

Cancer survival in Qidong between 1972 and 2011: A population-based analysis

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Abstract. Population-based cancer survival is an improved index for evaluating the overall efficiency of cancer health services in a given region. The current study analysed the observed survival and relative survival of leading cancer sites from a population-based cancer registry between 1972 and 2011 in Qidong, China. A total of 92,780 incident cases with cancer were registered and followed-up for survival status. The main sites of the cancer types, based on the rank order of incidence, were the liver, stomach, lung, colon and rectum, oesophagus, breast, pancreas, leukaemia, brain and central nervous system (B and CNS), bladder, blood [non-Hodgkin's lymphoma (NHL)] and cervix. For all malignancies combined, the 5-year observed survival was 13.18% and the relative survival was 15.80%. Females had higher observed survival and relative survival (19.32 and 22.71%, respectively) compared with males (9.63 and 11.68%, respectively). The cancer sites with the highest five-year relative survival rates were the female breast, bladder, cervix and colon and rectum; followed by NHL, stomach, B and CNS cancer and leukaemia. The poorest survival rates were cancers of oesophagus, lung, pancreas and liver. Higher survival rates were observed in younger patients compared with older patients. Cancers of the oesophagus, female breast and bladder were associated with higher survival in middle-aged groups. Improved survival rates in the most recent two 5-year calendar periods were identified for stomach,

lung, colon and rectum, oesophagus, female breast and bladder cancer, as well as leukaemia and NHL. The observations of the current study provide the opportunity for evaluation of the survival outcomes of frequent cancer sites that reflects the changes and improvement in a rural area in China.

Introduction

Cancer survival is an index for evaluating the effect of treatment of patients in specific settings, whether used to define outcomes in clinical trials or as an indicator of the overall efficiency of the cancer health services in a given region or country for the general public. There have been numerous reports on cancer survival revealing improvements through various therapies, derived from hospital-based datasets (1-4). However, there are few reports on the general efficiency of cancer health services derived from long-term population-based cancer registration systems (5-10).

Nation-wide population-based cancer registration, such as that found in Europe, makes survival analysis possible, and has revealed the impact of various socio-economic factors, natural histories, health-seeking behaviours, awareness, early detection practices and treatment availability and accessibility on cancer survivorship (5,10,11). In less developed countries, however, there were relatively few datasets to provide population-based cancer survival analyses until the first volume of the International Agency for Research on Cancer's report on Cancer Survival in Developing Countries (6) was published in 1998. It includes survival data from 10 cancer registries in 5 countries. In 2011, IARC published its second scientific publication on Cancer Survival in Africa, Asia, the Caribbean and Central America (7), which includes survival data from 27 cancer registries in 14 countries.

These international cancer survival studies (5-7,10) have provided important information concerning differences in populations observed between and within countries, and valuable insights for future planning and investment by governments in primary prevention activities, early detection initiatives and tertiary care to achieve meaningful cancer control (7). A global coordinative research report of survival from 279 population-based registries was published recently (12), and several nationwide research reports were issued to estimate

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Abbreviations: B and CNS, brain and central nervous system; NHL, non-Hodgkin's lymphoma; IARC, International Agency for Research on Cancer; DCN, death certificate notifications; DCO, death certificate only; MV, morphological verification; ASR_w, age-standardized rate by world population

Key words: neoplasm, observed survival, relative survival, population-based cancer registration, epidemiology

the prognosis of cancer, but these included only a short time period (13,14), or site-specific survival from population based data (15-17). For providing a long-term assessment of population-based cancer data, this paper provides a systematic analysis of cancer survival for the period of 1972-2011 in Qidong, China.

Materials and methods

The Qidong Cancer Registry. The Qidong Cancer Registry was designed as a population-based cancer registry in 1972 when the Qidong Liver Cancer Institute was established (18). Soon thereafter, this registry was designated by the local health authority as a compulsory reporting system implemented by health care workers in all health services. In 1974, the Qidong Cancer Registry started to establish an all cause-of-death certificate reporting system (Qidong All-Death-Cause Registration), as one of the seven national disease-monitoring rural locations for vital statistics under the supervision of the Health Ministry of PR China (19). This vital statistics system makes available the outcome of any patients with cancer patients who succumbed to the disease or are still alive. At present, this cancer registry has joined the national monitoring programme (the National Cancer Registration Network) of the National Central Cancer Registry of China supported by the Ministry of Health of China (20).

Case-finding. Mixed methods were employed for case finding and follow-up, as described elsewhere (6,7). Briefly, district and township health services (or hospitals) were responsible for the registration and follow-up of incident cases and mortalities from cancer cases diagnosed in outpatient departments, or during hospitalization (including those returning home following hospitalization outside of Qidong). Upon discovering any 'new' patient(s) with cancer in the covered area, registration personnel would first check to confirm the case was new, and then considered it as incident case for inquiring about the patient's demographic features such as name, gender, age, address, marital status and occupation, as well as main items on the date and basis of diagnosis, treatment (if any) and hospital name(s). These data were recorded on registers, lists, or cards issued by Qidong Cancer Registry, and then reported monthly to Qidong Cancer Registry. When incident case(s) later died at home or in a hospital, the registration personnel would add the date of death to the existing record in the registry. Meanwhile a death certificate, issued by the physician in charge of the case or collected from the registrants, would be sent to the current registry for entry and storage in the archives.

Follow-up methods. In practice, cancer lists and death certificate notifications (DCN) were reported monthly. Any cases of mortality from cancer were matched again with the DCN in our registry. For those alive, repeated scrutiny of medical records was performed regularly at six-month intervals; more careful follow-up was performed again for each 5-year calendar period (21,22). Due to the follow-up efforts, the proportion of death certificate only (DCO) cases was very low, and nearly 100% of the died-of-cancer cases had DCN records. Therefore, all new patients or patients who had died that were diagnosed and/or treated in Qidong, or even outside

of Qidong, were completely recorded and their outcomes were ascertained.

Cancer classification, coding and case confirmation. Due to the development of the International Classification of Diseases (ICD), three versions (8th, 9th, 10th) that were revised by the World Health Organization during the past four decades, ICD-8, ICD-9 and ICD-10, were used for the coding practice in the Qidong Cancer Registry. In the current study, the cancer data have been reclassified and recoded according to the ICD-10 criteria. The cut-off for the final follow-up for survival status was April 2012. The proportion of morphological verification (MV) was 39.94% (37,052/92,780), with a lower DCO rate of 0.23%. The survival duration of each case was determined as the time difference from the date of initial diagnosis to the date of mortality due to cancer, date of death due to other diseases or date when the patient was lost to follow-up, and the date of closing for those still alive.

Survival analysis. Cumulative observed survival rate and relative survival rate were calculated. Relative survival rate was defined as the ratio of the observed survival rate to the expected rate that was based on a group of people in the general population similar to the patient group with respect to gender, age and calendar period of observation. This means that the survival of patients was adjusted to the normal life expectancy of the general population of the same age (23). The all-cause mortality and the life table data of the general population, which contains the probability of death and the life expectancy for single year age-groups for both sexes, for the relevant calendar years, was generated from the Qidong Vital Registry (Qidong All-Death-Cause Registration) (19,24). This measure made the relative survival rate an estimate of the chance of surviving the effects of cancer (25-28). The observed survival and relative survival rates were computed with 6 age groups (15-34, 35-44, 45-54, 55-64, 65-74 and 75+) and 9 calendar periods (1972, 1973-1977, 1978-1982, 1983-1987, 1988-1992, 1993-1997, 1998-2002, 2003-2007 and 2008-2011) using Hakulinen's method performed using the SURV3.01 software developed at the Finnish Cancer Registry, including the statistical tests (H_0 - H_2 equal vs. unequal hazards), derived from the software (26); $P < 0.05$ was considered statistically significant.

Results

The basic characteristics of cancer data and their quality indices. A total of 92,780 cases of cancer were registered between January 1, 1972 and December 31, 2011, with a crude incidence rate of 206.39 per 100,000, and an age standardized rate by world population (ASR_w) of 159.11 per 100,000 (213.69 for males and 109.99 for females). The quality indices used for cancer cases are the percent of DCO, percent of morphological verification and the ratio of mortality to incidence. These quality indices by site have been described in our previous studies (18,24). Briefly, as presented in Table I, the age-group distribution and the quality indices for the main sites of the cancer were, in rank order: liver, stomach, lung, colon-rectum, oesophagus, breast, pancreas, blood (leukaemia), brain

Table I. Case age distribution and quality indices of the major sites of cancers in Qidong, 1972-2011.

Site	ICD-10	Age, years and no. of cases							Total	DCO		MV		M:I
		0-14	15-34	35-44	45-54	55-64	65-74	75+		No.	%	No.	%	
Oesophagus	C15	1	24	81	392	995	1,538	1,383	4,414	11	0.25	1,533	34.73	0.95
Stomach	C16	2	308	879	1,993	3,716	4,807	3,696	15,401	29	0.19	8,550	55.52	0.89
Colon-rectum	C18-21	2	183	373	749	1,251	1,774	1,703	6,035	2	0.03	4,819	79.85	0.75
Liver	C22	64	2,602	6,819	7,673	5,606	3,612	2,022	28,398	88	0.31	3,797	13.37	0.96
Pancreas	C25	3	42	142	347	732	1,111	902	3,279	7	0.21	774	23.6	0.95
Lung	C33-34	5	128	513	1,695	3,852	5,411	3,736	15,340	41	0.27	1,951	12.72	0.93
Breast ^a	C50	1	180	761	1,097	720	417	276	3,452	0	0	3,212	93.05	0.51
Cervix	C53	3	62	191	263	281	229	182	1,211	0	0	1,089	89.93	0.72
Bladder	C67	2	22	52	143	345	474	581	1,619	0	0	1,158	71.53	0.68
B and CNS	C70-72	104	189	221	384	377	350	160	1,785	6	0.34	480	26.89	0.9
NHL	C82-85/96	48	133	146	228	337	361	219	1,472	0	0	1,468	99.73	0.85
Leukaemia	C91-95	221	402	242	264	303	328	170	1,930	4	0	1,921	99.53	0.93
All sites	C00-96	538	4,897	11,150	16,633	20,301	22,429	16,832	92,780	212	0.23	37,052	39.94	0.88

^aIncludes 32 cases of male breast cancer. DCO, death certificate only; MV, morphological verification; B and CNS, brain and central nervous system; NHL, non-Hodgkin's lymphoma; ICD, International Classification of Diseases; M:I, mortality: incidence.

and central nervous system (B and CNS), bladder, blood [non-Hodgkin's lymphoma (NHL)] and cervix.

Observed survival rate and relative survival rate by site. Table II shows the 1-, 5-, 10-, 20- and 30-year observed survival and relative survival rates by site. For all sites combined, the observed survivals were 29.23, 13.18, 9.98, 7.09 and 5.00%, and the relative survivals were 30.29, 15.80, 14.52, 15.90 and 18.67%, respectively. The highest 5-year observed survival rate among the major cancers was found to be the female breast (58.75%), followed by the cervix (42.66%) and bladder (35.98%); the poorest 5-year observed survival rate was liver (4.26%), and then pancreas (4.87%) and lung (5.15%). For 5-year relative survival, the three sites with the best rates were the female breast (63.12%), bladder (50.06%) and cervix (48.82%); the worst rates were for the liver (4.69%), pancreas (6.30%) and lung (6.61%). The 20-year observed survival rates from highest to lowest were female breast (38.30%), cervix (23.82%), bladder (18.37%) and colon-rectum cancer (15.57%), NHL (9.54%), stomach (6.63%) and B and CNS cancer (4.66%), leukaemia (2.90%), pancreas (2.66%), lung (2.39%), liver (2.15%) and oesophageal cancer (1.83%). The 20-year relative survival rates were as follows: bladder (76.39%), female breast (56.36%), cervix (53.09%), colon-rectum (45.53%) and stomach cancer (21.96%), NHL (19.37%), pancreas (9.27%), lung (8.55%), oesophagus (8.30%) and B and CNS cancer (7.55%), leukaemia (4.35%) and liver cancer (3.40%).

Five-year observed survival and relative survival by sex. In general, for all sites combined, females had higher observed and relative survival (19.32 and 22.71%, respectively) than males (9.63 and 11.68%, respectively). This outcome reflects the higher proportion of female site-specific cancer types, such as cancer of the female breast and cervix, with higher survival

rates. Table III reveals minimal differences between the sexes in terms of 5-year observed and relative survival rates for the major cancer sites. For site-specific cancers, bladder cancer and stomach cancer had lower survival rates in females compared with males, whereas for cancers of the liver, lung, oesophagus, B and CNS and NHL, survival rates were higher in females than males.

Five-year observed survival and relative survival by age group. Table IV shows the 5-year observed and relative survival by age group (15-34, 35-44, 45-54, 55-64, 65-74, and 75+) for all the major cancer sites. Relatively higher survival rates were observed in younger patients (15-34, 35-44) compared with older patients (65-74, 75+), particularly for sites including the stomach, lung, pancreas, B and CNS, blood (NHL) and cervix. Cancer of the oesophagus, female breast and bladder had higher survival in middle-aged groups (45-54, 55-64) than at other age groups. Liver cancer had relatively stable low survival rates at each age group. For all sites combined, middle-aged patients had the highest survival results of 5-year observed and relative survival rates.

Five-year observed and relative survival by period. Table V reveals the 5-year observed and relative survival by calendar year for each of the main sites. The 5-year observed survival and relative survival rates in the period of 1973-1977 were used as the baseline for comparison. The survival rates of stomach, lung, colon-rectum, oesophagus and female breast cancer, leukaemia, bladder cancer and NHL in the most recent two 5-year calendar periods showed improvement compared with previous periods. The survival rate of liver cancer has shown modest improvement since the 1978-1982 period, although the total survival rate remains poor. The survival rate for pancreatic cancer is the only one exhibiting no real change during these periods.

Table II. Observed survival rate and relative survival rate by site.

Site	Observed survival rate, %					Relative survival rate, %				
	1-year	5-year	10-year	20-year	30-year	1-year	5-year	10-year	20-year	30-year
Liver	15.18	4.26	2.79	2.15	1.73	15.47	4.69	3.41	3.40	4.02
Stomach	33.82	14.18	10.35	6.63	4.19	35.43	18.13	17.50	21.96	32.84
Lung	16.69	5.15	3.75	2.39	2.03	20.65	6.61	6.44	8.55	18.84
Colon-rectum	52.91	27.83	21.59	15.57	10.19	55.48	35.58	35.85	45.53	54.40
Oesophagus	20.92	5.28	3.39	1.83	1.61	22.19	7.20	6.58	8.30	21.75
Female breast	83.61	58.75	48.56	38.30	29.19	84.76	63.12	56.81	56.36	62.59
Pancreas	12.69	4.87	3.76	2.66	1.28	13.34	6.30	6.47	9.27	10.65
Leukaemia	23.00	7.47	3.80	2.90	2.90	23.43	8.23	4.64	4.35	5.26
B and CNS	25.20	10.91	8.29	4.66	4.12	25.73	12.15	10.37	7.55	9.09
Bladder	59.91	35.98	26.91	18.37	12.24	64.07	50.06	52.42	76.39	115.75
NHL	32.48	15.78	12.76	9.54	7.63	33.49	18.46	17.79	19.37	22.44
Cervix	64.30	42.66	35.16	23.82	12.75	65.85	48.82	48.08	53.09	60.33
All sites	29.23	13.18	9.98	7.09	5.00	30.29	15.80	14.52	15.90	18.67

B and CNS, brain and central nervous system; NHL, non-Hodgkin's lymphoma.

Table III. Five-year observed survival rate and relative survival rate by sex.

Site	Male				Female			
	OS	2*SE _{OS}	RS	2*SE _{RS}	OS	2*SE _{OS}	RS	2*SE _{RS}
Liver	4.06	0.29	4.47	0.32	4.87	0.55	5.37	0.61
Stomach	14.40	0.74	18.67	0.95	13.80	0.96	17.21	1.20
Lung	4.68	0.43	6.14	0.57	6.36	0.82	7.78	1.00
Colon-rectum	27.43	1.78	35.96	2.33	28.20	1.73	35.24	2.16
Oesophagus	5.03	0.84	6.92	1.16	5.82	1.32	7.77	1.76
Female Breast	-	-	-	-	58.75	1.81	63.12	1.95
Pancreas	4.67	1.05	6.14	1.38	5.12	1.21	6.47	1.53
Leukaemia	7.39	1.72	8.28	1.92	7.58	1.91	8.19	2.06
B and CNS	8.87	1.89	10.12	2.15	13.58	2.59	14.69	2.80
Bladder	36.95	2.92	52.02	4.11	32.44	5.44	43.37	7.28
NHL	15.19	2.51	18.02	2.98	16.72	3.35	19.14	3.84
Cervix	-	-	-	-	42.66	3.01	48.82	3.44
All sites	9.63	0.26	11.68	0.31	19.32	0.45	22.71	0.53

2*SE_{OS}, twice the standard error of OS; 2*SE_{RS}, twice the standard error of RS. OS, observed survival rate; RS, relative survival rate; B and CNS, brain and central nervous system; NHL, non-Hodgkin's lymphoma.

Discussion

The current study used 4 decades of population-based data from a registry to analyse cancer survival, updated for the outcomes of patients with cancer from the Qidong population, which collectively reflects the long-term trends of cancer survival in a rural area that has recently undergone regional economic development, and subsequent improvements of comprehensive treatment regimes and changes in local health care and service. The present authors hope these data will

provide important information for further optimizing current therapies and policy.

Differences in cancer survival reported from any hospital-based observation between or within countries may not be used directly for comparison due to limitations of the number of patients receiving various cancer therapies, or variations in the availability, accessibility and the treatments from different health service practices. Therefore, the cancer survival estimated from hospital and clinical trial settings at best reflects the selective experiences of groups of patients in

Table IV. Five-year observed survival rate and relative survival rate by age group.

Site	Five-year observed survival rate, %							Total	Five-year relative survival rate, %							Total
	0-14 ^a	15-34	35-44	45-54	55-64	65-74	75+		0-14 ^a	15-34	35-44	45-54	55-64	65-74	75+	
Liver	4.69	4.37	4.19	4.76	4.30	3.74	3.00	4.26	4.71	4.42	4.29	4.96	4.67	4.67	6.35	4.69
Stomach	0.00	21.82	25.59	22.94	17.25	11.90	5.81	14.18	0.00	22.01	26.12	23.87	18.89	15.14	12.27	18.13
Lung	20.00	13.20	8.48	8.14	6.40	4.70	2.21	5.15	20.05	13.31	8.65	8.47	6.98	5.95	4.69	6.61
Colon-rectum	0.00	33.15	37.27	40.28	38.76	26.26	12.31	27.83	0.00	33.43	37.99	41.73	41.76	32.65	25.38	35.58
Oesophagus	0.00	6.50	8.03	10.07	8.27	4.06	2.86	5.28	0.00	6.56	8.22	10.50	9.09	5.20	6.22	7.20
Female breast	-	59.81	67.42	66.26	53.44	47.82	30.42	58.75	-	60.17	68.27	67.79	56.03	55.50	55.28	63.12
Pancreas	0.00	17.81	6.34	8.32	5.04	3.75	3.82	4.87	0.00	17.97	6.47	8.65	5.47	4.68	8.03	6.30
Leukaemia	6.86	6.76	10.23	9.91	6.95	6.27	6.42	7.47	6.88	6.80	10.43	10.25	7.48	7.81	12.60	8.23
B and CNS	10.32	18.91	16.81	12.13	10.18	6.12	2.82	10.91	10.35	19.03	17.13	12.56	11.00	7.49	5.77	12.15
Bladder	0.00	48.63	65.97	60.31	49.21	36.29	17.34	35.98	0.00	49.10	67.53	62.77	53.92	46.59	39.85	50.06
NNHL	22.92	20.36	18.07	20.19	17.26	13.93	5.11	15.78	22.99	20.51	18.42	20.96	18.72	17.32	10.60	18.46
Cervix	0.00	68.69	66.12	58.55	43.46	30.20	7.74	42.66	0.00	68.92	66.86	59.98	45.81	35.58	14.59	48.82
All sites	10.60	16.02	15.64	17.51	14.82	11.10	6.85	13.18	10.63	16.17	15.99	18.18	16.11	13.95	14.43	15.80

^aThe 0-14 age group may be negligible due to the small proportion of cases for these 12 sites, with the exception of the B and CNS, and leukaemia (Table I). B and CNS, brain and central nervous system; NHL, non-Hodgkin's lymphoma.

Table V. Five-year observed survival rate and relative survival rate by calendar year.

Site	Five-year observed survival rate, %						Five-year relative survival rate, %							
	1973-1977	1978-1982	1983-1987	1988-1992	1993-1997	1998-2002	2003-2007	1973-1977	1978-1982	1983-1987	1988-1992	1993-1997	1998-2002	2003-2007
Liver	2.56	1.33	2.38	4.41	4.20	4.60	6.26	2.75	1.43	2.56	4.74	4.67	5.10	7.09
Stomach	9.47	10.43	11.27	14.35	13.30	14.00	20.65	11.79	13.53	14.47	18.09	16.92	18.01	26.67
Lung	3.55	4.10	3.92	3.56	3.69	5.13	6.32	4.38	5.25	5.04	4.52	4.66	6.49	8.26
Colon-rectum	18.96	18.50	22.39	25.55	25.34	29.18	32.24	23.29	23.27	27.80	31.70	32.29	37.02	42.70
Oesophagus	3.22	3.96	4.67	4.38	2.90	6.12	8.20	4.22	5.21	6.38	5.91	4.05	8.18	11.48
Female breast	51.46	56.28	55.95	56.40	50.54	59.54	64.70	56.30	60.43	59.98	60.32	54.62	63.11	69.26
Pancreas	2.01	6.60	5.83	5.04	4.35	4.17	5.11	2.45	8.42	7.56	6.38	5.48	5.42	6.75
Leukaemia	3.33	2.87	4.87	7.44	4.58	10.00	11.88	3.56	3.16	5.32	8.17	5.02	10.93	13.28
B and CNS	9.47	8.26	7.58	7.55	10.77	7.47	14.48	10.11	8.83	8.18	8.13	11.85	8.52	16.63
Bladder	26.92	27.50	32.06	29.58	31.72	35.71	42.20	34.57	36.45	41.97	39.60	43.76	48.74	62.89
NHL	6.80	11.01	16.08	12.50	10.35	15.17	23.05	7.76	12.77	18.63	14.49	12.42	17.62	26.79
Cervix	44.75	22.31	34.55	27.66	30.23	32.56	49.49	52.88	26.84	40.21	33.34	34.93	36.92	53.66
All sites	9.50	9.09	10.33	12.29	10.89	12.50	16.82	11.02	10.83	12.21	14.53	13.02	14.95	20.67
B and CNS, brain and central nervous system; NHL, non-Hodgkin's lymphoma.														

B and CNS, brain and central nervous system; NHL, non-Hodgkin's lymphoma.

specific settings, and cannot be generalized as reflecting the overall efficiency of the cancer health services in a given region or country (7).

For international comparisons of cancer survival, only the estimates of population-based survival based on all patients with cancer diagnosed by all means in a geographical region or country are recommended (12,13). In European countries, this estimation has been performed since the 1990s, and the results have been published in the EURO CARE study series (5,11,29), and other journals (30-33). In Asian countries, reports on cancer survival from population-based registries have increased since the beginning of this century (8); the majority of them report regional data (13,34-37). There have been few studies referring to population-based cancer survival in mainland China. Previous studies have reported on population-based cancer survival in Shanghai (38) and Zhejiang (39); however, these studies primarily focused on a certain or some cancer sites over a short time period. In Taiwan, the survival rates for epithelial ovarian cancer and uterine cancer were reported based upon data from a population-based registry (40,41).

The data from 40 years of population-based registration have provided the opportunity for the estimation of long-term cancer survival in a rural area in China. At present, studies from population-based settings referring to 20-year or 30-year observed or relative survivals are limited. Germany has described the 5- and 10-year relative survivals for 24 common cancer types in the 1990-1992 cohort, and the 2000-2002 period (42), and by further follow-up, site-specific survival for tumour types such as pancreatic cancer was evaluated (43). The 5- and 10-year relative survival of patients with chronic myelocytic leukaemia from the Surveillance, Epidemiology, and End Results (SEER) Program of the United States in 1973-2004 were reported to show a dramatic increase in long-term survival of younger patients (44). Korea has reported the 5- and 10-year relative survivals for the 19 most common cancer types from 1993-2007 (45) using 8 population-based cancer registry databases. A population-based study of long-term outcomes with the 5-, 15- and 25-year overall survival of patients with head and neck cancer were reported from a Canadian province (46). More recently, long-term relative survival data among testicular germ cell tumour (TGCT) patients diagnosed in Norway between 1953 and 2012, was reported showing patients with TGCTs diagnosed prior to 1980 or after age 40 had lower relative survival (47). Almost all these papers are from developed countries or areas; such studies rarely emanate from undeveloped areas.

The 5-year relative survival rate is a common index for the estimation of cancer outcome, and is regarded as almost equivalent to a cure for a specific cancer. The index of 20-year or 30-year relative survival is not widely used as i) long-term data are challenging to obtain, and ii) high durations of relative survival may be affected not only by the biological characteristics of the cancer but also by the survival probability (27), otherwise known as the life expectancy of the patient following diagnosis and treatment. Due to the ratio of the observed survival rate to this expected rate, the relative survival rate may occasionally increase with the survival year, that is, the 30-year relative survival rate might be even higher than the 20-year relative survival rate. In the current data, for instance, the 20-year relative survival rate of patients with bladder is

76.39%, and the 30-year relative survival rate is 115.75% (Table II), meaning that those patients who survived >30 years have a higher survival than the comparable population.

The survival status of any patients with cancer may be affected by numerous risk factors, particularly for elderly patients. In the present series, we identified that cancer affecting the female breast, cervix, bladder and colon-rectum has higher observed and relative survival rates compared with other cancer sites. Oesophageal cancer had the lowest 20-year observed survival, followed by cancers of the liver, lung and pancreas; liver cancer had the poorest 20-year relative survival, followed by leukaemia, B and CNS and oesophageal cancer, reflecting the possible competing risks from other causes of mortality (48) or the longevity factors of the different patient populations. The present study will primarily focus on the 5-year relative survival rate for further site-specific comparisons.

Liver cancer was the most prevalent type of cancer with an ASR_w of 50.71 per 100,000 and a cumulative risk of 5.15% for the forty-year period in Qidong. It is the fourth most common cancer in China (14,49), and fifth common cancer site in the world (50). As this cancer type is rare in developed countries (51), most of the survival reports associated with liver cancer are from developing countries (6,7,13,52). The survival for patients with liver cancer is usually poor. A report from Taiwan revealed that the mean survival time of 3,850 patients with liver cancer was ~1.8 years (53). An American study demonstrated that the 5-year relative survival was 3% in the period from 1975-1977, 5% from 1987-1989 and 18% from 2003-2009 (50). A comparison study with data from European countries and the Philippines has shown that the 5-year relative survival rates for this cancer type in 1995-1999 were 9.1 and 5.3%, respectively, indicating the discrepancy between developed and undeveloped countries (54). In the current study, the 5-year relative survival for liver cancer was around 2% in the 1970's, about 2-3% in 1980's, 4-5% in the 1990's, and 5-7% in the early 2000s, showing low rates but with slight improvement. There were no significant differences between the sexes for the relative 5-year, 10-year and 15-year survival rates. No significant differences were observed among the 15-34, 35-44, 45-54, 55-64 and 65-74 age groups, but the patients with liver cancer aged >75 had higher 5-year relative survival compared with other ages.

Stomach cancer had an ASR_w of 25.59 per 100,000 and a cumulative risk of 3.10% over the 4 decades. It is the most common cancer type in China (14,49) and the second most common cancer site in the world (50). According to previous global reports, the incidence of stomach cancer has been decreasing over the past few decades due to changes in food preservation, and improved survival due to early detection (55,56), or perhaps improvement of therapies. In a recent Swedish study, the 5-year relative survival rate for gastric cardia adenocarcinoma was reported to be 11.1% in 1990-1999 and 14.3% in 2000-2008, with higher survival rates among males and younger patients. For gastric non-cardia adenocarcinoma, the 5-year relative survival rate was 19.0% in 2000-2008 and 20.2% in 1990-1999, with no differences between sexes, and among age groups (32). In the present data, an improvement in 5-year relative survival was identified during the 40-year period, increasing from 11.79% in 1973-1982 to 26.67% in

2003-2007. Middle-aged patients (35-44 and 45-54 years) had relatively higher 5-year observed survivals (21.77% and 18.63%, respectively) than those under 35 years (16.13%) and those aged 55-64 (12.61%), 65-74 (7.99%) and aged >75 (2.94%). These relatively poor results are in accordance with a previous report (57) that compared survival between patients with stomach cancer in China and the United States, indicating that Chinese patients have poorer outcomes than US patients due to larger tumours and a later stage at presentation.

Lung cancer was the third major cancer site with an ASR_w of 25.41 per 100,000 and a cumulative risk of 3.22% on average over the forty years, although it has recently overtaken liver cancer and stomach cancer as the most frequent cancer site in Qidong. It was also the most common cancer type for the period between 2003 and 2007 in China (49), and globally (50,58); both in rural areas such as Qidong (27,59) and urban areas including Shanghai (14,60). The increasing trend of the worldwide burden of lung cancer likely results from smoking (accounting for 80% of cases in males and ≥50% in females), and outdoor air pollution (61), but the relatively high burden of lung cancer in females may also reflect indoor air pollution from unventilated coal-fuelled stoves and from cooking fumes in China, India and other regions still reliant on biomass fuels (50,62). Lung cancer incidence rates are decreasing in the majority of Western countries, whereas in China and other countries in Asia and Africa, lung cancer incidence rates are increasing (18,22,49-51). The improvement in lung cancer survival in recent decades has been minimal, with 5-year survival rates of 13% in 1975-1977 and 1984-1986, and 16% in 1999-2005 (63). In the present series, lung cancer has increased with an annual percent change rate (ASR_w) of 2.21% since the 1970s; however, the relative survival rate shows no major improvements, with observed survival rates of 4.38% from 1973-1977 and 4.69% from 1998-2003, with an elevation to 8.26% in 2003-2007. A younger patient age was associated with improved outcomes, with observed survival of 13.31% at aged 15-34 and 4.69% in the age group >75 years.

Colorectal cancer (CRC) was the fourth most common site with an ASR_w of 9.80 per 100,000 and a cumulative risk of 1.15% during the 40-year period in Qidong. Globally, CRC is the third most prevalent cancer type for males and the second most common for females (58). It is a cancer type that has increased in the majority of countries since the 1950s, and the incidence rates among males in the Czech Republic and Japan have already exceeded the peak of incidence observed in the United States, Canada and Australia, where rates are declining or stabilizing (50). However, the survival rate for patients with this cancer type has also improved during previous decades. According to a recent report examining Danish patients, the overall 5-year survival improved from 39% to a predicted survival of 46% for those diagnosed in 2009-2011, corresponding to a 5-year adjusted mortality rate ratio of 0.76 compared with 2000-2002 (64). In China, CRC has been reported to be among the three most prevalent forms of cancer, after lung and stomach cancer (49); however, a recent study suggested that it was the fifth most common cancer site (14). In Zhejiang, China, where CRC is prevalent, the 5-year relative survival rate for patients with CRC was 58.73%, with significant variation between different age groups, from 63.07% at 35-44 years to 47.41% in those aged >75 (39). In the current

series, the survival rates of patients with CRC have slightly increased, but remain very poor compared with the relative survival rates of 50% in 1970-1977 and 66% in 2005-2011 for patients with CRC in the United States (65). There is even a disparity between the survival rates in Zhejiang and Qidong, with 5-year relative survival rates of 58.73 vs. 35.58%, which perhaps reflects the difference in the treatment opportunities between urban and rural areas.

Oesophageal cancer (OC) ranked as the fifth most prevalent cancer type, with an ASR_w of 7.08 per 100,000 and a cumulative risk of 0.88% in the period from 1972-2011 in Qidong. Worldwide, this cancer is more common among males (seventh most common cancer site) than females (below the tenth most common site), and had the highest incidence rates in Southern and Eastern Africa and Eastern Asia, and the lowest rates in Western and Middle Africa and Central America (58). China is a relatively high incidence area for OC, ranking sixth in the world according to the 2003-2007 statistics (49), and ranking third in China according to a more recent estimation (14). A recent review indicates that the OC survival is poor for all groups, and is significantly poorer in black patients compared with white patients; the 5-year relative survival for 2002-2008 from 18 SEER geographic areas was 16.9% (66). A Swedish study revealed an improved 5-year relative survival for OC, increasing from 12.5% in 1990-1999 to 14.6% in 2000-2008 (32). However, a recent study in the United Kingdom from a population-based cohort reveals that following oesophagectomy the 5-year survival of oesophageal adenocarcinoma may be 65.1% (114/175), demonstrating an improved outcome for patients with early-stage OC (67). In the present series, the 5-year relative survival was 7.20%, and slightly higher in females (7.77%) compared with males (6.92%). There was a higher relative survival in the 45-54 age group (10.50%) compared with other age groups (5.20-9.09%), and the relative survival of OC has improved from 4.22% from 1973-1977 to 11.48% from 2003-2007. The survival rates for patients with OC are lower than the average rates for urban (19.1%) and rural areas (21.2%) during the years 2003-2005 in China (68).

Breast cancer ranked sixth with an ASR_w of 6.13 per 100,000 and a cumulative risk of 0.64% during the 40 years. In females, breast cancer was the fourth most common cancer site, with an ASR_w of 11.78 per 100,000 in Qidong. Female breast cancer (FBC) has been the most common cancer site in women worldwide, with rapidly increasing trends in many Western countries since the late 1980s (50). It is also the commonest site in females in China (14,49). FBC has higher survival rates than other forms of cancer. It is hypothesized that the decrease in breast cancer mortality during the past two decades in Germany and the US was primarily due to early detection and advances in treatment, with 5-year relative survival of localized breast cancer of 98.7% in Germany and 97.3% in the US between 2005 and 2008 (69). An international comparison reveals that there were no major differences in survival between European countries, with 5-year relative survival rates of 90-99% for the patients with stage I and II disease (70). At the population-based level, the survival rates of female patients with breast cancer were 75% in 1975-1977, 84% in 1987-1989 and 91% in 2005-2011 from 9 SEER areas in the US (65). A Singapore-Malaysia hospital-based breast cancer study revealed that ethnicity is independently

associated with poorer survival, with 5-year overall survival rates of 75.8% in Chinese females, 68.0% in Indian patients, and 58.5% in Malay patients with breast cancer (1). However, the data in the present study revealed reduced 5-year relative survival rates for female patients with breast cancer ranging from 50.63 to 69.26% among time periods, and 55.28-68.27% among age groups, reflecting the wide gap in the early detection and treatment for this disease in this rural area.

The cancer types that were ranked seventh to twelfth most common for the 40-year period were pancreatic cancer, leukaemia, B and CNS and bladder cancer, NHL and cervical cancer. Pancreatic cancer is a rapidly progressing disease with a poor prognosis, and the improvement in 5-year survival over time has been very limited, with rates of 2.0, 2.1, 3.4 and 3.8% for the periods 1998-2000, 2001-2003, 2004-2006 and 2007-2009, respectively, according to a study from Denmark (71). Slight improvements in 5-year relative survival of 10.7% in Germany and 10.3% in the United States were observed from 1997-2010 (65). Generally, the outcome is very poor for pancreatic cancer, irrespective of whether the country is wealthy or poor, or whether the region is urban or rural. In Shanghai, for instance, the 5-year survival was 4.1% in 2004-2009 (38), whereas in the current data, the 5-year observed and relative survival in 1972-2011 were 4.87 and 6.30%, respectively. The largest improvements in survival have been observed from an American cancer statistical report, for leukaemia (from 34% in 1975-1977 to 59% in 2003-2009), NHL (from 47 to 71%, respectively), and B and CNS (from 22 to 35%, respectively), whereas bladder and cervical cancer have shown the least improvement (from 72 to 80%, and from 69 to 69%, respectively) (51). A study from the UK observed the ethnic differences in cancer survival, revealing that male South Asian patients experienced a higher excess mortality than non-South Asians for NHL, with 5-year survival rates of 48.4 vs. 50.3% in 1986-1995, and of 57.2% vs. 57.8% in 1996-2004, respectively (72). For the 5-year relative survival in patients with B and CNS cancer in Qidong, the present study identified no major changes for earlier time periods (8.13-11.85%), but it has improved recently, with a rate of 16.63% in 2003-2007. In Korea, bladder cancer had a relatively high 5-year relative survival rate of 80.2% in 2006-2010 (36); whereas in China, this rate was 67.3% in 2003-2005 (68). Although the 5-year relative survival of bladder cancer was lower in our data, the outcomes have improved from 34.57% in 1973-1977, to 39.60% in 1988-1992 and to 62.89% in 2003-2007. For cervical cancer, the 5-year relative survival was 48.82%, fell steeply with age and improved notably in 2003-2007 (53.66%), but was lower than the results from South Korea (79%) and Singapore (76%) (13). The 5-year relative survival of patients with leukaemia in Qidong during the 40-year study period was 8.23 and 13.28% in 2003-2007, which is very low as compared with that in the United States (50%) (73), and in the European countries (42.4%), but higher than that in the Philippines (2.7%) (54). The 5-year survival outcomes of leukaemia are varied worldwide with comparable poor results (2005-2009) identified in registries in India (6.0%), Libya (6.2%), and Jordan (7.1%); improved results have been reported in Cyprus (61.3%), Belgium (59.4%) and Sweden (59.2%) (12).

Stage is the most important factor determining survival, as optimal and 'curative' treatment may only be offered to patients

diagnosed at an early enough stage to benefit from it (74). In a SEER study (75), the 5-year relative survival for those diagnosed at early stage (stage I) was very good (100% for all ethnicities combined), but if metastatic disease is diagnosed (stage IV), survival drops rapidly, revealing the effect of early-stage diagnosis on the prognosis. However, in the current population-based cancer registration series, stage information was sporadically available, which is a common problem in population-based cancer registries worldwide (76). This may restrict our stage analysis but does not limit the assessment of the general changes in the survival rates, particularly the long-term survival rates of cancers in the population-based covered area. Another limitation of the present study is the possible errors in diagnosis in the first year of registration (77), but this effect would be minimal over the 40-year dataset, and for period comparison, the use of 1973-1977 data should be an optimum baseline of survival.

In conclusion, survival analyses from the present updated dataset, now spanning four decades, have described the short and long-term survival effects for the most prevalent cancer sites. Such population-based analyses may aid the evaluation of the current and future impacts of comprehensive health services on cancer detection and treatment in Qidong, and other undeveloped areas in China. From the present findings, we have revealed that there is a large gap in cancer survival rates between the Qidong region and other settings from developed areas in China and in developed countries. The improving trends in survival of most cancers that have gradually occurred in Qidong during the past four decades may accelerate with the advent of precision oncology for screening, early diagnosis and treatment in an efficient, effective and affordable manner for all populations, and particularly underserved populations. Greater effort is required to improve the survival rates of all cancer types.

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