



# Impact of climate change on arsenic concentrations in paddy rice and the associated dietary health risks in Asia: an experimental and modelling study

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## Summary

**Background** Rising global atmospheric carbon dioxide (CO<sub>2</sub>) concentrations and surface temperatures could negatively affect rice yields and nutritional quality; however, their effects on arsenic accumulation in paddy rice have not been assessed concurrently. We aimed to assess the impact of increases in CO<sub>2</sub> and temperature (individually and in combination) on arsenic concentrations in rice, characterise soil properties that might influence arsenic uptake, and model the associated risks of cancer and other health outcomes due to increased arsenic exposure.

**Methods** For this modelling study we performed in-situ multi-varietal trials using Free-Air CO<sub>2</sub> Enrichment platforms with and without supplemental temperature to examine the bioaccumulation of arsenic in paddy rice and the underlying biogeochemical mechanisms from 2014 to 2023. We modelled dietary inorganic arsenic exposure and the associated risks of cancer and non-cancer health outcomes via rice consumption for seven of the leading rice-consuming countries in east and southeast Asia.

**Findings** Concomitant increases in CO<sub>2</sub> and temperature resulted in a synergistic increase of inorganic arsenic in rice grain. The observed increase is likely to be related to changes in soil biogeochemistry that favoured reduced arsenic species. Modelled consumption of rice under these conditions resulted in projected increases in inorganic arsenic exposure and lifetime cancer and health risks for multiple Asian countries by 2050.

**Interpretation** Inorganic arsenic exposure and the associated health consequences might increase in rice grain grown in flooded systems with mid-century climate projections. The current assessment reinforces the urgent need for mitigation of arsenic exposure in rice relative to near-term climate change.

**Funding** National Key Research and Development Program of China, National Natural Science Foundation of China, Key-Area Research and Development Program of Guangdong Province, China, Carbon Peaking and Carbon Neutrality Special Fund for Science and Technology from Nanjing Science and Technology Bureau, Key Research and Development Program of Jiangsu Province, Erdos City Science and Technology Major Project, Science Foundation of the Chinese Academy of Sciences, Carbon Peaking and Carbon Neutrality Special Fund for Science and Technology from Jiangsu Science and Technology Department, and “0-1” Original Innovation Project of the Chinese Academy of Sciences.

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## Introduction

There is increasing evidence that climate change, in the form of rising temperatures and increased CO<sub>2</sub> concentrations, can directly affect rice yields<sup>1-3</sup> and nutritional quality.<sup>4-6</sup> Aside from drinking water, rice is the largest dietary source of inorganic arsenic.<sup>7,8</sup> Some evidence from greenhouse and growth chamber experiments suggests that rising temperatures and atmospheric CO<sub>2</sub> could increase inorganic arsenic accumulation in rice grains, largely due to increased reductive dissolution of arsenic and higher arsenic bioavailability.<sup>9-11</sup> However, the consequences of concurrent increases in temperature and atmospheric CO<sub>2</sub> on the bioaccumulation of total arsenic and

inorganic arsenic have not been assessed in the field for paddy rice.

From a health perspective, the toxicological effects of chronic inorganic arsenic exposure are well established and include cancers of the lung, bladder, and skin, as well as ischaemic heart disease. Ongoing evidence suggests that inorganic arsenic might also be linked to diabetes, adverse pregnancy and neurodevelopmental outcomes, immune effects, other cancers, and other diseases.<sup>12,13</sup> Rice consumption in southern China and southeast and south Asia is already recognised as an important contributor to dietary inorganic arsenic exposure and cancer risk.<sup>14,15</sup>

We used the Free-Air CO<sub>2</sub> Enrichment (FACE) platforms with and without supplemental temperature

*Lancet Planet Health* 2025

Published Online

April 16, 2025

[https://doi.org/10.1016/S2542-5196\(25\)00055-5](https://doi.org/10.1016/S2542-5196(25)00055-5)

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See Online for appendix

## Research in context

### Evidence collected before this study

We searched peer-reviewed articles from database inception to Feb 28, 2025, in Google Scholar, Web of Science, and the China National Knowledge Infrastructure, using the following key words and phrases: "rice, CO<sub>2</sub> arsenic", "paddy rice, climate change arsenic", "rice, elevated temperature, arsenic", "microbial mechanism of soil arsenic in flooded soils", and "rice, inorganic arsenic, health risks". Before this study, individual indoor experiments for CO<sub>2</sub> and temperature relative to arsenic accumulation had been conducted, but concomitant changes in both climate variables for a range of rice cultivars grown under paddy conditions in fields had not been provided. Similarly, we found no studies that had modelled the impact of rising temperatures and CO<sub>2</sub> concentrations on dietary exposures to arsenic in rice and their subsequent population-level cancer burdens. A thorough search of the existing literature (using Google Scholar, Web of Science, and the China National Knowledge Infrastructure) found a small number of studies that examined the impact of CO<sub>2</sub> or elevated temperature, but not both, on the accumulation of arsenic in rice. Furthermore, these studies were only available for a single rice cultivar growing in glasshouse or growth chamber conditions and did not quantify the health consequences of changing arsenic concentrations.

### Added value of this study

For this modelling study, we used in situ Free-Air CO<sub>2</sub> Enrichment (FACE / T-FACE) platforms to assess the effects of rising temperatures and CO<sub>2</sub>, independently and jointly, on the

accumulation of arsenic in 28 strains of paddy rice over 10 years of observation. These empirical measurements serve as the basis for modelling the added cancer and other disease burdens attributable to the increased dietary arsenic exposure stemming from climate-induced changes in arsenic accumulation in rice in Asia. We found that temperature and CO<sub>2</sub> act synergistically to increase arsenic concentrations in rice, compounding dietary arsenic exposures for rice consumers and leading to projected cancer cases in the tens of millions among populations of Asian countries in 2050. Our study provides potential mechanistic insight suggesting that increases in temperature and CO<sub>2</sub> change rates of arsenic accumulation in rice by altering the soil microbiome.

### Implications of all the available evidence

This is, to the best of our knowledge, the first field-based study showing that concurrent increases in temperature and CO<sub>2</sub> collectively increase arsenic concentrations in paddy rice. Our findings have important implications for rice cultivation and consumption. As a staple food in many countries around the world, increased arsenic accumulation could translate into a substantial increase in the global burden of cancer, cardiovascular disease, and other adverse health outcomes related to arsenic exposure. In documenting this burden and simultaneously identifying mechanisms of increased arsenic accumulation in rice, our research paves the way for identification of interventions aimed at climate adaptation to improve the safety of rice as a dietary staple.

(FACE and T-FACE) over multiple years to examine the bioaccumulation of arsenic in the grains of genetically diverse rice lines under paddy conditions in southern China. We aimed to: assess whether increases in CO<sub>2</sub> and temperature (individually and in combination) affect concentrations of different forms of arsenic in rice relative to current atmospheric conditions; characterise soil chemistry and soil biome properties that might influence arsenic uptake and speciation; and model dietary inorganic arsenic exposure and the associated risks of cancer and selected non-cancer health outcomes via rice consumption for seven of the leading rice-consuming countries in east and southeast Asia. Given the ubiquity of paddy rice production and anticipated climate changes, such information is crucial to assess future population health risks associated with inorganic arsenic exposure.

## Methods

### FACE system description, experimental sites, and growth conditions

The FACE platform allows open-air elevation of CO<sub>2</sub> with and without supplemental air temperature under field conditions.<sup>16</sup> The current study was conducted from

2014 to 2023; however, temperature as a treatment parameter was only added for the years 2020, 2021, and 2023. FACE was used to impose two CO<sub>2</sub> concentrations, ambient and ambient +200 ppm CO<sub>2</sub>; T-FACE was used to impose two temperatures, ambient and +2°C. This resulted in four treatment variables: Ambient, CO<sub>2</sub>, Temp, and CO<sub>2</sub>+Temp.

The four FACE facilities (FACE 1–4, appendix p 2) are within the Yangtze River Delta region, a quintessential rice-growing region in southern China, and its humid, subtropical climate makes it representative of other rice-growing regions in Asia. The distance between any two of the FACE sites was less than 150 km (range 43–148 km). FACE 1 is near Kongbo Village (31°30'N, 120°33'E), Guli Township, Changshu Municipality, Jiangsu Province (appendix p 2). The soil is a gleyic stagnic anthrosol and has been cultivated under continuous rice–wheat rotation. The soil in this area is a typical paddy soil developed from the parent material of lake deposits in the north of Taihu Lake Plain, which is characterised by the gley hydroponic soil. The top 20 cm soil contains 33.1 g organic matter kg<sup>-1</sup> and 1.9 g nitrogen kg<sup>-1</sup>. The total arsenic concentrations in this soil were 10.1–10.3 mg kg<sup>-1</sup>, with no significant

differences between the treatment scenarios. FACE 2 is near Tuqiao Town (31°52'N, 119°03'E), Jiangning District, Nanjing Municipality, Jiangsu Province (appendix p 2). The soil is a loess base and has been under long-term rice cultivation. The top 20 cm soil contains 33.9 g organic matter kg<sup>-1</sup> and 1.9 g nitrogen kg<sup>-1</sup>. The total arsenic concentrations in this soil were 7.9–8.0 mg kg<sup>-1</sup>, with no significant differences between the treatment scenarios. FACE 3 is near Zhongcun Village (32°35'5"N, 119°42'0"E), Yangzhou City, Jiangsu Province (appendix p 2). The soil is a Shajiang-aquic cambisol. The top 20 cm of soil contains 18.4 g carbon kg<sup>-1</sup> and 1.45 g nitrogen kg<sup>-1</sup>. The total arsenic concentrations in this soil were 6.0 mg kg<sup>-1</sup>, with no significant differences between the treatment scenarios. FACE 4 is in Baolin village (31.9°N, 119.5°E), Yanling Town, Danyang City, Jiangsu province (appendix p 2). The top 20 cm soil contains 21.1 g carbon kg<sup>-1</sup> and 1.1 g nitrogen kg<sup>-1</sup>. The total arsenic concentrations in this soil were 10.1–10.4 mg kg<sup>-1</sup>, with no significant differences between the treatment scenarios.

### CO<sub>2</sub> and temperature control in FACE

We simulated four climate scenarios (Ambient, CO<sub>2</sub>, Temp, CO<sub>2</sub>+Temp) at FACE sites 1–2, and two climate scenarios (Ambient, CO<sub>2</sub>) at FACE sites 3–4. The treatment scenarios were selected on the basis of projected increases in temperature and CO<sub>2</sub> reported by the International Panel on Climate Change 5th and 6th Assessment Reports.<sup>17,18</sup> Each FACE system consists of 6–12 octagonal rings varying in size with three rings for each climate treatment. Individual ring diameters and respective surface areas were 8 cm and 50 m<sup>2</sup> for FACE location 1, 12 cm and 120 m<sup>2</sup> for FACE location 2, 14 cm and 160 m<sup>2</sup> for FACE location 3, and 8 m and 50 m<sup>2</sup> for FACE location 4.

Additional CO<sub>2</sub> at each FACE location can be injected to compensate for wind direction and velocity by use of an on-site computerised monitoring system to achieve the target elevated CO<sub>2</sub> concentration (ambient+200 μmol mol<sup>-1</sup>). CO<sub>2</sub> was added with polyethylene tubes installed horizontally on the periphery of the octagonal FACE ring, which released pure CO<sub>2</sub> at 50 cm above the rice canopy to keep the daytime CO<sub>2</sub> concentration within the centre of the plot at approximately 200 μmol mol<sup>-1</sup> above ambient concentrations. CO<sub>2</sub> was monitored at each FACE site with 16 Li-820 CO<sub>2</sub> sensors (Li-COR, Lincoln, NE, USA) installed above the rice canopy and evenly distributed. CO<sub>2</sub> concentration was monitored automatically every 1 min and was recorded with a datalogger (CR1000, Campbell Scientific; Logan, UT, USA). Additional details are provided elsewhere.<sup>19</sup>

The temperature treatment was added to FACE locations 1 and 2 (ie, T-FACE). For the FACE 1 location at Changshu we adopted canopy heating facilities for 2020 and 2021 for the 12 octagonal rings (three for each of the four treatments). The infrared heating facilities were

designed as described by Kimball and colleagues.<sup>20</sup> Specifically, each T-FACE ring consisted of 12 infrared heaters (2000 W, 240 V, 1.65 m long × 0.14 m wide; HS-2420, Kalglo Electronics, Bethlehem, PA, USA). The height of the heaters was adjusted in response to canopy height during the rice growing season. The infrared heaters increased the canopy temperature by approximately 2.0°C. The canopy temperature was monitored with six infrared thermometers (Model SI-121, Apogee instruments, Logan, UT, USA) arranged in a regular hexagonal array in each ring. Based on the monitored canopy temperature in each ring, canopy temperature increases were automatically controlled by a computer feedback control system. As with CO<sub>2</sub> concentration, canopy temperature was monitored automatically every 1 min and recorded with a datalogger (CR1000, Campbell Scientific). In addition to canopy temperature, daily air temperature data and other weather variables were monitored and recorded by an onsite weather station (sensor: HMP155A; Campbell Scientific) for each day of the rice growing season for each FACE site. Additional details of the design and operation of the T-FACE system are available.<sup>21,22</sup>

For the Nanjing T-FACE study (FACE 2 location), canopy warming was achieved with 24 ceramic infrared lamps (SYTZ-FTE-1000, Ceramicx, Ireland). The infrared lamps were installed within a stainless steel casing measuring 250×65×44 mm (1000 W emitting wavelengths ranging 2–10 μm). The infrared lamps were fixed onto a stainless steel bracket designed to minimise light obstruction but provide sufficient support for their weight. The on–off function of the infrared lamps was operated by a Proportional-Integral-Derivative (PID) controller to ensure that the canopy infrared temperature in the warming zone was consistently 2°C higher than the non-warming zone. The infrared warming system operated continuously for 24 h but would automatically shut down in the event of rainfall. To warm the water and soil, heating tape (manufactured by Taizhou ShuoJia Electric Heating Materials, Taizhou, China) was used. The heating tape had a width of 8 mm and a thickness of 3 mm, and contained positive temperature coefficient materials wrapped in polyolefin materials, providing a power of 35 w/m, with a maximum water temperature of 40°C. The heating tapes were controlled by PID to ensure that the water temperature in the warming zone was consistently 2°C higher than the non-warming zone. Data collection and PID control processes for the warming system were performed with CR1000X (Campbell Scientific; Logan, UT, USA).

### Rice cultivation and field management

Diverse rice cultivars were grown in four FACE sites from 2014 to 2023 (appendix p 3). These 28 cultivars are genetically representative of lines currently grown and consumed in Asia. The growth periods from

transplanting to maturity stage were dependent on cultivar, year, and site location. Standard cultivation practices, common to a given region, were followed at all FACE sites. Three-leaf-stage seedlings grown under ambient air were manually transplanted at a spacing of 25.0×16.7 cm (equivalent to 24 hills m<sup>-2</sup>) to the FACE system. Rice fields were flood-irrigated and grown as paddy rice, and irrigation management and additional pesticides were consistent with local practices.

### Rice sampling

At rice maturity, from each FACE ring, six rice plants per cultivar were sampled (the number of cultivars in each ring varied across years); see the Open Science Framework data for details.<sup>23</sup> Plants were chosen to ensure representativeness, as follows: the numbers of tillers per hill, excluding the border rows, were counted for each cultivar in each ring. Rice plants were chosen to ensure that the mean number of tillers per hill on the sampled plants was equal to the mean number of tillers per hill across all hills. The six rice plants were then separated into leaves, stems, and grains. Within each plant part, the six samples were mixed together, representing one biological replicate each for leaf, stem, and grain. This process was repeated three times for each cultivar and each climatic treatment, yielding three biological replicates per cultivar, plant part, and treatment group.

### Arsenic analysis

Arsenic concentrations were assessed at seed maturity for unpolished (ie, brown) rice for all experimental treatment scenarios, rice cultivars, and FACE locations from 2014 to 2023. Grain samples were mixed and ground with a GT200 ball grinding instrument (Grinder Corp, Beijing, China), and the resulting powder collected for analysis. To analyse total arsenic concentration, a 0.5 g sample was digested with 5 mL of high-purity grade HNO<sub>3</sub> in a microwave digester (Mars 6, CEM Corporation). After digestion, excess acid was evaporated by heating at 160°C to approximately 0.1 mL. The digest was diluted with 5 mL of 2% HNO<sub>3</sub> and the concentration of total arsenic was assessed with an inductively coupled plasma mass spectrometer (ICP-MS, PerkinElmer NexIon 300X).<sup>24</sup> The certified reference material (rice GBW10045a) was included for quality assurance. For the FACE 1 location for 2021, in addition to grain, the leaf and stem were also sampled for all cultivars and experimental treatment scenarios to assess total arsenic concentrations. Arsenic species in the rice grain samples were extracted with 1% HNO<sub>3</sub> at 95°C in a microwave digester.<sup>25</sup> Arsenic species in the extracts were separated by an anion exchange column (PRP-X100, 150 mm×4.6 mm, Hamilton) with a mobile phase containing 8.5 mM NH<sub>4</sub>H<sub>2</sub>PO<sub>4</sub> and NH<sub>4</sub>NO<sub>3</sub> (pH 6.0) and quantified with high-performance liquid chromatography (HPLC) coupled with inductively coupled plasma mass spectrometry (ICP-MS).<sup>26</sup>

### Soil microbial genes involved in arsenic transformation

For the FACE 1 location, the T-FACE experiment in 2021 underwent additional biochemical sampling of the paddy soils for each experimental treatment (0–20 cm in depth) at three growth stages: booting, heading and grain filling. From each FACE ring, five soil subsamples were randomly taken within a ring with a 20 cm soil extractor, then thoroughly mixed to ensure a representative sample. Total DNA was extracted from soil samples with a Power Soil DNA isolation Kit (TransGen, Hilden, Germany). DNA concentration was measured with a NanoDrop 2000C spectrophotometer (Thermo Scientific, Wilmington, DE, USA). The abundances of bacterial microbial 16S rRNA, *arsM* (arsenite S-adenosylmethionine methyltransferase gene), *arsC* (arsenate reductase gene), *arrA* (arsenate respiratory reductase gene), *aioA* (arsenite oxidase gene), and *dsr* (dissimilatory sulfite reductase gene) genes were quantified with a RealTime PCR Detection System (Bio-Rad CFX96, Hercules, CA, USA) in 20 µL reaction mixtures containing 10 µL SYBR Green Master Mix (Vazyme, Nanjing, China), 2 µL DNA template (10 ng µL<sup>-1</sup>), and 0.5 µL of each primer (10 µM).<sup>27</sup> The primers<sup>27</sup> used are listed in the appendix (p 4). Additionally, soil pH was assessed with a suspension of soil and water (1: 2.5, w: v, the ratio of soil weight to water volume) and a glass electrode. Soil redox potential was measured in situ with a combined Pt/Ag-AgCl electrode inserted into the soil layer approximately 8 cm below the soil surface at the rice booting, heading, and filling stages.<sup>28</sup>

### Dietary inorganic arsenic exposure and risk assessment

Projected cancer burdens and selected non-cancer health hazards associated with inorganic arsenic exposure from polished rice consumption were modelled for the year 2050 under four scenarios corresponding to each of the FACE treatments: Ambient (unmodified climate), CO<sub>2</sub> (+200 ppm), Temp (+2°C), and CO<sub>2</sub>+Temp (+200 ppm, +2°C). Each scenario was modelled in accordance with populations,<sup>29</sup> rice intake, and the share of rice hectares with flood irrigation specific to seven Asian countries: Bangladesh, China, India, Indonesia, Myanmar, Philippines, and Viet Nam. These countries were selected because they are among the highest rice producing or rice-consuming (or both) countries in the world, and because the rice varieties typically consumed in these countries include those analysed in this study.

A detailed overview of our model is provided in the appendix (p 5). Briefly, we modelled rice consumption rates by country and inorganic arsenic concentrations in rice (adjusted for bioaccessibility and other factors) by scenario, then combined these data with bodyweight estimates to calculate inorganic arsenic doses by scenario and country. Health risks associated with calculated inorganic arsenic doses were then estimated with toxicity



values for cancer and non-cancer outcomes.<sup>30</sup> Given the uncertainty and variation among model input data, a Monte Carlo simulation with 5000 trials was used to account for the range of potential outcomes. On each trial, for selected input variables (detailed in the following sections), a random value was sampled from a distribution of possible values. Taken together, model outputs represent every permutation of scenario, country, toxicity value, and trial. Model inputs are discussed in further detail below. All modelling and associated calculations were done with Python (version 3.12); the code and data are available via the Open Science Framework.<sup>23</sup>

### Rice consumption rates

Estimates of per-person rice availability in 2021 by country, as reported in the Food and Agriculture Organization of the UN food balance sheets,<sup>31</sup> were used as the starting point for estimating rice consumption. These data represent quantities expressed in terms of unhusked (ie, paddy rice) equivalents. Since white rice accounts for more than 99% of rice availability in China and India,<sup>32</sup> a simplifying assumption was made that all rice is consumed as white rice. Thus, conversion factors<sup>33</sup> were used to convert unhusked equivalents to white (ie, milled) rice. Notably, the use of present-day (2021) availability data assumes per-person rice consumption rates (but not country totals) remain the same in 2050.

The uptake of inorganic arsenic in rice tissues occurs primarily under the anaerobic conditions associated with flooded rice paddies; thus, the share of rice grown in rainfed fields was excluded from the model as follows: for each country included in the model, hectares of irrigated rice production in 2020<sup>34</sup> were divided by total hectares of rice production in 2020.<sup>35</sup> Each country's per-person rice availability was then multiplied by the fraction of irrigated rice. Since food balance sheets account for supply chain losses up to but not including the retail stage, estimates of retail losses and household waste for rice<sup>36</sup> were applied, yielding loss-adjusted per-person rice supplies by country. These were used as the proxy for rice consumption.

### Inorganic arsenic concentrations in rice

Inorganic arsenic concentrations were then multiplied by the estimated bioaccessible fraction in rice, represented as a beta distribution (alpha=4.91, beta=1.85), as described in a meta-analysis.<sup>37</sup>

To convert inorganic arsenic concentrations in brown rice to white rice, inorganic arsenic concentrations were multiplied by the fraction remaining after milling. As per a recent review of the literature,<sup>38</sup> estimates specific to selected cultivars grown in Asia ranged from 0.59 to 0.74, so a uniform distribution ranging from the lowest to the highest estimate was used for the Monte Carlo simulation.

### Inorganic arsenic doses

The average daily dose of inorganic arsenic ( $D$ ) in mg per kg bodyweight per day associated with rice consumption under each scenario  $s$  and in each country,  $c$  was calculated as follows:

$$D_{s,c} = \left( \frac{IC_c \times C_s}{BW} \right)$$

Where  $IC$  is the per capita rice consumption rate by country in kg/day,  $C$  is the inorganic arsenic concentration in rice by scenario in mg/kg, and  $BW$  is adult median bodyweight in kg for the average adult in Asia.<sup>39</sup> Rice consumption was assumed to remain constant throughout the lifetime.

Since rice consumption and bodyweight vary by person, the SD of rice consumption per kg bodyweight from the US Environmental Protection Agency (EPA) data<sup>40</sup> was used to create a normal distribution for each country, using the country-specific rice consumption rates adjusted for bodyweight as the means. On each of the 5000 trials, a random value was sampled from the distribution.

### Cancer burden

The cancer burden (CB; ie, projected number of excess cancer cases) associated with inorganic arsenic exposure via rice consumption, for each scenario  $s$ , country  $c$ , and toxicity value  $o$ , was calculated as follows:

$$CB_{s,c,o} = D_{s,c} \times OSF_o \times Pop_c$$

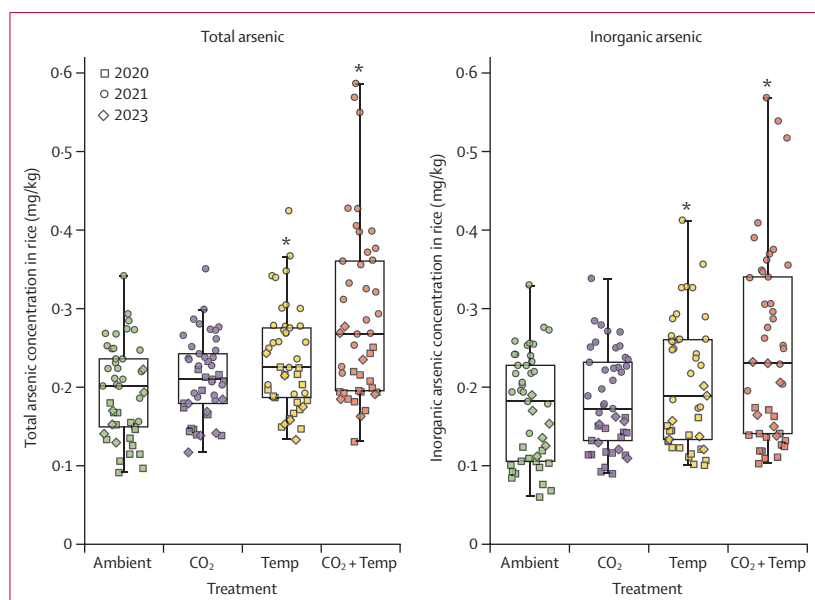
Where  $D$  is the average daily inorganic arsenic dose as defined above,  $OSF$  is the oral slope factor for inorganic arsenic, defined as the upper bound of increased cancer risk from lifetime oral exposure<sup>41</sup> expressed in mg inorganic arsenic per kg bodyweight per day, and  $Pop$  is the projected population of each country in 2050.<sup>29</sup> Multiplying  $D$  by  $OSF$  yielded the estimated excess risk of developing cancer over a person's lifetime given daily exposure to inorganic arsenic, which was calculated with both the current and proposed OSFs for inorganic arsenic. We used the inorganic arsenic OSF of 31.7 per mg/kg per day, corresponding to cancers of the bladder and lung, which was finalised by the EPA's Integrated Risk Information System in January 2025.<sup>30</sup> Multiplying by  $Pop$  yielded the projected number of cancer cases associated with exposure to inorganic arsenic via rice consumption over a lifetime.

### Non-cancer health hazards

Non-cancer health hazards were expressed in terms of hazard quotients (HQs), calculated for each scenario  $s$ , country  $c$ , and health outcome  $h$  as follows:

$$HQ_{s,c} = D_{s,c} \div RfD_h$$

Where  $D$  is the average daily inorganic arsenic dose as calculated above, and  $RfD$  is the reference dose in mg



**Figure 1: Arsenic concentrations in rice, by year and climatic conditions**

Total and inorganic arsenic concentrations (mg/kg) in brown (ie, unpolished) rice for multiple cultivars grown in situ by year and treatment. Treatments reflect climatic conditions: Ambient (unmodified climate), CO<sub>2</sub> (+200 ppm), Temp (+2°C), and CO<sub>2</sub>+Temp (+200 ppm, +2°C). Years indicate when rice plants were grown and harvested. Each treatment group included 45 biological samples (N=180 per panel). Compared to Ambient, total arsenic and inorganic arsenic concentrations were significantly higher for the Temp and CO<sub>2</sub>+Temp (\**p*<0.0001) treatments using mixed-effects models with cultivar as a random effect and controlling for year. Positive synergy between CO<sub>2</sub> and Temp treatments was observed for total arsenic (*p*=0.0034) and inorganic arsenic (*p*=0.0033) after adding an interaction term to the models. Independent of treatment effects, trial year was significantly and positively associated with total arsenic and inorganic arsenic concentrations (*p*<0.0001), probably as a result of natural warming (see figure 2). Boxes show IQRs and whiskers extend to 1.5 times the IQR. Regression tables are available via the Open Science Framework.<sup>23</sup>

inorganic arsenic per kg bodyweight per day. HQs are used for non-cancer health outcomes and are calculated as the level of exposure to a hazard (in this case, projected exposure to inorganic arsenic from paddy rice intake) divided by the exposure level at which no adverse effects are expected to occur (ie, the RfD).<sup>42</sup> Thus, an HQ of less than or equal to 1 indicates no appreciable risk, while an HQ above 1 suggests that a particular health outcome might be possible because of lifetime exposure under the specified conditions. We used a chronic oral RfD of  $6 \times 10^{-5}$  mg per kg bodyweight per day for inorganic arsenic corresponding to ischaemic heart disease and type 2 diabetes, as well as additional organ-specific or system-specific oral RfDs based on fetal, newborn, and infant health outcomes ( $7.9 \times 10^{-5}$  mg per kg bodyweight per day) and developmental neurocognitive effects ( $1.05 \times 10^{-4}$  mg per kg-day); these values were finalised by the EPA in 2025.<sup>30</sup>

### Statistical analysis

All statistical analyses were done with Python (version 3.12). To ensure reproducibility, all study data, code, and detailed results of statistical analyses are available via the Open Science Framework.<sup>23</sup>

Associations between FACE treatment and arsenic concentrations in brown (ie, unpolished) rice were

assessed with mixed-effects models, one each for total arsenic and inorganic arsenic, with treatment and year as predictors, rice cultivar as the random effect, and arsenic concentration as the outcome. Each treatment was represented in the model as a dummy variable assigned to 0 or 1 (the standard approach for categorical variables), and year was a continuous variable coded as 0 for 2020, 1 for 2021, or 3 for 2023. Mixed-effects models are the recommended approach for analysing clustered data (ie, when the data can be classified into groups, each with multiple observations).<sup>43</sup> In this case the data are clustered by rice cultivar (ie, observations from multiple biological replicates within the same rice cultivar might be more alike than observations across different cultivars). The arsenic concentration data are thus not independent, but the mixed-effect models account for this. In separate analyses, to assess potential synergies between CO<sub>2</sub> and temperature, each model was adapted to include an interaction term, assigned to 1 when both CO<sub>2</sub> and temperature were elevated in the treatment.

The same approach was used to compare arsenic III and dimethylarsenic (DMA) concentrations by treatment, but for 2021 and 2023 only; and also for total arsenic concentrations by plant organ (stem, leaf, and grain) across treatments; but since we only had data by organ for 2021, year was excluded as a covariate.

We examined the relationship between 10-year natural variations in seasonal air temperatures (average, minimum, and maximum) and total arsenic and inorganic arsenic concentrations in brown rice across 28 cultivars grown under different FACE treatments. Linear regression models were used, assuming independence of observations. Residual analysis, including histograms and Q-Q plots, indicated a generally normal distribution with some deviations in the tails. To address these departures from normality, we also implemented a generalised linear model (GLM) with a Gaussian family and log link function. This complementary analysis confirmed the robustness of the temperature–arsenic relationship without relying on normality assumptions.

Associations between FACE treatment and soil microbial counts in 2021 were assessed with mixed-effect models, one for each microbial gene (bacterial 16S rRNA, *aioA*, *arrA*, *arsC*, *arsM*, and *dsr* genes), with treatment as the predictor, rice growth stage (booting, heading, and grain-filling) as the random effect, and microbial count as the outcome. In separate analyses, to assess potential synergies between CO<sub>2</sub> and temperature, each model was adapted to include an interaction term as described above. The same approach was used to compare soil pH and redox potential by treatment.

Effects of treatment on soil microbes were further explored independently for each rice stage, based on the rationale that microbial counts during the grain-filling stage could have greater implications for inorganic arsenic concentrations in the edible rice

grain. A separate linear regression model (ie, a fixed-effects model) was used for each rice stage, with treatment as the categorical predictor and microbial count as the outcome. In separate analyses, to assess potential synergies between CO<sub>2</sub> and temperature, each model was adapted to include an interaction term as described above.

The Monte Carlo simulation is valuable for estimating the range of potential exposures and population health risks by country; however, differences between FACE treatments for a given country were driven exclusively by differences in inorganic arsenic concentrations in rice. All other variables (eg, rice consumption, bodyweight, and toxicity) were held constant across treatment scenarios within the same country. For these reasons, and to avoid inflating statistical power with simulated sample sizes, we did not run statistical tests to compare Monte Carlo results across FACE treatments.

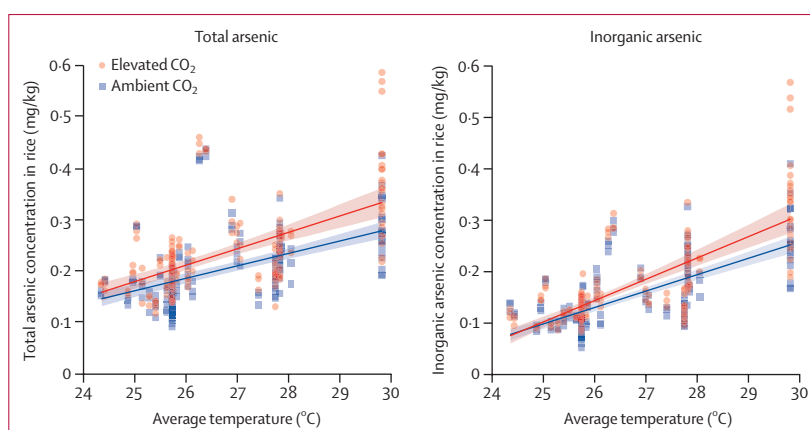
### Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report, or the decision to submit the manuscript for publication.

## Results

Genetically diverse cultivars of paddy rice (13 cultivars; appendix p 3) were grown using four treatments simulating different climatic conditions: Ambient (unmodified climate), CO<sub>2</sub> (+200 ppm), Temp (+2°C), and CO<sub>2</sub>+Temp (+200 ppm, +2°C) in 2020, 2021, and 2023. Elevated temperature negated the CO<sub>2</sub> fertilisation effect on rice yield with different magnitudes, consistent with previous work.<sup>2,21</sup> A 2°C increase was significantly associated with elevated total arsenic and inorganic arsenic concentrations in brown (unpolished) rice (both  $p < 0.0001$ ). Concomitant increases in both temperature and CO<sub>2</sub> resulted in a significant positive interaction on total arsenic and inorganic arsenic rice concentrations relative to either variable (both  $p < 0.0001$ ; figure 1). No significant effect on total arsenic or inorganic arsenic concentrations in rice was observed for elevated CO<sub>2</sub> alone (figure 1). Differences in total arsenic and inorganic arsenic concentrations by treatment for individual cultivars are provided in the appendix (pp 6–7).

A similar synergistic pattern was observed for stem and leaf arsenic total arsenic concentrations when averaged over all cultivars for 2021 (appendix pp 8–9) and for arsenic speciation (arsenic III and DMA) for brown rice in 2021 and 2023 (appendix pp 10–11). The proportion of DMA in total arsenic concentrations is relatively low, ranging from 2% to 21% among the four climatic conditions. The combination of elevated CO<sub>2</sub> and temperature increased DMA concentrations to 0.026 mg kg<sup>-1</sup> on average, compared with 0.014 mg kg<sup>-1</sup> for Ambient. Dimethylated monothioarsenate (DMMTA) was not detectable in the grain samples.

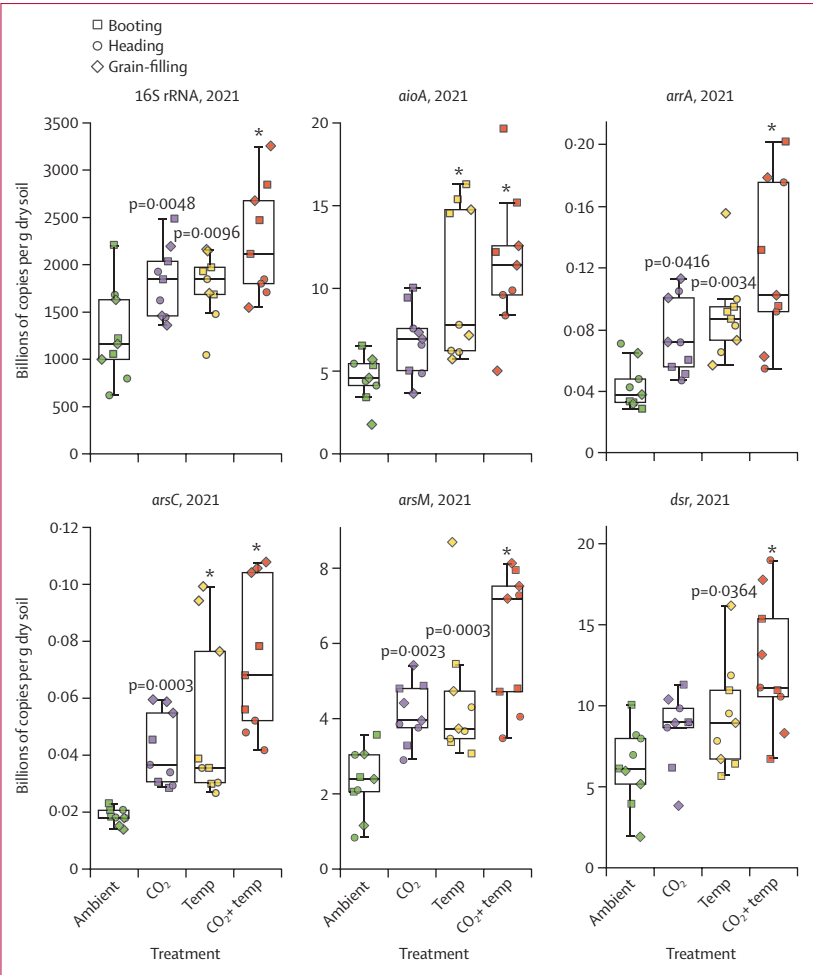


**Figure 2: Effect of seasonal average air temperature on arsenic concentrations in rice grain**

Total arsenic concentrations (mg/kg) in brown (ie, unpolished) rice grain from 28 cultivars across ten growing seasons (2014–23) are plotted against average seasonal air temperatures. Treatments reflect ambient CO<sub>2</sub> conditions (blue squares) or elevated CO<sub>2</sub> (+200 ppm, orange circles). Each treatment group included 180 biological samples (N=360 per panel). The x axis shows the true temperature for each treatment, including the +2°C increase for temperature-elevated conditions. The average daily temperatures (x axis) are calculated on the basis of daily temperatures of each day during the whole rice growing season, from transplanting to harvest (85–135 days depending on the cultivar, year, and experimental site). The number of cultivars varies from year to year. The blue line represents the association between average daily temperature and rice grain arsenic concentrations for growing sites with ambient CO<sub>2</sub> and the orange line represents the association for sites with elevated CO<sub>2</sub>. Linear regressions show significant positive associations between temperature and total arsenic concentrations for both ambient ( $y=24x-445$ ,  $R^2=0.265$ ,  $p<0.0001$ ) and elevated CO<sub>2</sub> ( $y=32x-621$ ,  $R^2=0.342$ ,  $p<0.0001$ ) conditions. The shaded areas around the regression lines represent 95% CIs. The steeper slope associated with elevated CO<sub>2</sub> suggests a potential synergistic effect of CO<sub>2</sub> and temperature on arsenic accumulation, but this was statistically not significant. This interaction shows a potential difference in temperature sensitivity between ambient and elevated CO<sub>2</sub> conditions. Similar trends were observed for inorganic arsenic and when using minimum or maximum seasonal temperatures (appendix pp 12–13). Linear regressions show significant positive associations between temperature and inorganic arsenic concentrations for both ambient ( $y=31x-680$ ,  $R^2=0.494$ ,  $p<0.0001$ ) and elevated CO<sub>2</sub> ( $y=41x-913$ ,  $R^2=0.549$ ,  $p<0.0001$ ) conditions. Regression tables are available via the Open Science Framework.<sup>23</sup>

The relationship between ambient temperature and total arsenic and inorganic arsenic using data from ten growing seasons (2014–23, 28 cultivars) was also assessed with and without treatment increases in CO<sub>2</sub>. Growing season temperature was significantly associated with elevated concentrations of inorganic arsenic and total arsenic in rice (both  $p < 0.0001$ ). Average seasonal temperatures differentially affected total arsenic and inorganic arsenic concentrations as a function of elevated CO<sub>2</sub> treatment, with the slope of regression steeper under elevated CO<sub>2</sub> than under ambient treatment (figure 2; appendix pp 12–13). These findings were consistent with those observed with the treatment synergy between CO<sub>2</sub> and temperature, although they did not reach statistical significance (figure 1).

The abundance of bacterial 16S rRNA, *aioA*, *arrA*, *arsC*, *arsM*, and *dsr* genes, measured as billions of copies per g of dry soil in paddy soils across three rice growing stages (booting, heading, and grain-filling), was characterised by treatment (figure 3). Bacterial 16S rRNA reflects the bacterial population, and others have a role in arsenate reduction (*arsC* and *arrA*), arsenite oxidation (*aioA*), arsenite methylation (*arsM*), or sulphate reduction (*dsr*). Compared to Ambient, elevated CO<sub>2</sub> or higher temperature significantly increased the abundance of all



**Figure 3: Abundance of soil microbial genes involved in the transformation of arsenic species, by climatic conditions**  
Abundance (billions of copies per g of dry soil) of soil microbial genes (bacterial 16S rRNA, *aioA*, *arrA*, *arsC*, *arsM*, and *dsr* genes) at different rice growth stages in paddy soils in 2021, by treatment. Although the substantial differences in abundance between different genes are associated with not only the number of bacterial cells possessing these genes in the soil but also the primers used to amplify the genes, the efficiencies of amplifications, and so on, it is reasonable to compare values of each gene across different treatments. Treatments reflect climatic conditions: Ambient (unmodified climate), CO<sub>2</sub> (+200 ppm), Temp (+2°C), and CO<sub>2</sub>+Temp (+200 ppm, +2°C). Each treatment group and rice stage included three biological replicates (N=36 per panel). Compared to Ambient, depending on the gene, counts were in most cases significantly higher in treatments with elevated CO<sub>2</sub>, or temperature, or both (\*p<0.0001 unless otherwise specified), in mixed-effects models with rice stage as a random effect. Adding an interaction term to the models did not identify any significant synergies between CO<sub>2</sub> and temperature. Boxes show IQRs and whiskers extend to 1.5 times the IQR. Regression tables are available via the Open Science Framework.<sup>23</sup>

microbial genes measured, except for *aioA* and *dsr* in the elevated CO<sub>2</sub> treatment, with combined CO<sub>2</sub> and temperature treatment producing the largest increase. No significant interactions were observed between CO<sub>2</sub> and temperature in a mixed-effects model with rice stage as the random effect. When the relationship between treatment and gene counts was modelled separately for each rice growing stage, treatment-induced changes were observed in two soil metrics, copies of *arsC* and *aioA* (table 1). Elevated CO<sub>2</sub> and temperature in combination had a positive interaction on *arsC* counts,

	Change in booting stage (%)	Change in heading stage (%)	Change in grain-filling stage (%)
<b>arsC</b>			
CO <sub>2</sub>	70% (15%)	78%* (-9%); p=0.0022	276%* (185%); p<0.0001
Temp	69% (26%)	65%* (-1%); p=0.0063	489%* (253%); p<0.0001
CO <sub>2</sub> +Temp	231%* (90%); p<0.0001	153%* (21%); p<0.0001	593%* (268%); p<0.0001
<b>aioA</b>			
CO <sub>2</sub>	60% (3%)	36% (-25%)	49% (18%)
Temp	202%* (126%); p=0.0010	44%* (-8%); p=0.0330	129% (49%)
CO <sub>2</sub> +Temp	207%* (73%); p=0.0008	99%* (1%); p=0.0004	140% (24%)

Treatments reflect climatic conditions: CO<sub>2</sub> (+200 ppm), Temp (+2°C), and CO<sub>2</sub>+Temp (+200 ppm, +2°C). *arsC* participates in the reduction of arsenic V to arsenic III, and *aioA* participates in the oxidation of arsenic III to arsenic V. Values outside parentheses show the percentage change in absolute abundance relative to Ambient; values inside parentheses show the percentage change in relative abundance. Compared to Ambient, the absolute abundance was significantly higher in treatments with elevated CO<sub>2</sub> or temperature, or both, as indicated above (\*p<0.05), in a separate linear regression model for each rice stage. Synergy between CO<sub>2</sub> and Temp (p=0.0070) was observed for *arsC* during the grain-filling stage after adding an interaction term to the model. Regression tables are available via the Open Science Framework.<sup>23</sup>

**Table 1: Percentage changes in the absolute and relative abundance of an arsenic reductive gene (*arsC*) and an oxidative gene (*aioA*) at different growth stages in paddy soils in 2021 as a function of projected climate change relative to ambient (unmodified climate) conditions**

with around six times higher counts in CO<sub>2</sub>+Temp compared to the Ambient treatment during the grain-filling stage, showing a synergism (table 1). For *aioA*, although early treatment differences were evident during booting, no significant treatment variation was observed by grain fill (table 1, figure 3).

Soil pH and redox potential were assessed in 2021 during booting, heading, and filling. Spatial and temporal changes in soil pH were not observed (appendix p 14). However, redox potential was consistently lower (more reductive) at the CO<sub>2</sub> and temperature treatment relative to the control (Ambient) during grain filling (appendix p 14).

The average daily consumption of inorganic arsenic and associated cancer and non-cancer risks from rice consumption, after converting brown (ie, unpolished) to white (ie, milled) rice intake, for the year 2050 was estimated with the four treatment scenarios (tables 2, 3; figure 4). Each scenario was modelled in accordance with populations, rice intake, and the share of rice hectares using flood irrigation specific to seven Asian countries: Bangladesh, China, India, Indonesia, Myanmar, Philippines, and Viet Nam (appendix p 5). Under Ambient conditions, mean inorganic arsenic exposures from rice consumption ranged from 1.54×10<sup>-4</sup> mg inorganic arsenic per kg bodyweight per day in India to 5.80×10<sup>-4</sup> mg inorganic arsenic per kg bodyweight per day in Viet Nam;



under CO<sub>2</sub>+Temp, exposures ranged from  $2.21 \times 10^{-4}$  mg inorganic arsenic per kg bodyweight per day in India to  $8.33 \times 10^{-4}$  mg inorganic arsenic per kg bodyweight per day in Viet Nam (table 2). The projected mean number of lifetime bladder and lung cancer cases in 2050 increased proportionally to exposures, with the highest risk projections observed for CO<sub>2</sub>+Temp (44% increase in mean cancer cases compared to Ambient; figure 4). Mean numbers of projected cancer cases under the Ambient treatment were highest for China, with 13.4 million cases attributable to inorganic arsenic exposure through rice consumption over the lifetimes of the population alive in 2050. Under the CO<sub>2</sub>+Temp treatment, the projected mean number of cancer cases in China increased to 19.3 million.

Non-cancer adverse health outcomes from rice inorganic arsenic exposure were assessed with HQs (table 3; appendix p 15). HQs of 1 or greater indicate that the corresponding adverse health effect might be possible given the estimated exposure. Median HQs ranged from 1.3 (India, Ambient, for developmental neurocognitive effects) to 12.0 (Viet Nam, CO<sub>2</sub>+Temp, for ischaemic heart disease and diabetes). As with cancer risk, mean HQs were 44% higher under CO<sub>2</sub>+Temp compared to Ambient. For every country and adverse health effect, median HQs were always above 1 regardless of treatment scenario.

## Discussion

This multi-season, multi-cultivar, and multi-T-FACE study of rice grown in paddy soils found that elevated temperature (+2°C) and concurrent increases in CO<sub>2</sub> and temperature (+200 ppm, +2°C) were significantly associated with higher concentrations of arsenic in rice. The concurrent increases were greater than that of temperature alone. This effect was observed with multiple cultivars genetically representative of lines currently grown and consumed in Asia. The projected excess cancer burden associated with dietary arsenic exposure under these scenarios for 2050 was in the tens of millions, and while elevated HQs do not directly translate to quantifiable increases in risk, our results can reasonably be interpreted to portend a greater incidence of heart disease, diabetes, and other non-cancer health effects.

Beyond temperature imposed as an experimental treatment, natural air temperature variation over a 10-year period (2014–23) was also associated with changes in arsenic concentrations. We observed a significantly positive relationship between arsenic concentration and air temperature with and without CO<sub>2</sub> enrichment. The steeper slope under elevated CO<sub>2</sub> indicates higher sensitivity of grain arsenic in response to temperature. These results, in both experimental climate scenarios and with real-world natural seasonal temperature variation, present a troubling trend towards increasing rice arsenic uptake in the context of climate change.

The current findings might be explained, in part, by soil biogeochemistry. In our analysis of paddy rice soils,

	Ambient	CO <sub>2</sub>	Temp	CO <sub>2</sub> +Temp
Viet Nam	$5.80 \times 10^{-4}$	$6.18 \times 10^{-4}$	$6.92 \times 10^{-4}$	$8.33 \times 10^{-4}$
Indonesia	$4.83 \times 10^{-4}$	$5.15 \times 10^{-4}$	$5.76 \times 10^{-4}$	$6.93 \times 10^{-4}$
China	$3.22 \times 10^{-4}$	$3.44 \times 10^{-4}$	$3.85 \times 10^{-4}$	$4.64 \times 10^{-4}$
Bangladesh	$2.61 \times 10^{-4}$	$2.78 \times 10^{-4}$	$3.11 \times 10^{-4}$	$3.74 \times 10^{-4}$
Philippines	$2.57 \times 10^{-4}$	$2.74 \times 10^{-4}$	$3.07 \times 10^{-4}$	$3.68 \times 10^{-4}$
Myanmar	$1.99 \times 10^{-4}$	$2.12 \times 10^{-4}$	$2.38 \times 10^{-4}$	$2.85 \times 10^{-4}$
India	$1.54 \times 10^{-4}$	$1.64 \times 10^{-4}$	$1.83 \times 10^{-4}$	$2.21 \times 10^{-4}$

Mean exposure (mg inorganic arsenic per kg bodyweight per day), by country, as a function of climate treatments: Ambient (unmodified climate), CO<sub>2</sub> (+200 ppm), Temp (+2°C), and CO<sub>2</sub>+Temp (+200 ppm, +2°C). We used a Monte Carlo simulation with 5000 trials to model exposure. Differences between treatments for a given country were entirely attributable to differences in inorganic arsenic concentrations in rice (figure 1), thus we did not run statistical comparisons on exposure estimates.

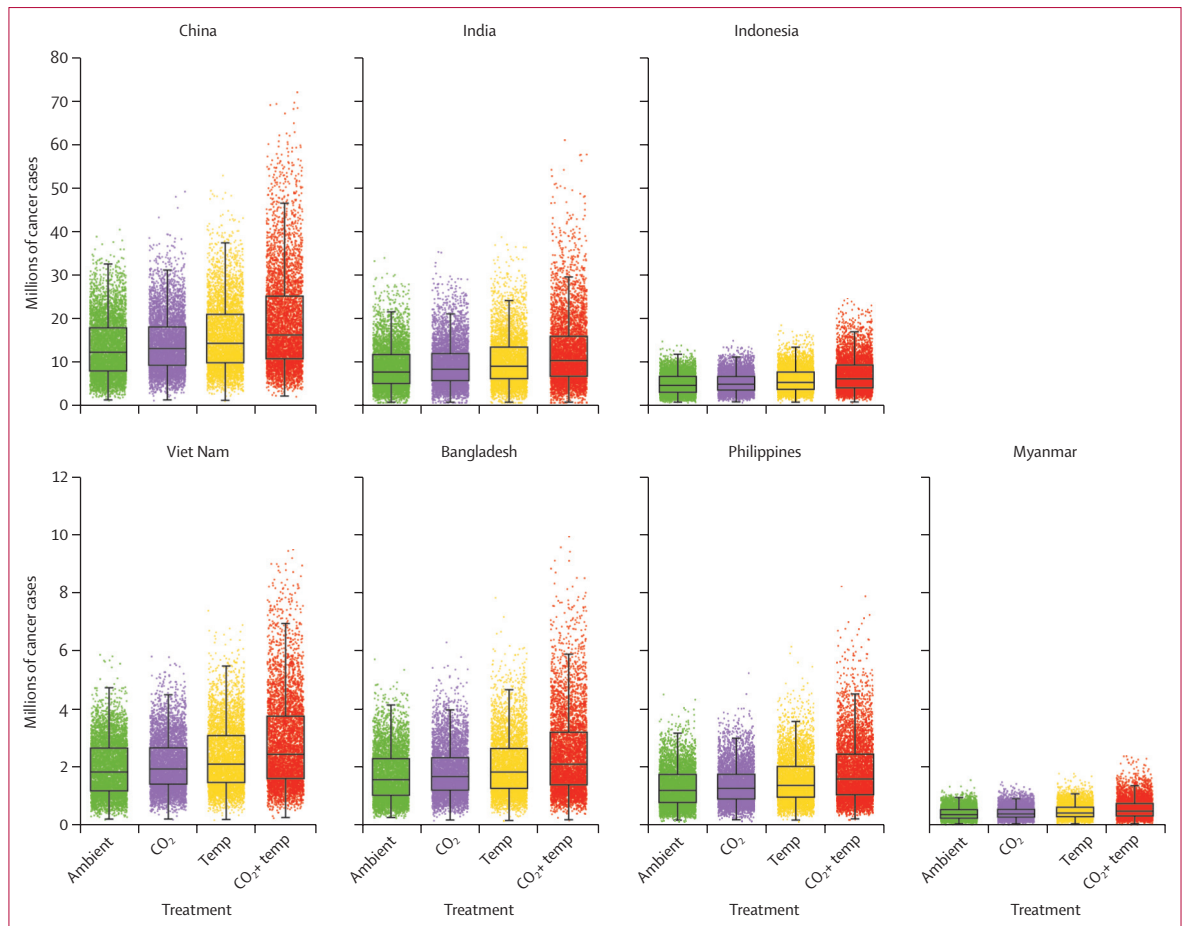
**Table 2: Mean inorganic arsenic exposure attributable to rice consumption, by country and treatment**

	Ambient	CO <sub>2</sub>	Temp	CO <sub>2</sub> +Temp
<b>Viet Nam</b>				
Ischaemic heart disease, diabetes	9.0 (5.9–13.0)	9.5 (7.0–13.1)	10.3 (7.3–15.1)	12.0 (7.9–18.4)
Fetal, newborn, and infant health outcomes	6.9 (4.5–9.9)	7.2 (5.3–9.9)	7.9 (5.5–11.5)	9.1 (6.0–14.0)
Developmental and neurocognitive outcomes	5.2 (3.3–7.5)	5.5 (4.0–7.5)	5.9 (4.1–8.7)	6.9 (4.5–10.5)
<b>Indonesia</b>				
Ischaemic heart disease, diabetes	7.5 (4.9–10.9)	8.0 (5.8–10.9)	8.6 (6.0–12.5)	10.0 (6.6–15.2)
Fetal, newborn, and infant health outcomes	5.7 (3.7–8.3)	6.1 (4.4–8.2)	6.6 (4.6–9.5)	7.6 (5.0–11.5)
Developmental and neurocognitive outcomes	4.3 (2.8–6.2)	4.6 (3.3–6.2)	4.9 (3.4–7.2)	5.7 (3.8–8.7)

Median hazard quotients (with IQRs) from Monte Carlo simulations with 5000 trials, shown for Viet Nam and Indonesia, the two countries (of seven analyzed) with the highest per-person intake of irrigated (flooded) rice. Differences between treatments for a given country were entirely attributable to differences in inorganic arsenic concentrations in rice (figure 1), thus we did not run statistical comparisons on hazard quotients. Detailed results for all seven countries are available via the Open Science Framework;<sup>23</sup> see also the appendix (p 15).

**Table 3: Median hazard quotients by country, health outcome, and treatment**

elevated CO<sub>2</sub> and temperature, independently and in combination, altered physical and biological soil metrics by lowering redox potential and shifting the abundance of microbial genes involved in the transformation of arsenic species. A lower redox potential favours the reductive dissolution of iron oxyhydroxides and the reduction of arsenate to arsenite, leading to both an increase in arsenic availability and its accumulation in rice plants.<sup>44–47</sup> Furthermore, the abundance of *arsC*, which participates in the reduction process of arsenic (from arsenate to arsenite), increased six times with elevated CO<sub>2</sub> and temperature during the grain-filling stage. These processes are potentially key drivers since rice is efficient at arsenic bioaccumulation owing in part to arsenite mobilisation<sup>8</sup> and inadvertent uptake of arsenite via the silicon transporters in rice roots.<sup>48</sup>



**Figure 4: Projected lifetime lung and bladder cancer cases among populations alive in 2050 attributable to inorganic arsenic exposure from paddy rice, by country and treatment**

We used a Monte Carlo simulation with 5000 trials to model projected cancer cases among the populations of seven Asian countries in 2050. Treatments reflect climatic conditions: Ambient (unmodified climate), CO<sub>2</sub> (+200 ppm), Temp (+2°C), and CO<sub>2</sub>+Temp (+200 ppm, +2°C). Differences between treatments for a given country were entirely attributable to differences in inorganic arsenic concentrations in rice (figure 1), thus we did not run statistical comparisons on cancer estimates. Note different y scales to account for differences in the magnitude of cancer cases across countries. Each dot is the result of a Monte Carlo trial. Boxes show IQRs and whiskers extend to 1.5 times the IQR.

Previous studies suggest the behaviour of the soil biota that drives arsenic bioaccumulation in rice depends, in part, on rising temperatures and CO<sub>2</sub> concentration.<sup>10,49</sup> Elevated CO<sub>2</sub> could also influence arsenic uptake in rice by stimulating root growth and increasing the root to shoot ratio<sup>50,51</sup> with additional carbon from root exudates stimulating microbial populations, arsenic availability, or arsenic biotransformation. Warmer temperatures, in turn, could promote CO<sub>2</sub>-induced root growth, exudate degradation, and increases in soil microbiota populations. Our study showed that elevated CO<sub>2</sub> and temperature could increase bacterial growth and differentially affect the abundance of reducing versus oxidative arsenic genes.

Previous investigations have explored independent effects of temperature or CO<sub>2</sub> concentration on arsenic in rice grain. Controlled environmental studies<sup>10,11,52</sup> with single cultivars under greenhouse or growth chamber conditions have reported that projected or inter-annual

variability in air temperature can increase arsenic in rice grain with negative effects on yield, due to facilitated microbial reduction and release of arsenic in flooded paddy soil. Elevated CO<sub>2</sub> alone might increase arsenic bioavailability and promote the transformation of arsenic V to arsenic III in the soil and arsenic uptake by rice.<sup>49,53</sup> We are aware of only one study<sup>9</sup> that examined simultaneous increases in temperature and CO<sub>2</sub> relative to arsenic accumulation and speciation; this study found that future climate conditions caused a nearly twofold increase of grain inorganic arsenic concentrations for a japonica cultivar, associated with increased dissolved arsenic and a greater proportion of arsenite in pore-water. These findings, under greenhouse conditions, are consistent with the amplified arsenic accumulation observed in the current study.

The use of FACE and T-FACE field systems reflect real-world growing conditions for paddy rice. The multi-year span of the study (3 years for T-FACE, 10 years including

both FACE and T-FACE) provides a robust dataset and the ability to explore the effects of ambient seasonal temperatures over time. The use of 28 cultivars represents the genetic diversity of rice consumed across major rice-consuming countries in Asia. A facilitated reduction process of arsenic characterised by substantial increases in *arsC* abundance at grain filling, and a lower soil redox potential, could account for the increased arsenic bioaccumulation in rice grain under the combination of elevated CO<sub>2</sub> and elevated temperature. Finally, a robust probabilistic modelling approach using the most recent epidemiological data, and accounting for arsenic bioaccessibility, arsenic losses during rice milling, and a range of other factors, allowed us to translate arsenic concentrations to potential population-level cancer and non-cancer health burdens specific to seven countries.

There are a few important factors that could influence the generalisability of our findings. There might be substantial geographical variation in the concentrations of arsenic in the underlying soil and irrigation water used to grow rice. Additionally, soil biogeochemistry can differ by locale, and thus climate-induced changes might be specific to the production environment in which rice is grown. The relationship between arsenic bioaccumulation in grain and soil temperature remains unclear. Furthermore, the distributions of input variables used in the study model exhibited variation and uncertainty; the SD of inorganic arsenic bioaccessibility in rice was 16% and that of inorganic arsenic remaining in rice after milling was 4%. The results of a sensitivity analysis (appendix p 16) showed that variability in inorganic arsenic concentrations in rice accounted for the widest range of variability in per-person cancer risk. Accounting for additional details about the variation in rice consumption by culture or ethnicity, preparation methods (eg, parboiling), use of arsenic-contaminated cooking water, and other factors would improve our confidence in estimated dietary arsenic exposures and associated health outcomes. We could not account for the toxicological effects of the consumption of organic arsenic species (eg, DMA)<sup>54</sup> present in rice due to a scarcity of quantitative toxicological values; lack of consideration of their contribution to disease processes might result in an underestimation of the health burden of arsenic related to climate change. Furthermore, excessive accumulation of DMA in rice grain can cause the physiological disorder straighthead disease in rice plants, resulting in substantial yield losses.<sup>28,55</sup> Although straighthead disease was not observed for any of the climate treatments used in the current study, probably due to relatively low DMA concentrations, increases in DMA in response to climate change can be a concern for rice production for farmers where the paddy soil has a high potential for microbial arsenic methylation.<sup>28</sup> Additionally, DMA can be converted to thiolated DMA (eg, DMMTA), and DMMTA is thought to be highly

toxic, with its cytotoxicity being three to ten times higher than that of inorganic arsenic in in-vitro studies,<sup>56,57</sup> but it was undetectable in our study.

Complicating matters, policy measures to control dietary arsenic exposures are inconsistent across countries and largely voluntary, inadequately comprehensive, or unenforced. For example, the US Food and Drug Administration has recommended a non-regulatory action level of 100 ppb of inorganic arsenic in infant rice cereal but does not formally regulate arsenic in rice or any other food. The European Union has established an enforceable inorganic arsenic standard of 100 ppb for rice used in foods for infants and children, as well as more tolerant standards for rice and other foods containing rice ranging from 200 to 300 ppb.<sup>58</sup> China has proposed a limit of 200 ppb for inorganic arsenic in paddy rice;<sup>59</sup> under elevated temperature and CO<sub>2</sub> conditions, more than half the rice samples in our study would have exceeded this limit (median: 231 ppb). To date, no countries or jurisdictions have established regulatory standards or guidance for organic arsenic species in foods.

While accounting for these factors is important, the current assessment might be sufficient to suggest actions that could reduce inorganic arsenic exposure going forward, given that rice is likely to remain a staple crop globally. Such actions could include plant breeding efforts that minimise arsenic uptake,<sup>60</sup> paddy soil management that would disrupt anaerobic conditions (eg, alternate wetting and drying),<sup>8</sup> or changes in soil management and amendments that hold promise for minimising the uptake of arsenic into rice. These efforts complement other public health measures aimed at rice processing and preparation, consumer education, and population exposure monitoring.<sup>61</sup> In summary, this work reinforces the urgent need to mitigate arsenic exposure in rice relative to near-term climate change.

#### Contributors

DW, CZ, LHZ, F-JZ, BFK, and KEN were responsible for conceptualisation of the study. CZ, BFK, KEN, IL, F-JZ, CCh, AG, AAC, LS, WZ, YJ, and DW were responsible for the methodology. DW, CZ, CCh, AG, LHZ, BFK, and KEN conducted the investigation of arsenic concentrations in rice, soil properties, and human health assessments. BFK, DW, and IL did the formal analysis. BFK, IL, DW, CZ, F-JZ, CCh, CM, LHZ, JH, and LS conducted the visualisation of the main and supplementary figures. CZ and CCh were responsible for funding acquisition. CZ, KEN, and LHZ were responsible for project administration. CZ, KEN, and LHZ were responsible for supervision of the experimental and modelling study. LHZ, DW, CZ, BFK, KEN, and F-JZ wrote the original draft. All authors contributed to the review and editing of the manuscript. All the authors had full access to all the data in the study and the corresponding author had final responsibility for the decision to submit the manuscript for publication.

#### Declaration of interests

We declare no competing interests.

#### Data sharing

To ensure reproducibility, all study data, code, and detailed results of statistical analyses are available via the Open Science Framework (<https://osf.io/harjx/>).

# Acknowledgments

We gratefully acknowledge fundings from the National Key Research and Development Program of China, National Natural Science Foundation of China, Key-Area Research and Development Program of Guangdong Province, China, Carbon Peaking and Carbon Neutrality Special Fund for Science and Technology from Nanjing Science and Technology Bureau, Key Research and Development Program of Jiangsu Province, Erdos City Science and Technology Major Project, Science Foundation of the Chinese Academy of Sciences, Carbon Peaking and Carbon Neutrality Special Fund for Science and Technology from Jiangsu Science and Technology Department, and "0-1" Original Innovation Project of the Chinese Academy of Sciences. We thank Genxin Pan and Xiaoyu Liu who made enduring contributions to the operation of FACE 1 platform (Changshu City) and thank Jianguo Zhu and Gang Liu who provided the technical support for FACE 3 (Yangzhou City). The FACE system instruments for FACE 3 were supplied by the National Institute of Agro-Environmental Sciences and the Agricultural Research Center of Tohoku Region (Japan). CZ received funding from the National Key Research and Development Program of China (grant 2023YFD1500801), National Natural Science Foundation of China (grant 31870423) Key-Area Research and Development Program of Guangdong Province, China (number 2020B020201006), the Carbon Peaking and Carbon Neutrality Special Fund for Science and Technology from Nanjing Science and Technology Bureau (number 20221103), Erdos City Science and Technology Major Project (grant 2022EEDSKJZDZX010), and "0-1" Original Innovation Project of the Chinese Academy of Sciences (ZDBS-LY-DQC020). YD received funding from the Key Research and Development Program of Jiangsu Province (grant BE2022308). CCa received funding from the Science Foundation of the Chinese Academy of Sciences (grant ISSAS2413). XY (Xiaoyuan Yan) received funding from the Carbon Peaking and Carbon Neutrality Special Fund for Science and Technology from Jiangsu Science and Technology Department (grant BM2022002).

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