Available online at www.sciencedirect.com

ScienceDirect

Journal of Policy Modeling 45 (2023) 103–120

www.elsevier.com/locate/jpm

The role of funding on research and science: The impact of glyphosate herbicides on health and the environment

Kodjo Barnor, James Caton, Dragan Miljkovic *,[1]

Department of Agribusiness and Applied Economics at North Dakota State University, Fargo, ND, USA

Received 15 September 2022; Received in revised form 30 October 2022; Accepted 19 November 2022
Available online 5 January 2023

Abstract

The objective of this research is to determine the factors that influence the outcomes of previous scientific research on the potential adverse effects of glyphosate-based herbicides (GBH) on human and animal health and the environment. The emphasis is placed on answering the questions about the causal linkages between who funds and performs the research and the research outcomes. A lack of change in use of the GBHs in agriculture stems directly from public (Government) support of the position how the GBHs are safe for humans and the environment. The results of our meta-analysis clearly demonstrate how large and growing majority of influential research on the subject suggests otherwise. Early research on the subject, prior to 2010, done by private and public sector researchers was strongly indicating how GBHs are safe for humans, animals and the environment. It is possible that there is inertia in food safety policy leading to this large gap and disconnect between the results of hundreds of more recent studies and the (current) course of public policy. This study helps us better understand why science on this subject has not been conclusive and thus not the main driver of "science-based" policies about the GBH based production of genetically modified foods. The importance and the implications of this research are obvious: Evidence-based decisions and policies informed by rigorous research and unimpeded by other interested parties are necessary when it comes to developing public policy that affects food safety and in turn human and animal health, and the environment.

Keywords: Directed acyclic graphs; Glyphosate-based herbicides; Human and animal health, and the environment; Research outcomes; Science policy

* Correspondence to: Department of Agribusiness and Applied Economics, North Dakota State University, NDSU Dept. 7610, Fargo, ND 58108-6050, USA.
E-mail address: Dragan.Miljkovic@ndsu.edu (D. Miljkovic).
[1] ORCID iD: 0000-0001-7511-7260

https://doi.org/10.1016/j.jpolmod.2023.01.001

1. Introduction

Global adoption of genetically modified organisms (GMOs) is a contentious issue due to a lack of conclusive scientific evidence about the consequences of GMO food production and consumption on humans, animals and the environment. The World Health Organization (WHO) defines GMOs as those organisms in which the genetic material has been altered in a way that does not occur naturally (WHO, 2022). In general terms, the safety assessment of GM foods should investigate: a) toxicity, b) allergenicity, c) specific components thought to have nutritional or toxic properties, d) stability of the inserted gene, e) nutritional effects associated with genetic modification, and f) any unintended effects which could result from the gene insertion (Food & Agriculture Organization of the United Nations-FAO, 2022). Accordingly, the GM products that are currently on the international market have all passed risk assessments conducted by national authorities. However, some of the recent studies sound alarm about the direct impacts of the GM foods on human and animal health, and the environment.

Special concern and emphasis are placed on the use of pesticide glyphosate, facilitated by developing GM varieties of crops such as soybeans or corn that are resistant to the use of glyphosate. Swanson et al. (2014) underscore these concerns: "A huge increase in the incidence and prevalence of chronic diseases has been reported in the United States (US) over the last 20 years. Similar increases have been seen globally. The herbicide glyphosate was introduced in 1974 and its use is accelerating with the advent of herbicide-tolerant genetically engineered (GE) crops. Evidence is mounting that glyphosate interferes with many metabolic processes in plants and animals and glyphosate residues have been detected in both. Glyphosate disrupts the endocrine system and the balance of gut bacteria, it damages DNA and is a driver of mutations that lead to cancer." Such evidence is very explicitly emphasized in some of the recent studies. US Department of Agriculture (USDA) data document dramatic increases in the use of glyphosate-based herbicides and GM soybeans is a major driver for this development (Benbrook, 2012, 2016). US GM soybeans thus represent a system that is influenced by glyphosate exposure and should be an ideal system in which to test whether crop management practices that include spraying with glyphosate might lead to accumulation of chemical residues, or other compositional differences, in the final soy product. Residue analysis is of particular interest, since there are no programs in the EU, US or Canada designed to monitor the main herbicides used in transgenic crop production. One of the most influential experimental studies to this effect on GM soybeans by Bøhn et al. (2014) uncovers that glyphosate tolerant GM soybeans contain high residues of glyphosate and rejects that, "…GM soy is "substantially equivalent" to non-GM soybeans." (Bøhn et al., 2014, p. 207).

In response to the findings of most recent scientific studies (e.g., Guyton et al., 2015), the International Agency for Research on Cancer (IARC, 2015) concluded that glyphosate is "probably carcinogenic to humans." As that announcement, a group of prominent scientists from the USA, Canada and the UK (Myers et al., 2016) have produced a Statement of Concern drawing on emerging science relevant to the safety of glyphosate-based herbicides (GBHs). Their Statement of Concern considers current published literature describing GBH uses, mechanisms of action, toxicity in laboratory animals, and epidemiological studies. It also examines the derivation of current human safety standards. They conclude that: (1) GBHs are the most heavily applied herbicide in the world and usage continues to rise; (2) Worldwide, GBHs often contaminate drinking water sources, precipitation, and air, especially in agricultural regions; (3) The half-life of glyphosate in water and soil is longer than previously recognized; (4) Glyphosate and its metabolites are widely present in the global soybean supply; (5) Human

exposures to GBHs are rising; (6) Glyphosate is now authoritatively classified as a probable human carcinogen; (7) Regulatory estimates of tolerable daily intakes for glyphosate in the United States and European Union are based on outdated science.

Concerns that global population and income growth may drive food demand beyond what can be supplied sustainably have intensified (e.g., Suweis, Joel, Maritan, Rinaldo, & D'Odorico, 2015). While improved food production technology, such as GM varieties of herbicide resistant crops, is often touted as a solution to the food security problems, there is growing concern about the environmental and health consequences of such technologies (e.g., Myers et al., 2016). Notably, there are solutions such as reducing post-harvest loss and food waste as alternative pathways to meeting rising food demand using existing environmentally sustainable systems (e.g., FAO, 2019; Miljkovic & Winter-Nelson, 2021). There is a need to properly examine food technologies through rigorous scientific research that will advise on their safe adoption and use by public policy. However, the outcomes of scientific research in this area are often ambiguous thus failing to provide clear guidance for best policy actions.

The objective of this research is to determine the factors that influence the outcomes of previous scientific research on the potential adverse effects of GBH on human and animal health and the environment. The emphasis is placed on answering the questions about the causal linkages between who funds and performs the research and the research outcomes. The study will help us better understand why science on this subject has not been conclusive and has not been able to be the main driver of "science-based" policies about the GBH based production of GMO foods. The importance and the implications of this research are obvious: Evidence-based decisions and policies informed by rigorous research and unimpeded by other interested parties are necessary when it comes to developing public policy, particularly when it affects food safety and in turn human and animal health, and the environment.

1.1. Literature review

In the past decade, there has been the adoption of meta-analysis to evaluate the effect, risk, and safety of GBH use. Lipsey and Wilson (2001) defined meta-analysis as a form of survey study in which scientific studies are assessed (surveyed). The researchers in this kind of study rely on the outcomes of previously completed studies as a source of data. The procedure of study selection and the analytical approach used in the meta-analysis are critical factors. Selection of acceptable research papers, accurate coding of their many characteristics, quantitative findings, and valid usable analysis, as well as interpretation of the combined results, are all critical considerations for meta-analysis. Chang and Delzell (2016) argued that the need to evaluate the literature on GBH risk has been warranted by the International Agency for Research on Cancer (IARC) classification of glyphosate as "probably carcinogenic to humans" in 2015. This was contrary to both earlier and subsequent assertions by organizations such as the US Environmental Protection Agency (EPA, 2017).

Researchers have sought to evaluate past studies through meta-analysis by employing various techniques to determine the safety, risks, and impacts associated with GBH use (e.g., Chang & Delzell, 2016; Nguyen et al., 2016; Cai et al., 2017; de Castilhos et al., 2016; Acquavella et al., 2016, pp. 1; Zhang et al., 2019; Battisti et al., 2021). Chang and Delzell (2016) looked into the link between glyphosate exposure and the risk of non-Hodgkin's lymphoma (NHL) and the main histopathological subtypes of NHL. Studies used for this meta-analysis were original experiments which estimated the RR (rate ratio, prevalence ratio, or odds ratio) of lymphohematopoietic cancer (LHC), NHL, leukaemia, and other subtypes of these

diseases associated with glyphosate exposure. A web scraping method was used to extract articles with certain keywords, which were evaluated for suitability. Certain key findings from the studies were extracted. The researchers calculated fixed-effects and random-effects meta-RRs with 95% confidence intervals for associations with at least two independent RR estimates from different study populations. The study found and concluded that there was no link between glyphosate exposure and the risk of NHL, HL, MM, leukaemia, or any subtype of LHC. Nguyen et al. (2016) found that different rates and formulations of herbicide application, the presence or absence of plants, and variability in soil parameters such as pH and organic carbon (OC) led to contradictory findings in research into the effect of glyphosate on soil microbial biomass and respiration. The authors sought to investigate this by using linear mixed-effect and boosted regression tree models. The researchers discovered that the dosage and duration of glyphosate exposure play a big role in the reaction of the whole soil microbial biomass and respiration. They proposed that, because soil microbial response is influenced by management and environmental factors, broad statements about glyphosate's toxicity or safety should be qualified by specifics about the conditions under which it was applied. Cai et al. (2017) conducted a meta-analysis to evaluate the potential adverse effects of GBH use on the reproductive function of male rodents. Eight studies were selected after a systematic and exhaustive literature search was conducted in the MEDLINE, TOXLINE, Embase, WANFANG, and CNKI databases. A random-effects model was run with a chi-square test used to determine the heterogeneity among the study results. The findings of a meta-analysis back up the hypothesis that glyphosate exposure reduces sperm concentration in mice. By estimating the natural logarithm of the response ratio from 81 studies, de Castilhos Ghisi et al. (2016) conducted a meta-analytical review of experimental studies on the relationship between exposure to glyphosate (GLY) and its formulations with the formation of micronuclei (MN). The cumulative effects size corroborated an overall positive association between GLY exposure and its formulations and MN in a woodland plot. The size of the cumulative effects was adversely related to exposure time and not obviously related to GLY dose, but it can be traced back to the various test systems, exposure routes, and protocols investigated. Finally, the study concluded and supports the theory that GLY and its formulations increase the likelihood of MN formation.

Battisti et al. (2021) used a meta-analysis to evaluate the impacts of GBH on bee mortality. A search of the databases Web of Science, CAPES (Coordination for the Improvement of Higher Education Personnel-Brazil), Scopus, and PubMed was conducted for this purpose. The researchers looked at papers published between 1945 and October 2020 that looked at the impact of GBH on bee mortality. A total of sixteen papers on mortality were selected, with a total of 34 data sets. The majority of the sets showed differences between the control and experimental groups, indicating that GBH treatments resulted in greater bee mortality. When compared to their respective control groups, the findings were different when considering the technique used (ingestion or contact), the phase of the biological cycle (adults or larvae), and the dosage (an ecologically significant dosage and recommended by the manufacturer). As a result, the study concluded that GBH was poisonous to bees.

2. Data

Appropriate original experiments and studies included in this meta-analysis were identified and selected through a web scraping method based on identified scientific keywords and terms using Python. The study accessed the CrossRef application programming interface (API) using the Habenero module in Python. The term "glyphosate" was looked up. This was followed by the

selection of a subset of data which included only entries that contained the following: “daily intake”, “dose”, “risk”, “endocrine”, “AMPA”, “A.M.P.A.”, “toxicology”, “cancer”, “health”, “human”, “carcinogen”. A total of 1523 entries (studies) were generated after the search process.

After a thorough evaluation of all 1523 studies from the search process, 503 studies were deemed appropriate or relevant to be considered in the meta-analysis. Several criteria were used to determine whether a study should be included or not. A study is expected to be an original experiment before it is included. This means reviews, literature reviews, and meta-analysis were excluded. Studies whose objectives were not to look at the effect or impact of glyphosate on humans, the environment, animals, and non-target organisms were also excluded. Studies excluded under this criterion were mainly looking into the efficacy of glyphosate on various weeds, the susceptibility of certain weeds to glyphosate, and the methodology of identifying glyphosate in water, food, and other substances such as chromatography. Also, articles comparing the efficacy of glyphosate with another herbicide were excluded.

Some articles could not be found online, even their abstracts. Others had only part of their full text-body available online. The abstracts of such articles excluded had very little information and were not enough to draw conclusions on their outcomes. Also, articles that were comments and responses to editors and authors of original experiments were dismissed from our meta-analysis. Articles on glyphosate regulatory and legal concerns were also excluded because they did not make a statement on the outcome of effect or impact of GBH. Some entries of articles on the list were repeated, hence only one entry was used. Finally, articles reporting the findings on cases of accidental and intentional direct ingestion of glyphosate published in medical journals were not included in the meta-analysis.

The 503 studies evaluated in the meta-analysis were published between 1987 and 2021. The number of studies over time is presented in Fig. 1, indicated by the total height of each bar in each of the subfigures. When considering researchers’ affiliation, university researchers were the most active in conducting research on the impacts of GBH, followed by public institutions such as regulatory agencies and state-funded research organizations. Private sector affiliation organizations include laboratories, research institutions, groups recognized as anti-glyphosate, and companies producing agricultural chemicals. Groups recognized as anti-glyphosate or producers of agricultural chemicals were also identified in this category. Even though international agencies such as the European Food Safety Authority were identified, they comprised a minuscule component of the study, and hence dropped out.

Finally, each study is coded concerning its findings with respect to health or the environment. If the study found that glyphosate was harmful to health or environment, the study result is recorded as a 1. If not harmful, the study result is coded as a 0. Conclusions from each study suggest either that GBH does or does not pose a potential risk even when used at recommended dosages, reference doses, and maximum contaminant levels. The recommended dose is the recommended producer dosage applied. The reference dose is an estimate of the amount of a chemical that a person might be exposed to on a daily basis for the remainder of their lives without experiencing significant adverse health consequences. Typically, reference doses are expressed as milligrams (mg) of chemical per kilogram (kg) of body weight per day. The maximum contaminant level (MCL) is the maximum contamination level that is legally permissible in drinking water. In the U.S., the reference dose (RfD) for glyphosate is 1.75 mg/kg/day and the maximum contaminant level (MCL) is 0.7 mg/L. For humans, the Acceptable Daily Intake (ADI) of glyphosate plus specific metabolites (AMPA, N-acetyl glyphosate, and N-acetyl AMPA) is 1.0 mg/kg. These figures change slightly depending on the country of use. The studies reviewed conducted their experiments using these dosages and limits as per the country

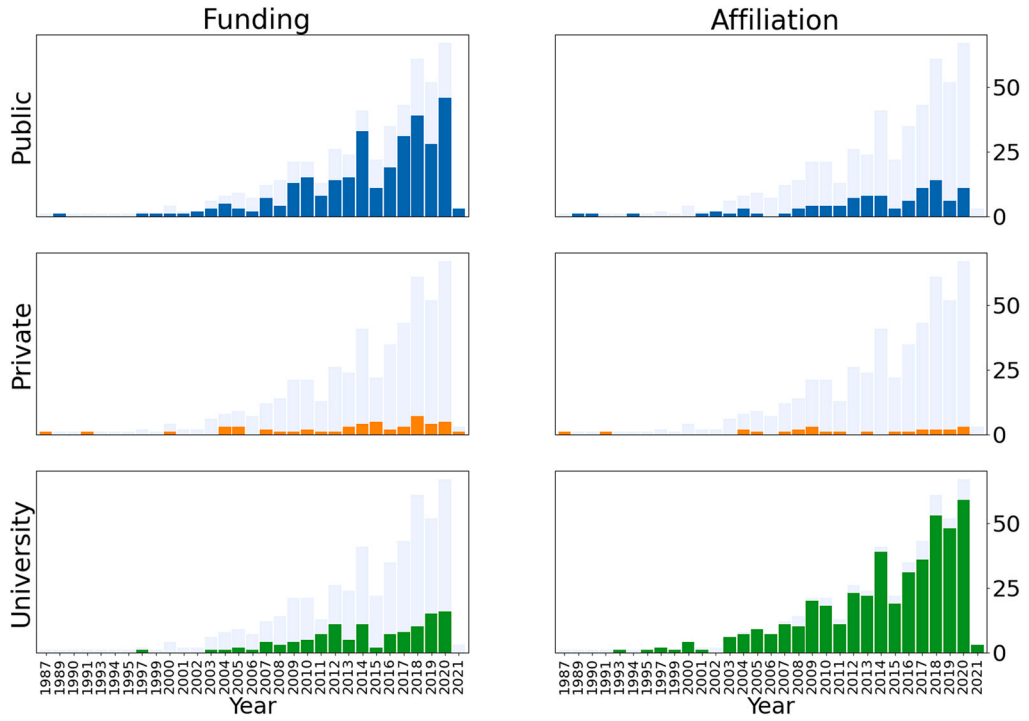

Fig. 1. Comparison of Number of Studies Each Year by Funding and Affiliation to All Inclusive Total.

of experiment as a benchmark. Studies asserted adverse effects on humans, the environment, or other non-target organisms based on these limits stipulated by the country of experiment.

In research, funding sources are a critical component of the study's outcome. Resnik (2000) asserts that there has been growing concern about the influence of financial interests and financing sources on research (outcomes). Recent publications require writers to disclose the sources of financing for their research and disclose any potential conflicts of interest. While others have argued that conflicting interests could jeopardize research and outcomes, this analysis focuses exclusively on the average outcome by funding source and affiliation. Our study identified the primary funding sources as public, university, private, and international, in descending order. The category of international is ambiguous and, thus, excluded from analysis. Project funding sources and affiliations as a share of all projects in a given year are indicated in Fig. 1. For the purposes of this study, university sources of funding were defined as funding sources from a university or a department. While we recognize that these sources could ultimately come from public, private, or international sources, we stick with university sources because these were what were available and acknowledged during data extraction from the analysed studies. Also, a study can be funded by many different sources, and some studies do not say where the money comes from at all. This has been considered in the analysis and discussion.

To illustrate the diversity of studies-sources for the data used in this meta-analysis, we classify them by country and journal quality as measured by the impact factor. Some countries stood out as being very productive in conducting original studies into the effects of GBH. The country of location was the country in which the study was carried out, even though the authors could be from a different country. Brazil was the leading country, with 102 (20.3%) of the papers

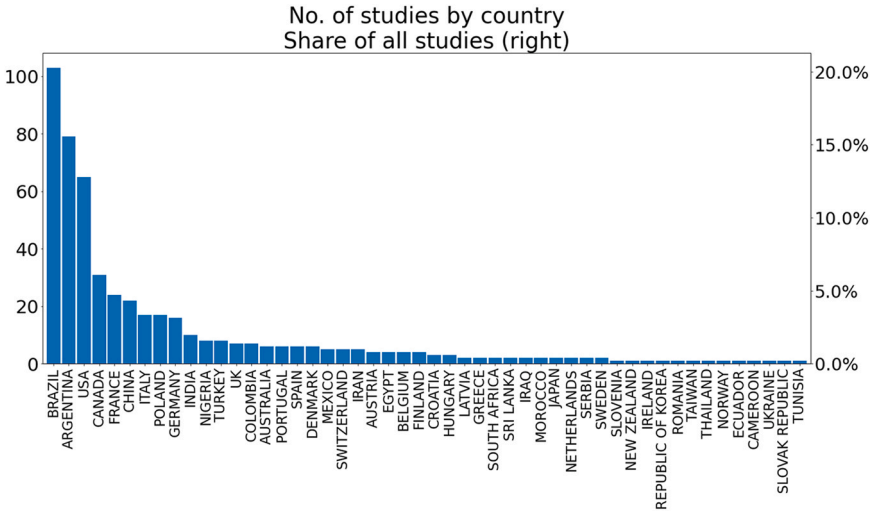

Fig. 2. Number and Share of Studies by Country and Share.

considered. This was followed by Argentina (79; 15.7%), the USA (63; 12%), Canada (30; 6%) and France (24; 4.8%) as the five leading countries. In their bibliometric analysis, Zyoud et al. (2017) also identified these five countries as the leading producers of research into glyphosate safety, but in different rankings. Fig. 2 ranks countries included in the dataset whose researchers have conducted any studies evaluating the impact of glyphosate on environment or health.

The impact factor of a journal is a good measure of the quality and impact of the journal. The journals with the highest impact factors whose papers were considered for the meta-analysis include Proceedings of the National Academy of Sciences (9.423), Journal of the National Cancer Institute (9.702), Water Research (9.15), Environmental Health Perspectives (8.326), and Environment International (7.577). Most journals in the sample were high-impact journals in their field. The overall distribution of results is presented in Fig. 3. The mean impact factor for each result is indicated by the vertical line of the colour associated with that result. Papers from studies that make it into these journals are considered to be high-quality due the rigorous review process and the influence in the field. People who write in these journals are generally considered experts in a field and help advance the knowledge in that field.

3. Methodology

Directed acyclic graphs (DAGs) are visual representations of identified causal flows between and among a series of variables (Pearl, 1995, 2000). DAGs use computer algorithms to visualize causal relationships based on statistical evidence (Pearl, 2000). DAGs are an alternative to Granger causality tests in that they look at non-time sequence asymmetry in causal interactions rather than the time sequence asymmetry used by the Granger test (e.g., Imbens, 2020; Barrera and Miljkovic, 2022). 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.

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

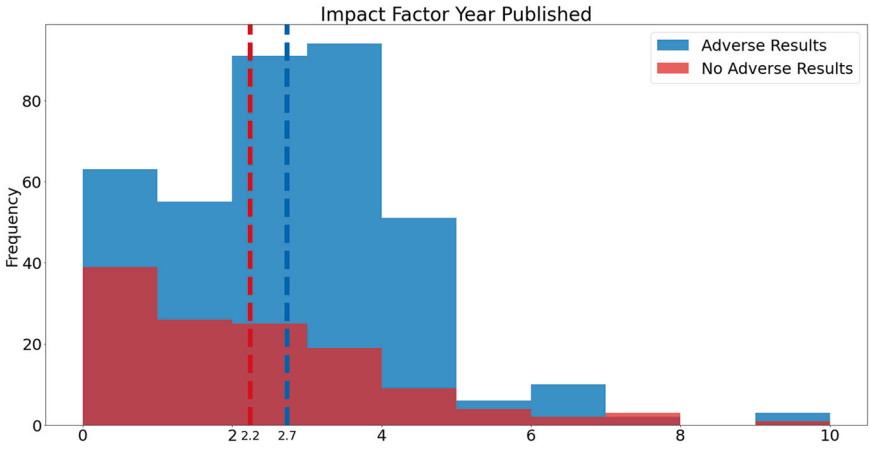

Fig. 3. Comparison of Average Results by Journal Impact Factor in the Year Published (bars are overlapping).

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. As a node on the directed route, B is an intermediary or mediator variable. It is on the causal path between A and C.

Because no node may have an arrow pointing to itself, and all edges must be directed (contain arrows), DAGs are acyclic (Greenland et al., 1999). In other words, there is no permissible directed path from any node to itself. The assumption that causes must come before effects is enforced by these rules. When assessing endogeneity from these graphs, variables with no causal input are exogenous, whereas variables with causal input are endogenous (Spirtes et al., 2000). According to Miljkovic et al. (2016), a DAG is mathematically represented as the conditional independence by the recursive product decomposition:

$$\Pr(v_1, v_2.....v_n) = \prod_{i=1}^{n} \Pr(v_i \mid p\pi_i) \tag{1}$$

where Pr is the probability of the variables $(v_1, v_2.....v_n)$. The product operator is denoted by Π, and $p\pi_i$ denotes the realization of a subset of variables that produce v_i in the order (i = 1,2,.n). The work of Pearl (2000) on D-separation allows independencies and causes to be visually expressed. D-separation is a criterion for determining if a set A of variables is independent of another set B, given a third set C, given a certain causal network. The concept is to identify "dependency" with "connectedness" (the presence of a connecting channel) and "independence" with "unconnectedness" or "separation." Pearl (2000) suggests D-separation as a graphical representation of conditional independence. In other words, D-separation characterizes the conditional independence relations defined by the equation. If we construct a directed acyclic graph in which the variables corresponding to $p\pi_i$ are represented as the parents (direct causes) of v_i, we may read off the graph the independencies suggested by the equation using the concept of D-separation (Pearl, 2000).

The DAGs in this study were created using the PC, Parallel PC, and Stable PC algorithms implemented in Python. We first explore the PC approach (Spirtes et al., 2000) for learning

directed acyclic graph Markov equivalence classes (DAGs). As a result of its use of conditional independence rules, the PC algorithm is called a constraint-based method. The PC algorithm begins with a fully connected network and determines whether an edge should be eliminated or preserved using conditional independence tests. However, there may be a drawback to the PC algorithm: the outcome of the PC method is variable-order dependent, i.e., the result may change depending on the order of the variables in the input dataset. We then use Parallel PC and Stable PC algorithms (Colombo & Maathuis, 2014) to overcome this problem and as a robustness check.

4. Results

Our goal is to generalize findings of research concerning the effect of glyphosate on human and animal health and the environment. To accomplish this task, we take several approaches. First, we compare the moving average of mean results from each year to approximate the evolution of scientific consensus. This allows us to evaluate the temporal evolution of scientific consensus. We are also interested in inferring whether or not there exists a statistically significant difference between findings by different categories of researchers. We divide project results according to funding source and institutional affiliation, each described as public, private, or university. We then compare this casual inference with probit regressions that estimate the relationship between study outcomes and categories of funding and affiliation. Finally, we employ DAGs to estimate the impact of funding sources and affiliation on study findings.

4.1. Cursory investigation

The result of a study is either 0, which indicates that the study found that glyphosate does not harm either health or environment, or 1, which indicates harm to either health or/and environment. The mean of the sample of studies within a year will therefore be between 0 and 1. The mean of sample means across a given time range approximates the findings of literature across that time period.

A given project can receive funding from or be affiliated with public, private, or university institutions. Fig. 4 approximates findings by funding source and affiliation using 10 year moving averages to approximate each subgroup as well as aggregate findings. In order for a moving average to be calculated, there must exist at least five years of data. According to the central limit theorem, the distribution of these annual sample means is normal if there exists a stable mean outcome for a given category of funding or affiliation. Of course, mean outcomes for research by affiliation and funding can change over time. Limited variation about the mean over time suggests that results are drawn from a stable distribution. The upward trend as the line progresses forward in time suggests growing consensus from scientific studies that glyphosate is harmful for health and the environment.

Findings from all three categories of funding and affiliation follow the trend and move in the direction of the aggregate mean. Thus, for results in most categories, findings have increasingly concluded that glyphosate is harmful to the health and environment. Somewhat surprisingly, this is true even for researchers affiliated with private institutions. There appears to a be greater convergence to the mean with regard to funding sources rather than affiliation. This is likely due to the change in the mix of researchers included in a given project as the presence of researchers with university affiliation as increased significantly over time (Fig. 1). As of the latest observation, the average outcome of all research is within the error term for the average outcome

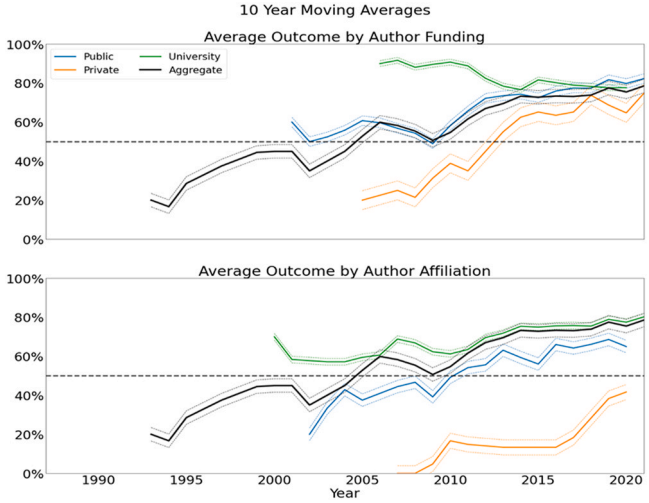

Fig. 4. 10 Year Moving Average of Study Outcomes (dotted lines indicate within group standard errors).

of privately funded research. Institutional affiliation of researchers operating outside of a university are associated with results that are notably different from aggregate findings.

To support the casual inferences drawn from Fig. 4, we conduct a preliminary probit regression. Probit is used to model discrete choice. The model asserts that the probability of y being 1 is a function of the explanatory variables, X. If $P(y = 1)X) \geq 0.5$, then we interpret the result as predicting that $y = 1$. Likewise, we predict that $y = 0$ in the case that $P(y = 1)X) < 0.5$. Errors are normalized by standard deviation in order to remove heteroskedasticity that would otherwise be generated from a standard OLS regression.

We regress the General Outcome on the variables identifying funding and affiliation by institutional type:

$$y_i = \alpha + \sum_{m=1}^{M} \beta_{m,i} x_{m,i} + \varepsilon_i \tag{2}$$

In Eq. (2), index i indicates an observation with no reference to the year that a study was conducted. There exist M different explanatory variables, which indicate the 6 variables that identify funding from or affiliation with public, private, or university institutions. For each explanatory variable we test the null hypothesis:

H_0: Studies subject to factor m do not generate results statistically different than studies lacking factor m.

Since we expect that the mean result should be a value other than 0 (zero), we estimate a constant, α, different from 0. This is consistent with the estimation of a constant in each of the OLS equations used to calculate partial correlations used to construct each DAG. (Table 1).

The preliminary regressions suggest that public funding is associated with a higher probability that a study finds that glyphosate is damaging to health or environment. Both private and public affiliation are associated with a lower probability that a study finds that glyphosate is damaging to health or environment. All three of these findings find support in one or more of the DAG results presented in the next section. Table 2 presents a confusion matrix that categorizes results by consistency of observed and predicted outcomes. The table indicates the percentage

Table 1
Probit Regression Results.

	y = General Outcome	
	(1)	
	All Obs n = 503	
	Param	P-Value
Public Funding	0.290	0.024
Public Affiliation	-0.386	0.042
Private Funding	-0.009	0.968
Private Affiliation	-1.153	0.000
University Funding	0.215	0.179
University Affiliation	0.181	0.435
Constant	0.444	0.073
Pseudo-r^2	0.067	
LL	-226.220	
LLR P-value	0.000	

of observations that lie in each of the four possible combinations of predicted and observed outcomes. Overall, regression (1) correctly predicts over 76% of results. 72.96% of all observations are correctly predicted as indicating a general outcome of 1, with 1.59% of all observed values of 1 being incorrectly predicted as 0. The probit model underpredicts outcomes finding no negative effect. 3.38% of all observations are correctly predicted as indicating a general outcome of 0, with 22.07% of all observed values of 0 being incorrectly predicted as 1.

4.2. Directed acyclic graphs

We follow this initial investigation by estimating directed acyclic graphs using the same variables. Directed acyclic graph simultaneously test every possible hypothesis concerning all possible statistically significant pairwise relationships among all variables. We employ partially directed acyclic graphs. When referring to these, will continue to use the abbreviation, DAG.

We calculate partial correlations in light of causation implied by the DAG. Suppose that a DAG indicates that variable A cause variable B. And suppose that the DAG also suggests that variable B is caused by variables C, such that $A \longrightarrow B \leftarrow C$. To estimate the impact of A on B, we must simultaneously control for variable C. Consistent with Miljkovic et al. (2016), we interpret undirected links as implying endogenous causation. Suppose, that holding all else constant in the scenarios described above, A and B mutually cause one another. And suppose that variable D causes variable A. Thus, $D \longrightarrow A \longleftrightarrow B \leftarrow C$. In this case, we would additionally calculate the impact the influence of B on A by controlling for D.

Table 2
Confusion Matrix.

	Observed 1	Observed 0
Predicted 1	72.96%	22.07%
Predicted 0	1.59%	3.38%

Figs. 5, 6, and 7 show the resultant DAGs estimated using three sets of variables. By figure number, variables included in the DAG are:

5. Private Funding, Public Funding, University Funding, and General Outcome
6. Private Affiliation, Public Affiliation, University Affiliation, and General Outcome
7. Private Funding, Public Funding, University Funding, Private Affiliation, Public Affiliation, University Affiliation, and General Outcome

Each Figure presents a 3 X 3 grid of results. On the vertical axis are indicated which PC algorithm is used, with options indicating the **original**, **stable**, or **parallel** PC algorithm. On the horizontal axis, the statistical significance is used for estimating the existence of a directed link. These include significance levels of 0.1, 0.2, and 0.3. We focus on results in the latter two

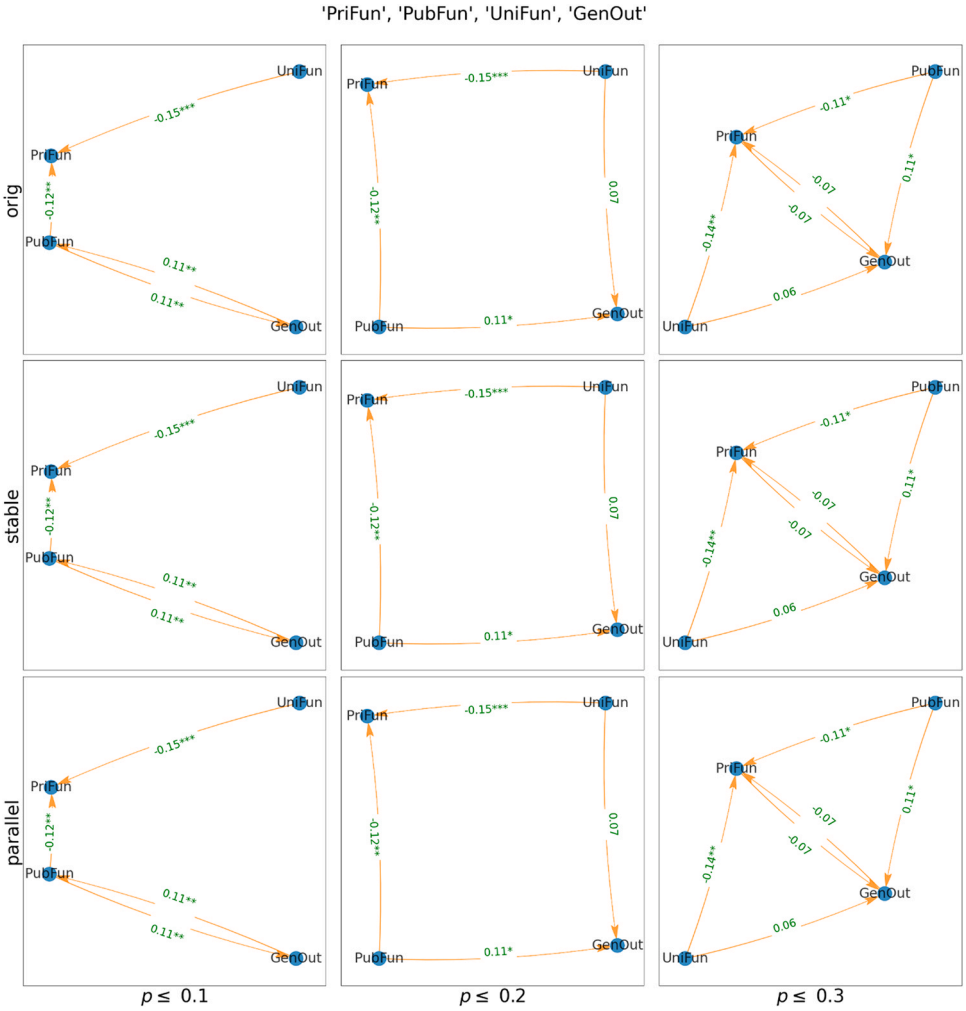

Fig. 5. DAG Inputs: Private Funding, Public Funding, University Funding, General Outcome.

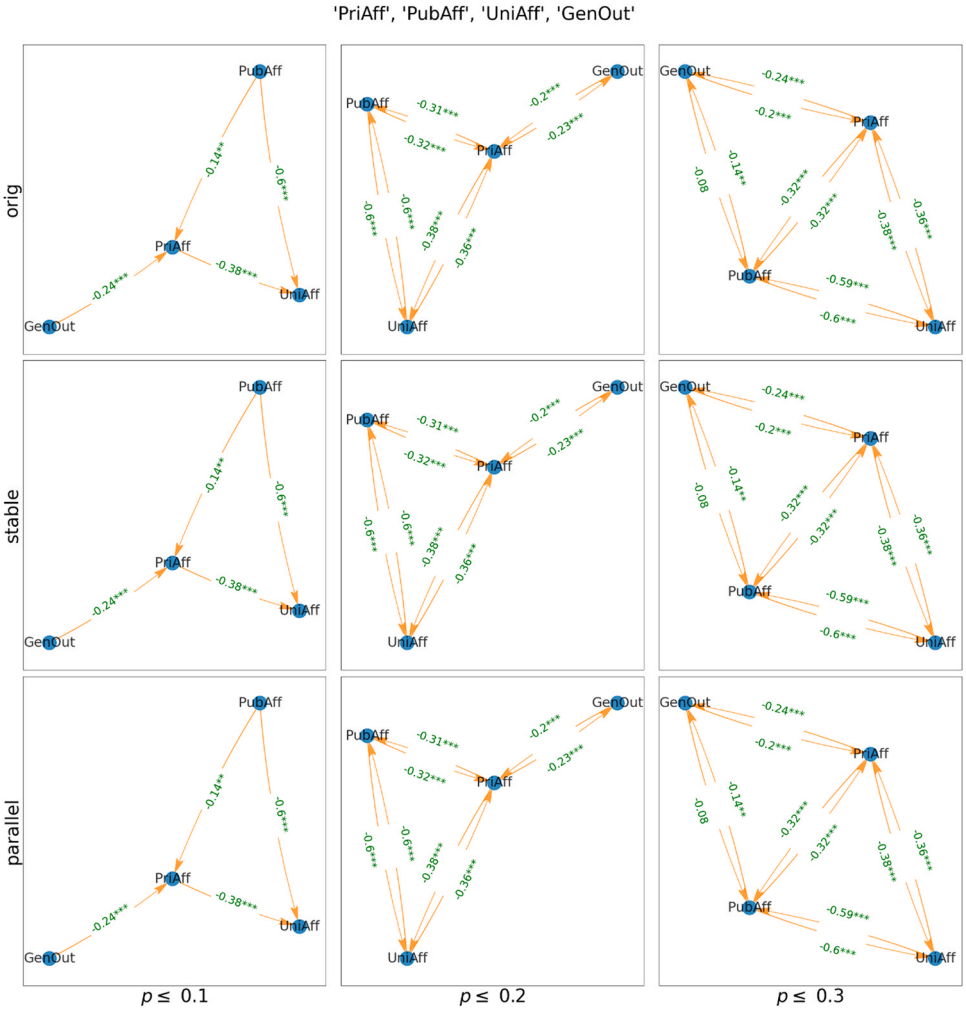

Fig. 6. DAG Inputs: Private Affiliation, Public Affiliation, University Affiliation, General Outcome.

columns, highlighting causal relationships that are reinforced by statistically significant partial correlations defined by $p \leq 0.05$. Within each subplot on this 3 X 3 grid, all links include partial correlations estimated in the manner explained in the previous paragraph. The statistical significance of a given link is indicated by the number of stars. One star (*) indicates a partial correlation with statistical significance $p \leq 0.05$, two stars (**) for $p \leq 0.01$, and three stars (***) for $p \leq 0.001$. We highlight the main result from each figure. We will focus on causal links that are related to general outcome and include statistically significant partial correlations.

In Fig. 5, only funding sources are included with general outcome. The DAGs suggest that public funding is associated with outcomes that are more likely to indicate that glyphosate is harmful to health and environment. The impact estimated by the partial correlation is.11, or 11%. University funding also apparently impacts the outcome, but the partial correlation estimated does not meet the standard for statistical significance.

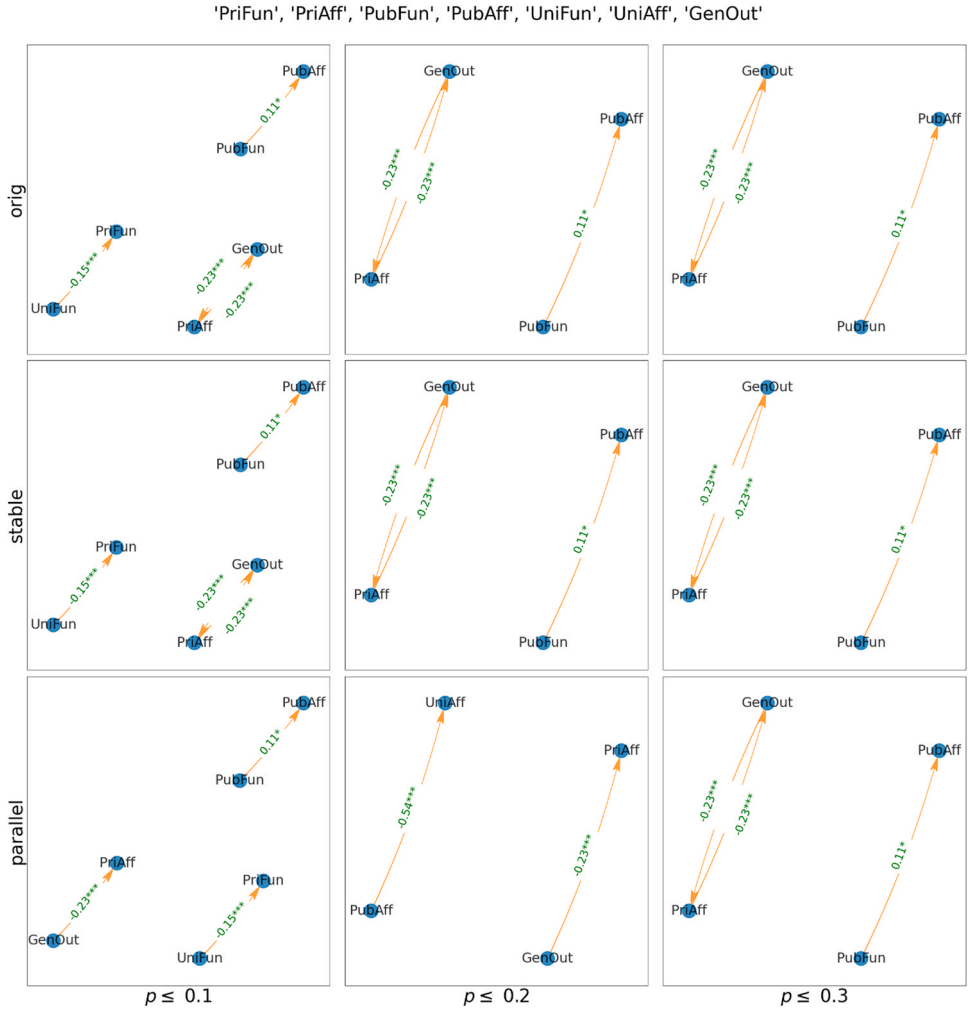

Fig. 7. DAG Inputs: Private Funding, Public Funding, University Funding, Private Affiliation, Public Affiliation, University Affiliation, General Outcome.

In Fig. 6 only institutional affiliations are included with general outcome. The DAGs suggest that both public and private affiliations tend to induce results that are less likely to indicate that glyphosate is harmful to health and environment. Further, causal arrow from general outcome to private affiliation suggests that studies that conclude that glyphosate is harmful (benign) are less (more) likely to be supported by actors affiliated with private institutions. The impact of private affiliation is most consistent, with estimates between $-$ 20% and $-$ 24%, depending upon the direction of the causal arrow. When the DAG is drawn using a statistical significance of $p \leq .3$ for each link, there is an estimated impact for public affiliation of 14% on general outcome. The partial correlation estimated for the causal arrow from general outcome to public affiliation is not statistically significant at the 5% level.

Finally, Fig. 7 include general outcome with both funding and affiliation by institutional type. The result reinforces the inference from Fig. 5 that private affiliation among researchers in a project reduce the likelihood that research will indicate that glyphosate is harmful to health and environment. The estimated partial correlation for this relationship is − 23%, being consistent with estimates from Fig. 5.

Some interesting ancillary results arose during the DAGs analysis. First, DAG in Fig. 5 reveals that university funded research causes reduced funding by the private sector. This may simply be due to the fact that funding sources are often substitutes. A single grant from a single institution may be sufficient for conducting a study. Alternately, this result may reveal an antagonistic relationship between private and university funders, possibly because of differing priors about the research outcome. Second, DAG in Fig. 6 reveals that university affiliation does not have causal impact on the research outcome; however, university affiliation does cause lesser involvement of private and public sector scholars and the vice versa. This result could be interpreted as the mutually exclusive relationship (rather than collaborative relationship) between the university scholars on one side, and private and public sector scholars on the other side. While relationships may span institutional types, the cost to maintain a network that is not biased toward one's own institutional type may be responsible for this result. Relationships of funding sources and institutional affiliation to general outcomes are indicated in Table 3.

4.3. Implications

The effects of GBH on human and animal health and the environment belong to what is known as trans-science questions. Weinberg (1972) defined trans-science questions as "questions which can be asked of science and yet which cannot be answered by science", although "they are, epistemologically speaking, questions of fact." (Weinberg, pp. 211) Since the time Weinberg introduced the term trans-science, we have come to view the interface between science and regulation as part fact, part policy and part decision making (Wirth, 1994). The factual aspect derives from scientific evidence, which makes some policies more politically feasible than others and some decisions more effective or more efficient than others. The policy aspect is reflected in the determination to base decisions on the best available scientific evidence. However, the policy implications of scientific knowledge are interpreted using default inference rules based on non-scientific considerations. The decisional aspect stems from the responsibility of the regulatory government to act expeditiously in effort to serve constituents effectively. Often, our scientific knowledge of consequences is incomplete. This mix of interacting factors often lead to policies that are vague and conflicting.

The decision a consumer makes when outcomes are uncertain is based on limited information. If more information were available, the consumer could make better predictions and reduce risk. Because information is a valuable commodity, people will pay for it. The value of

Table 3
Relationship of Funding Sources and Institutional Affiliation to General Outcomes.

Figure	Relationships to General Outcome
5	**Public Funding** ⟶ **General Outcome** (+)
6	**Public Affiliation** ⟶ **General Outcome** (−)
	Private Affiliation ⟶ **General Outcome** (−)(−)
7	**Private Affiliation** ⟶ **General Outcome** (−)(−)

complete information is the difference between the expected value of a choice when there is complete information and the expected value when information is incomplete. For instance, when we choose to buy cooking (vegetable or corn) oil, we are not sure what the quality is. Some of the information relevant to food safety attributes is available on the labels. However, not all the relevant information, e.g., is the oil coming from the soybeans or corn treated with the GBH, and the potential risk of GBH for health is provided. Thus, consumers would, according to economic theory, value the information, pay for it, and be able to make better informed choice. Although this information is not universally available for all options, some consumers do pay for this information by selecting a more expensive subset often under the heading of organic or non-GMO. Attributes of remaining food purchased by consumers are subject to uncertainty.

If we recall the presence of scientific uncertainty, that is, the inability of science to unambiguously answer the potential adverse effects of GBH on human and animal health and the environment food safety questions (trans-science) when creating food safety policies, the governments' role of arbiter in domestic and international markets, respectively, seems to be rather precarious. We are left with a corner solution, with more expensive options providing this information, but no means of differentiating attributes of low-cost food options. It is unclear where the responsibility of a government would be in case of erroneous standard setting in case of such as this one, i.e., when scientific research outcomes are ambiguous and changing over time. If the government sets standards for industry based on uncertain scientific results and then overlooks and re-enforces them, it seems obvious that the onus is on the government if adverse consequences ensue as a result of such policies. It is, however, unclear how the consumer is protected in the case where industry does comply with governmental regulation while generating outcomes hazardous to consumers. Perhaps, the strength of regulatory approval of potentially hazardous production methods should reflect the strength of scientific consensus.

It is important to emphasize that a lack of change in use of the GBHs in agriculture stems directly from public (Government) support of the position how the GBHs are safe for humans and the environment, e.g., "The draft human health risk assessment concludes that glyphosate is not likely to be carcinogenic to humans" (EPA, 2017). The results of our meta-analysis clearly demonstrate how large and growing majority of influential research on the subject suggests otherwise. Noteworthy reminder is that findings of early research on the subject, prior to 2010, done by private and public sector researchers was strongly indicating how GBHs are safe for humans, animals and the environment. It is possible that there is inertia in food safety policy leading to this large gap and disconnect between the results of hundreds of more recent studies and the (current) course of public policy. Even research conducted by privately and publicly affiliated scholars increasingly exhibit causal link with detrimental outcomes consistent with the overall trend in research outcomes pointing to harmful impacts of the GBHs on human and animal health and the environment. Still, here is a statistically significant gap between findings from private and public sector research as compared to overall findings. This gap certainly warrants further analysis. Perhaps stakeholders of the institutions exert greater influence over discourse generated directly by the institutions, as compared to discourse supported by funding from these institutions. In this vein, publicly funded research, mostly done by university scholars, very strongly points to harmful impacts of the GBHs. Public policy has not changed in light of growing consensus concerning the harmful effects of glyphosate. Risks to humans, animals, and the environment are clearly documented. Harm from glyphosate use will be costly to amend and, in many cases, may be irreversible.

References

Acquavella, J., Garabrant, D., Marsh, G., Sorahan, T., & Weed, D. L. (2016). Glyphosate epidemiology expert panel review: a weight of evidence systematic review of the relationship between glyphosate exposure and non-Hodgkin's lymphoma or multiple myeloma. *Critical Reviews in Toxicology, 46*(su), 28–43.

Battisti, L., Potrich, M., Sampaio, A. R., Ghisi, N.É. D. C., Costa-Maia, F. M., Abati, R., ... Sofia, S. H. (2021). Is glyphosate toxic to bees? A meta-analytical review. *Science of The Total Environment, 767*, Article 145397.

Benbrook, C. M. (2012). Impacts of genetically engineered crops on pesticide use in the US–the first sixteen years. *Environmental Sciences Europe, 24*(1), 1–13.

Benbrook, C. M. (2016). Trends in glyphosate herbicide use in the United States and globally. *Environmental Sciences Europe, 28*(1), 1–15.

Bøhn, T., Cuhra, M., Traavik, T., Sanden, M., Fagan, J., & Primicerio, R. (2014). Compositional differences in soybeans on the market: Glyphosate accumulates in Roundup Ready GM soybeans. *Food Chemistry, 153*, 207–215.

Cai, W., Ji, Y., Song, X., Guo, H., Han, L., Zhang, F., ... Xu, M. (2017). Effects of glyphosate exposure on sperm concentration in rodents: A systematic review and meta-analysis. *Environmental Toxicology and Pharmacology, 55*, 148–155.

de Castilhos Ghisi, N.É., Oliveira, E. C. D., & Prioli, A. J. (2016). Does exposure to glyphosate lead to an increase in the micronuclei frequency? A systematic and meta-analytic review. *Chemosphere, 145*, 42–54.

Chang, E. T., & Delzell, E. (2016). Systematic review and meta-analysis of glyphosate exposure and risk of lymphohematopoietic cancers. *Journal of Environmental Science and Health, Part B, 51*(6), 402–434.

Colombo, D., & Maathuis, M. H. (2014). Order-independent constraint-based causal structure learning. *Journal of Machine Learning Research, 15*(1), 3741–3782.

EPA. "Revised Glyphosate Issue Paper: Evaluation of Carcinogenic Potential." (2017). ⟨https://www.epa.gov/pesticides/epa-releases-draft-risk-assessments-glyphosate⟩ (last accessed on April 27, 2022).

FAO. (2019). State of Food and Agriculture: Moving Forward on Food Loss and Waste Reduction. (available at ⟨http://www.fao.org/3/ca6030en/ca6030en.pdf⟩; last accessed on March 24, 2022).

FAO. (2022). Codex Alimentarius: International food standards. (available at ⟨https://www.fao.org/fao-who-codexalimentarius/en/⟩; last accessed on March 24, 2022).

Greenland, S., Pearl, J., & Robins, J. M. (1999). Causal diagrams for epidemiologic research. *Epidemiology,* 37–48.

Guyton, K. Z., Loomis, D., Grosse, Y., Ghissassi, F. E., Benbrahim-Tallaa, L., Guha, N., ... Straif, K. (2015). Carcinogenicity of tetrachlorvinphos, parathion, malathion, diazinon, and glyphosate. *The Lancet Oncology, 16*(5), 490–491.

Imbens, G. W. (2020). Potential outcome and directed acyclic graph approaches to causality: Relevance for empirical practice in economics. *Journal of Economic Literature, 58*(4), 1129–1179.

International Agency for Research on Cancer (2015). *IARC Monographs Volume 112: evaluation of five organophosphate insecticides and herbicides. Lyon*: World Health Organization.

Lipsey, M. W., & Wilson, D. B. (2001). *Practical meta-analysis.* SAGE publications, Inc,.

Barrera, E. L., & Miljkovic, D. (2022). The link between the two epidemics provides an opportunity to remedy obesity while dealing with Covid-19. *Journal of Policy Modeling, 44*(2), 280–297.

Miljkovic, D., Dalbec, N., & Zhang, L. (2016). Estimating dynamics of US demand for major fossil fuels. *Energy Economics, 55*, 284–291.

Miljkovic, D., & Winter-Nelson, A. (2021). Measuring postharvest loss inequality: Method and applications. *Agricultural Systems, 186*, Article 102984.

Myers, Peterson, J., Antoniou, M. N., Blumberg, B., et al. (2016). Concerns over use of glyphosate-based herbicides and risks associated with exposures: a consensus statement. *Environmental Health, 15*(1), 19.

Nguyen, D. B., Michael, T. R., Rose, T. J., Morris, S. G., & van Zwieten, L. (2016). Impact of glyphosate on soil microbial biomass and respiration: a meta-analysis. *Soil Biology and Biochemistry, 92*, 50–57.

Pearl, J. (1995). Causal diagrams for empirical research. *Biometrika, 82*(4), 669–688.

Pearl, J. (2000). *Causality: Models, Reasoning, and Inference.* Cambridge, UK and New York: Cambridge University Press.

Resnik, D. B. (2000). Financial interests and research bias. *Perspectives on Science, 8*(3), 255–285.

Spirtes, P., C. Glymour, R. Scheines, S. Kauffman, V. Aimale, and F. Wimberly. "Constructing Bayesian network models of gene expression networks from microarray data." (2000).

Suweis, S., Joel, A. C., Maritan, A., Rinaldo, A., & D'Odorico, P. (2015). Resilience and reactivity of global food security. *Proceedings of the National Academy of Sciences, 112*(22), 6902–6907.

Swanson, N. L., Leu, A., Abrahamson, J., & Bradley, W. (2014). Genetically engineered crops, glyphosate and the deterioration of health in the United States of America. *Journal of Organic Systems, 9*(2), 6–37.

Weinberg, A. M. (1972). Science and trans-science. *Minerva,* (10), 209–222.

WHO. (2022). Food, genetically modified (available at: ⟨https://www.who.int/health-topics/food-genetically-modified#tab=tab_1⟩; last accessed on March 24, 2022).

Wirth, D. A. (1994). The role of science in the Uruguay Round and NAFTA trade disciplines. *Cornell International Law Journal,* (27), 817–859.

Zhang, L., Rana, I., Shaffer, R. M., Taioli, E., & Sheppard, L. (2019). Exposure to glyphosate-based herbicides and risk for non-Hodgkin lymphoma: A meta-analysis and supporting evidence. *Mutation Research/Reviews in Mutation Research, 781*, 186–206.

Zyoud, S. H., Waring, W. S., Al-Jabi, S. W., & Sweileh, W. M. (2017). Global research production in glyphosate intoxication from 1978 to 2015: A bibliometric analysis. *Human & Experimental Toxicology, 36*(10), 997–1006.