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Refinement of arsenic attributable health risks in rural Pakistan using population specific dietary intake values

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Highlights

- Comparison of international default or standard water and food intake values with local values of rural Pakistan.
- Higher cancer risk determined using population specific water or food intake data derived from 24 hour water consumption diary against the international default or standard values.
- An integrated cancer risk assessment that includes most of the intake sources should be considered for complete exposure characterization.

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Abstract

Background: Previous risk assessment studies have often utilised generic consumption or intake values when evaluating ingestion exposure pathways. If these values do not accurately reflect the country or scenario in question, the resulting risk assessment will not provide a meaningful representation of cancer risks in that particular country/scenario.

Objectives: This study sought to determine water and food intake parameters for one region in South Asia, rural Pakistan, and assess the role population specific intake parameters play in cancer risk assessment.

Methods: A questionnaire was developed to collect data on sociodemographic features and 24-hour water and food consumption patterns from a rural community. The impact of dietary differences on cancer susceptibility linked to arsenic exposure was evaluated by calculating cancer risks using the data collected in the current study against standard water and food intake levels for the USA, Europe and Asia. A probabilistic cancer risk was performed for each set of intake values of this study.

Results: Average daily total water intake based on drinking direct plain water and indirect water from food and beverages was found to be 3.5 L day^{-1} (95% CI: 3.38, 3.57) exceeding the US Environmental Protection Agency's default (2.5 L day^{-1}) and World Health Organization's recommended intake value (2 L day^{-1}). Average daily rice intake (469 g day^{-1}) was found to be lower than in India and Bangladesh whereas wheat intake (402 g day^{-1}) was higher than intake reported for USA, Europe and Asian sub-regions. Consequently, arsenic-associated cumulative cancer risks determined for daily water intake was found to be 17 in children of 3-6 years (95% CI: 0.0014, 0.0017), 14 in children of age 6-16 years (95% CI: 0.001, 0.0011) and 6 in adults of 16-67 years (95% CI: 0.0006, 0.0006) in a population size of 10000. This is higher than the risks estimated using the US Environmental Protection Agency and World Health Organization's default recommended water intake levels. Rice intake data showed early life cumulative cancer risks of 15 in 10000 for children of 3-6 years (95% CI: 0.0012, 0.0015), 14 in children of 6-16 years (95% CI: 0.0011, 0.0014) and later life risk of 8 in adults (95% CI: 0.0008, 0.0008) in a population of 10000. This is lower than cancer risks in countries with higher rice intake and elevated arsenic levels (Bangladesh and India). Cumulative cancer risk from arsenic exposure showed the relative risk contribution from total water to be51%, from rice to be44% and wheat intake 5%.

Conclusions: The study demonstrates the need to use population specific dietary information for risk assessment and risk management studies. Probabilistic risk assessment concluded the importance of dietary intake in estimating cancer risk, along with arsenic concentrations in water or food and age of exposed rural population.

Keywords: Water consumption, rice intake, wheat intake, dietary exposure, risk assessment, cancer risk assessment.

1. Introduction

Diet has been suggested to be the key causal factor for approximately 30% of cancers in industrialized countries (Doll and Peto, 1996) and about 20% in developing countries (Willet, 1995). However, water and food consumption patterns differ across the different regions of the world and can even vary within a country due to diverse socio-economic situations, dietary/cultural preferences, ethnicity, climatic conditions, age and sex (WHO, 2011). As such, careful consideration must be made when performing risk assessments of the intake patterns appropriate to the country/region or population for which cancer risks are being assessed.

In South Asia, there has been limited research into the association between diet and carcinogenic potential (Ganguli et al., 2011). Most such studies use data from epidemiological studies conducted in developed countries where diets and consumption patterns are usually very different. As an example, water consumption in South Asia might be considerably higher than the commonly used default water intake value of 2.5 L day^{-1} (USEPA 2011) and 2 L day^{-1} for an adult (WHO 2011; EFSA 2010) leading to an under estimate of exposure risk from waterborne chemicals such as arsenic. Similarly, rice consumption in South Asia is generally considerably higher than in many developed countries (FAO, 1998); but even within South Asia, there will be considerable variation with large areas of India consuming half the rice per capita of Bangladesh but higher levels of wheat (National Statistical Organisation India, 2012; Meharg and Zhao, 2012).

Variations in dietary consumption patterns between different subpopulations in the region were rarely considered. For instance, information on age or gender specific dietary differences can be used to define subgroups at highest risk (Zahm and Fraumeni, 1995). Children can have higher exposures to dietary chemicals than adults probably due to higher ratios of food consumption per kg body weight resulting in higher relative daily doses (Moy and Vannoort. 2013). A study by the US National Research Council (1993) found that children were at greater risk from ingestion of pesticide residues whilst a study by He et al. (2013) reported higher dietary cadmium exposure in men compared to women due to different consumption patterns of cadmium-containing foods such as cereals.

At a more local level, diets in urban areas are often very different to rural areas (Miller et al. 2012): for instance, in Pakistan, there has been an emphasis on metabolic and cardiovascular health risks from diet in urban areas that are not necessarily transferrable to rural areas with different social, cultural, economic and environmental factors affecting diets (Yakub et al. 2010; Hydrie et al. 2010; Jafar et al. 2009; Iqbal et al. 2004).

Dietary intake data must consider all potential dietary sources. However in the case of chemical risk assessment, some sources, particularly the contributions of indirect water intake and food, are often not adequately taken into consideration for consumption and associated risk assessment. Direct water is defined as tap water consumed directly as plain drinking water, whereas, indirect water is defined as water added to foods and beverages (e.g. tea, coffee, bottled water etc.) during final preparation at home or by food service establishments. Total water refers to combined direct and indirect water consumption (Bennet et al., 2000).

This study sought to gather food and water intake data from rural villages in Pakistan to examine the influence of regional rather than generic intake estimates on human health risk assessments, specifically for cancer risk. It focuses on the need to evaluate all key ingestion pathways including indirect water consumption, food intake and the role of socio-demographic factors such as sex, age and occupation on consumption patterns. A case study is provided based on arsenic exposure through ingestion of arsenic-contaminated water and food.

2. Materials and Methods

2.1 Dietary Intake methodology

Six villages in four districts (Kasur, Sahiwal, Bahawalpur and Rahim Yar Khan) of Pakistan were identified as study sites as they have at least one groundwater source with levels of arsenic in excess of 50 µg L^{-1} (Ahmad et al., 2004) (Figure-1). These sites consisted of 1776 households, with a population of 15647 (51% men; 49% women) and an average of 7 family members per house (Pakistan Bureau of Statistics, 2014). A sample size of 398 individuals from 220 households was recruited to the project, derived from a formula for estimating sample proportions from large populations (Collet, 2003). A 95% confidence level and standard error of 0.05, as recommended by Collet (2003), assumes a statistically significant sample size of 384 respondents for a large population.

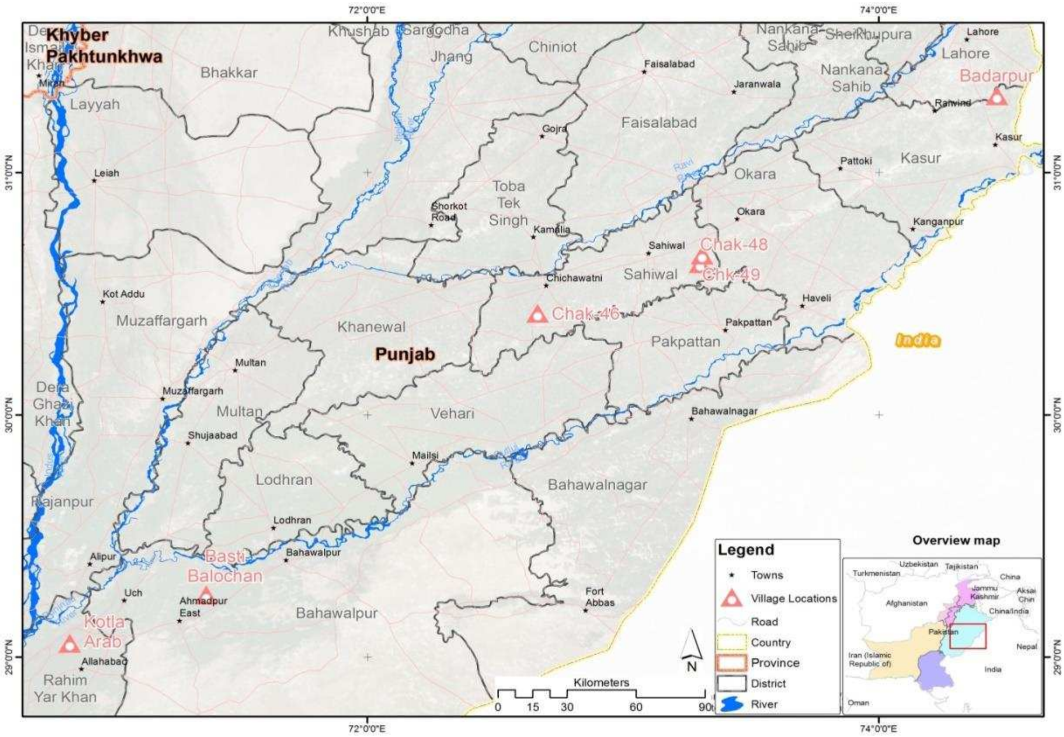

Figure 1: Location map of the study area and sampling points; villages Chak-46/12-L, Chak-48/12-I and Chak 49/12-I in district Sahiwal; Village Badarpur in district Kasur; villages Basti Kotla Arab and Basti Balochan RYK and Bahawalpur districts

The study was conducted in accordance with national and international guidelines for the protection of human subjects and the research protocol was approved by the National Bioethics Committee of Pakistan and University of Leeds Research Ethics Committee. Study participants were recruited during June-September 2014 by a field team fluent in English and the relevant local languages. Each participant completed a questionnaire with three sections: demographic features (age, sex, body weight, occupation, number of family members), 24-hour food intake diary and 24-hour water intake diary, and each household was supplied with appropriate kitchen utensils (glass: 200-250 ml, cups: 100-200 ml, plates: 150-400 g, and bowl: 100-300 g) with capacity measured and recorded by the field teams. The intake diaries used a semi-quantitative Food Frequency Questionnaire (FFQ) based on the 24 hour recall method (EFSA, 2010).

Water intake was calculated based on direct water sources (plain drinking water only) and indirect (water consumed in tea, lassi, and staple food such as rice, wheat and pulses) (Calderon et al., 1999; Ohno et al., 2007; Watanabe et al., 2004). Estimates of water volume provided by the U.S. Department of Agriculture's (USDA) National Nutrient Database were used to calculate indirect water intake (Agricultural Research Service, 2014) and were then combined with direct water intake estimates to make the total water intake. Equations 1-10 (Supplementary Information: Table S-1) show how the diary information was used to determine daily intakes across the sample population.

2.2 Risk assessment methodology

Water and food intake rates where used to calculate carcinogenic risk of arsenic exposure using the United States Environmental Protection Agency (USEPA) human health risk assessment model (Table 1). Risk calculations pertain to the villages and settings from which the primary water and food intake data were obtained. Mutagenic chemicals sometimes cause cancer by a mutagenic mode of action (MOA) which theoretically can lead to a 10 fold greater potency in the first 2 years of life and a 3 fold greater potency between ages 3 and 16 years of age (USEPA, 2005). This may pose a higher risk of cancer when exposure occurs during early life. In such cases, age-dependent adjustment factors (ADAFs) are used to assess the additional risk. Applying ADAFs, three main age groups (i.e. 3–6 years, 6–16 years, and >16 years) were used to quantify less than life time and life time cumulative cancer risks (USEPA, 2011b).

Table-1: USEPA equations (USEPA, 2011) for cancer risk calculation

Equation No.	Risk Parameters	Equation used
(1)	Lifetime Average Daily Dose (LADD)	$\text{LADD} = \dfrac{\text{C x IR} \times \text{ED x EF}}{\text{BW} \times \text{ATe}}$
(2)	Cancer Risk (CR)	$\text{CR} = \text{LADD} \times \text{CSF} \times \text{ADAF}$

Whereas;

C	Arsenic concentration: water (µg L^{-1}), rice/wheat (µg g^{-1}) *(for unit consistency multiplied by 0.001 to get water as (mg L^{-1}) and rice/wheat as (mg kg^{-1}))*
IR	Ingestion rate: water (L day^{-1}), food (g day^{-1}) *(for units consistency multiplied by 0.001 to get food as (kg day^{-1}))*
EF	Exposure frequency (days $year^{-1}$)
ED	Exposure duration: during life stage (years)
ATe	Average life expectancy (days) = 365 days/year * 67 years
BW	Body weight during life stage (kg)
CSF	1.5 per mg kg^{-1} body weight per day—the cancer slope factor (CSF) for oral ingestion of arsenic (ATSDR, 2007)
ADAF	Age dependent adjustment factor (USEPA, 2011b)

Two approaches were used to determine cancer risks: point estimates of cancer risks using intake values from USEPA, World Health Organization (WHO) and regionally appropriate intake values to assess the importance of dietary consumption patterns specific to the population in question (Table 2), and a probabilistic approach using the intake values from this study population. For this later risk assessment approach, a Monte Carlo simulation of 10,000 iterations was carried out. In this case, the input parameters defined as probability distributions are given in Table 2, and output is likewise presented as a probability distribution (USEPA, 2001).

Table-2: The input parameters used in calculation of arsenic attributable cancer

Input variable	Unit	Study area	Fitted distribution		values	Data source
			Point estimates	Probabilistic estimates		
As_{water}	$\mu g\ L^{-1}$	17 districts	mean	--	>10, >50 and >100 for point estimate	World Health Organization's (1993); Pakistan Standards Quality Control Authority, (2010); Tahir and Rasheed (2014); Ahmad et al. (2004)
			--	**Generalized Pareto (GP) Distribution k = 0.288 σ = 30.112 Θ = 10	>10 for probabilistic estimates	
$As_{raw\ rice}$	$mg\ kg^{-1}$	10 districts	mean	mean	0.082 ± 0.054	Rasheed et al. (2016)
As_{Wheat}	$mg\ kg^{-1}$	12 districts	mean	mean	0.012	Al-Othman et al.(2013)
Water intake (WI)	$L\ day^{-1}$	Study area	mean	mean values fitted with respect to age groups	***Children** Age 3-6 years: 1.9 Age 6-16 Years:2.9 **Adults >16** Male:3.9 Female:3.2 Overall mean 3.6	Present study
		Other	95th Percentile	NA	*Age 3-6 years: 0.33 *Age 6-16 Years: 0.5 Adults>:2.5	USEPA (2011a)
			mean	NA	*Age 3-6 years: 1 *Age 6-16 Years:1 Adults >16: 2	WHO (2011)
Rice intake rate (RI)	$g\ day^{-1}$	Pakistan	mean	mean	***Children** Age 3-6 years: 91 Age 6-16 Years:272 **Adults >16** Male: 576 Female: 463 Overall mean: 532	Present study
		Bangladesh	constant	NA	Male mean: 1789, Female mean: 1522 Children mean: 862	Khan et al. (2009)
		India		NA	Children: 400 Adults: 750	Roy Chowdhary et al. (2002)
		USA	constant	NA	Mean:172.6	USFDA (2016)
		Europe	constant	NA	Mean: 175	EFSA (2014)
Wheat intake (WhI)	$g\ day^{-1}$	Pakistan	mean	mean	**Children** Age 3-6 years: 149 Age 6-16 Years: 227. **Adults >16** Male 426 Female 358 Overall mean 400	Present study
		Bangladesh	mean	NA	Male: 179 Female: 131	Watanable et al. (2004)
		China	mean	NA	Children:13 Adults:44	Zeng et al. (2015)
		Europe	mean	NA	Mean: 182	FAO (2013)
		USA	mean	NA	Mean: 48 (Recommended)	U.S. Department of Health and Human Services and U.S. Department of Agriculture. 2015–2020
Body weight (BW)	kg	Study area	mean	NA	***Children** Age 3-6 years: 12 Age 6-16 years: 26 **Adults >16** Male: 68 Female: 55 **Overall mean 63**	Present study

			NA	Fourier Fit of Log (body weight) with respect to log (age)	Refer to Figure-S-1 (Supplementary information)	
Exposure duration (ED)	years	Study area	constant	Age 3-6 years: 6-Age (picked by Monte Carlo) Age 6-16 Years: 16-Age (picked by Monte Carlo) Adults >16 Year: 67- Age (picked by Monte Carlo)	***Children** Age 3-6 years: 3 years Age 6-16 Years: 10 years **Adults >16** Age 16-67 years: 51 years **Overall ED:** 64 years	Present study
Average Life expectancy	years	For all areas	constant	constant	67 (WHO data for Pakistan)	WHO (2015)
Age	years	Study area	mean	--	***Children** *Age 3-6 years *Age 6-16 Years **Adults** Age: 16 to >67 years	Present study
			--	Rician distribution	s (noncentrality parameter) = 27.4061 sigma (scale parameter) = 20.1825	
Averaging Time (AT)	days/years	For all participants	constant	constant	365	USEPA (2011a)
Age dependent adjustment factor (ADAF)			constant	constant	For 0-2 years = 10 For age 2-16 years =3 For age 16-67 years = 1	USEPA (2011b)
Reference dose (RfD)	mg kg^{-1} day^{-1}	For all participants	constant	constant	0.0003	USEPA (2011a)
Cancer slope factor (CSF)	$(mg/kg\text{-}day)^{-m}$	For all participants	constant	constant	1.5	ATSDR (2007)

**Results of children are presented in two age groups due to difference in mean body weights.*

***k*: shape parameter, *σ*: scale parameter, and *θ*: threshold parameter,

To calculate lifetime risk (cumulative risk) for a population with an average life expectancy of 67 years, the risk calculated for each of the age groups was summed after applying recommended ADAFs. Thus, the life time cancer risk is calculated for a total period of 64 years, starting at the minimum age of the study participants (3 years old). This will also help us determine lifetime risks based on exposure beginning very early compared with those that begin later in life for this region.

Cancer risks for water and most frequently consumed food stuffs i.e. wheat and rice were used to estimate cumulative as well as relative cancer risk from water and food. The USEPA acceptable cancer risk (CR) range is 10^{-4} to 10^{-6} which is dependent on the size of the target population (USEPA, 2001). As population size of six villages comprised of 15647 villagers, thus the USEPA's preferred risk goal (1.0 x 10^{-4}) was considered to rule out even the low risk.

2.3 Statistical analysis

The results of the household surveys and cancer risks were analysed using Microsoft Excel and SPSS 17.0 (IBM, New York, NY, USA) for descriptive statistics, two way analysis of variance (ANOVA), Pearson partial correlation analysis and independent samples t-test to identify inter-relationships within the parameters.

3. Results and Discussion

3.1 Estimation of total water intake

The 398 study participants included 249 men and 149 women; 66 participants <16 years of age (children) and 332 participants ≥16 years (adults); 67 persons < 35 kg body weight (mean body weight at 16 years of age) and 331 were ≥ 35 kg. (Detailed demographic features are given in Table-S-2 of Supplementary Information).

The average daily total water intake (direct plus indirect) across this sample population was determined to be 3.5 ± 1.0 L day^{-1} for all participants irrespective of age and sex (Table 3). Adult men (3.9 ± 1.0 L day^{-1}) and adult women (3.2 ± 0.7 L day^{-1}) of age ≥16 years consumed more water than children <16 years (2.8 ± 0.7 L day^{-1}). The overall average daily total water intake (3.5 L day^{-1}) comprised of 2.7 L day^{-1} (76% of total) of direct drinking water and 0.8 L day^{-1} (24%) of indirect water intake from food and other beverage sources: this was broadly consistent for males and females although children consumed less total, direct and indirect water than adult men and women. From an indirect water intake perspective, lassi and other dairy drinks contributed the most at around 42% followed by rice (21%), tea (18%), pulses (11%) and wheat chapatti (8%). (Supplementary information: Tables-S-3 and S-4).

Table-3: Summary of average daily total, direct and indirect water intake (L person^{-1} day^{-1}) of the study population

Sex	Age groups (Years)	Sample	Direct Water Intake (L person^{-1} day^{-1})				In-direct Water Intake (L person^{-1} day^{-1})				Total Water Intake (L person^{-1} day^{-1})			
			Mean	SD	95% *Confidence Interval*		Mean	SD	95% *Confidence Interval*		Mean	SD	95% *Confidence Interval*	
					Lower bound	*Upper bound*			*Lower bound*	*Upper bound*			*Lower bound*	*Upper bound*
Children	**3-6**	5	1.6	0.498	0.992	2.228	0.3	0.469	0.255	0.909	1.9	0.943	0.766	3.107
	6-16	61	2.3	0.494	2.219	2.472	0.6	0.391	0.476	0.677	2.9	0.660	2.752	3.090
	Overall < 16	66	2.3	0.528	2.160	2.419	0.6	0.399	0.459	0.656	2.8	0.725	2.669	3.025
Male	**≥16**	206	2.9	0.862	2.794	3.029	1.0	0.464	0.888	1.015	3.9	0.988	3.728	3.998
Female	**≥16**	126	2.4	0.541	2.307	2.496	0.8	0.371	0.709	0.838	3.2	0.692	3.054	3.296
Average intake (irrespective of sex)	**≥16**	332	2.7	0.795	2.632	2.804	0.9	0.439	0.837	0.931	3.6	0.947	3.500	3.704
Average intake	**All participants**	398	2.6	0.773	2.571	2.723	0.8	0.449	0.786	0.874	3.5	0.956	3.383	3.571

SD: Standard deviation, n: No. of samples

The mean total water intake of this study, 3.5 L day^{-1}, was found to be higher than most of the regional studies conducted in Canada, USA, Europe, Latin American and Asian Countries (Supplementary information: Table-S-5) except those reported by Hossain et al. (2012); Pokkamthanam et al. (2011) and Milton et al. (2006). Water intake differences might be due to regionally specific features as well as the use of different methodologies/definitions of intake values (such as using two different studies to calculate direct and indirect intake separately (Hossain et al. 2012)). Within South Asia, all of the studies undertaken in Bangladesh have quantified daily total water intake based on drinking water only (Supplementary information: Table-S-5) whereas, in India, Pokkamthanam et al. (2011) calculated an average total water intake of 4.5 L day^{-1} (4.8 ± 2.5 L day^{-1} for males and 3.3 ± 1.6 L day^{-1} for females) based on direct and indirect water intake (beverages and food).

Data that do exist in similar geographical regions, for example South Asia, showed considerable variation in water intake both within and between populations. A difference of 1 L day^{-1} between total water intake of the present study and that of Pokkamthanam et al. (2011) might be explained by differences in ambient temperature, dietary habits and/or different cultural practices that exist in India and Pakistan. These reasons may also explain the differences seen in comparison to dissimilar geographic regions: direct only intake values of 1.06 L day^{-1} (Kante and co-workers, 2009) and 1.1 L day^{-1} (Barraj et al. 2009) determined for the US population are lower than the present study (2.7 L day^{-1}) possibly due to different climatic and socio-economic conditions (including job types and working patterns), and different food and beverage (e.g. carbonated drinks) intake patterns and preferences.

Drewnowski et al (2013) reported an US average total water intake of 3.5 L day^{-1} (age group 20 to ≥71 years), of which 37% was from direct drinking water and the remainder (63%) deriving from indirect water intake as hot or cold beverages. This is almost the reverse of the situation reported in this study which puts indirect water intake at 24% of total consumption, similar to the 36% reported by Hossain et al (2012) in India and the USA study by Ershow and Cantor (1989) which reported 43% from indirect sources and 57% for direct water. This latter study found broadly the same level of indirect water consumption as the present study: 0.88 L day^{-1} (Ershow & Cantor, 1989) compared to 0.8 L day^{-1} although levels of direct water intake were lower as would be expected due to different climatic, social etc. factors. The role of climate, in particular temperature, in total water consumption is borne out by a number of studies in countries with high ambient temperatures reporting the highest intake levels e.g. Mexico (4.5 L day^{-1}; Del Razo et al., 2002), India (13.2 L day^{-1}; Pokkamthanam et al., 2011), and Bangladesh (6-10 L day^{-1}; Watanabe et al., 2004; Khan et al., 2009; and Chowdhury et al., 2000) as well as this study via the village with the highest ambient temperatures, Chak-48/12-I,which had a maximum total water intake of 4.5 L day^{-1} (for a children) and 7.4 L day^{-1} (for an adult).

3.2 Estimation of food intake pattern

An analysis of dietary choices and consumption frequency of key staples (wheat, rice, pulses, vegetables and chicken) by the study population over the 24 hour study period found that wheat chapattis were the most popular staple, consumed by 99% of participants, followed by pulses and rice at 42-47%; vegetables at 41% and chicken at 26% (Table 4).

Table-4 Average daily food intake (g day^{-1} $person^{-1}$) of children and adults

Sex	Age Group (Years)	Wheat intake			Rice intake			Pulses intake			Vegetable intake			Chicken intake			Total Food Intake		
		Mean ± SD	95% *Confidence Interval*		Mean ± SD	95% *Confidence Interval*		Mean ± SD	95% *Confidence Interval*		Mean ± SD	95% *Confidence Interval*		Mean ± SD	95% *Confidence Interval*		Mean ± SD	95% *Confidence Interval*	
			Lower bound	Upper bound		Lower bound	Upper bound		Lower bound	Upper bound		Lower bound	Upper bound		Lower bound	Upper bound		Lower bound	Upper bound
Children	3-6	149 ± 81	69	229	91± 7	85	98	75 ± 0	75	75	50 ± 0	50	50	150 ± 71	52	248	292 ± 102	202	382
	6-16	227± 58	212	242	272 ± 97	240	305	154 ± 58	133	176	104 ± 33	93	116	175 ± 45	149	201	526 ± 178	481	571
	Overall < 16	222 ± 62	207	237	253 ± 107	219	287	149 ± 59	127	170	103 ± 34	91	115	171± 47	147	196	508 ± 184	464	553
Male	> 16	426 ± 100	412	439	576 ± 175	538	614	252 ± 67	238	266	187 ± 59	175	200	169 ± 47	157	181	888 ± 269	852	925
Female	> 16	358 ± 101	341	376	463 ± 161	418	507	250 ± 73	232	268	181 ± 65	163	199	157± 50	138	176	773 ± 232	732	813
Average intake (irrespective of sex)	> 16	400 ± 105	389	412	532 ± 177	502	563	251± 70	240	262	185 ± 61	175	195	165 ± 48	155	175	844 ± 261	816	873
Average intake	All participants	372 ± 119	360	384	469 ± 202	439	500	234 ± 78	223	246	170 ± 65	160	180	166 ± 48	157	175	789 ± 279	761	816

SD: Standard deviation

Consumption of cooked rice was found to be higher in this study, at 469 g day^{-1}, than levels reported in USA, Europe, Africa, Middle East, and Latin America, where rice is not generally considered a staple food, but is broadly consistent with intake levels in South Asia with levels of 400-1789 g day^{-1} reported for Bangladesh and 450-1391 g day^{-1} in India (Signes et al. 2008; Meharg and Rahman, 2003) (Supplementary information: Table-S-6).

Average daily wheat intake by adults determined from this study (402 g day^{-1}) was found to be higher than in studies reported for USA, Europe and Asian sub-regions (Supplementary information: Table-S-6). However, wheat has been reported to be the staple food in Pakistan (Prikhodko and Zrilyi, 2013). Previous studies have not identified rice, wheat, vegetables, animal products and pulses intake values for Pakistan, either because these have not been considered in the study or the methodology has precluded inclusion. Thus, risk assessment studies have relied mostly on dietary consumption data from other geographical regions. For instance, Rehman and co-workers (2016) have conducted an arsenic risk assessment using the vegetable intake values reported for Jiangsu Province, China by Jiang et al. (2015).

3.3 Factors influencing dietary variations

As has already been noted, there is a difference in water consumption between men and women and between different age ranges. A two-way ANOVA found significant differences ($P<0.001$ *to* ≤ 0.05) between water and/or food intake and mean body weights (male: 68 kg and female: 56 kg), sex, age and villages. The most significant relationships were for sex and age, and can be linked to employment patterns identified by the sociodemographic questionnaire, supporting the association between labour and dietary intake already identified (WHO, 2007). Water consumption increased for men with age up to around 60 years (from 2.22 L day^{-1} to 2.75 L day^{-1}) and then fell (to around 2.52 L day^{-1}) possibly associated with physical labour in the crop fields: 47% of male participants were involved in agricultural activities and these individuals reported the highest levels of water consumption (3.86 L day^{-1}) as shown in Table 5. Women identifying as housewives (25% of the surveyed population) had a mean total water intake of 3.28 L day^{-1}.

Table-5 Average daily total water intake of various occupational categories

Category	Occupation	Count	Mean total water intake (L day^{-1} $person^{-1}$)
Labour intensive	Masonry workers	2	5.35
	Driver	1	3.91
	Farmers and agriculture labours	186	3.86
	Tailor	4	3.69
	Security Guard	1	3.55
Non-Labour intensive	House Wife	101	3.28
	Student	75	2.93
	Health Worker	1	2.69
	Police Man	1	1.90
	Homeopath Doctor	1	3.40
	Teacher	4	2.90
	Others (including old aged participants and non-school going children)	18	3.25
	NA including infants	3	1.50

3.4 Role of water intake values for cancer risk assessment

Human health risk assessment studies (Khan et al., 2015; Shah et al., 2012; Muhammad et al., 2011 and Muhammad et al., 2010) undertaken in Pakistan have used USEPA (1989) default water intake (2 L day^{-1}) and body weight (72 kg) values. This study has demonstrated that water intake was generally higher in the rural population of Pakistan than the revised USEPA (2011b) default water intake (2.5 L day^{-1}: updated from 2 L day^{-1} in 2011) with an average daily total water consumption of 3.5 L day^{-1} (men: 3.9 L day^{-1}, women: 3.2 L day^{-1}, children: 2.8 L day^{-1}). This difference in per capita drinking water consumption might contribute to considerably higher risks resulting from exposure to chemical contaminants in water. Using arsenic as an example, higher water intake levels might increase risk estimates for rural populations affected by arsenic-contaminated groundwater. To assess the impact of using default or generic as opposed to population specific intake levels, cancer risk assessment (Table-1: Equation-2) was carried out using intake variables (Table 2) from the present study and compared to USEPA default (2011b) and WHO recommended (2011) values. The only difference between the three scenarios (called present study; USEPA and WHO) is water intake (Table 2). The results of the risk assessment are provided in Table-6. Three risk levels were defined on the basis of risks above maximum allowable concentrations of 10 µg L^{-1} (WHO, USEPA), 50 μg L^{-1} (Pakistan Standards Quality Control Authority, 2010) and reported levels of >100 μg L^{-1} for arsenic concentration in drinking water (Table 2).

Table-6: Lifetime (Cumulative) Cancer risk point estimates of arsenic intake from water using input variables from the present study, USEPA and WHO

Water Intake data source	Parameters	Statistics	Children		Overall Adults (16-67 years)
			3-6 years	6-16 years	
Pakistan (Present study)	**Study participants**	***n***	5	61	332
	ADAF		3	3	1
	Body weight (kg)	***mean***	12	26	63
		SD	3	8	15
	Age-wise exposure duration	***years***	3*	10	51
	CR level-1	*mean (LB, UB)*	0.0017 (0.0014, 0.0017)	0.0014 (0.0011, 0.0014)	0.0006 (0.0006, 0.0006)
	CR level-2	*mean (LB UB)*	0.0087 (0.0072, 0.0088)	0.0070 (0.0057, 0.0072)	0.0033 (0.0032, 0.0034)
	CR level-3	*mean (LB, UB)*	0.0173 (0.0142, 0.0176)	0.0141 (0.0110, 0.0143)	0.0065 (0.0063, 0.0067)
USEPA**	**CR level-1**	***mean***	0.0006	0.0006	0.0005
	CR level-2	***mean***	0.0032	0.0029	0.0023
	CR level-3	***mean***	0.0064	0.0058	0.0045
WHO**	**CR level-1**	***mean***	0.0008	0.0006	0.0004
	CR level-2	***mean***	0.0039	0.0031	0.0018
	CR level-3	***mean***	0.0079	0.0062	0.0036

*minimum age of study participants
CR: Cancer risk, SD: Standard deviation
CR level-1 (>10 µg L^{-1}); CR level-2 (>50 µg L^{-1}); CR level-3 (>100 µg L^{-1})
** SDs not available for USEPA default and WHO recommended water intake values.

Cumulative cancer risks for an exposure duration of 3 to 67 years at all three risk levels and using three different water intake data sources (present study, USEPA and WHO) were found to be above the acceptable USEPA cancer risk criteria of 1.0 × 10^{-4} (i.e. 1 case of cancer per every 10,000) (Table 6). The, lifetime (cumulative) cancer risk at all three risk levels was found to be highest when applying total water intake values from this study (i.e. at lowest risk level, early life exposure with 17 chances in a population of 10000 children of age 3-6 years, 14 children in 10000 of age 6-16 years and 6 men or women in a population of 10000).

Whereas, cancer risk with USEPA default water intake (at lowest risk level, 6 chances in a population of 10000 children of both age groups 3-6 and 6-16 years, later age risk of 5 men or women in 10000 having 51 years of exposure (starting from 16 and continued to 67 years) and with WHO recommended water intake demonstrated an early age exposure of 8 in 10,000 children of 3-6 years, 6 in 10,000 children of 6-16 years and 4 in 10,000 adults, were found to be lower than this study (Table 6). Similarly cancer risk at risk levels 2 (>50 µg L^{-1}) and 3 (>100 µg L^{-1}) applying water intake from the present study compared to USEPA default and WHO recommended water intake values (Table 2) were revealed to be the highest for all age groups suggesting the significance of population specific water intake for cancer risk estimation.

These findings suggest that using the USEPA default water intake (i.e. 2.5 L day^{-1} for adults or 0.3-0.5 L day^{-1} for children aged 3-16 years) in regions having higher water intake than USA/Europe (e.g. South Asia, Africa etc.) may underestimate cancer risks and, conversely, for lower intake areas, the results might be over-estimated. USEPA default water intake values are based on the National Health and Nutrition Examination Surveys (1999–2010) but are used for worldwide risk assessment studies despite being lower than water intake values for warmer and developing areas of the world. Even in certain warmer parts of USA (i.e. California, Arizona) or during summer seasons, people may drink 4 to 4.5 L day^{-1} (USEPA, 1997; USEPA, 2000). Thus, the USEPA default value (2.5 L day^{-1}) or WHO recommendation of (1 L day^{-1} for children and 2.0 L day^{-1} for adults) may underestimate the risks for large numbers of people working in hot and humid environments (WHO, 2004). Cancer risk was calculated on the basis of total water intake (sum of direct and indirect water intake). Cancer risk determined from present study has also indicated that children are at higher risk than adults suggesting an increased carcinogenic potency during early life stages due to body weight and water intakes differences. This also suggests that lifetime cancer risk for children is much higher due to exposure during early life stages as compared to adults having exposure during later stages in life.

3.5 Role of food intake values for cancer risk assessment

In addition to water, food must be considered as an exposure pathway for arsenic although there have been much fewer studies for food than water (Schoof et al. 1999; Tao and Bolger. 1999; Hughes. 2006; Cascio et al. 2011). Human health risk assessments for arsenic in rice require a number of input parameters, such as amount of rice consumed and arsenic concentration in raw or cooked rice.

Past studies have reported rice arsenic levels as 0.32 mg/kg in France, 0.13-0.16 mg/kg in Spain, 0.13 mg/kg in California, 0.2 mg/kg in Arkansas, USA, 0.33-0.45 mg/kg in India, and 0.164 mg/kg in Pakistan (Saleem et al. 1988; Meharg et al. 2007; Bhattacharya et al. 2010). For the purposes of this risk assessment exercise, a conservative arsenic level reported for rice in Pakistan was selected (0.082 mg kg^{-1};Table-2; Rasheed et al. 2016) which is applicable to areas not traditionally associated with high environmental arsenic levels. Therefore, using the average daily rice intake determined in this study compared to intake parameters reported by other studies (Table 2) in Equations 1 and 2 (Table-1), it was possible to assess and compare the cumulative cancer risk of consumption of arsenic-contaminated rice (Figure-2).

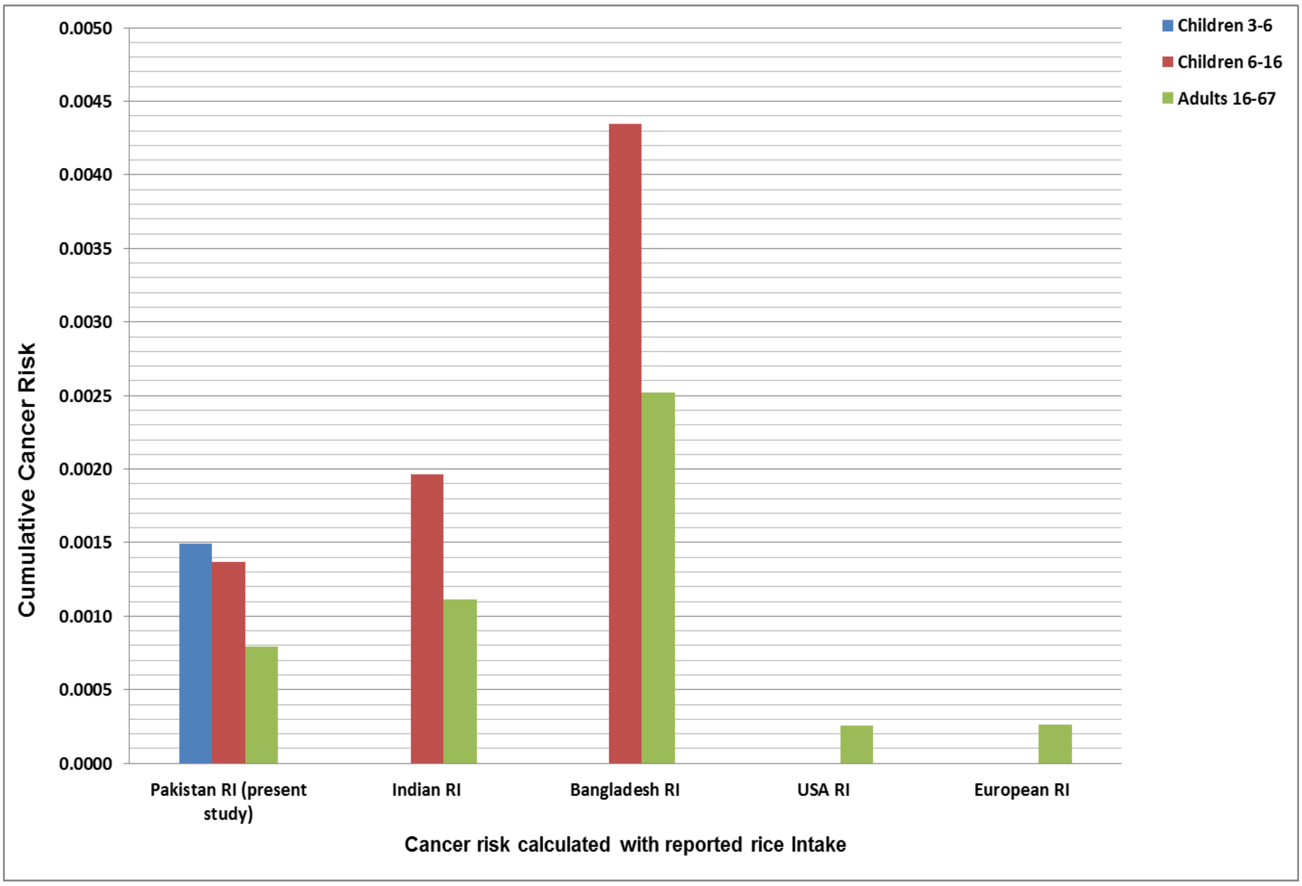

Figure-2: Cumulative cancer risk (point estimates at 95% CI) quantified from rice intake values of present study and previously published studies: the only parameter that is changed in each risk assessment is rice intake

Cancer risk due to rice consumption was found to be potentially higher in Bangladesh and India compared to the levels obtained for Pakistan in this study (Figure 2) based on differences in rice consumption values. Previous risk assessments for arsenic exposure through rice consumption in India reported risk results closer to this study using Indian intake values i.e. 7 adults in population of 10,000 (Meharg et al. 2009; Mondal and Polya. 2008). Past studies in Bangladesh (Meharg et al. 2009) also report quite similar levels of cancer risk (with 19 women and 22 men in a population of 10,000) in adult life as that shown in Figure 2. Cancer risk results using USA/European rice intake (i.e. 3 adults in population of 10,000) were also found to be similar to those identified by Meharg and co-workers (2009). So whilst the mean arsenic concentration used in the calculations is at the lower end of the reported arsenic concentration spectrum, residual cancer risk was still identified: using a higher arsenic concentration level, for instance, use of the recently established advisory limit of 0.2 mg kg^{-1} for arsenic in rice would lead to a higher cancer risk. This therefore suggests frequent rice consumption even at low arsenic concentrations may be a significant contributing factor for increased health risks from arsenic exposure. This fact is supported by the work of Banerjee and co-workers (2013), who showed that consuming arsenic-containing cooked rice as a staple food is associated with elevated genotoxic effects. It is further assumed that the arsenic concentration of raw rice and rice cooking water, volume of cooking water, cooking method and types of rice influence the arsenic level of cooked rice (Ohno et al. 2007). Rinsing, washing and cooking in a high volume of water and discarding excess water were found effective to reduce the inorganic arsenic content of cooked rice by 50% but had no effect on organic arsenic (Raab et al 2009). In the study area, most of the households had their own ground water source from where water was obtained for drinking, cooking, washing, bathing etc. Higher arsenic levels in their ground water sources is expected as evidenced from previous studies (Tahir and Rasheed, 2014; Mahar et al. 2015; Shakoor et al. 2015). Thus, rice cooking in a high volume of water was observed to be more prevalent however the arsenic level of cooking water is likely to be a reason for higher dietary arsenic exposure and requires further investigation.

In comparison to water and rice, there are very limited arsenic risk assessment studies for wheat. Studies show that wheat does take up arsenic from soil, indicating that wheat consumption is a potential exposure route (William et al. 2007). Arsenic has been identified in wheat grains at levels of 0.02 mg kg^{-1} in USA (Gartrell et al. 1986), 0.05 mg kg^{-1} in Netherlands (Wiersma et al. 1986), 362 mg kg^{-1} in India (Roychowdhury et al. 2002), 0.129 mg kg^{-1} in India (Bhattacharya et al. 2010), 0.127 mg kg^{-1} in Pakistan (Saleem et al. 1988) and 0.175-0.317 mg kg^{-1} in Sindh, Pakistan (Arain et al. 2009). A mean arsenic concentration of 0.012 mg kg^{-1} in wheat grains (Al-Othman et al. 2013) was used in the risk assessments, reflecting a conservative estimate of arsenic concentration for arsenic-affected countries whilst being applicable to regions with lower environmental arsenic levels. Using wheat intake values of this study and those reported for other countries or regions (Table 2), cancer risk was found to be within the USEPA acceptable cancer risk range of 1.0×10^{-4} for Bangladesh, China, Europe and the USA intake values. However, for Pakistan, where wheat intake is comparatively higher, cumulative cancer risk was found to be 2 persons (95% CI 0.0002, 0.0002) in a population of 10,000 with exposure initiating during 3-16 years.

3.6 Relative cancer risk (point estimates) from water and food sources

Multiple exposures are important when considering overall cancer risk hence it is important to consider the combined contributions made by water (>10 µg L^{-1}) and food to arsenic exposure. Using the water and food intake values (rice and wheat only) of this study, cumulative cancer risk is depicted in Figure 3 showing relative risk contribution by total water (51%), rice (44%) and wheat (5%) intake for different sub-populations (Figure 3). Food sources like rice are therefore a considerable contributing factor for exposure to waterborne contaminants such as arsenic, so knowledge of intake values (as well as contaminant loading) for different food stuffs is important to elucidate overall cancer risk.

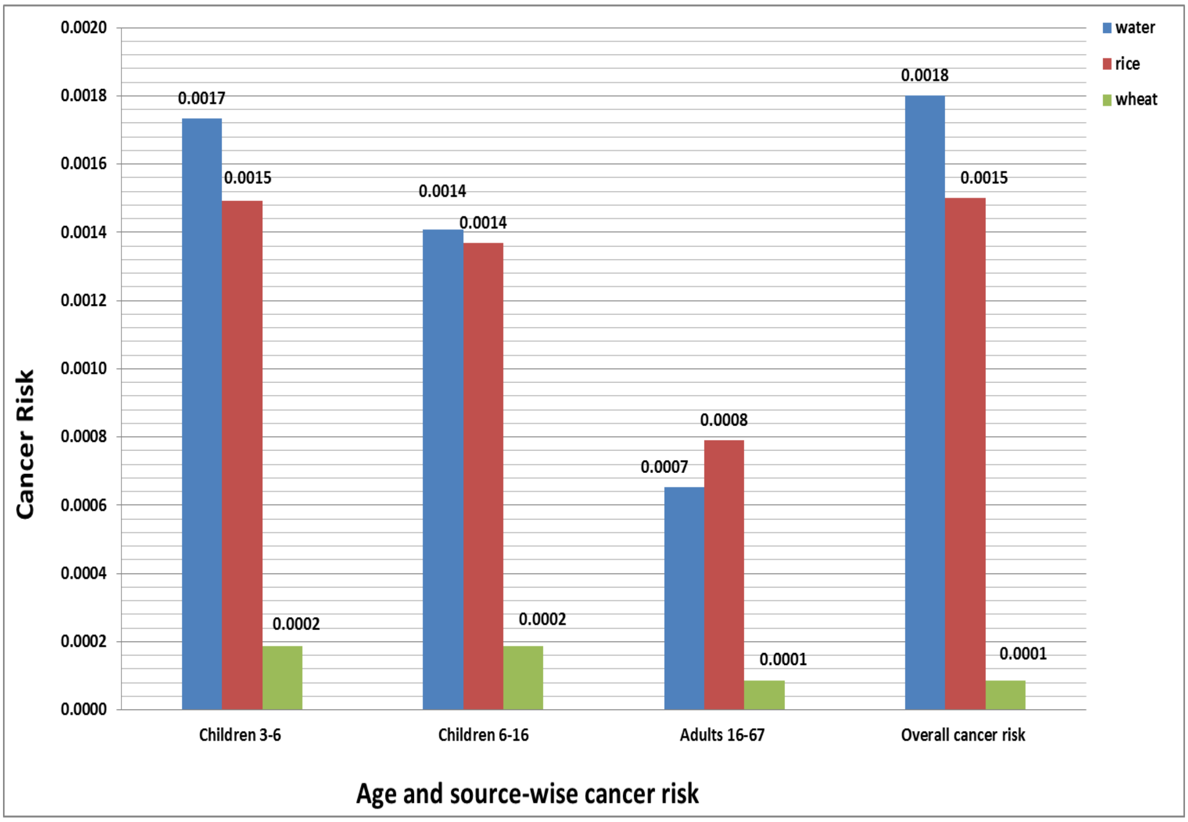

Figure-3: Cancer risk (point estimates at 95% CI) based on the average daily water, rice and wheat intake values of present study and exposure duration of 3-67 years of study participants

3.7 Probabilistic Risk Assessment approach

3.7.1 Results of probability distribution of input parameters

The sample data of arsenic concentration >10 µg L^{-1} of 17 districts (Tahir and Rasheed, 2014; Ahmad et al. 2004) and age data of 398 study participants were selected to define probability distributions. The optimal fitted distributions of arsenic concentration >10 µg L^{-1} and age of participants were characterised by a Generalized Pareto distribution and Rician distribution respectively as indicated by a set of parameters (Table 7).

Table-7 Probability distribution of arsenic in ground water and age of study participants

Probability Distribution	Arsenic concentration in water		Age of study participants	
	Original Data	**Generalized Pareto distribution**	**Original Data**	**Rician Distribution**
Minimum	10.0	10.0	3	3
Mean	52.5	52.6	36	34
Median	29.4	32.7	36	32
Percentile 95^{th}	166.0	154.4	62	64
Maximum	972.0	809.6	80	83
Standard deviation	63.3	63.7	17	16
Variance	4007.5	4052.7	289	272
Std. mean error	0.926	0.931	0.852	0.826
t-test for equality of means		***P= 0.392***		***P = 0.085***

The body weights of participants were fitted with respect to their ages based on Fourier fit in MATLAB (Supplementary information Figure S-1).

3.7.2 Probabilistic cancer risk

Probabilistic risk assessment is an improved approach to deterministic cancer risk estimation (point estimation). To better consider the uncertainty inherent in dietary data, probabilistic outputs were associated with seven different age groups as shown in Table 8. Using Monte Carlo simulations applied to ADAF transformed data for water, rice and wheat and combined dietary factors (Table 8 and 9), the results were found to be similar to point estimates with lifetime cancer risk of water and rice higher for intake values determined from this study compared to the USEPA regulatory threshold target cancer risk of 1.0 x 10^{-4} suggesting probable association between dietary intake and arsenic concentration levels.

Table-8 Probabilistic cancer risk (average risk from 10,000 permutations) exposed to arsenic in water at different age groups

Age groups (Years)	Mean	95% CI		Standard Deviation	Minimum	Maximum	Median	75th percentile	95th percentile
		LB	UB						
3-6	0.0073	0.0061	0.0084	0.0072	0.0016	0.0626	0.0056	0.0093	0.0183
6-16	0.0052	0.0049	0.0056	0.0055	0.0007	0.0624	0.0034	0.0064	0.0152
16-26	0.0042	0.0040	0.0044	0.0047	0.0006	0.0507	0.0027	0.0051	0.0128
26-36	0.0026	0.0025	0.0028	0.0031	0.0004	0.0439	0.0017	0.0031	0.0079
36-46	0.0016	0.0015	0.0017	0.0017	0.0003	0.0283	0.0010	0.0019	0.0045
46-56	0.0010	0.0009	0.0010	0.0011	0.0001	0.0097	0.0006	0.0012	0.0031
56-67	0.0003	0.0003	0.0004	0.0004	0.0000	0.0064	0.0002	0.0004	0.0011

CI: Confidence Interval, LB: Lower bound, UB: Upper bound

Table-9 Probabilistic cancer risk (average risk from 10,000 permutations) exposed to arsenic in rice and wheat at different age groups

Age groups (Years)	CR-Rice				CR-Wheat			
	Mean	95% CI		Standard Deviation	Mean	95% CI		Standard Deviation
		LB	UB			LB	UB	
3-6	0.0014	0.0014	0.0014	0.00005	0.0002	0.0002	0.0002	0.00001
6-16	0.0011	0.0011	0.0011	0.00029	0.0001	0.0001	0.0001	0.00003
16-26	0.0010	0.0010	0.0010	0.00020	0.0001	0.0001	0.0001	0.00002
26-36	0.0006	0.0006	0.0006	0.00008	0.0001	0.0001	0.0001	0.00001
36-46	0.0004	0.0004	0.0004	0.00005	0.0000	0.0000	0.0000	0.00001
46-56	0.0002	0.0002	0.0002	0.00004	0.0000	0.0000	0.0000	0.00000
56-67	0.0001	0.0001	0.0001	0.00004	0.0000	0.0000	0.0000	0.00000

CI: Confidence Interval, LB: Lower bound, UB: Upper bound

It is interesting to note that highest cumulative exposure from water and food sources initiating at age 3-6 years resulted in the risk probability of 89 children and ranging to 4 adults of age 56-67 in a population of 10,000. The findings are attributed to the incorporation of age dependent adjustment factors (ADAFs) which accounts for adjustment in cancer slope factor according to age. Thus, age adjusted probabilistic cancer risk from food intake of this study population hold a considerable contribution and cannot be neglected in risk quantification process (Figure-4 and 5).

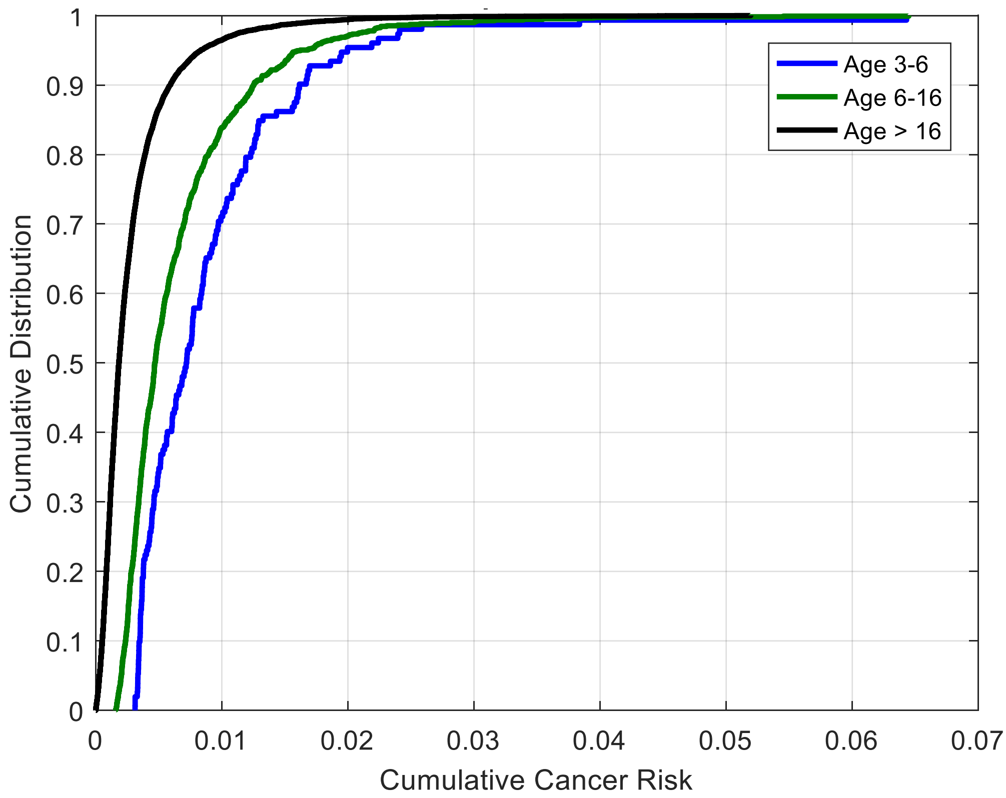

Figure-4 Cumulative probability distributions of age adjusted cancer risk from water and food intake for an exposure duration initiating at minimum age of study participant i.e. 3 years proceeding to age 67 years

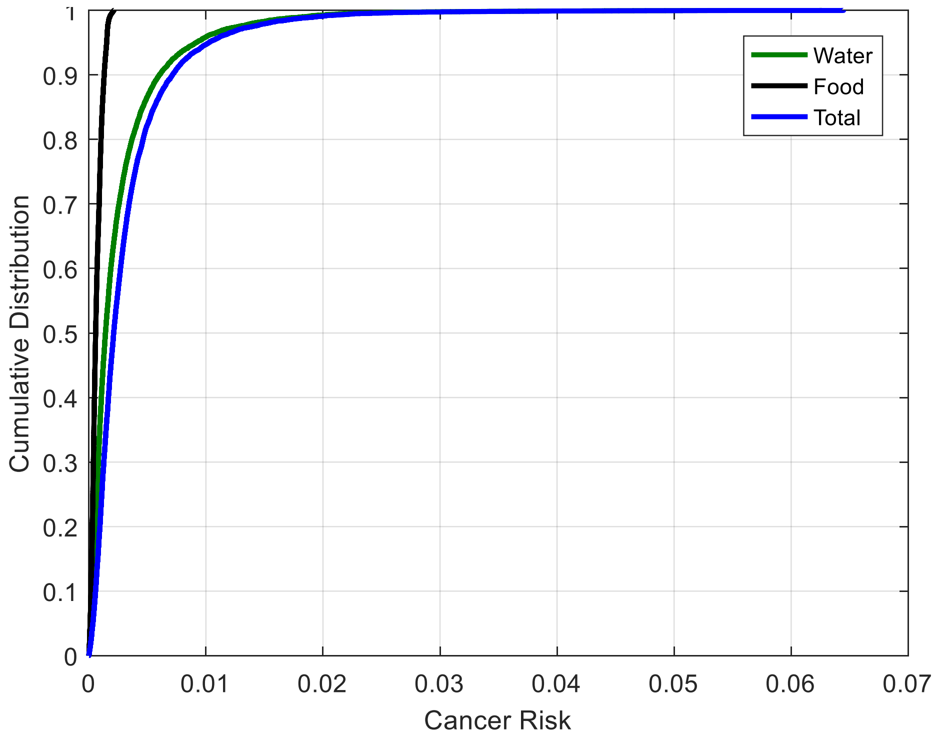

Figure-5 Cumulative probability distributions of age adjusted excess lifetime cancer risk from water and food intake (rice and wheat combined) and both (total risk) for the studied population

4. Conclusions

Mean total water intake (3.5 L day^{-1}) quantified on the basis of direct plain drinking water (2.7 L day^{-1}) and indirect water from food and beverages (0.8 L day^{-1}) for rural villages in Pakistan was found to be higher than the reported or recommended water intake of many developed countries. Comparison of the intake values determined for Pakistan with the USEPA default and the WHO recommended daily water intake in a cancer risk assessment model revealed a higher total cancer risk of 17 for children of 3-6 years (95% CI 0.0014, 0.0017), 14 for children of 6-16 years (95% CI 0.001, 0.0011) and 6 for adults of 16-67 years (95% CI, 0.0006, 0.0006) in a population of 10,000. This compares to respective figures of 6, 6 and 5 (USEPA) and 8, 6 and 4 (WHO). This difference at arsenic exposures above 10 µg L^{-1} shows the importance of population specific water intake values and the need to include indirect water sources in risk assessments.

Food is another significant exposure route for chemical risk. Mean average food intake in rural Pakistan was found to be 789 g day^{-1} consisting of wheat (402 g day^{-1}), rice (469 g day^{-1}), pulses (234 g day^{-1}), vegetables (170 g day^{-1}) and chicken (166 g day^{-1}). Consumption of rice was found to be higher than rice intake levels reported in USA (172.6 g day^{-1}), Europe (175 g day^{-1}), but consistent with intake levels reported for Bangladesh (1789 g day^{-1}) and India (862 g day^{-1}). Comparison of the rice intake values determined for Pakistan with these reported rice intake levels in the USEPA cancer risk assessment model revealed a lifetime cancer risk of 15 for children of3-6 years, 14 for children of6-16 years and 8 for adults. This compares to figures of 20 for children (6-16 years) and 11 for adults with Indian rice intake or 43 for children (6-16 years) and 25 for adults with Bangladesh rice intake). Using US/European rice intake values the risk for adults is 3) in a population size of 10000. This shows that countries with the highest consumption of rice have potentially higher cancer risks associated with arsenic exposure: India, Pakistan and Bangladesh all have environmental arsenic problems whilst US/European markets might import from these areas. Using wheat intake values from this study (402 g day^{-1}) has revealed a total cancer risk of 2 children (3-16 years) and 1 adult of 16-67 years. Whereas, with wheat intake reported for Bangladesh (131-179 g day^{-1}), China (13-44 g day^{-1}), Europe (182 g day^{-1}) and USA (48 g day^{-1}), cancer risk was found to be within the USEPA acceptable cancer risk range of 1.0×10^{-4} highlighting the role of the wheat intake and arsenic concentration level in the risk assessment process (a conservative estimate used). These results are further supported by uncertainty analysis using a probabilistic approach indicating the significance of population specific dietary intake values, arsenic concentrations in water and age of participants in determining cancer risk estimates.

The study findings demonstrate that population specific model values realistically reflect the local situation, whilst also showing that consideration of multiple exposure sources, e.g. water and food sources with respect to age provide a more robust risk assessment. The population specific dietary information from this study may hold significance for future studies to understand a range of age adjusted dietary exposure risks.

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Appendix A. Supplementary Information

Tables-S-1 to S-7

Figures S-1

References

Abdollahi, M., Naseri, E., Bondarianzadeh, D., Mohammadpour, B., and Houshiar-rad, A. (2013). Types and amounts of fluids consumed by the adult population of Tehran. *Iran J Nutr Sci Food Technol 8:71–80.*

Aga Khan University, Pakistan, Pakistan Medical Research Council (PMRC) and Nutrition Wing, Ministry of Health, Pakistan. National Nutrition Survey. (2011). UNICEF Pakistan. Available at: https://www.humanitarianresponse.info/system/files/documents/files/59_National%20Nutrition%20Survey-2011.pdf. (Accessed 01.04.16).

Agency for Toxic Substances and Disease Registry (ATSDR). (2007). Toxicological Profile for Arsenic. U.S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry. 2007; 1-559.

Agricultural Research Service. (2014). United States Department of Agriculture's (USDA) National Nutrient Database: Standard Reference Release 27. Available at: http://ndb.nal.usda.gov/ndb/search/list.(Accessed 01.01.15).

Agusa, T., Kunito, T., Fujihara, J., Kubota, R., Minh, T., Kim Trang, P., Iwata, H., Subramanian, A., Viet, P. and Tanabe, S. (2006). Contamination by arsenic and other trace elements in tube-well water and its risk assessment to humans in Hanoi, Vietnam. *Environmental Pollution*, 139(1), pp.95-106.

Ahmad, T., Kahlown, M., Tahir, A., and Hifza, R. (2004). Arsenic an Emerging Issue: Experiences from Pakistan. *Proceedings of 30th WEDC International Conference* Vietiane, Lao PDR.

Ahsan, H., Chen, Y., Parvez, F., Argos, M., Hussain, A., Momotaj, H., Levy, D., van Geen, A., Howe, G. and Graziano, J. (2006). Health Effects of Arsenic Longitudinal Study (HEALS): Description of a multidisciplinary epidemiologic investigation. *J Expos Sci Environ Epidemiol*, 16(2), pp.191-205.

Al-Othman, Z., Ali, R., Al-Othman, A., Ali, J. and A. Habila, M. (2013). Assessment of toxic metals in wheat crops grown on selected soils, irrigated by different water sources. *Arabian Journal of Chemistry*. Available at: http://dx.doi.org/10.1016/j.arabjc.2012.04.006. (Accessed 01.02.16).

Arain, M., Kazi, T., Baig, J., Jamali, M., Afridi, H., Shah, A., Jalbani, N. and Sarfraz, R. (2009). Determination of arsenic levels in lake water, sediment, and foodstuff from selected area of Sindh, Pakistan: Estimation of daily dietary intake. *Food and Chemical Toxicology*, 47(1), pp.242-248.

Azlan, A., Khoo, H., Idris, M., Amin, I. and Razman, M. (2012). Consumption Patterns and Perception on Intake of Drinking Water in Klang Valley, Malaysia. *Pakistan J. of Nutrition*, 11(6), pp.584-590.

Barraj, L., Scrafford, C., Lantz, J., Daniels, C. and Mihlan, G. (2008). Within-day drinking water consumption patterns: Results from a drinking water consumption survey. *J Expos Sci Environ Epidemiol*, 19(4), pp.382-395.

Batres-Marquez, S., Jensen, H. and Upton, J. (2009). Rice Consumption in the United States: Recent Evidence from Food Consumption Surveys. *Journal of the American Dietetic Association*, 109(10), pp.1719-1727.

Bellisle, F., Thornton, S., Hebel, P., Denizeau, M. and Tahiri, M. (2010). A study of fluid intake from beverages in a sample of healthy French children, adolescents and adults. *European Journal of Clinical Nutrition*, 64(4), pp.350-355. doi: 10.1038/ejcn.2010.4.

Banerjee et al., 2013. M. Banerjee, N. Banerjee, P. Bhattacharjee, D. Mondal, P.R. Lythgoe, M. Martínez, *et al.* High arsenic in rice is associated with elevated genotoxic effects in humans Scientific Reports, 3 (2013), p. 2195

Bennett, John B. & Stedge, Gerald D. (2000).. United States. Environmental Protection Agency. Office of Ground Water and Drinking Water. 2000, Proposed arsenic in drinking water rule regulatory impact analysis [electronic resource] Principal investigator Office of Ground Water and Drinking Water, U.S. Environmental Protection Agency Washington, D.C. pp:5-8.

Bhattacharya, P., Samal, A., Majumdar, J. and Santra, S. (2010). Arsenic Contamination in Rice, Wheat, Pulses, and Vegetables: A Study in an Arsenic Affected Area of West Bengal, India. Water, Air, & Soil Pollution, 213(1-4), pp.3-13.

Calderon, R., Hudgens, E., Le, X., Schreinemachers, D. and Thomas, D. (1999). Excretion of arsenic in urine as a function of exposure to arsenic in drinking water. *Environ Health Perspect*, 107(8), pp.663-667.

Cascio, C., Raab, A., Jenkins, R., Feldmann, J., Meharg, A. and Haris, P. (2011). The impact of a rice based diet on urinary arsenic. *J. Environ. Monit.*, 13(2), pp.257-265.

Cha, H., Han, G. and Chung, H. (2012). A study on the trend analysis regarding the rice consumption of Korean adults using Korean National Health and Nutrition Examination Survey data from 1998, 2001 and 2005. *Nutrition Research and Practice*, 6(3), p.254.

Chen, H., Lee, C., Huang, W., Huang, H., Wu, Y., Hsu, Y. and Kao, Y. (2015). Arsenic speciation in rice and risk assessment of inorganic arsenic in Taiwan population. *Environmental Science and Pollution Research*, 23(5), pp.4481-4488.

Chowdhury, U., Biswas, B., Chowdhury, T., Samanta, G., Mandal, B., Basu, G., Chanda, C., Lodh, D., Saha, K., Mukherjee, S., Roy, S., Kabir, S., Quamruzzaman, Q. and Chakraborti, D. (2000). Groundwater Arsenic Contamination in Bangladesh and West Bengal, India. *Environ Health Perspect*, 108(5), pp.393-397.

Collett D. (2003). Modelling survival data in medical research. 2nd Edition. London: Chapman & Hall.

Commonwealth scientific and industrial research organisation (CSIRO) and University of South Australia. (2008). Australian national children's nutrition and physical activity survey—main findings. Canberra: Commonwealth of Australia. ISBN: 1-74186-756-8. Available at: https://www.health.gov.au/internet/main/publishing.nsf/Content/8F4516D5FAC0700ACA257BF0001E0109/$File/childrens-nut-phys-survey.pdf. (Accessed 10.02.16).

Del Razo, L., Garcia-Vargas, G., Garcia-Salcedo, J., Sanmiguel, M., Rivera, M., Hernandez, M. and Cebrian, M. (2002). Arsenic levels in cooked food and assessment of adult dietary intake of arsenic in the Region Lagunera, Mexico. *Food and Chemical Toxicology*, 40(10), pp.1423-1431.

Dietary Reference Intakes: Water, a. (2004). *Dietary Reference Intakes: Water, Potassium, Sodium, Chloride, and Sulfate: Health and Medicine Division*. Nationalacademies.org. Available at: http://www.nationalacademies.org/hmd/Reports/2004/Dietary-Reference-Intakes-Water-Potassium-Sodium-Chloride-and-Sulfate.aspx (Accessed 01.01.16).

Doll, R., and Peto, R. (1996). Epidemiology of cancer. In: Weatherall DJ, Ledingham JGG, Warrell DA, eds. *Oxford textbook of medicine*. Oxford, Oxford University Press, 1996:197-221.

Drewnowski, A., Rehm, C. and Constant, F. (2013). Water and beverage consumption among adults in the United States: cross-sectional study using data from NHANES 2005-2010. *BMC Public Health*, 13(1), p.1068. doi: 10.1186/1471-2458-13-1068.

Duxbury, J., Mayer, A., Lauren, J. and Hassan, N. (2003). Food Chain Aspects of Arsenic Contamination in Bangladesh: Effects on Quality and Productivity of Rice. *Journal of Environmental Science and Health, Part A*, 38(1), pp.61-69.

European Food Safety Authority (EFSA). 2014. Dietary exposure to inorganic arsenic in the European population. *EFSA Journal 2014;12(3):3597*. European Food Safety Authority Parma, Italy

European Food Safety Authority (EFSA). (2010). Scientific Opinion on Dietary Reference Values for water**.** *EFSA Journal 2010; 8(3):1459*. European Food Safety Authority (EFSA), Parma, Italy.

Ershow, A.,G. and Cantor, K.,P. (1989). Total Water and Tap water Intake in the United States: Population-Based Estimates of Quantities and Sources. Life Sciences Research Office, Federation of American Societies for Experimental Biology, Bethesda, MD.

Food and Agriculture Organization (FAO). (2013). FAO Statistical Yearbook-2013. Food and Agriculture Organization of the United Nations. http://faostat.fao.org/site/567/DesktopDefault.aspx#ancor. (Accessed 10.03.16).

Food and Agriculture Organization and World Health Organization (FAO and WHO), 2009. Principles and Methods for the Risk Assessment of Chemicals in Food. Dietary Exposure Assessment of Chemicals in Food. Environmental Health Criteria 240. International Programme on Chemical Safety. A joint publication of the Food and Agriculture Organization of the United Nations and the World Health Organization. ISBN 978 92 4 157240 8. Wissenchaftliche Verlagsgesellschaft mbH, Stuttgart, Germany.

Food and Agriculture Organization (FAO). 1998. Report of the Fifth External Programme and Management Review of International Rice Research Institute (IRRI). TAC Secretariat. Food and Agriculture Organization of the United Nations. http://www.fao.org/wairdocs/tac/x5801e/x5801e00.htm#Contents. (Accessed 10.03.16).

Ferreira-Pego, C., Babio, N., Fenández-Alvira, J.,M., Iglesia, I., Moreno, L.,A. and Salas-Salvadó, J. (2014). Fluid intake from beverages in Spanish adults; cross-sectional study. *Nutr Hosp. 2014 May 1;29(5):1171-8*. doi: 10.3305/nh.2014.29.5.7421.

Farr, W (1852). Proportion of the sexes who die of cholera at different periods of an epidemic, and under different circumstances. Report on the mortality of cholera in England, 1848-49. Royal College of Physicians of London. p. xl. Available at: https://archive.org/details/b24751297. (Accessed 26.07.16).

Gandy, J. (2015). Erratum to: Water intake: validity of population assessment and recommendations. *European Journal of Nutrition*, 54(6), pp.1031-1031.

Ganguli, D., Das, N., Saha, I., Biswas, P., Datta, S., Mukhopadhyay, B., Chaudhuri, D., Ghosh, S. and Dey, S. (2011). Major dietary patterns and their associations with cardiovascular risk factors among women in West Bengal, India. *British Journal of Nutrition*, 105(10), pp.1520-1529.

Gartrell, M.J. ; Craun, J.C. ; Podrebarac, D.S.; Gunderson, E.L. Pesticides, selected elements, and other chemicals in adult diet samples. *J. Assoc. Off.Anal. Chem*., 1986, 69, 146-161.

Gilbert, P., Polya, D. and Cooke, D. (2015). Arsenic hazard in Cambodian rice from a market-based survey with a case study of Preak Russey village, Kandal Province. *Environ Geochem Health*, 37(4), pp.757-766.

Kennedy, G., Burlingame, B. and Nguyen, N. (2002). Nutrient impact assessment of rice in major rice-consuming countries.Newsletter 5. Rome:Food and Agriculture Organization.

Grandjean, A. (2004). Water requirements, impinging factors, and recommended intakes. Rolling revision of the WHO Guidelines for Drinking-Water Quality. World Health Organization. pp.5.

Guelinckx, I., Ferreira-Pego, C., Moreno, L., Kavouras, S., Gandy, J., Martinez, H., Bardosono, S., Abdollahi, M., Nasseri, E., Jarosz, A., Ma, G., Carmuega, E., Babio, N. and Salas-Salvado, J. (2015). Intake of water and different beverages in adults across 13 countries. *European Journal of Nutrition*, 54(S2), pp.45-55.

He P, Lu Y, Liang Y, Chen B, Wu M, Li S, He G, Jin T. Exposure assessment of dietary cadmium: findings from shanghainese over 40 years, China. BMC Public Health 2013; 13:590; PMID:23773573; http://dx.doi.org/10.1186/1471-2458-13-590

Helgesen, H. and Larsen, E. (1998). Bioavailability and speciation of arsenic in carrots grown in contaminated soils. *The Analyst*, 123(5), pp.791-796.

Hopkins, S., M. and Ellis, J., C. (1980) Drinking water consumption in Great Britain. Technical Report TR 137 Medmenhom Laboratory. Water Research Center.

Hossain, M., Rahman, M., Murrill, M., Das, B., Roy, B., Dey, S., Maity, D. and Chakraborti, D. (2012). Water consumption patterns and factors contributing to water consumption in arsenic affected population of rural West Bengal, India. *Science of The Total Environment*, 463-464, pp.1217-1224.

Hu, F. (2002). Dietary pattern analysis: a new direction in nutritional epidemiology. *Current Opinion in Lipidology*, 13(1), pp.3-9.

Hughes, M. (2006). Biomarkers of Exposure: A Case Study with Inorganic Arsenic. *Environ Health Perspect*. 2006 Nov; 114(11): 1790–1796. doi: 10.1289/ehp.9058.

Hydrie, M., Basit, A., Samad Sher, A., Hakeem, R. and Hussain, A. (2010). Dietary Patterns Associated with Risk for Metabolic Syndrome in Urban Community of Karachi Defined by Cluster Analysis. *Pakistan J. of Nutrition*, 9(1), pp.93-99.

Iqbal, S.,P., Dodani, S. and Qureshi, R. (2004) Risk factors and behaviours for coronary artery disease (CAD) among ambulatory Pakistanis. *J Pak Med Assoc 54, 261–266*.

Jafar, T.,H., Hatcher, J., Poulter, N., Islam, M., Hashmi, S., Qadri, Z., Bux, R., Khan, A., Jafary, F.,H., Hameed, A., Khan, A., Badruddin, S.,H., Chaturvedi, N. (2009). Hypertension Research Group. Community-based interventions to promote blood pressure control in a developing country: a cluster randomized trial. *Ann Intern Med. 2009 Nov 3;151(9):593-601*. doi: 10.7326/0003-4819-151-9-200911030-00004.

Jiang, Y., Zeng, X., Fan, X., Chao, S., Zhu, M. and Cao, H. (2015). Levels of arsenic pollution in daily foodstuffs and soils and its associated human health risk in a town in Jiangsu Province, China. *Ecotoxicology and Environmental Safety*, 122, pp.198-204.

Jones, A., Majowicz, S., Edge, V., Thomas, M., MacDougall, L., Fyfe, M., Atashband, S. and Kovacs, S. (2007). Drinking water consumption patterns in British Columbia: An investigation of associations with demographic factors and acute gastrointestinal illness. *Science of The Total Environment*, 388(1-3), pp.54-65.

Kahn, H. and Stralka, K. (2008). Estimated daily average per capita water ingestion by child and adult age categories based on USDA's 1994, 1996 and 1998 continuing survey of food intakes by individuals. *J Expos Sci Environ Epidemiol*, 19(4), pp.396-404.

Kant, A., Graubard, B. and Atchison, E. (2009). Intakes of plain water, moisture in foods and beverages, and total water in the adult US population--nutritional, meal pattern, and body weight correlates: National Health and Nutrition Examination Surveys 1999-2006. *American Journal of Clinical Nutrition*, 90(3), pp.655-663.

Khan, N., Bruce, D., Naidu, R. and Owens, G. (2009). Implementation of food frequency questionnaire for the assessment of total dietary arsenic intake in Bangladesh: Part B, preliminary findings. *Environ Geochem Health*, 31(S1), pp.221-238.

Kile, M., Houseman, E., Breton, C., Quamruzzaman, Q., Rahman, M., Mahiuddin, G. and Christiani, D. (2007). Association between total ingested arsenic and toenail arsenic concentrations. *Journal of Environmental Science and Health, Part A*, 42(12), pp.1827-1834.

Levallois, P., Guevin, N., Gingras, S., Levesque, B., Weber, J. and Letarte, R. (1998). New patterns of drinking-water consumption: results of a pilot study. *Science of The Total Environment*, 209(2-3), pp.233-241.

Liang, C., Wang, S., Kao, Y. and Chen, J. (2016). Health risk assessment of groundwater arsenic pollution in southern Taiwan. *Environ Geochem Health*. DOI: 10.1007/s10653-016-9794-4

Ma, G., Zhang, Q., Liu, A., Zuo, J., Zhang, W., Zou, S., Li, X., Lu, L., Pan, H. and Hu, X. (2012). Fluid intake of adults in four Chinese cities. *Nutrition Reviews*, 70, pp.S105-S110.

Mahmood, A., Malik, R., Li, J. and Zhang, G. (2014). Human health risk assessment and dietary intake of organochlorine pesticides through air, soil and food crops (wheat and rice) along two tributaries of river Chenab, Pakistan. *Food and Chemical Toxicology*, 71, pp.17-25.

Manz, F., Johner, S., Wentz, A., Boeing, H. and Remer, T. (2012). Water balance throughout the adult life span in a German population. *British Journal of Nutrition*, 107(11), pp.1673-1681.

Martinez, H. (2014). Fluid intake in Mexican adults; a cross-sectional study. *Nutr Hosp*. 2014 May 1;29(5):1179-87. doi: 10.3305/nh.2014.29.5.7447.

Mahar, M.T., Khuhawar, M.Y., Jahangir**,** T.M., 2015. Arab J Geosci. Determination of arsenic contents in groundwater of District Rahim Yar Khan Southern Punjab, Pakistan. (2015) 8: 10983. doi:10.1007/s12517-015-1979-0.

Meharg, A. and Zhao, F., J. (2012). Arsenic and Rice. Springer Netherlands. pp. 171. ISBN 978-94-007-2946-9. *doi:* 10.1007/978-94-007-2947-6.

Meharg, A. and Raab, A. (2010). Getting to the bottom of arsenic standards and guidelines. *Environmental Science & Technology*, 44(12), pp.4395-4399.

Meharg, A., Williams, P., Adomako, E., Lawgali, Y., Deacon, C., Villada, A., Cambell, R., Sun, G., Zhu, Y., Feldmann, J., Raab, A., Zhao, F., Islam, R., Hossain, S. and Yanai, J. (2009). Geographical Variation in Total and Inorganic Arsenic Content of Polished (White) Rice. *Environmental Science & Technology*, 43(5), pp.1612-1617.

Meharg, A. (2007). Levels of arsenic in rice – literature review, Food Standards Agency contract C101045, UK 2007.

Meharg, A. and Rahman, M. (2003). Arsenic Contamination of Bangladesh Paddy Field Soils: Implications for Rice Contribution to Arsenic Consumption. *Environmental Science & Technology*, 37(2), pp.229-234.

Melkonian, S., Argos, M., Hall, M., Chen, Y., Parvez, F., Pierce, B., Cao, H., Aschebrook-Kilfoy, B., Ahmed, A., Islam, T., Slavcovich, V., Gamble, M., Haris, P., Graziano, J. and Ahsan, H. (2013). Urinary and Dietary Analysis of 18,470 Bangladeshis Reveal a Correlation of Rice Consumption with Arsenic Exposure and Toxicity. *PLoS ONE*, 8(11), p.e80691.

Miller, P., Morey, M., Hartman, T., Snyder, D., Sloane, R., Cohen, H. and Demark-Wahnefried, W. (2012). Dietary Patterns Differ between Urban and Rural Older, Long-Term Survivors of Breast, Prostate, and Colorectal Cancer and Are Associated with Body Mass Index. *Journal of the Academy of Nutrition and Dietetics*, 112(6), pp.824-831.e1.

Milton, A.,H., Rahman, H., Smith, W., Shrestha, R. and Dear, K. (2006). *Water consumption patterns in rural Bangladesh: are we underestimating total arsenic load*? *J Water Health.2006 Dec;4(4):431-6*.

Moy, G., G and Vannoort, R.,W. (2013). Total Diet Studies. Pp. 184. Springer, NY.

Mondal, D., Banerjee, M., Kundu, M., Banerjee, N., Bhattacharya, U., Giri, A., Ganguli, B., Sen Roy, S. and Polya, D. (2010). Comparison of drinking water, raw rice and cooking of rice as arsenic exposure routes in three contrasting areas of West Bengal, India. *Environ Geochem Health*, 32(6), pp.463-477.

Mondal, D. and Polya, D. (2008). Rice is a major exposure route for arsenic in Chakdaha block, Nadia district, West Bengal, India: A probabilistic risk assessment. *Applied Geochemistry*, 23(11), pp.2987-2998.

Muhammad, S., Shah, M. and Khan, S. (2011). Health risk assessment of heavy metals and their source apportionment in drinking water of Kohistan region, northern Pakistan. *Microchemical Journal*, 98(2), pp.334-343.

Muhammad, S., Tahir, M. and Khan, S. (2010). Arsenic health risk assessment in drinking water and source apportionment using multivariate statistical techniques in Kohistan region, northern Pakistan. *Food and Chemical Toxicology*, 48(10), pp.2855-2864.

Munoz, O., Bastias, J., Araya, M., Morales, A., Orellana, C., Rebolledo, R. and Velez, D. (2005). Estimation of the dietary intake of cadmium, lead, mercury, and arsenic by the population of Santiago (Chile) using a Total Diet Study. *Food and Chemical Toxicology*, 43(11), pp.1647-1655.

National Health and Medical Research Council and National Resource Management Ministerial Council (NHMRC and NRMMC). (2011). Australian Drinking Water Guidelines Paper 6. National Water Quality Management Strategy. National Health and Medical Research Council, National Resource Management Ministerial Council, Commonwealth of Australia, Canberra. pp; 6–4

Norimah, K., Safiah, M., Jamal, K., Haslinda, S., Zuhaida, H., Rohida, S., Fatimah, S., Norazlin, S., Poh, K., Kandiah, M., Zalilah, S., Wan Manan, M., Fatimah, S., Azmi, Y. (2008). Food Consumption Patterns: Findings from the Malaysian Adult Nutrition Survey (MANS). *Malays J Nutr. 2008 Mar;14(1):25-39.*

National Statistical Organisation India. (2012). Nutritional Intake in India, 2011-12. National Sample Survey Office. Ministry of Statistics and Programme Implementation. Government of India.

Ohno, K., Yanase, T., Matsuo, Y., Kimura, T., Hamidur Rahman, M., Magara, Y. and Matsui, Y. (2007). Arsenic intake via water and food by a population living in an arsenic-affected area of Bangladesh. *Science of The Total Environment*, 381(1-3), pp.68-76.

Pokkamthanam, A., Ridederer, A. and Anchala, R. (2011). Risk Assessment of Ingestion of Arsenic-Contaminated Water Among Adults in Bandlaguda, India. *Blacksmith Institute Journal of Health and Pollution*, 1(1), pp.8-15.

Prikhodko, D. and Zrilyi, O. (2013). Review of the wheat sector and grain storage issues. Country Highlights prepared under the FAO/World Bank Cooperative Programme. Food and Agriculture Organization of the United Nations (FAO). http://www.fao.org/docrep/018/i3251e/i3251e.pdf. (Accessed 12.04.16).

Pakistan Standards Quality Control Authority (PSQCA)., 2010. Pakistan Standards Drinking Water. 3rd Revision. PS 1932-2010 (R). ICS. 13.060. 20.67.

Qureshi AS, Shah T, Akhtar M. 2003. The Groundwater Economy of Pakistan. IWMI Working Paper No. 64. Colombo, Sri Lanka: International Water Management Institute (IWMI). Available at: http://www.iwmi.cgiar.org/wp-content/uploads/2013/02/WOR64.pdf. (Accessed 13.04.16).

Raab A, Baskaran C, Feldmann J, Meharg AA. 2009. Cooking rice in a high water to rice ratio reduces inorganic arsenic content. J Environ Monit 11(1):41–44.

Rasheed, H., Slack, R., and Kay, P. (2016). A comparative assessment of arsenic distribution in rice produced in Pakistan and other geographical regions. *Proceedings of the 6th International Congress on Arsenic in the Environment (As2016)*, June 19-23, 2016, Stockholm, Sweden.pp:279-280.

Rehman, Z., Khan, S., Qin, K., Brusseau, M., Shah, M. and Din, I. (2016). Quantification of inorganic arsenic exposure and cancer risk via consumption of vegetables in southern selected districts of Pakistan. *Science of The Total Environment*, 550, pp.321-329.

Rintala, E., Ekholm, P., Koivisto, P., Peltonen, K. and Venalainen, E. (2014). The intake of inorganic arsenic from long grain rice and rice-based baby food in Finland-Low safety margin warrants follow up. *Food Chemistry*, 150, pp.199-205.

Roche, S., Jones, A., Majowicz, S., McEwen, S. and Pintar, K. (2012). Drinking water consumption patterns in Canadian communities (2001-2007). *Journal of Water and Health*, 10(1), pp.69.

Roychowdhury, T., Tokunaga, H. and Ando, M. (2003). Survey of arsenic and other heavy metals in food composites and drinking water and estimation of dietary intake by the villagers from an arsenic-affected area of West Bengal, India. *Science of The Total Environment*, 308(1-3), pp.15-35.

Roychowdhury, T., Uchino, T., Tokunaga, H. and Ando, M. (2002). Survey of arsenic in food composites from an arsenic-affected area of West Bengal, India. *Food and Chemical Toxicology*, 40(11), pp.1611-1621.

Ruangwises, S. and Saipan, P. (2009). Dietary Intake of Total and Inorganic Arsenic by Adults in Arsenic-Contaminated Area of Ron Phibun District, Thailand. *Bull Environ Contam Toxicol*, 84(3), pp.274-277.

Salomon, S., Gabriela, C.,, Veronica, O. and Lilianne, A. (2015). Inorganic Arsenic in Rice and Rice Products on the Swedish Market 2015. *Part 2 - Risk Assessment.* Rapport 16 – 2015.

Saleem M. Ahmad M. Anwar S. Jaffar M. (1988). Mineral Element Composition of Cereals Grains grown in Pakistan, Pak .J. Agric res. 9 .2; 1988.

Samal, A., Kar, S., Bhattacharya, P. and Santra, S. (2011). Human exposure to arsenic through foodstuffs cultivated using arsenic contaminated groundwater in areas of West Bengal, India. *Journal of Environmental Science and Health, Part A*, 46(11), pp.1259-1265.

Sapunarpostrunik, J., Bauli, D. and Kubala, H. (1996). Estimation of dietary intake of arsenic in the general population of the Republic of Croatia. *Science of The Total Environment*, 191(1-2), pp.119-123.

Schoof, E.A., Eickhoff, J., Yost, L.J., Crecelius, E.A., Cragin, D.W. and Meacher, D.M. (1999). Dietary exposure to inorganic arsenic. In: Arsenic Exposure and Health Effects (Chappell WR, Abemathy CO, Calderon RL, eds). *New York: Elsevier, 81–88*.

Shakoor, M.B.**,** Niazi, N.K.**,** Bibi, I.**,** Rahman, M.M.**,** Naidu, R.**,** Dong, Z.**,** Shahid, M.**,** Arshad, M.**,** 2015. Unraveling Health Risk and Speciation of Arsenic from Groundwater in Rural Areas of Punjab, Pakistan. Int. J. Environ. Res. Public Health**,** 12, 12371-12390.

Shah, M., Ara, J., Muhammad, S., Khan, S. and Tariq, S. (2012). Health risk assessment via surface water and sub-surface water consumption in the mafic and ultramafic terrain, Mohmand agency, northern Pakistan. *Journal of Geochemical Exploration*, 118, pp.60-67.

Shirreffs, S. (2012). Global patterns of water intake: how intake data affect recommendations. *Nutrition Reviews*, 70, pp.S98-S100.

Signes, A., Mitra, K., Burlo, F. and Carbonell-Barrachina, A. (2008). Contribution of water and cooked rice to an estimation of the dietary intake of inorganic arsenic in a rural village of West Bengal, India. *Food Additives & Contaminants*, 25(1), pp.41-50.

Smiciklas-Wright, H., Mitchell, C., Mickle, J., Cook, J. and Goldman, D. (2002). Foods Commonly Eaten in the United States: Quantities Consumed Per Eating Occasion and in a Day, 1994-96. U.S. Department of Agriculture, Agricultural Research Service and Pennsylvania State University. January. http://www.barc.usda.gov/bhnrc/foodsurvey/pdf/Portion.pdf. (Accessed 31.12.15).

Song, D., Zhuang, D., Jiang, D., Fu, J. and Wang, Q. (2015). Integrated Health Risk Assessment of Heavy Metals in Suxian County, South China. *International Journal of Environmental Research and Public Health*, 12(7), pp.7100-7117.

Su, Y., McGrath, S. and Zhao, F. (2009). Rice is more efficient in arsenite uptake and translocation than wheat and barley. *Plant Soil*, 328(1-2), pp.27-34.

Tahir, A. and Rasheed, H. (2014). Technical Report on Arsenic Monitoring and Mitigation in Pakistan. Pakistan Council of Research in Water Resources, Islamabad, Pakistan. Pp. 26-250.

Tao, S. and Michael Bolger, P. (1999). Dietary arsenic intakes in the United States: FDA Total Diet Study, September 1991-December 1996. *Food Additives and Contaminants*, 16(11), pp.465-472.

United States Environmental Protection Agency (US EPA. (2014). Recommended Default Exposure Factors (2014). OSWER Directive 9200.1-120. Human Health Evaluation Manual, Supplemental Guidance: Update of Standard Default Exposure Factors. U.S. Environmental Protection Agency Washington, DC 20460.

United States Environmental Protection Agency (US EPA). (2011a). Exposure Factors Handbook: 2011 Edition. EPA/600/R-09/052F. September 2011. National Center for Environmental Assessment Office of Research and Development, U.S. Environmental Protection Agency Washington, DC 20460.

United States Environmental Protection Agency (US EPA). (2011b).Age dependent adjustment factors application. Office of water policy document. Office of Water, U.S. Environmental Protection Agency Washington, DC.pp.7. Available at: https://hero.epa.gov/hero/index.cfm/reference/download/reference_id/783747 (Accessed 14.11.15).

United States Environmental Protection Agency (US EPA). (2005). Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens. Risk assessment forum. EPA/630/R-03/003F. Environmental Protection Agency Washington, DC.pp.30-36. Available at: https://www3.epa.gov/airtoxics/childrens_supplement_final.pdf (Accessed 24.09.16).

United States Environmental Protection Agency (US EPA). (2001). Risk Assessment Guidance for Superfund, vol. III-Part A, Process for Conducting Probabilistic Risk Assessment. EPA/540/R-02/002. United States Environmental Protection Agency, Washington DC. 2001. pp: 7-1.

United States Environmental Protection Agency (US EPA). (2000).Water Quality Standards, Establishment of Numeric Criteria for Priority Toxic Pollutants for the State of California. Accessed at: /http://www.epa.gov/fedrgstr/ EPA. (Accessed 24.11.15).

United States Environmental Protection Agency (US EPA) (1997). Exposure Factors Handbook. National Centre for Environmental Assessment Office of Research and Development, US Environmental protection agency. https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=12464. (Accessed 24.10.15). pp.3-3

U.S. Food and Drug Administration. (2016). Arsenic in Rice and Rice Products Risk Assessment Report. Centre for Food Safety and Applied Nutrition Food and Drug Administration. U.S. Department of Health and Human Services http://www.fda.gov/Food/FoodScienceResearch/RiskSafetyAssessment/default.htm. (Accessed 15.06.16).Page.240.

U.S. Department of Health and Human Services and U.S. Department of Agriculture. (2015). 2015–2020 Dietary Guidelines for Americans. 8th Edition. December 2015, pp.80. Available at http://health.gov/dietaryguidelines/2015/guidelines/. (Accessed 21.02.16).

U.S. National Research Council (NRC). (1993). Pesticides in the Diets of Infants and Children. ISBN: 0-309-58535-X. National Academies Press. pp. 5-6. Available at: http://www.nap.edu/catalog/2126.html. (Accessed. 01.08.2016).

Wang, H., Sthiannopkao, S., Chen, Z., Man, Y., Du, J., Xing, G., Kim, K., Mohamed Yasin, M., Hashim, J. and Wong, M. (2013). Arsenic concentration in rice, fish, meat and vegetables in Cambodia: a preliminary risk assessment. *Environ Geochem Health*, 35(6), pp.745-755.

Watanabe, C., Kawata, A., Sudo, N., Sekiyama, M., Inaoka, T., Bae, M., Ohtsuka, R. (2004). Water intake in an Asian population living in arsenic-contaminated area. Toxicol Appl Pharmacol. Aug 1;198(3):272-82.

Westrell, T., Andersson, Y. and Stenström, T. (2006). Drinking water consumption patterns in Sweden. *J Water Health. 2006 Dec;4(4):511-22*.

Wiersma, D., van Goor, B.,J and van der Veen, N.,G. (1986). Cadmium, lead, mercury, and arsenic concentrations in crops and corresponding soils in the Netherlands. *J. Agric.Food Chem.*, 34, 1067-1074.

World Health Organization (WHO). (2015). Global Health Observatory data repository. Available at: http://apps.who.int/gho/data/node.main.1?lang=en. (Accessed 24.12.15).

World Health Organization (WHO). (2011). Guidelines for drinking-water quality. 4th Ed. Geneva: World Health Organization, pp. 164–168.

World Health Organization (WHO). (2007). Addressing sex and gender in epidemic-prone infectious diseases. Departments of Gender, Women and Health, and Epidemic and Pandemic Alert and Response, WHO, Geneva. ISBN 978 92 4 159534 6. Available at: http://www.who.int/csr/resources/publications/SexGenderInfectDis.pdf. (Accessed 12.06.16).

World Health Organization (WHO). (2004). Water Requirements, Impinging Factors, and Recommended Intakes. pp.5. Geneva, Switzerland.

World Health Organization (WHO). (2003). Global Environment Monitoring System – Food Contamination Monitoring and Assessment Programme (GEMS/Food) in collaboration with Codex Committee on Pesticide Residues. Guidelines for predicting dietary intake of pesticide residues. WHO/FSF/FOS/97.7.pp: 32.

World Health Organization (WHO). (1993). Guidelines for drinking-water quality. Vol. 1. Recommendations. 2nd ed. Geneva, Switzerland.

World Health Organization (WHO). (1981). *Environmental Health criteria* 18: Arsenic. World Health Organisation, Geneva.

Williams, P.N.; Raab, A.; Feldmann, J.; Meharg, A.A. High levels of arsenic in South Central US rice grain: consequences for human dietary exposure. *Environ. Sci.Technol.,* **2007**, 41, 2178-2183.

Willet, M., C. (1995). *Diet, nutrition, and avoidable cancer*. *Environmental Health Perspectives*, 1995, 103(Suppl. 8):S165-S170.

Yakub, M., Iqbal, M. and Iqbal, R. (2010). Dietary Patterns Are Associated with Hyperhomocysteinemia in an Urban Pakistani Population. *Journal of Nutrition*, 140(7), pp.1261-1266.

Zahm, S. and Fraumeni, J. (1995). Racial, ethnic, and gender variations in cancer risk: considerations for future epidemiologic research. *Environ Health Perspect*, 103(Suppl 8), pp.283-286.

Zeng, X., Wang, Z., Wang, J., Guo, J., Chen, X. and Zhuang, J. (2015). Health risk assessment of heavy metals via dietary intake of wheat grown in Tianjin sewage irrigation area. *Ecotoxicology*, 24(10), pp.2115-2124.

Zhao, F., Stroud, J., Eagling, T., Dunham, S., McGrath, S. and Shewry, P. (2010). Accumulation, Distribution, and Speciation of Arsenic in Wheat Grain. *Environmental Science & Technology*, 44(14), pp.5464-5468.

Zhang, D., Liu, D., Tian, C. and He, L. (2009). Toxicity and accumulation of arsenic in wheat (Triticum sestivum L.) varieties of China. *Phyton-Int. J. Exp. Bot.*, 78: 147–154.

Appendix A. Supplementary Information

Table-S-1: Water and food intake calculation formulae

Table-S-2: Description of study area participants

Table-S-3 Food and beverages sources contributing in indirect water intake *(*L person $^{-1}$ day^{-1}*)*

Table-S-4: Village wise average daily water intake (L day^{-1} person^{-1}) of the study population

Table-S-5: Reported water intake values in different countries

Table-S-6: Average daily rice intake (g day^{-1} person^{-1}) reported in different countries/regions

Table-S-7: Water and Food intake rates with respect to age for probabilistic cancer risk assessment

Figure-S-1 Age and body weight of participant's- Fourier Fit

Table-S-1: Water and food intake calculation formulae

Equation No.	Food item	Unit and Eqv weight* (g)*	Water used* (g)	Weight per serving	Volume of water (ml)	***Equation used to calculate water*** *(L person $^{-1}$ day^{-1})* ***or food intake*** *(g person $^{-1}$ day^{-1})*
(1)	Tea, black, brewed, prepared with tap water (without milk)	1 cup (237 g)	236.29	120-200 ml	249.48	$WI_{tea} = No\ of\ cups\ consumed\ per\ day\ \times\ ml\ of\ water\ per\ cup\ \ /\ 1000$
(2)	Whole milk	1 cup (245 g)	215.38	5-10 ml (added in tea)	4.4-8.8	-
(3)	Fermented dairy drink (Lassi)	1 glass	96.2%**	250 ml	240	$WI_{lassi} = \ No.of\ glass\ consumed\ per\ day\ \times\ 240\ ml\ of\ water\ /\ 1000$
(4)	Rice, white, medium-grain, cooked	1 cup (186 g)	127.61 (69%)	300-414 g	206-284	$WI_{cooked\ rice}\ = cooked\ rice\ intake\ in\ gm\ \ \times\ 0.69\ /\ 1000$
(5)	Red and White, Lentil Soup, condensed	1 cup (252 g)	179.42	150 g	107	$WI_{pulses} = No.of\ servings\ (150\ g)\ \times\ ml\ of\ water\ (107\ ml)/1000$
(6)	Bread, Chapatti or Roti, plain, commercially prepared	1 piece (68 g)	22.44	80-90 g (Av: 85 g)	28	$WI_{chapatti}\ = No.of\ units\ consumed\ (85\ g)\ \times 28\ ml\ of\ water/1000$
(7)	Water intake from direct sources	-	-	-	-	$\mathrm{W_{direct}}\ \ = \text{size of glass}\ (200 - 250\ \text{ml}) \times \text{No. of glass per day}\ /\ 1000$
(8)	Water intake from indirect sources	-	-	-	-	$TW_{indirect} = \ \ WI_{tea\ +lassi+cooked\ rice+pulses+chapatti}$
(9)	Total water intake	-	-	-	-	$WI_{total}\ =\ TW_{direct}\ \ +\ TW_{indirect}$
(10)	Total daily intake of food (TDFI)	-	-	-	-	$TDIF = \ Weight\ of food\ measured\ on plate/bowl \times No.of\ servings\ per\ day$

Whereas: *WI= Water intake (L person $^{-1}$ day^{-1})*
*** Standard values recommended *by Standard Reference Release-27, National Nutrient Database of United States Department of Agriculture (USDA) (Agricultural Research Service, 2014)*
***Lassi containing 96.2% water (Padghan et al., 2015)*

Table-S-2: Description of study area participants

Parameter		unit	Villages						overall
			Chak-46/12-L	Chak-48/12-l	Chak 49/12-l	Basti Balochan	Badarpur	Basti Kotla Arab	
Households reported by PBS		n	447	412	522	260	395	319	1776
Average household size		n	7	7	7	7	8	8	29
Population reported by PBS		n	3,195	3,037	3,986	2036	3,393	2345	15647
Male population		n	1,599	1,559	2,071	1,006	1,714	1210	7949
Female population		n	1,596	1,478	1,915	1,030	1,679	1135	7698
Literacy ratio		%	34.1	53.7	59.1	24	43.4	23	14
Households willing to participate in the study		n	64	45	50	26	26	29	240
Sampled houses		%	15	11	10	10	10	15	14
Total participants		n	121	54	75	44	34	70	398
Men		n	79	49	59	14	20	28	249
Age range	< 16	n	19	4	6	6	0	8	43
	≥16	n	60	45	53	8	20	20	206
Body weight range (kg)	< 35 kg	n	19	0	13	25	.	6	--
	≥ 35 kg	n	69	52	55	32	51	48	--
Women		n							
Age range	< 16	n	7	2	2	2	1	9	23
	≥16	n	35	3	14	28	13	33	126
Body weight range (kg)	< 35 kg	n	20	1	13	16	0	19	--
	≥ 35 kg	n	68	14	41	30	38	36	--

Source: Pakistan Bureau of Statistics (PBS)

Table-S-3: Food and beverages sources contributing to indirect water intake (L person $^{-1}$ day^{-1})

Villages	Age groups	Indirect water intake				Sources				
						Wheat Chapatti	Rice	Pulses	Tea	Lassi
		Minimum	Maximum	Mean	SD	Mean	Mean	Mean	Mean	Mean
Chak-46/12-L	Age < 16	0.1	1.0	0.4	0.2	0.1	0.2	0.1	0.1	0.3
	Age > 16	0.2	2.0	0.8	0.4	0.1	0.4	0.2	0.2	0.5
Chak-48/12-I	Age < 16	0.3	1.9	1.1	0.6	0.1	0.2	0.2	0.3	0.9
	Age > 16	0.4	2.2	1.1	0.5	0.1	0.3	0.2	0.3	0.8
Chak 49/12-I	Age < 16	0.1	1.2	0.4	0.3	0.1	0.1	0.1	0.1	1.0
	Age > 16	0.3	2.3	0.9	0.4	0.1	0.4	0.2	0.4	0.5
Basti Balochan	Age < 16	0.1	1.0	0.6	0.3	0.1	0.2	0.1	0.2	0.3
	Age > 16	0.3	1.4	0.7	0.3	0.1	0.2	0.2	0.2	0.4
Badarpur	Age < 16	0.3	0.3	0.3	0.0	0.1	0.0	0.1	0.1	0.0
	Age > 16	0.3	2.4	1.0	0.5	0.1	0.4	0.2	0.2	0.7
Kotla Arab	Age < 16	0.1	1.4	0.6	0.4	0.1	0.1	0.1	0.2	0.7
	Age > 16	0.3	1.9	1.0	0.5	0.1	0.3	0.2	0.2	0.7
Total	**Age < 16**	**0.1**	**1.9**	**0.6**	**0.4**	**0.1**	**0.2**	**0.1**	**0.2**	**0.5**
	Age > 16	**0.2**	**2.4**	**0.9**	**0.4**	**0.1**	**0.4**	**0.2**	**0.3**	**0.6**
	Overall	**0.1**	**2.4**	**0.8**	**0.4**	**0.1**	**0.3**	**0.2**	**0.2**	**0.6**

Table-S-4: Village wise average daily water intake (L day^{-1} person^{-1}) of the study population

Village	Sex	Age groups (years)	Direct Water Intake (L person^{-1} day^{-1})		In-direct Water Intake (L person^{-1} day^{-1})		Total Water Intake (L person^{-1} day^{-1})		Total Water Intake (L kg^{-1} day^{-1})	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD
Chak-46/12-L	Children	3-6	1.6	0.2	0.1	0.0	1.8	0.2	0.1	0.0
		6-16	2.3	0.5	0.5	0.2	2.8	0.5	0.1	0.0
		Overall < 16	2.3	0.5	0.4	0.2	2.7	0.6	0.1	0.0
	Male	≥ 16	3.0	0.8	0.9	0.4	3.9	0.9	0.1	0.0
	Female	≥ 16	2.5	0.4	0.7	0.3	3.2	0.6	0.1	0.0
	Average intake (irrespective of sex)	≥ 16	2.8	0.7	0.8	0.4	3.6	0.8	0.1	0.0
	Average intake	**All participants**	**2.7**	**0.7**	**0.7**	**0.4**	**3.4**	**0.9**	**0.1**	**0.0**
Chak-48/12-I	Children	3-6	.	.	.	.	.	.	.	.
		6-16	2.6	0.3	1.1	0.6	3.8	0.6	0.1	0.1
		Overall < 16	2.6	0.3	1.1	0.6	3.8	.6	0.1	0.1
	Male	≥ 16	2.9	0.9	1.1	0.6	4.0	1.2	0.1	0.0
	Female	≥ 16	2.7	0.4	1.0	0.2	3.8	0.5	0.1	0.0
	Average intake (irrespective of sex)	≥ 16	2.8	0.9	1.1	0.5	3.9	1.2	0.1	0.0
	Average intake	**All participants**	**2.8**	**0.9**	**1.1**	**0.5**	**3.9**	**1.1**	**0.1**	**0.0**
Chak 49/12-I	Children	3-6	1.8	0.8	0.7	0.7	2.5	1.6	0.2	0.0
		6-16	2.4	0.7	0.3	0.1	2.7	0.8	0.1	0.0
		Overall < 16	2.3	0.8	0.4	0.3	2.7	0.9	0.1	0.0
	Male	≥ 16	2.7	0.9	0.9	0.4	3.6	0.9	0.1	0.0
	Female	≥ 16	2.0	0.3	0.8	0.3	2.8	0.5	0.1	0.0
	Average intake (irrespective of sex)	≥ 16	2.5	0.8	0.9	0.4	3.4	0.9	0.1	0.0
	Average intake	**All participants**	**2.5**	**0.8**	**0.8**	**0.4**	**3.3**	**0.9**	**0.1**	**0.0**
Basti Balochan	Children	3-6	1.2	0.0	0.1	0.0	1.3	0.0	0.1	0.0
		6-16	2.5	0.6	0.7	0.2	3.1	0.7	0.1	0.0
		Overall < 16	2.3	0.7	0.6	0.3	2.9	0.9	0.1	0.0
	Male	≥ 16	3.4	0.5	0.6	0.2	4.0	0.5	0.1	0.0
	Female	≥ 16	2.4	0.4	0.7	0.3	3.1	0.4	0.1	0.0
	Average intake (irrespective of sex)	≥ 16	2.7	0.6	0.7	0.3	3.3	0.6	0.1	0.0
	Average intake	**All participants**	**2.6**	**0.6**	**0.6**	**0.3**	**3.2**	**0.7**	**0.1**	**0.0**
Badarpur	Children	3-6	.	.	.	.	.	.	.	.
		6-16	2.4	0.0	0.3	0.0	2.7	0.0	0.1	0.0
		Overall < 16	2.4	0.0	0.3	0.0	2.7	0.0	0.1	0.0
	Male	≥ 16	3.2	0.4	1.0	0.5	4.2	0.6	0.1	0.0

	Female	≥ 16	3.0	0.5	0.9	0.6	3.9	0.7	0.1	0.0
	Average intake (irrespective of sex)	≥ 16	3.1	0.4	1.0	0.5	4.1	0.7	0.1	0.0
	Average intake	**All participants**	**3.1**	**0.4**	**0.9**	**0.5**	**4.0**	**0.7**	**0.1**	**0.0**
Kotla Arab	**Children**	3-6	.	.	.	.	.	.	.	.
		6-16	2.1	0.4	0.6	0.4	2.8	0.6	0.1	0.0
		Overall < 16	2.1	0.4	0.6	0.4	2.8	0.6	0.1	0.0
	Male	≥ 16	2.9	1.1	1.1	0.5	4.0	1.3	0.1	0.0
	Female	≥ 16	2.1	0.7	0.9	0.4	3.0	0.8	0.1	0.0
	Average intake (irrespective of sex)	≥ 16	2.4	0.9	1.0	0.5	3.4	1.2	0.1	0.0
	Average intake	**All participants**	**2.4**	**0.8**	**0.9**	**0.5**	**3.2**	**1.1**	**0.1**	**0.0**
Overall (All villages)	**Children (both sex)**	<16	2.3	0.5	0.6	0.4	2.8	0.7	0.1	0.0
	Male	≥ 16	2.9	0.9	1.0	0.5	3.9	1.0	0.1	0.0
	Female	≥ 16	2.4	0.5	0.8	0.4	3.2	0.7	0.1	0.0
	Average intake (irrespective of sex)	≥ 16	2.7	0.8	0.9	0.4	3.6	0.9	0.1	0.0
	Average intake	**All participants**	**2.6**	**0.8**	**0.8**	**0.4**	**3.5**	**1.0**	**0.1**	**0.0**

Table-S-5: Reported water intake values in different countries

Country	Male			Female			All adults			Type	Reference
	n	age range	L day^{-1}	n	age range	L day^{-1}	n	age range	L day^{-1}		
Australia	ND	19+	3.4	ND	19+	2.8	ND	19+	3.1	water, hot and cold beverage intake	CSIRO & University of South Australia (2008)
Australia	ND	ND	ND	ND	ND	ND	ND	ND	2	water	NHMRC and NRMMC (2011)
Canada	ND	ND	ND	ND	ND	ND	8,916	ND	1.2	water	Roche et al.(2012)
Canada	37	ND	ND	88	ND	ND	125	20 to 64	1.6	Water, beverages and liquid food	Levallois et al. (1998)
Canada	ND	ND	ND	ND	ND	ND	4532	ND	1	water	Jones et al. (2007)
USA	ND	>19	3	ND	ND	3	4,112	>19	3.17	total fluids intake	Kante et al. (2009)
USA	7614	ND	ND	8088	ND	ND	15702	20 to ≥71	3.5	water, hot and cold beverage intake	Drewnowski et al. (2013)
USA-Winters	ND	ND	ND	ND	ND	ND	2458	ND	0.983	water	Barraj et al. (2009)
USA-summers	ND	ND	ND	ND	ND	ND	1740	ND	1.1	water	Barraj et al. (2009)
USA	ND	ND	ND	ND	ND	ND	20,000	<1 month to >65 years	2.6	water	Kahn and Stralka (2009)
USA	11,888	<1 to >65	2.261	14193	<1 to >65	1.919	26081	20 to 65	2.07	direct and indirect water intake (beverages and food)	Ershow and Cantor (1989).
USA	ND	ND	ND	ND	ND	ND	ND	≥21	2.5	water	USEPA (2011a)
USA	ND	ND	1.3	ND	ND	1.18	20,261	<1 to >20	1	water	USEPA (2004)
Mexico	574	ND	1.77	ND	ND	1.84	1498	38.6	1.81	total fluids intake	Martinez (2014)
Mexico	ND	18 to ≥50	ND	ND	ND	ND	80	20–65	1.81	water	Del Razo et al. (2002)
Brazil	941	18 to ≥50	2.34	983	18 to ≥50	2.1	1924	ND	2.22	water, hot and cold beverage intake	Guelinckx et al. (2015)
Argentina	241	18 to ≥50	2.32	266	18 to ≥50	2.29	507	ND	2.3	water, hot and cold beverage intake	Guelinckx et al. (2015)
UK	1,758	1 to >55	1.07	1,800	1 to>55	1.87	3,564	1 to >55	1.59	water, hot and cold beverage intake	Hopkins and Ellis (1980)
UK	371	ND	2.24	526	ND	2.37	897	ND	2.32	total fluids intake	Gandy (2015)
Spain	630	18 to ≥50	1.94	610	18 to ≥50	1.87	1240	ND	1.9	total fluids intake	Ferreira-Pego et al. (2014)
France	ND	ND	ND	ND	ND	ND	1361	20 to 54	1.31	water, hot and cold beverage intake	Bellisle et al. (2010)
France	804	18 to ≥50	1.55	730	18 to ≥50	1.57	1534	ND	1.56	water, hot and cold beverage intake	Guelinckx et al. (2015)
Poland	517	18 to ≥50	1.7	545	18 to ≥50	1.57	1062	ND	1.64	water, hot and cold	Guelinckx et al. (2015)

									beverage intake	
Turkey	488	18 to ≥50	2.15	473	18 to ≥50	2.17	961	ND	2.21	water, hot and cold beverage intake	Guelinckx et al. (2015)
France	ND	ND	ND	ND	ND	ND	831	20 to 54	2	water, hot and cold beverage intake	Bellisle et al. (2010)
Germany	639	>17	3	889	>17	ND	1528	ND	ND	direct and indirect water intake (beverages and food)	Manz et al. (2012)
Germany	856	18 to ≥50	2.51	1012	18 to ≥50	2.45	1868	ND	2.47	water, hot and cold beverage intake	Guelinckx et al. (2015)
Sweden	585	ND	2	625	ND	2	1210	ND	ND	water, hot and cold beverage intake	Shirreffs (2012)
Sweden	ND	ND	ND	ND	ND	ND	10957	ND	1.86	water and hot beverages	Westrell et al. (2006)
Netherlands	1252	22 to 50	3	1472	22-50	2	2724	ND	1.5	water	EFSA (2010)
Indonesia	444	18 to ≥50	2.33	922	18 to ≥50	2.26	1366	ND	2.28	water, hot and cold beverage intake	Guelinckx et al. (2015)
Malaysia	ND	ND	102	103	ND	ND	ND	ND	ND	water	Azlan et al. (2012)
Pakistan	ND	ND	102	103	ND	ND	ND	ND	4	water	Arain et al. (2009)
India	ND	ND	4	ND	ND	3	9	ND	ND	water	Chowdhury et al. (2000)
India	219	≥15 years	6.1	204	≥15 years	4.84	423	7 months to 90 years	4.92	direct and indirect water intake (beverages and food)	Hossain et al. (2012)
India	50	19-68	4.8	50	19-68	3.3	100	19-68	4.5	Water, mixed drinks, rice and pulses	Pokkamthanam et al. (2011)
Bangladesh	127	>14	3.89	323	>14	3.02	ND	0 to >65	ND	water	Khan et al. (2009)
Bangladesh	ND	ND	73.97 ml kg^{-1} day^{-1}	ND	ND	72.07 ml kg^{-1} day^{-1}	640	15 to ≥45	3.53	water	Milton et al. (2006)
Bangladesh	28	16 to 80	3.1	23	20 to 70	2.9	77	6 to 80	3	water	Ohno et al. (2007)
Bangladesh	9	>20	3	9	>20	3	38	20 to 53	3	water	Watanabe et al.(2004)
Bangladesh	113	16 to 73	3.1	108	14 to 65	2.6	232	14 to 65	ND	water	Mondal et al. (2010)
Bangladesh	5042	ND	2.9	6704	ND	3.1	ND	ND	ND	water	Ahsan et al. (2006)
Bangladesh	ND	ND	ND	ND	ND	ND	936	20 to 65	2.55	water	Kile et al. (2007)
Pakistan	249	3 to 80	3.70	149	4 to 80	3.11	398	3 to 80	3.50	direct and indirect water intake (beverages and food)	Present study
Iran	283	ND	1.92	289	ND	1.92	572	ND	1.92	total fluids intake	Abdollahi et al.(2013)
China	733	ND	1.78	733	ND	1.75	1466	ND	1.76	total fluids intake	Ma et al. (2012)
Japan	698	18 to ≥50	1.47	683	18 to ≥50	1.52	1381	ND	1.5	water, hot and cold beverage intake	Guelinckx et al. (2015)
Taiwan	ND	ND	1.5	ND	ND	1	ND	ND	1.2	water	Liang et al. (2016)

n: No. of samples, ND: No data

Table-S-6: Average daily rice, wheat and vegetables intake (g day^{-1} $person^{-1}$) reported in different countries/regions

Country	Food item	Consumption g day^{-1}				Reference
		Children	Men	Women	Mean	
India	Rice (cooked)				450	Signes et al. (2008)
India	Rice (cooked)	400 around 10 years of age)	750	750	713	Roy Chowdhary et al. (2002)
China	Rice (cooked)	210			370	Song et al. (2015)
Sweden	Rice (cooked)				44	Sand et al. (2016)
Korea	Rice (cooked)		236.8	187	212	Cha et al. (2012)
Thailand	Rice (cooked)				>200	Ruangwises and Saipan (2010)
Bangladesh	Rice (cooked)	862	1789	1522	1391	Khan et al. (2009)
Bangladesh	Rice (cooked)				1782	Melkonian et al. (2013)
Bangladesh	Rice (cooked)		523	300		Watanabe et al. (2004)
Bangladesh	Rice (raw)				400	Duxbury et al. (2003)
Bangladesh	Rice (raw)				420	Meharg and Rahman.(2003)
Cambodia	Rice (cooked)				522	Gilbert et al. (2015)
Bangladesh	Rice (cooked)		776	553	665	Ohno et al. (2007)
Pakistan	Rice(cooked)	253	576	463	372	Present study
Pakistan	Rice(cooked)			259		Aga Khan University et al. (2011)
Finland	Rice(cooked)	24			83	Rintala et al. (2014)
USA	Rice (Raw)	5		11	17	FDA (2016)
USA	Rice (Cooked)	88			172.6	FDA (2016)
USA	Rice (Raw)	17				Marquez and Jensen (2009)
USA	Rice (cooked)				334	Smiciklas-Wright et al. (2002)
Europe	Rice (cooked)				175	EFSA (2014)
Europe	*Rice				12	WHO (2003)
Africa	*Rice				103	WHO (2003)
Middle East	*Rice				48	WHO (2003)
Far East	*Rice				279	WHO (2003)
Latin America	*Rice				87	WHO (2003)
Cambodia, Indonesia, Lao People's Democratic Republic, Mayanmar and Vietnam	Rice (raw polished rice)				>400	Kennedy (2002)
Cambodia	Rice (cooked)				522	Gilbert et al. (2015)
Vietnam	Rice (cooked)				460	Agusa et al. (2006)
Bangladesh	Wheat		179	131		Watanabe et al. (2004)
China		13			44	Zeng et al. (2015)
Europe					182	FAO (2013)
USA					48	U.S. Department of Health and Human Services and U.S. Department of Agriculture. (2015–2020)
Pakistan					250	Mahmood et al. (2014)
Pakistan				306		Aga Khan University et al. (2011)
Pakistan		222	426	358	402	Present study
Cambodia	Vegetables				417-656	Wang et al. (2013)

Republic of Croatia					275	Sapunar et al. (1996)
Chile					327	Munoz et al. (2005)
Denmark					376	Helgesen and Larsen (1998)
India					400-500	Samal et al. (2011) Roychowdhury et al. (2003)
Pakistan					100	Arain et al. (2009)
Pakistan		103	187	181	170	Present study

*raw or cooked status is not mentioned in the WHO/FSF/FOS/97.7.

Table-S-7: Water and food intake rates with respect to age for probabilistic cancer risk assessment

Age groups	Total water intake ($L\ day^{-1}$)	Rice intake ($g\ day^{-1}$)	Wheat intake ($g\ day^{-1}$)
Age 3-6	1.94	91.38	148.75
Age 6-16	2.92	272.10	226.91
Age 16-26	3.36	419.96	359.87
Age 26-36	3.71	499.16	417.67
Age 36-46	3.73	586.92	417.74
Age 46-56	3.59	583.15	425.00
Age 56-66	3.68	604.64	385.33
Age > 66	3.57	510.93	347.08

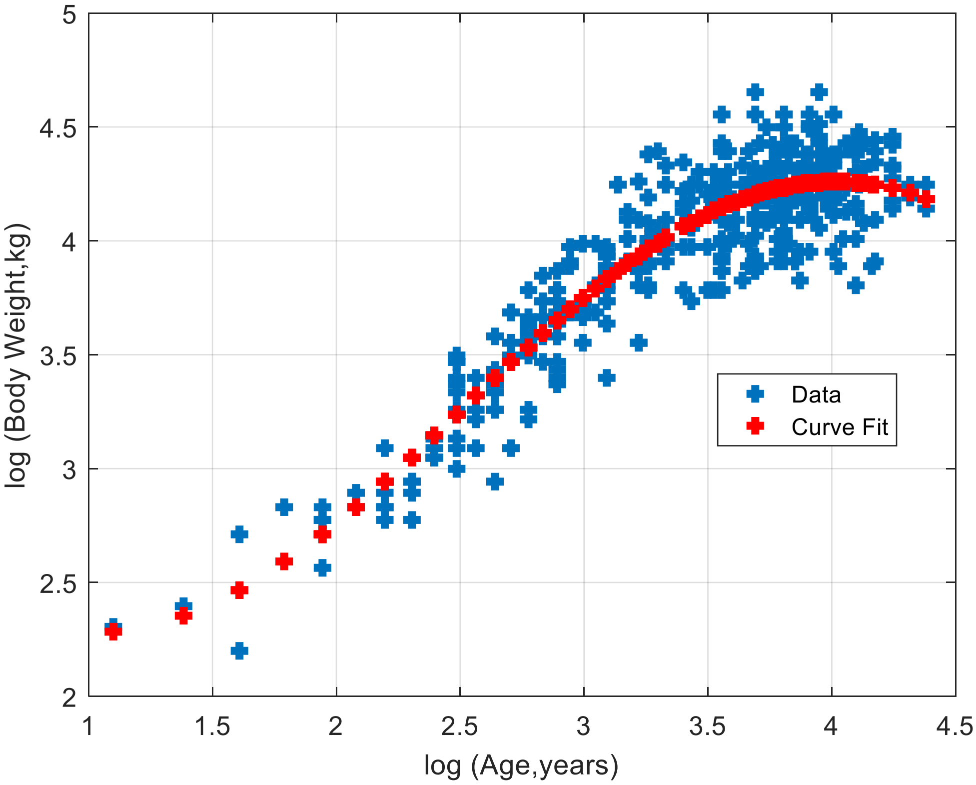

Figure-S-1 Age and body weight of participant's-linear regression

General model **Fourier Fit**: (Goodness of Fit R-sq 0.85)

f(x) = a0 + a1*cos(x*w) + b1*sin(x*w)

Coefficients (with 95% confidence bounds):
a0 = 3.269 (3.139, 3.399)
a1 = -0.4815 (-0.9603, -0.002601)
b1 = -0.8643 (-0.9992, -0.7294)
w = 1.047 (0.9079, 1.187)
x = ge (in log)
f(x) = Body Weight (in log)