A Meta-Analysis of Studies Addressing the Impact of Glyphosate on Human, Animal, and Environment

Abstract

Main (Introduction, Results, Discussion)

Introduction

Chemical herbicides, particularly glyphosate, have become a ubiquitous aspect of modern industrial agriculture. Although glyphosate was discovered as a herbicide in the 1970s, the introduction of glyphosate resistant genetically modified crops in 1994 resulted in a nearly 15-fold increase in global glyphosate usage[[1]](#footnote-1). Glyphosate usage worldwide grew from approximately 67 million kilograms in 1995 to 826 million kilograms in 2014. Glyphosate, also known scientifically as N-(phosphonomethyl) glycine, is the active ingredient in a large number of commercial broad-spectrum systemic herbicides used for weed management. Glyphosate kills broadleaf weeds and grasses that compete with crops. Monsanto chemists discovered it as a pesticide in 1970 and commercialized it under the trade name Roundup in 1974 for commercial agriculture and home usage[[2]](#footnote-2). Over the years, additional commercial/trade names of glyphosate such as Roundup Ultra®, Roundup UltraDRY®, Roundup UltraMAX®, Roundup WeatherMAX®, Touchdown w/IQ®, Cornerstone®, Clearout 41 Plus®, GlyphoMAX®, Glyfos Xtra® and Glyphomax Plus® have been sold on the market.

Glyphosate is an organophosphorus compound that inhibits the enzyme 5-enolpyruvoylshikimate-3-phosphate synthase (EPSPS), which catalyzes the aromatic amino acids tyrosine, tryptophan, and phenylalanine production in plants. Due to the absence of the 5-enolpyruvoylshikimate-3-phosphate synthase (EPSPS) pathway in humans, other mammals, fish, birds, and insects, glyphosate has traditionally been considered harmless to these species when applied in prescribed amounts for plants. Glyphosate based herbicides have been evaluated and approved by the FDA and USDA, as evidenced by numerous published research papers, indicating that they are safe for humans, animals, and the environment [[3]](#footnote-3) [[4]](#footnote-4) [[5]](#footnote-5).

Recent research has however established that glyphosate interferes with a variety of metabolic processes in plants, animals, and other organisms that contain glyphosate residues. Glyphosate has been shown to disrupt the endocrine system, the balance of gut bacteria, and DNA, and is a known cause of cancer-causing mutations. [[6]](#footnote-6) [[7]](#footnote-7). In line with this, the WHO's International Agency for Research on Cancer recently concluded that glyphosate is "probably carcinogenic to humans". Also, a group of highly regarded scientists [[8]](#footnote-8) issued a caution statement regarding emerging science concerning the safety and use of GBH, its mechanisms of action, toxicity in laboratory animals, and epidemiological studies, while considering the development in current human safety standards. In 2018, a California court determined and later upheld that Monsanto failed to disclose potential cancer risks associated with its Roundup herbicide and awarded claims that Roundup caused cancer [[9]](#footnote-9).

It is therefore necessary to investigate why research on the effect of glyphosate on non-target organisms has been inconclusive and why science was not the key driver in developing policies for the use and regulation of glyphosate. Factors such as the organization from which the research was conducted, the journal in which it was published, and the country in which the experiment was conducted are key factors worth considering. For instance, it has been demonstrated that public and private science organizations pursue distinct goals and incentives when conducting research, which can have an effect on the outcome[[10]](#footnote-10). Here we present a meta-analysis of impact of glyphosate on humans, environment and other nontarget organisms. Specifically, we identify the factors that influence the outcomes of scientific research to date regarding the potentially adverse impacts of GBH on human and animal health and the environment. Understanding the reason why science on this subject has been inconclusive is and was not able to establish itself as the primary driver in formulating science-based policies and regulations is important for not only glyphosate regulation but also other subjects with divergent science backed findings.

To ascertain the factors that influence the results of previous scientific research on the potential adverse effects of GBH on human, animal health and the environment, we conducted a systematic review of published studies on the effects of glyphosate-based herbicides on humans, animals, the environment, and non-target organisms. The CrossRef application programming interface (API) was used in conjunction with the Habenero module in Python to search for the term "Glyphosate," followed by the selection of a subset of data that included only entries containing the terms "daily intake", "dose", "risk", "endocrine", "AMPA", "A.M.P.A.", "toxicology", "cancer", "health", "human", and "carcinogen". Following the search process, a total of 1,523 entries (studies) were generated between 1987 and 2021, of which 503 were deemed appropriate or relevant for inclusion in the meta-analysis. Excluded searches were those that were not original experiments; additionally, studies that did not examine the effect or impact of glyphosate on humans, the environment, animals, or non-target organisms were excluded. Additionally, the meta-analysis excluded articles that were comments, responses to editors and authors of original experiments, articles on glyphosate regulatory and legal concerns, and articles reporting on cases of accidental and intentional glyphosate ingestion in medical journals.

This study applies a methodology that, to our knowledge, has not been adopted in conducting reviews and analyses of this area of research, the Directed Acyclic Graphs (DAGs). The DAG approach has not caught on in the field of economics, agricultural economics to be specific even though it presents an avenue to capture critical assumptions that demonstrate the path the researcher perceived the causal relationships (Imbens 2020). A directed acyclic graph (DAG) is an alternative method for determining contemporaneous causal relationships between variables. In causal structures, DAGs are used to represent researchers' a priori hypotheses about the relationships between and among variables. A DAG is a graphic illustration of a graph with directed edges (arrows), linking nodes (variables), and their paths. Computer algorithms generate graphs containing nodes (vertices, variables) and edges between nodes to discover these causal relationships.

Let A,B and C represent nodes which are variables. The edges can be directed or undirected, and they represent a causal relationship between nodes (indicated by the marks). A path is an unbroken sequence of distinct nodes connected by edges; a directed path, such as the path from A to C (A→B→C) follows the edges in the direction indicated by the arrows. An undirected path, such as the A to C path, does not follow the direction of the arrows. Kinship terms are usually employed in the representation of the relationship within a path. If a directed path exists from A to C, then A is C's ancestor and C is A's descendant. In the case of the directed path A→B→C, A is a direct cause or parent of B, and B is a child of A and parent of C, whereas A is an indirect cause or ancestor of C. The node B is an intermediary or mediator variable on the directed route since it is located on the causal path between A and C.

The DAGs were created using the PC and Parallel PC methods implemented in Python. These two algorithms were selected because they enable us to determine the reliability of the directions and relationships in the data provided by the PC algorithm. The PC algorithm is broken into two phases: first, it learns a skeleton graph from data consisting entirely of undirected edges, and secondly, it orients the undirected edges to construct an equivalence class of DAGs (Spirtes et al 2000). The theoretical underpinning of the PC algorithm is that if there is no connection (edge) between nodes X and Y, then there exists a set of vertices Z that are either neighbors of X or Y and hence independent of X and Y. In other words, Z disassociates X and Y. The PC algorithm begins with a fully linked network and determines whether an edge should be eliminated or preserved using conditional independence tests. The PC algorithm determines the independence of two variables connected by an edge, X and Y, conditional on a subset Z of all X and Y's neighbors.

Results

Three hundred and seventy-six studies, representing 74.8%, reported that GBH could have detrimental impacts on humans, non-target creatures, or/and the environment. Around 25.2% of studies found that GBH had no harmful effect; hence, they are considered safe for humans, animals, non-target creatures, and the environment. The bulk of these research, 270, examined the influence of GBH on non-target creatures and the environment, including other plants, aquatic organisms, rodents, bees, and microbes. The meta-analysis included 281 research that examined the effects or consequences on human health. This included cancer, hormone changes, and any other potential risk to human health that GBH may offer. The acceptable daily consumption of glyphosate in food and water was studied in 14 of the 503 research. The number of papers making statements about the impact of GBH has surged from less than ten in 2005 to 67 in 2020 over the last two decades.

Discussion

Methods

Data availability

Code availability

References

Acknowledgements

Author Information

Ethics declarations

Additional Information

Extended data figures and tables

Supplementary information

Rights and permissions

About this article

Comments

1. (Benbrook 2016) [↑](#footnote-ref-1)
2. (Stong 1990) [↑](#footnote-ref-2)
3. (Knox et al 2013) [↑](#footnote-ref-3)
4. (Areal, Riesgo, and Rodrãguez-Cerezo 2013) [↑](#footnote-ref-4)
5. (Séra 2013) [↑](#footnote-ref-5)
6. (Bohn et al 2014) [↑](#footnote-ref-6)
7. (Swanson et al 2014) [↑](#footnote-ref-7)
8. (Myers et al 2016) [↑](#footnote-ref-8)
9. (Glenna and Bruce 2021) [↑](#footnote-ref-9)
10. (Glenna and Bruce 2021) [↑](#footnote-ref-10)