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# Cancer risk assessment on trihalomethanes and haloacetic acids in drinking water of China using disability-adjusted life years

Shenling Pan[a], Wei An[a,*], Hongyan Li[a], Ming Su[a], Jinliang Zhang[b], Min Yang[a]

[a] State Key Laboratory of Environmental Aquatic Chemistry, Research Center for Eco-Environmental Sciences, Chinese Academy of Sciences, Beijing, 100085, China
[b] Department of Environmental Pollution and Health, Chinese Research Academy of Environmental Sciences, Beijing, 100012, China

## HIGHLIGHTS

- The median total cancer risk of THMs and HAAs in drinking water of China was calculated as $7.34 \times 10^{-7}$ DALYs ppy.
- The risk of TCAA was highest among the DBPs considered.
- Ingestion exposure was the most important pathway for the total risk.
- The risk in northeast China and Tianjin was highest.

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## ABSTRACT

The cancer risks from exposure to trihalomethanes (THMs) and haloacetic acids (HAAs) through multiple pathways were assessed based on the result of a water quality survey in 35 major cities of China. To express the risks in disability-adjusted life years (DALYs), the excess cancer incidence estimates were combined with a two-stage disease model for calculation. The median total cancer risk of THMs and HAAs was calculated as $7.34 \times 10^{-7}$ DALYs per person-year (ppy), lower than the reference level of risk ($10^{-6}$ DALYs ppy) set by WHO. The risk from ingestion and inhalation exposures contributed 93.6% and 6.3% of the total risk respectively, while dermal contact made a negligible contribution. The median risk of trichloroacetic acid (TCAA) ($2.12 \times 10^{-7}$ DALYs ppy) was highest among the disinfection by-products (DBPs) considered. The risk ratio of total HAAs (THAA) to total THMs (TTHM) was 1.12. The risk was highest in northeast China while lowest in northwest China. As for the 35 cities, Tianjin had the highest risk while Yinchuan had the lowest. This study attempted to use DALYs for the risk assessment of DBPs, which will provide useful information for risk comparison and prioritization of hazards in drinking water.



## 1. Introduction

Disinfection is a critical step in drinking water treatment to protect public health from pathogenic microbes. Chlorine is the most widely used disinfectant due to its low cost, ease of operation and high efficiency. However, chlorine reacts with natural organic matter to generate disinfection by-products (DBPs) during chlorination. So far, more than one thousand chlorinated DBPs have been reported [1], among which trihalomethanes (THMs) and haloacetic acids (HAAs) are the two most abundant classes on a weight basis [2], thus gaining particular attention and being regulated globally [3]. DBPs could introduce potential health risks of cancers as well as adverse developmental and reproductive effects [4]. An increased incidence of bladder cancer has been most consistently associated with chlorinated drinking water by epidemiologic studies [5].

Risk assessment has now become the most important basis for regulating and prioritizing pollutants in drinking water [6]. However, risks of different pollutants, usually expressed in terms of specific disease endpoints (e.g. cancer, diarrheal disease), cannot be compared directly [7]. To set a common unit for risk, the World Health Organization (WHO) recommends the use of disability-adjusted life years (DALYs) to assess the disease burden caused by environmental risk factors. DALYs is a time-based measure, combining the healthy life lost due to premature mortality and morbidity [8]. Many cancer risk assessments have been conducted on DBPs, but most of them conveyed the risk as the excess cancer

* Corresponding author. Tel.: +86 10 62923475; fax: +86 10 62923541.
*E-mail address:* anwei@rcees.ac.cn (W. An).

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incidence through lifetime exposure [9–16]. Havelarr et al. [17] calculated DALYs for renal cancer due to bromate, the major DBP in the ozone disinfection process. He eliminated morbidity burden, since it was very small compared with mortality burden for renal cancer. However, for some other cancer types (e.g. bladder cancer), morbidity burden usually accounts for a non-ignorable part of the DALY estimate [18]. To completely calculate the cancer risks of DBPs in DALYs, this study introduced the disease model that was designed by WHO for estimating the morbidity burden of cancers [19].

In China, approximately 99.5% of urban water supply systems use chlorine for disinfection [20]. Thus a significant number of people are exposed to DBPs through their lifetimes. Though some regional cancer risk assessments have been conducted for DBPs [11,14], nationwide risk assessment has never been conducted due to the limitation of information regarding the occurrences of DBPs. In this paper, the cancer risks of THMs and HAAs through multiple pathways were estimated and compared using DALYs, based on the nationwide DBP survey in China. This work will be useful in risk comparison and prioritization of hazards in drinking water.

## 2. Materials and methods

### 2.1. Data source

Between December 2009 and May 2012, two large-scale water quality survey activities were carried out across China. Finished water samples were collected in the distribution systems of 127 large drinking water treatment plants (DWTPs) in 35 major cities, as shown in Appendix Fig. A1. The name, location and scale of the cities is provided in Table A1.

Samples were analyzed for THMs and HAAs. The detailed information on sample collection, sample preparation, sample analysis and quality assurance and quality control can be found elsewhere [21]. HAAs have nine species. However, the cancer potency information is only available for dichloroacetic acid (DCAA) and trichloroacetic acid (TCAA). So this study will focus on these two HAAs and four THMs.

### 2.2. Exposure assessment

Since the populations served by the DWTPs are different, the concentration data of DBPs were weighted by the daily water supply of DWTPs, and then characterized by best-fitted statistical distributions. Based on the DBP distributions, an exposure assessment was conducted to evaluate their potential intake through multiple pathways. THMs are kinds of volatile organic compounds, whose health risks from inhalation and dermal exposures during regular indoor activities cannot be ignored [22]. In this study, showering was assumed to be the major activity for inhalation and dermal contact [12]. In contrast, HAAs are non-volatile. Xu et al. [23] measured the inhalation dose of HAAs during showering to be less than 1% of the ingestion dose. Also, the dermal dose of HAAs is expected to be negligible because of their very low skin permeability ($1–3 \times 10^{-3}$ cm/h, pH 7) [24]. So, for THMs, ingestion, inhalation and dermal contact exposures were considered, while for HAAs, only ingestion exposure was considered. Chronic daily intake (CDI) estimates for different pathways were calculated by the following equations [10]:

$$\mathrm{CDI_{ing}} = \frac{C_w \times \mathrm{IR} \times \mathrm{EF} \times \mathrm{ED} \times \mathrm{CF}}{\mathrm{BW} \times \mathrm{AT}} \quad (1)$$

$$\mathrm{CDI_{inh}} = \frac{C_{air} \times R \times t \times F \times \mathrm{EF} \times \mathrm{ED}}{\mathrm{BW} \times \mathrm{AT}} \quad (2)$$

$$\mathrm{CDI_{der}} = \frac{C_w \times A_s \times \mathrm{PC} \times t \times F \times \mathrm{EF} \times \mathrm{ED}}{\mathrm{BW} \times \mathrm{AT}} \quad (3)$$

where $\mathrm{CDI_{ing}}$, $\mathrm{CDI_{inh}}$, $\mathrm{CDI_{der}}$ are CDI values for ingestion, inhalation and dermal pathways (mg/kg/day).

The descriptions and values of all the parameters are summarized in Table A2. The concentrations of THMs in the air ($C_{air}$) were estimated by two-resistance model proposed by Little [25], and the comprehensive formulas were summarized in Table A2. Shower frequency (F) and shower duration (t) were estimated from the shower-habit survey data in one northern city (Shijiazhuang) and two southern cities (Ningbo and Xiamen) to characterize the big difference of shower-habit between northern and southern China. To minimize the biases of possible outliers, 10th, 50th and 90th percentile values of the survey data were used to generate triangular distributions [13].

### 2.3. Calculating the lifetime cancer incidence rates

The lifetime incidence rates (IR) of developing cancer from exposure to different DBPs through different pathways were calculated as Eq. (4). Using an additive model, the total cancer incidence rate (TIR) was calculated as Eq. (5).

$$\mathrm{IR}_{i,j} = \mathrm{CDI}_{i,j} \times \mathrm{SF}_{i,j} \quad (4)$$

$$\mathrm{TIR} = \sum_{i,j} \mathrm{CDI}_{i,j} \times \mathrm{SF}_{i,j} \quad (5)$$

where $i$ = exposure pathway, $j$ = THM or HAA, SF = slope factor.

The summary of slope factors is shown in Table A3. Slope factors are estimated from animal toxicity data by various models, approximating 95% confidence limits. So, the calculated cancer incidence can be interpreted as the upper bound lifetime probability of an individual's developing cancer. Chloroform (TCM), generally regarded as a non-genotoxic carcinogen, is likely to be carcinogenic to humans by all routes of exposure under high-exposure conditions that lead to cytotoxicity and regenerative hyperplasia, otherwise, not likely to be carcinogenic to humans by any route of exposure [26–29]. After the year 2000, EPA proposed a mode of action (MOA) approach (a nonlinear approach) for the risk assessment on TCM, and set a threshold (0.01 mg/kg/day, equal to its RfD), considered protective against cancer risk [29]. However, most risk assessments on TCM still adopted its previous oral slope factor [9–16], which was developed by EPA under the default assumption of linearity and has been deleted. Currently, the majority of evidence and documents support a MOA based risk assessment for TCM [30–32]. In our case, the estimated maximum CDI for TCM was 0.0010 mg/kg/day, much smaller than its RfD. So, this paper excluded TCM as a possible human carcinogen through any route of exposure. For the other three THMs [bromodichloromethane (BDCM), dibromochloromethane (DBCM), bromoform (TBM)] and two HAAs (DCAA, TCAA), slope factors from the IRIS [29] and the Risk Assessment Information System (RAIS) [33] were used.

### 2.4. Disease model and DALY estimation

To assess the disease burden of cancer, the cancer incidence estimates were combined with a two-stage disease model (Fig. 1) [19] for DALY estimation. The disease model simplifies each disease phase in the disease history. There are two possible outcomes for cancer cases: (1) some will die from cancer ($1 - S_x$); (2) some will be cured from cancer ($S_x$), and a proportion of them ($S_x \times P_{seq}$) live with cancer sequelaes for the rest of their lives.

Different cancer types usually differ in severity, thus causing different disease burden. The selection of DBPs associated cancer was based on human epidemiology. Numerous epidemiologic studies have explored the possible cancer risk in relation to some measure of chlorinated DBPs. Bladder cancer, with the most consistent evidence, has the greatest likelihood of being causally associated

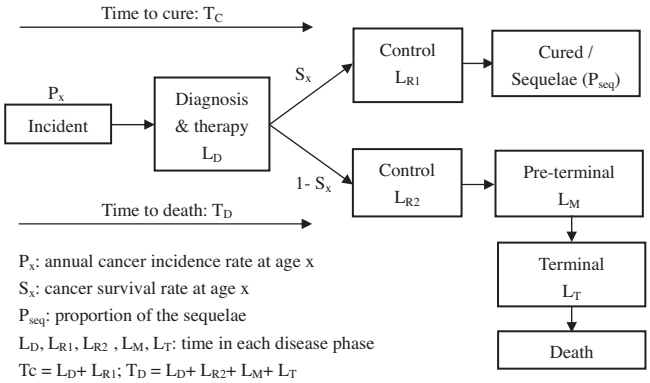


**Fig. 1.** Two-stage disease model.

with chlorinated DBPs [5]. As for other cancer types, the evidence is limited. So, this study chose bladder cancer as the disease endpoint.

DALYs combines premature mortality burden (years of life lost, YLLs) and morbidity burden (years lived with a disability, YLDs) of the disease. According to the disease model, morbidity burden should be considered during each disease phase except death, while mortality burden only in the death phase. The basic formulas of DALYs, YLLs and YLDs were shown as Eq. (6)–(8) [18]:

$$\mathrm{YLLs} = \sum_{x} n_x d_x e_x^* \tag{6}$$

$$\mathrm{YLDs} = \sum_{x,y} n_x i_{x,y} \mathrm{DW}_y L_y \tag{7}$$

$$\mathrm{DALYs} = \mathrm{YLLs} + \mathrm{YLDs} \tag{8}$$

where $n$ = number of population, $d$ = incidence of death, $e^*$ = standard life expectancy, $i$ = incidence, $DW$ = disability weight, $L$ = duration of disability, $x$ = age (to be consistent with the age structure of life expectancy and population statistics, stratified into 19 groups: 0–1, 1–5, 5–10, 10–15,. . ., 80–85, 85 and over), $y$ = disease phase.

Annual age-specific cancer incidence ($P_x$) and survival rate ($S_x$) were used to calculate the incidence of death ($d_x$) and incidence of each disease phase ($i_{x,y}$). Since those dead or those cured would gone through a period of time to death ($T_D$) or time to cure ($T_C$), ($e^* - T_D$) and ($e^* - T_C$) would be more accurate than $e^*$ to represent the life years loss of death and the rest of lives for those cured. So, Eqs. (6) and (7) can be expressed as:

$$\mathrm{YLLs} = \sum_{x} n_x P_x (1 - S_x)(e_x^* - T_D) \tag{9}$$

$$\mathrm{YLDs} = \sum_{x,y} n_x P_x [(1 - S_x)\mathrm{DW}_y L_y + S_x(\mathrm{DW}_y L_y + P_{\mathrm{seq}} \mathrm{DW}_{\mathrm{seq}}(e_x^* - T_C))] \tag{10}$$

where $P_{seq}$ = proportion of the sequelae, $DW_{seq}$ = disability weight of the sequelae.

The parameters used in the disease model and DALY estimation are illustrated below: (1) $P_x$: The lifetime cancer estimates (IR) should first be converted into annual estimates. Apparently, the probabilities of developing cancer at different age stages are not the same. To characterize this difference, we introduced the parameter age-specific relative sensitivity ($RS_x$), which was estimated by dividing the age-specific incidence rates of bladder cancer by the total incidence rate reported in cancer registration areas of China from 2003 to 2007 [34], as shown in Fig. A2(A). $P_x$ was calculated as: $P_x = IR \times RS_x/Sp_x$, where $Sp_x$ is age span for each age group (1 and 4 for 0–1 and 1–5 age groups, and 5 for others). (2) $S_x$: $S_x$ was estimated by 5-year relative survival [35], for which the complement of the ratio of cancer mortality ($M$) to incidence (I) [$1 - (M/I)$] is a good approximation [36]. Age-specific incidence rate and mortality rate of bladder cancer reported in cancer registration areas of China from 2003 to 2007 [34] were used to calculate $S_x$, as shown in Fig. A2(B). (3) $L$ and DW: Times for diagnosis and treatment ($L_D$), pre-terminal phase ($L_M$) and terminal phase ($L_T$) were set as 4 months, 3 months and 1 month, respectively [18]. The median time to death ($T_D$) and the median time to cure ($T_C$) of bladder cancer reported by the Cancer Registry of Norway were 2.20 years and 4.00 years [37]. According to the disease model, times for control of those cured ($L_{R1}$) and those dead ($L_{R2}$) were calculated as 3.67 years and 1.53 years. Disability weights quantify the severity of disabilities, ranging from 0 (full health) to 1 (death). Disability weights for each disease phase were derived from the Victorian burden of disease study [38]. The summary of the durations and disability weights are shown in Table A4. (4) Others: Number of population was based on the Chinese population structure in 2011 [39]. Standard life expectancy was based on model life-table West [8]. Sequelaes among bladder cancer survivors include incontinence, impotence and infertility. The proportions and disability weights of the sequelaes are summarized in Table A5, and the detailed information can be found in the literatures [40,41].

Monte Carlo simulation was used to incorporate uncertainty in the risk assessment, which comes from the variation of exposure and the uncertainty of parameter values. Following the distributions of the concentration data and the parameters, a total of 5000 simulations were performed to obtain the distribution of risk estimates. R (version 3.0.0) was used during the whole calculation process in this study.

## 3. Results and discussion

### 3.1. Concentrations of DBPs

The concentrations of DBPs are summarized and compared with the Chinese guideline values in Table 1. Except for the TCM concentrations of two samples, the DBP concentrations of all the samples were below the Chinese guideline values regulated by “Standards for Drinking Water Quality” (GB 5749-2006). For THMs, the average concentrations followed the order: TCM > BDCM > DBCM > TBM, while for HAAs, TCAA > DCAA, which was consistent with other studies [42–44]. The total concentrations of four THMs and nine HAAs ranged from 1.50 to 94.90 μg/L (median value: 16.48 μg/L) and from below the detection limit to 52.98 μg/L (median value: 7.46 μg/L), which were much lower than those reported for Canada and the United States [2,13]. TCAA and DCAA were found to be dominant among the nine HAA species in most of the samples, which on average accounted for 89.3% of the total HAAs (THAA). The dominance of TCAA and DCAA has also been reported in previous studies conducted in Canada and China [13,14].

The water-supply weighted histograms and box-plots of DBP concentrations are shown in Fig. 2. The weighted DBCM concentrations were best fitted with a logarithmic normal distribution, while the concentrations of other DBPs were all best fitted with exponential distributions, and the resulting distribution parameters are shown in Table 1. Some concentration data were beyond the limits in the box-plots, which might be outliers, but still important in the risk assessment [13].

### 3.2. Total cancer risk

The distribution of the total lifetime cancer incidence and its cumulative distribution were simulated, as shown in Fig. A3. The

**Table 1**
Summary of DBP concentrations (μg/L) and distribution parameters.

| DBPs | Range | Chinese guideline value | Median value | Mean value (SD) | Distribution parameter |
|---|---|---|---|---|---|
| TCM | 0.90–89.20 | 60 | 10.70 | 12.67 (12.41) | Exp(0.071) |
| BDCM | ND–25.20 | 60 | 2.50 | 3.81 (4.57) | Exp(0.24) |
| DBCM | ND–13.20 | 100 | 0.40 | 1.50 (2.77) | Lnorm(−1.80,2.48) |
| TBM | ND–7.00 | 100 | 0 | 0.23 (0.84) | Exp(5.00) |
| TCAA | ND–30.76 | 100 | 3.30 | 4.79 (5.01) | Exp(0.18) |
| DCAA | ND–32.68 | 50 | 1.90 | 3.11 (4.61) | Exp(0.29) |

ND: below the detection limits, SD: standard deviation, Exp: exponential distribution, Lnorm: logarithmic normal distribution.

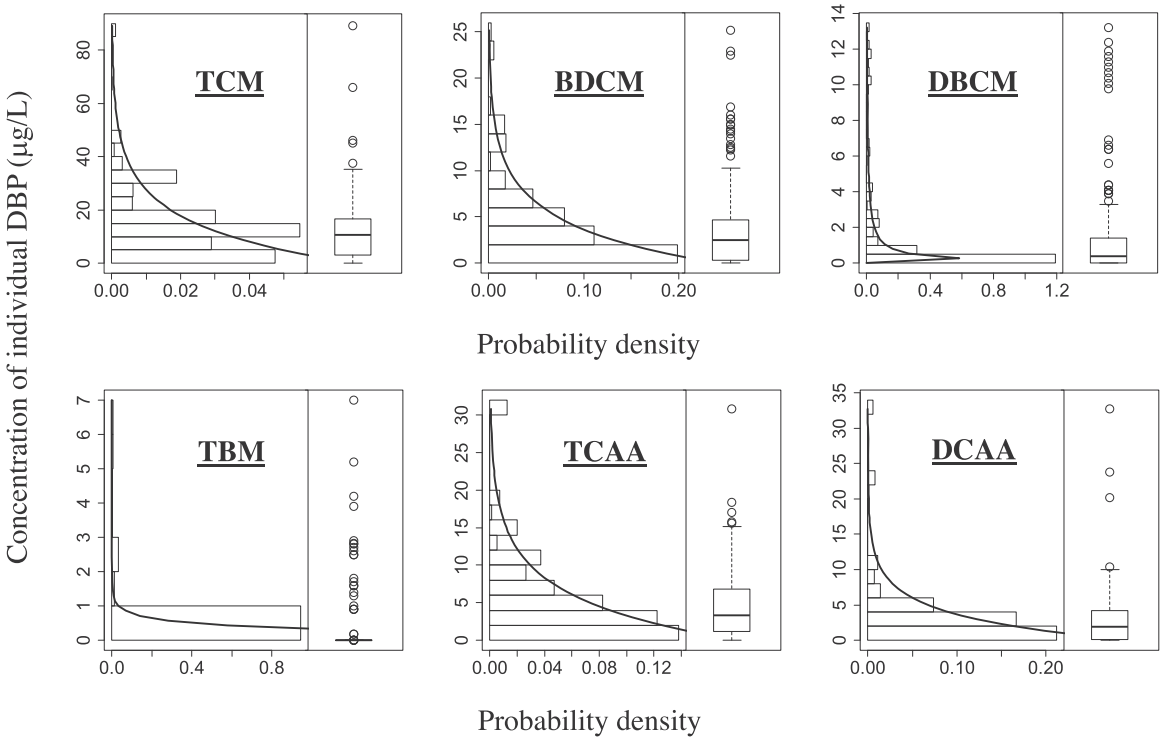


**Fig. 2.** Distribution plots and box plots of DBP concentrations.

median value of the total lifetime incidence was $2.94 \times 10^{-5}$, which was 29.4 times the minimum or negligible risk level set by the USEPA ($1 \times 10^{-6}$), but within the regulatory limit defined by USEPA ($10^{-6}$ to $10^{-4}$) [45].

Based on the median value of the total cancer incidence, the age-specific DALYs were calculated, shown as Fig. 3. The total DALYs of all age groups was 989.14 DALYs per year. The YLLs and the YLDs were calculated as 806.56 DALYs per year and 182.58 DALYs per year, which contributed 81.5% and 18.5% of the DALYs respectively. The morbidity burden of bladder cancer cannot be ignored because of its relatively high survival rate, long treatment phase and possible sequelaes among survivors, which has also been found in the Spanish burden of disease study [19].

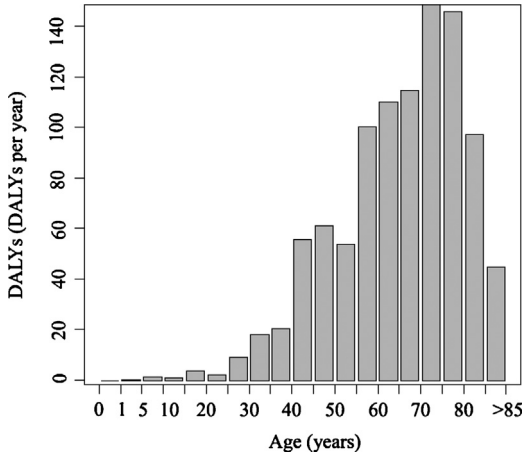


**Fig. 3.** Age-specific DALYs lost based on median cancer incidence.

Based on the distribution of the total cancer incidence, the corresponding distribution of total DALYs was simulated. Dividing the total DALYs by the total population resulted in the average individual DALYs lost, as shown in Fig. 4. In the WHO guidelines for drinking-water quality, the reference level of risk is defined as $10^{-6}$ DALYs per person-year (ppy), approximately equivalent to a $10^{-5}$ lifetime cancer incidence rate [6]. The median value of the individual DALYs ($7.34 \times 10^{-7}$ ppy) was below the reference level, and the exceeding probability was calculated as 28.3% according to the distribution of the individual DALYs.

### 3.3. Comparison of the cancer risks of THMs and HAAs through different pathways

The median values, 5th and 95th percentiles of the cancer risk distributions from exposure to different DBPs through different pathways are summarized in Table A6 and Table 2. In terms of excess cancer incidence, the risks of DBPs considered were all

**Table 2**
Cancer risks of DBPs through different pathways[a] ($\times 10^{-7}$ DALYs ppy).

| Route | TCM | BDCM | DBCM | TBM | TCAA | DCAA | Total |
|---|---|---|---|---|---|---|---|
| Ingestion | – | 1.40 (0.10, 6.23) | 0.69 (0.05, 2.79) | 0.09 (0.00, 0.37) | 2.12 (0.16, 9.18) | 0.93 (0.07, 3.96) | 6.59 (2.53, 15.22) |
| Inhalation | – | 0.26 (0.02, 2.10) | 0.11 (0.00, 0.81) | 0.00 (0.00, 0.00) | – | – | 0.44 (0.06, 2.65) |
| Dermal contact | – | 0.01 (0.00, 0.04) | 0.00 (0.00, 0.02) | 0.00 (0.00, 0.00) | – | – | 0.01 (0.00, 0.06) |
| Total | – | 1.78 (0.13, 8.17) | 0.84 (0.06, 3.51) | 0.09 (0.00, 0.38) | 2.12 (0.16, 9.18) | 0.93 (0.07, 3.96) | 7.34 (2.75, 17.10) |

[a] Data shown are median values of the risk distributions, and values in the parentheses are the 5th and 95th percentiles of the risk distributions.

below $1 \times 10^{-5}$, while except for TBM all above $1 \times 10^{-6}$. In terms of DALYs, the risks of DBPs were all below $10^{-6}$ DALYs ppy. The risk of DBPs followed the order: TCAA > BDCM > DCAA > DBCM > TBM. Though only the ingestion pathway was considered for HAAs, the median risk of TCAA ($2.12 \times 10^{-7}$ DALYs ppy) was highest because of its relatively high concentrations and oral slope factor. TCAA and DCAA made 36.8% and 16.1% contributions to the total risk respectively. For THMs, BDCM contributed the most (30.9%) to the total risk, followed by DBCM (14.6%) and TBM (1.6%).

The cancer risks from ingestion and inhalation exposures accounted for 93.6% and 6.3% of the total risk respectively, while dermal contact made a negligible contribution. Considering THMs alone, ingestion exposure was also the most important pathway for all the three THMs. The risks through ingestion, inhalation and dermal pathways accounted for 87.5%, 12.2% and 0.3% of the risk of total THMs (TTHM) respectively. The contribution of inhalation pathway was relatively small compared with the previous risk assessments on THMs [9,14], since we excluded TCM, which usually plays a major role in the risk of inhalation exposure.

The median cancer risks of THAA and TTHM were $3.54 \times 10^{-7}$ DALYs ppy and $3.17 \times 10^{-7}$ DALYs ppy respectively. The risk ratio of THAA to TTHM was 1.12. The real ratio must be a little bit larger, since only two dominant chlorinated HAAs were considered in this study. It has been reported that the concentrations of the brominated HAAs, which are generally more toxic than the chlorinated DBPs [46], can be comparable to those of the chlorinated HAAs in drinking waters that have moderate bromide in their source waters [47]. For areas with such drinking waters, the risk ratio might be much larger. However, except for TCAA and DCAA, cancer potencies of other HAAs have not yet been available. Understanding their occurrences and carcinogenicities is important to enable better regulation of HAAs.

### 3.4. Geographic difference of the cancer risks

China is generally divided into seven geographic regions: the northeast (NE), north (N), northwest (NW), southwest (SW), southern (S), east (E) and central (C) China. The concentrations and cancer risks of DBPs in seven regions and 35 sampling cities are shown in Tables A7–A10 and Fig. 5 (a darker color represents a higher cancer risk in the region). Since the limitation of the amount of concentration data in each region and city, the risks were estimated based on the average DBP concentrations instead of Monte Carlo simulation. The total cancer risk in NE ($1.16 \times 10^{-6}$ DALYs ppy) was highest, followed by N ($1.04 \times 10^{-6}$ DALYs ppy). The risks in the other five regions were all below the WHO reference level, with the lowest risk in NW ($0.45 \times 10^{-6}$ DALYs ppy). Among 35 cities, the top six of high risk cities are all located in NE and N. The risk in Tianjin ($2.87 \times 10^{-6}$ DALYs ppy) was highest, followed by Qingdao ($2.14 \times 10^{-6}$ DALYs ppy) and Jinan ($1.94 \times 10^{-6}$ DALYs ppy). Yinchuan (in NW) had the lowest risk ($9.62 \times 10^{-8}$ DALYs ppy), followed by Changsha ($1.84 \times 10^{-7}$ DALYs ppy, in C) and Xining ($2.53 \times 10^{-7}$ DALYs ppy, in NW). Beijing had the fourth lowest risk ($2.87 \times 10^{-7}$ DALYs ppy) though located in N.

The concentrations and composition of the DBPs varied considerably in 35 cities, and presented some geographical features (e.g. BDCM and DBCM were generally the major components of total risks in N, while TCAA was the major component in NE). Concentrations and composition of DBPs were associated with the level of key precursors and chlorine disinfection process (type and amount of the disinfectant, contact time, temperature, pH and whether using pre-chlorination). Since the two water quality surveys did not get comprehensive data on the source waters and treatment processes, the resulting geographic variations need further study.

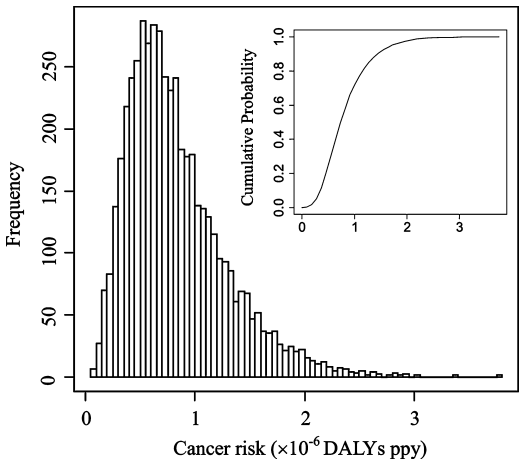


**Fig. 4.** The distribution of total cancer risk (in DALYs).

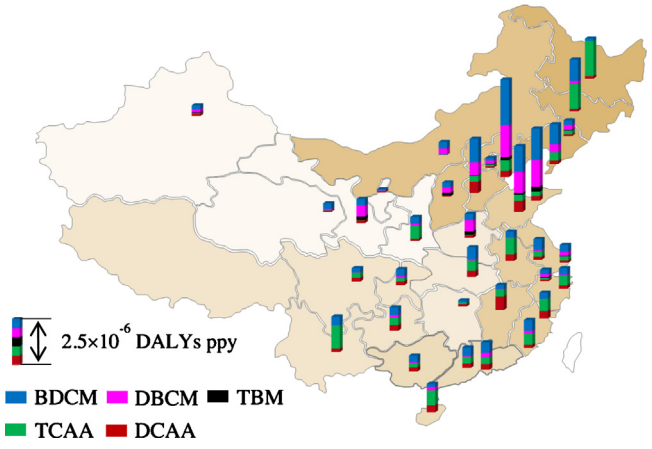


**Fig. 5.** Cancer risks of DBPs in different geographic regions and cities. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

### 3.5. Uncertainty analysis

This study adopted EPA-developed models for the estimation of excess cancer incidence. Uncertainties could come from lack of knowledge about the parameters and lack of data. For example, there is limited availability of toxicological data of HAAs. Also, due to the lack of human data, the slope factors used are all derived from animal studies, which may give rise to the issue of predictive validity by translating high-dose exposure data from animal to human who suffer long-term exposure at much lower concentrations [17]. Another important source of uncertainties come from day-to-day, place-to-place variations in concentrations and composition of DBPs. Monte Carlo simulation and geographic analysis can partly incorporate and characterize these uncertainties, but more comprehensive survey data are needed to support a further study. Uncertainties could also be caused by different water consumption habits and patterns (e.g. boiled water, bottled water) among people. Experimental data have shown that THMs can be almost completely removed upon boiling [48]. So considering this factor, the risk of THMs from ingestion exposure can be greatly reduced, and inhalation exposure will become the most important pathway for the risk of THMs when the removal rate exceeds 82.6%. As for HAAs, TCAA has shown to be readily removed by boiling water. However, additional DCAA could form in this process. The effect of boiling on the risk of THAA is dependent on the boil time, amount of DBP precursors and chlorine residual in the water [49]. When these survey data are available, boiling water should be considered as an important modifying factor in the exposure assessment, since most Chinese people boil water before they drink it.

In the DALY estimation, bladder cancer is the only considered disease endpoint because of its greatest likelihood of being causally associated with chlorinated DBPs. However, this causality has not yet been proven, and it is possible that the actual risk could be zero [5]. Among the parameters used in the disease model, the severity weights and durations were derived from the burden of disease study in other country, under the assumption on the applicability of international data to the Chinese situation. There is evidence that the major sources of variation in DALY estimates come from the problem of "getting the numbers of patients right", not so much from severity weights or durations [7]. So, the uncertain in severity weights and durations would not undermine the robustness of DALY estimates. In order to more accurately predict the cancer cases and survivors, we calculated age-specific parameters (incidence and survival rates) instead of average values by using Chinese cancer registration data. Though the registration data may not be fully applicable to the bladder cases caused by specific DBPs, we believe that the best available data were adopted.

This study excluded TCM as a carcinogen through any exposure pathway considering the toxicology of TCM. However, there are some inconsistent conclusions between different authorities. EPA deleted the oral slope factor for TCM, but remains its inhalation slope factor [29]. The Office of the Environmental Health Hazard Assessment (OEHHA) still has both the two slope factors [50]. To make a comparison, we also calculated the possible cancer risks including TCM (previous slope factors developed by EPA were used), as shown in Table A11. The total risk would rise to $1.03 \times 10^{-6}$ DALYs ppy, 40% higher than the original value. There is a big difference between the results of MOA-based and default linear approach. So, further reassessment of toxicity data is necessary for TCM to provide a unified method and information.

## 4. Conclusions

According to the above analysis, the following conclusions were reached: (1) The median total cancer risk of THMs and HAAs in drinking water of China was estimated as $7.34 \times 10^{-7}$ DALYs ppy, lower than the reference level of risk set by WHO. (2) The risk of TCAA was highest among the DBPs considered, and ingestion exposure was the most important pathway for the total risk. (3) The risk in northeast China ($1.16 \times 10^{-6}$ DALYs ppy) was highest while the risk in northwest China ($0.45 \times 10^{-6}$ DALYs ppy) was lowest. As for 35 cities, Tianjin had the highest risk ($2.87 \times 10^{-6}$ DALYs ppy) while Yinchuan had the lowest risk ($9.62 \times 10^{-8}$ DALYs ppy).

DALY method adds a public health dimension to the risk assessment process that may make the outcomes more informative for the regulators. At present, disease burden related to different hazards in drinking water (e.g. *Cryptosporidium*, arsenic and bromate) has been assessed. Expressing risk of DBPs in DALYs enables their risk comparison. And since DALYs is a standardized metric, it can also be calculated for cost-effectiveness analysis of quality-improving activities for drinking water, enabling the prioritization of hazardous agents as well as any other environmental risk factors.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jhazmat.2014.07.080.

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