



# **CASE-SPOUSE CONTROL STUDY DESIGN IN PRACTICE**

**—— An experience in estimating the relationship  
between smoking and cancer deaths in Chinese**

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# BACKGROUND

- China is the world's largest tobacco producer and consumer, with 20% of the world's population, accounting for 30% of the world's cigarette consumption.
- It is impossible to undertake classical epidemiological studies to assess the patterns of all mortality related to tobacco in a large developing country. We need to explore innovative and robust epidemiological method to assess the hazard of smoking on health.

# BACKGROUND

- Case-spouse control study design was raised by Chinese epidemiologists Boqi Liu et al. in 1991. The design was incorporated into a nationwide retrospective mortality survey in China from 1989 to 1991.



# STUDY DESIGN

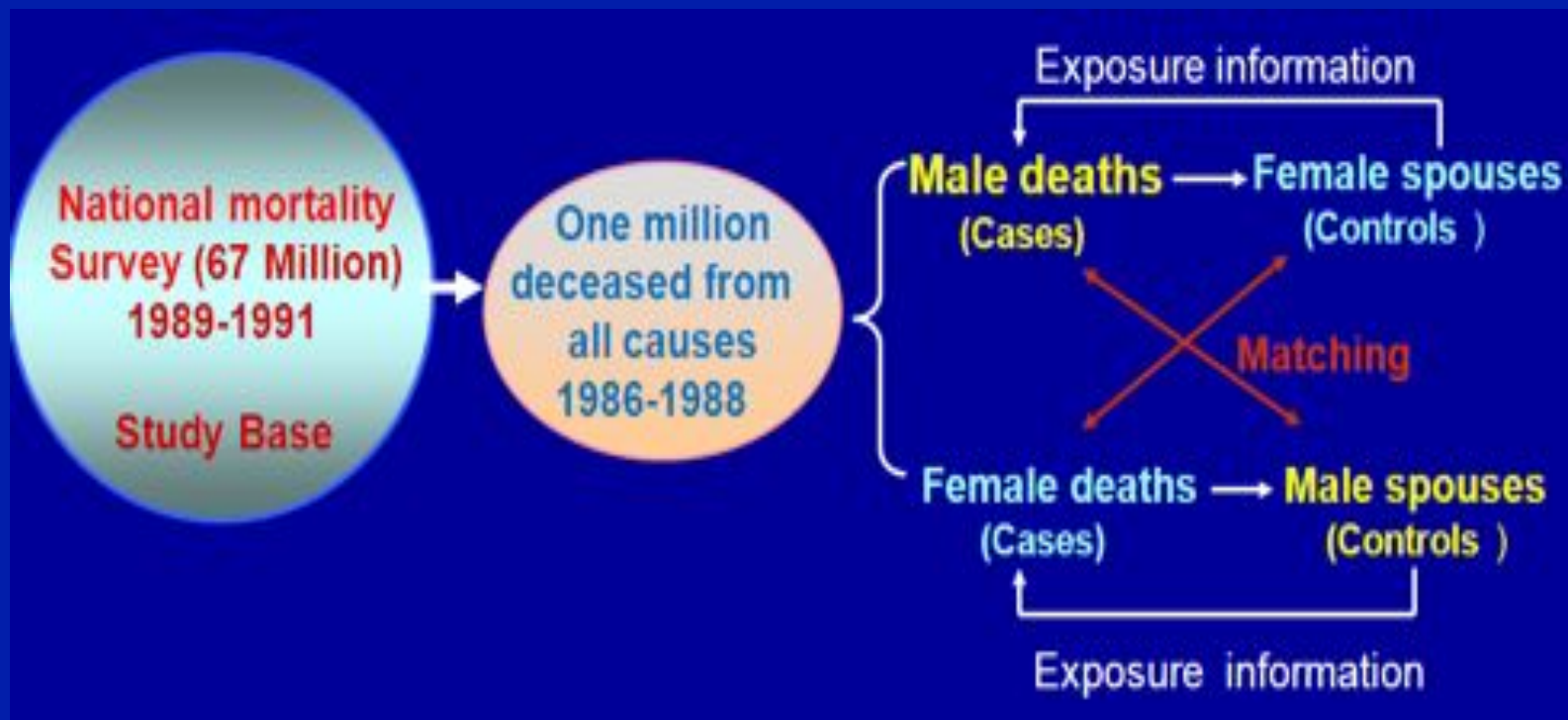
- In 1989-1991, a nationwide retrospective mortality survey was conducted in China, which involved 103 study areas and approximately 1,000,000 adult deaths from all causes during the years 1986-1988.



- **24 major cities** which were chosen to represent a wide geographical spread
- **79 rural counties** were selected through stratified random sampling among the 2,000 counties
- **Base population** including 67 million populations

# STUDY DESIGN

- Within the study base, all deceased aged 35 or over were identified. For those who died of causes related to smoking were taken as cases, whereas surviving spouses of those who died from any conditions during the same year were taken as controls. Exposure information for both cases and controls was provided by living spouses.



# STUDY DESIGN



- **The theoretical thinking of selecting controls**
  - The distribution of all causes of deaths in the base population is approximately at random, so is the spouse population.
- **Assumptions in selection of controls**
  - Individuals in the control group had smoking habits that were similar to those of the study base.
  - There is no significant relationship in tobacco use between couples.

# WHAT WE HAVE DONE

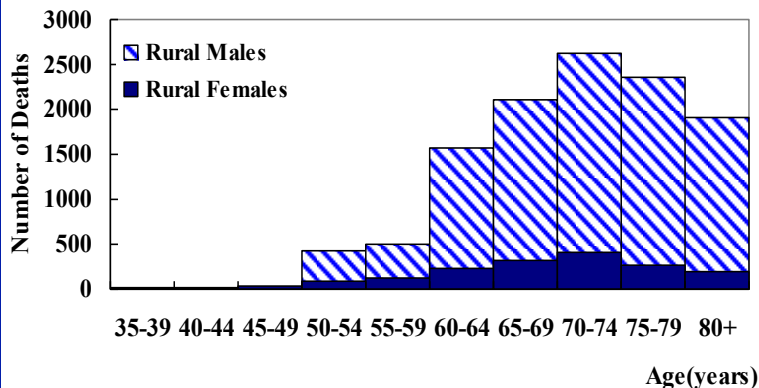
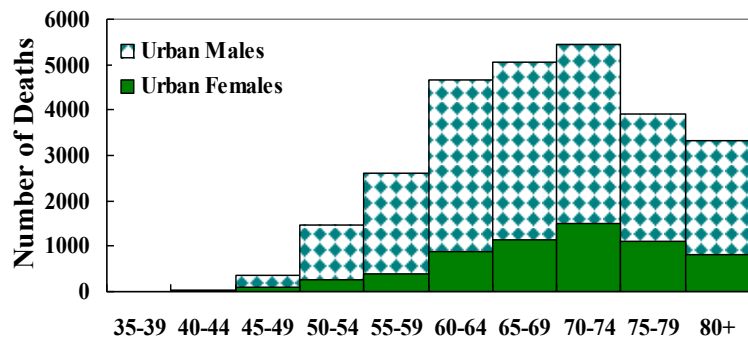
- **Application with the new design**

- To assess the hazard of smoking for...
  - { All causes of deaths
  - { Some conditions { TB
  - { Cancer deaths { COPD

- **Methodological study about the new design**

- Comparative study with the normal design
- Sample size and efficiency evaluation, etc

# Smoking causes early death



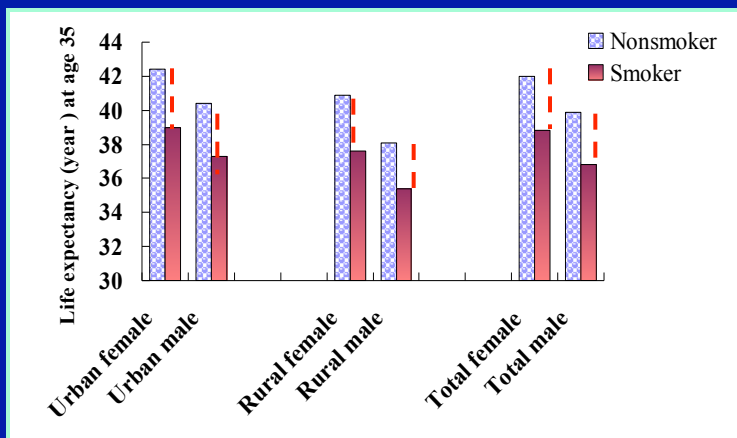
- More than two-thirds of smoking-attributable deaths occurred between the ages of 50 and 74 years
- This fact emphasizes the importance of preventing the initiation of smoking at a young age



# MAIN RESULTS — general

**Smoking reduces life expectancy same regardless of the poor and the rich**

- Although life expectancy was higher in urban than in rural areas, and was higher in women than in men, the years of life lost which were attributable to smoking were almost the same irrespective of the region or sex.



**Smokers at age 35 lost about 3 years of life expectancy in comparison with never smokers**

# MAIN RESULTS — general conclusion

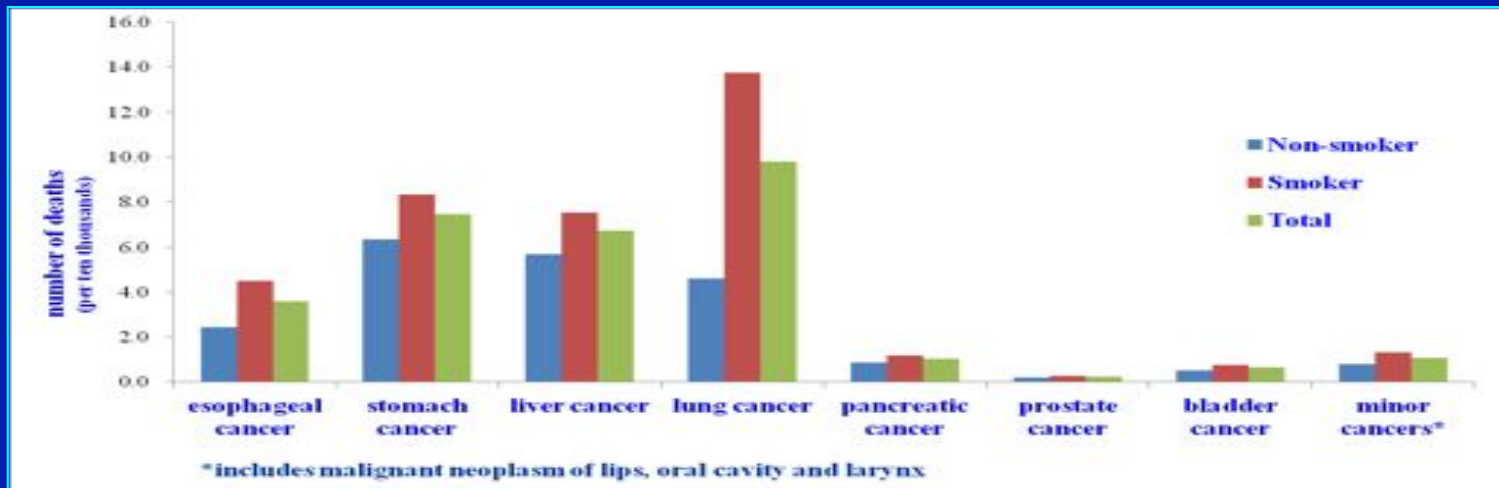
**Smoking plays an important role in difference between male and female's life expectancy**

- **More than 50% of the sex difference in life expectancy was accounted for smoking. Women who smoke had a higher risk in terms of reduced life expectancy, although the prevalence of smoking among women was much lower than men**

Categories	Life expectancy (years) at ages				
	35	45	55	65	75
Difference in life expectancy	3.8	3.6	3.3	2.8	1.8
Smoking-attributable	1.8	1.8	1.7	1.4	1.0
Not attributable to smoking	2.0	1.8	1.6	1.4	0.8
% smoking-attributable	47	50	52	50	56

# MAIN RESULTS – smoking on cancer

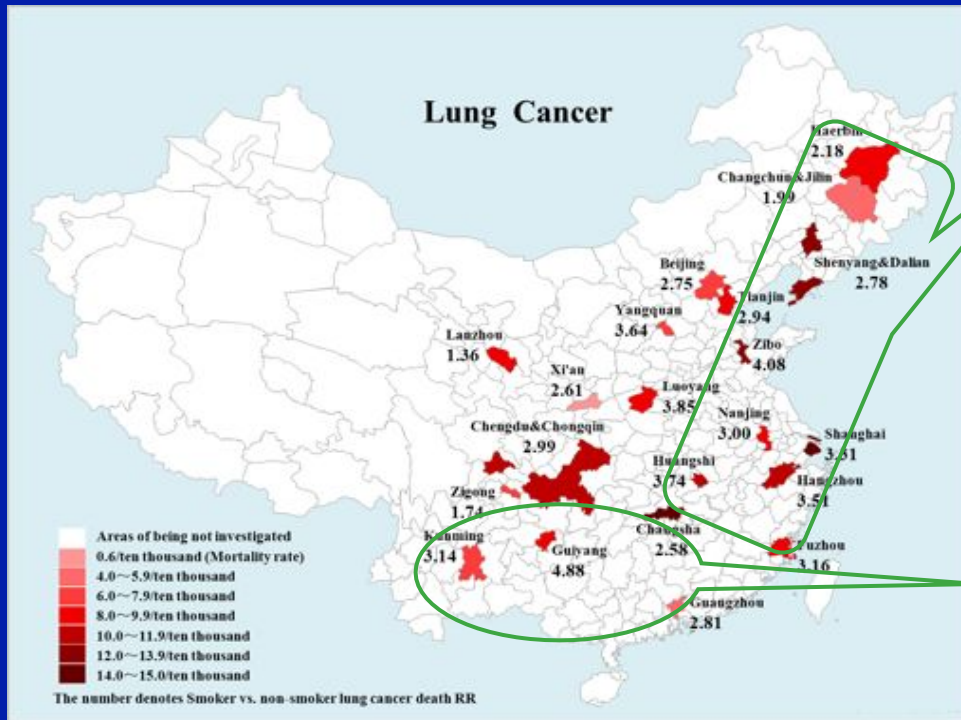
Smoking causes common cancer deaths more



- Of all smoking-related cancer death, lung, stomach, esophagus, and liver cancer had the highest death rates.
- 82% of lung cancer deaths were smokers. this suggests that lung cancer is about three times as common among smokers as non-smokers.

# MAIN RESULTS – smoking on cancer

The area distributions of cancer mortality are not identical with that of smoking hazard



The east costal areas have higher lung cancer mortality rates

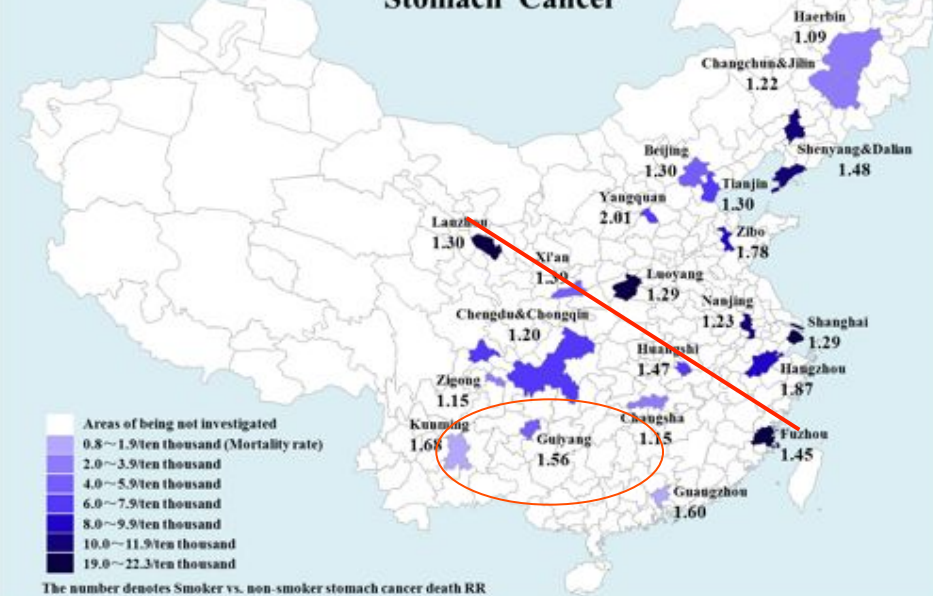
The tobacco-planting areas have higher smoking hazard

Fig. the distribution of areas-specific lung cancer mortality and smoking hazard; The darker the color is, the higher the mortality is.

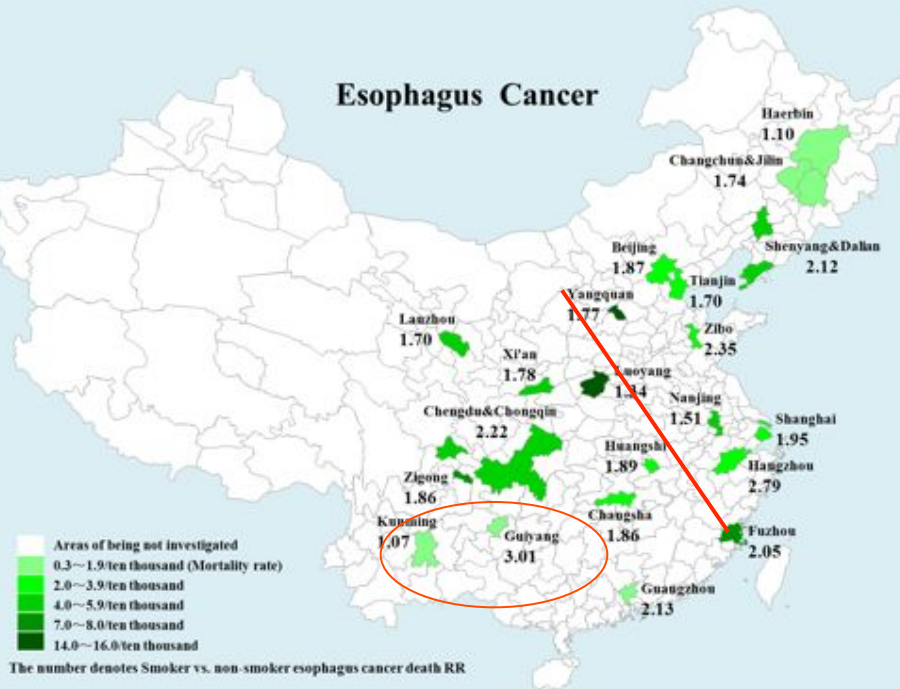
## Liver Cancer



## Stomach Cancer



## Esophagus Cancer



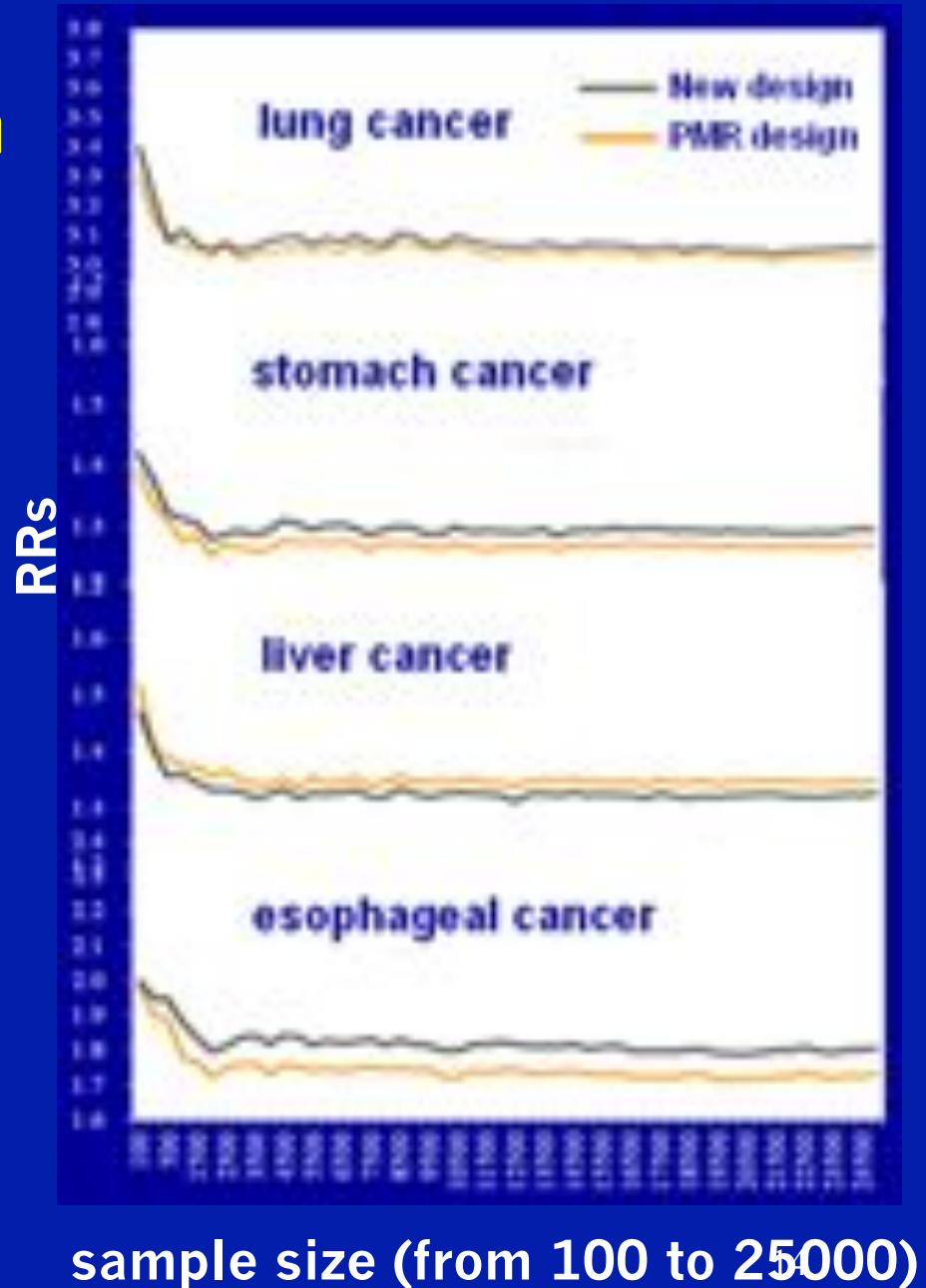
- The area-specific distribution of digestive cancer has its own characteristic. The mortality is higher in middle areas (from west to east) compared to others.
- The same as lung cancer, the RRs of smoking are higher in tobacco-planting areas compared to others.



# Methodological study

## —Stability of new design

- Comparison between new design and PMR design was conducted to assess the validity and stability by re-sampling method under various sample size(100-25000).
- Although both designs slightly overestimate the RRs when sample size is small (100-300), they show high consistence and stability regardless of sample size. The new design is more sensitive than PMR design .
- The results indicate the new design is also suitable for small-scale study.



# STRENGTH OF NEW DESIGN

- **This study design makes it possible**
  - To select a representative sample as controls within a huge population and study one exposure to the risk of any causes of death. Prospective studies take years to mature, however, the retrospective methods such as this study require much less time;
  - To produce one more control groups in one survey and enhance the evidence of etiology in epidemiological research;
  - To balance most confounding factors (known or unknown) naturally between such huge comparison groups.

# APPLICATION & DEVELOPMENT

- **The application of this design in other countries and areas**
  - Jha P, et al. A nationally representative case-control study of smoking and death in India. *N Engl J Med*. 2008.
  - Lam TH, et al. Mortality and smoking in Hong Kong. *BMJ*. 2001.
  - Gajalakshmi V, et al. Smoking and mortality from tuberculosis and other diseases in India. *Lancet*. 2003.
  - Sitas F, et al. Tobacco attributable deaths in South Africa. *Tob Control*. 2004.
- **As important reference for latter researches in China**
  - Gu D, et al. Mortality attributable to smoking in China. *N Engl J Med*. 2009.
  - Yang G, et al. Smoking in China. *JAMA*. 1999 .
  - Niu SR, et al. Emerging tobacco hazards in China. *BMJ*. 1998 .



# WHAT WILL WE DO ?

- This design will be put forward from population-based to hospital-based study



# Contributors in this Project

- We thank Cancer Research UK, the UK Medical Research Council, the US National Institutes of Health, the Chinese Ministry of Health, and the Chinese Academy of Medical Sciences who supported the original survey;
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Thanks!  
Greetings from China!

