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Weaponised uranium and adverse health outcomes in Iraq: a systematic review

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ABSTRACT

Background The US military first deployed depleted uranium (DU) weapons in Iraq during the Gulf War in 1990 and in the 2003 invasion of Iraq. Research into the health impacts of DU has been mired in debate and controversy. Research funded by the US government has denied the health risks posed by DU to the Iraqi population, while opponents have claimed that DU is responsible for increased rates of birth defects and cancers in Iraq. Others assert that the public health impacts of DU weapons remain uncertain. This systematic review identified, appraised and synthesised all human observational studies assessing adverse health outcomes associated with DU exposure among the Iraqi population. To our knowledge, no systematic review has been conducted on the topic previously.

Methods We searched 11 electronic databases for human observational studies published between 1990 and 2020 that measured association between exposure to weaponised uranium and health outcomes (including cancer, birth defects, immune system function and mortality) among the Iraqi population. We assessed risk of bias using the Navigation Guide's risk of bias tool and rated certainty of the evidence using the Grading of Recommendations, Assessment, Development and Evaluations approach (PROSPERO: CRD42018108225).

Results Our searches identified 2601 records, of which 28 met our inclusion criteria. We identified five additional eligible reports from other sources. Two articles reported the results of multiple relevant studies; our final set included 33 articles reporting on 36 eligible studies. Most studies (n=30, 83%) reported a positive association between uranium exposure and adverse health outcomes. However, we found that the reviewed body of evidence suffers from a high risk of bias.

Conclusion The available evidence suggests possible associations between exposure to depleted uranium and adverse health outcomes among the Iraqi population. More primary research and the release of missing data are needed to design meaningful health and policy interventions in Iraq.

Key questions

What is already known?

- Depleted uranium (DU) is a chemotoxic and radiotoxic heavy metal and is classified by the International Agency for Research on Cancer (IARC) as a group I carcinogen (*limited evidence* in humans and *sufficient evidence* in experimental animals).
- The US and UK militaries used DU weapons in Iraq during the First Gulf War in 1991 and the Iraq War starting in 2003.
- Many studies have investigated the association between DU exposure in Iraq and adverse health outcomes, but to our knowledge no systematic review (SR) on the topic has been previously conducted.

What are the new findings?

- Most of the included reports in this SR were published in the year 2010 or later (after US Gulf War sanctions had been lifted).
- Most of the included reports showed a positive association between uranium exposure and adverse health outcomes among the Iraqi population.
- Our risk of bias assessment rated all the included reports as *high* or *probably high* in the domain of confounding.

What do the new findings imply?

- US sanctions on Iraq may have played a role in limiting research and publication on the health impacts of weaponised uranium on the Iraqi population.
- More primary research on this topic is needed, with adequate assessment and control of important confounders.

INTRODUCTION

Depleted uranium (DU) is a heavy metal possessing chemotoxic and radiotoxic properties.[1] In nature, uranium exists in three isotopic forms, U-238, U-235 and U-234, with mass percentages of 99.284%, 0.711% and 0.005%, respectively.[2] Of those, only U-235 is fissionable, that is, will readily undergo a nuclear chain reaction.[3] In order to produce fuel for commercial nuclear energy reactors, the mass percentage of U-235 in *natural uranium* (0.711%) must be increased through the enrichment process.[3] The US Nuclear Regulatory Commission defines *highly enriched*

uranium as uranium with a mass percentage of U-235 of 20% or greater, *enriched* uranium as uranium with a mass percentage of U-235 of 2%–5% and *depleted* uranium as uranium with an abundance of U-235 less than 0.7% (by mass).[4] DU is created as a by-product of uranium enrichment and contains fewer U-235 isotopes than natural uranium.[1]

Due to its density, pyrophoricity (ie, the ability to ignite on impact) and availability, the US military deployed DU weapons in 1991 during the first Gulf War in Iraq and again in the 2003 US invasion of Iraq.[5] Recent studies have suggested that the US military may also use *slightly enriched* uranium (U-235 mass percentage >0.711%, <2%) in conventional weapons in Iraq.[6] Therefore, we use the term *weaponised uranium* to refer to metallic uranium (of uncertain isotopic composition) that has been introduced to the environment in Iraq via the use of conventional weapons (ie, non-nuclear missiles, bullets and armour).

The possible routes of exposure to weaponised uranium among the Iraqi population are ingestion, inhalation, dermal contact and embedded fragments (eg, shrapnel).[3] On impact with a hard target (eg, an armoured tank), weaponised uranium generates a cloud of uranium oxide particles of varying solubility, a property known as pyrophoricity.[7] Exposure to uranium oxides via inhalation or ingestion has been shown to induce carcinogenic and teratogenic effects in non-human in vivo animal studies.[3 8 9] After absorption, uranium oxides are metabolised to uranyl ions that readily bond with other molecules, including proteins and bioligands, and are transported throughout the body via systemic circulation.[3] Most uranium that is absorbed is excreted in urine within 24 hours, but that which remains is stored in the bones, the kidneys and the liver.[1] Uranium is also capable of crossing the blood–brain barrier and the placental barrier.[10] Once absorbed, uranium has been shown to increase the presence of reactive oxygen species, break DNA strands and alter gene expression leading to adverse clinical effects.[10] Chronic exposure scenarios put local populations at greater risk to adverse health effects than veteran populations.[11–13] According to the WHO, children might be at greater risk of exposure via ingestion due to hand-to-mouth transfer of dust and uranium oxide particles.[14] Other vulnerable groups include scrap metal workers and civilians living near highly contaminated areas such as the Umm Qasr tank storage area in Southern Iraq.[15]

Exactly where, or how much, DU was used in Iraq by US forces since 1991 is still not fully known.[16–18] The International Atomic Energy Agency (IAEA) estimates that between 170 and 1700 t of DU was deployed in Iraq by the US military since 2003, while other conservative estimates place the total amount of DU used by the US military in Iraq since 1991 at 440 t.[18 19] The UK has also reported firing 1.9 t DU weapons in Iraq since 2003.[20] More than 300 DU-contaminated sites in Iraq have been identified by the Iraqi Ministry of the Environment Radiation Protection Center (RPC).[20] While all sites identified by the RPC were located south of Baghdad, additional research has reported high concentrations of uranium in soil samples from Mosul.[21] In 2014, the Dutch NGO PAX published a set of US DU firing coordinates in the Dutch area of operation in Basrah that were provided at the request of the Dutch Ministry of Defense out of concern for their military personnel serving in the area.[20] Additionally, in 2016, George Washington University and the Dutch NGO PAX released data on DU firing coordinates obtained via a Freedom of Information Act request.[16 18] The data contain precise locations of 783 out of 1116 airstrikes carried out by DU-armed A-10 Warthogs in Iraq between 20 March and 15 April 2003.[18] While the data do not contain total amounts of DU rounds fired during each strike, they do indicate a far more widespread use of DU during the 2003 Iraq War than had previously been indicated. The target locations are scattered across Iraq, in every governorate.[16 18]

While many recent reviews attempted to summarise the evidence regarding toxicity of weaponised uranium,[8 11 22–26] only one was conducted systematically—and it focused on US Gulf War veterans.[24] Compared with veterans, the Iraqi population has received scant attention in the DU literature, due partly to the politicisation of DU research.[11–13] In 2013, Webster PC[27] published a World Report in *The Lancet* raising concern about a national congenital birth defect (CBD) study carried out by the Iraqi Ministry of Health (IMOH) in 2012. The IMOH study found *no proof* of unusually high CBD incidence in the country, although Iraqi doctors in DU-impacted zones had been voicing concerns for decades. Webster sharply criticised the IMOH's methodology, its (lack of) peer-review process, and cited three studies on CBD incidence in Iraq whose findings disagreed with the IMOH report.[28–30] This controversy speaks to the need for a systematic review (SR) of all the available evidence. Previous (non-systematic) reviews on this topic have lacked comprehensive, transparent search strategies and inclusion criteria, which may have introduced bias into the reviews.

The present study aimed to systematically review the evidence on the associations between weaponised uranium exposure and adverse health impacts among the Iraqi population and to judge the certainty of the evidence. SRs have long been considered the standard approach to synthesising a body of evidence in the field of clinical medicine and are increasingly considered so in the field of environmental health.[31] Their thorough, transparent and reproducible methods make SRs the ideal tool for approaching controversial and politicised questions of environmental exposures.

METHODS

Eligibility search strategy and selection criteria

We defined our research question and eligibility criteria using the Population, Exposure, Comparator, Outcome,

Study Design (PECOS) Statement (online supplemental material 1, table S1).[32] The population of interest consists of individuals of any age residing in Iraq at any time between 1990 and 2020 and of the children of those individuals. We did not limit our exposure inclusion criteria to strictly DU (U-235 content <0.7%), because it has been reported that slightly enriched uranium might also be used in conventional weapons by the US military.[33] Regarding outcomes, we included studies that reported mortality and morbidity outcomes such as cancer and birth defects. Only human observational studies were eligible for inclusion in this review. In order to overcome possible publication bias, we did not restrict our inclusion criteria based on publication status (eg, peer-reviewed studies).

We developed our search strategy with the assistance of a medical librarian and searched the following 11 electronic databases: MEDLINE, Embase, PubMed, Scopus, Toxline, Iraqi Academic Scientific Journals, WHO Digital Library, United Nations Environment Programme Knowledge Repository, IAEA Scientific and Technical Publications, Google Scholar and ProQuest Dissertations and Theses Global. Complete search strategies for each database are provided in the online supplemental material 1, table S2.

We restricted our initial search to human observational studies published between January 1990 and April 2020, and we used no language restrictions. In addition to database searches, we hand searched reference lists of included studies and forward-tracked citations of included studies in Google Scholar in order to identify additional relevant studies.

Title/abstract and full-text screening was conducted by independent screeners with two screeners per article (SS, MI and MA-L), using the reference management software EndNote V.X8 and following the prespecified eligibility criteria (see online supplemental material 1, 'Screening form'). Calibration exercises were carried out prior to beginning title/abstract and full-text screening, in order to test the clarity of the screening protocol and to ensure a high level of agreement between the three primary reviewers (SS, MI and MA-L). During the calibration exercises, the reviewers met and reviewed the screening forms. Then, each reviewer independently screened the same subset of records and full texts, and the reviewers compared their results and discussed any disagreements.

Studies deemed eligible for inclusion by any reviewer during the title and abstract screening phase underwent full-text screening. At the full-text screening phase, reviewers again screened full texts independently and in duplicate. However, after screening at the full text phase, the two reviewers assigned to each study met to compare screening decisions. In cases of disagreement, the two reviewers discussed their justifications or invited a third reviewer for input (RRH and LAK) until consensus was achieved.

This study is reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (online supplemental material 1, Table S3). The study protocol is available online (PROSPERO, number CRD42018108225, see https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=108225).

There were no patient or public involvement in the study protocol of this SR.

Data analysis

Two reviewers abstracted data from full-text articles in duplicate and independently by using a prespecified data abstraction form designed by the authors in Microsoft Excel (for Office 365) (see online supplemental material 1, 'Data abstraction items'). A data abstraction calibration exercise was conducted with a small sample of full texts prior to initiating data abstraction. After abstracting data independently, the two reviewers met to compare their results and resolve disagreements. Data abstraction items included summary measures from individual studies, such as difference in means and relative risk.

Risk of bias was assessed using the Navigation Guide's risk of bias tool (provided in online supplemental material 1, 'The Navigation Guide instructions for making risk of bias determinations') that is adapted from the Cochrane Collaboration's Risk of Bias tool and the Agency for Healthcare Research and Quality's Methods Guide.[34] The Navigation Guide's risk of bias tool includes nine domains: recruitment strategy, blinding, confounding, exposure assessment, outcome assessment, incomplete outcome data, selective outcome reporting, conflict of interest and other sources of bias. For each domain, reviewers documented the risk of bias for each individual study as 'low risk of bias', 'probably low risk of bias', 'probably high risk of bias', 'high risk of bias' or 'not applicable' following prespecified criteria. Complete definitions of each domain and rating criteria are found in the online supplemental material 1 'The Navigation Guide instructions for making risk of bias determinations'. Regarding the domain of confounding, we judged a study to be low risk of bias if it accounted for all five of the following confounders: age of participants, sex of participants, tobacco use, obesity and toxic environmental exposures. For studies that assessed birth defects, we required four additional confounders to be accounted for: maternal folate deficiency, maternal age (at birth), maternal education (at birth) and consanguinity. Two reviewers (SS and MI) rated risk of bias for each included study in duplicate and independently, and then met to compare their results. In cases of disagreement, input from a third reviewer (RRH) was sought.

We analysed data using a *narrative synthesis*, following guidelines produced by the Center for Reviews and Dissemination at the University of York. As per the Popay *et al*[35] guidelines, our synthesis sought to organise findings by health outcome, explore patterns in the results (including direction and magnitude of effects) and

examine relationships in the data. We organised our synthesis by eight health outcomes: CBDs, other birth-related outcomes, cancer, BCL-2 oncogene expression, PTEN gene expression, kidney failure, immune system function and other outcomes.

We assessed the certainty of evidence for each outcome using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach.[36] The GRADE approach defines the certainty of a body of evidence as the extent to which one can be confident that an estimate of effect is close to the true value for an outcome.[37] The certainty of evidence is assessed for each outcome separately. According to the GRADE approach for assessing the certainty of the evidence for non-randomised studies (NRS), the rating of the certainty of evidence for NRS may be initially rated as high certainty.[38] Next, the rating considers five factors for which the certainty of evidence is rated down, and three factors for which the certainty can be rated up.[39] The five rating-down factors are: (1) risk of bias, (2) indirectness of evidence, (3) inconsistency, (4) imprecision of effect estimates and (5) risk of publication bias. The three rating-up factors are: (1) large effect, (2) dose–response gradient and (3) plausible confounders or other biases increase the certainty in the effect. We judged whether each of these factors (and for one outcome at a time) is of no serious, serious, or very serious concern, except for the risk of bias domain where 'extremely serious' may apply. The final assessment of the certainty of a body of evidence is one of four grades: high, moderate, low or very low (online supplemental material 1, table S4).[40]

There was no funding source for this study.

RESULTS

Search results

Our database searches retrieved 2601 unique records. Of those, 235 met our inclusion criteria at the title and abstract screening phase (figure 1 – diagram style adapted from ROSES).[41] The full-text reports for 15 of those records could not be retrieved. The records for all of the unretrievable texts came from our grey literature search and either (A) contained insufficient bibliographic data for tracking the source of the records (n=5) or (B) a request was made for the full text by a medical librarian, but the text was not supplied (n=10). Of the 220 reports that underwent full-text screening, 28 met our inclusion criteria. Reasons for exclusion at the full-text screening

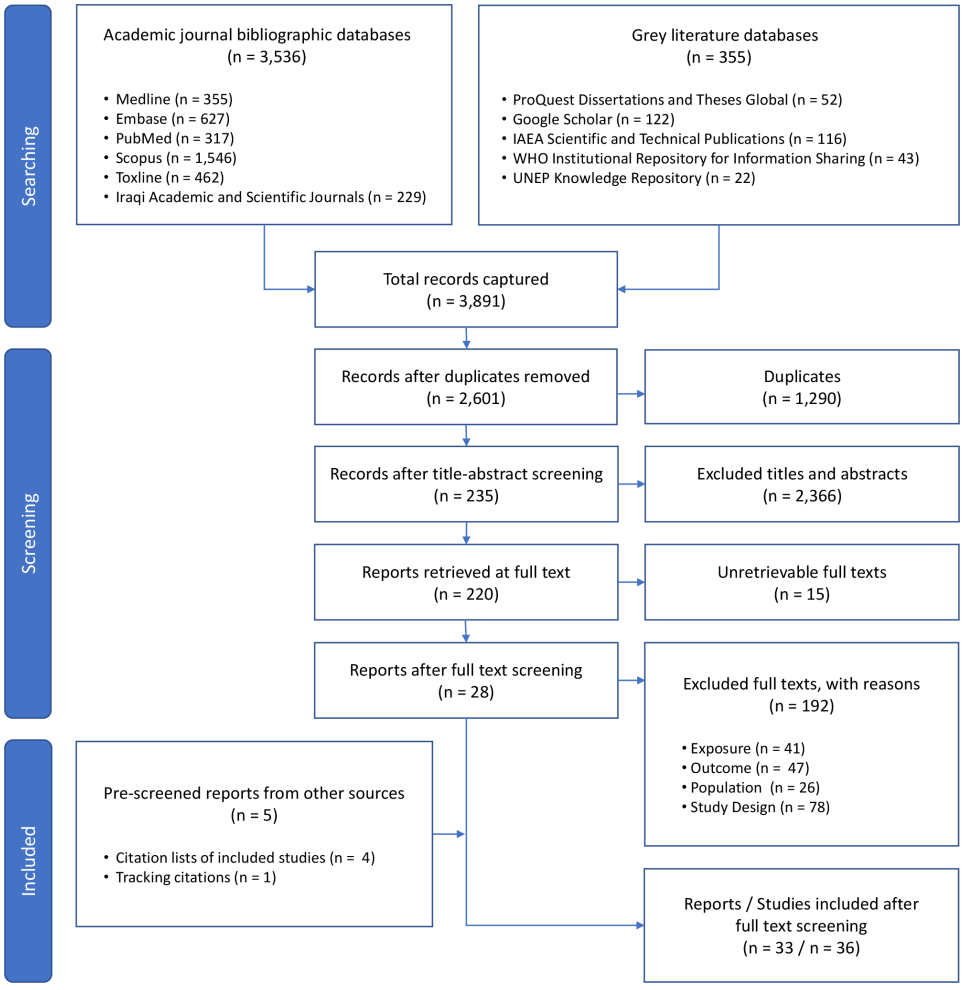

Figure 1 Study selection, diagram style adapted from ROSES.[41]

stage are provided in the online supplemental material 1, 'Full text exclusion justifications'. By screening the citation lists of included reports and by tracking their citations forward in Google Scholar, we identified five additional records that were not captured in our database searches, bringing our total number of included reports to 33. Of the 33 included reports, two reported results from the same study.[42 43] Additionally, three articles reported the results of more than one relevant study,[28 44 45] and thus the final number of studies included in our evidence synthesis was 36 (online supplemental material 1, tables S5–S12).

Characteristics of included studies

The timeframes of 26 included studies ranged from 1980 to 2017 (10 studies did not report their research timeframe). The most common study design was case–control, which was used in 61% of studies (n=22) (refs 6 28 (study 2); refs 30 42–44 (study 2); ref 44 (study 3); ref 45 (study 1); ref 45 (study 2); refs 46–59).[30 33 42–59] Other study designs used were cross-sectional (14%, n=5) (refs 29 44 (study 1); refs 60–62 ecological time trend (22%, n=8) (ref 28 (study 1); refs 63–69) and ecological geographic comparison (3%, n=1).[70]

Publication dates of included reports ranged from 1999 to 2020, with the majority of articles (82%) published in the year 2010 or later (n=27). Eighteen studies (50%) focused on populations at the city or district level (Baghdad: n=6; Fallujah: n=7; Basrah city: n=3; Nasriyah: n=1; and Ramadi: n=1), 13 studies (36%) focused on populations at the governorate or province level (Babylon governorate: n=1; Baghdad governorate: n=1; Basrah governorate: n=7; Ninawa province: n=1; Diyala governorate: n=1; Karbala governorate: n=1; and Muthanna governorate: n=1) and 5 studies (14%) focused on populations at the regional level (Southern Iraq) (figure 2). One of the included studies was a national household survey.[29] However, that study only used the subset of data collected from Basrah governorate for the analysis of the association between birth defects and warfare contamination.

Methods of exposure assessment

Eleven studies (30%) used place of residence, 9 (25%) used historical controls or time periods, 15 (42%) directly measured uranium concentrations in human biological samples and a single study (3%) used the source of bullets among patients with gunshot wounds to assess uranium exposure (online supplemental material 1, tables S5–S12). Most studies that assessed exposure by place of residence used prior knowledge of locations where military attacks involving the use of weaponised uranium took place, or cited literature that documented those locations. Only one included study conducted primary environmental monitoring to measure uranium concentrations in their study area.[61]

Outcomes

Regarding health outcomes, 28% of included studies assessed CBDs (n=10) (online supplemental material 1, table S5). Other birth-related outcomes among included studies were: anthropometric measurements of newborns (3%, n=1), sex ratio at birth (3%, n=1) and infant mortality rate (IMR) (3%, n=1) (online supplemental

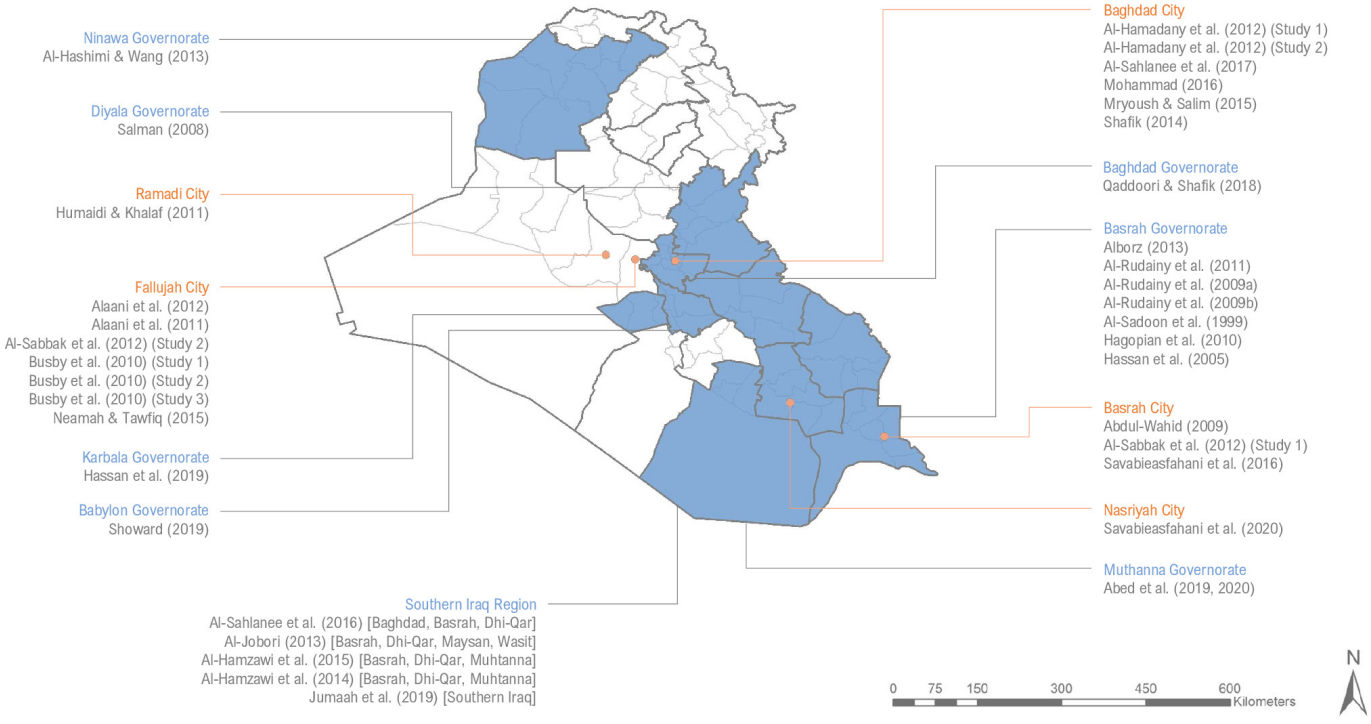

Figure 2 Summary of the geographic scope of included studies, highlighting each governorate (shaded blue) and city (orange dot) in Iraq that was a focus of an included study.

material 1, table S6). Additionally, 15 studies assessed cancer (41%) (online supplemental material 1, table S7), and three studies (8%) measured outcomes related to immune system function (online supplemental material 1, table S8). A single study assessed kidney failure (3%) (online supplemental material 1, table S9), a single study assessed the expression of the oncogene BCL-2 (an important prognosis indicator for breast cancer) (3%) (online supplemental material 1, table S10) and a single study assessed PTEN gene expression (3%) (online supplemental material 1, table S11). Two case–control studies (5%) assessed multiple outcomes (they defined cases as patients with cancer, or parents of children born with CBDs, and then grouped both outcomes together in their analysis) (online supplemental material 1, table S12).

Risk of bias assessment

By assessing study quality using the Navigation Guide's risk of bias tool,[34] we concluded that there was generally a high risk of bias across the body of evidence (figure 3A). We found that confounding was the domain with the highest risk of bias, followed by other sources of bias, exposure assessment, blinding and recruitment (figure 3B). The domain with the lowest risk of bias was incomplete outcome data, followed by conflict of interest. Only two

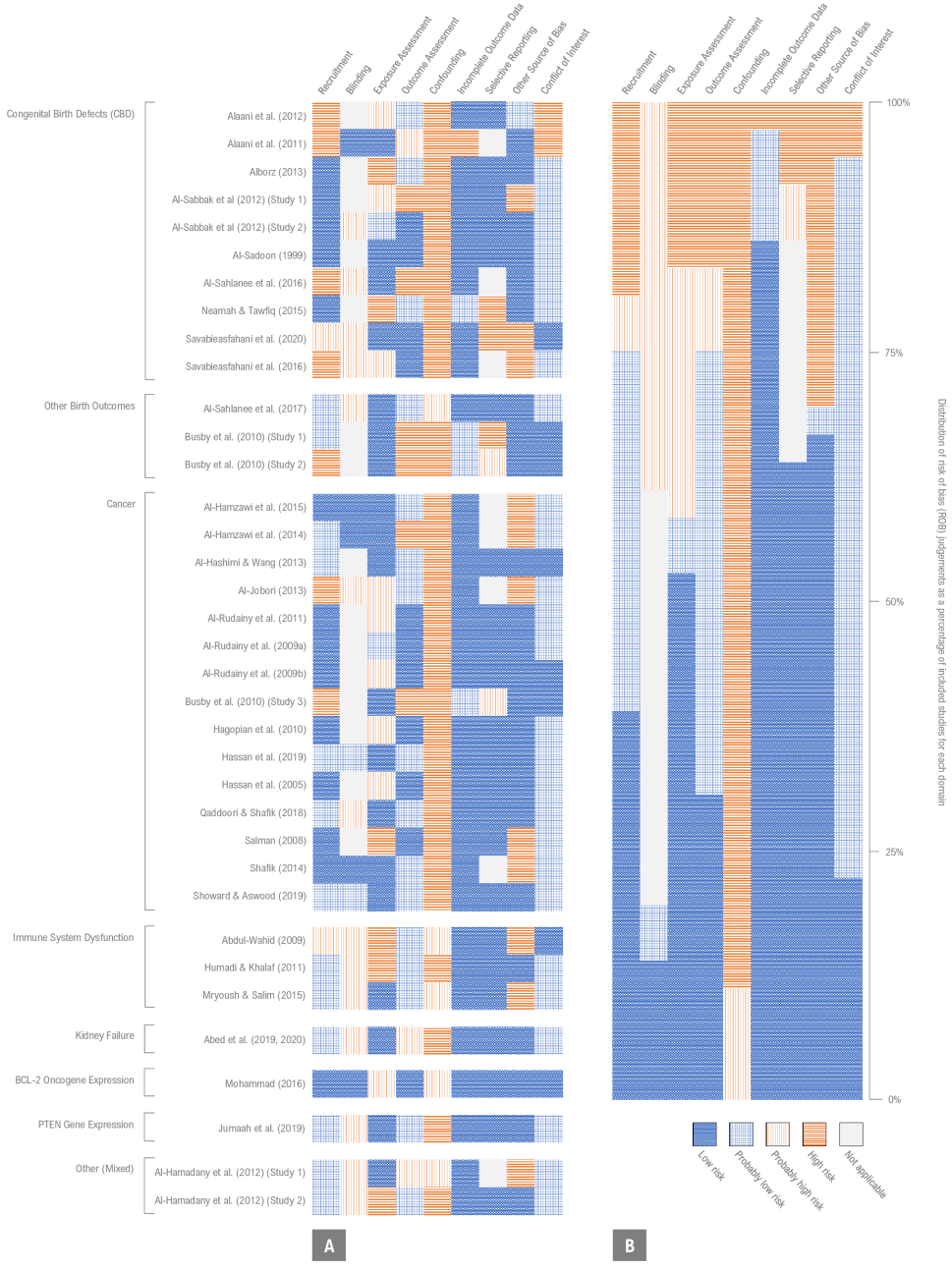

Figure 3 Risk of bias assessments (low, probably low, probably high and high risk) for each included study (A) and given as percentages across all included studies (B). Justifications for risk of bias determinations for individual studies are provided in the online supplemental material 1, tables S13–S48.

studies (6%) were rated high risk of bias in the conflict of interest domain, and all other studies were rated low or probably low risk of bias in that domain. Justifications for risk of bias determinations for each included study are provided in the online supplemental material 1, tables S13–S48.

Congenital birth defects

Ten studies selected CBD as their health outcome of interest. Of those, four studies examined CBD incidence rate, all of which found higher incidence in their exposed population compared with their control population. However, only two of the studies measuring incidence of CBD tested their observed differences for statistical significance. Alborz[29] found that a significantly higher proportion of children with birth defects in Basrah were living in households that reported exposure to warfare contamination, than children without birth defects (p<0.001).[29] Al-Sadoon *et al*[65] found CBD incidence during the period 1995–1998 (4.57/1000 live births) to be significantly higher than during the period 1991–1994 (2.5/1000 live births) (p<0.01).[65] Although no statistical test of significance was conducted, Al-Sabbak *et al*[28] (study 1) observed that CBD incidence in 2003 in Basrah (23/1000 live births) was 17 times higher than the CBD incidence in 1994 (1.37/1000 live births).[28] Six CBD studies compared uranium concentrations in biological samples collected from parents who had given birth to children with CBDs (cases) and healthy controls, of which five found mean uranium concentrations to be higher in samples collected from cases compared with controls.

Eight of the 10 studies that selected CBD as their outcome of interest were judged to have low or probably low risk of bias for the domain of conflict of interest. All 10 studies that selected CBD as their outcome of interest were judged to have high risk of bias in the domain of confounding, because they did not account for one or more of this review's prespecified confounders. One study of CBD incidence in Fallujah found that consanguinity among parents (defined as marriage to first, second or third cousins) was present in 56.8% of the observed CBD cases (n=162), but the study did not assess the rate of consanguinity among parents who gave birth to infants without CBD or account for consanguinity in their analysis.[28]

Another problematic feature among the CBD studies is directness of exposure measurement. The studies that assessed CBD incidence did not directly measure uranium exposure (ie, biomarkers, radiation dose measurements and direct environmental monitoring). Instead, they used time period or geographic location as a proxy for exposure or used a questionnaire for self-reported exposure. For the CBD case–control studies that *did* measure uranium concentrations in human biological samples, it was not known whether the source of uranium exposure came from natural or artificial sources (ie, conventional weapons used by the US or coalition forces in Iraq). Exposure to natural uranium can be elevated by agricultural phosphate fertilisers, tobacco use, as well as proximity to fertiliser plants or phosphate and uranium mines.[71] Only one study, carried out in Fallujah, measured the isotopic ratio of uranium in participants' samples and found that the uranium had a slightly enriched, rather than depleted, isotopic signature.[6] While this finding suggests that the source of uranium in participants was not natural, it is questionable whether the uranium was derived from US weapons. One possible source of non-natural uranium exposure in Iraq is the Al-Tuwaitha Nuclear Research Centre in Baghdad (40 km east of Fallujah) that was bombed and looted during the 2003 invasion.[72] Hundreds of barrels of uranium oxide went missing from the plant after it was destroyed, and only a fraction of the barrels was recovered. In some instances, empty (but still radiologically contaminated) barrels were found in nearby towns and were being used as household food and water storage containers.[72]

We judged the certainty of the evidence for this outcome (CBDs) to be very low mainly due to the extremely serious risk of bias, serious indirectness and serious publication bias (table 1).

Other birth-related outcomes

All three studies on birth-related outcomes other than CBDs found uranium exposure to be associated with adverse health impacts. However, all studies were found to have high risk of bias in at least one domain.

Al-Sahlanee *et al*[60] carried out a cross-sectional study at a hospital in Baghdad to measure association between uranium exposure and anthropometric measurements of infants.[60] The study used a CR-39 fission track detector to measure uranium concentration in maternal and umbilical blood samples in 50 mother–infant volunteer pairs. They found that uranium concentrations in both maternal and umbilical cord blood samples were negatively correlated with measurements for body length, birth weight and head circumference. However, the isotopic ratio of uranium detected in maternal and umbilical cord blood samples was not examined and so the study cannot be said to strictly measure uranium derived from weapons used by the US or coalition forces. Although the study collected data on maternal age, it did not account for maternal age or other confounders in its tests for association.

Busby *et al*[44] (study 1) sought to examine the association between birth sex ratio and radiation exposure in Fallujah using a cross-sectional household survey.[44] They found that the sex ratio of boys to girls for children born during the period 2006–2010 was 0.86, compared with 1.182 for children born between 2001 and 2005, 1.109 for children born between 1996 and 2000 and 1.010 for children born between 1991 and 1995. The birth sex ratio for children born between 2006 and 2010 was found to differ significantly from the expected ratio (p<0.01). However, the study did not account for any confounders, including parental age or consanguinity. Additionally, the study did not explicitly discuss or report in their narrative text

Table 1 GRADE summary of findings for all outcomes

Outcome	No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Factors than increase the certainty	No. of patients and findings	Certainty
Congenital birth defect (CBD)	10	Observational	Very serious*	Not serious	Serious†	Not serious	Serious‡	None	Although most studies are of small sample size, one study has a very large sample size (n=16 746), and its findings are both precise and consistent with the results of the remaining studies.	Very low
Cancer	15	Observational	Very serious§	Not serious	Serious¶	Not serious	Serious‡	None	The total number of participants included in all the studies was 997. Some studies reported small significant increase in cancer incidence among exposed populations, and other studies (mainly ecological studies) reported 'non-significant results'. The findings of one population-based study of 711 households were both precise and consistent with the results of the remaining studies.	Very low
BCL-2 oncogene	1	Observational	Very serious**	Not serious	Not serious	Serious††	Serious‡	None	The total number of participants included in the study was 80 (low sample size). The study reported BCL-2 expression was found to be significantly higher among exposed populations.	Very low
Immune system function	3	Observational	Very serious‡‡	Not serious	Not serious	Not serious	Serious‡	None	The total number of participants included in all the studies was 365. All studies reported worse immune system function among exposed populations.	Very low
Kidney failure	1	Observational	Very serious§§	Not serious	Not serious	Serious¶¶	Serious‡	None	The total number of participants included in the study was 26. The study found higher exposure among kidney failure patients than healthy controls.	Very low

Continued

Table 1 Continued

Outcome	No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Factors than increase the certainty	No. of patients and findings	Certainty
PTEN gene	1	Observational	Serious***	Not serious	Serious†††	Serious‡‡‡	Serious‡	None	The total number of patients included in the study was 43. The study found that PTEN gene expression mean fold change was greater among the exposed group than the unexposed group.	Very low

*All 10 studies were judged to have high risk of bias related to confounding, because none accounted for any confounders known to be associated with birth defects, including consanguinity, maternal age, maternal nutritional status (ie, folate deficiency) or exposure to other environmental teratogens.
†We judged the evidence to have serious indirectness as the studies that assessed CBD incidence did not directly measure uranium exposure. For the case–control studies, which did measure uranium concentrations in human biological samples, it was not known whether the source of uranium exposure came from natural or artificial sources (ie, conventional weapons used by the US or coalition forces in Iraq). One study, carried out in Fallujah, measured the isotopic ratio of uranium in participants' samples and found that the uranium had an enriched, rather than depleted, isotopic signature.
‡We suspect publication bias given that the sanctions played a role in limiting research publications on the health impacts of weaponised uranium in Iraq.
§All 15 studies were judged to have high risk of bias related to confounding. Five studies were rated high risk of bias in the domain 'other sources of bias'. One study was potentially subject to recall bias or over-reporting.
¶We judged the evidence to have serious indirectness as the studies that assessed cancer incidence did not directly measure uranium exposure. For the case–control studies that did measure uranium concentrations in human biological samples, it was not known whether the source of uranium exposure came from natural or artificial sources (ie, conventional weapons used by the US or coalition forces in Iraq).
**The study was rated high risk of bias due to lack of adjusting for confounding and reporting of adequate blinding.
††The total number of patients included in the study was almost 80 (low sample size). The study reported BCL-2 expression was found to be significantly higher among exposed populations.
‡‡All three of the studies were rated high risk of bias due to lack of adjusting for confounding and probably high risk of bias due to lack of reporting of adequate blinding.
§§The study was judged to have high risk of bias due to lack of adjusting for confounding and probably high risk of bias due to lack of reporting of adequate blinding.
¶¶The study found higher exposure among kidney failure patients than healthy controls, but the sample size for the study was small (n=26).
***The study was rated probably high risk of bias in the domains of exposure assessment and confounding.
†††The study did not directly measure uranium exposure.
‡‡‡The total number of patients included in the study was 43 (low sample size).

the birth sex ratio for age cohorts above 19 years. The next age cohort (20–24 years, children born between 1986 and 1990) has a birth sex ratio even lower than the 0–4 years age cohort (which represents children born between 2006 and 2010); the study data show a birth sex ratio of 776 males per 1000 females in the 20–24 years age cohort (although the ratio was not calculated or reported by the study authors) compared with 860 males per 1000 females in the 0–4 years age cohort (which was calculated and explicitly reported). Hence, the study was also judged to be high risk for the domain of selective reporting.

In the same household survey, Busby *et al*[44] (study 2) also investigated the IMR in Fallujah between 2006 and 2010.[44] They found the IMR in Fallujah over that time period to be 80 per 1000 births, which was four times higher than the IMR reported in Egypt and Jordan (p<0.00001) and nine times higher than the IMR in Kuwait (p value not reported). However, the study did not account for any confounding variables and was rated high risk of bias in the domain of confounding.

We were unable to rate the certainty of evidence for studies of 'other birth-related outcomes', because the three studies in this category each assessed a different type of birth-related outcome (anthropometric measurements, birth sex ratio and infant mortality).

Cancer

Fifteen studies selected cancer (specific types of cancer or *all* cancer) as their health outcome of interest, of which seven assessed cancer incidence. Two of the seven studies that assessed cancer incidence found a higher incidence among their exposed populations compared with their controls. In contrast, all seven of the case–control studies that compared uranium concentrations in biological samples collected from patients with cancer (cases) and healthy controls found mean uranium concentrations to be higher among cases, but only two of the four studies tested the difference in means for statistical significance. Like the CBD case–control studies, the cancer case–control studies that measured uranium concentrations in participants' samples did not assess the source of uranium (natural or artificial).

All 15 studies that selected cancer as their outcome of interest were rated low or probably low risk for conflict of interest. However, all 15 were rated high risk of bias in the domain of confounding. Additionally, 5 of the 15 studies were rated high risk for the domain 'other sources of bias'.[47–49 58 69] Among the 'other sources of bias', two studies did not report their research timeframe (or the year that blood samples obtained from hospitals were collected from cancer patients),[47 48] one study examined cancer case counts (as opposed to cancer incidence)[69] and two studies had very small sample sizes (n=5 and n=12).[49 58]

We judged the certainty of the evidence for the association between uranium exposure and cancer among the Iraqi population to be very low mainly due to the extremely serious risk of bias and serious publication bias (table 1).

Immune system function

All three of the studies that selected outcomes related to immune system function reported finding an association between uranium exposure and adverse health outcomes. Abdul-Wahid[46] found that individuals with higher levels of uranium exposure had lower levels of selected lymphocytes compared with individuals with lower levels of exposure (no p values reported from statistical test).[46] Humadi and Khalaf[52] investigated several outcomes related to immune system function among patients who had been injured by bullets fired by US and coalition forces (a proxy for DU exposure) compared with patients injured by bullets from other sources (controls).[52] They found that DU exposure was associated with adverse health outcomes including lower blood haemoglobin concentrations and faster erythrocyte sedimentation rates. The third immune system study found that higher exposure to uranium was associated with higher mitotic index scores.[61] However, they did not test the difference for statistical significance.

Although all three immune system studies were consistent in their findings of direction of effect, they were all rated probably high risk of bias in the domain of blinding. For all three studies, blinding of key personnel for either exposure or outcome measurement was not reported, and lack of blinding could have introduced bias. All were rated high risk or probably high risk in the domain of confounding. All three studies were rated low or probably low risk of bias in the domain of conflict of interest.

We judged the certainty of the evidence for the association between uranium exposure and adverse impacts on immune system function among the Iraqi population to be very low mainly due to the extremely serious risk of bias in the domains of blinding and confounding, and serious publication bias (table 1).

Kidney failure

Our search strategy captured two reports of the same case–control study that assessed uranium concentration in blood and urine samples from kidney failure patients (cases) and healthy controls in a hospital in Al-Muthanna governorate.[42 43] The study found that uranium concentrations were higher in both urine and blood samples of kidney failure patients than healthy controls, but the differences were not tested for statistical significance. The study was rated probably high risk of bias in the domain of blinding, because no procedures accounting for blinding were reported. It was also rated high risk of bias in the domain of confounding. Although the study collected data on age and sex of participants, these confounders were not controlled for, and neither were any other confounders.

We judged the certainty of the evidence for the association between uranium exposure and kidney failure in patients in the Iraqi population to be very low mainly

due to the extremely serious risk of bias in the domains of blinding and confounding, serious imprecision and serious publication bias (table 1).

BCL-2 oncogene expression

One case–control study examined the expression and intensity of the oncogene BCL-2 (an important prognostic factor for breast cancer) in Iraqi patients with breast cancer (n=50) and compared findings with a control population in Italy (n=30).[54] The study found that BCL-2 expression in Iraqi breast cancer tissue samples was significantly higher (p=0.037) than in Italian samples, and among individuals for which BCL-2 was positively expressed, Iraqi participants had higher intensities than Italian participants.

However, the study was rated high risk of bias in the domain of confounding and probably high risk in the domain of blinding. Additionally, the study was rated probably high risk of bias in the domain of outcome assessment, because the authors reported that differences in tissue processing time, tissue quality and timing for embedding tissues in paraffin between cases and controls may have impacted outcome measurements, but data are not available for those variables.[54]

We judged the certainty of the evidence for the association between uranium exposure and BCL-2 expression among the Iraqi population to be very low mainly due to the extremely serious risk of bias in the domains of blinding and confounding, serious imprecision and serious publication bias (table 1).

PTEN gene expression

A single study measured the expression of the tumour-suppressor gene, PTEN, in endometrial carcinoma patients living in DU-exposed areas (cases) and unexposed areas (controls) in Southern Iraq.[53] The study found that PTEN gene expression mean fold change was greater among the exposed group (0.139±0.185) than the unexposed group (0.0031±0.0029), but the difference in means was not statistically significant when tumour grade and cancer stage were controlled for (p=0.286 and p=0.98, respectively).

The study did not conduct environmental monitoring to determine uranium exposure in the study area, nor directly measure uranium concentration in biological samples from study participants. Hence, the study was rated probably high risk of bias in the domain of exposure assessment. The study was also rated probably high risk of bias in the domain of confounding. While the study controlled for the age and sex of participants, it did not control for any other important confounders, such as obesity and tobacco use.

We judged the certainty of the evidence for the association between uranium exposure and PTEN gene expression among the Iraqi population to be very low mainly due to the extremely serious risk of bias in the domains of exposure assessment and confounding, serious imprecision and serious publication bias (table 1).

Other outcomes

Two included studies (with the same set of participants, published in the same article) used case–control study designs and selected cases based on multiple outcomes—they defined cases as patients with cancer, or parents of children born with CBDs—in Baghdad.[45]

The stated objective of the study by Al-Hamadany *et al*[45] (study 1) was to compare uranium concentration in blood samples collected from cases and (healthy) controls.[45] The study recruited participants from Baghdad in five categories: patients with cancer prior to treatment (n=15), patients with cancer currently receiving treatment (n=15), women who had given birth to children with CBDs (n=15), volunteers who were occupationally exposed to ionising radiation (n=14), residents of areas of Baghdad that were reportedly contaminated with DU (n=15) and healthy volunteers residing in areas of Baghdad not reported to be contaminated with DU (n=14). The study reported the mean uranium concentration measured in blood samples collected from the healthy unexposed group (n=14) and the mean uranium concentration in blood samples from participants from all other groups (n=74). The study found that mean uranium concentration from the control population (0.11ppm ±0.009 SE) was significantly lower than the mean uranium concentration in samples from participants from all other recruitment groups (0.21 ppm±0.01 SE) (p<0.05).

The second study by Al-Hamadany *et al*[45] (study 2) assessed outcomes related to immune system function but used the health condition of patients as an indicator for the exposure to uranium.[45] Patients with cancer, and mothers of children with birth defects, were defined as exposed, as were individuals occupationally exposed to ionising radiation in a medical setting and individuals residing in areas of Baghdad that were reportedly contaminated with DU. Controls were defined as healthy individuals living in uncontaminated areas of Baghdad. The study found that white cell counts were significantly higher among participants defined as exposed, and haemoglobin concentrations were significantly lower, compared with the group defined as unexposed (p<0.05).

The definition of cases (exposed) and controls (unexposed) in the studies by Al-Hamadany *et al*[45] was problematic and undermined the quality of the study results.

We were unable to rate the certainty of evidence for the association between uranium exposure and other outcomes among the Iraqi population, because the definition of cases in these two studies included individuals with a variety of health conditions and a number of exposure scenarios (including environmental uranium exposure and occupational exposure to ionising radiation).

GRADE summary of findings

The certainty of the evidence was rated *very low* across all outcomes (table 1).

DISCUSSION

The investigation of a possible causal link between DU exposure and adverse health outcomes is essential for designing interventions. In this SR, we sought to synthesise the evidence on the association between uranium exposure and adverse health outcomes in Iraq. To our knowledge, this is the first SR on the topic.

Among the 36 studies that met inclusion criteria for this SR, the most common study design was case–control. This study design may have been selected due to the fact that the outcomes of interest among our included studies were either illnesses with long latency periods (such as cancer) or CBDs, which were identified in hospital settings. The most common method of exposure assessment among our included studies was direct measurement of uranium in human biological samples, and the most common technique used was CR-39 fission track detectors. This is probably explained by the fact that uranium is an alpha particle emitter and use of fission track detectors was the most feasible technique for measuring alpha particles.

The findings of our included studies are relatively consistent in the direction of effect; most of the included studies (n=30, 83%) reported a positive association between uranium exposure and adverse health outcomes, including CBDs and cancer. Although the data suggests that there is an association between uranium exposure and adverse health outcomes, the evidence is very uncertain. The very low certainty of the evidence across outcomes is mainly due to the extremely serious risk of bias (especially in the domain of confounding), serious indirectness and imprecision and the very serious publication bias. Until now, the mantra in the literature has been that not enough studies have been conducted to assess whether DU has adversely impacted the health of the Iraqi population.[22 73] The findings from this SR allow us to make a new argument: the body of evidence does not lack studies, it lacks *high quality* studies.

Publication bias and missing data

Study publication bias is a well-documented problem in medical research and health sciences.[74] Typically, studies that find significant results are more likely to be published, leading to bias in the literature, but the problem can also arise when other factors influence the production and publication of research.[74] By examining the characteristics of our included studies in a historical context, we observed patterns that suggest that publication bias may have occurred. The sanctions imposed on Iraq by the UN Security Council in 1990 after the Iraqi invasion of Kuwait (specifically resolution 661) restricted the flow of physical goods and financial resources into and out of Iraq and effectively acted as an intellectual embargo, incapacitating Iraq's medical research abilities.[75 76] The sanctions were modified after the 2003 US invasion of Iraq, and then lifted in 2010. Even though the investigation of health impacts of DU has been a priority for Iraqi scientists since the early 1990s, we found that the majority of the studies included in this SR (82%) were published in 2010 or later, after the sanctions had been lifted. The sanctions may have limited access by Iraqi researchers to specialised equipment needed for detecting and measuring uranium concentration in environmental and human biological samples. All of the included studies in this SR that used specialised equipment, such as inductively coupled plasma mass spectrometry (ICP-MS), or CR-39 fission track detectors, were published in 2011 or later. This suggests that the sanctions played a role in limiting research and publication on the health impacts of weaponised uranium in Iraq. Additionally, the difficulties inflicted by the 20-year intellectual embargo may have impacted the quality of research that has been produced on this topic. A sanction-specific publication bias may have prevented the publication of high-quality studies that found positive results on the association between exposure to DU and adverse public health burdens in Iraq or studies that were authored by Iraqi nationals.[76 77]

The lack of public access to important data may have also inhibited high-quality research on the public health impacts of DU exposure in Iraq. One source of missing data is the complete set of US firing coordinates for DU weapons in Iraq. Over the last decade, multiple nongovernmental organizations (NGOs) in the USA and abroad have filed Freedom of Information Act requests with the US Department of Defense and Department of State, but only a fraction of the requested data has been publicly released.[18] Another source of missing data is the IMOH national CBDs study that was carried out in 2012. Summary results from the study were published in 2013, but to date neither a full report has been published, nor has the study data been made accessible to independent researchers for analysis and verification.[18]

Strengths and limitations

Many previous reviews have attempted to summarise the body of evidence regarding the effects of DU on public health in Iraq. However, the present study is the first to do so systematically. One of the strengths of the SR methodology is the sensitivity and transparency of the search strategy. To our knowledge, this study assembled in a single collection more human observational studies investigating associations between exposure to weaponised uranium and health outcomes among the Iraqi population than any publication has before. Additionally, we assessed the quality of individual studies and rated the certainty of the body of evidence in a transparent and reproducible manner. Even though the risk of bias within our body of evidence was generally high, we found a low risk of bias in the conflict of interest domain. This is a notable strength in our included studies and speaks to both the importance of this topic in Iraqi society and the tenacity of Iraqi academic researchers, who pursued this topic despite technical and political challenges.

A possible limitation of this SR is that in our inclusion criteria and PECOS statement, we did not account for 'length of residence' among our study population. If we had applied an additional participant inclusion criteria

regarding length of residence, such as living in the study location continuously for at least 5 years, it may have reduced our total number of included studies. Another limitation of this SR is that we were only able to judge the certainty of evidence using the GRADE approach for six of the eight outcome categories. Specifically, we were unable to judge the certainty of the evidence for other birth-related outcomes and other (mixed) outcomes, because studies assessed a variety of outcomes within those outcome categories.

Meta-analysis

We did not carry out a meta-analysis in this review. The lack of similarity in study outcomes and study designs precluded our ability to conduct a meta-analysis of summary measures among the included studies.

Implications for future research

The sparsity of high-quality human observational studies on the health impacts of DU among the Iraqi population led to very low certainty in the quality of the evidence. This, however, does not negate the possibility that DU weapons have adversely affected public health in Iraq. A number of experts have expressed concern that the politicisation of DU research might have limited international collaborations and interdisciplinary approaches to the topic, isolating Iraqi scientists over the past decades.[17 75] Similarly, we suspect that efforts to assess, evaluate and clean-up DU might have been undermined by lack of security, financing or attention to environmental health impacts of war. To date, research on the impact of war in Iraq has mainly focused on body counts and infrastructure damage,[75] and critical data, like the complete set of US DU firing coordinates or data from the IMOH national birth defect survey, are unavailable. Consequently, the ability of Iraqi scientists to conduct research on DU has been limited. More research on this topic is warranted, specifically observational studies with improved methods of exposure assessment, adequate blinding of key personnel and assessment and control of important confounders.

Improved methods of exposure assessment

The most common method of exposure assessment among the included studies was the measurement of uranium concentration in human biological samples, using equipment such as ICP-MS and CR-39 fission track detectors. The direct measurement methods used in such biomarker studies are typically reliable and robust. However, only one of the included studies measured the isotopic ratio of uranium in samples, using ICP-MS,[33] a step that is critical to determining the source and potential toxicity of the uranium. Hence, there is a need for more observational studies that assess uranium exposure via the use of biomarkers and that determine the isotopic ratio of detected uranium using methods such as ICP-MS.[3] Additionally, only one of the included studies used environmental monitoring methods to assess uranium exposure.[61] Future observational studies should use environmental monitoring to assess the presence, concentration and isotopic ratio of uranium in water, soil, dust and other environmental media. Recent reports that the US military has used DU weapons in Syria highlight the need for primary studies to be carried out in countries outside of Iraq as well.[78 79]

More SRs and health risk assessments

In addition to high-quality primary research, we call for SRs on related topics to be conducted. This SR does not represent an assessment of studies that measured uranium or radiological contamination in Iraq without also assessing health outcomes. Although studies that estimated future health risks based on absorbed dose or effective dose calculated from environmental radioactivity measurements in Iraq (as opposed to reporting current health outcomes among participants or target populations) did not meet our inclusion criteria, they still offer insight into possible health hazards faced by the Iraqi population, for example, see Almayahi[80] and Mohammed and Ahmed.[81]. An SR of these and similar studies is merited. Furthermore, no SRs on evidence of uranium toxicity from animal studies, or on DU-exposed populations outside of Iraq (such as the Balkans), have been conducted. A large body of primary studies exist for these topics, but they have yet to be systematically synthesised and critically appraised.

In conclusion, more research on DU and other war remnants is imperative for understanding the long-term, environmental health impacts of armed conflict. DU weapons are still in use in other countries, and therefore the study of the health impacts of DU remains essential.[79] We believe that funding for continued research should be provided in tandem with funding for clean-up and personnel training for the removal of debris from known DU-contaminated sites in Iraq. The global health community has been scrutinised for its inadequate response to the 2003 Iraq War.[82] International health organisations (including the WHO) had not been held accountable for their work during and after the war, and unnecessary suffering occurred because of that failure.[82] We are concerned that the global health community may have also failed to adequately support research into the health impacts of DU in Iraq. There is a need for an international regulation to allow and protect research conducted on this sensitive topic going forward. We call on garnering funding, training and collaboration to Iraqi researchers who continue to investigate this unforgotten topic.

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SS and RRH wrote the first draft. SS, RRH, LAK, and EAA revised the subsequent versions of the manuscript. All authors approved the final manuscript.

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Supplemental Material

Title

Weaponized uranium and adverse health outcomes in Iraq: A systematic review

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Table S1. PECOS Statement and inclusion/exclusion criteria

Study Aspect	Inclusion Criteria	Exclusion Criteria
Population	Humans (of any age) residing in Iraq at any time between 1990-2020	Non-humans
	Children born to those individuals	Military veterans (U.S. or other nationalities)
Exposure	Chemical exposure to metallic uranium that has been introduced to the environment in Iraq via the use of conventional weapons (i.e. non-nuclear missiles, bullets, and armor)	Physical exposure to ultraviolet radiation (e.g. solar radiation)
	Chemical exposure to decay and corrosion products of weapon uranium in Iraq	Physical exposure to ionizing radiation emitted from medical radioisotopes
	Physical exposure to ionizing radiation emitted from radioisotopes in weaponized uranium or its decay or erosion products	Physical or chemical exposure to nuclear materials not originating from metallic uranium weapons used by US and coalition forces
Comparator	Individuals not exposed to uranium	Studies that document health impacts among an exposed population without comparison to a non-exposed (or lesser exposed) group or population
	Individuals exposed to lower levels	
	Can include historical controls	
Outcomes	Human health-relevant outcomes, including measures of general wellbeing, mental health, or self-rated health	Studies that measure the concentration of uranium (or decay/corrosion products) in environmental or human biological samples without measuring a health outcome
		Studies that measure radiation levels in food, water, or environmental samples without measuring a health outcome
Study Design	Observational study designs including case-control, case-report, cohort, and cross-sectional	Randomized control trials or other experimental study designs
		Reviews (including systematic reviews) that do not include or report primary research

Table S2. Full search strategy

Database	**MEDLINE** Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily, 1946 to April 06, 2020
Search	(exp URANIUM COMPOUNDS/ or exp URANIUM/ or exp RADIOLOGIC HEALTH/ or THORIUM/ or PLUTONIUM/ or PROTACTINIUM/ or exp THORIUM COMPOUNDS/ or (uranium* or diuranium* or triuranium* or DU or "U(VI)" or "U(IV)" or U-235 or U235 or U-238 or U238 or Qmetal* or (Q adj metal*) or depletalloy* or (deplet* adj alloy*) or uranyl or radiation* or radioactiv* or radioisotop* or radionuclide* or radiologic* or dosimet* or ((gamma* or beta* or alpha* or nuclear) adj3 (ray? or radiation? or emitt* or emission* or decay*)) or plutonium* or thorium* or protactinium*).mp.) AND (exp IRAQ/ or exp IRAQ WAR, 2003-2011/ or exp GULF WAR/ or (Iraq* or (operation* adj2 ((new adj dawn*) or freedom*)) or (gulf adj2 (war* or Arab* or Persian*)) or (operation* adj2 (desert* adj (storm* or shield*))) or mosul* or Falluja* or Al-Anbar* or alanbar* or Anbar* or Babil* or Baghdad* or Al-Basra* or Albasra* or Basra* or ((Dhi or Thi*) adj Qar) or Al-Qadisiy* or Alqadisiy* or Qadisiy* or Diyala* or Dohuk* or Erbil* or Halabja* or Karbala* or Kirkuk* or Maysan* or Al-Muthan* or almuthan* or Muthan* or Najaf* or Ninev* or Saladin* or Sulaymaniy* or Wasit* or kurd*).mp.) AND (1990:2020.(sa_year).) NOT (Animals/ not (Animals/ and Humans/))
Results	355
Database	**Embase**
Search	('uranium'/exp OR 'uranium derivative'/exp OR 'radiation and radiation related phenomena'/exp OR 'thorium'/exp OR 'plutonium'/exp OR 'protactinium'/exp OR 'thorium derivative'/exp OR uranium*:ab,ti OR diuranium*:ab,ti OR triuranium*:ab,ti OR du:ab,ti OR 'u(vi)':ab,ti OR 'u(iv)':ab,ti OR 'u-235':ab,ti OR u235:ab,ti OR 'u-238':ab,ti OR u238:ab,ti OR qmetal*:ab,ti OR ((deplet* NEAR/2 alloy*):ab,ti) OR uranyl:ab,ti OR radiation*:ab,ti OR radioactiv*:ab,ti OR radioisotope*:ab,ti OR radionuclide*:ab,ti OR radiological*:ab,ti OR dosimet*:ab,ti OR

	plutonium*:ab,ti OR thorium*:ab,ti OR protactinium*:ab,ti OR (((gamma* OR beta* OR alpha* OR nuclear) NEAR/3 (ray* OR radiation* OR emitt* OR emission* OR decay*)):ab,ti)) AND ('iraq'/exp OR 'iraqi'/exp OR 'iraqi kurdistan'/exp OR 'persian gulf'/exp OR iraq*:ab,ti OR ((operation* NEAR/2 new* NEAR/2 dawn*):ab,ti) OR ((operation* NEAR/2 freedom*):ab,ti) OR ((gulf NEAR/2 war*):ab,ti) OR ((gulf NEAR/2 arab*):ab,ti) OR ((gulf NEAR/2 persian*):ab,ti) OR ((operation* NEAR/2 desert* NEAR/2 storm):ab,ti) OR ((operation* NEAR/2 desert* NEAR/2 shield*):ab,ti) OR mosul*:ab,ti OR falluja*:ab,ti OR 'al-anbar*':ab,ti OR alanbar*:ab,ti OR anbar*:ab,ti OR babil*:ab,ti OR baghdad*:ab,ti OR 'al-basra*':ab,ti OR albasra*:ab,ti OR basra*:ab,ti OR ((dhi* NEAR/2 qar):ab,ti) OR ((thi* NEAR/2 qar):ab,ti) OR 'al-qadisy*':ab,ti OR alqadisy*:ab,ti OR qadisy*:ab,ti OR diyala*:ab,ti OR dohuk*:ab,ti OR erbil*:ab,ti OR halabja*:ab,ti OR karbala*:ab,ti OR kirkuk*:ab,ti OR maysan*:ab,ti OR 'al-muthan*':ab,ti OR almuthan*:ab,ti OR najaf*:ab,ti OR ninev*:ab,ti OR saladin*:ab,ti OR sulaymaniy*:ab,ti OR wasit*:ab,ti OR kurd*:ab,ti) AND [1990-2020]/py NOT ([animals]/lim NOT [humans]/lim)
Results	627
Database	**PubMed**
Search	(((iraq[mesh]) OR (iraq war, 2003-2011[mesh]) OR (gulf war[mesh]) OR Iraq*[tw] OR operation new dawn*[tw] OR operation iraqi freedom[tw] OR gulf war*[tw] OR persian gulf*[tw] OR arab gulf*[tw] OR operation desert storm*[tw] OR operation desert shield*[tw] OR mosul*[tw] OR Falluja*[tw] OR Al-Anbar*[tw] OR alanbar*[tw] OR Anbar*[tw] OR Babil*[tw] OR Baghdad*[tw] OR Al-Basra*[tw] OR Albasra*[tw] OR Basra*[tw] OR dhiqar*[tw] OR thiqar*[tw] OR dhi-qar*[tw] OR thi-qar*[tw] OR Al-Qadisiy*[tw] OR Alqadisiy*[tw] OR Qadisiy*[tw] OR Diyala*[tw] OR Dohuk*[tw] OR Erbil*[tw] OR Halabja*[tw] OR Karbala*[tw] OR Kirkuk*[tw] OR Maysan*[tw] OR Al-Muthan*[tw] OR almuthan*[tw] OR Muthan*[tw] OR Najaf*[tw] OR Ninev*[tw] OR Saladin*[tw] OR Sulaymaniy*[tw] OR Wasit*[tw] OR kurd*[tw]) AND ((uranium[mesh]) OR (uranium compounds[mesh]) OR (radiologic health[mesh]) OR (thorium[mesh]) OR (thorium compounds[mesh]) OR (plutonium[mesh]) OR (protactinium[mesh]) OR (uranium*[tw] OR uranyl*[tw] OR plutonium*[tw] OR thorium*[tw] OR protactinium*[tw] OR qmetal*[tw]

	OR depletalloy*[tw] OR q-metal*[tw] OR deplete-alloy*[tw] OR radiation*[tw] OR du[tw] OR u235[tw] OR u238[tw] OR u-235[tw] OR u-238[tw] OR radiologic*[tw] OR radioactiv*[tw] OR radioisotop*[tw] OR radionuclide*[tw] OR dosimet*[tw] OR gamma-ray*[tw] OR gamma-emit*[tw] OR gamma-emission*[tw] or gamma-decay*[tw] OR beta-ray*[tw] OR beta-emit*[tw] OR beta-emission*[tw] OR beta-decay*[tw] OR alpha-ray*[tw] or alpha-emit*[tw] OR alpha-emission*[tw] OR alpha-decay*[tw] OR nuclear-ray*[tw] or nuclear-emitt*[tw] or nuclear-emission*[tw] or nuclear-decay*[tw]))) NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])) AND ("1990/01/01"[PDAT] : "2020/12/31"[PDAT])
Results	317
Database	**Scopus**
Search	TITLE-ABS-KEY("Iraq*" OR (Gulf W/2 War*) OR ((Persia* or Arab*) W/2 Gulf) OR (operation* W/2 new* W/2 dawn*) OR (operation* W/2 freedom*) OR (operation* W/2 desert* W/2 storm*) OR (operation* W/2 desert* W/2 shield*) OR mosul* or Falluja* or *Anbar* or Babil* or Baghdad* or *Basra* or ((Dhi or Thi*) W/2 Qar) or *Qadisiy* or Diyala* or Dohuk* or Erbil* or Halabja* or Karbala* or Kirkuk* or Maysan* or *Muthan* or Najaf* or Ninev* or Saladin* or Sulaymaniy* or Wasit* or kurd*) AND TITLE-ABS-KEY(*uranium* OR thorium* OR plutonium* OR protactinium* OR DU OR "U(VI)" OR "U(IV)" OR U235 OR U-235 OR U238 OR U238 OR qmetal* OR q-metal* or depletalloy* OR (deplet* W/2 alloy*) or uranyl or radiation* or radioactiv* or radioisotop* or radionuclide* or radiologic* or dosimet* or ((gamma* or beta* or alpha* or nuclear) w/3 (ray* or radiation* or emitt* or emission* or decay*))) AND PUBYEAR > 1990
Results	1546
Database	**TOXLINE**

Search	((uranium OR "uranium 238" OR 7440-61-1 [rn]) OR uranyl OR plutonium* OR thorium* OR protactinium* OR qmetal* OR depletalloy* OR "q-metal" OR "deplete-alloy" OR radiation* OR du OR u235 OR u238 OR "u-235" OR "u-238" OR radiologic* OR radioactiv* OR radioisotop* OR radionuclide* OR dosimet* or “alpha-ray” or “alpha ray” or “alpha-emitter” OR “alpha emitter” OR “alpha-emission” OR “alpha emission” OR “alpha-decay” or “alpha decay” or “beta-ray” or “beta ray” or “beta-emitter” or “beta emitter” or “beta-emission” or “beta emission” or “beta-decay” or “beta-decay” or “gamma-ray” or “gamma ray” or “gamma-emitter” or “gamma emitter” or “gamma-emission” or “gamma emission” or “gamma-decay” or “gamma decay” or “nuclear-ray” or “nuclear ray” or “nuclear-emitter” or “nuclear emitter” or “nuclear-emission” or “nuclear emission” or “nuclear-decay” or “nuclear decay”) AND (iraq* OR "gulf war" OR "persian gulf" OR "arab gulf" OR "desert storm" OR "desert shield" OR "operation iraqi freedom" OR "operation new dawn" OR mosul* OR falluja* OR al-anbar* OR alanbar* OR anbar* OR babil* OR baghdad* OR al-basra* OR albasra* OR basra* OR dhi-qar OR thi-qar OR dhiqar OR thiqar OR al-qadisiy* OR alqadisiy* OR qadisiy* OR diyala* OR dohuk* OR erbil* OR halabja* OR karbala* OR kirkuk* OR maysan* OR al-muthan* OR almuthan* OR muthan* OR najaf* OR ninev* OR saladin* OR sulaymaniy* OR wasit* OR kurd*) AND 1990:2020 [yr]
Results	462
Database	**Iraqi Academic Scientific Journals**
Search	(all:Uranium* all:or all:U-235 all:or all:U-238 all:or all:U235 all:or all:U238) Publication Year: 1990 to 2020
Results	229
Database	**ProQuest Dissertations and Theses Global**

Search	TI,AB,SU((uranium* OR uranyl OR plutonium* OR thorium* OR protactinium* OR qmetal* OR depletalloy* OR "q-metal" OR "deplete-alloy" OR radiation* OR du OR u235 OR u238 OR "u-235" OR "u-238" OR radiologic* OR radioactiv* OR radioisotop* OR radionuclide* OR dosimet* or “alpha-ray” or “alpha ray” or “alpha-emitter” OR “alpha emitter” OR “alpha-emission” OR “alpha emission” OR “alpha-decay” or “alpha decay” or “beta-ray” or “beta ray” or “beta-emitter” or “beta emitter” or “beta-emission” or “beta emission” or “beta-decay” or “beta-decay” or “gamma-ray” or “gamma ray” or “gamma-emitter” or “gamma emitter” or “gamma-emission” or “gamma emission” or “gamma-decay” or “gamma decay” or “nuclear-ray” or “nuclear ray” or “nuclear-emitter” or “nuclear emitter” or “nuclear-emission” or “nuclear emission” or “nuclear-decay” or “nuclear decay”) AND (iraq* OR "gulf war" OR "persian gulf" OR "arab gulf" OR "desert storm" OR "desert shield" OR "operation iraqi freedom" OR "operation new dawn" OR mosul* OR falluja* OR al-anbar* OR alanbar* OR anbar* OR babil* OR baghdad* OR al-basra* OR albasra* OR basra* OR dhi-qar OR thi-qar OR dhiqar OR thiqar OR al-qadisiy* OR alqadisiy* OR qadisiy* OR diyala* OR dohuk* OR erbil* OR halabja* OR karbala* OR kirkuk* OR maysan* OR al-muthan* OR almuthan* OR muthan* OR najaf* OR ninev* OR saladin* OR sulaymaniy* OR wasit* OR kurd*)) AND YR(1990-2020)
Results	52
Database	**Google Scholar**
Search	Allintitle: Uranium Iraq Publication Year: 1990-2020
Results	122
Database	**IAEA Scientific and Technical Publications**

Search	Search: Uranium Publication Year: 1990-2020 Search: Iraq Search: Iraqi
Results	116
Database	**WHO Institutional Repository for Information Sharing**
Search	Iraq* AND Uranium
Results	43
Database	**UNEP Knowledge Repository**
Search	Iraq
Results	22

Table S3. Preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6-7
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6; Supplemental Material (Table S1)
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6; Supplemental Material (Table S2)
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplemental Material (Table S2)
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6; Supplemental Material “Screening Form” and “Full text exclusion justifications”
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7; Supplemental Material “Data

			abstraction form"
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7-8; Supplemental Material Tables S6-S13
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7; Supplemental Material "Navigation Guide instructions for making risk of bias determinations"
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	No meta-analysis was conducted
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7-8, Supplemental Material Table S5
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	No meta-analysis was conducted
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9, Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9-10; Supplemental Material Tables S5-S13
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	10-15, Figures 3A & 3B, Supplemental Material Tables S14-S49
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9-15, Table 1, Supplemental Material Tables S5-S13
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	No meta-analysis was conducted
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10-15, Table 1, Figure 3A & 3B

Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	No meta-analysis was conducted
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10-15, Table 1
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	16-19
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	20

Table S4. Quality of evidence grades (Schünemann et al. 2013)

Grade	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very Low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Table S5. Study characteristics of human observational studies measuring association between exposure to weaponized uranium and **congenital birth defects** among the Iraqi population

Study ID	**Study Design**	**Study Timeframe**	**Population/ Location**	**Sample size**	**Exposure**	**Outcome(s)**	**Statistical test(s)**	**Results**
Alaani et al. (2012)	Case-control	Nov. 2009 – Sept. 2010	Births in Fallujah	Population based	Place of residence (Exposed = Fallujah, Unexposed = Egypt, Kuwait, and UAE, i.e. historical control)	CBD incidence rate (number of infants born with CBD per 1000 live births in population)	No statistical test	CBD incidence in Fallujah for the 11 month period was reported to be between 48-144/ 1000 live births. This rate is many times higher that CBD incidence reported for other (unexposed) Arab countries (Giza, Egypt 31.7, Kuwait 12.5, UAE 7.9)
Alaani et al. (2011)	Case-control	2009-2010	Parents who gave birth to children with CBD at Fallujah General Hospital	Cases = 25 Controls = 99, (Israeli) 114 (Swedish), 2 (Iraqi)	Uranium concentration in hair scalp samples (U mg·kg^{-1}) and uranium concentration along length of hair (mg·kg^{-1}per length interval), ICPMS	Infant with CBD	Mann-Whitley U-Wilcox non-parametric test	The Fallujah cohort (cases) were found to have significantly higher levels of uranium in scalp hair samples (0.16 U mg·kg^{-1}± 0.11 SD) than the control population (historical control) in Southern Israel (0.062 U mg·kg^{-1}) (p=0.016); Uranium concentrations in long-hair samples from the Fallujah cases (0.26 U mg·kg^{-1}± 0.09 SD) were found to be more that 2 SD from the mean for control population (historical control) in Northern Sweden (0.057 U mg·kg^{-1}± 0.065 SD), uranium content does not fall along the length of hair in Fallujah cases as compared to Swedish controls, indicating higher exposure among the Fallujah population in the past compared to present

Alborz (2013)	Cross-sectional	2010	Residents of Basrah governorate	Households = 6032 Children = 10,714	Place of residence - Self-reported exposure to "warfare contamination" (Exposed = Yes, Unexposed = No)	Child with CBD	Chi-squared	A significantly higher proportion of children with birth defects in Basrah (105 out of 383) were found to be living in households that reported exposure to "warfare contamination" than children without birth defects (1349 out of 9547) ($p<0.001$)
Al-Sabbak et al. (2012) (Study 1)	Ecological: Time trend	1994-2011	Births in Al-Basrah city	Population based	Time period (Unexposed = 1994, Exposed = 2003-2011)	CBD incidence rate (number of infants born with CBD per 1000 live births in population)	No statistical test	The CBD incidence rate in Al-Basrah increased 17-fold between 1994 (1.37 CBD per 1000 live births) and 2003 (23 CBD/1000 live births)
Al-Sabbak et al. (2012) (Study 2)	Case-control	May – Aug. 2010	Parents who gave birth to children with CBD at Fallujah General Hospital	Cases = 103 Controls = 9	Uranium concentration in hair ($\mu g \cdot kg^{-1}$), ICPMS	Diagnosis of infant at time of delivery at Fallujah General Hospital (Cases = stillbirths or infants with CBD, Controls = healthy live births)	Independent sample t-test	Uranium concentrations in hair from cases (parents of children with birth defects) and was higher than in controls (parents of healthy children), but the difference was not statistically significant ($p > 0.05$)
Al-Sadoon et al. (1999)	Ecological: Time trend	1990-1998	Residents of Basrah	Population based	Time period - Year of congenital anomaly registration (Unexposed = 1990, Exposed = 1991-1998, later years are equated with greater exposure)	CBD incidence	SND test for difference in proportions (z-test)	A significant increase in CBD incidence in Basrah was found between the periods 1991-1994 (2.5 CBDs/1000 live births) and 1995-1998 (4.57 CBDs/1000 live births) (SND=5.37, $p<0.01$)
Al-Sahlanee et al. (2016)	Case-control	N/R*	Infants born in Baghdad, Dhi-Qar and Basrah.	Participants = 47 mother-neonate pairs	Uranium concentration in maternal and umbilical cord blood samples (ppb), CR-39 fission track detector	Diagnosis at time of delivery in Baghdad (Hospital of Al-Yarmuk and Hospital of Al-Alwiyah), Basrah (Hospital of Gezwan) and Dih-Qar (Hospital of	Independent sample t-tests	Mean uranium concentrations in the maternal and umbilical cord blood samples of deformed infants (2.43 ppb ± 0.89 SD, and 1.99 ppb ± 0.78 SD, respectively) were found to be significantly higher than those samples from normal infants (1.26 ppb ± 0.51 SD, and 0.97

						Al-Shatrah and Hospital of Al-Nasriah), (Cases = infants born dead and deformed, Controls = infants born normal and alive)		ppb ± 0.38 SD, respectively) ($p<0.05$), samples from Basrah also had significantly higher uranium concentrations than the other two regions (Baghdad and Dhi-Qar)
Neamah & Tawfiq (2015)	Cross-sectional	Jan. 01 – May 31, 2011	Residents of Fallujah	N/R	Place of residence (Exposed = Fallujah, Unexposed = Baghdad)	CBD incidence (number of infants born with CBD per 1000 live births) recorded during a five month period at Fallujah General Hospital (Fallujah) and Yarmouk Teaching Hospital (Baghdad)	Autoregressive model	The coefficient values were found to be higher for Basrah (exposed region) than for Baghdad (unexposed region)
Savabieasfa-hani et al. (2020)	Case-control	Summer and Fall of 2016	Nasriyah (Bint Al-Huda Maternity Hospital)	Cases = 19 Controls = 10	Uranium and thorium concentration in hair (ICPMS)	Congenital birth defects	ANOVA	The mean concentrations of uranium and thorium in hair samples from cases (43.51 +/- 29.14 and 6.09 +/- 3.22, respectively) and were higher than those from controls, but the differences were not statistically significant
Savabieasfa-hani et al. (2016)	Case-control	April 2013	Children born with CBDs in Basrah city	Cases = 3 Controls = 6	Uranium and thorium concentrations (ppm) in deciduous teeth, LA-ICP-MS elemental bioimaging	Child with CBD	No statistical test	Uranium and thorium were not detected in any of the samples (detection limit of LA-ICP-MS method was in the ppb range)

Note: CBD = Congenital birth defects, ICP-MS = inductively coupled plasma mass spectrometry, N/R = Not reported; *Paper suggests that the study was conducted after 1991

Table S6. Study characteristics of human observational studies measuring association between exposure to weaponized uranium and **birth-related outcomes** (excluding congenital birth defects) among the Iraqi population

Study ID	**Study Design**	**Study Timeframe**	**Population/ Location**	**Sample size**	**Exposure**	**Outcome(s)**	**Statistical test(s)**	**Results**
Al-Sahlanee et al. (2017)	Cross-sectional	N/R*	Infants born at maternity hospitals in Baghdad	Participants = 50 mother-neonate pairs	Uranium concentration in maternal and umbilical cord blood samples (ppm), CR-39 fission track detector	Infant anthropometric measurements (birth weight, body length, head circumference), determined at time of delivery	Adjusted regression model	Uranium concentrations in maternal blood samples (0.95 ppm ± 0.62 SD) and umbilical cord blood samples (0.68 ppm ± 0.39 SD) were found to be negatively, significantly correlated with the anthropometric measurements (infant birth weight, body length, and head circumference) ($p<0.05$), except for infant umbilical cord blood uranium concentrations and body length (correlation was negative but not significant, $p>0.05$)
Busby et al. (2010) (Study 1)	Cross-sectional	Jan. 20 - Feb. 20, 2010	Residents of Fallujah	Households = 711 Children = 2,132	Time period - Year of birth (Exposed = births after 2005, Unexposed = births prior to 2005)	Birth-sex ratio (ratio of male births to 1000 female births), as reported by subjects in household survey	A statistical test was reportedly used, but not described	Birth-sex ratio decreased to 0.86 for children born between 2006-2010, compared to 1.182 for children born between 2001-2005, 1.109 for children born between 1996-2000, and 1.010 for children born between 1991-1995; the birth-sex ratio for children born between 2006-2010 was found to differ significantly from the expected ratio
Busby et al. (2010) (Study 2)	Case-control	Jan. 20 - Feb. 20, 2010	Residents of Fallujah	Households = 711	Place of residence (Exposed = Fallujah, Unexposed = Egypt, Jordan, and Kuwait)	Infant mortality rate (IMR)	Z-test	IMR in Fallujah between 2006-2010 was four times higher than IMR in Egypt and Jordan ($p < 0.00001$), and nine time higher that the IMR in Kuwait

Note: IMR = Infant mortality rate, N/R = Not reported; *Paper suggests that the study was conducted after 1991

Table S7. Study characteristics of human observational studies measuring association between exposure to weaponized uranium and **cancer** among the Iraqi population

Study ID	**Study Design**	**Study Timeframe**	**Population/ Location**	**Sample size**	**Exposure**	**Outcome(s)**	**Statistical test(s)**	**Results**
Al-Hamzawi et al. (2015)	Case-control	N/R*	Residents of Southern Iraqi governorates (Basrah, Muthanna, and Dhi-Qar)	Cases = 24 Controls = 12	Uranium concentration in tissue ($\mu g \cdot kg^{-1}$), CR-39 fission track detector	Cancer (Cases = kidney, breast, stomach, and uterus cancer tissues, Controls = kidney, breast, stomach, and uterus tissues from healthy individuals)	Independent sample t-test	Significant differences in mean uranium concentrations were found between tissues from cancer patients compared to healthy controls for all cancer types: **Kidney** ($p < 0.001$) Cancer: 6.51 $\mu g \cdot kg^{-1}$ ± 0.20 SD Normal: 4.11 $\mu g \cdot kg^{-1}$ ± 0.38 SD **Breast** ($p < 0.01$) Cancer: 5.04 $\mu g \cdot kg^{-1}$ ± 0.27 SD Normal: 2.96 $\mu g \cdot kg^{-1}$ ± 0.16 SD, **Stomach** ($p < 0.01$) Cancer: 5.22 $\mu g \cdot kg^{-1}$ ± 0.22 SD Normal: 3.11 $\mu g \cdot kg^{-1}$ ± 0.29 SD **Uterus** ($p < 0.01$) Cancer: 4.61 $\mu g \cdot kg^{-1}$ ± 0.32 SD Normal: 2.28 $\mu g \cdot kg^{-1}$ ± 0.51 SD
Al-Hamzawi et al. (2014)	Case-control	N/R*	Residents of Southern Iraqi governorates (Basrah, Muthanna, and Dhi-Qar)	Cases = 30 Controls = 30	Uranium concentrations in blood samples (ppb), CR-39 fission track detector	Leukemia (Cases = leukemia patients in selected hospitals, Controls = healthy volunteers residing in the same areas as hospitals)	Independent sample t-test	Uranium concentrations in blood samples from the leukemia patients (2.87 ppb ± 0.11 SD) were found to be significantly higher than those from the healthy group (1.43 ppb ± 0.07 SD) ($p<0.001$), and uranium concentrations from cases and controls from Basrah were higher than concentrations in blood samples from the other governorates ($p<0.05$)
Al-Hashimi & Wang (2013)	Ecological: Time trend	1980-2010	Residents of Ninawa Province	Population based	Time period (Unexposed = 1980-1990, Exposed = 1991-	Cancer incidence rate ratio (IRR)	Poisson regression analysis	IRR for most cancer types in Ninawa significantly decreased in the second (1991-2000) and third period (2001-2010)

					2000 and 2001-2010)			compared to the first period (1980-1990) ($p < 0.01$), leukemia increased in the third period (IRR: 0.2152, CI: 0.1976-0.2346) compared to the second period (IRR: 0.1731, CI: 0.1505-0.1990), but not to the first period (IRR: 0.2964, CI: 0.2433-0.3611)
Al-Jobori (2013)	Case-control	N/R*	Cancer patients residing in the South of Iraq	Cases = 9 Controls = 3	Uranium concentration in tissues (CR-39 fission track detector)	Cancer (Cases = samples from kidney, bone, breast, lung and liver cancer patients, Controls = samples from kidney, bone, and breast cancer patients)	No statistical test	Uranium was not detected in tissue samples from any of the non-cancerous controls
Al-Rudainy et al. (2011)	Ecological: Time trend	2004-2009	Residents of Basrah Governorate	Population based	Time period (Least exposed = 2004, Most exposed = 2009)	Incidence of childhood Leukemia (0-14 years old)	Standard linear regression, test for trend using parameter estimates of regression model	Incidence of childhood leukemia did not change over the 6 year study period. Leukaemia rates decreased by 0.123 per 100,000 between 2004-2009, but the test for trend was not significant (p=0.81)
Al-Rudainy et al. (2009a)	Ecological: Geographic comparison	2006	Residents of Basrah Governorate	Population based	Place of residence - Locations of DU contaminated sites in Basrah governorate were compiled through a literature and meta-geographic-analysis	Cancer incidence rate by district	Spearman correlation analysis	No statistical correlation was found between level of DU contamination and cancer incidence rate by district (r= -0.01, p= 0.98)
Al-Rudainy et al. (2009b)	Ecological: Time trend	2003-2007	Residents of Basrah Governorate	Population based	Time period (Least exposed = 2003, Most exposed = 2007)	Incidence of childhood Leukemia (1-14 years old)	No statistical test	Over the 5 years study period, no increase in childhood leukemia incidence was observed.

Busby et al. (2010) (Study 3)	Case-control	Jan. 20 - Feb. 20, 2010	Residents of Fallujah	Households = 711 Residents = 4,843	Place of residence (Exposed = Fallujah, Unexposed = Egypt, Jordan, and Kuwait)	Cancer incidence	Z-test	Relative Risk (RR) for cancer incidence in Fallujah between 2005-2010 compared to Egypt was 4.22 (CI: 2.8 - 6.6, p < 0.00000001)
Hagopian et al. (2010)	Ecological: Time trend	1993-2007	Children (0-14 years of age) residing in Basrah Governorate	Population based	Time period - Year of leukemia registration (recent years equates with greater weaponized uranium exposure, earlier years with less exposure)	Leukemia incidence among children aged 0-14 years, over three year periods	Standard linear regression	A significant (p=0.03) trend of increasing incidence of childhood leukemia in Basrah between 1993-2007 was found; incidence more than doubled over the study period (ratio of 2005–2007 incidence to 1993–1995 incidence=2.7; CI=1.437, 5.124)
Hassan et al. (2019)	Case-control	Oct.-Dec. 2017	Cancer patients in Karbala Governorate	Cases = 10 Controls = 2	Uranium concentration in blood samples (ppm), LR-115 type II SSNTD	Cancer	No statistical test	The mean uranium concentration in blood samples from cancer patients (1.4 ppm) was higher than that for healthy controls (0.1 ppm), but no statistical test was performed.
Hassan and Hamadi (2005)	Ecological: Time trend	1997-2002	Residents of Basrah Governorate	Population based	Time period - Year of death or diagnosis (max. exposure = 2002, min. exposure = 1997)	Cancer incidence rate (IR) and mortality rate (MR)	No statistical test reported in study, but a linear regression performed by authors of this SR using reported IR showed a positive trend and moderate effect size (r-squared = 0.58)	No significant increases in cancer IR or MR were observed in Basrah over the study period.
Qaddoori & Shafik (2018)	Case-control	N/R*	Bladder cancer patients in Baghdad Governorate	Cases = 60 Controls = 30	Uranium concentration in urine (μg/L) using CR-39 fission track detector.	Bladder cancer	No statistical test	Bladder cancer patients were found to have a higher average concentration of uranium in urine (1.79004 μg/L) compared to controls (0.89308 μg/L), but the difference was not tested statistically.

Salman (2008)	Ecological: Time trend	1989-2004	Residents of Diyala Governorate	Population based	Time period - Year of cancer diagnosis (Exposed = 2004, Unexposed = 1989)	Number of diagnosed cancer cases per year (Baquba General Hospital, Primary care center of Baquba and medical centers for cancer treatment in Baghdad)	No statistical test	The number of lung cancer cases recorded was higher in 2004 (105 cases) than in 1989 (26 cases), as well as for breast cancer (85 and 17 cases, respectively), and leukemia (92 and 22 cases, respectively) – note: cancer case counts per year do not account for population growth
Shafik (2014)	Case-control	N/R*	Female breast cancer patients in Baghdad	Cases = 41 Controls = 5	Uranium concentrations in 24-hour urine samples ($\mu g \cdot L^{-1}$), KPA-11	Breast cancer (Cases = women with breast cancer living in Baghdad, Controls = healthy women living in Baghdad)	No statistical test	The mean concentration of uranium in urine samples was higher among cases (breast cancer patients, 1.6 $\mu g \cdot L^{-1} \pm$ 0.027 SD) than controls (healthy women, 1.03 $\mu g \cdot L^{-1} \pm$ 0.0202 SD)
Showard & Aswood (2019)	Case-control	N/R*	Patients at Morgan Hospital in Babylon Governorate	Cases = 24 Controls = 6	Concentration of radon-emitted alpha particles in blood samples (Bq/m3), CR-39 fission track detector	Leukemia	No statistical test	The concentration of alpha particles in blood samples for leukemia patients was higher than for controls (7.79 Bq/m3 and 4.39 Bq/m3, respectively), but the difference was not tested statistically.

Note: SSNTD = Solid state nuclear track detector, N/R = Not reported; *Paper suggests that the study was conducted after 2003

Table S8. Study characteristics of human observational studies measuring association between exposure to weaponized uranium and **immune system function** among the Iraqi population

Study ID	**Study Design**	**Study Timeframe**	**Population/ Location**	**Sample size**	**Exposure**	**Outcome(s)**	**Statistical test(s)**	**Results**
Abdul-Wahid (2009)	Case-control	June 2007	Residents of a district in northern Al-Basrah city	Cases = 50 Controls = 50	Place of residence (Exposed = Basrah, Unexposed = Baghdad)	Immune system function (lymphocyte phenotyping: % of cells as lymphocytes in blood sample)	T-test	Cases were found to have lower levels of selected lymphocytes (CD3, CD4, CD8, CD19, and CD56) compared to controls (p-values not reported)
Humaidi & Khalaf (2011)	Case-control	Aug. 2005 – Aug. 2009	Bullet wounded Iraqi's in Ramadi	Cases = 196 Controls = 19	Bullet type (Exposed = shot by US or coalition forces, unexposed = shot by other source)	W.B.C. count, hemoglobin concentration, erythrocyte sedimentation ratio, total serum Bilirubin, alkaline phosphates enzyme concentration, serum transferees enzymes concentration, serum Creatinine concentration, blood urea concentration, mitotic index.	ANOVA	There were significant differences ($p<0.05$) between cases and controls for all outcomes measured
Mryoush & Salim (2015)	Cross-sectional	N/R**	Residents of Baghdad	Participants = 50	Place of residence - Uranium concentration in soil samples (ppm) from five neighborhoods in Baghdad (North -	Mitotic index (MI) analysis (number of cells undergoing mitosis/1000 cells in blood sample)	No statistical test	The North of Baghdad had the highest mean uranium concentration in soil samples (12.90 ppm ± 0.7 SD) and the West had the lowest mean (0.60 ppm ± 0.21 SD), and the mean Mitotic Index in blood samples from the North (2.3 ± 0.059 SD)

					Al-Taji, East - Diyala Bridge, South - Al-Mhmodya, West - Abu Ghraib, Central - Bab-Al-Sharqee)			was higher than the mean MI in samples from the West (0.20 ± 0.3 SD), suggesting a negative correlation

Note: W.B.C. = White blood cell, N/R = Not reported; **Paper suggests that the study was conducted after 1991

Table S9. Study characteristics of human observational studies measuring association between exposure to weaponized uranium and **kidney failure** among the Iraqi population

Study ID	**Study Design**	**Study Timeframe**	**Population/ Location**	**Sample size**	**Exposure**	**Outcome(s)**	**Statistical test(s)**	**Results**
Abed et al (2019, 2020)	Case-control	N/R*	Al-Muthanna Governorate	Cases=21 Controls=5	Uranium concentration in blood (ppm) and urine(μg/L), CR-39 nuclear track detector	Kidney failure	No statistical test	The mean uranium concentration in blood samples from kidney failure patients (0.243 ppm) was higher than that for healthy controls (0.137 ppm), but no statistical test was performed. The mean uranium concentration in urine samples from kidney failure patients (1.90 μg/L) was higher than that for healthy controls (1.16 μg/L), but no statistical test was performed.

Note: N/R= Not reported; * Paper suggests that the study was conducted after 2003

Table S10. Study characteristics of human observational studies measuring association between exposure to weaponized uranium and **BCL-2 oncogene expression** among the Iraqi population

Study ID	**Study Design**	**Study Timeframe**	**Population/ Location**	**Sample size**	**Exposure**	**Outcome(s)**	**Statistical test(s)**	**Results**
Mohammad (2016)	Case-control	2007-2009	Breast cancer patients in Baghdad	Cases = 50 Controls = 30	Place of residence (Exposed = Iraq, Unexposed = Italy)	Bcl-2 oncogene expression and intensity in breast cancer tissue samples	Chi-squared (for Bcl-2 expression) No statistical test (for Bcl-2 intensity)	Bcl-2 expression in Iraqi breast cancer tissue samples was found to be significantly higher ($p = 0.037$) than in Italian samples, and among individuals for which Bcl-2 was positively expressed, Iraqi participants had higher intensities than Italian participants

Table S11. Study characteristics of human observational studies measuring association between exposure to weaponized uranium and **PTEN gene expression** among the Iraqi population

Study ID	**Study Design**	**Study Timeframe**	**Population/ Location**	**Sample size**	**Exposure**	**Outcome(s)**	**Statistical test(s)**	**Results**
Jumaah et al. (2019)	Case-control	Oct. 2006 - Oct. 2007	Female patients at hospitals in central and southern Iraq	Cases (exposed) = 21 Controls (unexposed) = 22	Place of residence (conflict zone vs. peaceful area)	PTEN gene expression	Student's T-test	The PTEN gene expression mean fold change was greater among the exposed group (0.139 ± 0.185) than the unexposed group (0.0031 ± 0.0029), but the difference in means was not statistically significant when tumor grade and cancer stage were controlled for (p=0.286 and p=0.98, respectively).

Note: N/R= Not reported; * Paper suggests that the study was conducted after 2003

Table S12. Study characteristics of human observational studies measuring association between exposure to weaponized uranium and **mixed adverse health outcomes** among the Iraqi population

Study ID	**Study Design**	**Study Timeframe**	**Population/ Location**	**Sample size**	**Exposure**	**Outcome(s)**	**Statistical test(s)**	**Results**
Al-Hamadany et al. (2012) (Study 1)	Case-control	2009-2010	Residents of Baghdad	Cases = 74 Controls = 14	Uranium concentration in blood samples (ppm), CR-39 fission track detector	Illness (Cases = patients with cancer and mothers of children with CBD, Controls = healthy adults)	T-test	Results comparing predefined cases and controls were not reported; Rather, mean uranium concentrations in blood samples are compared between a portion of the control samples (only those healthy individuals living in uncontaminated areas) (0.11ppm ± 0.009 SE), and the cancer patient samples plus the other controls (0.21 ppm ± 0.01 SE) and the difference was statistically significant ($p<0.05$)
Al-Hamadany et al. (2012) (Study 2)	Case-control	2009-2010	Residents of Baghdad	Cases = 74 Controls = 14	Place of residence, health status, or occupation (Exposed = cancer patients, mothers of children with CBDs, employees of the Institute and Hospital of Radiotherapy and Nuclear Medicine, or individuals	Total and Differential W.B.C. Count, Hemoglobin Concentration, neutrophils phagocytic activity, IFN-γ concentrations, IL-2 concentrations	Independent sample t-tests	WBC counts were significantly higher among groups defined as "exposed" and hemoglobin concentrations were significantly lower compared to the group defined as unexposed ($p<0.05$)

					residing in areas of Baghdad identified by UNEP as contaminated, Unexposed = healthy individuals residing in areas reported to be free of weaponized uranium)			

Table S13. Risk of bias assessment for Abed et al (2019, 2020) (Reference 27)

Domain	Rating	Justification
Recruitment	Probably low risk	The recruitment methods in this study were not fully described, but it is suggested that participants were selected from the same area during the same time period.
Blinding	Probably high risk	Blinding of key personnel for outcome measurement is not reported, and lack of blinding could introduce bias.
Exposure Assessment	Low risk	The method for uranium exposure measurement (CR-39 fission track detector) is robust.
Outcome Assessment	Probably low risk	The authors do not sufficiently describe how kidney failure patients were diagnosed, but the use of the term 'patients' suggests that they were diagnosed by medical professionals.
Confounding	High risk	The study collected data on (but did not control for) age and sex of participants. No other confounders were controlled for.
Incomplete Outcome Data	Low risk	Study is free of missing outcome data.
Selective Reporting	Low risk	All pre-specified outcomes were reported.
Other Bias	Low risk	Study appears free of other sources of bias.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S14. Risk of bias assessment for Abdul-Wahid (2009) (Reference 1)

Domain	Rating	Justification
Recruitment	Probably high risk	Study lacks complete description of recruitment criteria, but it is suggested that participants from the unexposed population were selected to be predisposed towards normal ("healthy") immune system function, while the same criteria was not applied to the selection of participants from the exposed population.
Blinding	Probably high risk	Study does not report blinding of key personnel (e.g. personnel counting the number of labeled cells).
Exposure Assessment	High risk	The city of Baghdad does not represent an unexposed geographic location with certainty, as heavy fighting took place in the city during the 2003 invasion by US and coalition forces.
Outcome Assessment	Probably low risk	Outcomes were assessed and defined consistently across all study participants, using a valid and reliable measures (biomarkers) – no Quality assurance/Quality control.
Confounding	Probably high risk	The study controlled for age and sex, but it is unclear whether is accounted to for other important confounders including tobacco use and obesity.
Incomplete Outcome Data	Low risk	The study did not have incomplete outcome data.
Selective Reporting	Low risk	The study is free of suggestion of selective outcome reporting. All of the study's specified outcomes were adequately reported.
Other Bias	High risk	The study reportedly performed t-test to measure association between cases and controls, but the p-values for the test were reported inaccurately.
Conflict of Interest	Low risk	The authors report no conflict of interest, and associated funds and persons appear to be from government and/or academia only.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S15. Risk of bias assessment for Alaani et al (2012) (Reference 14)

Domain	Rating	Justification
Recruitment	High risk	Recruitment strategies for the control populations are not described.
Blinding	Not applicable	Blinding is not an element of study design capable of introducing risk of bias in the study.
Exposure Assessment	Probably high risk	While Egypt (Giza) and Jordan represent unexposed populations, depleted uranium has previously been detected in Kuwait.
Outcome Assessment	Probably low risk	Diagnoses of congenital anomalies were made a professional pediatrician (consistent and valid) – no Quality assurance/Quality control.
Confounding	High risk	The study used a questionnaire to collect data on most important confounders among study participants. However, no confounding variables were accounted for between study groups.
Incomplete Outcome Data	Low risk	The study did not have incomplete outcome data.
Selective Reporting	Low risk	The study is free of suggestion of selective outcome reporting. All of the study's specified outcomes were adequately reported.
Other Bias	Probably low risk	The method for assessing the incidence of congenital birth defects per 1000 live births in Fallujah was not precise (the denominator was estimated), but the explanation provided in the report suggests that the method was reasonably accurate.
Conflict of Interest	High risk	Authors report no conflict of interest, but funding for the study was partially provided by Swedish non-profit International Foundation for Research on Radiation Risk (IFRRR), which has a stated agenda of disputing the

		International Commission on Radiological Protection (ICRP) radiation risk model.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S16. Risk of bias assessment for Alaani et al (2011) (Reference 13)

Domain	Rating	Justification
Recruitment	High risk	Cases and controls were recruited from different populations (Iraq, Israel, and Sweden). Descriptions of the recruitment strategies for the Israeli population (historical control) and Swedish population (historical control) are not reported, nor is the recruitment criteria for Fallujah participants fully reported.
Blinding	Low risk	Hair samples for uranium concentration analysis were re-coded to ensure blinding of key personnel.
Exposure Assessment	Low risk	The method of uranium concentration measurement in hair samples using Inductively coupled plasma mass spectrometry (ICMPS) is robust.
Outcome Assessment	Probably high risk	Cases were diagnosed by a medical doctor at Fallujah General Hospital, however it is not known if or how outcomes were assessed among the participants in the comparator group (Southern Israel, historical control). It is not known if or how outcomes were assessed among the participants in the Swedish (historical control) comparator group.
Confounding	High risk	The study did not account for many important confounders including consanguinity, obesity, maternal folate deficiency or maternal education.
Incomplete Outcome Data	High risk	Birth outcomes were not reported for either historical control group (Israeli and Swedish).
Selective Reporting	Not applicable	In this case-control study, cases were selected on the basis of outcome, thus selective outcome reporting is not capable of introducing risk of bias in the study.
Other Bias	Low risk	The study appears to be free of other sources of bias.
Conflict of Interest	High risk	Authors report no conflict of interest, but funding for the study was partially provided by Swedish non-profit

		International Foundation for Research on Radiation Risk (IFRRR), which has a stated agenda of disputing the International Commission on Radiological Protection (ICRP) radiation risk model.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S17. Risk of bias assessment for Alborz (2013) (Reference 15)

Domain	Rating	Justification
Recruitment	Low risk	The strategy for recruiting participants was consistent across study groups.
Blinding	Not applicable	Blinding is not an element of study design capable of introducing risk of bias in the study.
Exposure Assessment	High risk	Self-reported exposure to war contamination is not a robust method of measuring uranium exposure.
Outcome Assessment	Probably low risk	Outcomes were assessed and defined consistently across all study participants, using a method (questionnaires) that were valid and reliable for the outcome of interest (birth defects) – no Quality assurance/Quality control.
Confounding	High risk	Although the study accounted to other environmental exposures, it did not account for any other important confounders.
Incomplete Outcome Data	Low risk	Study is free of missing outcome data.
Selective Reporting	Low risk	All pre-specified outcomes are reported.
Other Bias	Low risk	Study appears free of other sources of bias.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S18. Risk of bias assessment for Al-Hamadany et al (2012) (Study 1) (Reference 2)

Domain	Rating	Justification
Recruitment	Probably low risk	Study lacks a complete description of recruitment methods.
Blinding	Probably high risk	Blinding of key personnel for outcome measurement is not reported, and lack of blinding could introduce bias.
Exposure Assessment	Low risk	The method for uranium exposure measurement (CR-39 fission track detector) is robust.
Outcome Assessment	Probably high risk	The study does not clearly define the outcome of interest or report how the outcomes were assessed.
Confounding	High risk	Study did not control for any confounders.
Incomplete Outcome Data	Low risk	Study appears to be free of missing outcome data.
Selective Reporting	Not applicable	In this case-control study, cases were selected on the basis of outcome, thus selective outcome reporting is not capable of introducing risk of bias in the study.
Other Bias	High risk	The study did not report uranium concentrations for all six study groups. The decision to lump occupationally exposed individuals, and healthy individuals living in neighborhoods suspected to be contaminated with depleted uranium, into the same group as cancer patients and mothers who gave birth to children with congenital birth defects (cases) for comparison to the health, unexposed group, introduces a serious methodological flaw into the study.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S19. Risk of bias assessment for Al-Hamadany et al (2012) (Study 2) (Reference 2)

Domain	Rating	Justification
Recruitment	Probably low risk	Study lacks a complete description of recruitment methods.
Blinding	Probably high risk	Blinding of key personnel for outcome measurement is not reported, and lack of blinding could introduce bias.
Exposure Assessment	High risk	The study defined uranium "exposed" cases as cancer patients, mothers of children with congenital birth defects, employees of the Institute and Hospital of Radiotherapy and Nuclear Medicine, or individuals residing in areas of Baghdad identified by the United Nations Environmental Program (UNEP) as contaminated. This is a highly problematic definition of "exposed".
Outcome Assessment	Probably low risk	The methods used for outcome assessments (direct assessment of biomarkers) were valid and robust – no Quality assurance/Quality control .
Confounding	High risk	Study did not control for any confounders.
Incomplete Outcome Data	Low risk	Study appears to be free of missing outcome data.
Selective Reporting	Low risk	All pre-specified outcomes were reported.
Other Bias	Low risk	Study appears to be free of other sources of bias.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S20. Risk of bias assessment for Al-Hamzawi et al (2015) (Reference 4)

Domain	Rating	Justification
Recruitment	Low risk	The strategy for recruiting participants was consistent across study groups.
Blinding	Low risk	Tissue samples for uranium concentration analysis were re-coded to ensure blinding of key personnel.
Exposure Assessment	Low risk	The methods for uranium concentration measurement in blood samples (CR-39 fission track detector) are robust.
Outcome Assessment	Probably low risk	All samples were collected from a histopathology clinic in Southern Iraq, which presumably used valid and reliable methods to record or determine if samples came from subjects diagnosed with cancer, or healthy subjects – No Quality assurance/Quality control .
Confounding	High risk	Data on age, sex, and tobacco use of participants was collected and reported. However, the confounders were not accounted or controlled for in analysis.
Incomplete Outcome Data	Low risk	The study did not have incomplete outcome data.
Selective Reporting	Not applicable	In this case-control study, cases were selected on the basis of outcome, thus selective outcome reporting is not capable of introducing risk of bias in the study.
Other Bias	High risk	Neither the time frame during which tissue samples of cancer patients (cases) were collected by the histopathology clinic, nor the year that cancer was diagnosed for study subjects are reported. Cancerous tissue samples collected before 1991 or 2003, or collected from patients who were diagnosed before 1991 or 2003, cannot inform the question of whether uranium exposure (independent variable) is association with cancer (dependent variable). Samples from patients with inherited-type cancers also cannot inform the question of association. Some cancer treatment drugs

		can affect kidney function, which could hypothetically reduce the excretion rate of uranium, leading to higher concentrations of uranium in tissues among patients receiving treatment than in healthy volunteers, although the levels of environmental exposure may be the same. Likewise, cancer of the kidney can impair kidney function, leading to a reduction in the rate of uranium excretion and an accumulation of uranium in kidney tissues.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from government and/or academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S21. Risk of bias assessment for Al-Hamzawi et al (2014) (Reference 3)

Domain	Rating	Justification
Recruitment	Probably low risk	Study participants were not all recruited from the same population, but proportions of participants from each population in each study group are uniform. Study lacks a complete description of recruitment methods, but otherwise no reason to suspect there were substantial differences between comparison groups other than uranium exposure.
Blinding	Low risk	Blinding methods are not reported, but the authors of this SR judge that the neither the outcome and the outcome measurement, nor exposure and exposure measurement are likely to be influenced by lack of blinding.
Exposure Assessment	Low risk	The methods for uranium concentration measurement in blood samples (CR-39 fission track detector) are robust.
Outcome Assessment	High risk	The outcome of interest (Leukemia) was not assessed consistently across all study participants.
Confounding	High risk	The study accounted for age and sex of participants, but it did not account for any other important confounders.
Incomplete Outcome Data	Low risk	The study did not have incomplete outcome data.
Selective Reporting	Not applicable	In this case-control study, cases were selected on the basis of outcome, thus selective outcome reporting is not capable of introducing risk of bias in the study.
Other Bias	High risk	Neither the year that blood samples of leukemia patients were collected by hospitals, nor the year that cancer was diagnosed for the leukemia patients are reported. Leukemia blood samples collected before 1991 or 2003, or collected from patients who were diagnosed before 1991 or 2003, cannot inform the question of whether uranium exposure (independent variable) is association

		with leukemia (dependent variable). Samples from patients with inherited-type leukemia also cannot inform the question of association. Some leukemia treatment drugs can affect kidney function, which could hypothetically reduce the excretion rate of uranium, leading to higher concentrations of uranium in blood among patients receiving treatment than in healthy volunteers, although the levels of environmental exposure may be the same.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from government and/or academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S22. Risk of bias assessment for Al-Hashimi & Wang (2013) (Reference 5)

Domain	Rating	Justification
Recruitment	Probably low risk	Data for this study was obtained from the Directorate of Health in Ninawa. The methods by which the Directorate collected the data between years was not reported, but there is no suggestion that methods of data collection differed between years.
Blinding	Not applicable	As a purely statistical analysis, blinding is not an element of study design capable of introducing risk of bias in the study.
Exposure Assessment	Low risk	Given the study design (ecological: time trend), the method of exposure measurement in this study (year) is robust.
Outcome Assessment	Probably low risk	Data was collected from the Directorate of Health of the Ninawa province in Iraq.
Confounding	High risk	While the study controlled for age and sex in its analysis, it did not control for tobacco use or other environmental exposures.
Incomplete Outcome Data	Low risk	The study did not have incomplete outcome data.
Selective Reporting	Low risk	The study is free of suggestion of selective outcome reporting. All of the study's specified outcomes were adequately reported.
Other Bias	Low risk	The study appears to be free of other sources of bias.
Conflict of Interest	Low risk	The authors report no conflict of interest, and associated funds and persons appear to be from government and/or academia only.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S23. Risk of bias assessment for Al-Jobori (2013) (Reference 6)

Domain	Rating	Justification
Recruitment	High risk	Participants were not recruitments not recruited from the same population. The timeframe during which participants were recruited is not reported.
Blinding	Probably high risk	Blinding of key personnel for outcome measurement is not reported, and lack of blinding could introduce bias.
Exposure Assessment	Probably high risk	While the method used for uranium concentration measurement in tissues samples (CR-39 fission track detector) is robust, the finding that control samples contained no detectable levels of uranium is highly questionable.
Outcome Assessment	Probably low risk	All subjects (cases and controls) were recruited from hospitals in Iraq where the health outcome of interest (cancer) was diagnosed by a medical doctor.
Confounding	High risk	Study did not account for any confounders.
Incomplete Outcome Data	Low risk	Study appears free from missing outcome data.
Selective Reporting	Not applicable	In this case-control study, cases were selected on the basis of outcome, thus selective outcome reporting is not capable of introducing risk of bias in the study.
Other Bias	High risk	The study did not clearly state whether the specimens were collected from affected organs. The sample size was small (controls, n=3).
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S24. Risk of bias assessment for Al-Rudainy et al (2011) (Reference 16)

Domain	Rating	Justification
Recruitment	Low risk	The strategy for recruiting participants was consistent across study groups.
Blinding	Not applicable	Blinding is not an element of study design capable of introducing risk of bias in the study.
Exposure Assessment	Probably high risk	The time frame for this study was 2004-2009, and thus no data for an unexposed population (prior to 1991 or 2003) was used in this study. The assumption that later year of diagnosis (more recent) equates with higher uranium exposure is questionable.
Outcome Assessment	Low risk	Health outcome data was collected from the Pediatric Oncology Ward in Basrah Maternity & Children's Hospital and the Basrah Health Authorities Statistical Office.
Confounding	High risk	While the study controlled for age and sex in its analysis, it did not control for tobacco use or other environmental exposures.
Incomplete Outcome Data	Low risk	Study is free of missing outcome data.
Selective Reporting	Low risk	All pre-specified outcomes are reported.
Other Bias	Low risk	Study appears free of other sources of bias.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S25. Risk of bias assessment for Al-Rudainy et al (2009a) (Reference 7)

Domain	Rating	Justification
Recruitment	Low risk	The strategy for recruiting participants was consistent across study groups.
Blinding	Not applicable	Blinding is not an element of study design capable of introducing risk of bias in the study.
Exposure Assessment	Probably low risk	Given the study design (ecological: geographic comparison), the method of exposure measurement in this study (meta-synthesis of depleted uranium impacted sites) is robust.
Outcome Assessment	Low risk	Health and population data was compiled from a valid and reliable source.
Confounding	High risk	While the study controlled for age and sex in its analysis, it did not control for tobacco use or other environmental exposures.
Incomplete Outcome Data	Low risk	Study is free of missing outcome data.
Selective Reporting	Low risk	All pre-specified outcomes are reported.
Other Bias	Low risk	Study appears free of other sources of bias.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S26. Risk of bias assessment for Al-Rudainy et al (2009b) (Reference 8)

Domain	Rating	Justification
Recruitment	Low risk	The strategy for recruiting participants was consistent across study groups.
Blinding	Not applicable	Blinding is not an element of study design capable of introducing risk of bias in the study.
Exposure Assessment	Probably high risk	The time frame for this study was 2007-2009, and thus no data for an unexposed population (prior to 1991 or 2003) was used in this study. The assumption that later year of diagnosis (more recent) equates with higher uranium exposure is questionable.
Outcome Assessment	Low risk	Health outcome data was collected from the Pediatric Oncology Ward in Basrah Maternity & Children's Hospital and the Basrah Health Authorities Statistical Office.
Confounding	High risk	Study did not account for tobacco use among participants or population, nor other environmental exposures.
Incomplete Outcome Data	Low risk	Study is free of missing outcome data.
Selective Reporting	Low risk	All pre-specified outcomes are reported.
Other Bias	Low risk	Study appears free of other sources of bias.
Conflict of Interest	Low risk	Authors declared no conflict of interest. Associated funds and persons appear to be from academia only and free of financial interests in study results.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S27. Risk of bias assessment for Al-Sabbak et al (2012) (Study 1) (Reference 9)

Domain	Rating	Justification
Recruitment	Low risk	Recruitment criteria were consistent across study groups.
Blinding	Not applicable	Blinding is not an element of study design capable of introducing risk of bias in the study.
Exposure Assessment	Probably high risk	The control period (1994) does not represent an unexposed period, as depleted uranium weapons were used in Basra by US forces in 1991.
Outcome Assessment	High risk	Data was obtained from the Al-Basrah Maternity Hospital (a reliable source). However, health outcomes among the control population were only assessed over a 1 year period, compared to the exposed population for with birth defects incidence was calculated over a 9 year period. The impact of economic sanctions in Iraq on health care infrastructure during that period (1994) may have impacted cancer surveillance and registration.
Confounding	High risk	No confounding variables in the study population were measured or accounted for.
Incomplete Outcome Data	Low risk	The study did not have incomplete outcome data.
Selective Reporting	Low risk	The study is free of suggestion of selective outcome reporting. All of the study's specified outcomes were adequately reported.
Other Bias	High risk	Only a fraction of the total births in Al-Basrah take place in a hospital setting, or at Al-Basra Maternity hospital specifically, which could introduce a form of selection bias into the study deign.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from government and/or academia only and free of financial

		interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S28. Risk of bias assessment for Al-Sabbak et al (2012) (Study 2) (Reference 9)

Domain	Rating	Justification
Recruitment	Low risk	The strategy for recruiting participants was consistent across study groups.
Blinding	Probably high risk	The study does not discuss blinding of key personnel (e.g. personnel conducting ICPMS analysis), and it is possible that lack of blinding could introduce bias.
Exposure Assessment	Probably low risk	The method of uranium concentration measurement in hair samples using Inductively coupled plasma mass spectrometry (ICPMS) is robust, as long as hair samples were collected from the scalp (not specified in study).
Outcome Assessment	Low risk	Diagnosis of birth defects by a medical doctor at the Fallujah General Hospital at the time of delivery is a valid and robust methods for outcome assessment.
Confounding	High risk	A questionnaire was reportedly used to collect data on many important confounders (including consanguinity and maternal health status) and the authors also tested hair samples for other environmental teratogens including lead and mercury. However, these confounding variables to do appear to have been accounted for in the statistical analysis comparing uranium concentration in hair samples between cases and controls.
Incomplete Outcome Data	Low risk	The study did not have incomplete outcome data.
Selective Reporting	Low risk	The study is free of suggestion of selective outcome reporting. All of the study's specified outcomes were adequately reported.
Other Bias	Low risk	The study appears to be free of other sources of bias.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from government and/or academia only and free of financial

		interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S29. Risk of bias assessment for Al-Sadoon et al (1999) (Reference 10)

Domain	Rating	Justification
Recruitment	Low risk	The strategy for recruiting participants was consistent across study groups.
Blinding	Not applicable	Blinding is not an element of study design capable of introducing risk of bias in the study.
Exposure Assessment	Low risk	Given the study design (ecological: time trend), the method of exposure measurement in this study (year) is robust.
Outcome Assessment	Low risk	Data was obtained from the Al-Basrah Maternity Hospital (a reliable source).
Confounding	High risk	No confounding variables in the study population were measured or accounted for.
Incomplete Outcome Data	Low risk	Study is free of missing outcome data.
Selective Reporting	Low risk	All pre-specified outcomes are reported.
Other Bias	Low risk	Study appears free of other sources of bias.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S30. Risk of bias assessment for Al-Sahlanee et al (2017) (Reference 12)

Domain	Rating	Justification
Recruitment	Probably low risk	Study lacks a complete description of recruitment criteria. Namely, it does not specify if participants were recruited from a single hospital or multiple hospitals in Baghdad, or explicitly define the time period during which participants were recruited.
Blinding	Probably high risk	The study does not discuss blinding of key personnel (e.g. personnel counting CR-39 fission detector tracks), and it is possible that lack of blinding could introduce bias.
Exposure Assessment	Low risk	The methods for measuring uranium concentration measurement in blood samples (CR-39 fission track detector) are robust.
Outcome Assessment	Probably low risk	Details on the methods used to obtain anthropometric of measurements of newborns are lacking, but presumably performed by a nurse at the hospital at the time of birth – No Quality assurance/Quality control.
Confounding	Probably high risk	Data on all important confounders except consanguinity were collected. It is suggested (but not explicitly stated) that they were controlled for in the adjusted regression analysis.
Incomplete Outcome Data	Low risk	Study is free of missing outcome data.
Selective Reporting	Low risk	All of the pre-specified outcomes are reported.
Other Bias	Low risk	The study appears to be free of other sources of bias.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from government and/or academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S31. Risk of bias assessment for Al-Sahlanee et al (2016) (Reference 11)

Domain	Rating	Justification
Recruitment	High risk	Study lacks a complete description of recruitment criteria. Participants were recruited from different populations, and the number of participants from each population are not reported. The time period during which blood samples were collected from participants is not reported.
Blinding	Probably high risk	Blinding of key personnel (e.g. personnel conducting track density counts) was not reported.
Exposure Assessment	Low risk	The method of uranium concentration measurement in maternal and umbilical cord blood samples (CR-39 fission track detector) is robust.
Outcome Assessment	High risk	Details are lacking on how birth outcomes were defined or diagnosed during this study. It unclear whether cases included still births without diagnosed congenital malformations.
Confounding	High risk	Data on maternal age was collected, but not controlled for in analysis.
Incomplete Outcome Data	Low risk	The study did not have incomplete outcome data.
Selective Reporting	Not applicable	In this case-control study, cases were selected on the basis of outcome, thus selective outcome reporting is not capable of introducing risk of bias in the study.
Other Bias	Low risk	The study appears to be free of other sources of bias.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from government and/or academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S32. Risk of bias assessment for Busby et al (2010) (Study 1) (Reference 17)

Domain	Rating	Justification
Recruitment	Probably low risk	Recruitment criteria was applied similarly across study groups. The response rate for the household survey was reportedly 60%, and the majority of the non-responses came from a single neighborhood where household residents were suspicious of the surveyors. The study authors provide a reasonable explanation that the non-responses were unlikely to be related to exposures or outcomes.
Blinding	Not applicable	Blinding is not an element of study design capable of introducing risk of bias in the study.
Exposure Assessment	Low risk	Given the study design (cross-sectional), the method of exposure measurement in this study (year) is robust.
Outcome Assessment	High risk	This study determined the yearly birth-sex ratio in Fallujah by conducting a household cross-sectional survey, and document the age and sex of children in each household. This is a problematic method, because it does not account for deaths, adoptions, or immigration. The study design was also potentially subject to recall bias or overreporting bias. Differential child mortality rates between sexes could also impact outcomes measured.
Confounding	High risk	No confounding variables in the study population were measured or accounted for.
Incomplete Outcome Data	Probably low risk	The study does not report any missing data (but they also do not report that all questionnaires were completed in full).
Selective Reporting	High risk	The study does not report the birth-sex ratio for age cohorts above 19 years. The next age cohort (20-24 years) has a birth-sex ratio even lower than the 0-4 years age cohort (776 compared to 860 males per 1000 females, respectively).

Other Bias	Low risk	The study appears to be free of other sources of bias.
Conflict of Interest	Low risk	Authors declare no conflict of interest.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S33. Risk of bias assessment for Busby et al (2010) (Study 2) (Reference 17)

Domain	Rating	Justification
Recruitment	High risk	The recruitment strategies differed between exposed (Fallujah) and unexposed (Egypt) populations.
Blinding	Not applicable	Blinding is not an element of study design capable of introducing risk of bias in the study.
Exposure Assessment	Low Risk	Egypt represents an unexposed population.
Outcome Assessment	High Risk	The method of data collection among the exposed population (Fallujah) was indirect (cross-sectional survey) potentially subject to recall bias or overreporting bias.
Confounding	High risk	No confounding variables in the study population were measured or accounted for.
Incomplete Outcome Data	Probably low risk	The study does not report any missing data (but they do not report that all questionnaires were completed in full). The study suggests that parents may have underreported cases of birth defects, but the study accounted for that by collecting data on still births (with the reasonable assumption that families effected by stigma surrounding birth defects would report cases as still births or infant mortality).
Selective Reporting	Probably high risk	The questionnaire used in the study aimed to collected data on health status, birth history, and infant mortality among study participants for a ten year period, but only the most recent five year period was reported.
Other Bias	Low risk	The study appears to be free of other sources of bias.
Conflict of Interest	Low risk	Authors declare no conflict of interest.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S34. Risk of bias assessment for Busby et al (2010) (Study 3) (Reference 17)

Domain	Rating	Justification
Recruitment	High risk	The recruitment strategies differed between exposed (Fallujah) and unexposed (Egypt) populations.
Blinding	Not applicable	Blinding is not an element of study design capable of introducing risk of bias in the study.
Exposure Assessment	Low risk	Egypt represents an unexposed population.
Outcome Assessment	High risk	The method of data collection differed across study groups, and the method of data collection among the exposed population (Fallujah) was potentially subject to recall bias or overreporting bias.
Confounding	High risk	The only confounding variable controlled for in this study was age.
Incomplete Outcome Data	Probably low risk	The study does not report any missing data (but they do not report that all questionnaires were completed in full).
Selective Reporting	Probably high risk	The questionnaire used in the study aimed to collected data on health status, birth history, and cancer history among study participants for a ten year period, but only the most recent five year period was reported.
Other Bias	Low risk	The study appears to be free of other sources of bias.
Conflict of Interest	Low risk	Authors declare no conflict of interest.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S35. Risk of bias assessment for Hagopian et al (2010) (Reference 18)

Domain	Rating	Justification
Recruitment	Low risk	The strategy for recruiting participants was consistent across study groups.
Blinding	Not applicable	Blinding is not an element of study design capable of introducing risk of bias in the study.
Exposure Assessment	Probably high risk	The time frame for this study was 1993-2007, and thus no data for an unexposed population (prior to 1991) was used in this study. The assumption that later year of diagnosis (more recent) equates with higher uranium exposure is questionable.
Outcome Assessment	Low risk	Data was obtained from the Ibn Ghazwan Hospital's leukemia registry.
Confounding	High risk	No confounding variables in the study population were measured or accounted for.
Incomplete Outcome Data	Low risk	Study is free of missing outcome data.
Selective Reporting	Low risk	All pre-specified outcomes are reported.
Other Bias	Low risk	Study appears free of other sources of bias.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S36. Risk of bias assessment for Hassan et al (2019) (Reference 29)

Domain	Rating	Justification
Recruitment	Probably low risk	The recruitment methods in this study were not fully described, but it is suggested that participants were selected from the same area during the same time period.
Blinding	Probably low risk	It is reported that samples were recoded, which suggests that blinding procedures were implemented.
Exposure Assessment	Low risk	The method for uranium exposure measurement (Solid State Nuclear Track Detector) is robust.
Outcome Assessment	Probably low risk	Patients were reportedly diagnosed at a cancer hospital in Karbala Governorate.
Confounding	High risk	The study did not control for any confounders.
Incomplete Outcome Data	Low risk	Study is free of missing outcome data.
Selective Reporting	Low risk	All pre-specified outcomes were reported.
Other Bias	Low risk	Study appears free of other sources of bias.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S37. Risk of bias assessment for Hassan et al (2005) (Reference 19)

Domain	Rating	Justification
Recruitment	Low risk	The strategy for recruiting participants was consistent across study groups.
Blinding	Not applicable	Blinding is not an element of study design capable of introducing risk of bias in the study.
Exposure Assessment	Probably high risk	The cancer registry from which data was obtained for this study was created in 1997, and thus no data for an unexposed population was used in this study. The assumption that later year of diagnosis (more recent) equates with higher uranium exposure is questionable.
Outcome Assessment	Low risk	Data was obtained from the Basrah Oncology Center, Basrah Health Office, and Central Statistical Bureau.
Confounding	High risk	Study accounts for sex, but does not account for average age of population between years (increase in cancer rate is expected with an ageing population). No other confounders were accounted for.
Incomplete Outcome Data	Low risk	Study is free of missing outcome data.
Selective Reporting	Low risk	All pre-specified outcomes are reported.
Other Bias	Low risk	Study appears free of other sources of bias.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S38. Risk of bias assessment for Humaidi & Khalaf (2011) (Reference 20)

Domain	Rating	Justification
Recruitment	Probably low risk	Study lacks a complete description of recruitment methods, but otherwise no reason to suspect there were substantial differences between comparison groups other than uranium exposure (as defined within the context of the study).
Blinding	Probably high risk	Blinding of key personnel for outcome measurement is not reported, and lack of blinding could introduce bias.
Exposure Assessment	High risk	Not all bullets used by US or coalition forces contain weaponized uranium.
Outcome Assessment	Probably low risk	The methods used for outcome assessments (direct assessment of biomarkers) were valid and robust – no Quality assurance/Quality control.
Confounding	High risk	Study does not account for age, severity of bullet injury, or location of injury.
Incomplete Outcome Data	Low risk	Study has no suggestion of missing outcome data.
Selective Reporting	Low risk	All pre-specified outcomes were reported.
Other Bias	Low risk	Study appears to be free of other sources of bias.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S39. Risk of bias assessment for Jumaah et al (2019) (Reference 30)

Domain	Rating	Justification
Recruitment	Low risk	Recruitment strategies were the same across study groups.
Blinding	Low risk	Participant data was coded and blinding procedures were implemented.
Exposure Assessment	Probably high risk	Categorization of place of residence as 'exposed' or 'unexposed' was not verified by environmental or biological monitoring.
Outcome Assessment	Low risk	Study reports that "All cases were examined by two independent pathologists to confirm the diagnosis."
Confounding	Probably high risk	The study controlled for age and sex of participants, as well as other environmental exposures. It did not control for tobacco use or obesity.
Incomplete Outcome Data	Low risk	Study is free of missing outcome data.
Selective Reporting	Low risk	All pre-specified outcomes were reported.
Other Bias	Low risk	Study appears free of other sources of bias.
Conflict of Interest	Low risk	The authors declare no funding for this study and no competing interests.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S40. Risk of bias assessment for Mohammad (2016) (Reference 23)

Domain	Rating	Justification
Recruitment	Probably low risk	Study lacks complete description of recruitment criteria for each population, but it is reported that samples were collected from patients in both populations during the same time frame.
Blinding	Probably high risk	Blinding of key personnel for outcome measurement is not reported, and lack of blinding could introduce bias.
Exposure Assessment	Low risk	The Italian control population represents an appropriate (unexposed) control.
Outcome Assessment	Probably high risk	The study reports that the difference in tissue processing time, the difference in tissue quality, and the timing for embedding tissues in paraffin may have impacted outcome measurements, but data is not available for those variables - no Quality assurance/Quality control reported.
Confounding	High risk	Only age and sex were accounted for in this study.
Incomplete Outcome Data	Low risk	Study is free of missing outcome data.
Selective Reporting	Low risk	All pre-specified outcomes are reported.
Other Bias	Low risk	The study appears to be free of other sources of bias.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from government and/or academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S41. Risk of bias assessment for Mryoush & Salim (2015) (Reference 21)

Domain	Rating	Justification
Recruitment	Probably low risk	Study lacks a complete description of recruitment criteria, but otherwise no reason to suspect there were substantial differences between comparison groups other than uranium exposure.
Blinding	Probably high risk	Blinding of key personnel for either exposure or outcome measurement is not reported, and lack of blinding could introduce bias.
Exposure Assessment	Low risk	The method of measuring uranium concentration in soil samples (CR-39 fission track detector) is robust.
Outcome Assessment	Probably low risk	Outcomes were assessed and defined consistently across all study participants, using valid and reliable measures – no Quality assurance/Quality control reported.
Confounding	Probably high risk	The study accounted for age, sex, and tobacco use among study participants. However, it did not account for body fat (obesity) or other environmental exposures.
Incomplete Outcome Data	Low risk	Study is free of missing outcome data.
Selective Reporting	Low risk	All of the pre-specified outcomes are reported.
Other Bias	High risk	The authors of the study reported that the use of phosphate fertilizers, or proximity to fertilizer production facilities, could lead to higher concentrations or uranium in soil samples in the study area.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from government and/or academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S42. Risk of bias assessment for Neamah & Tawfiq (2015) (Reference 22)

Domain	Rating	Justification
Recruitment	Low risk	The strategy for recruiting participants was consistent across study groups.
Blinding	Not applicable	Blinding is not an element of study design capable of introducing risk of bias in the study.
Exposure Assessment	High risk	The city of Baghdad does not represent an unexposed geographic location with certainty, as heavy fighting took place in the city during the 2003 invasion by US and coalition forces.
Outcome Assessment	Probably low risk	Not enough information to permit a judgement of low risk of bias, but the article suggests that outcomes were assessed and defined consistently across all study participants, using valid and reliable measures (direct observation by medical professional in prospective cohort study).
Confounding	High risk	The study did not control for any confounders.
Incomplete Outcome Data	Probably low risk	The data in this study is presented in the form of matrices prepared for statistical analysis, from which missing outcome data cannot be interpreted. The authors do not report any missing outcome data in the narrative text.
Selective Reporting	High risk	The study does not report total number of births at each hospital.
Other Bias	Low risk	The study appears free of other sources of bias.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S43. Risk of bias assessment for Qaddoori & Shafik (2018) (Reference 31)

Domain	Rating	Justification
Recruitment	Probably low risk	The recruitment methods in this study were not fully described, but it is suggested that participants were selected from the same area during the same time period.
Blinding	Probably high risk	Blinding of key personnel for outcome measurement is not reported, and lack of blinding could introduce bias.
Exposure Assessment	Low risk	The method of uranium concentration measures (CR-39 fission track detector) was robust.
Outcome Assessment	Probably low risk	All cancer patients were recruited from hospitals in the Baghdad governorate.
Confounding	High Risk	The study did not control for any confounders.
Incomplete Outcome Data	Low risk	Study is free of missing outcome data.
Selective Reporting	Low risk	All pre-specified outcomes were reported.
Other Bias	Low risk	Study appears free of other sources of bias.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S44. Risk of bias assessment for Salman (2008) (Reference 24)

Domain	Rating	Justification
Recruitment	Low risk	The strategy for recruiting participants was consistent across study groups.
Blinding	Not applicable	Blinding is not an element of study design capable of introducing risk of bias in the study.
Exposure Assessment	High risk	Study findings may reflect changes in cancer detection (diagnostic abilities), and not true change of cancer incidence in the population.
Outcome Assessment	Low risk	Data on cancer cases was obtained from the Baquba General Hospital.
Confounding	High risk	The study did not control for any confounders.
Incomplete Outcome Data	Low risk	Study is free of missing outcome data.
Selective Reporting	Low risk	All pre-specified outcomes are reported.
Other Bias	High risk	Study reports cases, not incidence of cancer.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S45. Risk of bias assessment for Savabieasfahani et al (2020) (Reference 32)

Domain	Rating	Justification
Recruitment	Probably high risk	Recruitment strategies were the same across study groups, but a high non-response rate was reported (39%).
Blinding	Probably high risk	Blinding of key personnel for outcome measurement is not reported, and lack of blinding could introduce bias.
Exposure Assessment	Low risk	The method of uranium and thorium detection in hair samples Inductively coupled plasma mass spectrometry (ICP-MS) was robust.
Outcome Assessment	Low risk	Study reports that "Determination of congenital anomalies was done by medical doctors at Bint Al-Huda Maternity Hospital."
Confounding	High risk	The study controlled for age and sex of participants, tobacco use, maternal health status, and maternal age at birth. However, it did not assess or control for maternal folate deficiency, consanguinity, or other environmental exposures.
Incomplete Outcome Data	Low risk	Study is free of missing outcome data.
Selective Reporting	High risk	The article states that 43 families were recruited into the study. However, results for only 30 participants are reported (20 cases, 10 controls) were reported.
Other Bias	High risk	The Journal Pre-Proof of this article (published online in August 2019) identified the US military base of interest as Camp Taji. When published, the article was revised and 'Camp Taji' was replaced with "Tallil Air Base' without any explanation. This raises concerns

		about the certainty in identification of the US military base. Additionally, Table 1, reported 20 cases were included in the study, but the manuscript text reports that 19 cases were included (Section 6. Biological Samples).
Conflict of Interest	Low risk	The authors declare no competing interest.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S46. Risk of bias assessment for Savabieasfahani et al (2016) (Reference 25)

Domain	Rating	Justification
Recruitment	High risk	Participants from the control group (children without congenital birth defects) were selected from populations outside of Iraq.
Blinding	Probably high risk	Blinding of key personnel for outcome measurement is not reported, and lack of blinding could introduce bias.
Exposure Assessment	Probably high risk	The method selected for exposure assessment (elemental bioimaging using laser ablation Inductively coupled plasma mass spectrometry) may have a detection limit above the expected range of uranium concentration in human teeth.
Outcome Assessment	Low risk	Outcomes were assessed and defined consistently across all study participants, using valid and reliable measures.
Confounding	High risk	The study did not control for any confounders.
Incomplete Outcome Data	Low risk	Study is free of missing outcome data.
Selective Reporting	Not applicable	In this case-control study, cases were selected on the basis of outcome, thus selective outcome reporting is not capable of introducing risk of bias in the study.
Other Bias	High risk	Very small sample sizes (Cases, n=3; Controls, n=6)
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Table S47. Risk of bias assessment for Shafik (2014) (Reference 26)

Domain	Rating	Justification
Recruitment	Low risk	Study lacks a complete description of recruitment methods, but otherwise no reason to suspect there were substantial differences between comparison groups other than uranium exposure.
Blinding	Low risk	Urine samples for uranium concentration analysis were re-coded to ensure blinding of key personnel.
Exposure Assessment	Low risk	The method for monitoring uranium concentration in urine samples (Kinetic Phosphorescence Analyzer, KPA-11) is robust.
Outcome Assessment	Probably low risk	Study lacks a complete description of outcome assessment methods.
Confounding	High risk	Of the important confounders pre-specified in the present systematic review, Shafik (2014) only controlled for sex of participants and tobacco use. The study did not control for age, obesity, or other environmental exposures.
Incomplete Outcome Data	Low risk	Study was free of missing outcome data.
Selective Reporting	Not applicable	In this case-control study, cases were selected on the basis of outcome, thus selective outcome reporting is not capable of introducing risk of bias in the study.
Other Bias	High risk	Very small sample size (Controls, n=5). No statistical test of difference in uranium concentrations was performed.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, “The Navigation Guide instructions for making risk of bias determinations”

Table S48. Risk of bias assessment for Showard & Aswood (2019) (Reference 33)

Domain	Rating	Justification
Recruitment	Probably low risk	The recruitment methods in this study were not fully described, but it is suggested that participants were selected from the same area during the same time period.
Blinding	Probably low risk	Study reports that samples were coded, which suggests blinding measures were implemented.
Exposure Assessment	Low risk	The method of alpha particle concentration assessment (CR-39 fission track detector) was robust.
Outcome Assessment	Probably low risk	The authors do not sufficiently describe how leukemia patients were diagnosed, but the use of the term 'patients' suggests that they were diagnosed by medical professionals.
Confounding	High risk	The study collected data on age and sex of participants, but did not control for those or any other confounders.
Incomplete Outcome Data	Low risk	Study is free of missing outcome data.
Selective Reporting	Low risk	All pre-specified outcomes were reported.
Other Bias	Low risk	Study appears free of other sources of bias.
Conflict of Interest	Probably low risk	Associated funds and persons appear to be from academia only and free of financial interests in study results. However, no claim denying conflicts of interest was made.

Note: For more information, please see Supplemental Material, "The Navigation Guide instructions for making risk of bias determinations"

Data abstraction items

Study Characteristic Items	**Risk of Bias Items**
Target population	Recruitment strategy for participants
Total number of study participants	Recruitment strategy for comparator/controls
Characteristics of participants (age, gender, etc.)	Response Rate
Type of exposure assessed	Blinding measures in place
Characteristics of comparator/controls	Confounding variables measured/assessed
Type of health outcome assessed	Exposure assessment methods
Method of health outcome assessment	Time of exposure measurement
Time of health outcome measurement	Location of exposure measurement
Year of publication	Strategy for addressing missing outcome data
Study setting	Evidence of selective outcome reporting
Study design	Other sources of methodological bias
Publication status	Financial conflict of interest
Association measured	
Major finding/conclusions of study	
Notes	

Screening form

Does the publication report or measure uranium, its corrosion products, or ionizing radiation in Iraq or surrounding areas?

Uranium corrosion products may include uranium oxides and uranyl ions, while exposure to ionizing radiation may include alpha, beta, or gamma rays. Studies that only measure or report exposure to UV radiation (i.e. solar radiation) are excluded. Levels or concentrations of ionizaing radiation or uranium should be measured/reported in Iraq or surrounding areas such as Kuwait.

☐ NO → Exclude, and note reason in Excel
☐ Yes → Go to the next question

Does the publication report or measure health outcomes or disease states in humans?

Do not restrict to only birth outcomes at this stage. Outcomes ought to be clinical or "patient important", i.e. exclude if they only measure uranium concentrations in human tissues.

☐ NO → Exclude, and note reason in Excel
☐ Yes → Go to the next question

Is the study population Iraqi?

Does the human population for which health outcomes are reported include or consist entirely of Iraqi nationals? Exclude studies that only report health outcomes in populations of military veterans (of the US or other nationalities) who fought during the 1990 or 2003 Iraq Wars.

☐ NO → Exclude, and note reason in Excel
☐ Yes → Go to the next question

Does the publication include or report primary research?

Exclude review articles, including systematic reviews, which do not contain or report primary research.

☐ NO → Exclude, and note reason in Excel
☐ Yes → Go to the next question

Does the study include a nonexposed (or lesser exposed) comparator or control group?

Exclude single-arm, non-comparator studies.

☐ NO → Exclude, and note reason in Excel
☐ Yes → INCLUDE

The Navigation Guide instructions for making risk of bias determinations

1. **Was the strategy for recruiting participants consistent across study groups?**

   Criteria for a judgment of 'YES' (i.e. low risk of bias):

   Protocols for recruitment and inclusion/exclusion criteria were applied similarly across study groups, and any one of the following:

   - Study participants were recruited from the same population at the same time frame; or
   - Study participants were not all recruited from the same population, but proportions of participants from each population in each study group are uniform

   Criteria for the judgment of 'PROBABLY YES' (i.e. probably low risk of bias):

   There is insufficient information about participant selection to permit a judgment of 'YES', but there is indirect evidence that suggests that participant recruitment and inclusion/exclusion criteria was consistent, as described by the criteria for a judgment of 'YES'.

   Criteria for the judgment of 'NO' (i.e. high risk of bias)

   Any one of the following:

   - Protocols for recruitment or inclusion/exclusion criteria were applied differently across study groups; or
   - Study participants were recruited at different time frames; or
   - Study participants were recruited from different populations and proportions of participants from each population in each study group are not uniform

   Criteria for the judgment of 'PROBABLY NO' (i.e. probably high risk of bias):

   There is insufficient information about participant selection to permit a judgment of 'NO', but there is indirect evidence that suggests that participant recruitment or inclusion/exclusion criteria was inconsistent, as described by the criteria for a judgment of 'NO'.

   Criteria for the judgment of 'NOT APPLICABLE' (risk of bias domain is not applicable to study):

   There is evidence that participant selection is not an element of study design capable of introducing risk of bias in the study.

2. **Was knowledge of the exposure groups adequately prevented during the study?**

   Criteria for a judgment of 'YES' (i.e. low risk of bias):

Any one of the following:

- No blinding, but the review authors judge that the outcome and the outcome measurement are not likely to be influenced by lack of blinding; or
- Blinding of key study personnel ensured, and unlikely that the blinding could have been broken; or
- Some key study personnel were not blinded, but outcome assessment was blinded and the non-blinding of others unlikely to introduce bias.

Criteria for the judgment of 'PROBABLY YES' (i.e. probably low risk of bias):

There is insufficient information about blinding to permit a judgment of 'YES', but there is indirect evidence that suggests the study was adequately blinded, as described by the criteria for a judgment of 'YES'.

Criteria for the judgment of 'NO' (i.e. high risk of bias):

Any one of the following:

- No blinding or incomplete blinding, and the outcome or outcome measurement is likely to be influenced by lack of blinding; or
- Blinding of key study personnel attempted, but likely that the blinding could have been broken; or
- Some key study personnel were not blinded, and the non-blinding of others likely to introduce bias.

Criteria for the judgment of 'PROBABLY NO' (i.e. probably high risk of bias):

There is insufficient information about blinding to permit a judgment of 'NO', but there is indirect evidence that suggests the study was not adequately blinded, as described by the criteria for a judgment of 'NO'.

Criteria for the judgment of 'NOT APPLICABLE' (risk of bias domain is not applicable to study):

There is evidence that blinding is not an element of study design capable of introducing risk of bias in the study.

3. Were exposure assessment methods robust?

Criteria for a judgment of 'YES' (i.e. low risk of bias):

The reviewers judge that there is low risk of exposure misclassification and any one of the following:

- There is high confidence in the accuracy of the exposure assessment methods; or
- Less-established or less direct exposure measurements are validated against well-established or direct methods AND if applicable, appropriate QA/QC for methods are described and are satisfactory, with at least three of the following items reported, or at least two of the following items reported plus evidence of

satisfactory performance in a high quality inter-laboratory comparison: Limit of detection or quantification; standards recovery; measure of repeatability; investigation and prevention of blanks contamination.

Criteria for the judgment of 'PROBABLY YES' (i.e. probably low risk of bias):

There is insufficient information about the exposure assessment methods to permit a judgment of 'YES', but there is indirect evidence that suggests that methods were robust, as described by the criteria for a judgment of 'YES'. Studies only reporting that the QA/QC items above were satisfactory but not reporting all of the actual numbers may receive a judgment of "probably yes."

Criteria for the judgment of 'NO' (i.e. high risk of bias):

The reviewers judge that there is high risk of exposure misclassification and any one of the following:

- There is low confidence in the accuracy of the exposure assessment methods; or
- Less-established or less direct exposure measurements are not validated and are suspected to introduce bias that impacts the outcome assessment (example: participants are asked to report exposure status retrospectively, subject to recall bias)
- Uncertain how exposure information was obtained

Criteria for the judgment of 'PROBABLY NO' (i.e. probably high risk of bias):

There is insufficient information about the exposure assessment methods to permit a judgment of 'NO', but there is indirect evidence that suggests that methods were not robust, as described by the criteria for a judgment of 'NO'.

Criteria for the judgment of 'NOT APPLICABLE' (risk of bias domain is not applicable to study):

There is evidence that exposure assessment is not an element of study design capable of introducing risk of bias in the study.

4. Were outcome assessment methods robust?

Criteria for a judgment of 'YES' (i.e. low risk of bias):

The reviewers judge that there is low risk of outcome misclassification, i.e.:

- Outcomes were assessed and defined consistently across all study participants, using valid and reliable measures; or
- Less-established or less direct outcome measurements are validated against well-established or direct methods; or
- Appropriate sensitivity analyses were conducted that suggest the influence of outcome misclassification would be minimal

- AND, if applicable, appropriate QA/QC for methods is described and is satisfactory.

Criteria for the judgment of 'PROBABLY YES' (i.e. probably low risk of bias):

There is insufficient information about the outcome assessment methods to permit a judgment of low risk of bias, but there is indirect evidence which suggests that methods were robust, as described by the criteria for a judgment of low risk of bias. Appropriate QA/QC for methods are not described but the review authors judge that the outcome and the outcome assessment are objective and uniform across study groups.

Criteria for the judgment of 'PROBABLY NO' (i.e. probably high risk of bias):

There is insufficient information about the outcome assessment methods to permit a judgment of high risk of bias, but there is indirect evidence which suggests that methods were not robust, as described by the criteria for a judgment of high risk of bias.

Criteria for the judgment of 'PROBABLY NO' (i.e. probably high risk of bias):

The reviewers judge that there is high risk of outcome misclassification and any one of the following:

- There is low confidence in the accuracy of the outcome assessment methods; or
- Less-established or less direct outcome measurements are not validated and are suspected to introduce bias that impacts the outcome assessment
- Uncertain how outcome information was obtained

Criteria for the judgment of 'NOT APPLICABLE' (risk of bias domain is not applicable to study):

There is evidence that outcome assessment methods are not capable of introducing risk of bias in the study.

5. Was confounding adequately addressed?

Criteria for a judgment of 'YES' (i.e. low risk of bias):

The study accounted for (i.e., matched, stratified, multivariate analysis or otherwise statistically controlled for) important potential confounders, or reported that potential confounders were evaluated and omitted because inclusion did not substantially affect the results. The determination of specific confounders may be informed by the data, including the studies included in the review.

Criteria for the judgment of 'PROBABLY YES' (i.e. probably low risk of bias):

The study accounted for most but not all of the important potential confounders AND this lack of accounting is not expected to introduce substantial bias.

Criteria for the judgment of 'NO' (i.e. high risk of bias):

The study did not account for or evaluate important potential confounders.

Criteria for the judgment of 'PROBABLY NO' (i.e. probably high risk of bias):

The study accounted for some but not all of the important potential confounders AND this lack of accounting may have introduced substantial bias.

6. Were incomplete outcome data adequately addressed?

Criteria for a judgment of 'YES' (i.e. low risk of bias):

Participants were followed long enough to obtain outcome measurements and any one of the following:

- No missing outcome data; or
- Reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias); or
- Missing outcome data balanced in numbers across exposure groups, with similar reasons for missing data across groups; or
- For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a biologically relevant impact on the intervention effect estimate; or
- For continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes not enough to have a biologically relevant impact on observed effect size; or
- Missing data have been imputed using appropriate methods

Criteria for the judgment of 'PROBABLY YES' (i.e. probably low risk of bias):

There is insufficient information about incomplete outcome data to permit a judgment of 'YES', but there is indirect evidence that suggests incomplete outcome data was adequately addressed, as described by the criteria for a judgment of 'YES'.

Criteria for the judgment of 'NO' (i.e. high risk of bias):

Participants were not followed long enough to obtain outcome measurements OR any one of the following:

- Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across exposure groups; or

- For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce biologically relevant bias in intervention effect estimate; or
- For continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes enough to induce biologically relevant bias in observed effect size; or
- Potentially inappropriate application of imputation.

Criteria for the judgment of 'PROBABLY NO' (i.e. probably high risk of bias):

There is insufficient information about incomplete outcome data to permit a judgment of 'NO', but there is indirect evidence that suggests incomplete outcome data was not adequately addressed, as described by the criteria for a judgment of 'NO'.

Criteria for the judgment of 'NOT APPLICABLE' (risk of bias domain is not applicable to study):

There is evidence that incomplete outcome data is not capable of introducing risk of bias in the study.

7. Are reports of the study free of suggestion of selective outcome reporting?

Criteria for a judgment of 'YES' (i.e. low risk of bias):

All of the study's pre-specified (primary and secondary) outcomes outlined in the protocol, methods, abstract, and/or introduction that are of interest in the review have been reported in the pre-specified way.

Criteria for the judgment of 'PROBABLY YES' (i.e. probably low risk of bias):

There is insufficient information about selective outcome reporting to permit a judgment of 'YES', but there is indirect evidence that suggests the study was free of selective reporting, as described by the criteria for a judgment of 'YES'.

Criteria for the judgment of 'NO' (i.e. high risk of bias):

Any one of the following:

- Not all of the study's pre-specified primary outcomes (as outlined in the protocol, methods, abstract, and/or introduction) have been reported; or
- One or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. subscales) that were not pre-specified; or
- One or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected effect); or
- One or more outcomes of interest are reported incompletely

Criteria for the judgment of 'PROBABLY NO' (i.e. probably high risk of bias):

There is insufficient information about selective outcome reporting to permit a judgment of 'NO', but there is indirect evidence that suggests the study was not free of selective reporting, as described by the criteria for a judgment of 'NO'.

Criteria for the judgment of 'NOT APPLICABLE' (risk of bias domain is not applicable to study):

There is evidence that selective outcome reporting is not capable of introducing risk of bias in the study.

8. Was the study apparently free of other problems that could put it at a risk of bias?

Criteria for a judgment of 'YES' (i.e. low risk of bias):

The study appears to be free of other sources of bias.

Criteria for the judgment of 'PROBABLY YES' (i.e. probably low risk of bias):

There is insufficient information to permit a judgment of 'YES', but there is indirect evidence that suggests the study was free of other threats to validity.

Criteria for the judgment of 'NO' (i.e. high risk of bias):

There is at least one important risk of bias. For example, the study:

- Had a potential source of bias related to the specific study design used; or
- Stopped early due to some data-dependent process (including a formal-stopping rule); or
- Had extreme imbalance of characteristics among exposure groups; or
- Had differential surveillance for outcome between exposure groups or between exposed/unexposed groups
- The conduct of the study is affected by interim results (e.g. recruiting additional participants from a subgroup showing greater or lesser effect); or
- An insensitive instrument is used to measure outcomes (which can lead to under-estimation of both beneficial and harmful effects); or
- Selective reporting of subgroups; or • Has been claimed to have been fraudulent; or
- Had some other problem

Criteria for the judgment of 'PROBABLY NO' (i.e. probably high risk of bias):
There is insufficient information to permit a judgment of 'NO', but there is indirect evidence that suggests the study was not free of other threats to validity, as described by the criteria for a judgment of 'NO'.

Criteria for the judgment of 'NOT APPLICABLE' (risk of bias domain is not applicable to study):

There is evidence that other potential threats to validity are not capable of introducing risk of bias in the study.

9. Was the study free of support from a company, study author, or other entity having a financial interest in any of the exposures studied?

Criteria for a judgment of 'YES' (i.e. low risk of bias):

The study did not receive support from a company, study author, or other entity having a financial interest in the outcome of the study. Examples include the following:

- Funding source is limited to government, non-profit organizations, or academic grants funded by government, foundations and/or non-profit organizations;
- Chemicals or other treatment used in study were purchased from a supplier;
- Company affiliated staff are not mentioned in the acknowledgements section;
- Authors were not employees of a company with a financial interest in the outcome of the study;
- Company with a financial interest in the outcome of the study was not involved in the design, conduct, analysis, or reporting of the study and authors had complete access to the data;
- Study authors make a claim denying conflicts of interest;
- Study authors are unaffiliated with companies with financial interest, and there is no reason to believe a conflict of interest exists;
- All study authors are affiliated with a government agency (are prohibited from involvement in projects for which there is a conflict of interest or an appearance of conflict of interest).

Criteria for the judgment of 'PROBABLY YES' (i.e. probably low risk of bias):

There is insufficient information to permit a judgment of 'YES', but there is indirect evidence that suggests the study was free of support from a company, study author, or other entity having a financial interest in the outcome of the study, as described by the criteria for a judgment of 'YES'.

Criteria for the judgment of 'NO' (i.e. high risk of bias):

The study received support from a company, study author, or other entity having a financial interest in the outcome of the study. Examples of support include:

- Research funds;
- Chemicals provided at no cost;
- Writing services;
- Author/staff from study was employee or otherwise affiliated with company with financial interest;

- Company limited author access to the data;
- Company was involved in the design, conduct, analysis, or reporting of the study;
- Study authors claim a conflict of interest

Criteria for the judgment of 'PROBABLY NO' (i.e. probably high risk of bias):

There is insufficient information to permit a judgment of 'NO', but there is indirect evidence that suggests the study was not free of support from a company, study author, or other entity having a financial interest in the outcome of the study, as described by the criteria for a judgment of 'NO'.

Criteria for the judgment of 'NOT APPLICABLE' (risk of bias domain is not applicable to study):

There is evidence that conflicts of interest are not capable of introducing risk of bias in the study.

Full text exclusion justifications

Include Report met all inclusion criteria, as specified in the PECOS statement	[1-33]
Exclude – Exposure Study did not measure or report exposure to weaponized uranium in Iraq	[34-74]
Exclude – Outcome Study did not measure or report patient-important health outcomes	[75-121]
Exclude – Population Study population was not Iraqi	[122-147]
Exclude – Study Design: Primary research Study did not contain original data or analysis	[148-203]
Exclude – Study Design: Comparator Non-comparator study	[204-225]

Include

1. Abdul-Wahid R. 2009. Depleted uranium effects on immunophenotyping of human lymphocytes in southern iraq. Iraqi Journal of Community Medicine 22(4):249-253.
2. Al-Hamadany WS, Saleh DS, Shanshal MA. 2012. Radiation pollution in cancer and other diseases using some immunological and clinical parameters. The Iraqi Journal of Veterinary Medicine 36(2):33-40.
3. Al-Hamzawi AA, Jaafar MS, Tawfiq NF. 2014. Uranium concentration in blood samples of southern Iraqi leukemia patients using CR-39 track detector. Journal of Radioanalytical and Nuclear Chemistry 299:1267-1272. PMID: 26224958, https://doi.org/10.1007/s10967-013-2808-0.
4. Al-Hamzawi AA, Jaafar MS, Tawfiq NF. 2015. Concentration of uranium in human cancerous tissues of southern Iraqi patients using fission track analysis. Journal of Radioanalytical and Nuclear Chemistry 303:1703-1709. https://doi.org/10.1007/s10967-014-3682-0.

5. Al-Hashimi MMY, Wang X. 2013. Comparing the cancer in Ninawa during three periods (1980-1990, 1991-2000, 2001-2010) using poisson regression. Journal of Research in Medical Sciences 18(12):1026-1039. PMID: 24523792.
6. Al-Jobori S. 2013. Track detection technique using cr-39 for determining depleted uranium in biological specimens. Journal of Medenat Alelem College 5(2):5-14.
7. Al-Rudainy LA, Ajeel NA, Al-Saad HT. 2009a. Depleted uranium and incidence of cancer in Basrah: A preliminary ecological study. The Medical Journal of Basrah University 27(1):1-6.
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