RESEARCH COMMUNICATION

Appropriateness of the Standard Mortality/Incidence Ratio in Evaluation of Completeness of Population-Based Cancer Registry Data

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Abstract

Background: The magnitude of differences in mortality incidence (M:I) ratios derived from the national mortality source and those derived from cancer registry (CR) databases may be used to determine associated factors. Methods: All information on cancer incidence cases and mortality cases from January 1, 2003 to December 31, 2007 were retrieved from 5 population-based cancer registries in four regions of Thailand. Two sources of mortality were used: death cases within the cancer registries and mortality statistics obtained from the Ministry of Public Health (MOPH). Plots of percentage M:I ratios from cancer registry databases and from national mortality sources against 1 minus 5 years relative survival (1-5yrRS) were used to visualize the correlation between the two mortality sources. A Poisson regression model was used to determine the influence of cancer sites and registries on the M:I ratio/[1-5yrRS]. Results: There was high variability between the standard M:I ratio derived from national mortality compared with 1-5 year RS. The factors affecting M:I ratios are sources of mortality data and misclassification of topographic site as the cause of death. Conclusions: Use of the M:I ratio is not recommended to evaluate completeness of cancer registry data when the quality of mortality data is poor.

Keywords: Mortality/incidence ratio - cancer registry - source of death database - Thailand

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Introduction

A population-based cancer registry (CR) routinely collects information on patients diagnosed with cancer from hospitals, pathological laboratories as well as other sources, and gives estimates of the magnitude of cancer problems in the community. Cancer registries are expected to contain high quality cancer information. A number of quantitative indices to assess data completeness of cancer registry information are regularly reported in the Cancer Incidence in Five Continents (CI5) series of monographs (Parkin et al., 1994). Indices of completeness usually used in monitoring the quality process include those of historic data methods, proportion of morphologically verified cases, proportion of cases with unknown basis of diagnosis, mortality incidence ratio, death certificate only cases and completeness of case ascertainment by capture-recapture methods (Parkin and Bray, 2009).

Monitoring sources of cancer cases is one of the most useful methods in evaluating the completeness of case ascertainment for all cancer registries. Therefore, the mortality incidence ratio (M:I ratio) method, an example of the independent ascertainment method (Parkin and Bray, 2009), which handles data sources, is considered a good indicator to assess the completeness in terms of coverage of case ascertainment. To calculate the M:I ratio, the incidence from a cancer registry and reported mortality statistics in the same period are used (Parkin and Muir, 1992). Registry generated mortality statistics (based on cases in the registry's database who die during the period) are not acceptable for calculation of the M:I ratio since they do not constitute independent data sources. When the quality of the reported mortality data is good, the M:I ratio is positively related to case fatality, and 1 minus 5 year relative survival (1-5yrRS) (Parkin and Hakulinen, 1991).

Mortality statistics are one of the most important indicators as it can reflect health problems of the

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population and influence resource allocation to health care sectors. Thailand is among the countries with a low quality of mortality data, with 49% of all causes of deaths are recorded as "ill-defined" (Mathers et al., 2004). The mortality data in Thailand, especially cause of death, still has a substantial proportion of errors and misclassifications (Pattaraarchachai et al., 2010; Polprasert et al., 2010). In one study, agreement between cause of death recorded in hospital and that from death certificates was only 25% (Chuprapawon, 2003).

Due to the low quality of mortality data in Thailand, especially for specific cancer primary sites, M:I ratios derived from the national mortality source would not reflect the quality of completeness of case ascertainment. It would lead to a misperception of quality of cancer registries and also their cancer burden statistics.

Since cancer registries collect follow up information of all registered cases until death, the mortality rates can be estimated from CR databases. Limitations of using the mortality statistics are mentioned elsewhere (Chuprapawon, 2003; Pattaraarchachai et al., 2010; Polprasert et al., 2010;). In countries where national mortality source data is not available or lacks accuracy, mortality statistics derived from CR databases may be valuable.

Inaccuracy of cancer specific cause of death occurs in many developing and the third world countries and M:I ratios reported from these nations might be misleading in evaluating the quality of their CRs. In this study, we estimate the magnitude of differences between M:I ratios calculated from the national mortality source with those derived from five selected CR databases in Thailand and determine the factors which affect these differences.

Materials and Methods

Sources of data

Cancer incident cases and deaths occurring between January 1, 2003 and December 31, 2007 were retrieved from 5 selected population-based cancer registries in three regions of Thailand. The registries included in this study were Chiang Mai and Lampang registries in the Northern region, Khon Kaen and Udon Thani registries in the Northeastern region, and Songkhla registry in the Southern region. We also obtained cancer mortality data from the 5 aforementioned provinces, based on the 10th revision of the International Classification of Diseases and Health Related Problems (ICD-10), from the Bureau of Policy and Strategy, Ministry of Public Health, Thailand.

International Classification of Diseases for Oncology (ICD-O-3) codes (Fritz A et al, 2000) are currently used for coding cancer diagnoses in the 5 study registries and ICD-10 codes are automatically generated from ICD-O by the database software used by the registries (Ferlay J, 2005). In the 5-year study period there were 46,589 cases recorded in the cancer registry databases. The 22 most common cancers, sorted by ICD-10 code, are shown in Table 1.

The M:I ratio was calculated from two mortality sources: cancer registries (observed deaths) and the national mortality source (reported deaths). Incidence cases were extracted from CR databases in the same time period, as mortality 2003-2007.

Five-year relative survival (5yrRS) estimates from 1998 to 2002 were calculated for each cancer group. Since the M:I ratio is approximately equal to 1 - 5yrRS (Parkin and Hakulinen, 1991) the expected M:I ratio can be estimated from the pooled analysis of 5yrRS rates using the survival function (Prasartkul P and Rakchanyaban U, 2002). The M:I ratios were calculated from the mortality rates and the cancer incidence rates in the same time period for each cancer group shown in Table 1. The M:I ratios were calculated from three different sources, namely, the national mortality source (standard M:I ratio), deaths within CRs (estimated M:I ratio), and that derived from 1-5yrRS, which is the expected M:I ratio as it has been shown to be correlated with the standard M:I ratio in many cases (Parkin and Bray, 2009).

A linear model was used to determine the variation for cancer groups between expected mortality derived from 1-5yrRS and observed mortality obtained from CR databases in males and females separately. Since the expected mortality (expected deaths) was derived from 1-[5yrRS] x Incidence, year of death was included in the model to determine the period effect.

The relationship between the M:I ratio calculated from CR databases and that from the national mortality source against 1-5yrRS were plotted to visualize the correlation. A line of slope 1 was superimposed to facilitate evaluation of the relationship.

If the M:I ratio correlates well with 1-5yrRS, the ratio between M:I ratio and 1-5yrRS should be approximately 1 for all cancer sites and the degree of variation from 1, as well as the factors affecting the variation, can be determined by fitting a linear regression model. Such a ratio can be used to standardize the M:I ratio so that it is

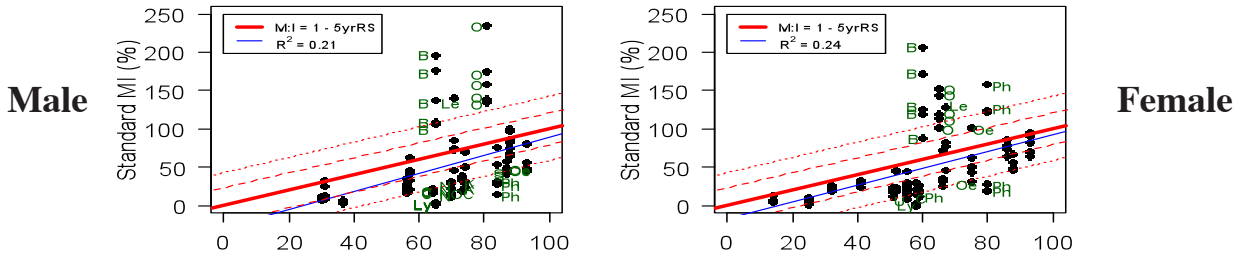

Figure 1. Plots of M:I Ratios (%) against 1 minus 5yr Relative Survival (%). M:I ratios were computed from the national mortality sources; B, brain; C, colon; K, kidney; Le, leukaemia; Li, liver; Lu, lung; La, larynx; Ly, lymphoma; O, other and unspecified; OC, oral cavity; Oe, oesophagus; Ph, pharynx; Pr, prostate; S, stomach; Th, thyroid; U, urinary tract

not dependent on survival. A Poisson regression model was used to determine the influence of cancer groups and registries on the ratio of M:I ratio/1-5yrRS. R software was used for all statistical analysis (R Development Core Team, 2010).

Results

We pooled data from the 5 CRs and after fitting a linear regression model between deaths within CR and expected death, we found no heterogeneity among registries. A period effect for year of death was not observed and so we pooled the cancer sites and registries in further statistical analysis of the M:I ratio. Figure 1 shows plots of the M:I ratio against 1-5yrRS for males and females where M:I ratios were computed from the national mortality source. Figure 2 shows a similar plot except that the M:I ratio was calculated from the cancer registries.

In Figures 1 and 2, the dashed lines represent ± 20% from the line of slope 1 while the dotted lines represent ± 40%. Figure 1 shows a lot of points beyond ± 20%, and even beyond ± 40% of the perfect correlation. In Figure 2 there are less dots beyond ± 20%. The slope of regression lines when the national mortality source is used (Figure 1) are significantly higher than 1 and it is significantly lower than 1 when CR is used (Figure 2).

Multiple linear regressions of M:I ratio against 1-5yrRS, topographic sites and registries when data from the national mortality source were used show that only registry A among males and registry C among females have lower estimated M:I ratios than others registries, while registries A,B and C have lower estimated M:I ratios than registries D and E when deaths within CRs are used to calculate the M:I ratio.

Almost all topographic sites in both sexes have significantly low standard M:I using the data from the national mortality source to calculate the M:I ratio. In contrast, many topographic sites, such as colon and urinary bladder in both sexes, prostate and kidney in males and oesophagus and ovary among females, have statistically lower estimated M:I ratio than the others when deaths within CR are used to calculate the M:I ratio.

The slopes of regression lines shown in Figure 1, are 1.18 with 95% CI [0.71, 1.64] and 1.09 with 95% CI [0.71,1.47] for males and females, and in Figure 2 are 0.61 95% CI [0.40,0.83] and 0.75 95% CI [0.56,0.93],

Table 1. The 22 Most Common Cancer Site Groups, Sorted by ICD-10 Code, from 2003 - 2007

No.	Cancer group	Sex	ICD-10	Specific Sites
1	Oral cavity	both	C00-C08	Lip, tongue, salivary gland and mouth
2	Nasopharynx	both	C11	Nasopharynx
3	Pharynx	both	C09-C10, C12-C14	Oropharynx, hypopharynx and pharynx (unspecified)
4	Oesophagus	both	C15	Oesophagus
5	Stomach	both	C16	Stomach, including oesophago-gastric junction
6	Colorectal	both	C18-C21	Colon, rectum and anus
7	Liver and gallbladder	both	C22-C24	Liver, bile duct and gallbladder
8	Larynx	both	C32	Supraglottis, glottis and subglottis
9	Trachea, bronchus and lung	both	C33-C34	Trachea, bronchus and lung
10	Melanoma and other malignant skin neoplasm	both	C43-C44	Skin
11	Breast	female	C50	Breast and axillary tail of breast
12	Cervix uteri	female	C53	Cervix uteri
13	Ovary	female	C56	Ovary
14	Penis	male	C60	Penis
15	Prostate	male	C61	Prostate
16	Kidney	both	C64	Kidney, excluding renal pelvis
17	Urinary tract	both	C65-C67	Renal pelvis, ureter and urinary bladder
18	Brain and nervous system	both	C70-C72	Meninges, brain, spinal cord and cranial nerves
19	Thyroid	both	C73	Thyroid
20	Lymphoma	both	C81-C85, C96	Hodgkin's disease and all types of non-Hodgkin lymphoma
21	Leukaemia	both	C91-C95	All types of leukaemia

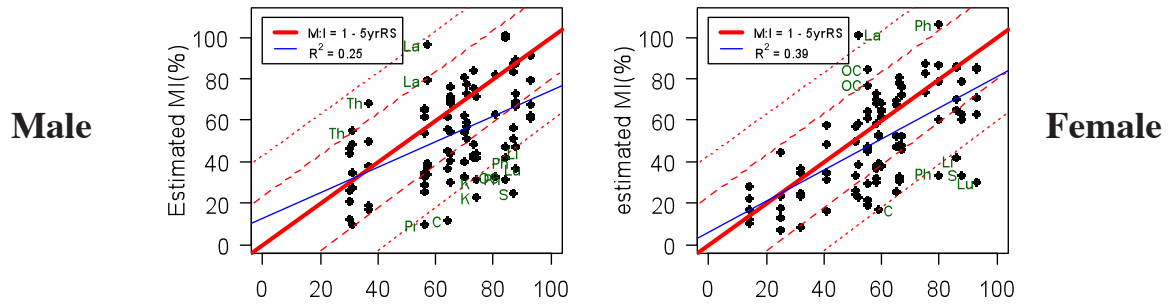

Figure 2. Plots of M:I Ratios (%) against 1 minus 5yr Relative Survival (%). M:I ratios were computed from cancer registries; B, brain; C, colon; K, kidney; Le, leukaemia; Li, liver; Lu, lung; La, larynx; Ly, lymphoma; O, other and unspecified; OC, oral cavity; Oe, oesophagus; Ph, pharynx; Pr, prostate; S, stomach; Th, thyroid; U, urinary tract

Table 2. Poisson Regression Standardized Model, 5 CRs

Topography site	National mortality			
	Males		Females	
	Coeff.	95% CI	Coeff.	95%CI
Oral cavity	-0.6	(-2.3,0.6)	-0.5	(-2.0,0.6)
Nasopharynx	-0.9	(-3.1,0.4)	-0.9	(-3.0,0.4)
Pharynx	-0.5	(-2.1,0.6)	0.3	(-0.7,1.1)
Oesophagus	-0.2	(-1.5,0.9)	-0.1	(-1.3,0.9)
Stomach	-0.3	(-1.8,0.8)	-0.3	(-1.8,0.7)
Colorectal	-1.0	(-3.2,0.4)	-1.0	(-3.1,0.3)
Liver	0.2	(-1.0,1.1)	0.1	(-1.1,1.0)
Larynx	-0.1	(-1.4,0.9)	-0.2	(-1.6,0.8)
Bronchus & lung	0.2	(-1.0,1.1)	0.0	(-1.2,1.0)
Skin	-1.0	(-3.2,0.4)	-1.3	(-3.9,0.2)
Breast	-	-	-0.2	(-1.5,0.8)
Cervix uteri	-	-	-0.3	(-1.7,0.8)
Ovary	-	-	-0.8	(-2.7,0.4)
Penis	-1.9	(-6.0,-0.0)	-	-
Prostate	-0.5	(-2.1,0.7)	-	-
Kidney	-0.4	(-1.9,0.7)	-0.4	(-1.8,0.7)
Urinary tract	-0.8	(-2.8,0.5)	-1.0	(-3.3,0.3)
Brain	1.1	(0.3,1.7)	1.0	(0.3,1.7)
Thyroid	-0.4	(-1.9,0.7)	-0.5	(-2.0,0.6)
Lymphoma	-3.3	(-8.3,-0.4)	-3.5	(-9.0,-0.5)
Leukaemia	0.4	(-0.6,1.2)	0.4	(-0.6,1.9)
Other& unspecified	1.0	(0.2,1.7)	0.8	(0.0,1.5)

CI,Confidence Interval; Coeff,Coefficient, Registries are omitted since none is significantly different

Table 3. Poisson Regression Standardized Model, 5 CRs

	National mortality			
	Males		Females	
	Coeff.	95% CI	Coeff.	95% CI
Oral cavity	-0.4	(-1.6,0.6)	-0.1	(-1.2 ,0.8)
Nasopharynx	-0.4	(-1.7,0.6)	-0.3	(-1.6,0.6)
Pharynx	-0.4	(-1.7,0.6)	-0.2	(-1.4,0.7)
Oesophagus	-0.4	(-1.7,0.6)	-0.0	(-1.1,0.8)
Stomach	-0.6	(-1.8,0.5)	-0.5	(-1.8,0.6)
Colorectal	-0.3	(-3.2,0.4)	-1.0	(-3.1,0.3)
Liver	-0.1	(-1.9,0.5)	-0.5	(-1.9,0.5)
Larynx	-0.1	(-1.2,0.8)	-0.0	(-1.1,0.8)
Bronchus & lung	-0.4	(-1.6,0.6)	-0.4	(-1.8,0.6)
Skin	-0.1	(-1.3,0.8)	-0.3	(-1.5,0.7)
Breast	-	-	-0.3	(-1.6,0.6)
Cervix uteri	-	-	-0.2	(-1.4,0.7)
Ovary	-	-	-0.4	(-1.7,0.6)
Penis	-0.09	(-1.2,0.8)	-	-
Prostate	-0.52	(-1.9,0.5)	-	-
Kidney	-0.7	(-2.2,0.4)	-0.3	(-1.5,0.6)
Urinary tract	-0.4	(-1.7,0.6)	-0.5	(-1.9,0.5)
Brain	-0.2	(-1.3,0.7)	-0.1	(-1.2,0.8)
Thyroid	-0.0	(-1.1,0.9)	0.1	(-0.9,1.0)
Lymphoma	-0.4	(-1.6,0.6)	-0.3	(-1.5,0.7)
Leukaemia	-0.2	(-1.4,0.7)	-0.2	(-1.4,0.7)
Other& unspecified	0.4	(-1.6,0.6)	-0.3	(-1.7,0.6)

CI,Confidence Interval; Coeff,Coefficient, Registries are omitted since none is significantly different.

respectively. 5yrRS explained the ratio of M:I ratio/[1-5yrRS]. Thus, the Poisson regression model with cancer sites and registries with intercept omitted is shown in the equation below.

$$\text{M:I ratio/[1-5yrRS]} = \text{cancer site} + \text{registry}$$

Tables 2 and 3 show the full Poisson regression model the ratio of M:I ratio/[1-5yrRS], cancer registries and topographic sites. The results from the model show positive coefficient values in some sites such as lung, liver, brain, leukaemia, and other and unspecified site when national mortality is used. There is statistical significance for brain and other and unspecified site in both sexes. Registry is not correlated with M:I ratio/[1-5yrRs].

Discussion

In evaluating the magnitude and factors affecting the M:I ratios, data from 5 population-based CRs were used. The reason for pooling the data was to increase the power of statistical analysis in detecting a difference in cancer site groups. The authors first assessed the variability by registry, cancer site group and year of death by simple linear regression. The result showed no significant difference by those factors and confirmed that pooling the data from the 5 CRs could be done without causing any bias.

Figures 1 and 2 allows one to visualize the distribution of standard M:I ratio and 1-5yrRS against the theoretical perfect correlation between the two where the slope of a line equals one. Figure 2 shows less variation than Figure 1 for both males and females. In calculation of the M:I ratio, national mortality and cancer registry are the usual sources of mortality and incidence as they are independent sources (Parkin DM and Bray F, 2009) when the quality of the mortality data is good. Brain and other and unspecified sites are two topographic sites in both sexes where standard M:I ratio is much higher than the expected M:I ratio. The phenomenon may be explained by coding errors resulting in over-reporting of death from brain and unspecified sites, which are common sites for metastasis from other primary sites. Therefore, the validity of coding cause of death affects the validity of the M:I ratio. Thus, invalid M:I ratio causes difficulties in comparison of M:I ratio from CRs in Thailand with those reported from other countries with good quality mortality statistics.

In a cross-sectional study to verify causes of death in Thailand in 2005 (Pattaraarchachai et al, 2010; Rao C, 2010), an uncertainty of causes of death was identified. However, the study could not answer the uncertainty of cancer death since ICD-10 was used. The problem of using ICD-10 codes for classifying cancer deaths is the fact that both primary and metastatic cancers to an organ are often coded identically, even though unknown primary has its own code. The ICO-O coding system classifies metastatic cancer according to the primary (origin) site of cancer. If the cases were not traced back long enough, the primary cancer might be missed and the true cause of death might not be revealed, when ICD-10 was used in the study. Such the fact of miscoding the metastatic site as primary tumour might under by the higher percentage of standard

M:I ratio calculated from the national mortality source than that expected from 1-5yrRS (Figure 1).

Figure 2 shows a better correlation when compared with the expected M:I ratio of estimated M:I ratio derived from CR than that of the standard M:I ratio. However, the estimated M:I ratio has lower values when 1-5yrRS is high or, on the other hand, when 5yrRS is low. Some biases can be expected when the estimated M:I ratio is used instead of the standard M:I ratio, since mortality is a subset and dependent on incidence. In a country where national mortality data are not reliable, use of the estimated M:I ratio derived from CR may be better than to the use of the standard M:I ratio which is more biased in classification of primary cancer site.

As mentioned in the methods section, RS for all cancer sites was calculated by pooling together the data from all registries, thus, the life table of the country was used. However, variation in life span of populations in different regions of the country exists, since RS is related to socioeconomic differences of people covered by a registry (Quaglia A et al, 2005; Howlader et al, 2010; Davies EA et al, 2010), and also health care facilities in the area (Vostakolaei FA et al, 2010). Such variation in these two factors among different registries should be considered in the calculation of RS. However, in the existence of regional/ provincial variation, the difference in RS is minor and the pooled estimation of RS is acceptable in this study since regional/ provincial life table is unavoidable.

The fact that brain and unspecified organs are common metastatic sites of cancers, higher standard M:I ratio of these sites is evident in Figure 1 while it is not in Figure 2 where dead cases are already registered in CR. Pharynx is a cancer site commonly used for any cancer within the throat so that it also showed higher standard M:I ratio than estimated M:I ratio. Leukemia is usually the late stage of many lymphoma cases, the same phenomenon as that of brain and unspecified sites is observed in Figures 1 and 2. The feature results in over-reported number of deaths in those four topographic sites while deaths in other sites are under-reported. This phenomenon is also reported in a study in northern European countries and the US (Vostakolaei FA, 2010).

From our results the total number of deaths from the national mortality source was higher than that recorded in CRs by 16.1% and 17.2% for males and females, respectively. It is possible that the number of cancer deaths in the national mortality source is slightly overestimated by those ambiguous topographic sites. The study of a standard verbal autopsy to verify causes of death in Thailand showed a tendency towards under-reported of cause-specific deaths including cancer (Polprasert W, 2010). However, reclassification to specific cancer site using ICD-10 by verbal autopsy might lead to over reporting of death from lung, liver, and brain cancers since they are common organs for cancer metastases.

Poisson regression was used to fit a model to the data in which the outcome was the ratio of M:I ratio and 1-5yrRS, while cancer site and registry were determinants. There is no difference of the values among 5 registries. Brain and other unspecified cancer have significantly higher ratio than other cancers. Results from the model correspond with Figure 1 and 2. When the national mortality data source is used, cancers with positive coefficient were liver, lung, brain, and leukaemia in both sexes and also that of pharynx in females. These are the common metastatic sites for many cancers or final presentation of the disease which can be coded as cause of death when ICD-10 is applied. Misclassification may also occur in pharyngeal cancers site it is commonly used for any cancer within the throat and neck.

In conclusion, the use of the M:I ratio is limited by the fact that the quality of national mortality data is poor in some countries, including Thailand. We also found that factors affecting M:I ratios are source of mortality, topographic sites, and relative survival. In registries where registration of death is satisfactory, the use of death within registries instead of unfavorable national mortality is another option. We also propose a comprehensive Poisson regression model where topographic site is the predictor of the M:I ratio/[1-5yrRS] ratio to check the cancer sites that have significantly deviated M:I ratio.

In conclusion and recommendation, in countries in which quality of mortality data is doubtful M:I ratio should not be used to evaluate completeness as it does not reflect quality of cancer registry procedures. On the other hand, it actually reflects quality of mortality data. Plots between M:I ratio and 1-5yrRS, and a Poisson regression model can demonstrate deviation of M:I ratio for a particular cancer.

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