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Comprehensive risk-benefit assessment of chemicals: A case study on glyphosate

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ABSTRACT

The integrity of environmental toxicology is undermined by selective risk assessments that focus intently on certain chemicals while overlooking others. Glyphosate, one of the most widely used herbicides, serves as a case study of how regulatory decisions can be shaped by incomplete or biased evidence. This paper argues for a holistic approach to toxicology, calling for balanced assessments that consider both health risks and societal benefits. It critically examines current regulatory practices concerning glyphosate, investigating its association with non-Hodgkin's lymphoma and its positive effects on agricultural productivity and food security. While definitive evidence linking glyphosate to cancer remains inconclusive, its role in enhancing crop yields, by as much as 20 % in some regions, has had measurable benefits for food security and public health. The paper advocates for regulatory frameworks that transparently weigh these societal benefits against potential health risks, particularly in settings of occupational exposure, where the need for balanced assessment is especially pressing. Through a narrative review of major studies, this paper underscores the need for transparency, accountability, and evidence-based approaches in environmental regulation. Such practices are essential for crafting policies that not only mitigate risk but also promote global food security and well-being. By integrating both risks and benefits into the regulatory process, the study proposes an inclusive and data-driven approach to chemical policy that aligns with the broader goals of sustainability and public health.

1. Introduction

Replacing selective risk avoidance with comprehensive risk assessment and mitigation, as proposed by Thompson et al. [77], Li and Ellingwood [49], Lacasse, Nadim, and Hoeg [48], Georgesen and Lipner [34], Aqlan and Ali [9], and Boretti [16], requires a shift from a reactive approach to a proactive, holistic strategy for managing potential hazards. This approach is applicable across various contexts, including environmental, industrial, and public health settings.

In a selective risk avoidance approach, decisions are often made based on specific risks, while other potential risks might be overlooked. This can result in a fragmented approach where only certain hazards are addressed, leaving room for other risks to emerge. By applying the linear no-threshold model, see Boretti [16], Calabrese, Selby and Giordano [19], Doss [26], Agathokleous, and Calabrese [5], Agathokleous, and Calabrese [6], Oakley, and Harrison [59], Fernández [31], and Jargin [39], almost any substance being considered is harmful, as exposure in large amounts is generally negative. Also, the attribution of likely carcinogenicity by organisms such as the International Agency for Research on Cancer (IARC), is by no way a reason to proceed to the ban of specific chemicals, see Boretti [16] or Kabat [42]. Statistically, almost none of the substances examined by the IARC has escaped the attribution of carcinogen or likely carcinogen, from red meat to hot coffee, from Chinese-style salted fish to alcohol, and this does not mean these substances must be banned. Other substances not considered by the IARC may have an objective risk profile even worse than the risk profile of those who are considered carcinogenic or likely carcinogenic by the IARC. Assessments should be based on carefully determined risk profiles, with proof of correlation and causation for specific pathologies to specific exposures, see Boretti [16].

A comprehensive risk assessment entails a detailed and systematic evaluation of all potential risks related to a specific activity, substance, or situation, see Fraum et al. [33], Gharabagh et al. [35], Kastrinos et al. [46], Jay et al. [40], Meltzer et al. [55], Kah et al. [43], Yang et al. [85], Luo et al. [50], and Rabi et al. [68]. It considers a wide range of factors, including known hazards, potential exposure pathways, uncertainties, and interactions between different risks. Comprehensive risk assessment goes beyond avoiding isolated risks and focuses on developing strategies

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to manage, minimize, or eliminate risks across the board. Mitigation efforts can include engineering controls, administrative measures, personal protective equipment, and education and training. A comprehensive approach takes into account the interconnectedness of different risks and their impacts. It acknowledges that addressing one risk might have unintended consequences on other aspects of a system, and therefore strives for a balanced and informed decision-making process. If for example, one substance has negative and positive aspects, only a holistic perspective may clarify the best trade-off for the permitted use.

Instead of waiting for risks to materialize and then responding, comprehensive risk assessment aims to anticipate potential risks and take preventive measures to reduce their likelihood or impact, see Fraum et al. [33], Gharabagh et al. [35], Kastrinos et al. [46], Jay et al. [40], Meltzer et al. [55], Kah et al. [43], Yang et al. [85], Luo et al. [50], Rabi et al. [68]. This proactive stance is particularly important in preventing large-scale incidents or disasters. By considering a broader spectrum of risks and their interactions, comprehensive risk assessment contributes to long-term sustainability. It aligns with the goals of environmental protection, public health, and the preservation of resources for future generations. Comprehensive risk assessment provides decision-makers with a more accurate and nuanced understanding of potential risks. This enables them to make informed choices that balance the benefits of certain activities against the associated risks. Embracing comprehensive risk assessment can lead to more effective and adaptable regulations and policies. It helps regulatory agencies create guidelines that are better equipped to address complex and evolving risks. Adopting a comprehensive approach also stimulates scientific research and innovation. It encourages the development of new methods for risk assessment, data collection, and modeling, enhancing our ability to predict and manage risks. A transparent and comprehensive risk assessment process enhances public trust in regulatory agencies and industries. Open communication about risks, uncertainties, and mitigation measures fosters understanding and cooperation. There are practical challenges associated with implementing comprehensive risk assessment to replace selective risk avoidance based on the linear no-threshold model or likely carcinogenicity. Adopting a holistic perspective in substance evaluation allows for a more balanced consideration of diverse factors, fostering sustainable and responsible decision-making in real-world scenarios. The definition of appropriate risk profiles suffers from the complexities and obstacles in establishing concrete links between substances and specific pathologies. While there is a clear need for a comprehensive risk assessment, there are certainly many challenges to overcome, such as data limitations and the interdisciplinary nature of the assessment, as well as potential hurdles in predicting and mitigating emerging risks and uncertainties.

Glyphosate has become a focal point in global debates over its safety and environmental impact. The International Agency for Research on Cancer (IARC) classified glyphosate as a “probable carcinogen,” a designation that diverges from the U.S. Environmental Protection Agency (EPA)’s stance, which does not consider glyphosate carcinogenic. This inconsistency has fueled public debate, legal challenges, and regulatory discrepancies worldwide, underscoring the urgent need for transparent, evidence-based regulatory practices.

In response to these controversies, recent advancements in eco-friendly agricultural compounds and nanotechnology are offering potential alternatives for pest and weed management. Nano-based herbicides, for example, leverage nanotechnology to improve the efficacy and precision of herbicides, enabling more targeted application and potentially lowering the required dosages while reducing environmental impacts [44]. Using nano-carriers like nanoparticles and encapsulation methods, these herbicides can deliver active ingredients precisely to target weeds, minimizing risks of leaching and contamination in soil and water [67]. Additionally, bio-stimulants, derived from natural compounds or microorganisms, have emerged as eco-friendly solutions to enhance crop growth and resilience against stress factors such as drought and pests. By improving nutrient uptake efficiency and enhancing natural plant defenses, bio-stimulants indirectly help crops compete against weeds and boost overall resilience [27]. These innovations support a more sustainable approach to agriculture by reducing the need for synthetic chemical inputs, offering pathways to lessen the environmental footprint of conventional farming practices.

While these developments are promising, it is essential to recognize that they remain in early stages and do not yet offer a proven alternative that matches the cost-effectiveness and broad efficacy of synthetic herbicides like glyphosate across all criteria. Due to its broad-spectrum weed control, reliable yield impact, and relatively low environmental persistence under regulated use, glyphosate remains one of the most widely employed herbicides worldwide [12]. Though nano-based and bio-stimulant alternatives show great potential, "new" does not automatically mean "better" when considering critical agricultural factors, such as scalability, yield consistency, environmental persistence, and economic feasibility. The same is true for health impact. The real challenge lies in advancing research and field trials for these novel solutions to verify their consistent performance and safety on a large scale. Rigorous assessment is essential to understand the long-term impacts and confirm whether these innovations can truly deliver sustainable improvements over existing synthetic herbicides.

2. Methodology and data

This analysis employed a narrative review approach, selecting studies that investigate glyphosate’s health impacts, agricultural productivity benefits, and regulatory frameworks. The inclusion criteria prioritized peer-reviewed studies published within the last decade, with a particular focus on those examining glyphosate’s epidemiological links to cancer, especially non-Hodgkin lymphoma, alongside its role in enhancing agricultural productivity. Data were extracted based on the relevance, methodological rigor, and clarity of findings to ensure a robust analysis. Where available, quantitative data on glyphosate exposure levels and their health impacts were incorporated to enhance analytical depth. This structured selection and review process aims to provide transparency and reproducibility, facilitating a balanced assessment of glyphosate’s associated risks and benefits.

3. Results and analysis

The case of Glyphosate, which is a popular herbicide with extremely positive effects on agricultural yields, see Brookes, Taheripour, and Tyner [18], Cuhra, Bøhn, and Cuhra [24], Wynn, and Webb [83], Wiese, and Steinmann [80], Kanissery, Gairhe, Kadyampakeni, Batuman, and Alferez [45], necessitates a more grounded approach for a ban than a selective quest for total risk avoidance, which is discussed as an example. Glyphosate, a widely used herbicide, has been at the center of significant controversies, illustrating challenges in regulatory decision-making within the field of environmental toxicology. One of the major controversies surrounding Glyphosate involves its classification as a potential carcinogen by the IARC, a branch of the World Health Organization (WHO). However, other regulatory bodies, including the U.S. Environmental Protection Agency (EPA), did not reach the same conclusion, leading to conflicting assessments and raising questions about the consistency of regulatory standards. Glyphosate has been the subject of numerous lawsuits, particularly against the product Roundup, which contains Glyphosate and is widely used in agriculture. Individuals and groups have claimed that exposure to Glyphosate-based products led to cancer, particularly non-Hodgkin lymphoma. Studies examining occupational glyphosate exposure have shown varying levels of risk association with non-Hodgkin lymphoma, underscoring data inconsistency. Data limitations include variations in sample sizes and control groups across studies, which may affect generalizability and reliability.

Legal battles and large settlements have fueled debates about the adequacy of regulatory oversight and the need for more stringent safety evaluations. Controversies have emerged regarding the permissible

levels of Glyphosate residues in food and water. Regulatory agencies face challenges in setting appropriate residue limits that balance agricultural needs with potential health risks. Glyphosate's environmental impact is another source of controversy. It has been associated with negative effects on non-target plants, insects, and aquatic ecosystems. There have been claims for the herbicide's potential contribution to the decline of pollinators, such as bees, and its impact on biodiversity. Controversies have arisen regarding potential conflicts of interest in regulatory decision-making. Critics argue that regulatory agencies may be influenced by economic and political interests. This has raised questions about the independence and objectivity of regulatory assessments. Challenges exist in ensuring transparency and access to data related to Glyphosate through independent scrutiny. The accessibility of data is crucial for regulators and independent researchers to conduct thorough evaluations. Different regulatory agencies around the world have reached varying conclusions about the safety of Glyphosate. While some countries have banned or restricted its use, others continue to permit widespread application. This regulatory divergence adds complexity to global trade and raises questions about the adequacy of harmonized international standards.

The debate surrounding the use of Glyphosate, a widely used herbicide, see Duke [29], Carlisle, and Trevors [22], Sammons, and Gaines [70], Duke, and Powles [28], Johal, and Huber [41], is complex and multifaceted. Glyphosate is a key component in many herbicides and has been used extensively in agriculture to control weeds. It has been associated with both benefits, such as increased crop yields and cost-effective weed control, as well as concerns related to its potential environmental and health impacts.

Arguments for banning glyphosate include health and safety concerns, see Myers et al. [57], Richmond [69], Xu, Smith, Smith, Wang, and Li [84], as some studies have suggested potential links between glyphosate exposure and health issues, including cancer, and specific non-Hodgkin's lymphomas, see Acquavella [3], Weisenburger [79], Meloni et al. [54]. These concerns have led regulatory agencies in some countries to consider or implement restrictions on its use, following the pressure of environmental activists and the organic foods industry. Glyphosate may also have unintended impacts on non-target plants and organisms, potentially affecting ecosystems and biodiversity, and possibly producing resistance development. Overreliance on glyphosate for weed control has led to the development of glyphosate-resistant weeds, which can reduce the effectiveness of the herbicide and increase the need for alternative weed control methods.

Many more arguments speak against banning glyphosate, see Brookes, Taheripour, and Tyner [18], Cuhra, Bøhn, and Cuhra [24], Wynn, and Webb [83], Wiese, and Steinmann [80], Kanissery, Gairhe, Kadyampakeni, Batuman, and Alferez [45], Duke [29], Carlisle, and Trevors [22], Sammons, and Gaines [70], Duke, and Powles [28], and Johal, and Huber [41]. Glyphosate is credited with contributing to increased agricultural productivity by allowing for efficient weed control, which can lead to higher crop yields and lower costs for farmers. Glyphosate is a cost-effective herbicide, and banning it could increase production costs for farmers. This could disproportionately affect small-scale farmers and food production in regions with limited resources. With the global population projected to grow, maintaining high levels of agricultural productivity becomes crucial. Banning glyphosate could potentially impact food production and contribute to food security challenges. Additionally, those studies claiming correlation and causation between the use of glyphosate and health effects are mostly flawed. Additionally, while concerns exist about glyphosate, it is important to consider viable alternatives for effective weed control that reduce rather than increase environmental and health risks.

Recently, Finger, Möhring, and Kudsk [32] discussed that the Glyphosate ban will have economic impacts on European agriculture. While the ban on Glyphosate has much worse consequences on a global scale than a simple loss of profit for agriculture businesses across Europe, as this may affect food security causing famine among the world's poor, the work has been negatively commented as science biased by commercial interests, see aa.vv. [1]. This is fundamentally incorrect. Commercially and politically motivated science is rather one that supports decisions based on questionable science favoring a restricted elite while hurting humanity at large.

The science behind the ban on Glyphosate is everything but solid' see Boretti [15]. The correlation between exposure to Glyphosate and the development of specific pathologies is questionable, and even more obscure is the causation. In the specific case of Non-Hodgkin Lymphoma, which is one of the most popular alleged pathologies that Glyphosate should produce, there is no proof of correlation and no causation, see Boretti [15]. We do not know yet what causes non-Hodgkin lymphoma following which mechanism, see cancer.org.au [21], nhs.uk [58], mayoclinic [52], or cancer.org [20]. We do not know yet how to cure non-Hodgkin lymphoma. However, it is enough to argue an association between exposure to Glyphosate and non-Hodgkin lymphoma, and this may result in the ban of a product that has a hugely beneficial impact on agricultural yields across the world.

The war on Glyphosate was prompted by the attribution of "probably carcinogenic" issued in 2015 by the IARC. The process through which the IARC initiated and concluded its assessment of Glyphosate exhibited a bias and was marred by conflicts of interest, see Kelland [47] or Kabat [42]. The agency initiated the assessment with a preconceived conclusion and manipulated the final report to align with the intended outcome. This involved disregarding and altering findings from the draft that contradicted the presupposition that Glyphosate is carcinogenic, see Kelland [47] or Kabat [42]. The IARC's opinion provided the basis for litigation to United States law firms, which likely promoted the examination of the chemical, see Kabat [42]. The IARC's opinion helped considerably the above-mentioned law firms, also delivering powerful ammunition to environmental activists, anti-GMO groups, NGOs, and the organic foods industry in both Europe and North America, in their campaign to ban Glyphosate for various other reasons than its carcinogenicity, which was only an excuse.

Talking about toxicological assessments in general, there is a common problem which is the degree of exposure. The questionable assessment by the IARC did not take into consideration the degree of exposure to Glyphosate. Everything is likely dangerous to human health in large amounts, but this does not mean that even negligible exposures to almost everything are dangerous, and, consequently, almost every chemical substance has to be banned.

The ban on Glyphosate will hurt farmers and consumers by decreasing crop yields and increasing the costs of produce, see Wynn, and Webb [83], Antier et al. [8], Böcker, Britz, Möhring, and Finger [13], Pardo, and Martínez [65]. It will require the substitutional use of other herbicides only less known and effective, which may also pose a greater health risk, which is only presently unassessed. Decreasing crop yields will have even more significant implications on the world's poorest populations, potentially leading to famine. There is indeed a strong link between decreasing crop yields, poverty, and famine, see Mellor, and Gavian [53].

Pesticides in general are used to protect crops against pests, see Abubakar et al. [2], Sharma, Sharma, and Chopra [72], Begum, Alam, and Uddin [11]. They include herbicides, insecticides, fungicides, and other substances. They have been used in agriculture for millennia. The naturally occurring elements of the past have been replaced by the synthetic products of the present to better target specific pests. Pesticides are important for corps protection and increases in yields. Pesticides may certainly have negative impacts on biodiversity and can be toxic to farmers more than consumers. However, a balanced approach that objectively assesses their risk-to-benefit ratio, as well as the risk-to-benefit ratio of every other threat to the environment and human health, should be adopted.

In recent years, there has undeniably been an upsurge in the utilization of pesticides, ourworldindata [60]. This increase has corresponded with the expansion in crop yields, ourworldindata [61].

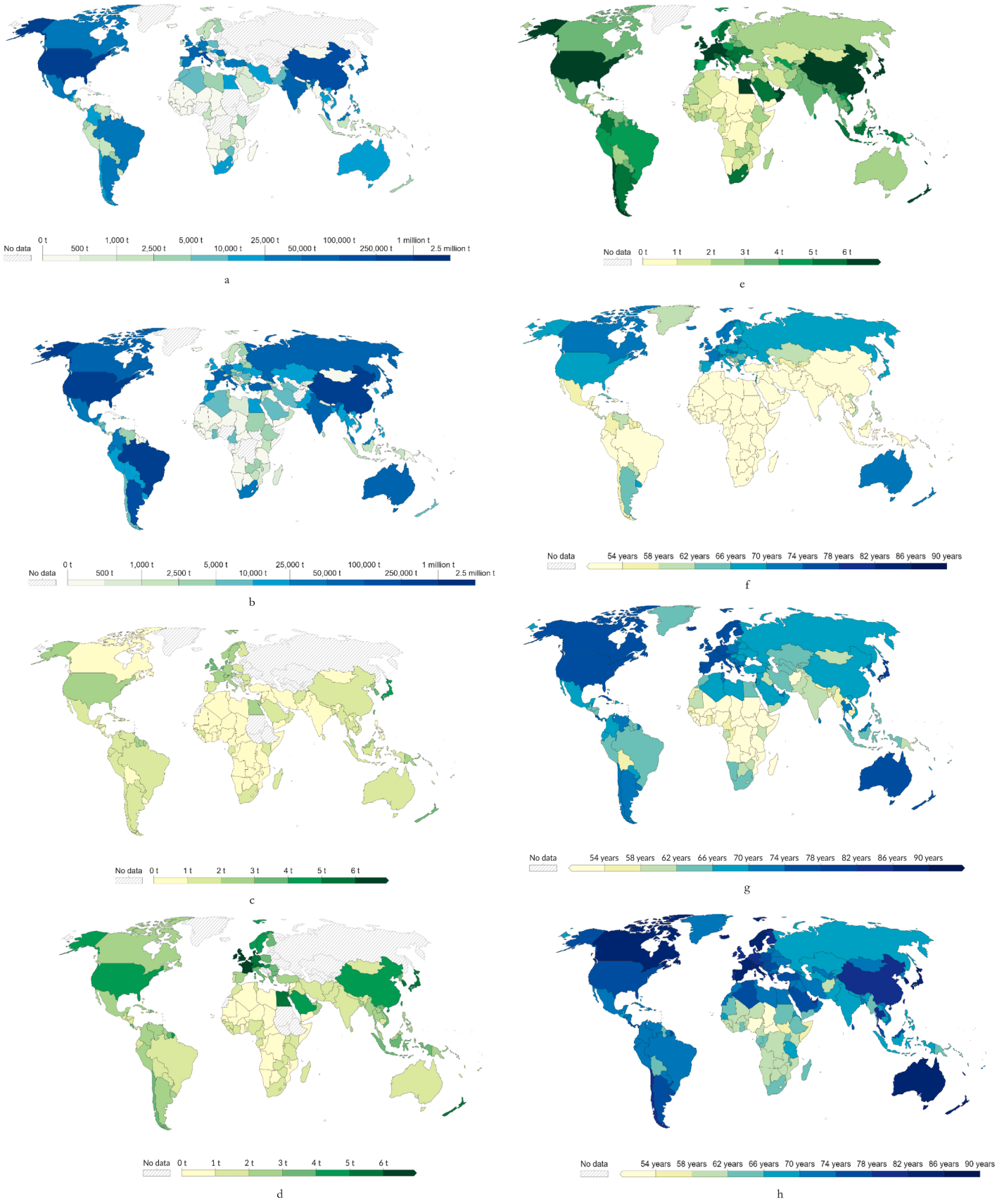
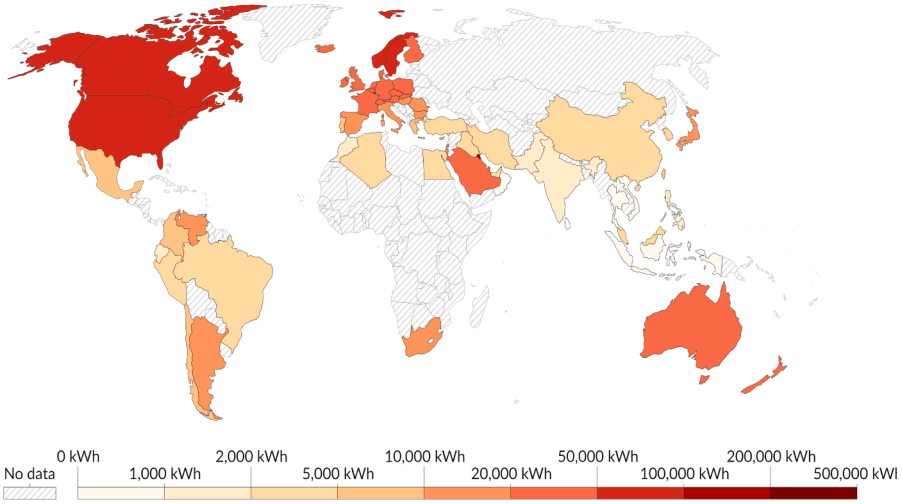


Fig. 1. (a) and (b) geographical change of pesticide use over the last 30 years. (c), (d) and (e) geographical change of cereal yields over the last 30 and 60 years. (f), (g) and (h) geographical change in life expectancy over the last 30 and 60 years. (i), (j), and (k) geographical change in energy use per capita over the last 30 and 60 years. Data for pesticide use in 1960 is unavailable in the selected database. Images from Our World in Data. CC BY.



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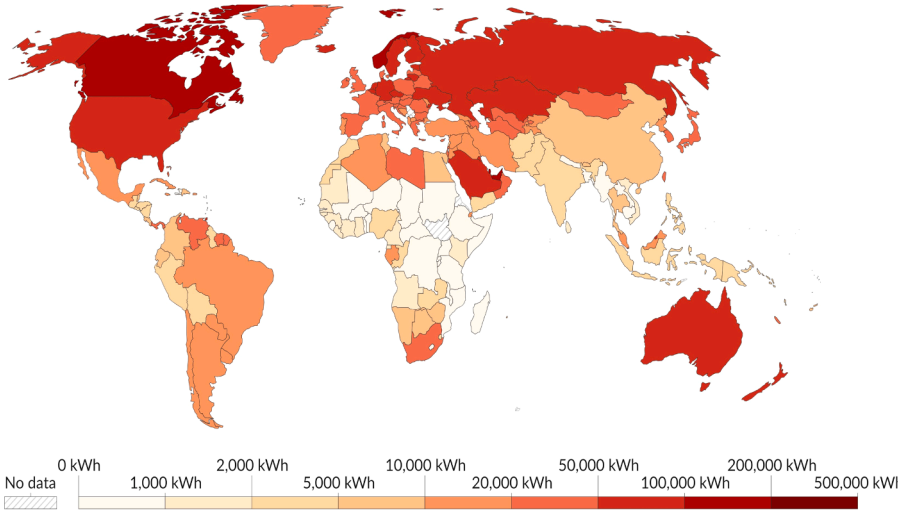

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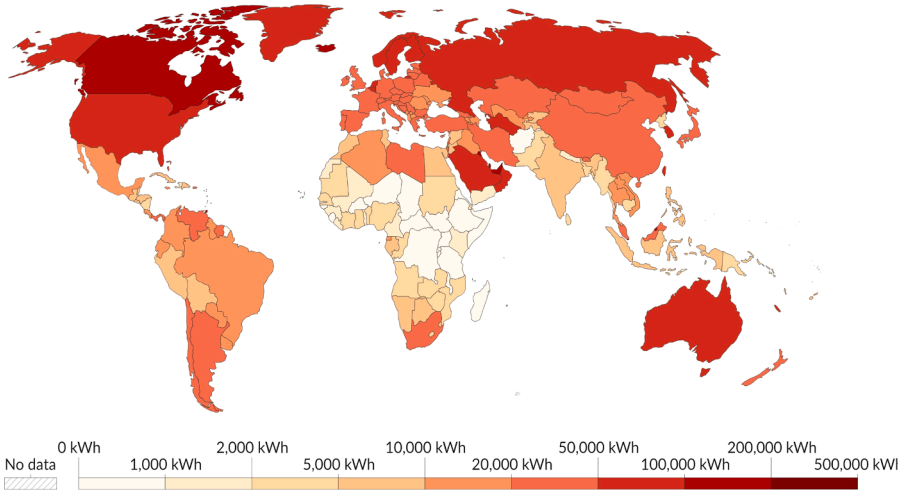

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Fig. 1. (*continued*).

Enhancements in crop yields are essential to meet the nutritional needs of a growing global population, ourworldindata [62] characterized by increasing life expectancy, ourworldindata [63]. This simultaneous increase in productivity plays a pivotal role in mitigating the environmental impact associated with food production, as depicted in Figure 1. The figure also proposes the energy use per capita, ourworldindata [64]. Undoubtedly, enhancements in quality of life, exemplified by increased life expectancy, have been achieved through improved access to energy and, notably, the greater availability of food, with the latter facilitated by the expanded use of pesticides.

Prohibiting specific pesticides in certain countries can result in a deterioration of pest, weed, and disease control. Additionally, it often leads to an increase in food prices, see Alcántara-de la Cruz et al. [7]. Instead of an outright ban, a more prudent approach is to make necessary adjustments when a particular pesticide poses manageable risks.

Crop yields determine the amount of food that can be produced. A shortage of food supply causes prices to rise due to increased demand and limited availability. Rising food prices disproportionately affect low-income households and those living in poverty. This may lead to malnutrition and food can insecurity, see Alcántara-de la Cruz et al. [7], Gustafson [36], worldbank [81]. Malnutrition have severe and long-lasting effects on physical and cognitive development, leading to a cycle of poverty, see fao [30], Stephenson et al. [75], Müller and Krawinkel, [56], Saunders and Smith [71], Peña and Bacallao [66]. Famine and malnutrition weaken immune systems, making individuals more susceptible to diseases and leading to health crises in already vulnerable regions. Scarcity of food can also lead to social unrest and conflict as people compete for limited resources, with broader implications for stability and security, affecting entire regions. Thus, there are many very good reasons why comprehensive risk assessments should replace risk avoidance for targeted products, trying to figure out the best way to move forward in the world of the many, rather than moving backward in the world of the very few.

In the case of Glyphosate, before any ban, it should be made clear through proper studies of correlation and causation, which is the risk of developing specific pathologies for exposures in a given amount. It should be also made clear which is then the overall impact of a ban on Glyphosate, not only on the economy of rich countries but also on the access to food of the world's poor, who are at perennial risk of famines also because of European (and North American) colonization. There is a need for sustainable agricultural practices, global cooperation, targeted interventions, and objective toxicological assessments, to ensure food security and equitable access to nutrition for all, rather than to please elites.

The ban on glyphosate will have immediate economic impacts. Glyphosate is a widely used herbicide in agriculture, and a ban could potentially lead to a decline in crop yields. Farmers may struggle to manage weed control effectively, impacting the productivity of their crops. Farmers may incur higher costs due to the need for alternative herbicides, increased labor for manual weeding, or the adoption of alternative farming practices. This could lead to a rise in the overall cost of agricultural production. Transitioning away from glyphosate may involve the need for farmers to adapt to new methods, technologies, or herbicides. The initial transition period may be economically challenging for some farmers. Glyphosate is not only used by farmers but is also a key component in many agricultural supply chains. A ban could disrupt these supply chains, affecting the availability and cost of certain agricultural products. The ban on glyphosate may have global consequences on food security and the livelihoods of small-scale farmers. The ban on glyphosate could potentially impact global food security if it leads to a decrease in crop yields. As glyphosate is commonly used in large-scale agriculture, any significant disruption could affect the availability and affordability of food.

Small-scale farmers, who may be more resource-constrained than larger industrial farms, could face significant challenges in adapting to alternative herbicides or practices. This may threaten their livelihoods and economic sustainability. In regions heavily dependent on glyphosate for agriculture, a ban could disproportionately affect developing countries, where small-scale farming is prevalent. These countries may face challenges in ensuring food security and supporting the livelihoods of their rural populations. The alternative herbicides have environmental/health risk profiles not well assessed as superior. Paraquat is one alternative herbicide, but it has been associated with health risks, including toxicity. It has been banned or restricted in several countries due to safety concerns.

2, 4-D and Dicamba are herbicide alternatives to glyphosate, which have been linked to drift issues, posing risks to non-target plants and crops. Their use has raised environmental concerns and led to legal challenges. Glufosinate, also considered an alternative, has its own set of environmental concerns. It may impact non-target plants and has been associated with negative effects on aquatic ecosystems. While some farmers may opt for organic farming practices as an alternative to synthetic herbicides, these practices considered more environmentally friendly, also present their own set of challenges, including much lower yields and potential economic constraints.

Comparisons with studies such as those by Meloni et al. [54] and Richmond [69] reveal similar findings on glyphosate's impact on both agricultural efficiency and associated health risks, reinforcing the need for comprehensive risk assessment models.

Table 1 below summarizes the Key Studies on Glyphosate's Health Impacts and Agricultural Benefits.

Findings reveal that while glyphosate has significant productivity benefits—such as crop yield increases of up to 20 % in regions dependent on large-scale agriculture—there is conflicting evidence on its health impacts, particularly concerning cancer risk. Studies with occupational exposure groups have shown a possible association between glyphosate and non-Hodgkin lymphoma, though inconsistencies in sample size and control groups create limitations in generalizability. For

Table 1
Summary of Key Studies on Glyphosate's Health Impacts and Agricultural Benefits.

Study	Health Impact Findings	Agricultural Benefit Findings	Comments
Meloni et al. [54]	Found increased risk of non-Hodgkin lymphoma with high occupational exposure.	Not assessed.	Adds evidence of risk for occupational exposure; focuses on human health aspect only.
Richmond [69]	Highlights glyphosate's potential health effects across species; lacks conclusive data.	Notes glyphosate's effectiveness in enhancing crop yield by 15–20 % in controlled environments.	Indicates need for more consistent, cross-species health data.
Brookes et al. [18]	Not the focus of the study.	Reports increased crop yields by up to 20 % due to weed control effectiveness, improving farmer productivity.	Demonstrates glyphosate's role in agricultural productivity; lacks health impact assessment.
Acquavella [3]	Reviewed epidemiological studies with mixed findings on glyphosate exposure and lymphoma.	Not assessed.	Calls for more controlled studies to clarify exposure levels and health impacts.
Alcántara-de la Cruz et al. [7]	Highlights potential health risks but suggests current data is inconclusive.	Discusses challenges of weed control without glyphosate, which would likely increase production costs.	Addresses agricultural impacts of a ban; notes potential for increased costs and yield reductions.

example, Meloni et al. [54] demonstrated elevated lymphoma risk with high exposure levels, whereas Brookes et al. [18] focused on agricultural yield improvements and did not assess health impacts. Such contrasts highlight the need for comprehensive risk-benefit assessments that recognize data limitations and the diverse outcomes associated with glyphosate use.

4. Discussion

The IARC is known for its subjective classification of substances based on their potential to cause cancer. However, its assessments have faced criticism and controversy due to perceived flaws in its methodologies and decision-making processes. IARC's classifications often do not take into account the level of exposure to a substance. The risk of cancer is often associated with the dose and duration of exposure, but IARC classifications typically focus on hazard identification without considering exposure levels, leading to potential overestimation of risk. IARC has been criticized for inconsistencies in its classifications. Some substances that are classified as Group 1 (carcinogenic to humans) have lower levels of evidence compared to other substances in the same category. This has led to questions about the reliability and consistency of IARC's decision-making process. IARC's assessments have been often accused of selectively using evidence that supports a particular classification while disregarding conflicting data. This cherry-picking of data leads to biased conclusions and may not accurately represent the overall scientific consensus. Some critics have raised concerns about the lack of transparency in IARC's decision-making process. The criteria used for classification and the specific studies considered are not always transparently disclosed, making it difficult for independent experts to scrutinize the assessments. IARC assessments may not always consider real-world exposure scenarios or take into account factors such as differences in exposure levels between occupational and general populations. This limitation may result in an overestimation of risk in situations where exposure is significantly lower than those observed in occupational settings. IARC's evaluations sometimes do not adequately consider the mode of action by which a substance may cause cancer. Understanding the biological mechanisms through which a substance exerts its carcinogenic effects is crucial for accurate risk assessment, and a failure to consider this aspect leads to flawed classifications. Finally, IARC classifications typically focus on hazard identification without giving due consideration to risk reduction measures and regulatory actions. This results in an incomplete understanding of the overall risk-benefit balance associated with the use of certain substances.

The degree of exposure to glyphosate is fundamental to toxicological assessments. The degree of exposure to glyphosate is a crucial factor in toxicological assessments, influencing the potential health and environmental risks associated with the herbicide. Exposure occurs through various routes, including occupational, dietary, and environmental pathways. Understanding the levels and patterns of exposure is essential for accurate risk assessment. Farmers, agricultural workers, and pesticide applicators may experience higher levels of occupational exposure to glyphosate. This group of individuals is at an increased risk due to direct contact during the application of the herbicide. The residue of glyphosate and its metabolites can be found in food items, particularly in crops treated with the herbicide. Dietary exposure is a significant concern, as it contributes to the overall intake of glyphosate by the general population. Glyphosate can contaminate soil, water, and air in agricultural areas, leading to exposure to non-target organisms, including wildlife. This exposure pathway is important for assessing the broader ecological impact of glyphosate. Toxicological assessments should consider these exposure pathways and levels, taking into account real-world scenarios to provide a comprehensive understanding of the potential risks to human health and the environment. Pesticides impact the environment and human health. Pesticides, including glyphosate, can have adverse effects on non-target organisms, leading to a decline in biodiversity. Insecticides, for example, may harm pollinators like bees, while herbicides can affect plants and soil organisms, disrupting ecosystems. Pesticides can leach into groundwater or be carried by runoff into surface water, leading to water contamination. This can have implications for aquatic ecosystems and may pose risks to human health if contaminated water sources are used for drinking or irrigation. Residues of pesticides in food items can contribute to human exposure. Chronic exposure to low levels of pesticides through the diet raises concerns about potential long-term health effects, including the development of chronic diseases. Current agricultural practices heavily reliant on pesticides raise concerns about long-term environmental sustainability. The overuse of certain pesticides can lead to the development of resistance in target pests, requiring higher doses or the introduction of new, potentially more harmful, chemicals. Sustainable agricultural practices, such as integrated pest management (IPM), organic farming, and agroecological approaches, aim to reduce the dependence on synthetic pesticides. These methods prioritize ecological balance, biodiversity conservation, and minimizing the environmental impact of agricultural activities.

Given the global nature of agriculture and environmental issues, there is a critical need for global cooperation in managing the use of pesticides. Developing and harmonizing international regulations can ensure consistent standards for pesticide use, safety, and environmental protection across borders. Facilitating the exchange of knowledge and research findings on pesticide impacts, alternatives, and best practices can enhance global understanding and inform decision-making. Supporting developing countries in building capacity for sustainable agricultural practices, including alternatives to pesticides, can contribute to global efforts in reducing environmental and health risks. Establishing mechanisms for global monitoring and reporting of pesticide use and its impacts allows for the timely identification of emerging issues and facilitates evidence-based decision-making. Encouraging research and innovation in alternative pest management strategies can contribute to the development of sustainable practices that reduce reliance on conventional pesticides. Addressing the challenges posed by pesticides, including glyphosate, requires a comprehensive understanding of exposure levels, consideration of the broader environmental and health impacts, and a concerted global effort to promote sustainable agricultural practices. Global cooperation is essential to ensure the long-term health of ecosystems, the viability of agriculture, and the well-being of both the environment and human populations worldwide. A more comprehensive and informed debate on the ban on Glyphosate should encompass economic, environmental, and global considerations.

Environmental toxicology, as detailed in Wright, and Welbourn [82], Cockerham, and Shane [23], Shaw, and Chadwick [73], is a scientific discipline dedicated to comprehending the impact of harmful substances on living organisms and ecosystems. Its primary objective is to assess and mitigate potential risks posed by pollutants and chemicals, safeguarding both the environment and human health, and ultimately shaping a brighter future for all. It is imperative to ensure that this field remains entrenched in scientific principles and impartial research, recognizing and rectifying the inappropriate influence of various stakeholders in distorting environmental policies and public awareness.

The case of glyphosate is not an isolated incident. Another recent case emerging is the per and polyfluorinated substances (PFAS), see Boretti [17], popular human-made chemicals that are resistant to heat, water, and oil and are used in many industrial and consumer products. Apart from a 2001 US class-action lawsuit filed targeting perfluorooctanoic acid (PFOA), the war on all the PFAS, a total of about 4, 700 different, popular, compounds, was suddenly started by the US EPA in 2019, with at the time very little evidence to support such a measure, see acsh.org [4]. Recent reviews, such as those by Sunderland et al. [76] or De Silva et al. [25], indicate only a weak correlation between PFAS exposure and the health effects studied, without establishing causation. Furthermore, these reviews focus on only a few of the numerous PFAS chemicals, leaving many others unexamined in detail regarding their potential health impacts. While Western governments often downplay

certain potential health risks, such as those linked to COVID-19 mRNA vaccines or depleted uranium bullets, they express significant concerns about the potential harm posed by glyphosate and PFAS. These concerns have prompted urgent calls for banning these two chemicals, despite any potential benefits they may offer. However, it is crucial to weigh the potential risks against the benefits, considering the possibility that their removal could lead to more harm than good.

Systemic CD30+ Hodgkin lymphomas have traditionally been treated with the CHOP regimen (cytotoxic drugs) since 1974 [14]. It wasn't until 2019 that the groundbreaking BV+CHP regimen was introduced in clinical practice [37]. BV, which combines an antibody with a cytotoxic drug, represents a significant advancement; however, it is still administered alongside three of the four components of the CHOP regimen. There are several promising therapies under development that could offer superior outcomes, yet they struggle with limited financial backing. These include BV monotherapy [74], BV combined with alternative chemotherapy regimens [78], BV with immunotherapy [51], BV with targeted therapies [10], and most notably CAR-T cell therapy [38], which holds the potential to be a truly transformative solution. It is deeply troubling to see substantial resources diverted towards speculative claims—such as glyphosate causing non-Hodgkin lymphoma—instead of being dedicated to advancing and improving treatments for those suffering from this disease.

As a sign of growing dystopia and hypocrisy, countries where public opposition to glyphosate is particularly vocal, citing concerns about potential links to lymphomas, are paradoxically the same places where there is minimal advocacy for access to modern, highly effective therapies in hospitals to cure lymphomas. Consequently, patients who could benefit from life-saving treatments face limited options, often reliant on outdated and less effective medical therapies. This imbalance highlights a troubling reality. While there is intense scrutiny and resistance against potential risks from agricultural chemicals, the urgency to advance healthcare access and improve survival outcomes for serious diseases receives comparatively little attention.

5. The question of glyphosate and its potential link to NHL in the realm of science

The question of glyphosate and its potential link to non-Hodgkin lymphoma (NHL) spans the complex intersection of science, law, and politics. Each domain offers different approaches and conclusions, shaped by their unique principles and methodologies.

- **Glyphosate and Non-Hodgkin Lymphoma:**
  - **International Agency for Research on Cancer (IARC)**: In 2015, the IARC, a branch of the World Health Organization, classified glyphosate as "probably carcinogenic to humans" (Group 2 A). This designation was based on limited evidence in humans and stronger evidence in animals, igniting concerns over a possible connection between glyphosate and cancer.
  - **Epidemiological Studies**: While some research suggests a possible link between high glyphosate exposure—especially among agricultural workers—and an increased risk of NHL, the data remains inconclusive. Some studies find no statistically significant association between glyphosate and NHL, leading to mixed conclusions within the scientific community.
  - **Regulatory Agencies**: Regulatory bodies such as the U.S. Environmental Protection Agency (EPA) and the European Food Safety Authority (EFSA) have not classified glyphosate as a carcinogen. They assert that, when used according to guidelines, glyphosate is unlikely to pose a cancer risk to humans, including for NHL.
  - **Mechanism of Action**: The biological mechanism by which glyphosate might contribute to NHL remains unclear, adding to the complexity of determining its role in the disease.
- **Causes of Non-Hodgkin Lymphoma:**
- **Multifactorial Disease**: NHL is considered a multifactorial condition, meaning its cause can be attributed to a combination of genetic, environmental, and lifestyle factors. Known risks include immunosuppression, certain viral infections (e.g., Epstein-Barr, HIV), family history, autoimmune disorders, and exposure to various chemicals. However, for most individuals diagnosed with NHL, the precise cause remains unknown, making it difficult to link the disease to a specific environmental factor like glyphosate.
- **Legal Context:**
  - **Lawsuits**: Glyphosate has been at the center of numerous lawsuits in which plaintiffs with NHL claim their condition was caused by exposure to the herbicide. In some high-profile cases, U.S. juries have awarded significant settlements, finding glyphosate to be a substantial factor in causing cancer. However, legal judgments are made based on the balance of probabilities rather than scientific certainty. The fields of law and science operate on different evidentiary standards, and a legal verdict does not equate to scientific proof.
- **Distinctions Between Science, Law, and Politics:**

The domains of science, law, and politics each serve distinct functions. Science is rooted in empirical research, where hypotheses are tested through experimentation and peer review, resulting in knowledge that is always open to revision as new evidence emerges. Law, on the other hand, interprets statutes and regulations, often balancing evidence to reach conclusions based on legal principles and societal values rather than scientific inquiry. Politics, focused on governance and resource distribution, is driven by debates over ideology, public opinion, and power, and its decisions are often influenced by competing interests that may or may not align with scientific consensus.

While these domains sometimes overlap—especially in matters like public health and environmental regulation—their methods and goals differ significantly. Scientific research seeks to uncover truths through evidence; the law aims to maintain social order; and politics navigates the complexities of governance. For contentious issues such as the safety of glyphosate, it is crucial to rely on sound scientific evidence to guide legal and political decisions.

- **Bottom Line:**
  - **Scientific Uncertainty**: There is no definitive scientific consensus that glyphosate causes NHL. Although some studies suggest a potential link, the evidence remains inconsistent. Regulatory bodies generally maintain that glyphosate, when used as directed, is unlikely to pose a cancer risk.
  - **NHL Causes**: Non-Hodgkin lymphoma is likely caused by multiple factors, and most cases cannot be attributed to a single environmental trigger like glyphosate. While the herbicide remains under scrutiny, its role in NHL has not been conclusively established.

In sum, the question of whether glyphosate causes non-Hodgkin lymphoma yields different answers depending on the lens through which it is examined. In the realm of science, the answer is that "nobody knows for sure what causes most cases of NHL." While glyphosate is still under investigation, it has not been definitively proven as a cause of the disease.

6. Conclusions

This paper offers a balanced risk-benefit analysis that contrasts with studies often focused exclusively on either health risks or agricultural productivity. By highlighting regulatory inconsistencies and advocating for transparent, evidence-based policymaking, it addresses a significant gap in current toxicological literature. A key contribution of this work is

the call for a comprehensive risk-benefit assessment model in regulatory toxicology, urging a shift towards greater transparency and accountability, both essential for effective global environmental health management. This paper addresses the lack of integrated assessments of health and agricultural impacts in regulatory evaluations, proposing a novel framework that balances health risks with productivity benefits and emphasizes transparency and international cooperation as pillars for future regulatory practices. Achieving a balance between glyphosate's agricultural benefits and potential health risks requires nuanced, transparent policies that aim to sustain agricultural productivity while prioritizing public health through enhanced safety protocols. International cooperation in establishing regulatory standards would further bolster global food security and environmental health.

Future research should focus on longitudinal studies to evaluate glyphosate's health impacts over time, with an emphasis on comprehensive exposure assessments and cross-species health impacts to yield more reliable data on long-term effects. Recognizing limitations, such as variability in study quality and data consistency, this paper underscores the importance of additional research. Policymakers are encouraged to adopt an evidence-based, globally coordinated approach that balances health considerations with agricultural needs, fostering public trust and promoting sustainable agricultural policies.

A shift from selective risk avoidance to a thorough, balanced approach to risk assessment and mitigation necessitates specific actions in evaluating substances like glyphosate. This requires adopting innovative methodologies, updating data requirements, and enhancing interdisciplinary collaboration to facilitate informed decision-making that considers agricultural productivity, environmental sustainability, and public health. Emphasis should be placed on long-term resilience, prioritizing practices that strengthen ecosystems and communities. Given the global scale of environmental challenges, promoting international collaboration to manage the risks associated with glyphosate is critical, including the development of frameworks for global cooperation. Transparency in communication and trust-building among stakeholders are essential to this process, as is the role of scientific research in bridging knowledge gaps. Drawing from cases like the regulatory treatment of per- and polyfluoroalkyl substances (PFAS) illustrates the importance of evidence-based approaches. Only an inclusive decision-making process—incorporating diverse perspectives, especially from vulnerable populations, can ensure that regulatory actions are collaborative, fair, and mindful of disproportionate impacts.

Ethical approval

Not applicable, because this article does not contain any studies with human or animal subjects.

Author statement

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Trial registration

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