# **RESEARCH COMMUNICATION**

# **Representativeness of Population-Based Cancer Registration** in China - Comparison of Urban and Rural Areas

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# Abstract

<u>Objective</u>: Chinese cancer registration data provide information on the national cancer burden but how representative they are of the real situation is uncertain. Mortality data from cancer registration and the third national death survey were therefore compared to determine the accuracy of estimates in China. <u>Methods</u>: The data were from the Cancer Registration Annual Report, 2004, China and the third National Death Survey, 2004-205. Negative binomial regression was used to estimate site-specific cancer mortality rate ratios between the two. <u>Results</u>: The estimated cancer mortality for all sites from national cancer registration was representative for China, especially in urban areas, but mortality was over-estimated for rural areas, with large differences in some cancer site-specific mortalities. <u>Conclusion</u>: Although cancer registration data are representative at the country level and for urban areas, they may not reflect real cancer burden in rural areas, particularly with some cancer types. Setting up new cancer registries in non-high risk areas in rural areas should be enhanced in further cancer surveillance plans.

Key Words: Cancer registry - Mortality - Negative binomial regression - Poisson regression - China

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# Introduction

Cancer is the second leading cause of death in China (Ministry of Health, 2008). Cancer incidence and mortality for most cancers are showing upward trends so that the disease is becoming one of the serious public health issues with socioeconomic development and aging of the population. In 2000, the total number of cancer deaths was 1,500,000 (Dong et al., 2002).

Since 1950, cancer prevention and control have attracted increasing concern and support from the central government and great progress has been made, for example with cancer registration. In the early 1960s, there were only two population-based cancer registries, one in an urban area and one in an rural area. Limited cancer registration data were published from 1988 to 2002 (Li et al., 2000; 2002; Zhang et al., 2006). However, in 2002, a Central Cancer Registry office was established by the Health Ministry to enhance systematic management of cancer surveillance. Since then, quantity and quality of cancer registration have markedly improved and the number of cancer registries has now reached 43, covering 5.53% of the national population (National Office for Cancer Prevention and Control, 2008). The problem is that cancer case reporting is voluntary and there are still one third of provinces are without any cancer registry. The representativeness of the available data might therefore be questioned.

In 2006, Health Ministry carried out the third National Death Survey focusing on cancer death, in order to assess the current health situation in China. In this survey, 160 Death Surveillance points were selected to determine the death status at the national level. We here retrieved the death database from cancer registration for comparison with the countrywide findings of this survey.

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We here retrieved the death database from cancer registration comparing with the death data from the survey to study the presentation of cancer registry.

# **Materials and Methods**

#### National cancer mortality

The Chinese Third Death Survey was carried out in 2006 and covered all deaths occurring in 2004 and 2005 in 142,660,482 person-years equal to 5.49% of the national population. Disease Surveillance Point which was used by CDC (Chinese Disease Control and Prevention) was applied for the survey. A stratified random sample of 160 counties/ districts was selected so as to be representative of national level mortality. The representation in cancer site specific mortality was approved by comparing with national cancer mortality using first national death survey

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#### Guang Lin Li and Wan Qing Chen

in 1973-1975 which covered whole national population. When a county was selected, all deaths in 2004 and 2005 were identified from death registries, hospitals and the Civil Administration Bureau. Population information was also obtained from official registration records. Cause of death was found out from the death certificate provided by hospitals. If a death certificate was unavailable, households were visited and information on cause of death collected by interviews with relatives. All cancer deaths were retrieved from database including cause, sex, age and urban /rural status. The year of age was divided as 5 categories, 0-49, 50-59, 60-69, 70-79 and 80 years and over. Cancer cause was coded using ICD-10.

#### Cancer registration data

The cancer registries identified new cancer cases and cancer deaths in the respective areas from all hospitals, community health centers, death registries and the Civil Administration Bureau, which holds cremation records. Population information was obtained from official registration records. National Cancer Annual Report 2004 has been published by National Central Cancer Registry in 2008. We pooled 34 individual cancer mortality data as registration death database covered 4.09% of the country's population.

#### Statistical analysis

According to the ICD-10 coding system, 17 major cancer mortalities were compared between cancer registration and the third death survey including sites of lung and bronchus, liver, stomach, esophagus, colon, rectum, pancreas, breast, brain and other nervous system, gallbladder, non-Hodgkin's lymphoma, bladder, nasopharynx, leukemia, ovary, prostate, cervix and all cancer sites. Cancer site, sex, urban/rural, year specific mortality data were retrieved from two databases for comparison. Correspondent population data were also obtained for analysis.

Negative binomial regression and Poisson regression models were used to estimate mortality rate ratios between the cancer death data groups. The appropriate model was selected through comparison of goodness of fit. Mortality rate ratios were tested adjusted by sex, urban/rural and age against hypothesis of no difference of mortality between two data in all areas, urban areas and rural areas. Analyses were performed using the Genmod model with SAS (Statistical Analysis System) version 9.1 (SAS Institute Inc., Cary, NC, USA).

### Results

In the third death survey, there 193,841 cancer death in sampling areas in 2004 and 2005 with adjusted mortality of 91.24/100,000 with the 1982 national population structure. Cancer registration in 2004 recorded 88,334 cancer deaths in 34 cancer registries with adjusted mortality of 85.80/100,000.

Goodness of fit method for negative regression and Poisson regression depends on the residual. The value of Pearson chi-square divided by degree of freedom was used to test which model will be fit well. Table 1 displays that the values in negative binomial regression were closer to 1 than that in Poisson regression so that mortality data was more consistent with negative binomial regression.

Table 1. Test for Goodness of Fit between Negative Binomial and Poisson Regression Models

| Parameter          |         | Negative re        | gression model     | Pois     | Poisson regression model |                    |  |  |
|--------------------|---------|--------------------|--------------------|----------|--------------------------|--------------------|--|--|
|                    | $All^1$ | Urban <sup>2</sup> | Rural <sup>3</sup> | $All^1$  | Urban <sup>2</sup>       | Rural <sup>3</sup> |  |  |
| Pearson chi-square | 20.3178 | 20.0559            | 19.565             | 616.7428 | 2736.502                 | 516.218            |  |  |
| Degrees of freedom | 13      | 14                 | 13                 | 13       | 14                       | 13                 |  |  |
| Value/DF           | 1.5629  | 1.4326             | 1.5204             | 47.4418  | 195.4644                 | 39.7097            |  |  |

<sup>1</sup>All areas: Adjusted for age, sex and urban/rural.<sup>2,3</sup>Urban and rurals: Adjusted for age and sex

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| Cancer type/site     | Number          | of Deaths    | Both     | n sexes    | Ma          | ale      | Fer        | nale     |
|----------------------|-----------------|--------------|----------|------------|-------------|----------|------------|----------|
|                      | Cancer Registry | Death Survey | Rate rat | io p value | Rate ration | p value  | Rate ratio | p value  |
| Lung and bronchus    | 21,848          | 43,989       | 1.04     | 0.2083     | 1.03        | 0.2453   | 1.05       | 0.2189   |
| Liver                | 13,330          | 37,459       | 0.78     | 0.0029     | 0.81        | < 0.0001 | 0.74       | < 0.0001 |
| Stomach              | 12,956          | 35,248       | 0.81     | < 0.0001   | 0.80        | < 0.0001 | 0.81       | 0.0019   |
| Esophagus            | 8,510           | 21,692       | 0.87     | 0.0098     | 0.85        | 0.0011   | 0.85       | < 0.0001 |
| Rectum               | 3,320           | 6,548        | 1.07     | 0.0165     | 1.00        | 0.9849   | 1.18       | < 0.0001 |
| Colon                | 3,158           | 3,788        | 1.74     | < 0.0001   | 1.65        | < 0.0001 | 1.89       | < 0.0001 |
| Pancreas             | 3,164           | 3,735        | 1.79     | < 0.0001   | 1.77        | < 0.0001 | 1.80       | < 0.0001 |
| Breast               | 2,473           | 4,131        |          |            |             |          | 1.42       | < 0.0001 |
| Brain/nervous system | 1,866           | 4,462        | 0.97     | 0.2263     | 0.90        | 0.0067   | 1.05       | 0.221    |
| Gallbladder          | 1,529           | 1,801        | 1.74     | < 0.0001   | 1.75        | < 0.0001 | 1.75       | < 0.0001 |
| NHL                  | 1,434           | 1,766        | 1.81     | < 0.0001   | 1.76        | < 0.0001 | 1.88       | < 0.0001 |
| Bladder              | 1,244           | 2,016        | 1.24     | < 0.0001   | 1.19        | 0.0013   | 1.35       | < 0.0001 |
| Nasopharynx          | 1,190           | 2,079        | 1.29     | < 0.0001   | 1.32        | < 0.0001 | 1.25       | < 0.0001 |
| Leukemia             | 1,080           | 4,223        | 0.66     | < 0.0001   | 0.70        | < 0.0001 | 0.59       | < 0.0001 |
| Ovary                | 782             | 1,007        |          |            |             |          | 1.91       | 0.0389   |
| Prostate             | 733             | 1,382        |          |            | 1.04        | 0.3574   |            |          |
| Cervix               | 656             | 1,995        |          |            |             |          | 0.73       | < 0.0001 |
| All cancers          | 88,334          | 193,841      | 1.00     | 0.8339     | 0.98        | 0.3751   | 1.01       | 0.5398   |

| Cancer type/site     | Number of Deaths<br>Cancer Registry Death Survey |        | Both sexes<br>Rate ratio p value |          | Male<br>Rate ratio p value |          | Female<br>Rate ratio p value |          |
|----------------------|--|--------|----------------------------------|----------|----------------------------|----------|------------------------------|----------|
|                      |  |        |                                  |          |                            |          |                              |          |
| Lung and bronchus    | 17,765   | 19,627 | 0.95                             | 0.4829   | 0.95                       | 0.5475   | 0.96                         | 0.6596   |
| Liver                | 8,566  | 11,942 | 0.79                             | 0.0088   | 0.81                       | < 0.0001 | 0.77                         | < 0.0001 |
| Stomach              | 7,406  | 11,004 | 0.75                             | 0.0007   | 0.74                       | 0.0007   | 0.74                         | 0.0084   |
| Esophagus            | 3,549  | 5,257  | 0.75                             | 0.0005   | 0.78                       | 0.0044   | 0.69                         | 0.0022   |
| Rectum               | 2,738  | 2,778  | 1.05                             | 0.5319   | 0.97                       | 0.7846   | 1.14                         | 0.244    |
| Colon                | 2,768  | 1,907  | 1.53                             | < 0.0001 | 1.44                       | 0.0022   | 1.64                         | < 0.0001 |
| Pancreas             | 2,601  | 2,126  | 1.30                             | < 0.0001 | 1.35                       | 0.0003   | 1.26                         | 0.0072   |
| Breast               | 2,057  | 1,905  |                                  |          |                            |          | 1.24                         | 0.0013   |
| Brain/nervous system | 1,422  | 1,808  | 0.89                             | 0.0023   | 0.82                       | < 0.0001 | 0.98                         | 0.6721   |
| Gallbladder          | 1,316  | 1,022  | 1.30                             | 0.0221   | 1.33                       | 0.0945   | 1.28                         | 0.0737   |
| NHL                  | 1,155  | 841    | 1.52                             | < 0.0001 | 1.49                       | < 0.0001 | 1.56                         | 0.0003   |
| Bladder              | 1,017  | 953    | 1.09                             | 0.5889   | 1.03                       | 0.8961   | 1.16                         | 0.5288   |
| Nasopharynx          | 798  | 764    | 1.17                             | 0.0317   | 1.17                       | 0.1037   | 1.13                         | 0.1031   |
| Leukemia             | 757  | 1,371  | 0.65                             | < 0.0001 | 0.69                       | < 0.0001 | 0.60                         | < 0.0001 |
| Ovary                | 687  | 630    |                                  |          |                            |          | 1.46                         | 0.2897   |
| Prostate             | 618  | 638    |                                  |          | 0.79                       | 0.4278   |                              |          |
| Cervix               | 422  | 669    |                                  |          |                            |          | 0.68                         | < 0.0001 |
| All cancers          | 62,990   | 71,936 | 0.95                             | 0.4088   | 0.93                       | 0.3668   | 0.97                         | 0.7256   |

Table 3. Urban Cancer Mortality Rate Ratios - Cancer Registration Compared with the National Death Survey

Table 4. Rural Cancer Mortality Rate Ratios - Cancer Registration Compared with the National Death Survey

| Cancer type/site     | Number of Deaths |              | Both sexes |            | Male        |           | Female     |          |
|----------------------|------------------|--------------|------------|------------|-------------|-----------|------------|----------|
|                      | Cancer Registry  | Death Survey | Rate rat   | io p value | Rate ration | o p value | Rate ratio | p value  |
| Lung and bronchus    | 4,083            | 24,362       | 0.90       | 0.0328     | 0.92        | 0.0285    | 0.88       | 0.0315   |
| Liver                | 4,764            | 25,517       | 0.98       | 0.8143     | 1.02        | 0.8826    | 0.93       | 0.3714   |
| Stomach              | 5,550            | 24,244       | 1.23       | 0.0003     | 1.24        | < 0.0001  | 1.23       | 0.0037   |
| Esophagus            | 4,961            | 16,435       | 1.68       | < 0.0001   | 1.57        | < 0.0001  | 1.79       | < 0.0001 |
| Rectum               | 582              | 3,770        | 0.84       | < 0.0001   | 0.82        | 0.0009    | 0.87       | 0.0471   |
| Colon                | 390              | 1,881        | 1.13       | 0.0274     | 1.08        | 0.3235    | 1.20       | 0.0271   |
| Pancreas             | 563              | 1,609        | 1.93       | < 0.0001   | 1.79        | < 0.0001  | 2.12       | < 0.0001 |
| Breast               | 416              | 2,226        |            |            |             |           | 1.07       | 0.2271   |
| Brain/nervous system | 444              | 2,654        | 0.99       | 0.8841     | 0.99        | 0.8847    | 1.00       | 0.9577   |
| Gallbladder          | 213              | 779          | 1.48       | < 0.0001   | 1.40        | 0.0041    | 1.53       | < 0.0001 |
| NHL                  | 279              | 925          | 1.74       | < 0.0001   | 1.82        | < 0.0001  | 1.60       | < 0.0001 |
| Bladder              | 227              | 1,063        | 1.13       | 0.0954     | 1.14        | 0.1234    | 1.11       | 0.5092   |
| Nasopharynx          | 392              | 1,315        | 1.75       | < 0.0001   | 1.78        | < 0.0001  | 1.69       | < 0.0001 |
| Leukemia             | 323              | 2,852        | 0.72       | < 0.0001   | 0.75        | 0.0002    | 0.67       | < 0.0001 |
| Ovary                | 95               | 377          |            |            |             |           | 0.69       | 0.7272   |
| Prostate             | 115              | 744          |            |            | 0.80        | 0.0238    |            |          |
| Cervix               | 234              | 1,326        |            |            |             |           | 0.99       | 0.9241   |
| All cancers          | 25,344           | 121,905      | 1.13       | 0.001      | 1.16        | 0.0067    | 1.11       | 0.0085   |

Adjusted cancer mortality rate ratios for cancer registries compared with the third death survey are shown in Table 2. For all cancers, there was no significant difference. Mortality of lung cancer was higher by 4% and of brain and other nervous system tumor 3% (p>0.05). Cancer registration data had a lower mortality in liver cancer and esophageal cancer, but higher in rectal cancer (0.05<p<0.0001).

The data for urban and rural areas treated separately are summarized in Table 2 and 3, respectively. The overall cancer mortality rate ratio compared between two death data was 0.95 standing for 5% lower of mortality in cancer registries than death surveyed areas with 0.93 for male and 0.97 for female. The difference was not statistically significant at the 0.05 level of significance (p=0.408, 0.367 and 0.726, respectively). For site specific mortality, lung cancer mortality was 5% lower in cancer registries than in death survey areas, 5% and 9% higher for rectal cancer and bladder cancer with no significant difference. At the 0.001 level of significance, mortalities of liver cancer, gallbladder cancer, nasopharyngeal cancer and tumor of brain and other nervous system were not statistical different between two data. For male in urban areas, mortalities of lung cancer, rectal cancer, bladder cancer, gallbladder cancer, nasopharyngeal cancer and prostate were no significant difference; for females, mortalities of lung cancer, rectal cancer, tumor of brain and other nervous system, gallbladder cancer, bladder cancer and nasopharyngeal cancer were similar in teh two death data sets (Table 3).

In rural areas, the overall cancer mortality rate ratio compared between two death data was 1.13 standing for 13% higher of mortality in cancer registries than death surveyed areas with 1.16 for male and 1.11 for female. The difference was statistical in 0.05 levels of significance by not in 0.001 levels. For site specific mortality, liver cancer and tumor of brain and other nervous system mortalities were 2% and 1% lower in cancer registries than in death survey areas, 13% higher for bladder cancer with no significant difference.

#### Guang Lin Li and Wan Qing Chen

For males in rural areas, mortalities of liver cancer, colon cancer, tumor of brain and other nervous system and bladder cancer demonstrated no significant differences; for females, mortalities of liver cancer, colorectal cancer, breast cancer, tumor of brain and other nervous system, bladder cancer, ovary cancer and cervical cancer were no significant differences in the two death data sets (Table 4).

### Discussion

Cancer registration could provide useful information about cancer burden and play an important role on making cancer control plan. Recently, cancer registration is still lagging behind compared with other countries and far from being able to meet the needs. So far, there were 43 cancer registries doing population based cancer registration, reporting cancer new cases and cancer death data to National Central Cancer Registries covered nearly 6% of whole country's population. For these cancer registries, most of them are located in eastern of China- more developed areas in term of economic status. There are still 11 provinces which have no any cancer registry. Cancer morbidity and mortality is from estimation based on limited resources. In order to provide valid cancer burden information, national cancer data is necessary. How representative is the recent cancer registration data of China is needed to be tested.

The cancer incidence and mortality in China were always estimated by limited resources (Yang et al., 2003; 2004; Ling et al., 2005), including cancer registration data, continuing mortality surveillance data from Center of Health Information and Statistics, disease surveillance points from Chinese Center of Disease Control and Prevention, also three times of death surveys statewide. The popular data quoted by researchers is the data in the Cancer Incidence in Five Continents included several cancer registries data in China that was thought less representative (Parkin et al., 2002). A similar study compared mortality data from SEER (Surveillance, Epidemiology, and End Results) tumor registries with cancer mortality data for US to access its representation to US using mortality ratio tested by Poisson regression (Ray and Kirk, 2004). Although there are no any nationalwide death surveillance like US mortality data, completely true cancer mortality is unavailable.

Fortunately, Ministry of Health carried out the third national death survey for evaluation disease burden in the early 21st century. The surveyed areas was selected as Disease Surveillance Points (DSP) by Chinese Center of Disease Control and Prevention according to 3 sampling steps: geographical location (east, middle and west), type (urban and rural) and economical status (GDP). 160 counties were identified and proven having representative of whole country's population. In order to test DSP's representativeness for mortality, especially for site-specific cancer mortality, comparison has been done using historical data from the first national death survey between DSP's cancer mortality and national data that has shown representative for site-specific cancer mortality. The result of the third national death survey published in 2008 gave a good resource for testing representativeness of cancer registration data.

For the third national death survey, all deaths in 2004 and 2005 in surveyed counties were identified from death registries, hospitals and the Civil Administration Bureau. Causes of death were confirmed by checking medical records in relevant hospitals if available. Otherwise, household visits and interviewed were done by trained medical workers. For cancer registries, all different resources were supplied by local hospitals, death registries and Civil Administration Bureau. Registrars compared those data with incidence database, rechecked from hospitals and interviewed for those who medical records were unavailable. The two cancer mortality data are relatively complete and valid.

For all cancer mortality, cancer registration data could represent national cancer burden, also for male and female after adjusted age. For urban areas, the mortality was similar between two data. But mortality could be overestimated in rural areas. That is reasonable to explain that most of rural cancer registries were cancer high risk areas which were identified from the first national death survey, especially high incidence and mortality for esophageal cancer and stomach cancer. Some cancer types were also representative, such as lung cancer, prostate cancer and tumor of brain and other nervous system in all cancer registries; lung cancer, rectal cancer, bladder cancer and nasopharyngeal cancer in urban areas; liver cancer, rectal cancer, tumor of brain and other nervous system and bladder cancer in rural areas.

According to that useful information, we have made a new plan on structuring national cancer registration network in 2009 trying to provide cancer registration data more close to reality. We have made a principle how to choose areas to do cancer registration considering location, economic status, population size, cancer incidence/ mortality level. On of them is to establish new cancer registries in rural areas which should be not high cancer risk areas, especially in west of China. When enough cancer registries are established, we are able to choose appropriate data to estimate and project cancer burden in national level and even in provincial level. At present, we could evaluate cancer incidence and mortality in China based on the results using mortality data from death survey and then calculate incidence with M/I ratio from cancer registration data.

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Guang Lin Li and Wan Qing Chen