Received 19.12.2023
Accepted 16.07.2024

EDN: CHYTNG

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DOI: 10.24287/1726-1708-2024-23-3-44-50

A comparison of radon and uranium concentrations with the concentrations of some trace elements in lung cancer samples

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Lung cancer is one of the deadliest cancers in the world. Since this malignancy is influenced by a variety of genetic, environmental, and occupational factors, early diagnosis helps to enhance care and improve treatment outcomes. In this study, we measured the concentrations of some trace elements using the atomic absorption spectroscopy, while radon and uranium concentrations were measured using a nuclear track detector (CR-39) and were then compared to the levels of the trace elements. The study protocol was approved by the local ethics committee. Lung cancer samples were collected at the National Hospital for Oncology and Hematology and medical clinics in the Najaf Governorate, between March 2022 and June 2023. The levels of uranium and four elements (zinc, copper, lead and cadmium) were measured in the serum samples of the affected patients and the controls of both genders. While the cancer patients of both genders had the highest average radon concentrations, lifetime risk ratios and uranium levels, their zinc concentrations were lower than in the healthy controls. The average amounts of copper, cadmium, and lead in the blood samples from the lung cancer patients were greater than those in the control group. There was a positive correlation between uranium concentrations and copper, lead and cadmium levels (indicating that these elements are influenced by mechanical and biological changes), while zinc and uranium concentrations were inversely correlated. A statistical comparison of radon concentrations in both studied groups of both genders revealed that the mean radon levels were significantly higher in the cancer patients compared to the healthy subjects.
Key words: *trace elements, uranium, lung cancer, Iraq*

Ahmed Ali Ghali Al-Khayfawee, et al. Pediatric Hematology/Oncology and Immunopathology 2024; 23 (3): 44–50. DOI: 10.24287/1726-1708-2024-23-3-44-50

Trace elements are nutritionally essential and must be included in a person's diet. They support such important biological functions as metabolism, tissue healing, growth, and development. People must consume these through their diet or take them as supplements because the human body cannot produce them naturally [1]. However, these elements can be dangerous if consumed in excess. Iron, copper, cobalt, zinc, selenium, chromium, iodine, and molybdenum are all essential micronutrients [2]. Numerous epidemiological studies and experiments on animals demonstrated that trace element deficiencies are the root cause of many health issues [3]. It was shown that a lack of certain trace elements (zinc, in particular) contributes to immune dysfunctions, faster HIV progression, abnormal pregnancies, developmental delays in children and taste disorders [3]. Selenium deficiency was reported to be linked to an increase in cancer and ischemic heart disease rates, while chromium deficiency was associated with the onset of diabetes mellitus and atherosclerosis [4]. This is evidenced by epidemiological studies on hundreds of uranium miners around the world (UNSCEAR, 2000) [5]. Lung cancer can also result from radon exposure in homes (WHO, 2002) [6] and when radon exposure and smoking are combined, the risk of developing lung cancer increases dramatically. It is thought to rise in a linear fashion with radon exposure. Although the risk increases with higher levels of radon concentration and longer periods of exposure, lung cancer from domestic radon exposure is significantly less common than that from radon exposure in mines [8]. The lifetime risk (LTR) of developing lung cancer from residential radon exposure levels of 20 $Bq \cdot m^{-3}$ is 0.3% (3 deaths per 1000 people) (WHO, 2002).

Heavy metal and trace element concentrations in humans have drawn a lot of attention in recent years. It is important to understand whether variations in the concentration of these elements can lead to toxicity or malignant disorders [9]. Since trace elements are required by living organisms only in minute amounts, their excess can result in death or severe dysfunctions. In living tissues, trace element concentrations range from 0.01 to 100 mg/kg. If people or animals consume large amounts of food over an extended period of time, all these necessary trace elements can become harmful [10]. Trace elements do not have detrimental effects when present in low concentrations, which is the primary distinction between them and heavy metals. Heavy metals are generally dangerous even in relatively small amounts. Body fluids and tissues accumulate a large number of trace elements which, depending on their chemical makeup, can perform a variety of functions [11]. One study showed that patients newly diagnosed with infections had the highest concentrations of trace elements and that the chemotherapy group had higher levels of uranium, radium, and radon in female plasma samples compared to the healthy population. The daily dose of alpha particles from radon progeny (^{218}po, ^{214}po) was the lowest in the healthy controls, while the largest dose was reported in the cases with new infections, followed by the patients undergoing chemotherapy [12]. There were many studies comparing trace element concentrations in healthy subjects and breast cancer patients [13]. Some researchers also studied concentrations in nails, hair and blood serum samples of diabetic patients [14, 15]. Another study carried out in Najaf, Iraq, that included 101 blood serum samples collected from the patients at the Middle Euphrates Cancer Centre revealed that the cancer patients had higher lead and cadmium concentrations in their blood [16]. There were many studies on the effect of trace element concentrations on lung cancer and breast cancer [13, 17].

The aim of this study was to compare trace element levels with uranium concentration and determine whether high or low concentrations of trace elements in the body can increase the risk of developing lung cancer.

MATERIALS AND METHODS

The study protocol was approved by the local ethics committee.

Cadmium

Food is the main source of cadmium exposure, and tobacco smoking is a major cause of cadmium toxicity which can lead to other health issues like cancer, heart disease, and hypertension. Cadmium is classified as a human carcinogen [18]. It is a highly toxic metal that can enter the environment through natural processes or industrial pollution and is found in many places including Belgium, Sweden, the United Kingdom, Japan and China. Cadmium exposure occurs mainly through the consumption of contaminated drinking water or food (such as leafy vegetables, cereals, organ meats, and crustaceans), inhalation of polluted air or work in certain industries. Because tobacco leaves accumulate cadmium similarly to some plant-based foods, smoking tobacco adds an additional burden of cadmium. Smokers have around twice as much cadmium in their bodies as non-smokers [18].

Copper

Copper is essential for the function of numerous enzymes, which play a significant role in human metabolism. Acidic environments facilitate the solubility of copper ions, thus allowing them to enter the food chain in cupric or cuprous form. In contrast to copper deficiency, copper toxicity is very uncommon in plants. Copper toxicity is usually caused by environmental exposures in animals and humans that have genetic defects in copper metabolism. The richest dietary sources of copper include liver, oysters and other shellfish, dried fruit, milk and dairy products, sesame seeds, sunflower seeds, tahini, and sun-dried tomatoes [19]. Copper in human blood is mostly found in plasma and red blood cells. In red blood cells, around 60% of copper is bound to the metalloenzyme copper-zinc superoxide dismutase; the remaining 40% is weakly bound to other proteins and amino acids [20].

Lead

There is no feedback mechanism which would limit the absorption of lead in case of a large body burden of this element. Absorbed lead is mostly eliminated through urinary excretion, while lead that is not absorbed is mostly excreted in the feces. Lead and calcium share similar properties, meaning that the distribution of lead throughout the body is somewhat similar to that of calcium. Physiological regulators of calcium metabolism regulate lead metabolism in a similar manner. The bones contain over 90% of total lead in the body. Increased bone turnover in some pathological conditions, such as osteoporosis, and physiological states, such as pregnancy or breastfeeding, result in a higher release of lead from bones. Lead and calcium are released during bone resorption. Lead can be remobilized from bones back into the bloodstream by competing with calcium for binding and transport sites [21].

Zinc

Zinc is an omnipotent metal of amphoteric nature that tends to react both with acidic and alkaline compounds. The adult body contains about 2–3 grams of zinc. Around 95% of body zinc is intracellular, and the rest is distributed in plasma. The daily need for zinc is between 15 and 20 mg. Copper and zinc compete for absorption from the small intestine. Zinc is primarily excreted through the gastrointestinal tract (2–5 mg every day). It can also be excreted via urine and sweat. Reduced plasma zinc levels are caused by infections, cancer, acute myocardial infarction, blood loss, pregnancy, fluid loss, and the use of oral contraceptives [19].

Experimental methods

Atomic absorption spectroscopy

This is a method of analytical chemistry used for the quantitative measurement of certain elements (analytes) in samples. Atomic absorption spectroscopy (*figure 1*) can be applied to identify more than 70 different elements in solutions or directly in solid samples by means of electrothermal vaporization [22]. The radiation source (a lamp) emits a sharp line spectrum characteristic of the analyte element. The emission beam from the radiation source is then modulated, and the modulated signal passes through the atomic vapour where the radiation is absorbed by the atoms of the analyte. After selection of the desired spectral line by the monochromator, the isolated analyte line falls on the detector, where the light signal is converted into the electric signal. This signal is then amplified by a selective amplifier and recorded by a computer or other reading device [23].

Solid-state nuclear track detectors

Solid-state nuclear track detection (SSNTD) method is easy to use and reasonably priced. The formation of latent tracks and their subsequent development (visualization) via chemicals or other techniques are the two key processes in SSNTD. SSNTDs are widely used in a large number of fields, including nuclear physics, dosimetry, biology, and medical physics. SSNTDs can be generally divided into 2 types:

– organic detectors made of polymers like Lexan, Makrofol, LR-115, CR-39, CN-85, etc;

– inorganic detectors, such as crystals or glasses.

Methodology

This type of device can be used to determine radon concentrations (*figure 2*) by recording tracks of alpha particles emitted from radon. Track density (tracks/cm^2) is calculated using the following formula [12]:

$$\textit{Track density } (\rho) = \frac{\textit{Average number of tracks}}{\textit{field of view area}} \quad (1),$$

After determining the density of the tracks, radon activity concentration C^a_{Rn} (Bq/m^3) can be measured in the headspace of the container at the top of the sample. Radon activity concentration is calculated using the following formula [25]:

$$C^a_{Rn} = \frac{\rho}{KT} \quad (2),$$

where ρ is radon-related alpha track density, K is a calibration factor (or diffusion constant) which varies depending on the geometric dimensions of diffusion chambers), and T is time of detector exposure.

Figure 1
Atomic absorption spectroscopy device

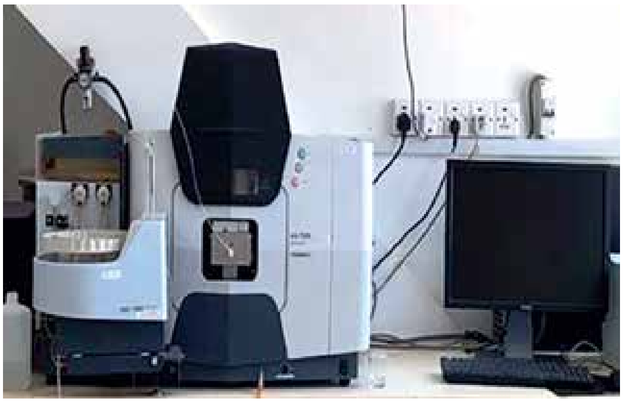
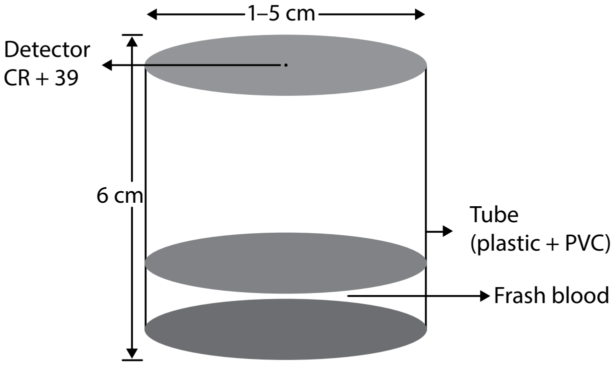


Figure 2
Schematic of the container for the measurement of radon concentration



Using the formula for radioactive equilibrium:

$$\lambda_U N_U = \lambda_{Rn} N_{Rn} \quad (3),$$

where λ_U is the decay constant of uranium, 4.9 × 10^{-18}/s, one may calculate the number of uranium atoms (N_U).

The weight of uranium (W_U) in a dry sample is calculated using the following formula [4]:

$$W_U = \frac{N_U A_U}{N_a} \quad (4),$$

where, A_U is the mass number of uranium (^{238}U), N_a is Avogadro's number, 6.02 × 10^{23}.

The concertation of uranium in a sample can be calculated using formula 5 [3]:

$$C_U = \frac{WU}{ws} \quad (5),$$

where *ws* is sample weight.

We also calculated the LTR (%) of developing lung cancer from radon exposure (ICRP, 1993).

Sample preparation and collection

A total of 50 blood and serum samples were collected from the patients with lung cancer (25 females and 25 males) at the National Hospital for Oncology and Hematology. Blood samples were processed (dried and grinded) as required by the methods used to measure radon concentration and other variables [12].

Serum samples were used to measure the concentrations of the studied trace elements. They were prepared using the digestion method [26]. In our study, there were 10 samples obtained from the female healthy controls and 15 samples obtained from the male controls. These samples were collected in cooperation with the Oncology Center and the Blood Bank. The female participants were aged between 40 and 50 years, and the male participants were aged between 40 and 60 years, both healthy controls and lung cancer patients. The preparation, storage, and digestion of the samples were carried out according to the international recommendations [23].

RESULTS AND DISCUSSION

Tables 1, 2 show radon concentration and LTR of developing lung cancer from exposure to radon. We measured radon concentration in the blood samples of the males and the females and compared the mean, maximum and minimum values in the lung cancer patients and the healthy controls of both genders.

As seen in *tables 1, 2*, the mean radon concentration in the blood samples of the healthy females was higher than the mean radon concentration in the blood samples of the healthy males. The same observation was found for LTR.

As regards radon concentration in the blood samples of the lung cancer patients, the females showed lower radon concentration than the males, as well as lower LTR.

Using the aforementioned formulas, we determined radon concentration levels in the headspace of the containers with blood of lung cancer patients and healthy controls. The mean radon concentration in the female lung cancer patients was 85.771 (Bq/m^3), compared to 17.4424 (Bq/m^3) in the healthy females. A similar correlation between the mean radon concentration levels was observed in males: 104.58 (Bq/m^3) – in the male lung cancer patients, 15.7284 (Bq/m^3) – in the healthy males.

We also compared radon concentration levels between the males and females and found that the male lung cancer patients had higher radon concentration levels than the female lung cancer patients, while the healthy males had lower radon concentration levels than the healthy females.

When comparing values of LTR (%) of developing lung cancer from the exposure to radon, we observed a positive correlation between radon concentration level and LTR for both genders.

Using statistical analysis, we drew *figure 3, 4* demonstrating a comparison between two genders.

Table 1
Radon concentrations (Bq/m^3) in the blood samples of the male and female healthy controls and their LTR (%) of developing lung cancer from the exposure to radon

Sq.	Female		Male	
	H.C.	LTR %	H.C.	LTR %
1	35.614	0.00356	21.687	0.00217
2	28.651	0.00287	18.253	0.00183
3	8.619	0.00086	19.970	0.00200
4	19.112	0.00191	8.714	0.00087
5	19.970	0.00200	11.290	0.00113
6	23.404	0.00234	12.148	0.00121
7	6.902	0.00069	21.687	0.00217
8	9.573	0.00096	20.829	0.00208
9	10.431	0.00104	23.404	0.00234
10	12.148	0.00121	20.829	0.00208
11	-	-	11.290	0.00113
12	-	-	21.687	0.00217
13	-	-	13.007	0.00130
14	-	-	6.806	0.00068
15	-	-	4.326	0.00043
Mean	17.4424	0.00174	15.7284	0.00157
Max	35.614	0.00356	23.404	0.00234
Min	6.902	0.00069	4.326	0.00043

Note. H.C. – healthy controls.

Table 2
Radon concentrations (Bq/m^3) in the blood samples of the male and female lung cancer patients and their LTR (%) of developing lung cancer from the exposure to radon

Sq.	Female		Male	
	H.C.	LTR %	H.C.	LTR %
1	136.349	0.01363	71.195	0.00712
2	76.442	0.00764	78.159	0.00782
3	64.136	0.00641	79.876	0.00799
4	79.876	0.00799	95.521	0.00955
5	48.587	0.00486	100.767	0.01008
6	95.521	0.00955	81.688	0.00817
7	51.258	0.00513	89.415	0.00894
8	167.639	0.01676	124.139	0.01241
9	100.767	0.01008	96.379	0.00964
10	68.619	0.00686	61.656	0.00617
11	92.086	0.00921	101.626	0.01016
12	33.897	0.00339	110.307	0.01103
13	43.436	0.00434	112.024	0.01120
14	81.688	0.00817	125.951	0.01260
15	58.222	0.00582	110.307	0.01103
16	33.897	0.00339	200.55	0.02006
17	88.557	0.00886	138.925	0.01389
18	110.307	0.01103	72.912	0.00729
19	130.244	0.01302	85.027	0.00850
20	39.048	0.00390	138.067	0.01381
21	75.583	0.00756	124.139	0.01241
22	153.711	0.01537	135.491	0.01355
23	141.501	0.01415	129.386	0.01294
24	142.550	0.01426	90.274	0.00903
25	30.368	0.00304	60.797	0.00608
Mean	85.771	0.00858	104.583	0.01046
Max	167.639	0.01676	200.55	0.02006
Min	30.368	0.00304	60.797	0.00608

Note. L.C. – lung cancer patients.

Figures 3, 4 and table 3 showed that radon concentration (Bq/m^3) in the blood serum of the women with lung cancer was higher than that in the healthy women, and it had a high statistical significance; the same result was observed in the men, which indicated that radon concentration was higher in those with lung cancer (for both genders). It is possible to say that it may be among the causes of lung cancer development.

Using statistical analysis, we drew *figure 3, 4* demonstrating a comparison between two genders. *Figures 3, 4* and *table 3* showed that radon concentration (Bq/m^3) in the blood serum of the women with lung cancer was higher than that in the healthy women, and it had a high statistical significance; the same result was observed in the men, which indicated that radon concentration was higher in those with lung cancer (for both genders). It is possible to say that it may be among the causes of lung cancer development.

The mean concentration of uranium was compared with the mean concentration of the four elements (zinc, copper, lead, and cadmium) for both healthy controls and lung cancer patients. It was observed that the female patients had a higher level of uranium content than the healthy females (*figure 5*).

A similar observation was found for copper, lead, and cadmium, indicating that the elements are subject to mechanical and biological changes. Our findings concurred with those of multiple research studies [16, 17, 27, 28]. As regards zinc, the correlation was opposite: the healthy controls had a higher level of zinc content than the lung cancer patients.

Our analysis showed that the male patients had a higher level of uranium concentration than the male healthy controls. Moreover, a similar observation was found for copper, lead, and cadmium, indi-

Figure 3
Comparison of the mean differences in radon concentrations in blood samples of the healthy females and the female lung cancer patients

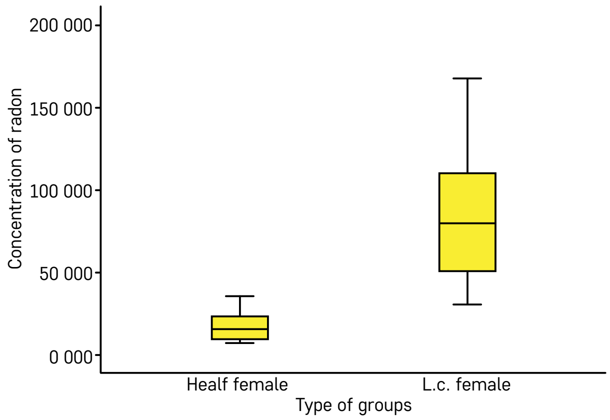


Figure 4
Comparison of the mean differences in radon concentrations in the blood samples of the healthy males and the male lung cancer patients

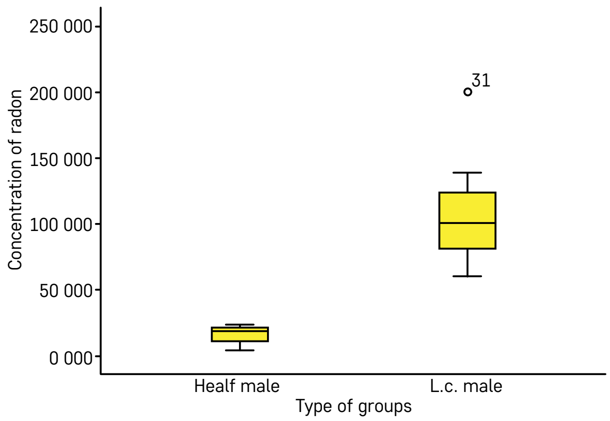


Table 3
Statistical results of Levene's test using the SPSS Statistics program for the analysis of radon concentration in the participants of both genders

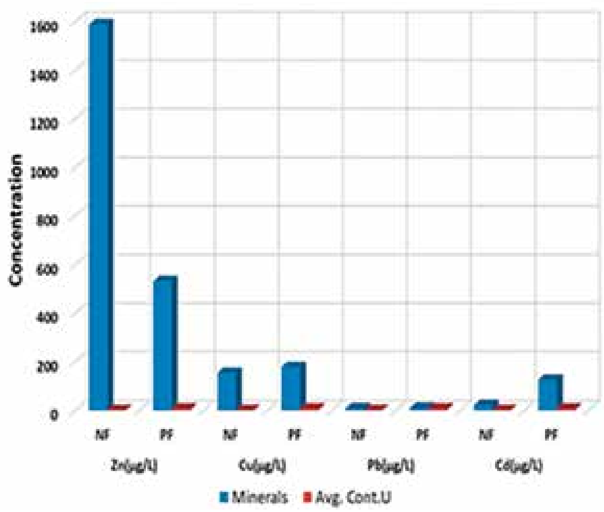
Group	*n*	Mean	SD	Levene's test		*p*-value
				F	Sig.	
H.C. (female)	10	17.4424	9.5952	12.153	0.001	0.000**
L.C. (female)	25	85.7715	40.7826			
H.C. (male)	15	15.7284	6.3261	13.303	0.001	0.000**
L.C. (male)	25	104.5831	31.040			

*Note. ** – p-value was significant; H.C. – healthy controls; L.C. – lung cancer patients.*

Table 4
Mean concentrations of the trace elements and uranium in blood and serum samples of the healthy controls and the lung cancer patients (both genders)

Type of element	Study group	Female	Male
Zn, μg/L	Healthy controls	1588.83	1247.02
	Lung cancer patients	531.54	666.75
Cu, μg/L	Healthy controls	152.45	155.61
	Lung cancer patients	176.46	218.59
Pb, μg/L	Healthy controls	8.3	5.38
	Lung cancer patients	10.28	13.4
Cd, μg/L	Healthy controls	21.41	14.02
	Lung cancer patients	123.74	60.87
U, ppb	Healthy controls	1.371	1.237
	Lung cancer patients	6.745	8.224

Figure 5
Mean concentrations of uranium and the trace elements in the healthy females and the females patients

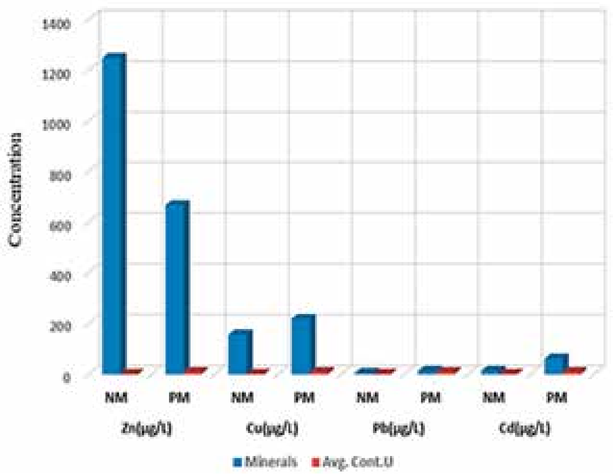


cating that these elements are subject to biological and mechanical changes. In contrast, zinc exhibited an opposite correlation, as shown in *table 4* and *figure 6*: zinc concentration level was higher in the healthy controls when compared to the male patients.

CONCLUSION

The values of radon concentrations and the percentage of LTR in the cancer patients were higher than in the healthy controls; moreover, these values were higher in the male cancer patients when compared to the female cancer patients.

Figure 6
Mean concentrations of uranium and the trace elements in the healthy males and the male patients



Statistical tests showed that radon concentrations in the serum of females and males with lung cancer were higher when compared to healthy controls of both genders, which indicates that an increased radon concentration level is one of the causes of lung cancer.

Another conclusion was made in terms of the correlation between trace elements and uranium concentrations. We observed a positive correlation between high levels of copper, lead, and cadmium and high mean concentration of uranium. An inverse correlation was seen between the level of zinc and high mean concentration of uranium. Thus, we can assume that an increase in radon concentration may have a connection to other elements and induce cancer.

ACKNOWLEDGMENTS
We thank all staff members of the Oncology Center (Iraq) for the facilities provided to accomplish this study.

FUNDING
The study was not supported by external funding.

CONFLICT OF INTEREST
The authors have no conflicts of interest to disclose.

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