Survival differences between the USA and an urban population from China for all cancer types and 20 individual cancers: a population-based study

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Summary

Background The systematic comparison of cancer survival between China and the USA is rare. Here we aimed to assess the magnitude of survival disparities and disentangle the impact of the stage at diagnosis between a Chinese metropolitan city and the USA on cancer survival.

Methods We included 11,046 newly diagnosed cancer patients in Dalian Cancer Registry, China, 2015, with the follow-up data for vital status until December 2020. We estimated age-standardised 5-year relative survival and quantified the excess hazard ratio (EHR) of death using generalised linear models for all cancers and 20 individual cancers. We compared these estimates with 17 cancer registries' data from the USA, using the Surveillance, Epidemiology, and End Results database. We further estimated the stage-specific survival for five major cancers by region.

Findings Age-standardised 5-year relative survival for all patients in Dalian was lower than that in the USA (49.9% vs 67.9%). By cancer types, twelve cancers with poorer prognosis were observed in Dalian compared to the USA, with the largest gap seen in prostate cancer (Dalian: 55.8% vs USA: 96.0%). However, Dalian had a better survival for lung cancer, cervical cancer, and bladder cancer. Dalian patients had a lower percentage of stage I colorectal cancer (Dalian: 17.9% vs USA: 24.2%) and female breast cancer (Dalian: 40.9% vs USA: 48.9%). However, we observed better stage-specific survival among stage I-II lung cancer patients in Dalian than in the USA.

Interpretation This study suggests that although the overall prognosis for patients was better in the USA than in Dalian, China, survival deficits existed in both countries. Improvement in cancer early detection and cancer care are needed in both countries.

Abbreviations: AJCC, American Joint Committee on Cancer; CI, Confidence interval; EHR, Excess hazard ratio; GDP, Gross Domestic Product; ICD-10, International Classification of Diseases 10th Revision; ICD-O-3, International Classification of Diseases for Oncology, 3rd edition; ICSS, International Cancer Survival Standards; SEER, Surveillance, Epidemiology and End Results; TNM, Tumour-Node-Metastasis; The USA, The United States

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Keywords: 5-year relative survival; Population-based study; Urban China, Dalian; The United States

Research in context

Evidence before this study

Population-based survival comparison is important to assess the overall effectiveness of a cancer care system. Without setting language or date restriction, we searched PubMed, Web of Science, Google Scholar, and China Academic Journals database for papers and their references using "cancer survival", "population-based", or "comparison". Several studies reported marked differences between developed countries and developing countries. It was also reported that within China, survival gaps existed between urban and rural areas. To explain the survival differences, the information on the stage at diagnosis may help to investigate whether differences in cancer survival can be explained by early detection. However, information on the stage at diagnosis and survival is rarely available in population-based cancer registries in developing countries including China. There is still a lack of systematic survival comparisons between China and the USA using the updated population-based cancer survival statistics including detailed information on stage at diagnosis.

Added value of this study

We provided the first systematic and timely population-based study that presents direct international survival comparison for all cancers and 20 individual cancers in a metropolitan city in China and the USA. Our study showed that age-standardised 5-year relative survival for all cancer types combined and twelve individual cancer types was lower in Dalian, China than in the USA. However, survival was higher for lung cancer, cervical cancer, and bladder cancer in Dalian, China than in the USA. International differences in lung cancer and colorectal cancer survival are partly explained by differences in stage at diagnosis, and partly by differences in stage-specific survival. Whereas for female breast cancer survival, disparities are mainly by the differences in stage at diagnosis.

Implications of all the available evidence

The study results contribute to the evidence base for the policy of cancer control in both China and the USA. Our study highlights the importance of access to diagnostic and therapeutic facilities.

Introduction

Population-based cancer survival reflects the overall prognosis of cancer patients and provides important information on the effectiveness of a cancer care system including diagnostic tools and treatment. Population-based national survival studies have been systematically reported in the United States (USA), Europe, and other developed countries such as England.[1–3] There were several collaborative projects for international survival comparisons of some individual cancers, such as CONCORD-3,[4] EUROCARE-5,[2] SURMARK-2,[5] and SURVCAN-3.[6] Existing studies have shown that marked differences exist between high-income countries and middle/low-income countries. Though cancer survival has improved in many countries, the gap between middle/low-income countries and high-income countries remains wide. China and the USA, represent two countries with differences in socioeconomic status, cancer profile, cancer biology, use of screening, stage at diagnosis, and access to high-quality cancer treatment care. Quantifying the magnitude of survival disparities and understanding their potential mechanisms may provide important evidence to improve the cancer care system and help to design more effective interventions to minimize survival disparities.

The latest survival statistics showed that the age-standardised 5-year relative overall cancer survival was 40.5% in 2012–2015 based on population-based cancer registries in China,[7] which was much lower than that in the USA.[8] It was also reported that survival gaps existed between urban and rural areas within China.[7] Contributors to the survival differences are perceived to vary across the regions. Stage at diagnosis is a key prognostic factor. Comparisons of stage-specific survival can partially explain the disparities, which have been reported in many developed countries or regions.[9–11] However, population-based cancer registries in developing countries including China do not routinely collect information on the stage at diagnosis. Therefore, there is still a lack of systematic and in-depth comparison of cancer survival between developed countries and developing countries including stage at diagnosis.[12–14]

Dalian is one of the most economically developed cities in northeast China. Dalian Cancer Registry has been collecting population-based cancer incidence data since the 1980s. In 2008, Dalian Cancer Registry developed an electronic data management system for data abstraction and reporting, which enabled the updated collection of detailed information on stage at diagnosis. As one of three representative urban areas for the latest Chinese national cancer survival report,[15] the population-based cancer survival data from Dalian was included in the CONCORD-3 program, a worldwide comparative analysis of cancer survival. However, previous survival data from Dalian Cancer Registry were collected only based on passive follow-up methods, which resulted in less reliable estimates of survival due to incomplete follow-up.[7,15]

In this study, we leveraged the updated population-based cancer survival data using both passive follow-up and active follow-up methods in Dalian Cancer Registry. This is the most updated and systematic examination of cancer survival between China and the USA using population-based cancer registry data including stage at diagnosis, with standardised quality control and analytic methods. We aimed to compare the survival for all cancer types and 20 individual cancers in Dalian with the USA. We further compared the distribution of stage at diagnosis and stage-specific survival for five major cancers (lung cancer, colorectal cancer, thyroid cancer, female breast cancer, and stomach cancer) between the regions.

Methods

Study population and data collection

Dalian is located in northeast China and has a massive population of over 2.3 million. Especially, the Per Capita Disposable Income in Dalian ($5816) was higher than the national average ($3486), but much lower than that in the USA in 2015 ($41,382) (Supplementary Table S1). This study included patients who were newly diagnosed with cancer in 2015 from Dalian population-based cancer registry. We collected patients' demographic information, primary tumour site, tumour morphology, and stage at diagnosis, and obtained their vital status as of December 31, 2020. Institutional Review Board approval for this study was granted by the Ethics Committee of National Cancer Center/Cancer Hospital, Chinese Academy of Medical Science and Peking Union Medical College. The patients' survival status was annually updated by linking their identifiable information to the Dalian Vital Statistic System, and we classified the linked cases as deceased patients.[16] We also linked patients' information to the Dalian Civil Registration system, the health insurance system, and hospital medical records. In these datasets, the successful linkage of patient records was considered as evidence that the patient was alive on a particular date. We further actively followed up on the unlinked cases by contacting the patients or their families to determine their vital status. Patients who could not be followed up by both passive and active methods were classified as lost to follow-up. The proportion of patients who were lost to follow-up was 0.3% (Supplementary Figure S1).

Cancer records in Dalian Cancer Registry were coded according to the International Classification of Diseases for Oncology, 3rd edition (ICD-O-3) and the International Statistical Classification of Diseases 10th Revision (ICD-10). We used the Tumour-Node-Metastasis (TNM) staging system (7th edition) of the American Joint Committee on Cancer (AJCC) for stage abstraction.[17] Information on stage was extracted from the diagnostic records, imaging tests, pathological reports, surgical records, and hospital discharge records from local hospitals in Dalian, China. Stage at diagnosis was determined based on the pathological stage data if available. Otherwise, the clinical stage at diagnosis was used. If both were unavailable, we identified the cases with the unknown stage.

We included newly diagnosed cancer patients with the first invasive, malignant primary tumour, and excluded patients younger than 15 years. We further excluded the patients diagnosed with carcinoma in situ given that "in situ cancer registration is not mandatory according to the Chinese Cancer Registration Guidelines.[18,19] Registry staff routinely checked and verified patient data using CanReg4 software.[20] We also adopted a rigorous quality control process to quantify the registration data and vital status of each record. First, we examined the adherence of the dataset to protocol and the distribution of variables. We considered values that were out of range as errors and double-checked with the cancer registry staff. Second, we applied standardised quality control to the submitted records according to the International Agency for Research on Cancer guideline.[21] Impossible combinations (eg: sex-site errors, invalid dates, and impossible date sequence) were classified as errors and sent back to the registry for clarification or correction. We used the same procedures to recheck the resubmitted cases. Cases that still had other invalid, missing or inconsistent values were marked as errors and excluded from the analyses. Patients (0.3%) with unknown vital status were also excluded.

We obtained patients' data in the USA from 17 population-based cancer registries in the Surveillance, Epidemiology and End Results (SEER) program, covering approximately 26.5% of the USA population using the same data inclusion criteria as Dalian's data. These registries are from Alaska Native Tumour Registry, Connecticut, Atlanta, Greater Georgia, Rural Georgia, San Francisco-Oakland, San Jose-Monterey, Greater California, Hawaii, Iowa, Kentucky, Los Angeles, Louisiana, New Mexico, New Jersey, Seattle-Puget Sound, Utah. We included cancer patients diagnosed in 2014 with follow-up data until December 2019 in the SEER database because they were diagnosed in the closest period and had been followed up for at least full 5 years as the patients from Dalian, China (the closet period for such data that are available) (Supplementary Figure S1). The survival outcomes of patients were obtained using passive and active follow-up methods. In passive follow-up, cancer registry staff obtained patients' vital status by linking the records from vital statistics, hospital admission, outpatient records, and health information management departments without directly contacting the patients. The cancer registry staff further actively followed up with the patients or family members by using telephone or home visits. For each case, we retrieved detailed information including area, age at diagnosis, year of diagnosis, AJCC 7th edition staging information, vital status, and survival. We used the same protocol of data extraction, standardised quality control, and a single, centralised analysis for individual records both from Dalian and the SEER database.

Statistical analysis

We estimated 5-year relative survival for all cancer types combined and separately for each cancer type. Relative survival was calculated using the cohort approach, as the ratio between the observed survival of cancer patients and the expected survival of the general population in the registry's territory. Observed survival was estimated using the life table method, and expected survival was estimated using regional life tables by the Ederer II method.[22] Abridged life table for all-cause mortality by sex, 5-year age group and calendar year in Dalian, China was provided by Dalian Center for Disease Control and Prevention and then smoothed to complete life table by a single year of age using the Elandt-Johnson method.[23] Complete life table by sex, race, single year of age, and calendar year in the USA was obtained from the SEER program by using SEER*Stat software (version 8.4.1). We calculated 95% confidence interval (CI) for relative survival using the Greenwood method.[24] To account for a possible difference in the age profile of patients, relative survival was age-standardised according to the International Cancer Survival Standards weights, using five age groups (15–44, 45–54, 55–64, 65–74, and 75+).[25] We calculated the absolute difference in survival between Dalian, China and the USA to quantify the survival gaps. We further calculated the excess hazard ratio (EHR) for death (Dalian, China versus the USA as a reference) and tested the statistical differences for significance between Dalian and the USA using generalised linear models assuming a Poisson error structure, adjusted for sex and age. We tested the statistical difference for relative survival after adjusting for age in a poisson regression model.[26] The advantage of estimating the model in the framework of generalised linear models based on collapsed data using exact survival times and Poisson assumption is that we have access to a rich theoretical framework and can utilize regression diagnostics.[27] Implementation of this approach is user-friendly in *strs* in Stata (version 16) for survival analysis. In the calculation of the EHR, we assumed that the hazard was constant within the pre-specified bands of the time.

For patients with missingness on stage, we assumed that the stage was missing at random, and imputed this variable using multiple imputation with chained equations.[28] We first used χ^2 tests to evaluate the association between the candidate covariates and stage distribution as well as the missingness of stage (Supplementary Tables S2 and S3). We further reviewed the existing publications on imputation of missing values of cancer stage in population-based cancer registration.[10,29–32] We selected the variables for the imputation model based on any of the three reasons: 1) variables were associated with stage completeness; 2) variables were associated with stage distribution; 3) variables were included in the multiple imputation model in previous studies. Therefore, the variables we included in the multiple imputation were: age, sex, marital status, race (USA only), survival time, vital status, cancer type, the Nelson-Aalen estimator, and the non-linear effect of age at diagnosis (Supplementary Table S4).[10,33] We ran the imputation model 50 times for the USA and Dalian, China separately and combined estimators for each imputed dataset using Rubin's rules.[33]

To further evaluate the age-standardised relative survival between cancer patients from Dalian and those who were Asian Americans from the USA, we restricted the SEER dataset by including the cancer patients of non-Hispanic Asian/Pacific Islander only. We considered counties in metropolitan areas to be urban areas of the USA and compared the survival statistics in urban areas of the USA with Dalian as well.

We conducted several supplementary analyses. First, to adjust for the potential impact of the different profiles in cancer type in the comparison of survival for all cancers combined between two countries, we constructed an all-cancer survival index with a weighted average for each combination of sex, cancer type, and age group (15–44, 45–54, 55–64, 65–74, and 75+ years) using patients' data from the USA, assuming that the age, sex, and cancer type distribution of the Dalian cancer patients had been the same as that of the standard weights derived from the USA distribution. Second, to evaluate whether using a different standard may introduce significant changes in the results, we further constructed another all-cancer survival index with a weighted average for each combination of sex, cancer type, and age group (15–44, 45–54, 55–64, 65–74, and 75+ years) using patients' data from both Dalian, China and the USA. Third, to test whether multiple imputation under the missing at random assumption may introduce any bias in the results, we presented the distribution of stage and estimated the stage-specific survival for five major cancer types by including patients with unknown stage at diagnosis without multiple imputations. We further used the pattern-mixture model approach to conduct multiple imputation under the assumption of missing not at random. Fourth, to test whether the EHRs were constant over time between Dalian and the USA, we further presented 1-, 3-year relative survival and corresponding EHRs for death (Dalian, China versus the USA as a reference). Fifth, we further adjusted for stage distribution among five major cancers, to compare the survival assuming the stage distribution was the same between the two populations.

We used R software (version 4.1.2) for descriptive analyses.[34] We conducted survival analyses and multiple imputation in Stata (version 16.0).[29,35] We conducted multiple imputation under the mechanism of missing not at random using the pattern-mixture model in SAS (version 9.4).[36] All statistical tests were two-sided, and P-value less than 0.05 were considered statistically significant.

Role of the funding source
The funding sources of the study had no role in study design, data collection, data analysis, data interpretation or report writing. The corresponding author has full access to all the data and is responsible for the decision to submit and publish the paper.

Results

Our study included 11,046 cases from Dalian, China and 312,069 cases from the USA (Table 1, Supplementary Figure S1). The proportion of cancer types was different between Dalian, China and the USA. The five major cancers in Dalian, China (lung cancer, colorectal cancer, thyroid cancer, female breast cancer and stomach cancer) accounted for 61.4% (6787/11,046) of the patients (Supplementary Table S5). In the USA, the proportion of these cancer types comprised 41.6% (129,942/312,069) of all cases. The mean age at diagnosis was similar in all cancer types combined and most individual cancer types, with the exception of prostate cancer and brain cancer. Patients with prostate cancer at diagnosis in the USA (66.2 ± 9.2) were much younger than those in Dalian (75.9 ± 8.3), China. The proportion of men patients was similar for all cancer types combined in Dalian, China (51.4%) and the USA (49.2%).

The age-standardised 5-year relative survival and EHRs overall and by cancer type in Dalian, China and the USA are shown in Fig. 1 (Supplementary Table S6). For all cancer types combined, the age-standardised 5-year relative survival was 18.0% lower for patients in Dalian, China (49.9%, 95% CI: 48.9%–51.0%) than in the USA (67.9%, 95% CI: 67.7%–68.1%) (P < 0.001), corresponding to an EHR of 1.9 (95% CI: 1.8–1.9). By sex, for all cancers combined, age-standardised 5-year relative survival for patients in men was 41.6% (95% CI: 40.2%–43.1%), which was lower than for women patients (58.2%, 95% CI: 56.7%–59.7%) (P < 0.001) (Supplementary Figure S2). By cancer type, Dalian, China had lower age-standardised 5-year relative survival than the USA for female breast cancer, kidney cancer, lymphoma, colorectal cancer, prostate cancer, leukaemia, oral cavity and pharynx cancer, brain cancer, gallbladder cancer, liver cancer, oesophageal cancer, and pancreatic cancer (P < 0.05), in which the absolute differences ranged from 2.3% in brain cancer to 40.2% in prostate cancer. Especially, prostate cancer patients in Dalian, China had more than a 5-fold of risk of death, compared with those in the USA (EHR 6.1, 95% CI: 4.2–8.9). However, patients had a higher survival for bladder cancer, cervical cancer, and lung cancer in Dalian, China than in the USA (P < 0.05), with an absolute difference of 20.0% in bladder cancer, 4.6% in cervical cancer and 14.2% in lung cancer. No significant differences in 5-year survival were found for cancers of the thyroid, uterus, larynx, ovary, and stomach between the two study populations.

We further compared the age-standardised 5-year relative survival and EHRs overall and by cancer type in Dalian, China, in Asian American population from the USA, in urban population from the USA (Fig. 2). The number and characteristics of cancer patients from Asian Americans and the USA urban population are shown in Supplementary Table S7. Age-standardised 5-year relative survival was lower for patients in Dalian, compared to patients from Asian Americans (63.2%, 95% CI: 62.5%–64.0%) and the USA urban population (68.7%, 95% CI: 68.5%–68.9%), but higher than that in 17 cancer registries of China (40.5%, 95% CI: 40.3%–40.7%) (Supplementary Table S8).

Given that stage at diagnosis is an important prognostic factor of cancer, we further presented the distribution of stage at diagnosis for the five major cancer types in Dalian, China and the USA (Supplementary Table S9). Patients in the USA generally had a higher proportion of known stage at diagnosis than those in Dalian, China. The proportion of unknown stage ranged from 3.3% to 13.1% for five major cancers in the USA, whereas in Dalian, China, it ranged from 11.9% to 38.7%. After multiple imputation for unknown stage at diagnosis (Fig. 3, Table 2), Dalian, China had a higher proportion of stage I lung cancer patients than the USA (29.6% vs 18.3%). However, advanced-stage (stage III/IV) colorectal cancer and female breast cancer were more common in Dalian, China than in the USA. Stage-specific survival differed across cancer types between the two populations (Fig. 4). For example, 5-year survival for patients with stage I lung cancer was higher in Dalian, China (79.5%, 95% CI: 77.1%–81.8%) than in the USA (67.9%, 95% CI: 67.6%–68.2%) (P < 0.001). However, the 5-year survival for stage III colorectal cancer was higher in the USA (68.1%, 95% CI: 67.8%–68.3%) than in Dalian, China (58.6%, 95% CI: 56.4%–60.7%) (P < 0.05).

In the supplementary analysis, given that the cancer profile may be different in Dalian, China and the USA,

Cancer site	Number (%)		Mean age at diagnosis (standard deviation)		Sex (men), N (%)	
	Dalian	USA	Dalian	USA	Dalian	USA
Oral cavity and pharynx	141 (1.3)	7791 (2.5)	61.9 (13.2)	62.4 (12.6)	105 (74.5)	5643 (72.4)
Oesophagus	188 (1.7)	2929 (0.9)	64.9 (10.9)	66.5 (11.8)	172 (91.5)	2308 (78.8)
Stomach	943 (8.5)	5264 (1.7)	68.1 (12.7)	65.7 (14.3)	636 (67.4)	3240 (61.6)
Colorectum	1275 (11.5)	29,360 (9.4)	68.1 (12.4)	64.5 (14.2)	773 (60.6)	15,251 (51.9)
Liver	746 (6.8)	7413 (2.4)	64.4 (12.9)	64.5 (10.9)	549 (73.6)	5378 (72.5)
Gallbladder	145 (1.3)	2257 (0.7)	71.3 (12.1)	68.8 (12.8)	78 (53.8)	999 (44.3)
Pancreas	314 (2.8)	9094 (2.9)	70.8 (11.9)	68.5 (12.8)	180 (57.3)	4676 (51.4)
Larynx	69 (0.6)	2071 (0.7)	63.0 (10.2)	64.4 (11.0)	66 (95.7)	1678 (81.0)
Lung	2501 (22.6)	34,984 (11.2)	68.3 (12.0)	68.9 (11.1)	1449 (57.9)	18,211 (52.1)
Female breast	1003 (9.1)	49,214 (15.8)	56.7 (12.8)	60.6 (13.5)	–	–
Cervix	247 (2.2)	3077 (1.0)	53.4 (12.2)	50.2 (15.0)	–	–
Uterus	175 (1.6)	11,547 (3.7)	58.8 (12.1)	61.5 (11.8)	–	–
Ovary	135 (1.2)	4683 (1.5)	58.7 (12.7)	61.3 (15.5)	–	–
Prostate	206 (1.9)	40,209 (12.9)	75.9 (8.3)	66.2 (9.2)	206 (100.0)	40,209 (100.0)
Kidney	431 (3.9)	11,605 (3.7)	63.1 (12.9)	62.6 (13.4)	294 (68.2)	7389 (63.7)
Bladder	315 (2.9)	6108 (2.0)	69.4 (12.3)	71.8 (11.9)	245 (77.8)	4565 (74.7)
Brain	128 (1.2)	4252 (1.4)	63.0 (14.8)	56.4 (18.0)	70 (54.7)	2455 (57.7)
Thyroid	1065 (9.6)	11,120 (3.6)	48.1 (12.7)	49.1 (15.4)	268 (25.2)	2589 (23.3)
Lymphoma	247 (2.2)	22,769 (7.3)	63.9 (13.9)	64.0 (16.7)	139 (56.3)	12,690 (55.7)
Leukaemia	145 (1.3)	11,479 (3.7)	60.6 (17.7)	63.5 (17.4)	83 (57.2)	6377 (55.6)
All others	627 (5.7)	34,843 (11.2)	66.3 (15.1)	60.4 (17.7)	360 (57.4)	19,729 (56.6)
All cancer sites	11,046 (100.0)	312,069 (100.0)	63.9 (14.4)	63.3 (14.5)	5673 (51.4)	153,387 (49.2)

Table 1: **Number and characteristics of patients included in the survival analysis in Dalian, China and the USA.**

we further estimated the 5-year relative survival with the adjustment for sex, age and cancer profile using patients' data from the USA. We found the overall age-standardised 5-year relative survival was still higher in the USA than in Dalian, China, where the survival gap narrowed after adjusting for the cancer profile. Using the weight from a combined dataset from both the USA and Dalian registries did not materially change the results (Supplementary Table S10). We also presented stage-specific survival without multiple imputation (Supplementary Table S11). We found the multiple imputation did not materially change the results of the stage-specific survival. By assuming the missing mechanism as missing not at random, the results of multiple imputation did not change the conclusions (Supplementary Table S12).

To test whether the EHRs were constant over time between Dalian and the USA, we further presented age-standardised 1-, 3-year relative survival and corresponding EHRs. The results further supported our assumption that the EHRs were constant over time (Supplementary Table S13). By assuming the stage distribution was the same between Dalian and the USA, we further presented age- and stage-adjusted relative survival of five cancers. We consistently found that the 5-year relative survival for lung cancer was better in Dalian than in the USA (Supplementary Table S14).

Discussion

To our knowledge, this is the most comprehensive and up-to-date study on the direct comparison of survival for all cancer types and 20 individual cancer types between a metropolitan city in China and the USA. We systematically assessed the magnitude of survival disparities and disentangled the impact of the stage at diagnosis on cancer survival. We found there were survival advantages in the USA for twelve cancer types, with an absolute difference ranging from 2.3% to 40.2%. However, survival is similar or even slightly worse for the other eight cancer types in the USA. Survival disparities were mainly driven by the stage at diagnosis for lung cancer, female breast cancer and colorectal cancer. Given that early diagnosis is possible for these cancers, our study highlights the importance of screening and early detection of these cancers in high-risk populations both in China and the USA. By improving access to health care, including cancer screenings and follow-up care, international cancer survival disparities can be narrowed.

The quality and completeness of cancer registration data and follow-up are prerequisites for accurate estimates. Incomplete follow-up and failure to capture all incident cases may bias survival comparisons.[37] Previously, Dalian's data on population-based cancer survival were collected entirely by passive follow-up. The incomplete follow-up yielded less reliable estimates.[4,38]

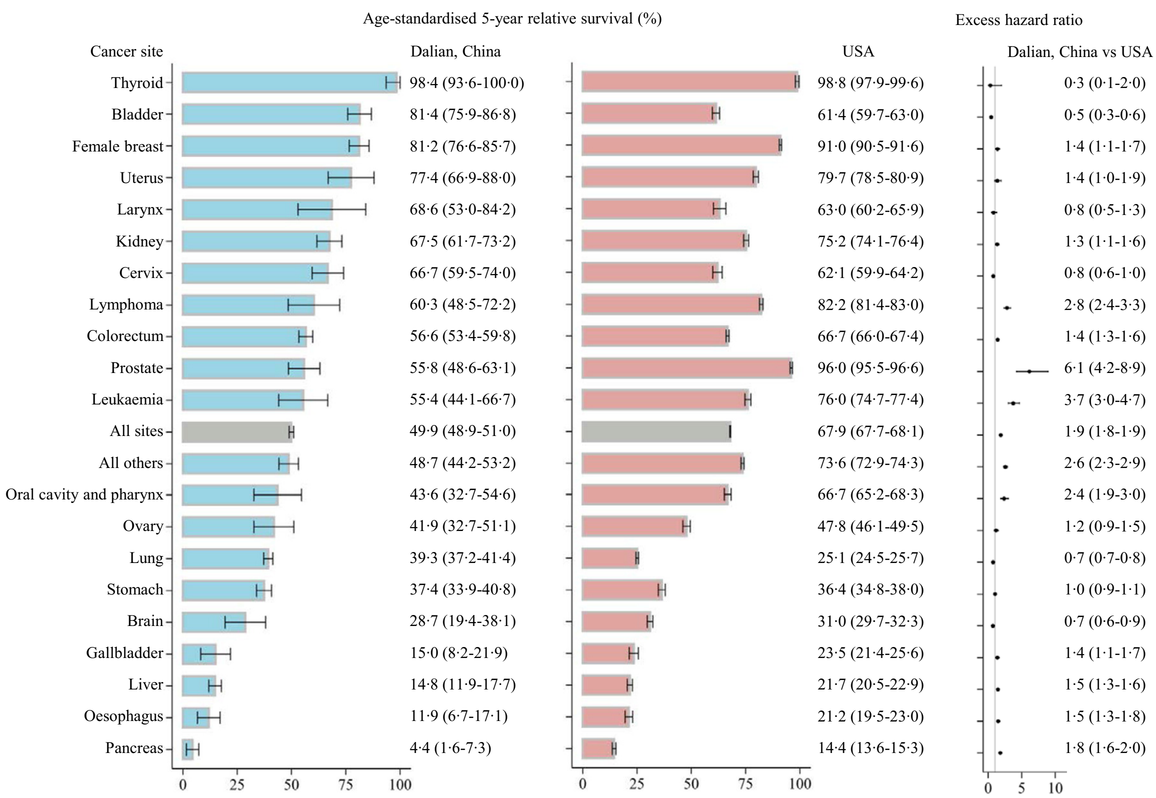
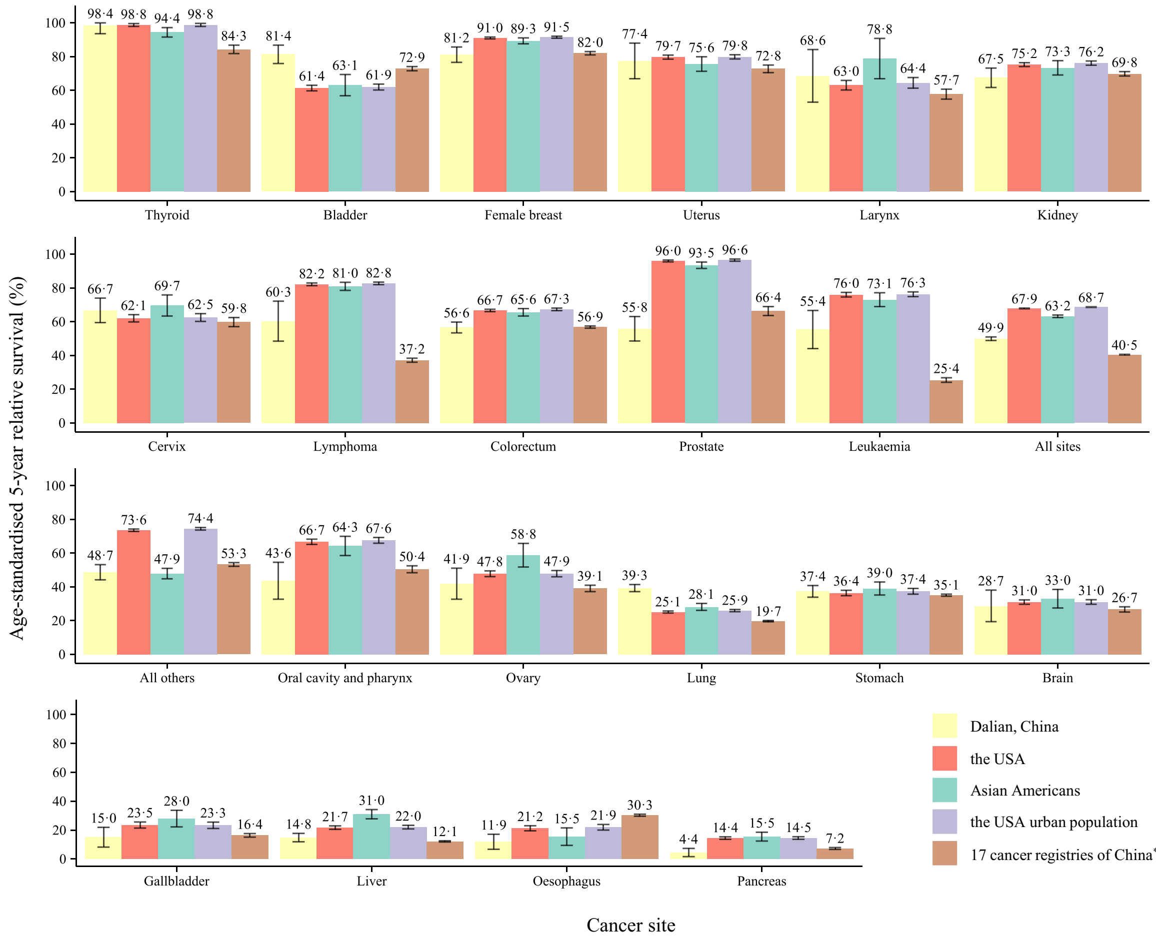


Fig. 1: Age-standardised 5-year relative survival in cancer patients from Dalian and the USA, overall and by cancer type.

To address this issue, we used both active and passive follow-up methods to obtain the patients' vital status. We used the same protocol, standardised quality control, and a centralized analysis for individual records. After extensive checks on data quality, the proportion of incomplete follow-up dropped substantially.[39] In our study, we found the 5-year cancer survival in Dalian ranging from the highest for thyroid cancer to the lowest for pancreatic cancer, which is plausible. The survival patterns across cancer types and by stage at diagnosis are similar to the most existing results,[7] which further speaks for the reliability of our study results.

In China, population-based cancer survival has been recognised as a key indicator for the overall effectiveness of the health systems. The national plan of "Healthy China 2030" had issued the overarching goal of cancer control using the age-standardised 5-year relative survival estimate for all cancer types combined as a measure of monitoring the progress of cancer control.[40] The index of relative survival for all cancer types combined provides a convenient number that summarises the overall patterns of cancer survival in a population. For the first time, we systematically reported the 5-year survival for all-cancers and 20 individual cancers in Dalian and made comparisons with the USA, which will inform what priorities of research and health policy should be made in these regions. Compared with the average level of urban Chinese cancer patients, we found overall cancer patients in Dalian had a better survival advantage (49.9% vs 46.7%) (Supplementary Table 15).[7] However, compared with the USA, we found a poorer survival for all cancer types combined in Dalian, China. Considering that the profiles of cancer types might affect the comparison of survival for all cancers combined, we assumed if the age, sex, and cancer type distribution of the Dalian cancer patients had been the same as that of the USA patients, we found the weighted all-cancers survival in Dalian, China was still worse than the USA. Moreover, the sensitivity analysis by using a different weight of all cancers combined did not introduce material change in the results, indicating the robustness of our findings. Our results indicated overall better management of these cancer types in the USA than in Dalian, China, wherein from cancer early diagnosis to improved treatment and care. The quality of cancer management is influenced markedly by health-related investments. For instance, the expansion of the Medicaid program in the USA has been shown to be associated with an increased proportion of patients receiving active surveillance and with



*: Data was extracted from Zeng et al study (Lancet Glob Health 2018; 6: e555–67)

Fig. 2: Age-standardised 5-year relative survival in cancer patients from Dalian, the USA, the Asian American population, the urban population from the USA, and 17 cancer registries of China.

early-stage disease,[41,42] which resulted in improved survival. In 2016, the overall health-related investment was markedly higher in the USA than in China,[43] or in Dalian, China.[44] Therefore, increasing investments in human and financial resources for cancer management needs to be strengthened.

The stage at diagnosis is an important factor for cancer prognosis, which can be markedly improved by early detection and screening programmes as well as diagnostic procedures. Studies have also shown that the stage at diagnosis partly explains international differences in cancer survival.[45,46] Screening for colorectal cancer and breast cancer has been proven effective in detecting cancer at an early stage and reducing the burden of the disease.[46,47] We observed higher proportions of early-stage female breast cancer and colorectal cancer in the USA than in Dalian, China, indicating that disparities in early detection contribute to the between-region survival disparities for these cancers. In the USA, 76.4% of women aged 50–74 years had a mammogram, which allows for the earlier detection of breast cancer, which, if followed by timely treatment, can help reduce deaths due to the disease. For colorectal cancer, 67.1% of adults who were 50–75 years old had received colorectal cancer screening based on the most recent guidelines.[48] However, in Dalian, China, there were no large-scale colorectal cancer and breast cancer screening programmes during the same period, which may partially explain the diagnostic and survival disparities for breast cancer and colorectal cancer. The slightly better survival may also in part be attributable to the disparities in treatment practice for patients with advanced-stage colorectal cancer in the USA, given that we observed better prognosis in patients with stage III colorectal cancer in the USA.

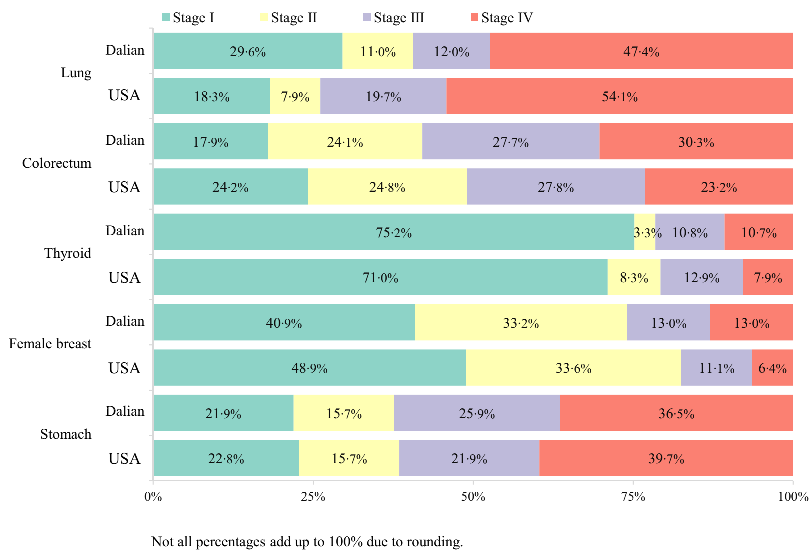


Fig. 3: Stage distribution after the multiple imputation for the five major cancer types in Dalian and the USA.

Cancer site	Stage	Stage distribution (%, 95% CI)		Age-standardised 5-year survival (%, 95% CI)		
		Dalian	USA	Dalian	USA	P-value
Lung						
	I	29.6 (27.6–31.6)	18.3 (17.8–18.7)	79.5 (77.1–81.8)	67.9 (67.6–68.2)	<0.001
	II	11.0 (9.6–12.5)	7.9 (7.6–8.1)	61.5 (57.5–65.5)	44.9 (44.3–45.4)	<0.001
	III	12.0 (10.2–13.7)	19.7 (19.3–20.2)	20.2 (17.1–23.8)	23.5 (23.3–23.8)	0.037
	IV	47.4 (44.9–49.9)	54.1 (53.6–54.7)	6.8 (6.0–7.7)	6.2 (6.1–6.2)	<0.001
	Overall	100.0	100.0	39.3 (37.2–41.4)	25.1 (24.5–25.7)	<0.001
Colorectum						
	I	17.9 (15.5–20.4)	24.2 (23.7–24.7)	91.6 (86.6–95.3)	92.9 (92.6–93.2)	0.399
	II	24.1 (21.4–26.9)	24.8 (24.3–25.4)	84.3 (80.2–87.9)	83.6 (83.4–83.8)	0.645
	III	27.7 (24.9–30.5)	27.8 (27.3–28.4)	58.6 (56.4–60.7)	68.1 (67.8–68.3)	0.010
	IV	30.3 (27.5–33.0)	23.2 (22.7–23.6)	11.4 (9.8–13.2)	13.8 (13.6–14.0)	0.665
	Overall	100.0	100.0	56.6 (53.4–59.8)	66.7 (66.0–67.4)	<0.001
Thyroid						
	I	75.2 (72.4–78.0)	71.0 (70.2–71.9)	99.0 (98.6–99.3)	99.0 (99.0–99.0)	<0.001
	II	3.3 (2.0–4.6)	8.2 (7.7–8.8)	88.2 (45.8–99.9)	99.0 (98.9–99.1)	0.319
	III	10.8 (8.8–12.8)	12.9 (12.3–13.5)	98.8 (96.2–99.8)	99.0 (98.9–99.1)	0.130
	IV	10.7 (8.8–12.7)	7.9 (7.3–8.4)	72.9 (60.7–83.9)	66.7 (65.9–67.4)	<0.001
	Overall	100.0	100.0	98.4 (93.6–100.0)	98.8 (97.9–99.6)	0.224
Female breast						
	I	40.9 (37.6–44.1)	48.9 (48.5–49.3)	98.2 (91.7–99.8)	99.0 (99.0–99.0)	0.091
	II	33.2 (30.1–36.2)	33.6 (33.2–34.0)	94.5 (90.5–97.2)	91.9 (91.7–92.1)	<0.001
	III	13.0 (10.7–15.2)	11.1 (10.8–11.4)	64.3 (56.4–72.2)	69.2 (68.8–69.6)	0.309
	IV	13.0 (10.7–15.3)	6.4 (6.2–6.6)	32.2 (28.4–36.3)	28.7 (28.3–29.2)	0.337
	Overall	100.0	100.0	81.2 (76.6–85.7)	91.0 (90.5–91.6)	0.002
Stomach						
	I	21.9 (18.9–24.9)	22.8 (21.6–24.0)	76.6 (72.7–80.2)	76.1 (75.4–76.9)	0.553
	II	15.7 (13.1–18.4)	15.7 (14.6–16.7)	58.1 (51.9–64.5)	56.8 (55.4–58.2)	0.576
	III	25.9 (22.5–29.3)	21.9 (20.7–23.1)	33.0 (29.5–36.8)	29.8 (28.7–30.8)	0.609
	IV	36.5 (32.8–40.2)	39.7 (38.3–41.0)	5.5 (4.2–7.3)	5.2 (4.9–5.6)	0.496
	Overall	100.0	100.0	37.4 (33.9–40.8)	36.4 (34.8–38.0)	0.466

Table 2: **The proportion of stage at diagnosis and age-standardised 5-year relative survival after multiple imputation for five major cancers in Dalian, China and the USA.**

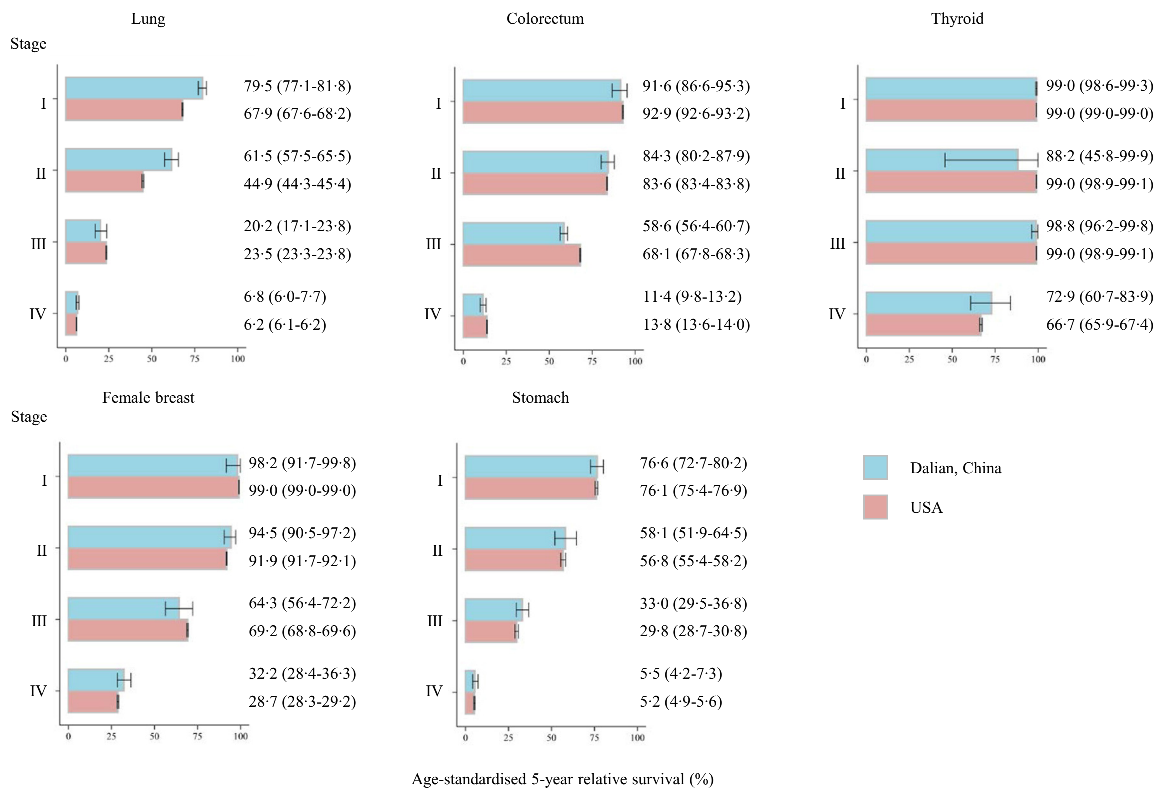


Fig. 4: Age-standardised 5-year relative survival by stage for the five major cancer types in Dalian and the USA after the multiple imputation.

For lung cancer, we observed a higher proportion of early-stage lung cancer in Dalian, China than that in the USA. The stage-specific survival for stage I/II lung cancer was also higher in Dalian, China than in the USA, partially explaining that the better prognosis was attributable both to early detection and treatment of this disease in Dalian, China. Serving nearly half of the cancer patients in Dalian, China, the First Affiliated Hospital of Dalian Medical University initiated lung cancer screening in 2006 and since then has conducted extensive health education on early detection of lung cancer for the residents. Dalian, China also started the health-related education program "Healthy Lifestyle Action" in 2009, which substantially enhanced the population's health awareness. Furthermore, the higher smoking rates among Chinese men than among the USA population,[49,50] may contribute to the greater awareness of lung cancer screening among the Chinese population. However, only 4.5% of adults aged 55–80 years who were at risk for lung cancer due to smoking had a screening by computed tomography in the USA.[48] A previous study also showed that Asian American patients with lung cancer had better survival outcomes compared to the White population within the USA, even after adjustment on smoking status and other factors, suggesting that the biological roles in racial/ethnic disparities cannot be ruled out.[51] In 2020, 20.6% of lung cancer patients underwent surgery nationally in the USA,[52] where the corresponding proportion was 37.0% in the urban areas of China.[53] Taken together, improved cancer awareness, early cancer detection, and better cancer management in Dalian, China may partly contribute to the improved lung cancer early detection and survival in this area.

While using cancer survival as one measure of a health system's effectiveness has merit, it also needs to be interpreted in the context of lead time bias–particularly for those cancer types that are amenable to screening. Survival disparities may be attributable to the difference in the intensity of diagnostic activities, lead-time bias, and to overdiagnosis. Overdiagnosis occurs more often in regions where people have increased accessibility and affordability of health care than in other areas. In the USA, it was estimated that 28% of over-diagnosed patients resulted from prostate cancer screening programs.[54] Whereas in China, PSA screening is not popular and the PSA screening rate is low.[55] Therefore, overdiagnosis may have a large effect on the survival gap for prostate cancer patients between regions. A recent study also reported that China seemed to display the typical epidemiological features of overdiagnosis of thyroid cancer.[56] Similarly, we found the percentage of stage I thyroid cancer was slightly higher in Dalian than that in the USA. Given that ultrasonography was affordable and can detect small and predominantly papillary thyroid tumours,[56] overdiagnosis may play a role in the favourable stage distribution as well as survival for thyroid cancer in both regions.

There are several strengths of our study. First, this is the first comprehensive population-based report that allows for a direct comparison of survival for all cancer types and 20 individual cancer types between Dalian and the USA. This comparison based on population-based cancer registry has important implications for cancer control, allowing us to borrow lessons from each other. The study results contribute to the evidence base for the policy of cancer control in both China and the USA. Our study highlights the importance of access to diagnostic and therapeutic facilities. Second, our study is the first high-resolution data on stage information to compare survival for the five major cancer types in Dalian, China and the USA. The well-established electronic medical reporting system covering the city linked with the Dalian Cancer Registry's electronic data management system allows the automatic routine collection of patients' information on cancer diagnosis. We used the same AJCC 7th edition staging system as the USA SEER database, which helps to elucidate the causes of the international variations in cancer survival between the two regions.

Our study has some limitations. First, this study only included newly diagnosed cancer patients in Dalian, China in a single year, based on a single population-based cancer registry. A multi-centre population-based study for the international comparison will provide more representative results on survival disparities. Nonetheless, the survival estimates reported in this study will serve as a baseline for future comparisons and provide insights into areas of the greatest need. Second, information related to socioeconomic status and detailed cancer treatment modalities is not routinely collected by the Dalian Cancer Registry. Further survival analysis based on the clinical information at the individual level could provide more clues on factors associated with survival gaps. Third, the proportion of unknown stage at diagnosis was higher in Dalian, China than in the USA. Anyhow, we imputed the original datasets for both populations. Multiple imputation under different assumptions of missing mechanism did not significantly alter the comparison results. Fourth, although we established a standardised study protocol for stage abstraction and conducted rigorous quality control, inconsistencies in the staging of cancer might have resulted in stage misclassification.

The comparison of survival estimates between the USA and a metropolitan city in China indicates persisting survival advantage in the USA for many of the most common cancers. Nevertheless, for some cancers, survival is similar or even worse for cancer patients in the USA. The results highlight the importance of cancer control activities for both countries, including early detection and treatment of cancer.

Contributors
Each author's contribution was listed as follows. RF, KS, XW, DM, and HZ drafted the study protocol. RF, KS, XW, JM, SN, TW, and BL contributed to the conception and design of the study. RF, KS, and XW did the data analysis. RF, KS, XW, LA, SZ, LL, SW, RC, KS, and BH contributed to the data quality control. RF, KS, XW, JM, SN, TW, BL, HL, LA, SZ, LL, SW, RC, KS, BH, HL, HW, DL, YW, YL, and QZ contributed to the data collection, data transmission, and data correction after quality control, and checking of the results. RF, KS, XW, HM, QG, FS, HZ, XZ, LL, DM, HZ, and WW drafted the paper and interpreted the results. All authors contributed to data interpretation and rewriting the paper, and reviewed and approved the final version. RF, KS, XW, DM, and HZ had access to the all raw data.

Data sharing statement
The study group welcomes potential collaboration to maximize the use of data. A data dictionary and a detailed study protocol can be reached by contacting the corresponding authors of this paper. Due to Chinese legal restrictions and the current ethical approval for the study, data are not publicly available to share, but the research group can provide descriptive data in table form. Requests can be made to Hongmei Zeng (hongmeizeng@cicams.ac.cn).

Editor note
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Declaration of interests
The authors disclose no conflicts.

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Appendix A. Supplementary data
Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2023.100799.

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