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Misleading nomenclature in the IARC Monographs Programme: a straightforward solution to improve accuracy and clarity

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Abstract

The International Agency for Research on Cancer (IARC) Monographs Programme plays an important role in cancer prevention by identifying potential carcinogenic hazards. However, the terminology used in IARC's classifications and Monographs can confuse the public, health professionals, and policymakers. Terms like "carcinogenic to humans" imply causation, although classifications only indicate increased risk under certain conditions. For example, the lifetime incidence of mesothelioma among firefighters is approximately 14 in 10,000, compared to 7 in 10,000 in the general population. Despite doubling the risk, occupational exposure as a firefighter does not cause this type of cancer in 9,986 out of 10,000 firefighters. However, the IARC concludes that "occupational exposure as a firefighter causes mesothelioma" (IARC Working Group on the Identification of Carcinogenic Hazards to Humans. Occupational Exposure as a Firefighter. Lyon: IARC; 2023. pp. 1–730. PMID: 37963216). In addition, the lack of essential information about dosage and context in the IARC carcinogen lists can lead to agents with health benefits under certain conditions (e.g., solar radiation, red meat consumption, approved drugs) being perceived as universally harmful, discouraging beneficial exposures, behaviors, or treatments. Here, I propose renaming the groups of agents classified by the IARC and adding basic labels to specific agents to improve the accuracy and interpretability of the IARC classification lists. These adjustments do not interfere with the IARC's objective of identifying potential hazards, are easy to implement, and enhance accuracy and clarity, providing stronger support to guide cancer prevention strategies.

Keywords

International Agency for Research on Cancer, IARC classification, IARC groups, IARC list, carcinogen, carcinogenesis

Introduction

The Monographs Programme of the International Agency for Research on Cancer (IARC), a branch of the World Health Organization (WHO), plays a key role in cancer prevention by identifying potential

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carcinogenic hazards. Although IARC does not make policy recommendations, its classifications have a significant global impact, often influencing regulations and policies. Governments worldwide rely on IARC cancer classifications to develop a wide range of regulations, such as communicating cancer hazards, setting monitoring and reporting requirements, imposing usage restrictions, and establishing exposure limits to carcinogens [1–3]. For example, in 2009, the IARC Monographs Programme classified the use of UV-emitting tanning devices in Group 1 (carcinogenic to humans). After this classification, restrictions or bans on these devices were recommended or implemented, and a meta-analysis showed that the global use of indoor tanning significantly decreased following these restrictions [4]. This example shows how identifying hazards can encourage actions to prevent cancer [3].

As stated in its preamble, the IARC Monographs focus on identifying potential carcinogenic hazards, not on assessing the actual risk of cancer in exposed individuals. A carcinogenic hazard refers to an agent capable of causing cancer under specific conditions, while cancer risk measures the likelihood of cancer occurring at a specific level of exposure. The Monographs assess the strength of the evidence that an agent is a carcinogenic hazard under specific conditions, providing the first step in understanding potential risks associated with certain agents [1, 2, 5].

In risk assessment, there are four main steps: hazard identification, dose-response assessment, exposure assessment, and risk characterization. The IARC Monographs focus on hazard identification. This is an essential step but does not offer a complete risk assessment. Although the Monographs have been criticized for not performing all four steps [6], their objective is to identify hazards and encourage regulatory bodies to conduct the full risk assessments that guide specific policies and protections, a task beyond the scope of the Monographs Programme [7].

However, focusing on identifying potential hazards without undertaking a complete risk assessment can lead to confusion and concern if the findings are not presented accurately and clearly. For example, some agents provide health benefits at moderate exposures but may become harmful at higher exposures. Since the Monographs identify agents that can potentially cause cancer under certain, sometimes uncommon, conditions, beneficial agents at normal exposures can be classified as carcinogenic to humans under the IARC protocol. If dosage and context are not clearly specified, labeling these agents as carcinogenic to humans can confuse the public, health professionals, and policymakers [8].

The terminology used in the IARC classifications is another source of unnecessary confusion and concern. The term "carcinogenic to humans" used for Group 1 agents implies an inevitability of cancer causation. Etymologically, carcinogenic means "producing cancer" or "causing cancer". Many dictionaries define carcinogenic this way, which influences how the general population understands the term "carcinogenic to humans". For instance, according to the Oxford English Dictionary, carcinogenic means "that causes cancer or induces the malignant transformation of cells". Importantly, this literal meaning is also used in the final evaluation section of all Monographs for agents classified in Group 1. For example, according to the IARC's Monographs, "solar radiation causes cutaneous malignant melanoma, squamous cell carcinoma of the skin and basal cell carcinoma of the skin" [9], and "occupational exposure as a firefighter causes mesothelioma" [10]. These examples show that the IARC Monographs often use the terms "causes cancer" and "increases the risk of cancer" interchangeably.

The following example may clarify the distinction between "causes cancer" and "increases the risk of cancer". Based on SEER Incidence Data, 1975–2021, the lifetime incidence of mesothelioma in the general population is approximately 7 in 10,000 individuals. This estimate derives from an annual incidence rate of about 0.9 per 100,000 people, which, accumulated over an average lifespan of 80 years, yields a lifetime risk of 0.072%. Firefighters have about twice the risk of mesothelioma compared to the general population [11], resulting in a lifetime incidence of approximately 14 in 10,000 among firefighters. These data indicate that, while being a firefighter increases the risk of developing this cancer, it does not cause it in 9,986 out of 10,000 firefighters. However, the IARC states that "occupational exposure as a firefighter causes mesothelioma" [10]. If exposure to an agent results in cancer for 14 people but not for 9,986 people, is it accurate to say that exposure to the agent causes cancer? Wouldn't it be more precise to say that exposure to the agent increases the risk of cancer?

Using this inaccurate and alarming terminology might help discourage exposure to agents that are harmful in almost all scenarios, like tobacco smoke. However, the same terminology is also used for agents that are beneficial at certain doses or in specific contexts. For example, excessive exposure to solar radiation increases the risk of skin cancer, but normal sun exposure is essential for producing vitamin D, which is vital for human health. When dose or context determines whether an agent is beneficial or harmful, labels like "carcinogenic to humans" or "causes cancer" can mislead the public and discourage beneficial behaviors, ultimately harming their health. This misunderstanding has already occurred. The fact that the IARC, the cancer agency of the WHO, labels solar radiation as "carcinogenic to humans" has likely led many people to avoid sunlight. Observational studies have shown that avoiding sun exposure is a risk factor for all-cause mortality [12]. A risk analysis of a prospective study found that nonsmokers who avoided sun exposure had a life expectancy similar to smokers with high sun exposure [13]. Compared to those with the highest sun exposure, sun avoiders had a reduced life expectancy of 0.6–2.1 years [13, 14].

The IARC rarely specifies dose and context in its list of carcinogens, even though these factors are crucial in determining actual cancer risk. For example, while red meat is classified as "probably carcinogenic to humans" (Group 2A), moderate consumption offers high-quality protein and essential nutrients such as B vitamins, iron, and zinc. In regions with limited food availability, red meat may be a difficult-to-replace source of these nutrients. Without clarifying the level of consumption at which red meat poses a risk, people might avoid it entirely, missing out on its health benefits. Similarly, several approved drugs are classified as Group 1 carcinogens, even though they are standard treatments for specific diseases and offer significant health benefits when used appropriately. These examples show that imprecise labels that lack dose and context may discourage beneficial behaviors, treatments, or exposures that have positive health effects.

The need for more accurate terminology is evident to avoid unnecessary confusion and ensure that people, health professionals, and policymakers make informed decisions based on a clear understanding of risk. The IARC recognizes the need to improve communication of its evaluation results and has recently added user-friendly features like "frequently asked questions" and infographics to explain its classifications and the supporting evidence [7]. However, the ongoing use of imprecise terminology and the lack of essential context, especially in the IARC's classification list of carcinogens, will likely continue to cause confusion and concern until these issues are properly addressed. This manuscript proposes a straightforward solution for the IARC Monographs to enhance the accuracy and clarity of its communications.

A straightforward solution to improve accuracy and prevent unnecessary confusion

The first step to improve accuracy and prevent unnecessary confusion is to rename the groups of agents classified by the IARC Monographs. As shown in Table 1, Group 1 (carcinogenic to humans) could be renamed as "agents that increase cancer risk in humans"; Group 2A (probably carcinogenic to humans) as "agents that probably increase cancer risk in humans"; Group 2B (possibly carcinogenic to humans) as "agents that possibly increase cancer risk in humans"; and Group 3 (not classifiable as to its carcinogenicity to humans) as "agents with insufficient or no evidence for cancer risk in humans".

Since IARC classifications only indicate evidence of increased risk under certain conditions, these new group names emphasize cancer risk rather than implying direct causation. As shown in the firefighter example, the term "increases cancer risk" is more precise than "is carcinogenic" or "causes cancer" and is easier for most people to understand, including health professionals and policymakers. The proposed name for Group 3 reflects IARC's recent merging of two categories: the former Group 3 (not classifiable as to its carcinogenicity to humans) and the now-eliminated Group 4 (probably not carcinogenic to humans). This change is important to clarify that not all agents in this group are suspected of increasing cancer risk.

The second step to improving accuracy and reducing unnecessary confusion is to add concise labels to specific agents to provide essential context and minimize misinterpretation. At least two basic labels should be used for specific agents: "excessive" for agents where dose determines whether the agent is beneficial or

Category	Current classification system	Proposed classification system
Group 1	Carcinogenic to humans	Agents that increase cancer risk in humans
	Tobacco smoke, plutonium, occupational exposure as a firefighter, solar radiation, etoposide, etc.	Tobacco smoke, plutonium, occupational exposure as a firefighter, excessive solar radiation, etoposide (beneficial under certain conditions), etc.
Group 2A	Probably carcinogenic to humans	Agents that probably increase cancer risk in humans
	Consumption of red meat, acrolein, malathion, etc.	Excessive consumption of red meat, acrolein, malathion, etc.
Group 2B	Possibly carcinogenic to humans	Agents that possibly increase cancer risk in humans
	Radiofrequency electromagnetic fields, aspartame, digoxin, etc.	Radiofrequency electromagnetic fields, aspartame, digoxin (beneficial under certain conditions), etc.
Group 3	Not classifiable as to its carcinogenicity to humans	Agents with insufficient or no evidence for cancer risk in humans
	Diazepam, coffee drinking, tea, etc.	Diazepam, coffee drinking, tea, etc.

Current and proposed classification system for agents evaluated in the International Agency for Research on Cancer (IARC) Monographs, with examples provided in each group to show how specific agents could be labeled

harmful, and "(beneficial under certain conditions)" for agents where context determines whether the agent is beneficial or harmful. For agents where dose and context do not offer any health benefits, such as tobacco smoke or occupational exposure as a firefighter, no labels are necessary (Table 1).

The label "excessive" could precede agents that are beneficial at moderate exposures (e.g., solar radiation, red meat consumption) to clarify that moderate exposure can have health benefits. In contrast, the label "excessive" would be unnecessary for agents lacking demonstrated health benefits at moderate exposures or that can be easily substituted, such as aspartame. While aspartame and other agents on the IARC lists might pose cancer risks only at high doses, renaming the groups as shown in Table 1 would be sufficient to help prevent misleading headlines like "Aspartame is a possible carcinogen" [15]. The existence of such headlines, even in respected scientific journals, suggests that the current IARC group names can be misinterpreted even by scientists [15].

The label "(beneficial under certain conditions)" could apply to agents that, at normal exposure levels, provide health benefits in specific contexts despite potential cancer risks at the same exposure levels. Examples include approved drugs like etoposide or digoxin. Adding this basic context would help people understand that certain agents offer health benefits while carrying a potential cancer risk. Without these clarifications, the IARC lists might unintentionally discourage the use of essential treatments; for example, etoposide and digoxin are actually included in the WHO Model List of Essential Medicines (23rd list, 2023) [16].

Conclusions

In conclusion, the changes proposed in this manuscript offer a straightforward and effective solution for the IARC Monographs Programme to enhance both the accuracy and clarity of its scientific communications. By updating the classification language from "carcinogenic to humans" to more precise terms like "agents that increase cancer risk in humans", the proposed system reduces the likelihood of misinterpretation while preserving the IARC's focus on identifying potential hazards without conducting full risk assessments. Since "carcinogenic hazards to humans" can be defined as "agents that increase cancer risk in humans", the current title, IARC Monographs on the Identification of Carcinogenic Hazards to Humans, remains fully consistent with the proposed group names in Table 1. Additionally, adding context-sensitive labels, such as "excessive" or "(beneficial under certain conditions)", provides essential context for agents that offer health benefits at moderate exposure levels or in specific situations. These adjustments neither alter the IARC's foundational mission nor require significant changes, yet they would improve clarity, enhance accuracy, and provide stronger support for cancer prevention strategies.

Abbreviations

IARC: International Agency for Research on Cancer WHO: World Health Organization

Declarations

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