fell from the 1960s to the 1990s in all educational groups. At the same time the proportion of adults in the basic educated group, with the highest mortality, decreased substantially. Absolute inequalities in mortality denoting deaths among the basic education groups minus deaths among the high education groups doubled in men and increased by a third in women. Inequalities on a relative scale widened more, from 1.33 to 2.24 (P=0.01) among men and from 1.52 to 2.19 (P=0.05) among women. Among men, absolute inequalities mainly increased as a result of cardiovascular diseases, lung cancer, and chronic lower respiratory tract diseases. Among women this was mainly due to lung cancer and chronic lower respiratory tract diseases. Unlike the situation in men, absolute inequalities in deaths due to cardiovascular causes narrowed among women. Chronic lower respiratory tract diseases contributed more to the disparities in inequalities among women than among men.

### Bias, confounding, and other reasons for caution
Different coding practices at different time points could have biased our results, but as the groups were broad this should not be a major problem. The accuracy of the education variable might have changed, as errors in measuring education may have been decreased over time, and this could be a partial reason for increasing inequalities. Furthermore, the meaning of education has probably changed over time, especially for women.

### Generalisability to other populations
Our study included data from Norway only, but the mechanisms behind our findings are likely to be generalisable to other Western countries, especially those with an egalitarian social policy.

### Study funding/potential competing interests
This study was funded by the Norwegian Institute of Public Health and the University of Oslo and approved by the Norwegian Data Inspectorate. We have no competing interests.

**EDUCATIONAL INEQUALITIES IN MORTALITY IN NORWEGIAN POPULATION AGED 45-64, BY DECADE**

| | Men | | Women | |
|---|---|---|---|---|
| Decade | Absolute inequality* (95% CI) | Relative inequality† (95% CI) | Absolute inequality* (95% CI) | Relative inequality† (95% CI) |
| 1960-70 | 460 (396 to 524) | 1.33 (1.28 to 1.38) | 356 (307 to 405) | 1.52 (1.43 to 1.60) |
| 1970-80 | 625 (577 to 674) | 1.48 (1.43 to 1.52) | 377 (342 to 412) | 1.66 (1.58 to 1.74) |
| 1980-90 | 878 (830 to 925) | 1.80 (1.74 to 1.86) | 371 (339 to 403) | 1.73 (1.65 to 1.81) |
| 1990-2000 | 943 (901 to 985) | 2.24 (2.16 to 2.32) | 471 (442 to 501) | 2.19 (2.08 to 2.30) |
| P value for trend | 0.012 | 0.014 | 0.102 | 0.048 |

*Slope index of inequality.
†Relative index of inequality.

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