A META-ANALYSIS OF STUDIES ADDRESSING THE IMPACT OF GBH ON HUMAN, ANIMAL HEALTH AND THE ENVIRONMENT

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

By

Kodjo Barnor

The Supervisory Committee certifies that this ***disquisition*** complies with North Dakota State University's regulations and meets the accepted standards for the degree of

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SUPERVISORY COMMITTEE:

Dragan Miljkovic
Chair

James Caton

Megan Orr

Approved:

April 14, 2022
Date

William Nganje
Department Chair

ABSTRACT

The herbicide glyphosate has been tested and approved by both the FDA and the USDA, as evidenced by many published research papers, i.e., they are deemed safe for humans, animals, and the environment. However, evidence is mounting that glyphosate interferes with many metabolic processes in plants and animals, and glyphosate residues have been detected in both. 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 were investigated.

Using DAGs and Granger causality tests, the study found that while private and public organizations were more likely to generate research indicating that GBH was not harmful, public funding and universities were more likely to produce research indicating that GBH was hazardous. Policy actions should be guided by independent research comprised of actors from major stakeholders and research organizations.

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DEDICATION

I dedicate this thesis to my wife, children, mother, and brother for their assistance in getting me started and eventually completing graduate school. - Kodjo

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LIST OF ABBREVIATIONS

ADF.....Augmented Dickey Fuller.

AMPA.....A-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid.

API.....Application Programming Interface.

CI.....Conditional Independence.

DAG.....Directed Acyclic Graph.

DNA.....Deoxyribonucleic Acid.

ECM.....Error Correction Model.

EPA.....Environmental Protection Agency.

GBH.....Glyphosate Based Herbicide.

GMO.....Genetically Modified Organism.

PC.....Peter Spirtes and Clark Glymour.

PO.....Potential Outcome.

USDA.....United States Department of Agriculture.

VAR.....Vector Autoregressive.

VECM.....Vector Error Correction Model.

WHO.....World Health Organization.

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1. INTRODUCTION

Glyphosate is the active ingredient in many commercial broad-spectrum systemic herbicides used to control weeds. It is also known scientifically as N-(phosphonomethyl) glycine. Glyphosate is a herbicide that is effective against broadleaf weeds and grasses that compete with crops. It was discovered as a herbicide by Monsanto scientists in 1970 and was commercialized under the brand name Roundup in 1974 for commercial cultivation and household usage (Stong 1990). Commercial and trade names for glyphosate have been coming out over the years, like Roundup Ultra, Roundup UltraDRY, Roundup UltraMAX, Roundup WeatherMAX, Touchdown w/IQ, Cornerstone, Clearout 41 Plus, GlyphoMAX, Glyfos Xtra, and Glyphomax Plus.

Crop varieties resistant to glyphosate have been developed, notably soybeans, maize, and cotton, to maximize the usage of glyphosate-based herbicides (GBH) in post-emergence crops. Crops that are Roundup-ready have acquired broad acceptance and adoption (genetically modified types that are entirely resistant to glyphosate). In the United States and other major producers, roundup-ready maize and soybeans dominate production. Around 94 percent of soybeans grown in the United States in 2012 were Roundup Ready (USDA 2014). As a consequence, the use of GBH for weed management has increased significantly. Global glyphosate usage has roughly doubled since the introduction of Roundup-ready genetically engineered crops in 1994. (Benbrook 2016). Between 1974 and 2016, the US used 19 percent of the world's glyphosate, or nearly 1.6 billion kilograms of the 8.6 billion kilograms consumed. According to Benbrook (2016) two thirds of the entire glyphosate used in the US prior to 2014 was used between 2004-2014, demonstrating the surge in the use of GBH

Glyphosate is an organophosphorus compound that functions by inhibiting the enzyme 5-enolpyruvoylshikimate-3-phosphate synthase (EPSPS), which catalyzes the formation of the

aromatic amino acids tyrosine, tryptophan, and phenylalanine in plants. Because humans, other mammals, fish, birds, and insects lack the 5-enolpyruvoylshikimate-3-phosphate synthase (EPSPS) pathway, it is considered benign for these species (Duke et al 2018). As a result, the assertion that it may have little or no effect on non-target species when used at prescribed levels for plants is made. There are a lot of regulatory bodies that make sure that glyphosate-based herbicides and Roundup-ready crops are safe for people and the environment when they are used at the right doses (Knox et al. 2013: Areal, Riesgo, and Rodrguez-Cerezo 2013: Séralina et al 2011).

A current visit to the EPA website espouses that glyphosate is safe for humans, the environment and other organism when used in recommended doses (Environmental Protection Agency, 2017). After a January 2020 review of glyphosate by the EPA, it found that; No risks of concern to human health from current uses of glyphosate; No indication that children are more sensitive to glyphosate; No evidence that glyphosate causes cancer in humans; No indication that glyphosate is an endocrine disruptor; Potential risk to terrestrial and aquatic plants and birds, and low toxicity to honeybees; Residues of glyphosate on any food or feed item are safe for consumers if they comply with the established tolerances. This confirms that GBH are perceived to be safe by the relevant public agencies.

On the contrary, other studies have found evidence that glyphosate disrupts 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 (Bohn et al 2014; Swanson et al 2014). Additionally, the WHO's International Agency for Research on Cancer recently concluded that glyphosate is "probably carcinogenic to humans." In accordance with this, a group of prominent

scientists (Myers et al. 2016) issued a caution statement regarding emerging science regarding the safety and use of GBH, its mechanisms of action, toxicity in laboratory animals, and epidemiological studies. This is also considered the process by which current human safety standards were developed.

Concerns that global population and income growth may drive food demand beyond what can be supplied sustainably have intensified (Pinstrup-Anderson et al 1997; Suweis et al 2015). While improved food production technology is often touted as a solution to the food security problems, there is growing concern about the environmental and health consequences of many production technologies (Myers et al 2016; Swanson et al 2014; International Agency for Research on Cancer 2015). Opponents of the population's justification for food system intensification without careful consideration of negative consequences have proposed solutions such as reducing post-harvest loss and food waste as alternative pathways to meeting rising food demand using existing environmentally sustainable systems (Food and Agricultural Organization of the United Nations 2019). 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.

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 health, safety, and the environment. Scientific and technical data, evidence, and information are critical for public health, safety, and prosperity, as well as for the development, evaluation, and formulation of policy. It has been observed that certain interests can interfere with this process. For instance, Fabbri et al. (2018) opined those corporate interests may steer research agendas away from the most pressing public health questions. Commercial

organizations now have the capacity to influence policymakers via their influence on the types of evidence provided and the types of public-interest solutions considered.

According to Fabbri et al. (2018), increased transparency of funding sources, declaration of conflicts of interest, and increased support for independent research, as well as tight standards governing the interaction of research institutions with commercial companies, should be implemented. Could this address the issue of why research on some topics has proved inconclusive, resulting in divergent outcomes that also impact policy decisions? In this scenario, research on the effect of GBH was unable to establish itself as the key driver in developing scientific-based policy on the adoption and usage of GBH.

Reviews of research on the impact and effect of glyphosate-based herbicides on humans, animals, and the environment employ statistical analysis of glyphosate bioassay data, Cochran-Armitage (C-A) linear trend tests, and qualitative and descriptive analysis of studies conducted over a period of time (Crump et al 2020: Zyoud et al 2017; Portier 2020; Mink 2012). These studies, however, fail to identify the factors that influence or contribute to the disparate findings of scientific research on the potential adverse effects of GBH on human and animal health and the environment to date. It's important to look into why research on this subject has not been conclusive and has not been a big factor in the development of science-based policies for the use of GBH.

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 purpose of this paper is to contribute to the body of knowledge by reviewing and examining scientific research on the effects of glyphosate use. The study will help

us 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 use of GMO foods.

This study employs a methodology that has not previously been used to conduct reviews and analyses in this field of study. A causality test employing directed acyclic graphs, a relatively new statistical technique for analyzing contemporaneous causal relationships. Computer science, epidemiology, and other social sciences make use of the DAG approach. However, it has not gained traction in the field of economics, specifically agricultural economics, despite the fact that it provides a mechanism for capturing critical assumptions that demonstrate how the researcher perceives causal relationships (Imbens 2020). Use of glyphosate will be explained in this way. It will show how scientific studies have come to this conclusion.

The remainder of the thesis is as follows: The following section, two, will review pertinent literature on the subject. Section three will discuss the data and the methodology used to obtain it. The fourth section discusses the empirical methodology; the fifth section discusses directed acyclic graphs. Finally, in Section 5, we talk about the results of the models we made and our closing remarks.

2. LITERATURE REVIEW

In this chapter, a review of studies looking into meta-analysis, meta-analysis of effect or impact of GBH use and application of directed acyclic graphs are presented.

2.1. Meta-analysis

Meta-analysis is a critical tool for assessing aggregate reports and research. It has been used in a broad variety of disciplines and fields, including the assessment of the impact or effect of GBH usage. Lipsey et al. (2001) defined meta-analysis as a form of survey study in which scientific studies (rather than people) 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.

According to Rosenthal and DiMatteo (2002), the cumulation or review of studies in the social sciences and other related disciplines has been mainly qualitative and not quantitative in design. They opined that meta-analysis could provide a quantitative summary of research domains, which has emerged as a more systemic, repeatable, and rigorous method of evidence accumulation. A meta-analysis provides a statistical synthesis of results from a collection of studies. Qualitative or narrative reviews of studies have the main limitation of the subjectivity inherent in the approach (Rosenblad 2009). Researchers in many fields began to move away from narrative reviews in the mid-1980s, and systematic reviews and meta-analysis became popular in the 1990s. A straightforward set of outlined guidelines used in a meta-analysis to find studies and then decide which studies will be included or excluded from the analysis is clearly

defined (Rosenthal and DiMatteo 2002; Rosenblad 2009). Because all the steps in the procedure are defined in detail, the procedure is transparent and repeatable.

Meta-analyses are carried out for several reasons, including to synthesize data on the impacts of interventions, as well as to promote evidence-based policy or practice. Important considerations or questions include when a meta-analysis should be done; what model should be used to analyze the data; what sensitivity analyses should be performed; and how the findings should be interpreted. The intent of the meta-analysis has ramifications. As a result, there is not a one-size-fits-all statistical tool for meta-analysis. Instead, the statistical tool chosen for a meta-analysis is based on its goal (Rosenblad 2009).

After its very first introduction by Glass (1976), meta-analysis has enjoyed widespread use in several fields of study, including the health sciences, psychology, education, marketing, and the social sciences (Nelson and Kennedy 2009). In economics and its related fields, the use of meta-analysis began in 1989–1990 with studies such as Stanley and Jarrell (1989), Walsh et al. (1989, 1990), Weitzman and Kruse (1990), Smith and Kaoru (1990a, b) playing pioneering roles. Meta-analysis has becoming more common in economics, particularly in environmental and resource economics (Nelson and Kennedy 2009).

According to Nelson and Kennedy (2009), results from their study of about 150 meta-analysis studies in economics-related fields revealed that a third of the meta-analysis in economics were in the area of environmental and resource economics. Also, most meta-analyses in economics employ a method known as "meta-regression analysis," in which the researcher gathers a set of primary studies with a common empirical outcome, such as the willingness-to-pay (WTP) for freshwater quality or the impact of air pollution on property values. Even though the current study is situated in the field of applied or agricultural economics, the field from

which it seeks to conduct the meta-analysis is within the biological sciences, with parameters and outcomes making it difficult to use meta-regression analysis.

2.2. Meta-analysis of Effect or Impact of GBH Use

In the past decade, there has been the adoption of meta-analysis to evaluate the effect, risk, and safety of GBH use. Chang and Delzell (2016) opined 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 earlier assertions by organizations such as the US Environmental Protection Agency (EPA), the German Federal Institute for Risk Assessment (BfR), the Joint Meeting on Pesticide Residues (JMPR), sponsored by the Food and Agriculture Organization of the United Nations, and the World Health Organization (WHO).

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 (Chang and Delzell 2016; Nguyen et al 2016; Cai et al 2017; de Castilhos Ghisi et al 2016; Acquavella et al 2016; Zhang et al 2019; Battisti et al 2021).

One of the early meta-analyses on the GBH was carried out by Chang and Delzell (2016) using human epidemiologic studies. The researchers 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 scrapping 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 percent 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, leukemia, or any subtype of LHC, according to the findings.

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 was 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.

2.3. Application of Directed Acyclic Graphs

The bulk of prior research on causal links between economic variables has mainly relied on the Granger (1969) causality approach, which is predicated on the observation that a cause precedes its related effect (and thus an effect does not precede its cause). However, Pearl introduced DAG as a framework for defining contemporaneous causal interactions (Pearl 1985). Directed acyclic graphs (DAGs) are visual representations of identified causal flows between and

among a series of variables (Pearl (2000); Spirtes et al. (2000)). DAGs use computer algorithms to visualize causal relationships based on statistical evidence (Lauritzen and Richardson, 2002).

In observational science, causal inference approaches are widely used, with directed acyclic graphs (DAGs) being particularly common (Krieger et al 2016). The causal interactions between variables are represented as arrows between nodes in a DAG. No causal effect is shown by the absence of an arrow between nodes, and nodes may be calculated or unmeasured (Pearl, 2009). Any variable that has an effect on at least two other variables should be considered. When calculating the influence of one variable on another, DAGs use the "backdoor criteria," a statistical ruleset, to decide which variables should be monitored. Consequently, DAGs are useful instruments for guiding analysis and thinking about relationships (Greenland et al., 1999).

In the applied economics literature, the use of DAGs is gaining popularity. David Bessler has been a pioneer in employing DAG as an analytic tool in applied economics. DAG was used to analyze supermarket beef and pork prices in the report by Bessler and Akleman (1998). DAGs are used in an empirical analysis of traffic occupant fatalities by Roh and Bessler (1999), who used Crandall's data on US traffic fatalities from 1947 to 1981 and expanded the survey to cover 1982–93. Bessler et al. (2003) examine the relationships between five regional wheat markets and DAGs, VARs, and VECMs, concluding that the United States and Canada are the pioneers of wheat pricing. Also, for the VAR and ECM studies of the world's major financial exchanges, Bessler and Yang (2003) use DAGs to assess the causal orderings of inventions for VAR and ECM. Haigh and Bessler (2004) used DAGs and ECMs to look at grain prices in Illinois, grain prices in the US Gulf, and the barge market, and discovered that the Illinois grain market is heavily influenced by the barge and commodity export markets.

DAGs have also been used by other authors to demonstrate causal interactions in applied economics works (Awokuse and Bessler (2003); Miljkovic et al. (2016); Ji et al. (2018)). Miljkovic et al. (2016) used DAGs to demonstrate direct causal interactions and explain endogeneity problems within variables within the energy complex. Using DAGs and ECM, Xu (2017) looked at corn prices in seven Midwestern states and discovered that Iowa led corn pricing during the crop year. Miljkovic and Goetz (2020) used Granger causality and DAGs to assess causal relationships and cointegration checks to determine long-run relationships to investigate the relationship between spot prices, futures prices, and ending stocks for storable commodities. To reproduce Sims' 1986 model of the US economy, Awokuse and Bessler (2003) use DAGs and VAR; oddly, they present DAGs with a significance level of up to 30% to achieve an unambiguous causal direction. Awokuse (2005) re-examined the complex relationship between monetary policy variables and agricultural prices over the time frame (1975–2000) observed using DAGs as an alternative to VAR.

Ji et al. (2018) use a DAG and an ECM to analyse the generators of natural gas markets and discover that oil prices cause natural gas prices. In his essay "Potential result and guided acyclic graph approaches to causality: Relevance for analytical practice in economics," Imbens (2020) noted that DAGs have not caught on in the mainstream in the field of economics, specifically agricultural economics, despite the fact that they provide a way to capture important hypotheses that show the researcher's conception of causal relationships. He went on to say that DAGs would make a significant contribution to the field, but that the most critical thing holding them back is a lack of compelling scientific applications in economics.

Even though the use of meta-analysis to evaluate the impact or effect of GBH use in the current study is not novel, the use of DAGs to establish contemporaneous causality between

research characteristics and the outcome of the research is. This will help with the scientific use of DAGs in applied economics and other fields.

3. METHODOLOGY

3.1. Selection of Studies for Meta-Analysis

The selection of studies is a critical process when conducting a meta-analysis seeking to assess the outcomes of scientific research regarding potential adverse impacts of GBH. 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 1,523 entries (studies) were generated after the search process.

After a thorough evaluation of all 1,523 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. These were considered not to be original experiments or studies. 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. Such studies excluded under this criterion were mainly looking into the efficacy of glyphosate on various weeds, the susceptibility of certain weeds to glyphosate, and articles looking at 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 part of their full articles available online. These were mostly very old papers (mainly before 1995). The abstracts of such articles excluded had very little information and were not enough to draw conclusions on their outcomes. These were mainly old articles from the Toxicology Letters. Also, articles that were comments and responses to editors and authors of original experiments were dismissed and were not included in the 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 were published in medical journals. These were not included in the meta-analysis.

3.2. Directed Acyclic Graphs

In The Book of Why by Pearl and Mackenzie (2018), the Ladder of Causality is a taxonomy of causal problems with three rungs designated as association (correlation and regression), intervention (causation), and counterfactuals, in order of complexity. In the first tier, association, researchers passively observe and make predictions based on their observations. The idea of correlation or association is important. According to the discussion in The Book of Why (TBOW), methods on this tier include regression, as well as several current machine learning methods such as regression trees, random forests, and deep neural networks. Of course, regression is used as a causal method in many disciplines, but TBOW views regression in a framework similar to what econometricians would call the best linear predictor framework, where the regression function is simply a parametric way of setting the conditional expectation (Goldberger, 1991), with little causality in this rung.

The intervention level is the second. The questions on this rung are mostly about manipulations. These are the questions on which much of the causal inference work is concentrated. Randomized trials are one of the most important statistical designs in this context. These topics are far more difficult to answer in observational research, yet they are investigated in a variety of fields using a variety of methodologies. Much of the empirical work in economics is done here. The difficulties usually stem from the inclusion of unobserved confounders of some kind because economists frequently simulate the behavior of maximizing agents, who are frequently more informed than the researcher and take into consideration the predicted outcomes of their actions. The identification procedures described in (Angrist and Krueger, 2001) are applicable here.

The third step of the causality ladder is concerned with counterfactuals. The questions on this third level are more difficult to answer and provide definitive answers to such issues, which are delicately dependent on individual-level variation. The association between potential outcomes provided a treatment and those without a treatment among subpopulations homogeneous in observed characteristics is not point-identified in the Potential Outcome (PO) framework. As a result, estimates that rely on this association, which includes the majority of third-rung questions, are only partially recognized. The economics literature does not devote as much attention to this sort of inquiry as it does to the second.

Formally, Bayesian networks are directed acyclic graphs (DAGs) whose nodes represent variables in the Bayesian sense (Pearl 1985): they may be observable quantities, latent variables, unknown parameters, or hypotheses. Edges represent conditional dependencies; nodes that are not connected (no path connects one node to another) represent variables that are conditionally independent of each other. Each node is associated with a probability function that takes, as

input, a particular set of values for the node's parent variables and gives (as output) the probability (or probability distribution, if applicable) of the variable represented by the node. Pearl and Mackenzie (2018) say that Bayesian networks are ideal for taking an event that occurred and predicting the likelihood that any one of several possible known causes was the contributing factor (Pearl and Mackenzie 2018).

A directed acyclic graph (DAG) is a method for determining contemporaneous causal relationships between variables. 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 (Bessler and Yang 2003). 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 make graphs that have nodes (variables) and edges (connections) between nodes to show 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. 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:

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

where Pr is the probability of the variables $(v_1, v_2 \ldots\ldots v_n)$. 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 Pearls' (1985) 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 "unconnected-ness" or "separation." Pearl (1985) 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, 1985).

Consider the three variable sets A, B, and C while describing d-separation. We can say these variables are d-separated if the flow of information between these nodes is blocked. This is known as d-separation, and it can occur in two ways, first of all if one variable, such as B in

A←B⟶C, is the cause of the other two variables, or if there is a passthrough variable, such as B in A→B→C; and second, when a variable is caused (influenced) by two variables, such as B in A→B←C. Spirtes et al (2000) incorporated the concept of d-separation into the PC algorithm.

In comparison to the econometrics set up in terms of employing instruments, DAG highlights the essential assumptions and structure of the relationship. The DAGs are clearer than the standard econometrics setup, which presents the important assumptions in terms of the correlation between residuals and instruments. DAGs can assist researchers define and share their opinions about the underlying data generation process, which may then assist analyse the statistical relationships found in the data. Developing DAGs is not always simple, and it may need a heuristic approach in which assumptions are checked and amended based on observable statistical associations. A methodical approach to creating DAGs might be beneficial for presenting results and justifying covariate selection. DAGs are also useful for causal modelling since they may infer identifiability from a complicated model.

A mediator is a variable in the causal pathway that connects the cause and the outcome (Pearl & Mackenzie 2018). The mediator is influenced by the cause (A), which in turn influences the outcome. Confounders are factors that influence both the treatment (A) and the outcome (B). Colliders, also known as common effects, are variables that are the children of two other variables (Pearl & Mackenzie 2018). Because the two arrows from the parents "collide" at the descendant node, the word "collider" is employed. The purpose of a causal analysis is to adjust for these other factors such that we receive the same effect size for the target variable as if the target predictor were altered in a controlled intervention (Lederer et al 2019).

Confounding, for instance, is more specific than having a variable that connects with predictor and responder. To find genuine confounders, direction is critical. Although the collider

correlates with cause and result, incorporating it (or adjusting for it) in a multiple regression creates a collider bias on the causal relationship of interest (Pearl 2009). The bottom line of this debate is that in order to show causality for a given link, we must seal the so-called back-door routes for this link (Lederer et al. 2019; Pearl 2009), by controlling for confounders, not adjusting for colliders, mediator bias, and other similar linkages. Due to the nature of the results from the causal inference described above, this approach has been used to argue for the inclusion or exclusion of variables in a regression and, more generally, specification.

3.2.1. DAG Algorithm Used

The DAGs in this study were created using the PC, Parallel PC, and Stable PC algorithms implemented in Python. These algorithms were selected because they enable us to determine the reliability of the directions and relationships in the data provided by the PC algorithm. We 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 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.

However, there are two significant drawbacks to the PC algorithm, particularly when applied to large biological datasets: the runtime of the PC algorithm, which is exponential in terms of the number of nodes (variables) when applied to high-dimensional datasets such as gene expression datasets, which was not a concern in our investigation. Second, 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. Colombo et al. (2012) demonstrated experimentally that approximately 40% of the edges (2000 edges) learned from a real gene expression dataset are not stable, i.e., these edges exist in less than half of the results produced with all possible node orderings.

To overcome this, the concept of parallelism has been employed, which is the process of breaking down a large task into several smaller subtasks and distributing them across multiple cores of the computer's CPU to perform them in parallel. After that, the outcomes of all subtasks will be combined to make the outcome of the main task. The parallel PC algorithm suggests a technique that parallelizes the CI tests inside each level of the stable PC algorithm, not across levels. This approach is practical because conditional independence tests (CI) at a given level are self-contained. Because the graph is updated only at the conclusion of each level, the result of one CI test has no effect on the results of the others. As a result, the CI tests at a given level can be run concurrently without affecting the final outcome. Additionally, this approach has the advantage of predetermining the number of CI tests for each level. Distributing the CI tests evenly across the available cores lets a parallelized method achieve its highest possible speedup.

PC-Stable, a prominent constraint-based approach for causal discovery, is an order-independent variation of the PC algorithm (Colombo et al 2014). As with the original PC method, this technique begins with an undirected, completely connected graph and then performs

conditional independence tests to remove edges between any two variables. To begin, unconditional independence tests are performed on X and Y, and if X is found to be independent of Y, an edge connecting X and Y is eliminated. The program next expands the conditioning set and checks for conditional independence on any remaining edges in the resultant graph that are dependent on some subset of their neighbors. This procedure is continued until no further edges can be removed in this manner.

The algorithm then determines causal direction by (i) orienting colliders (variables with two "parents"), (ii) avoiding the insertion of new colliders, and (iii) avoiding directed cycles (loops) (Colombo et al. 2014). The PC-Stable makes the following assumptions: the causal graph does not contain feedback loops; each variable is independent of its direct effects given its direct causes (causal Markov assumption); the conditional independence relations in the data are the result of applying the causal Markov assumption to the causal graph (causal faithfulness assumption); and the data does not contain unobserved confounders or selection bias.

3.3. Granger Causality

Granger (1969) causality tests are commonly used to determine causal links between different time series. This is accomplished by determining if the lags of one variable are beneficial for explaining another variable. Consider the case when Y and X are two stationary series. In essence, if previous values of X are significant predictors of the current value of Y even after including prior values of Y in the model, then X has a causal effect on Y. To do this, we regress Y on delayed values of Y and X, yielding our unrestricted regression.

$$y_t = \alpha + \sum_{k=1}^{K} \gamma_K y_{t-k} + \sum_{k=1}^{K} \beta x_{t-k} + \varepsilon_t \text{ with } t = 1 \ldots, T. \quad (1)$$

We estimate a constrained regression in which we regress Y against just its lagged values. The F-test is then used to determine if the group of coefficients associated with the lagged values of X is substantially different from zero.

$$H_o = \beta_1 = \cdots = \beta_K = 0$$

If they are significant, we can reject the hypothesis that X does not cause Y since previous values of X contribute to the explanation of the current level of Y. When the lags of one variable aid in the explanation of another, we might assert that X Granger causes Y. The x and y variables can be interchanged to test for causation in the reverse directions, and bidirectional causality can be seen (also called feedback). The traditional Granger Causality can be extended for detecting causal relationships in panel data. The fundamental regression is as follows:

$$y_{i,t} = \alpha_i + \sum_{k=1}^{K} \gamma_{i,k} y_{i,t-k} + \sum_{k=1}^{K} \beta x_{i,t-k} + \varepsilon_{i,t} \quad \text{with } i = 1..., N \text{ and } t = 1..., T \qquad (2)$$

where y and x are two stationary variables measured on t periods with i cross-sectional dimensions. The different types of panel causality tests vary in their assumptions about the coefficients' homogeneity across cross-sections. There are two methods for determining causality in panels. The first step is to consider the panel data as a single large, stacked set of data and then apply the normal Causality test, except that data from one cross - section is not allowed to enter the lagged values of data from the following cross - section. This approach is predicated on the assumption that all coefficients are constant throughout all cross sections, i.e.

$$\alpha_{0,i} = \alpha_{0,k}, \alpha_{1,i} = \alpha_{1,k}, \ldots . \alpha_{n,i}, = \alpha_{n,k}, \forall i, k$$

$$\beta_{1,i} = \beta_{1,k}, \ldots . , \beta_{n,i} = \beta_{n,k}, \forall i, k$$

Dumitrescu and Hurlin (2012) take a more generic method, allowing all coefficients to vary across cross-sections:

$$\alpha_{0,i} \neq \alpha_{0,k}, \alpha_{1,i} \neq \alpha_{1,k}, \ldots . \alpha_{n,i}, \neq \alpha_{n,k}, \forall i, k$$

$$\beta_{1,i} \neq \beta_{1,k}, \ldots., \beta_{n,i} \neq \beta_{n,k}, \forall i, k$$

This test is computed by performing unique Granger Causality regressions on each cross-section. The following step is to average the test statistics, which is referred to as the W-bar statistic. They demonstrate that when properly weighted in unbalanced panels, the standardized form of this statistic follows a conventional normal distribution. The Z-bar statistic is used to describe this. The method/test utilized in this study is Dumitrescu and Hurlin. As with the standard Granger Causality test, the approach for establishing causality is to examine the influence of past values of x on the present value of y. Thus, the null hypothesis is defined as:

$$H_o = \beta_{1,i} = \cdots = \beta_{1,K} = 0$$

This indicates that there is no causal relationship between any of the panel's cross-sections. The test assumes that causation is possible for some cross-sections but not necessarily for all. In other words, if the null hypothesis is rejected, causation may exist for some cross-sections but not necessarily for all, but if the null hypothesis is not rejected, there is no causality in any cross-sections. The panel granger causality test is intended to determine causality at the panel level, thus rejecting the null hypothesis does not rule out the possibility of noncausality for certain cross-sections. Dumitrescu and Hurlin (2012) demonstrate via Monte Carlo simulations that the Wald statistic calculated is asymptotically well performed and may be applied to explore panel causality.

Assuming that the Wald statistics are distributed independently and identically across individuals, it is possible to demonstrate that the standardized statistic Z when $T \rightarrow \infty$ comes first and then $N \rightarrow \infty$ (sometimes interpreted as "T should be large in comparison to N") follows a standard normal distribution (Lopez and Weber 2017). Finally, the null hypothesis testing approach is based on $\bar{Z}$ and $\tilde{Z}$. If these values are greater than the standard critical values, then

the null hypothesis should be rejected and Granger causality should be assumed. $\bar{Z}$ may be considered for large N and T panel datasets. $\tilde{Z}$ should be preferred for datasets with a big N but a modest T. We explore the $\tilde{Z}$ statistic in this research.

3.4. Granger Causality

To test for unit roots, we use both the Fisher ADF and the Levin, Lin, and Chu unit root tests separately. There is a need to determine the presence of unit roots when conducting cross-sectional time series analysis of panel data, which is a standard procedure. This panel unit root testing evolved from time series unit root testing, but unlike time series testing, we consider the asymptotic behavior of time series and cross-sectional dimensions. In general, the following procedure is used for panel unit root testing:

$$\Delta y_{it} = \alpha y_{it-1} + \sum_{j-1}^{\rho i} \beta_{ij} \Delta y_{it-j} + X'_{it}\delta + \varepsilon_{it}$$

In this case, we assume a common α=ρ-1 but allow the lag order for the difference terms, ρ_i to vary across cross-sections. X'_{it}represents the deterministic (exogenous) component in the model. The null and alternative hypotheses for the tests can be written as H_o: α = 0, H_1:α<0 indicating that there is a unit root under the null hypothesis and no unit root under the alternative.

4. RESULTS

4.1. Overviews of Studies Included in the Meta-Analysis

A total of 503 studies were evaluated for the meta-analysis. These studies were published between 1987 and the latest being published in 2021. A total of 378 representing 75.1% of the studies reported that GBH had potentially adverse effects on humans, non-target organisms, or/and the environment. Approximately 24.9% of the studies were found to report that GBH had no adverse effect, hence they are deemed safe for humans, animals, other non-target organisms, and the environment. This determination of adverse or no adverse effect was made after reviewing the articles for pronouncements or conclusions which suggest GBH could pose a potential risk even when used at recommended dosages.

Out of the 378 studies reporting that GBH had adverse effects, 215 concluded that GBH had adverse effect on non-target organisms and the environment. These included other plants, aquatic organisms, rodents, bees, and microorganisms. A total of 154 of the studies used in the meta-analysis concluded that GBH had adverse effect on human health. This ranged from cancer, hormonal effects, and all forms of potential health risk that GBH poses to human health. A total of 9 out of the 503 studies concluded that the daily accepted daily intake of glyphosate in food and water was too high.

In the last two decades, the number of papers that made pronouncements on the impact of GBH had increased from less than 10 papers in 2005 to 67 in 2020. The earliest study used in this meta-analysis was performed by Monsanto scientists, A. P. Li and T. J. Long, who sought to assess the potential genotoxicity of glyphosate using in-vitro and in-vivo assays (Li & Long 1987). The study did not observe any form of genotoxic activity and concluded that glyphosate

posed no genetic risk to humans. This paper was published in the Fundamental and Applied Toxicology journal and has been cited 70 times.

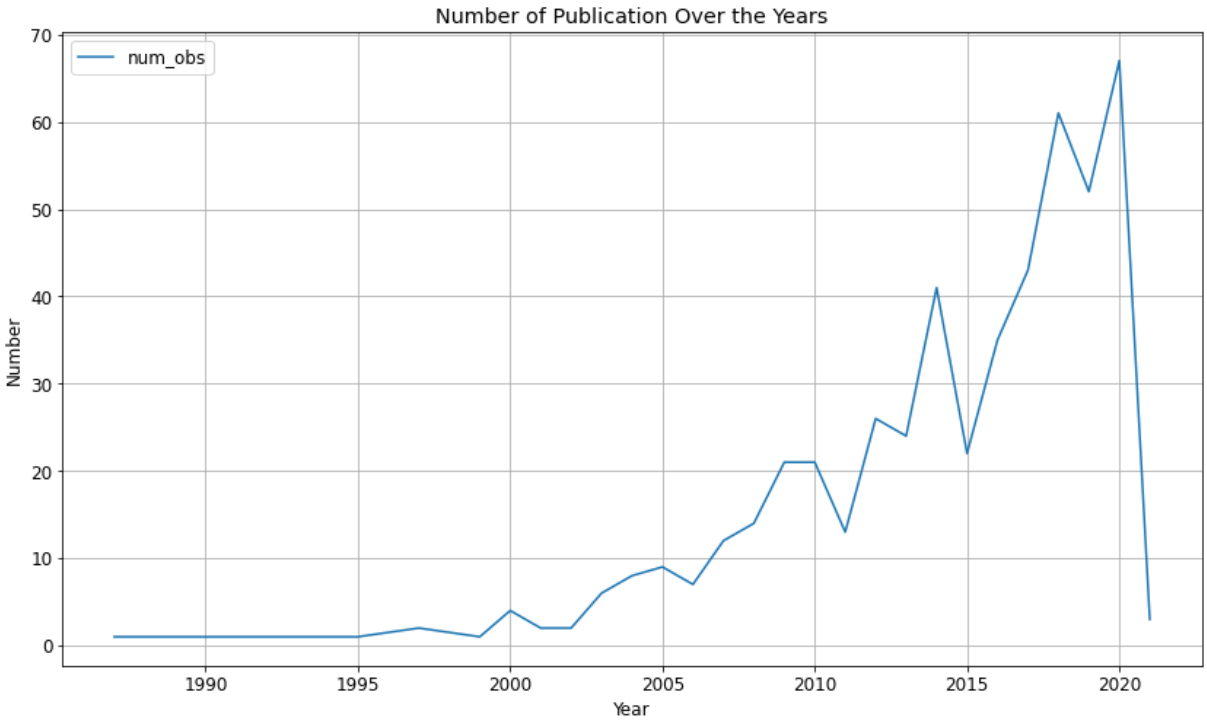

Figure 1. Publications included in the meta-analysis over time.

The first study within our list to produce an adverse result indicated that even though glyphosate residual levels dissipated to approximately 4% and 6% after 61 and 63 days in blueberry and raspberry, respectively. The residual levels were not below the maximum permissible residue level (0.01ppm), that becomes harmful as stipulated by Health and Welfare Canada (Roy et al 1989). Subsequent studies between 1989 and 1994 all produced results that indicated that there was no adverse effect or impact of GBH use on humans and other non-target organisms (Sundaram 1990; Brewster 1991; Rank 1993; Cessna 1994). The trend of scientific studies with no adverse effects began to change after 1995, when there was a mix of adverse and no adverse effects of GBH use on humans, other non-target organisms, or/and the environment, as shown in figure 2.

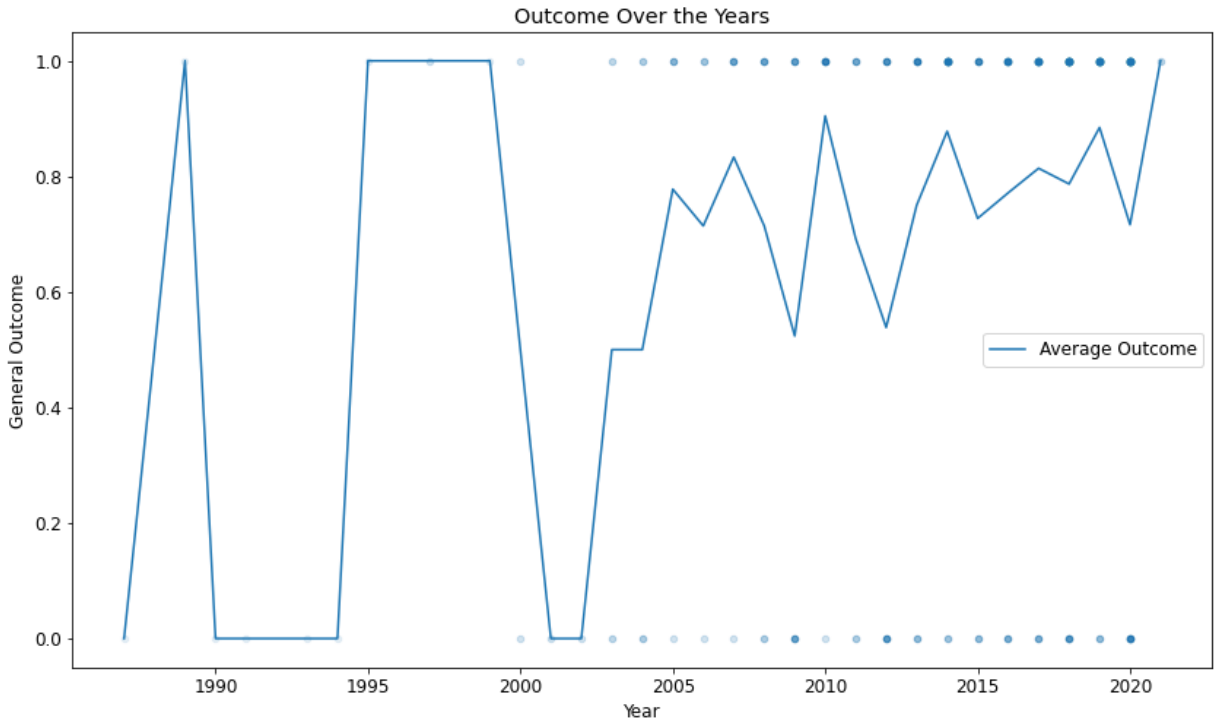

Figure 2. Distribution of research outcome over years.

According to Aksnes et al. (2019), the number of citations is a good measure of the quality, importance, and impact of research or studies in a field of study. The mean number of citations for the studies included in the study was 44, with the least cited studies having no citations at all and the highest being 691 citations. This meant the number of citations of the articles used in the meta-analysis had received a fair number of citations. It is, however, important to note that the median number of citations was 17, which is much lower than the mean and presents a better estimation of central tendency due to a few studies having very high citations. The top three most cited studies were carried out in France, with some of the authors having a common affiliation with the CRIIGEN (Committee for Independent Research and Information on Genetic Engineering).

The top seven most cited studies all espoused that GBH had some form of adverse effect or concluded that it had an adverse effect on humans, the environment, and other non-target

organisms. Specifically, the study with the highest number of citations (691), was by Richard et al. (2005), published in the Environmental Health Perspective, which sought to determine whether glyphosate is toxic to human placental cells of agricultural workers exposed to GBH with concentrations lower than those recommended. The study concluded that Roundup and its active ingredient glyphosate had endocrine and toxic effects that can be observed in mammals, hence the outcome of adverse effects of GBH.

Gasnier et al. (2009) was the second most cited study with 618 citations which was published in Toxicology. The study exposed human liver cells to different formulations of doses of glyphosate below the recommended agricultural usage. It measured the cytotoxicity, genotoxicity, anti-estrogenic, and anti-androgenic effects. The study found that all parameters were disrupted at doses below the recommended agricultural levels within 24 hours of exposure. This can be concluded that GBH had an adverse effect on human beings.

Benachour et al. (2009), which was the third most cited study, concluded that Roundup's adjuvants, such as Polyethoxylated tallow amine (POEA), affected human cells, rendering them permeable and increasing the toxicity already presented by Glyphosate through apoptosis and necrosis. The study was published in Chemical Research in Toxicology, which was also the journal that published the paper with the fourth-highest citation. The fourth most cited study was an Argentine study by Paganelli et al. (2010), which inferred that GBH-induced phenotypes occurred primarily due to an increase in endogenous retinoid activity. This is in line with the suppression of otx2 expression, as well as the disturbance of cephalic neural crest development and the decrease of Sonic hedgehog (Shh) signaling from the embryonic dorsal midline. They concluded that glyphosate had a direct effect on early morphogenesis processes in vertebrate embryos.

Howe et al. (2004) was the fifth most cited study. It found GBH of various formulations and their surfactants to have a toxic effect on frogs in an experiment in North America (Canada). This study was published in Environmental Toxicology and Chemistry: An International Journal. Mesnage et al. (2013) established and challenged the current acceptable daily intake of glyphosate because studies, experiments, and protocols used to set these considered just glyphosate when their adjuvants also posed toxicity to non-target organisms. This was the sixth most cited work and was published in Toxicology.

Thongprakaisang et al. (2013) inferred that glyphosate exhibited weak estrogenic activity, which implied that the use of glyphosate led to contamination of soybean products which may pose a risk of breast cancer. This Turkish study was the seventh most cited study. It was published in Food and Chemical Toxicology. The eighth most cited piece of research was the first to conclude that GBH has no negative consequences, which was reported in Environmental Health Perspectives. This was a study by De Roos et al. (2005). They used the Agricultural Health Study (AHS), a prospective cohort study of 57,311 licensed pesticide applicators in Iowa and North Carolina, to look at the relationship between glyphosate use and cancer incidence. The study found that glyphosate was not linked to cancer in general or to any of the different types of cancer.

The ninth most cited study examined the toxicity of glyphosate (Roundup) in silver catfish, which found that glyphosate concentrations used in agriculture can alter metabolic and enzymatic parameters in fish, including AChE inhibition, lipid peroxidation, and protein catabolism (Glusczak 2007). The study was carried out in Brazil and published in Comparative Biochemistry and Physiology Part C: Toxicology and Pharmacology and has 298 citations. The tenth most citations (295) went to an American study led by Monsanto scientist Acquavella and

published in Environmental Health Perspectives. The researchers tested 48 growers, their wives, and 79 children (4–18 years old) for glyphosate levels in their urine. Urine from days 1, 2, and 3 before and after glyphosate use was analyzed. None of the measured systemic doses in this study came close to the glyphosate reference dose of 2 mg/kg/day set by the US Environmental Protection Agency (Acquavella et al., 2004).

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 considered. This was followed by Argentina (79; 15.7%), the USA (63; 12%), Canada (30; 6%) and France (24; 4.8%) as the top five leading countries. In their bibliometric analysis, Zyoud et al. (2016) also identified these five countries as the leading producers of research into glyphosate safety, but in different rankings.

It is also important to look at the journals that published the most papers that were considered in this meta-analysis. Ecotoxicology and Environmental Safety (7.4%), Bulletin of Environmental Contamination and Toxicology (6.4%), Aquatic Toxicology (4.6%), Environmental Toxicology and Pharmacology (4.6%), and Planta Daninha (4.6%) were the top five leading journals. Four of these top five journals were also identified as the most productive journals by Zyoud et al. (2016) in their bibliometric analysis of GBH global intoxication research production from 1978 to 2015.

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. These were high-impact journals in their field. 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 experts in a field and help people learn more about that field.

4.2. Average Outcome of Countries

India had the highest average outcome of 90%, followed by Argentina, France, China, and Brazil with 89.87 %, 87.5 %, 86.36 %, and 80.58 % of studies revealing GBH had detrimental impacts, respectively. The remaining top ten most productive countries had over 70% of research suggesting detrimental effects, except for the USA and Canada, which had 55.55% and 43.33 percent of studies indicating adverse effects on non-target organisms, respectively. To gain additional insight, we studied the average outcome for nations in two time periods, prior to and following 2010, and showed the results in Figure 3, with dot size of countries scaled by the average impact factor of journals in which studies conducted in those countries are published. Average outcome is presented on the y-axis and number of observations recorded by each country is presented on the x-axis.

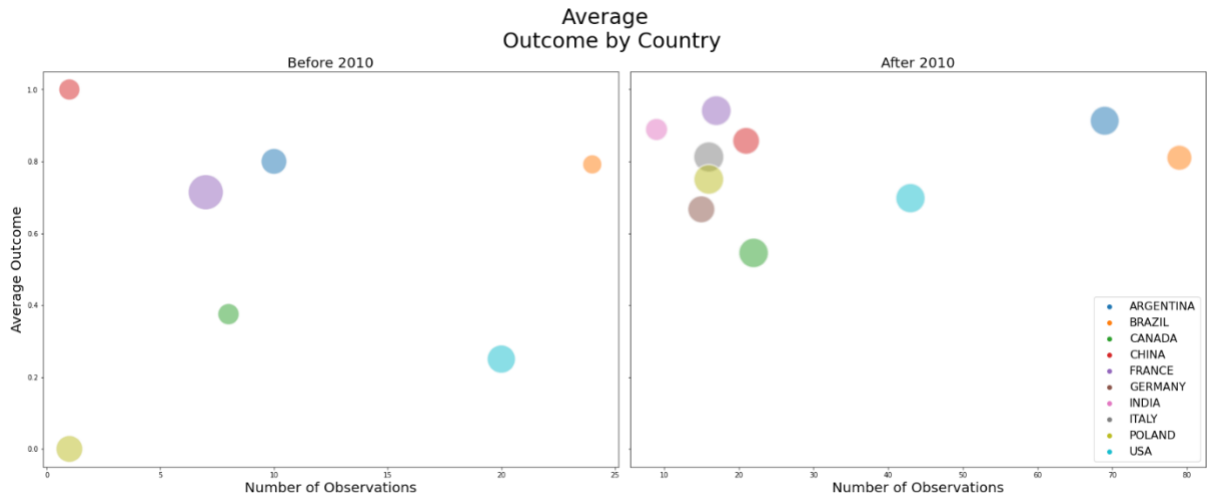

Figure 3. Average outcome of top 10 countries scaled by average impact factor of journals.

It can be noticed that prior to 2010, France stood out as the nation whose papers were published in journals with relatively high impact factor of about 3.6 followed by the Argentina, USA and Poland where papers were published in journals of about 1.7, 1.6 and 1.3 impact factor respectively. The rest were in journals of less than 1.0 impact factor. After 2010, papers have been published in journals with relatively high impact factor, 3 countries had papers published in journals with average impact factor above 3.0, six other countries had papers published in impact factor of between 2 and 3 on an average. GBH impact has become a topical issue which is gaining interest from top journals which publish quality research work.

According to our analysis, the majority of countries in the top ten have shifted slightly upward, showing a shift in the outcome of research following 2010. Among these is the instance of the United States of America and Canada; prior to 2010, the United States of America recorded only 25% of its research as having a harmful effect, compared to 69.77% after 2010. Canada also saw a rise in the number of studies reporting negative effects, from 37.5% before 2010 to 45.45% after 2010.

4.3. Average Outcome of Countries

The study investigated the average outcome for journal publications. In doing so, it is critical to examine the journals that published the most papers included in this meta-analysis. The top five most occurring journals had general outcome of Ecotoxicology and Environmental Safety (average outcome of 81.08%), Bulletin of Environmental Contamination and Toxicology (average outcome of 73.91%) Aquatic Toxicology average outcome of (91.30%) Environmental Toxicology and Pharmacology (average outcome of 86.95%), and Planta Daninha (average outcome of 78.26%). Generally, the most appearing journals had high general outcomes which

meant GBH studies published in were more likely to conclude that glyphosate had adverse effect on non-target organisms and the environment.

Additionally, we investigated the average outcome for the top journals in two time periods, prior to and following 2010, and showed the results in Figure 4 with dot size of journals scaled by the average impact factor of those journals. Average outcome is presented on the y-axis and number of observations recorded by each journal is presented on the x-axis. According to our analysis, most top journals actually increased somewhat in terms of the number of observations in the meta-analysis, indicating that high impact journals began to see an increase in papers focusing on effect on GBH. The total upward shift shown in the figure shows that after 2010 studies in the most cited and top journals are concluding that GBH had an adverse effect.

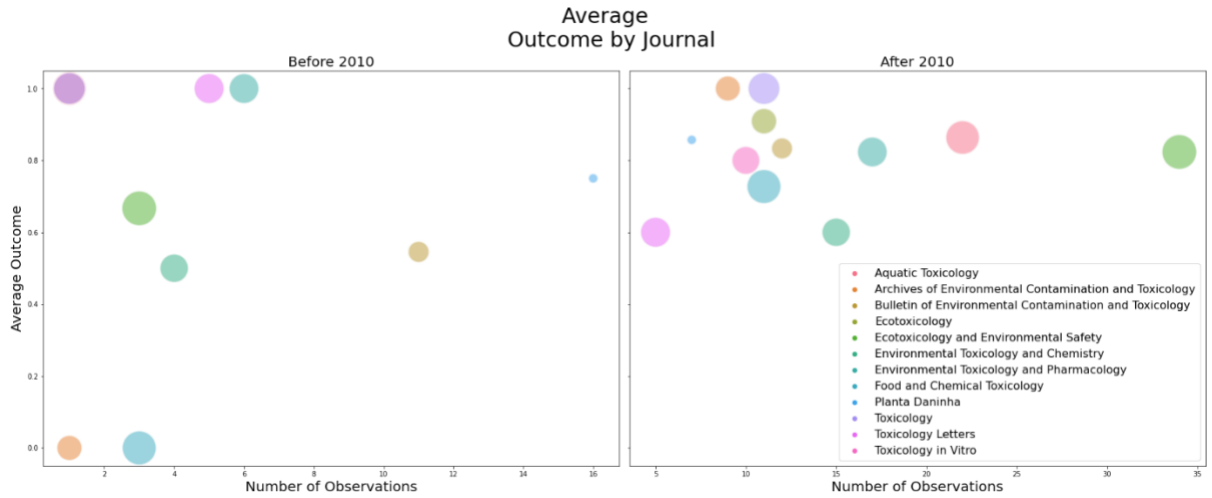

Figure 4. Average outcome for top 10 most observed journals scaled by average impact factor.

Figure 5 presents the impact factors of journals in which studies were published for two time periods (before 2010 and after 2010), with their outcomes. This provides information about the outcome based on the influence of the journal in which it was published. The impact factor of a journal is a good measure of the quality and impact of the journal.

The period prior to 2010 saw research into the impact of GBH published in journals with impact factor mostly below impact factor of 4 with a few between 4 to 6. From the shade of the dots, it can be observed that research which indicated that GBH was harmful were published in higher impact journals as compared to papers which conclude that GBH was not harmful. Specifically, papers with conclusion that GBH had adverse effects were more evenly spaced across journals with impact factors from 1.00 to 4.00 with a few appearing in journals with impact factor of over 4. Studies which concluded that GBH had no adverse effect were mainly clustered between impact factor of 0.00 (journals with no impact factor) and 3.00 with a few appearing in journals with impact factor of over 3.

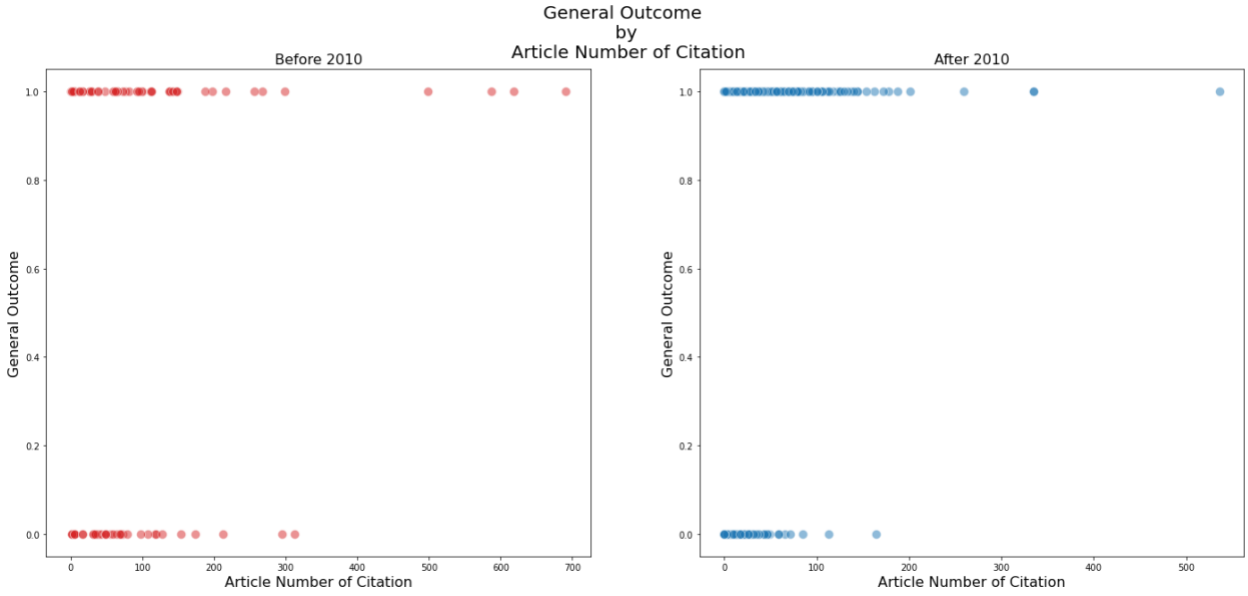

Figure 5. General outcome for studies and the impact factor of journals published in.

After 2010, it can be concluded that studies on the impact of GBH were published in higher-impact journals since it had become a topical issue of scientific concern. Studies concluding that GBH had adverse effects were evenly distributed in journals with an impact factor from 0.00 to about 5.00, after which a few studies from 5.00 to 7.00 and three studies from journals with an impact factor above 7 recorded adverse effects. Studies with no adverse effects

were also evenly distributed, even though less dense, from journals with impact factors of 0.00 to about 6.00, after which 4 studies were published in journals with an impact factor of between 7.00 and 9.00.

With regards to the number of citations over the two time periods, the period prior to 2010 had more citations as shown in figure 6. That time period had more papers with over 500 citations concluding that GBH had an adverse effect as compared to the period after 2010. From the figure, papers that indicated GBH had an adverse effect had more citations. This could mean that papers that indicated GBH was harmful got more attention from academics.

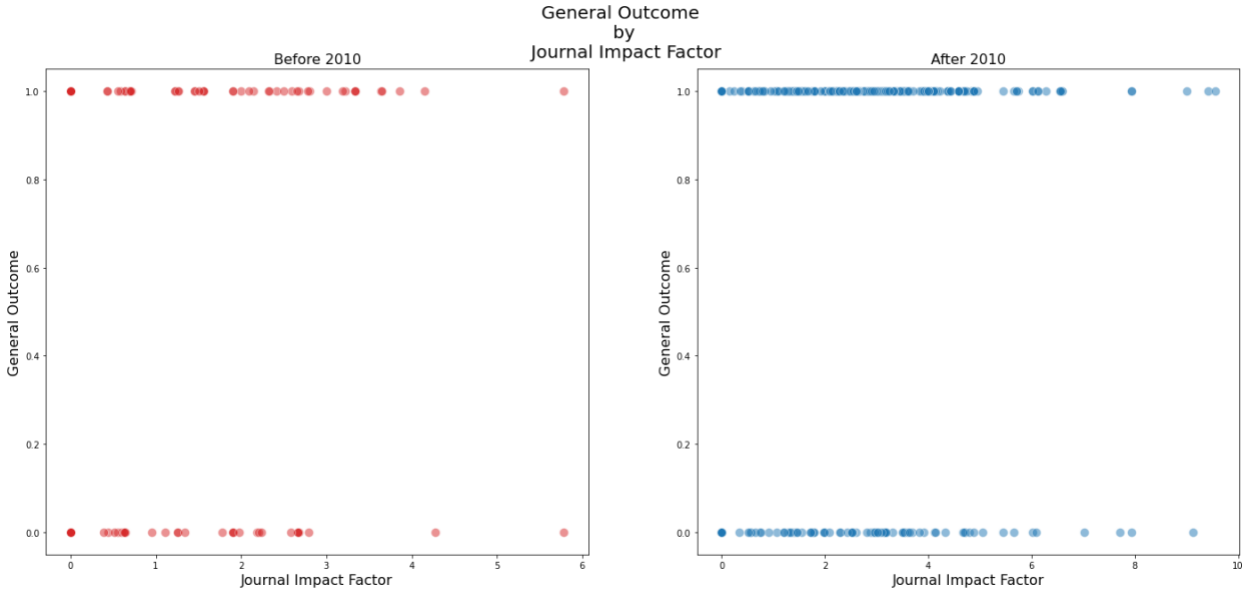

Figure 6. General outcome for studies and their number of citations.

4.4. Average Outcome of Affiliation

In general, 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, and companies producing agricultural chemicals. Groups recognized as anti-glyphosate or producers of agricultural chemicals were 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, hence dropped out.

The study acknowledges that some studies involve multiple authors from various institutions. To address this, we chose to identify each author's affiliation based on publicly available information in papers and to display all types of institutions per study. In all, 87.87% of studies had at least one author who was linked with a university, followed by public and private institutions at 20.08 and 4.72 percent, respectively. As shown in a breakdown of the average outcome (adverse or no adverse effect), studies having at least one author from a university had the highest average outcome of 75.57%, suggesting GBH had a detrimental effect on non-target organisms. This was followed by articles authored by individuals affiliated with public institutions, with 64.36 percent of the outcomes indicating that GBH had a variety of adverse effects. Only 32% of the research done by private institutions found that GBH had a negative effect on people, which was the lowest average outcome or negative impact.

Figure 7. Average outcome per institution of study.

To shed more light on the evaluation of study results by author affiliation, we present Figure 7, which depicts the progression of the major types of affiliation institutions and their associated outcomes across the time of analysis. The figure shows a graph that exhibits a general upward trend throughout time. This is particularly noticeable in studies conducted with university-based authors after the year 2000. This trend is similar for research conducted by members of public institutions. Even though this trend can be observed with research outcome from private entities, the fluctuations in this trend is more severe as compared to universities and public organizations. Previous research has proven that an author's affiliation with or the venue of a study, such as public or private research organizations, might influence the study's conclusion, as they seek various aims and incentives when conducting research (Glenn and Bruce, 2021).

4.5. Average Outcome of Various Funding Sources

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. 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. Our study identified the primary funding sources as public, university, private, and international, in descending order. 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 analyzed studies. In addition, a study can be

funded by many different sources, and some studies don't say where the money comes from at all. This has been considered in the analysis and discussion.

The government funded 61.14 percent of the research included in this meta-analysis. This was followed by university funding, which accounted for 24.65 percent of all studies, and private sector funding, which accounted for 10.14 percent. This is congruent with the reality that governments have been the largest source of funding for research and development since World War II (Resnik 2000), indicating the importance of balancing privately funded research and increasing public input into government funding decisions. Our findings indicated that university-funded studies had the highest average outcome of 80.65 percent, showing that GBH had a detrimental influence.

Furthermore, 77.67% of studies supported by public funds demonstrated that GBH was toxic to non-target organisms. Private funded research had an outcome of 60.78 percent of the research that found GBH had a negative effect on non-target organisms, which is a relatively low rate compared to other funding sources. This substantially higher general outcome figures for funding sources as compared to the author of affiliation could be explained by the fact that public funds are important in research, particularly co-financing, thus offsetting the effects of private funding in potential bias.

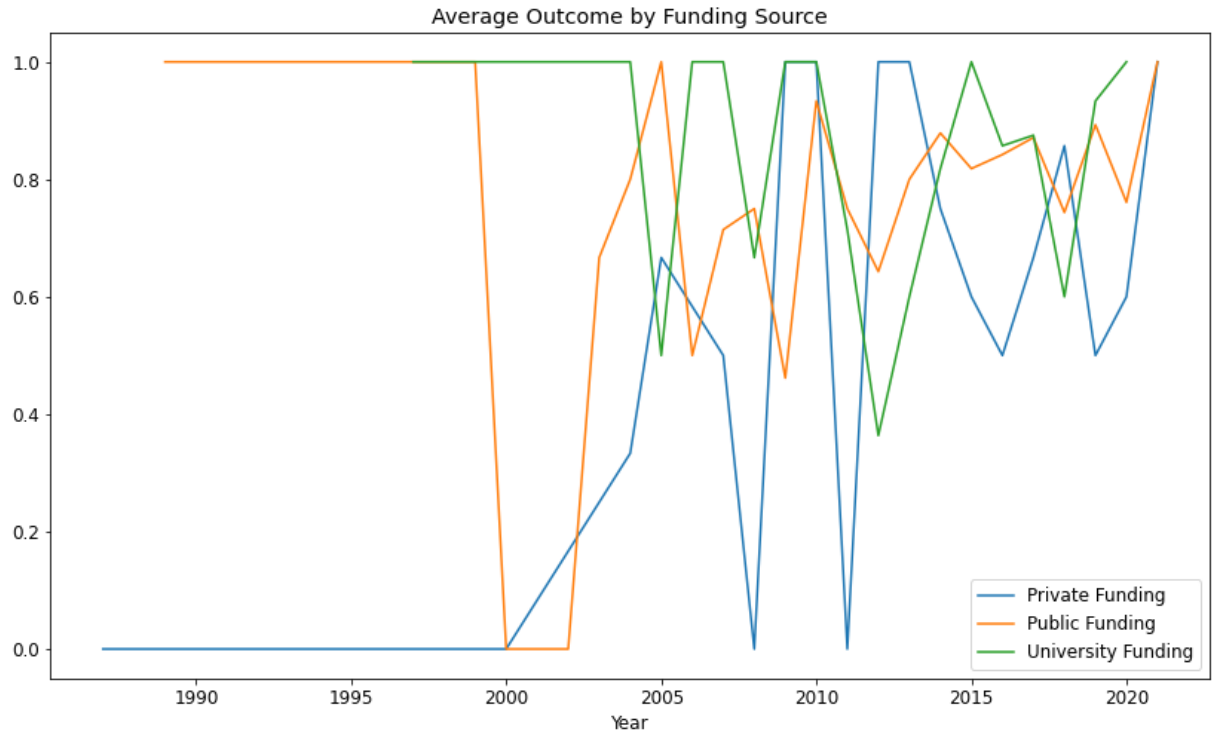

Figure 8. Average outcome of various funding sources.

In Figure 8, we also included a historical trend analysis of the average outcome for the various major financing sources. Prior to 2000, university and public sources tended to have high averages, implying that the majority of research had unfavorable outcomes, in contrast to private sources, which tended to have no negative effect. After 2000, the results have been mixed, but the increased trend in funding sources, particularly university and public funds, indicates that these funding sources are producing outputs revealing the adverse effect of GBH on non-target organisms. Private finance has seen a wave of volatility but is now converging to the top, signaling a reversal of previous outcomes. They can be explained by the different goals and motivations for funding and conducting research, as shown by the funding organizations in this case, a public institution and commercial organizations (Glenn & Bruce 2021).

4.6. DAG Results

The Directed Acyclic Graph results establishes contemporaneous causal relationships between some key factors of the studies included in the meta-analysis. The study examined the effect that these properties have on the outcomes of the studies that were conducted. The various funding sources, the organization type they support, and the results of studies on the impact of glyphosate and their relationship were examined. The results are presented in a matrix with rows representing the algorithm and columns representing the significance level tested. The PC technique is commonly used for predicting DAGs due to its computational efficiency. This algorithm is known to be order-dependent in that the result is conditional on the order in which the variables are specified. As a result, we compute two order-independent adaptations, the Stable PC and Parallel PC Algorithms, in addition to the classic PC Algorithm.

It is critical to highlight that the results reported in this section of the thesis are the most pertinent extractions, which are combinations of funding sources and type of organization. These include public affiliation, private affiliation, university affiliation, and general outcome, as well as public financing, private funding, university funding, and general outcome. Additional combinations are presented in the appendix to this work, which will be referred to during the discussions.

The significance level for updating the links in the DAGs computed were 0.05, 0.10, and 0.20. In DAGs, it is acceptable to use significance levels up to 0.30. A higher degree of significance prevents a limited sample size from producing an underfit result with too few edges (Bessler and Yang 2003; Scheines et al. 1994). Awokuse and Bessler (2003) also found that a significance level of up to 30% can show a clear structural result when there are only a few samples.

Three time periods are analyzed and presented, these are the total dataset (1987-2021), before 2010 and after 2010. The United States Environmental Protection Agency (EPA) conducted a review of glyphosate's registration in 2009 and directed pesticide registrants to conduct further research to support human health and ecological risk assessments from 2010. This was a critical milestone in researching the impact of GBH that extended to other countries. The EPA, for example, collaborated with Canada's Pest Management Regulatory Agency to offer risk assessment data. Results for prior and after 2010 are presented in the Appendix.

The results discussed in this sub-section, start from the interaction of funding and author affiliation with general outcome from one source, i.e. Private, Public and University sources. This helps to discern which factor, i.e. funds or affiliation directly indirectly or has more power in determining the general outcome of research from those sources. After these series, the results from interaction of all funding sources with general outcome and all affiliation with general outcome is presented to determine sources directly, indirectly or has more power in determining the general outcome of research for all funding sources and affiliation.

4.6.1. Private Funding, Private Affiliation, General Outcome

The first DAG presented is from the interaction between Private Funding, Private Affiliation, and Outcome. The results revealed that private funding has a positive causation (marginal effect of 27%) on private affiliation, whereas the study's outcome has a negative causation (marginal effect of 19%) on private affiliation. The results for all three algorithms and significance levels were consistent; the only difference was that the identified links in the significance levels of 0.10 and 0.20 had a bidirectional relationship (which can be interpreted as endogenous variables), whereas the 0.05 had a unidirectional relationship, implying that they are exogenous variables. All the marginal effects of causations identified were direct effects with a

99% level of confidence. This finding implies that the relationship between private organizations and non-harmful glyphosate research findings was supported by financial support from private entities. According to the DAG, private research which are likely to be funded by private groups was more likely to show that glyphosate did not harm non-target organisms.

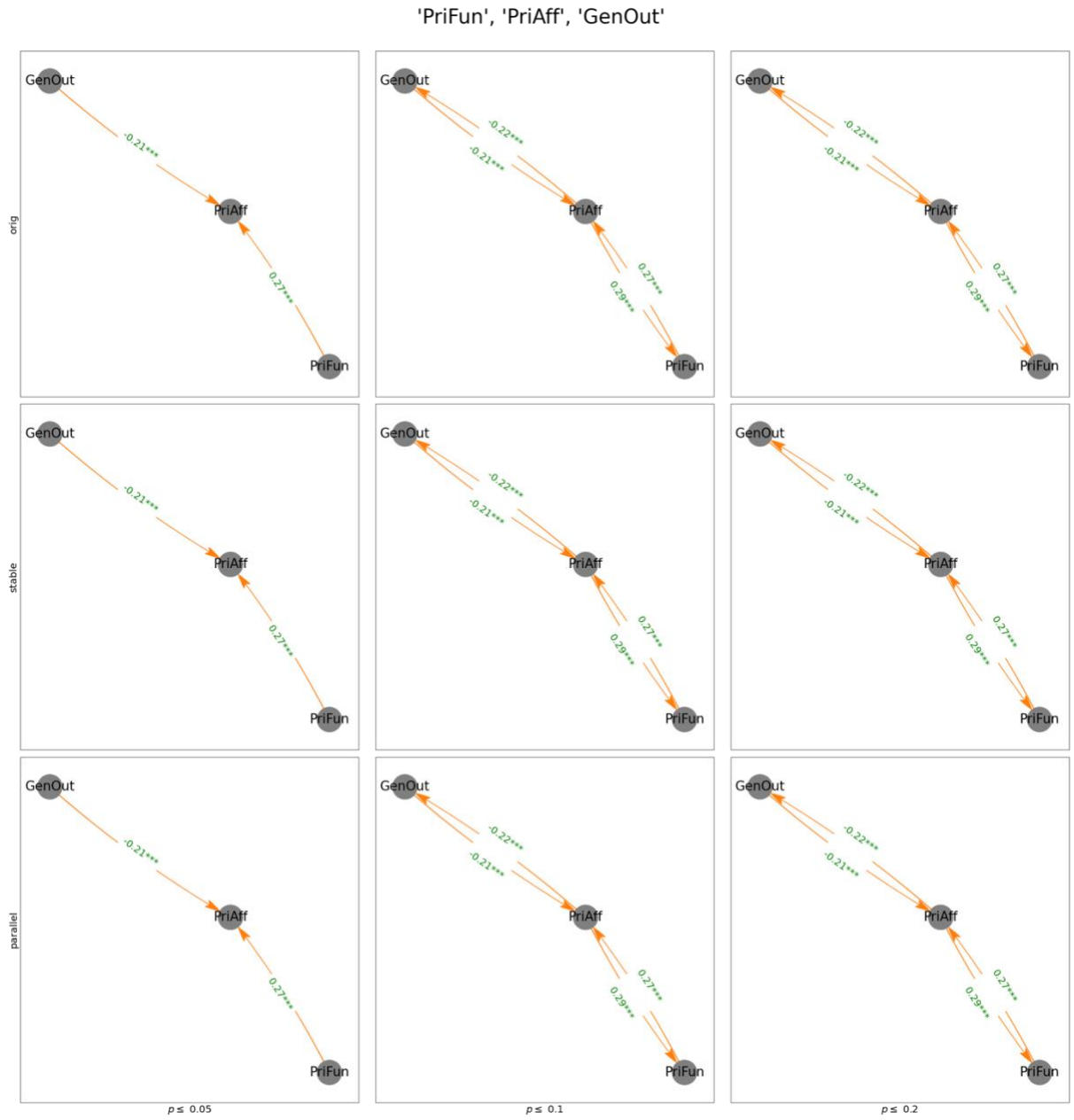

Figure 9. Private funding, private affiliation, general outcome.
*, ** and *** denote statistically significant causations at 10%, 5% and 1% respectively

4.6.2. Public Funding, Public Affiliation, General Outcome

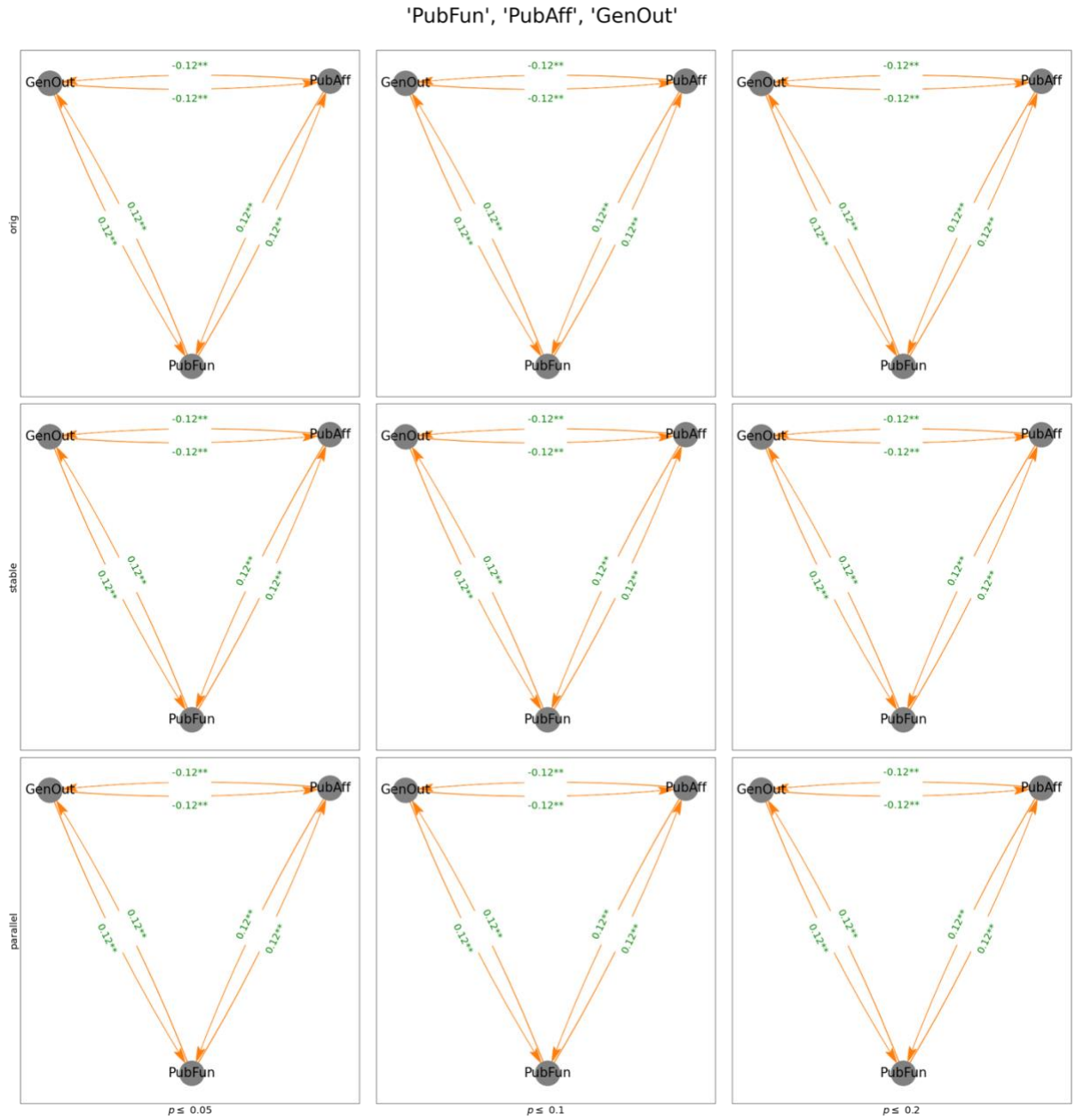

Figure 10. Public funding, public affiliation, and general outcome for full dataset.
*, ** and *** denote statistically significant causations at 10%, 5% and 1% respectively

The next result was examining the relationship between public funding, public affiliation, and outcome. The results from all 3 algorithms and significance level of updating the links (0.05, 0.10, and 0.20) yielded identical results. These were bi-directional causations between public funding, general outcome, and public affiliation, inferring that these are endogenous. The

magnitudes of the margins for all the three causations were 12% with a confidence interval of 90% in all cases. Public funding had a positive causation with general outcome and public affiliation. This means that publicly funded research was likely to yield results that indicate GBH had detrimental effect to humans, the environment or other non-target organisms. Also, since public institutions are almost exclusively funded by public funds by virtue of state budgetary allocation, public funding causes public affiliation. It is however interesting to note that public affiliation has a negative causation with general outcome that means that research from public institution were more likely to indicate that GBH are not harmful. This is consistent with earlier assertions and information from most public agencies.

This leads to question why does public funding and public organization have different directional causation with outcomes of studies they sponsor or conduct. It is important to note that public funding is the main driver of research after world war II as asserted by (Resnik 2000). This funding goes to public, universities and in some cases private organizations. Hence the deviation of public funds from the direction of public organizations could be as a result from the research outcome from the other publicly funded research by other institutions.

4.6.3. University Funding, University Affiliation, General Outcome

As part of their mission, universities, and for that matter, the ones identified in the meta-analysis, are committed to research as a central part of their existence. The results from all three algorithms and significance levels had consistent graphs, but the graphs from significance levels of 0.10 and 0.20 showed bidirectional causation, which infers that all three variables were endogenous. The marginals for all the algorithms and confidence intervals were approximately 15%, where university funding and general outcome both cause university affiliation. The

marginal effect of causation all had confidence interval of 99%. From the DAG results obtained, the outcome of the study and university funding, cause university affiliation.

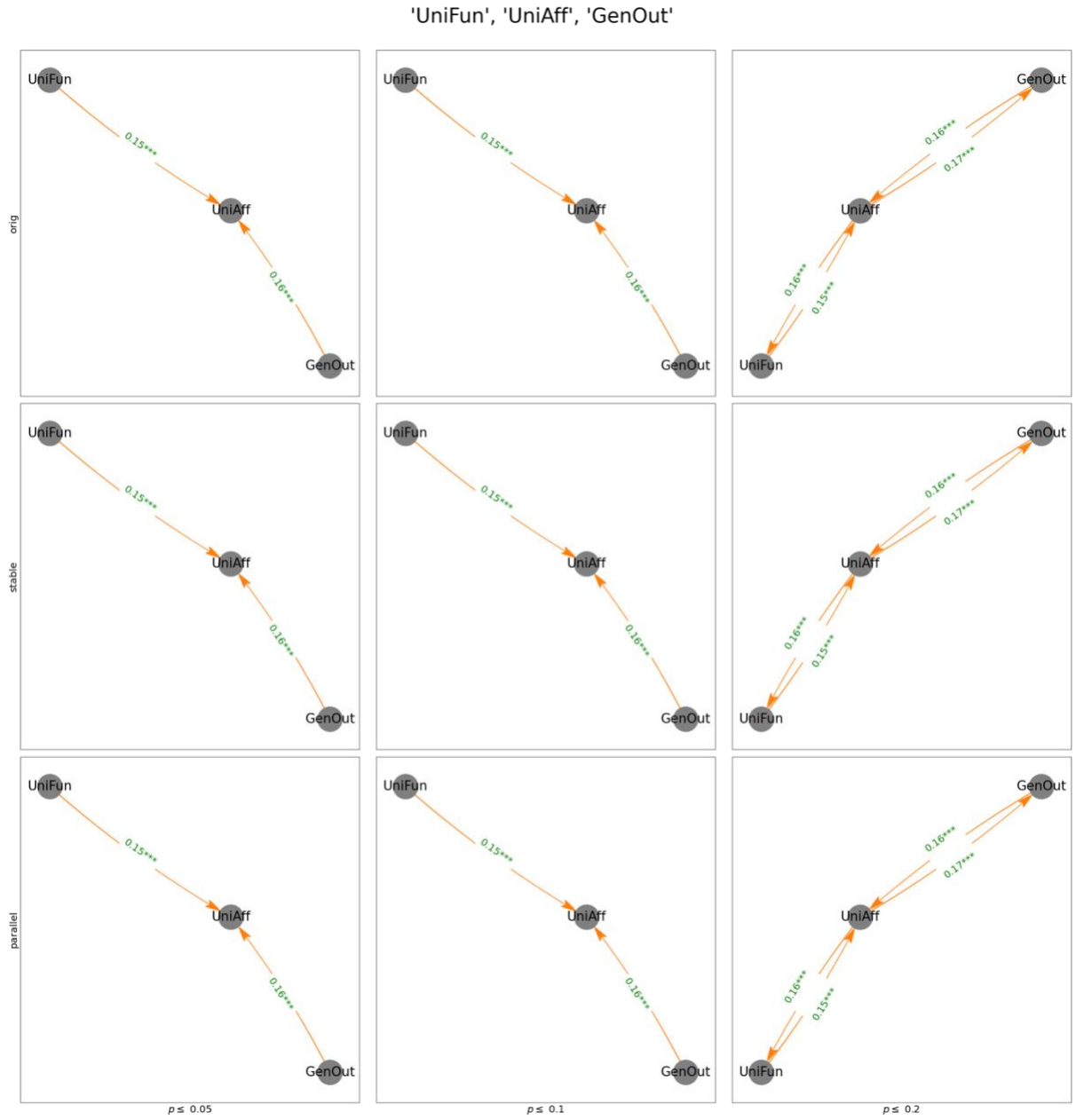

Figure 11. University funding, university affiliation, and general outcome for full dataset. *, ** and *** denote statistically significant causations at 10%, 5% and 1% respectively

University funding almost always goes into university research conducted within the university, which is illustrated by this finding. The general outcomes that reported adverse effects of GBH were likely to come from university affiliated research. In the face of university

funding and affiliation, it was university affiliation that had direct causation with general outcome.

4.6.4. Public Affiliation, Private Affiliation, University Affiliation, General Outcome

The study investigated the effect the various organizations had on the general outcome- public affiliation, private affiliation, university affiliation, general outcome. The results showed that for significance levels of 0.05 and 0.10 generated identical graphs where public affiliation negatively caused private affiliation with a marginal effect of 14% at a confidence level of 95%. Also, public affiliation negatively caused university affiliation with a marginal effect of 60% at 99% confidence level. This could be explained as researchers from public institutions were less likely to engage with university and private researchers to conduct GBH studies. We can infer from this those public institutions primarily conduct their own research with little collaboration from other organizations.

General outcome was linked to only private affiliation in this graph, the relationship was a negatively significant with a marginal effect of 22% at 99% confidence level. Meaning there was some level of likelihood that research from authors of private organizations were more likely to generate outcomes with no adverse effect. It could also be interpreted as general outcomes indicating that GBH is harmful are least associated with research from private institutions. This result was also evident in the combination between private funding, private affiliation and general outcome. It can be inferred that in the face of the three affiliations, it is private affiliation that has a direct causation with general outcome, the rest, i.e. public and university affiliation caused each other and private affiliation.

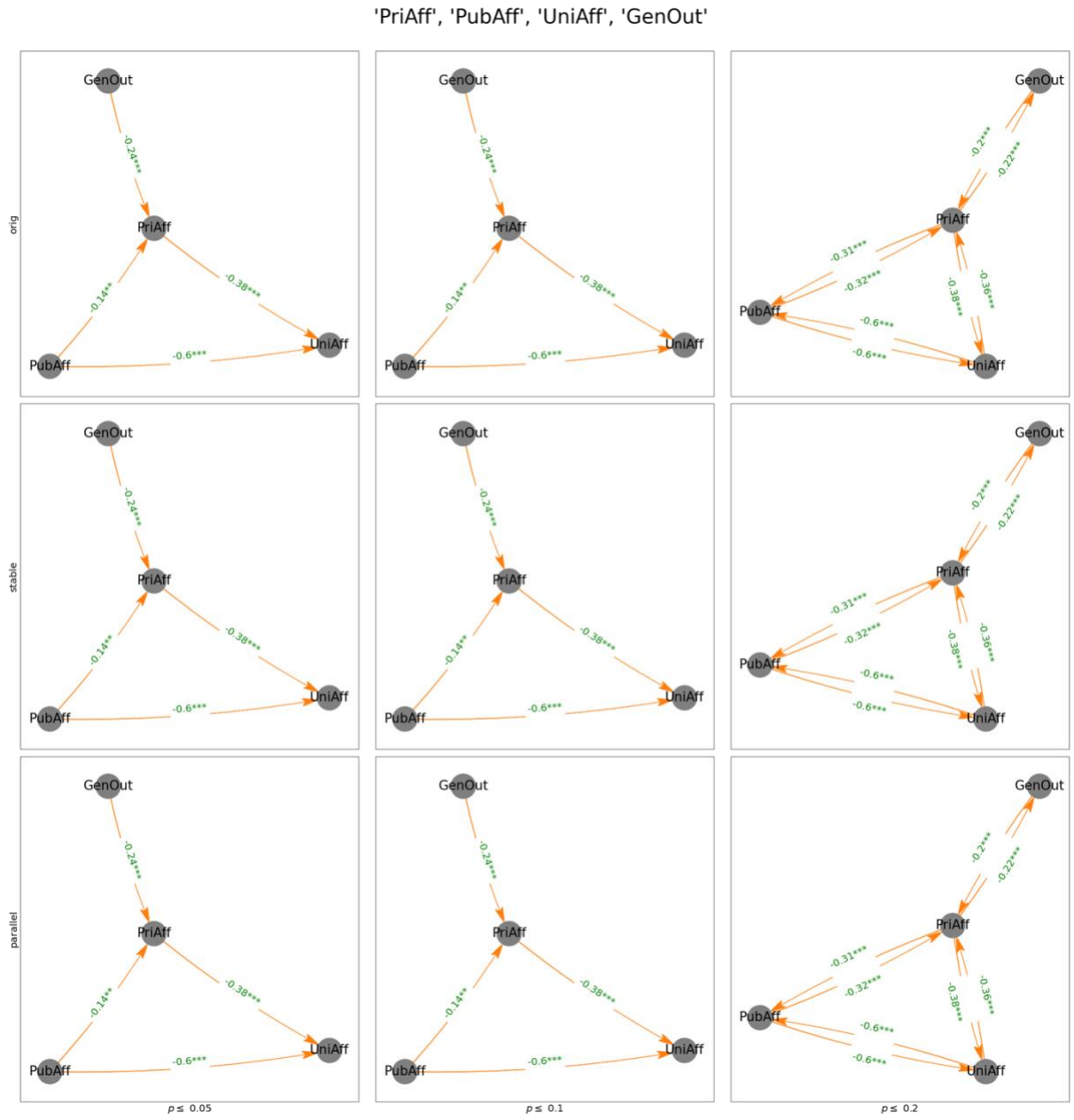

Figure 12. Public affiliation, private affiliation, university affiliation, general outcome for full dataset.
*, ** and *** denote statistically significant causations at 10%, 5% and 1% respectively

When using the definition of indirect effect in DAGs from Pearl (2009), there is an indirect effect from general outcome to university affiliation through private affiliation of magnitude 60%. In the combination between university affiliation, university funding and general outcome, general outcome was found to influence university affiliated research. Also

using the same concept of indirect effect, general outcome will be found to influence public affiliated research which is consistent with DAGs of public funding, funding affiliation and general outcome presented in the appendix.

The graph from significance level of 0.20 was identical in structure with the ones from 0.05 and 0.10 but the directions in this case (0.20) were bi-directional inferring that all the variables were endogenous.

4.6.5. Public Funding, Private Funding, University Funding, General Outcome

It is important to investigate the effect the various funding sources had on the outcome of the studies into the impact of glyphosate use on humans, the environment, and other non-target organisms. The results from graphs of all 3 significance levels and algorithm except Parallel PC showed that the general outcome had a positive effect on public funding and university funding had a negative relationship with private funding. This meant that research with findings that GBH had harmful effects was likely to come from publicly funded projects with a marginal effect of 11% at 90% confidence level. This could be interpreted as research indicating that glyphosate has an adverse effect on non-target organisms and the environment were likely to come from public organizations. It could be further inferred that an increase in research concluding GBH is harmful leads to the state allocating funds to further investigate the phenomenon as a public health concern.

The graph from the 0.10 significance level for all algorithms showed a relationship between private funding and university funding. There was however a negative relationship between public funding and private funding. From this result, both public and university funding affected private funding negatively meaning it were less likely to come together to sponsor a research project. Private funding usually fully supports its own studies. Also, the general

outcome has an indirect effect on private funding, with a marginal effect of 1% through public funding.

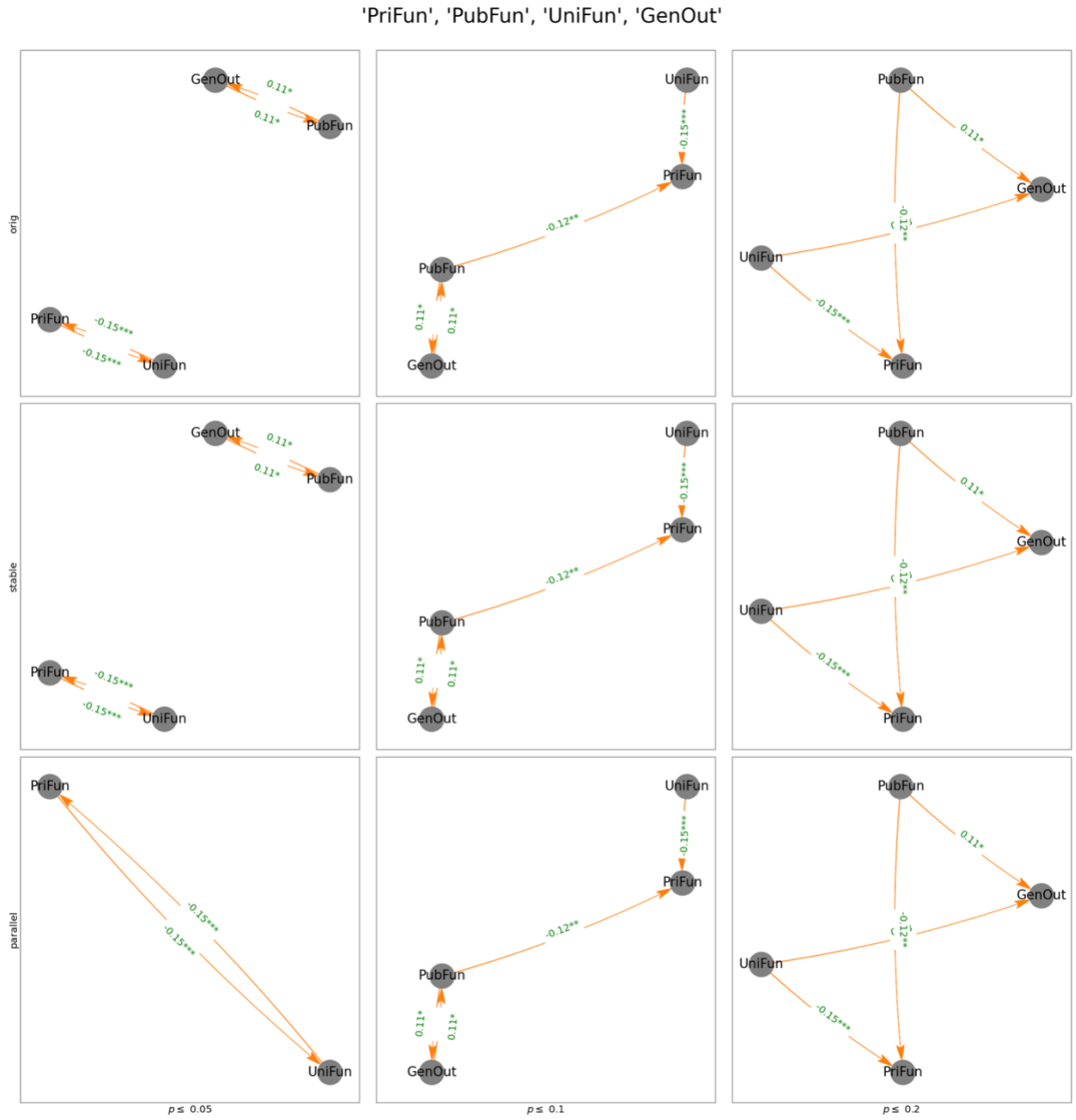

Figure 13. Public funding, private funding, university funding, general outcome for full dataset. *, ** and *** denote statistically significant causations at 10%, 5% and 1% respectively

The graph from the 0.20 significance level also maintained the relationship between public funding, private funding, and university funding as in the result from the 0.10 significance

level, where public funding and university funding negatively caused private funding with marginal effects of 12% and 15% at 95% and 99% confidence.

In this DAG, public funding and university funding jointly positively caused the general outcome with a margin of 11% and 8%, respectively. However, only the public funding and general outcome relation was statistically significant at 95%. This result showed that public funding usually led to outcomes which suggested GBH had harmful effects. The new relationship identified in this case between university funding and general outcomes, which suggested that university-funded studies were more likely to also generate outcomes, which meant GBH had harmful effects on non-target organisms, was however, not significant.

4.7. Panel Granger Causality Results

4.7.1. Unit Roots Results

Table 1. Summary of panel unit root test.

	Fisher ADF Null hypothesis: assumes individual unit root process		Levin, Lin and Chu test Null hypothesis: assumes common unit root process	
Variable	No Trend	Trend	No Trend	Trend
Avg_Gen_Out	27.4571	28.6843	-4.21465	-5.16054
	0.0006 ***	0.0004 ***	0.0000 ***	0.0000 ***
Avg_Uni_Fun	30.2470	25.2029	-4.49746	-3.88104
	0.0002 ***	0.0014 ***	0.0000 ***	0.0001 ***
Avg_Pri_Fun	51.7070	38.5388	-8.19431	-6.64438
	0.0000 ***	0.0000 ***	0.0000 ***	0.0000 ***
Avg_Pub_Fun	41.4754	28.7203	-4.63348	-4.26114
	0.0000 ***	0.0004 ***	0.0000 ***	0.0000 ***
Avg_Pri_Aff	16.7801	11.4841	-4.37101	-4.23680
	0.0101 ***	0.0745 **	0.0000 ***	0.0000 ***
Avg_Pub_Aff	37.4231	39.4760	-4.15117	-7.70426
	0.0000 ***	0.0000 ***	0.0000 ***	0.0000 ***
Avg_Uni_Aff	33.9723	23.9146	-5.29967	-3.02327
	0.0000 ***	0.0024 ***	0.0000 ***	0.0013 ***

*, ** and *** denote statistically significant level at 10%, 5% and 1% respectively

Panel unit root tests are performed on all variables used in the panel granger causality analysis. The results of the panel unit root tests are presented in the appendix. Both the Fisher ADF and the Levin, Lin, and Chu tests show that all the series are stationary at less than a 1%

significance level. This implies that the meanings and/or trends of all the averages are likely to change over time.

4.7.2. Causality Results

In computing the panel granger causality, the locations of the experiments were grouped into continents: North America, South America, Europe, and all other continents grouped into others. The variables used were computed as the averages of the average outcome, organization affiliation, and funding sources, which can be inferred as the percentage of the total number of studies with an outcome indicating an adverse effect, authors affiliated with private, public, or universities, and funding sources from private, public, or universities per a cross-section. Because granger causality uses information from lagged values, it requires full dataset with no missing observation for some years. Hence the dataset used for this granger causality is from 2004 to 2020 that has 62 observations.

The results from the granger causality for funding sources and general outcome is presented in table 2. From the results we can reject the null hypothesis that public funding does not cause general outcomes and accept the alternative that public funding causes general outcomes for at least one panel variable with a 99% confidence interval. This result reinforces the results from the DAGs that public funding causes general outcome. When public funding and public affiliation were interacted with the general outcome in the original PC, stable and parallel PC algorithms at 5%, 10% and 20% significance levels. Similar results were obtained when private, public, and university funding were combined with the overall outcome. Public funding was found to cause a general outcome in the original PC, stable and parallel PC algorithms at 10% and 20% significance levels, with 10% for all algorithms being a bidirectional causation

and 20% for all algorithms being a unidirectional causation. If you look at these results, it can be inferred from them that public money is behind the results of studies on the effects of glyphosate.

Table 2. Public funding, private funding, university funding, general outcome.

		X			
		Avg_Gen_Out	Avg_Uni_Fun	Avg_Pri_Fun	Avg_Pub_Fun
Y	Avg_Gen_Out	-0.0580	1.0194	-0.4397	**2.6817**
		(0.9538)	(0.3080)	(0.6602)	**(0.0073) *** **
	Avg_Uni_Fun	**4.7504**	0.6520	**4.8960**	0.2309
		(0.0000) * **	(0.5144)	**(0.0000) *** **	(0.8174)
	Avg_Pri_Fun	-0.8199	-0.0043	0.7305	-0.3680
		(0.4123)	(0.9966)	(0.4651)	(0.7129)
	Avg_Pub_Fun	0.1229	-0.2904	**2.3514**	-0.5036
		(0.9022)	(0.7715)	**(0.0187) *** **	(0.6145)

*, ** and *** denote statistically significant causations at 10%, 5% and 1% respectively

There is evidence from the results obtained from the panel granger causality test to reject the null hypothesis that general outcome does not cause university funding and accept the alternative that general outcome causes university funding for at least one panel variable with a 99% confidence interval. This result is unique, however, when compared with results from the DAGs. The reverse causation from the granger causality (university funding causing general outcome) was found not to be significantly significant, which is consistent with the DAGs results from interacting public, private, university, and general outcome. There was a link between university funding and general outcome, but this was not statistically significant. It can then be inferred that university funding does not directly cause general outcomes.

With 99% confidence, we can reject the null hypothesis that private funding does not cause university funding and accept the alternative that private funding does cause university funding. However, the reverse causation of this was found not to be statistically significant. The results from DAGs consistently showed that university funding had a negative correlation with private funding with 99% confidence. A similar trend was found where private funding was

found to cause public funding with a 99% confidence interval, while the results from DAGs showed that public funding was found to have a negative significant relationship with private funding. In these instances, even though there was causation found within private and university funding, the directions were different.

Table 3. Public affiliation, private affiliation, university affiliation, general outcome.

		X		
		Avg_Gen_Out	Avg_Pri_Aff	Avg_Pub_Aff
Y	Avg_Gen_Out	-0.0580	0.0236	-0.8653
		(0.9538)	(0.9812)	(0.3869)
	Avg_Pri_Aff			
	Avg_Pub_Aff	**2.4064**	-1.0983	**1.9378**
		(0.0161) ***	(0.2721)	**(0.0526) ****
	Avg_Uni_Aff	-0.4483	-1.2426	-0.4960
		(0.6539)	(0.2140)	(0.6199)

*, ** and *** denote statistically significant causations at 10%, 5% and 1% respectively

For the granger causality test of the various affiliation and general outcome, private affiliation had insufficient observations to allow computation of the granger causality test. This led to an omission of results from this variable. At least one panel variable with a 99% significance level found that general outcome causes public affiliation for at least one panel variable. Even though this relationship was a unidirectional one, the DAG results also indicated a significant relationship between general outcome and public funding that was rather bidirectional in nature. The results from the granger causality indicate that general outcomes lead public entities to venture into studying the impact of GBH. As a public safety issue, when there is an increase in findings that GBH is harmful, state agencies are required to investigate this phenomenon to influence policy.

From the panel granger causality test, university affiliation causes public affiliation at a 95% confidence level. University affiliation was also found to cause public affiliation in the

DAGs when all the various affiliation organizations were interacted with a general outcome. The Granger test indicated a causality, but the DAGs went further to show the nature of this causality, which was negative, indicating that researchers from public institutions did not engage with researchers to conduct GBH studies, which was significant.

5. CONCLUSION

To determine the factors that influence the findings of previous scientific research on the possible adverse effects of GBH on human and animal health and the environment, we conducted a meta-analysis of GBH-related studies. Relevant original experiments and papers were identified and selected for inclusion in this meta-analysis by utilizing a web scraping algorithm based on recognized scientific keywords and terms in Python. For this study, Directed Acyclic Graphs were utilized to determine causality, followed by a modified Granger causality test for panel data to determine causation between factors and study outcomes.

Key players in research into the effect of GBH are private corporations, who are mainly producers of agricultural chemicals, state agencies and regulatory authorities whose role is to safeguard the public interests and universities, which are supposed to be independent scientific knowledge-generating entities. And in recent times, there has been a rise in some private entities that were established with the main aim of protecting the environment and public health interests. These entities provide funding to themselves and cross-funding to other organizations to conduct research into the effects of GBH on health, the environment, and other non-target organisms. By virtue of establishment, these entities have their own interests, purposes, and perspectives, which could drive the nature of the outcome of research they conduct into GBH. This is not supposed to be the case, because scientific findings are intended to direct and finalize public policy, not to create polarization in public discourse.

Public policies, particularly those affecting public health, safety, and the environment, must be established on scientific evidence. Ambiguous and inconclusive scientific results on critical issues can influence policy development, posing risks to public health and safety. The increase in research output that is presented in a narrowly focused way based on interests and

perspectives has become a significant source of worry. This might be interpreted as polarization in research, which results in the division of scientific communities based on completely opposite viewpoints on a particular problem. Climate change, vaccination, and the health effects of GBH are just a few examples of critical subjects that have divided the scientific community. While professional disagreement is necessary for scientific progress, polarization stifles it by fostering static, entrenched stances that result in ineffective policy development to protect the public interest. Being able to determine what factors account for divergence in research outcomes is a critical step in discerning why science on some subjects, particularly the impact of GBH on non-target organisms and the environment, has been inconclusive.

From the empirical results based on the meta-analysis of 503 studies into GBH impact, it can be visually observed from figures 2 to 8 that there is a change in the average outcome of GBH studies by country, journal, journal impact factor, author affiliation, and funding. It is crucial to note that the EPA of the United States of America began reviewing glyphosate's registration in 2009 and then ordered pesticide registrants to do additional research to support 2010 human health and ecological risk assessments. Additionally, the EPA partnered with Canada's Pest Management Regulatory Agency to provide risk assessment information. The difference in the findings of GBH impact studies after this time is readily apparent and warrants more investigation into the underlying variables. Our investigation discovered that the kind of organization with which the authors are affiliated, and the type of funding source influenced the study's overall result. For instance, as expected, university funding had a causal relationship with university affiliation, and the same with public and private funding and affiliation. Additionally, some financing sources have been proven to relate to the types of organizations as predicted, while others have been shown to be unrelated or even detrimental to one another.

The general outcome of research was revealed to have a negative causality and, in certain circumstances, bidirectional causation with the authors' private affiliation. This meant that private sector research was more likely to conclude that GBH was not dangerous because the primary private sector players in GBH research were large corporations such as Monsanto and Bayer, who perform studies to demonstrate the safety of their products. On the other hand, the general outcome may push private entities to do more studies to demonstrate that their products are not detrimental to non-target organisms or the environment. Earlier investigations into the effects of GBH were first driven mostly by the private sector, followed by public organizations and universities, as seen in figures 7 and 8. These were the main research results that were used to write the story and talk about GBH use.

While publicly sponsored research is likely to provide findings suggesting that GBH is detrimental, research conducted by public institutions is likely to demonstrate that GBH is not hazardous. Public funds often support research conducted beyond only government organizations, most notably in universities, which explains the difference in the direction of causality in terms of public funds and affiliation on general outcome. Clearly, GBH is still used in the most nations because governmental authorities with the authority to regulate it claim it is safe. Universities are perceived as organizations dedicated to the production and advancement of knowledge, even though some are privately owned and may have other purposes. University authors' conducted studies established that GBH was hazardous. Universities play a key role in research, and this result raises significant concerns about contradictions between university findings and those of other organizations, particularly public organizations whose research has a direct impact on policy. While these contradictions are readily apparent, they have not been statistically examined and confirmed, as this work has done.

From the entire dataset, which spans from 1987 to 2021, and the decomposition into prior and after 2010, and the granger causality results, it has been demonstrated that results from private, public, and universities generate divergent results. Organizations, by their nature, have interests that can drive research agendas away from questions that are the most relevant for public policy and welfare. Strategies to counteract organizational influence on the research agenda are needed. We recommend policy actions beyond disclosure of funding and conflict of interest to adopting independent research which could comprise actors from major stakeholders and adhere to strict guidelines to regulate the interaction of research organizations.

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APPENDIX

A.1. Public Affiliation, Private Affiliation, University Affiliation, General Outcome

Prior 2010

Figure A1. Public affiliation, private affiliation, university affiliation, general outcome for prior 2010.
*, ** and *** denote statistically significant causations at 10%, 5% and 1% respectively

The study investigated the effect the various organizations had on the general outcome prior to 2010. The DAG revealed two distinct interactions between two variables for data prior to 2010. The findings suggested that public affiliation had a negative relationship with university affiliation, with a marginal effect of 60% at a 95% level of confidence. Furthermore, the overall outcome was associated with private affiliation in this graph; the association was negative significant, with a marginal effect of 35% at 99% confidence.

Both of the two relationships were two-way causation. Similar causal links may be deduced from the complete dataset's results, showing marginal effects that are slightly different and additional interactions between other variables. It is determined that a long-standing causal link exists between general outcome and private affiliation, as well as between university affiliation and public affiliation. However, there have been more connections between some of the funding sources over time, even though the relationship from the beginning is still visible.

A.2. Public Affiliation, Private Affiliation, University Affiliation, General Outcome After 2010

The results from the interaction of the various organizations with general outcomes for data after 2010 showed that 10% and 20% significance for all the algorithms yielded identical results, while the 5% significance also yielded same results for all algorithms. The DAGs from all the algorithms at 5% significance showed that public affiliation and private affiliation negatively caused university affiliation. This was consistent with some of the results from the same interaction in the entire dataset.

From the results of 10% and 20% significance for all the algorithms, general outcome negatively caused private affiliation while public affiliation negatively caused university affiliation. Meaning, there was some level of likelihood that research from authors of private

organizations was more likely to generate outcomes with no adverse effect, while public-affiliated authors were less likely to conduct studies into the impact of GBH with university researchers. These results were similar to those produced in the data prior to 2010, with the main difference being that the results here were unidirectional as compared to the bidirectional causations identified in the data prior to 2010. Also, the relationships identified can be teased out from parts of the DAGs generated from the entire dataset.

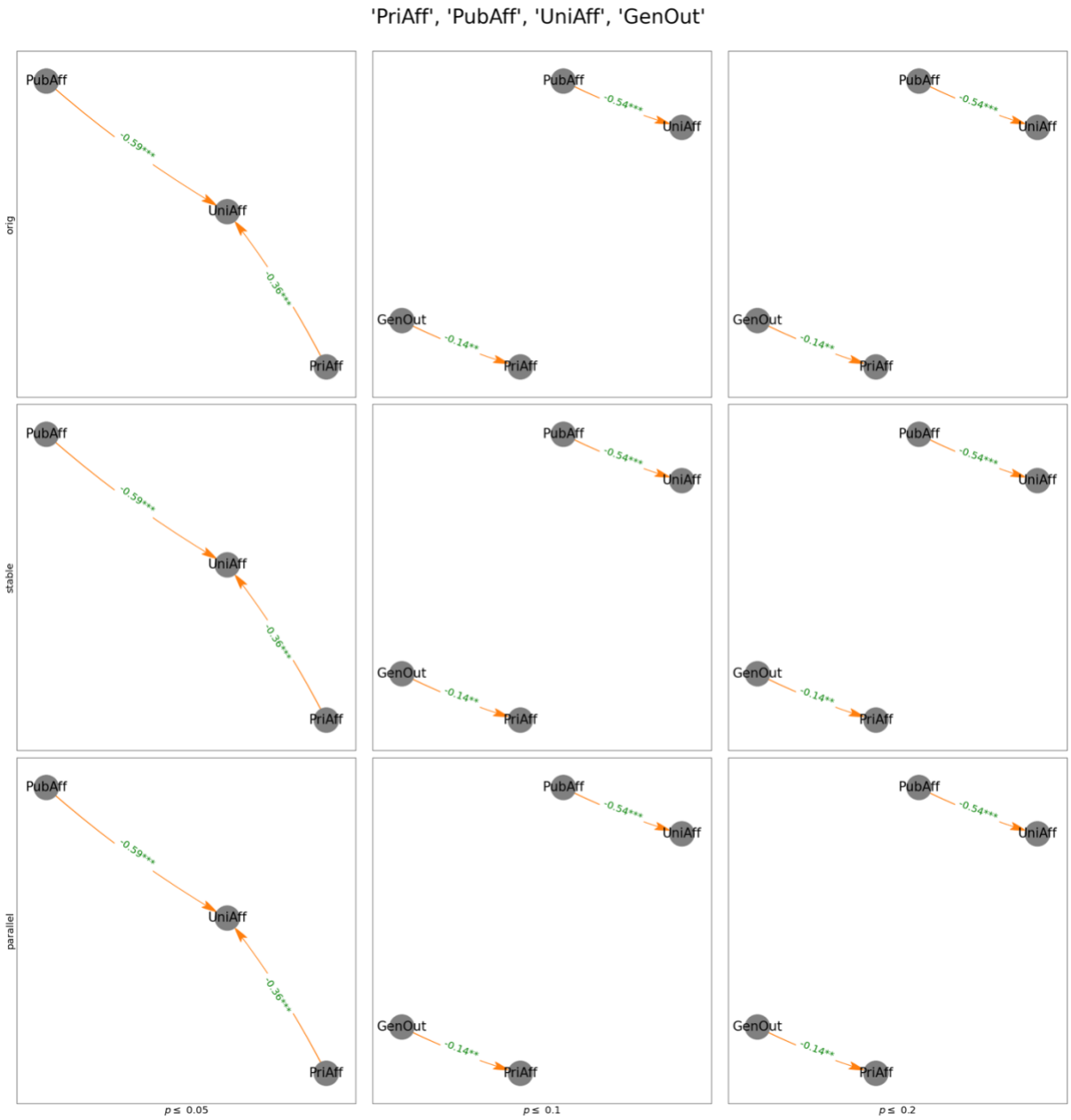

Figure A2. Public affiliation, private affiliation, university affiliation, general outcome for after 2010.

*, ** and *** denote statistically significant causations at 10%, 5% and 1% respectively

A.3. Public Funding, Private Funding, University Funding, General Outcome Prior 2010

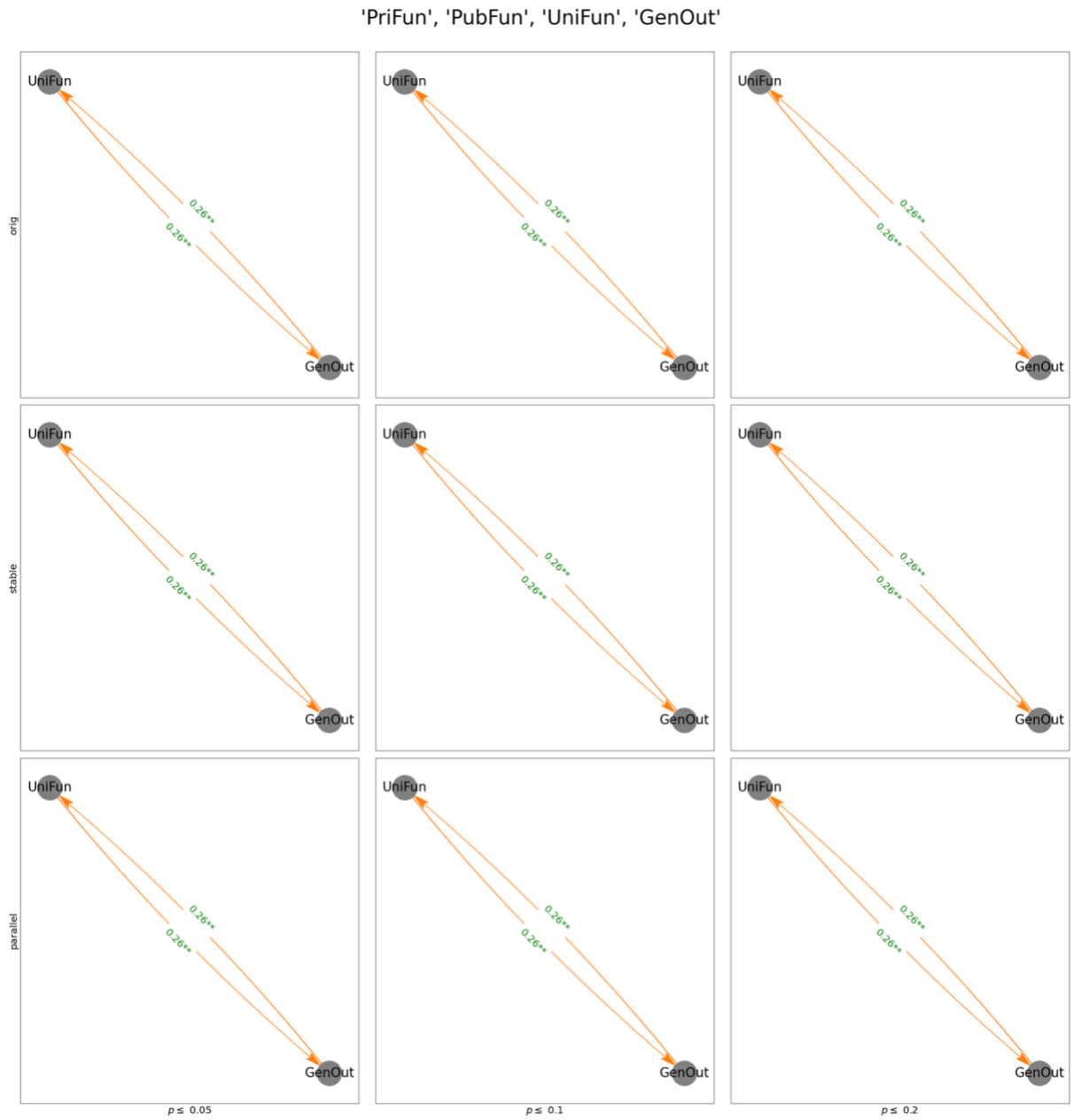

Figure A3. Public funding, private funding, university funding, general outcome prior to 2010. *, ** and *** denote statistically significant causations at 10%, 5% and 1% respectively

The DAG generated from the interactions of public, private, and university funding on the outcome of studies conducted prior to 2010 had the identical graph for all three confidence intervals and algorithm. The funding of universities demonstrated a bidirectional link with the general outcome, with a marginal effect of 26% at the 5% level of significance. This meant that

research funded by universities was likely to demonstrate that GBH had a detrimental effect on non-target creatures. This is in contrast to the DAG generated from the entire dataset, which found no significant relationship between university funding and general outcome but a significant negative relationship between private and university funding. While public funding showed a strong positive link with an overall positive outcome in the entire dataset, it was not the case prior to 2010. University funding and general outcome were linked before 2010, but this relationship has been weakening statistically over time as new causal links have been made as new variables have been linked to these two things.

A.4. Public Funding, Private Funding, University Funding, General Outcome After 2010

The results from graphs of all 3 algorithms with a confidence level of 95% and parallel PC at 10% significance showed that university funding had a negative bidirectional causation with private funding with a marginal effect of 16%. This finding was found as part of the DAG results from the same interaction using the entire dataset. The output from the original PC and stable PC at 10% confidence maintained the relationship between private funding and university funding as in the 5%. The new addition is a bidirectional causation of public funding and general outcome with a marginal effect of 10% which is consistent with other DAG results.

The graph from the 0.20 significance for all the algorithms maintained the relationship between public funding, private funding, and university funding as in the result of 0.10%. In this case, public and university funding jointly positively caused private funding negatively with a margin of 13% and 16%, respectively. These results are not identical to the results of the entire dataset but can be teased out. However, this relationship is very divergent from that of the DAG-generated data prior to 2010. These results meant private funding usually stood alone in

conducting studies into the impact of GBH. They did not come together with public and university sources of funding.

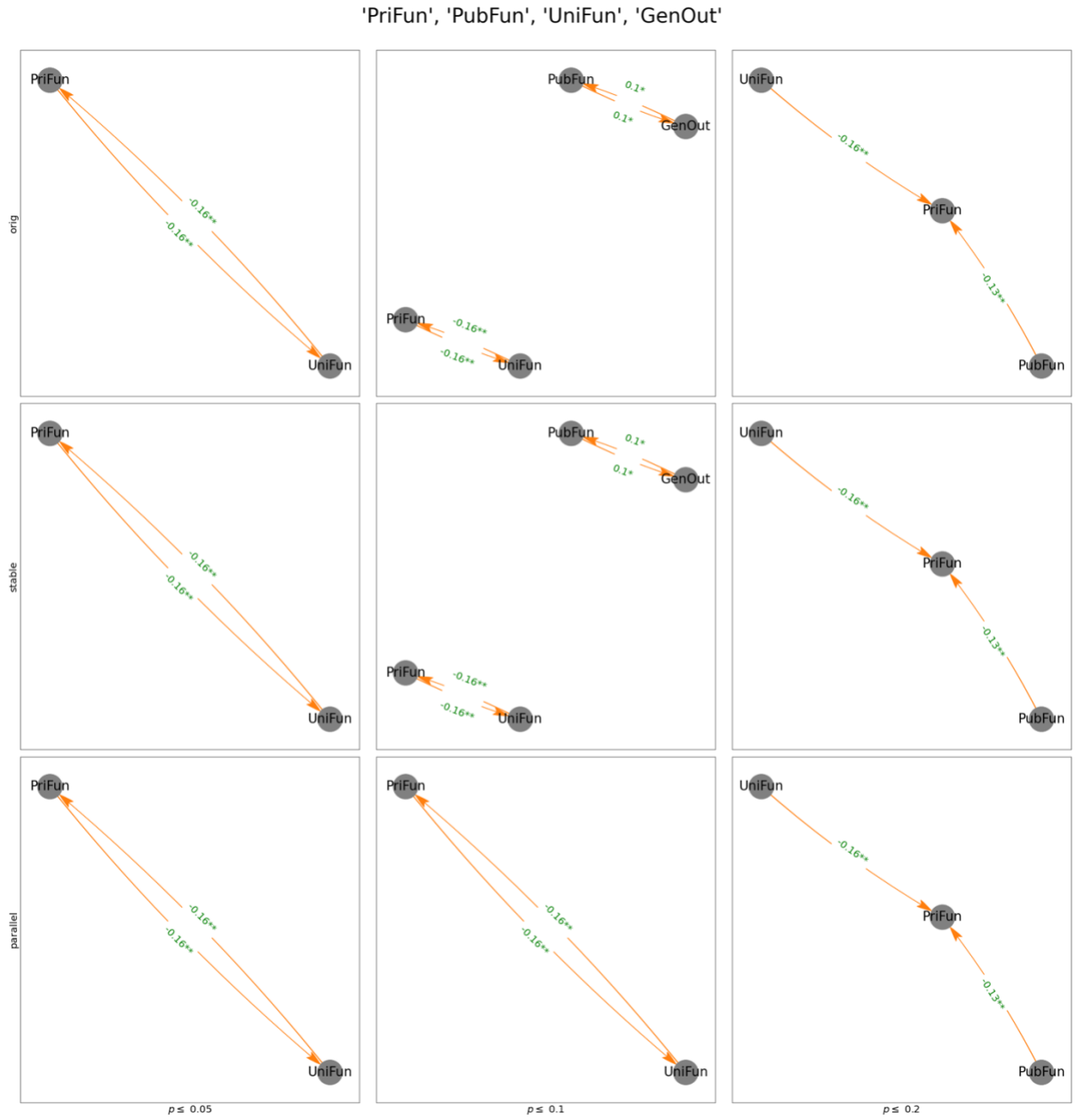

Figure A4. Public funding, private funding, university funding, general outcome after 2010. *, ** and *** denote statistically significant causations at 10%, 5% and 1% respectively

A.5. Public Funding, Public Affiliation, Private Funding, Private Affiliation, University Funding, University Affiliation, General Outcome

The causal relationship between the author's affiliation (public, private, or university), the sources of funding for the research, and the general outcome were investigated. While cross-funding between funding sources and affiliations, particularly in the case of public funding to all other organizations, was expected, the DAG-identified relationship demonstrates the statistically significant causal relationships. From the DAG obtained from the interaction between the various authors' affiliations and funding sources considered for the meta-analysis, all the graphs from the 3 significance levels were different.

The result of the DAG from the PC and Stable PC Algorithm with a confidence interval of 0.05 indicates a positive causal relationship between public funding and public organizations (at 90% confidence) with a marginal effect of 11%, and a negative relationship between university funding and private affiliation (at 99% confidence) with a marginal effect of 15%. The Parallel PC algorithm had identical relationships between university funding and private funding, but this time had a negative relationship between public affiliation and university affiliation with a marginal effect of 54% at 99% confidence.

The results from the 10% significance level were identical for all 3 algorithms. There was a positive causal relationship between public funding & public organizations (at 90% confidence) with a marginal effect of 11%, and a negative relationship between university funding & private affiliation (at 99% confidence) with a marginal effect of 15%. There was an additional negative bi-directional causal relationship indicating endogenous variables between private affiliation and general outcome with a marginal effect of 21% at 99% confidence,

inferring private organizations were more likely to generate research with outcomes that showed that GBH had no adverse effect, which has been consistent throughout this study.

The result of the DAG from the PC and Stable PC Algorithm with a confidence interval of 0.20% indicates a positive causal relationship between public funding and public organizations (at 90% confidence) with a marginal effect of 11%. There was a negative relationship between private affiliation and general outcome with a marginal effect of 21% at 99% confidence, with a bidirectional link indicating endogenous variables. Private funding also had a negative causal relationship with university affiliation and a marginal effect of 25% at 99% confidence. There was also a positive relationship with a marginal effect of 29% at a 99% confidence between private affiliation and private funding, as expected.

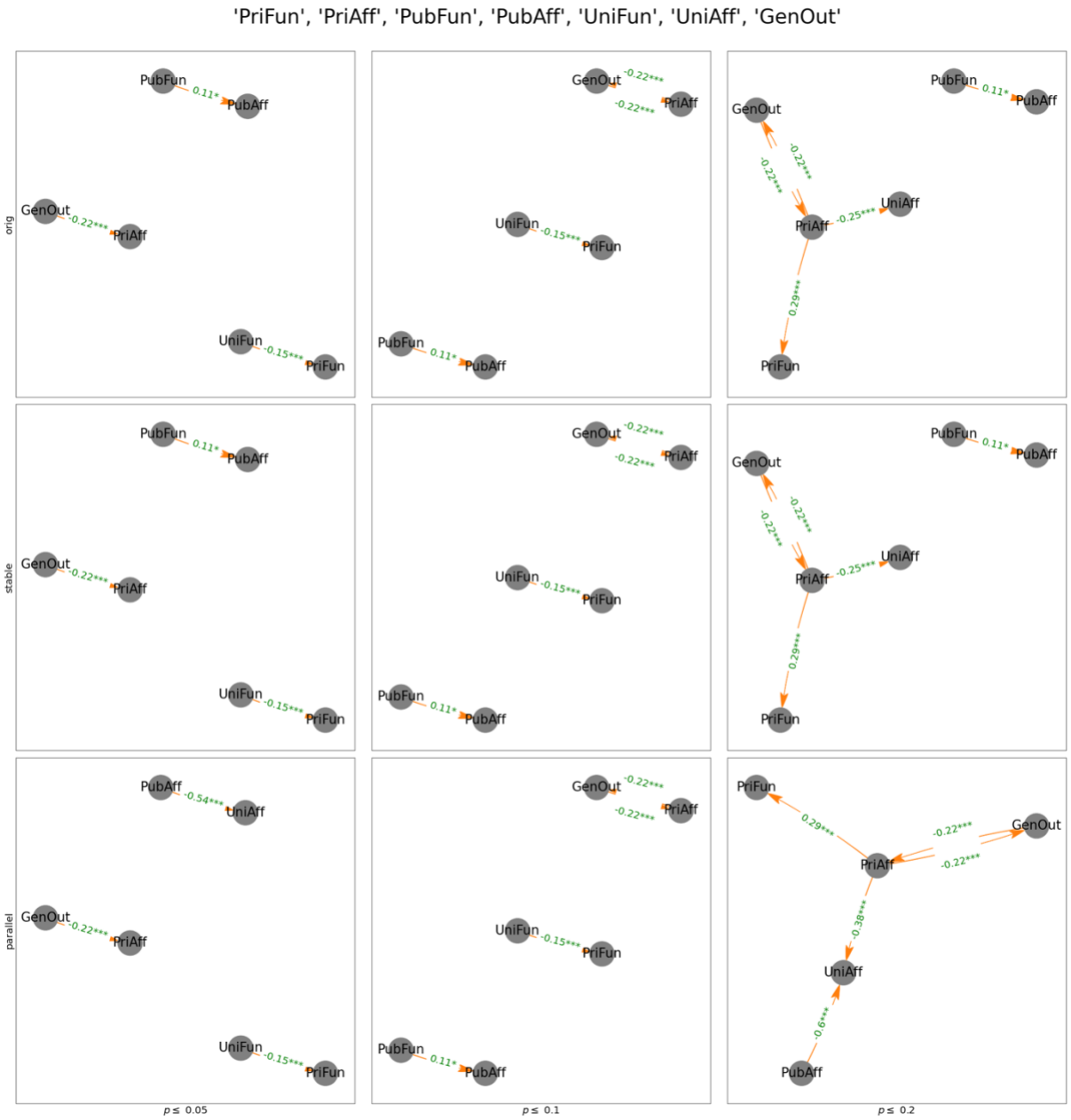

Figure A5. Public funding, public affiliation, private funding, private affiliation, university funding, university affiliation, general outcome for full dataset.
*, ** and *** denote statistically significant causations at 10%, 5% and 1% respectively

The Parallel PC algorithm had a causal relationship between private affiliation and general outcome and university affiliation. and a positive relationship between private affiliation and private funding. There was a negative relationship between university affiliation and public

affiliation with a marginal effect of 60% at 99% confidence as presented in the earlier analysis between the organization of affiliation and general outcome.

A.6. Private Funding, Private Affiliation, General Outcome Prior to 2010

The study then partitioned the DAG data into periods prior to and following 2010 in order to have a better understanding of how the variables' interactions changed over time. For the two time periods, all interactions were computed exactly as they were in the whole data study (1987–2021). We shall begin by discussing the outcomes before the year 2010.

Prior to 2010, the DAG results for private funding, private affiliation, and outcome were comparable to those for the entire dataset, with the main distinction being the marginal effects. For example, it was discovered that private financing has a positive influence on private affiliation (marginal effect of 53% compared to 27% in the whole data), but the general outcome had a negative effect on private affiliation (marginal effect of 19%). By and large, the marginal effects created by the interaction of data prior to 2010 were almost twice as large as those obtained by the entire dataset analysis. The other distinction was that the significance intervals of 5% and 10% produced unidirectional relationships, but the confidence interval of 20% generated bidirectional relationships. The confidence level for all of the causation was 99 percent. Prior to 2010, the data show a consistent pattern of this interaction, with overall data results indicating a decrease in magnitude or causality over time. Private organizations, private money, and overall outcomes have all had a similar effect or interaction over time.

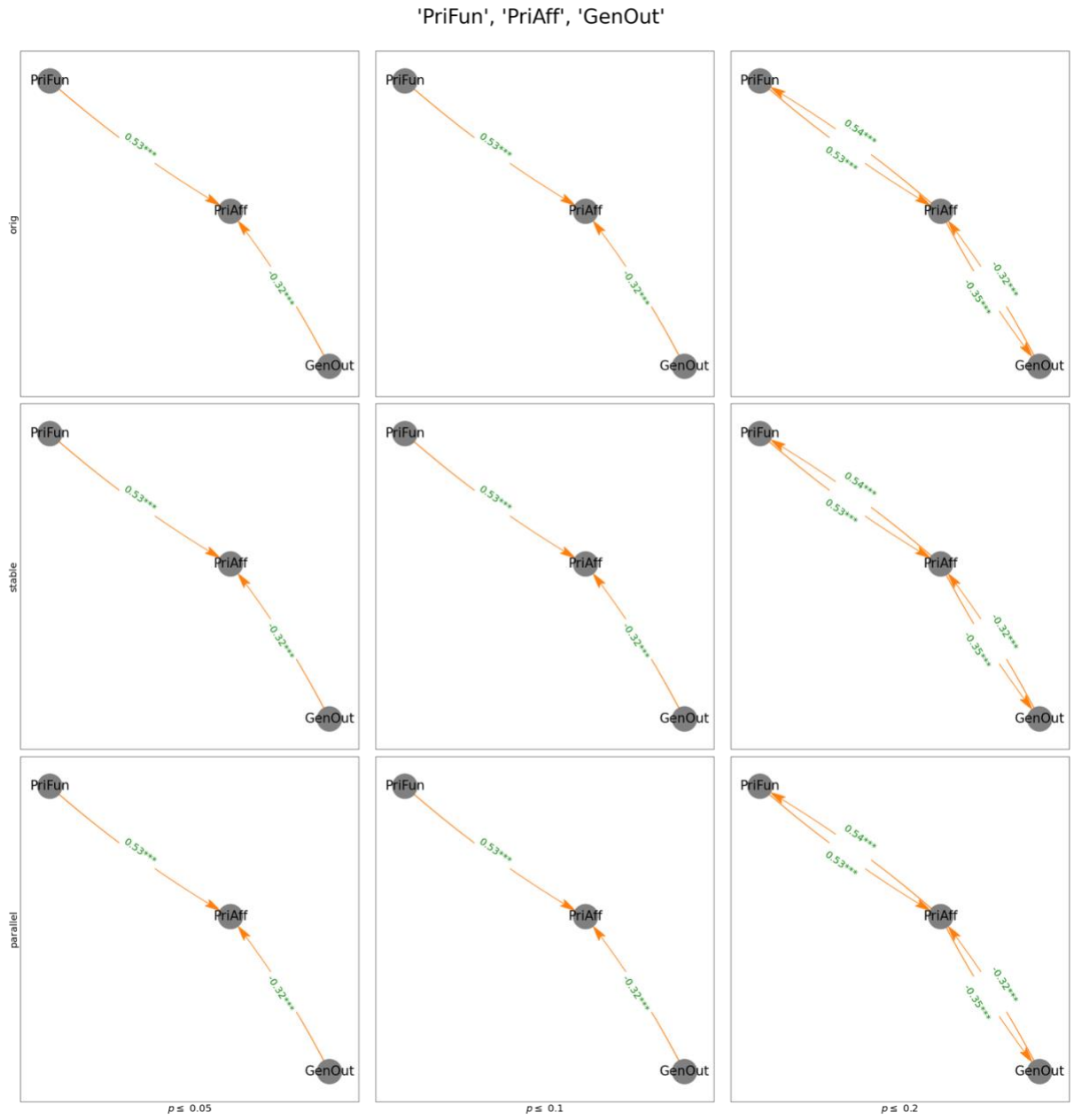

Figure A6. Private funding, private affiliation, general outcome prior to 2010.
*, ** and *** denote statistically significant causations at 10%, 5% and 1% respectively

A.7. Public Funding, Public Affiliation, General Outcome Prior to 2010

For the time prior to 2010, the interaction between public funding, public affiliation, and general outcome produced DAG outcomes that were completely contrary to the aggregate dataset results. A direct link could not be found between the 5% and 10% significance for any of the three algorithms that were used.

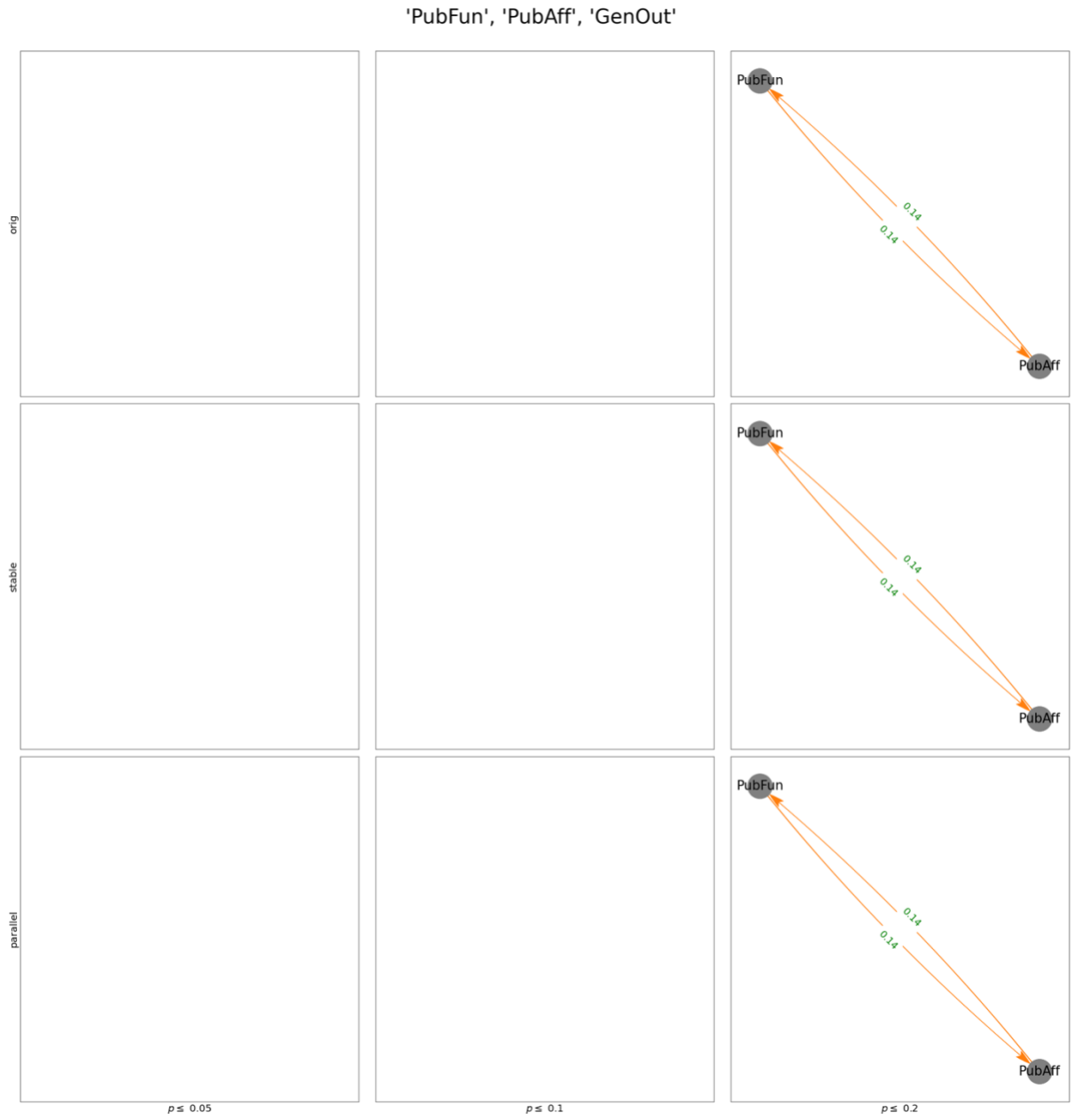

Figure A7. Public funding, public affiliation, general outcome prior to 2010.
*, ** and *** denote statistically significant causations at 10%, 5% and 1% respectively

The only association observed was between public financing and public affiliation for all three algorithms at a 20% significance. However, because this association was not statistically significant, no conclusions can be drawn. This result implies that, in general, public organizations were sponsored by public funds, as they are now, although this was not significant. Additionally, no relationship could be drawn between study findings from public organizations

or public financing, which is contrary to the results of the whole dataset, which indicated that public money had a positive effect on general outcome and public affiliation had a negative effect on general outcome.

A.8. University Funding, University Affiliation, General Outcome Prior 2010

It is critical to note that the overall dataset indicated that university funding was directed toward universities where research that revealed that GBH had detrimental effects was likely to be conducted. There was a bidirectional relationship between university funding and general outcome before 2010. The marginal effect from general outcome to university funding was 26 percent at a 5% significance level for all algorithms and confidence intervals, and the marginal effect from university funding to general outcome was 22 percent at the same level.

The significance of 10% and 20% revealed an additional causal relationship between university funding and the general outcome. Additionally, university affiliation exhibited a bidirectional causal relationship with the general outcome, with a marginal effect of 24% from the general outcome to university affiliation and 20% from university affiliation to general outcome at a 5% significance level. As a result of this finding, it is obvious that prior to 2010, there was a clearer relationship between general outcome and university money and affiliation, with their research indicating that GBH was toxic to non-target species.

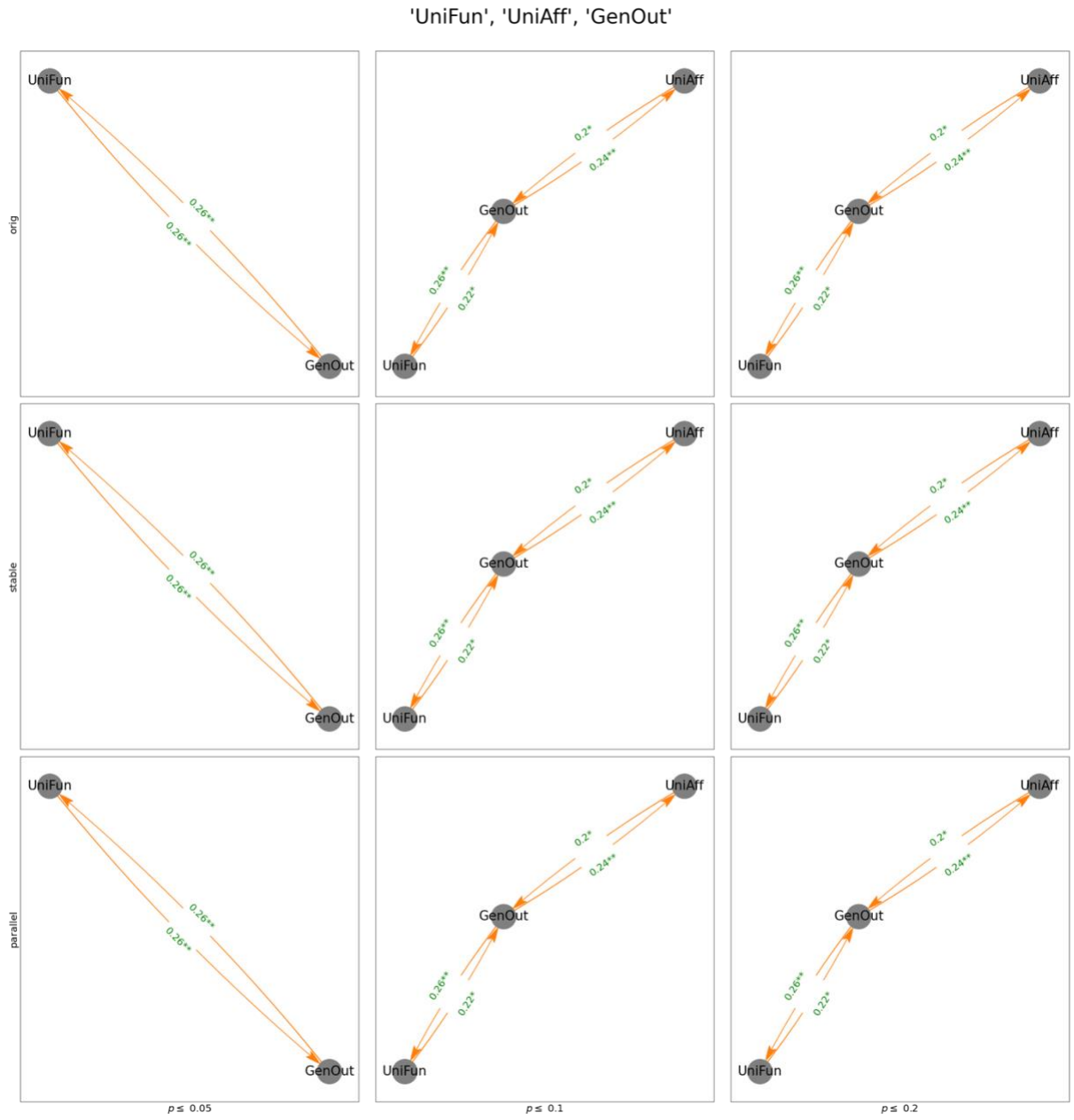

Figure A8. University funding, university affiliation, general outcome prior 2010.
*, ** and *** denote statistically significant causations at 10%, 5% and 1% respectively

A.9. Public Funding, Public Affiliation, Private Funding, Private Affiliation, University Funding, University Affiliation, General Outcome Prior to 2010

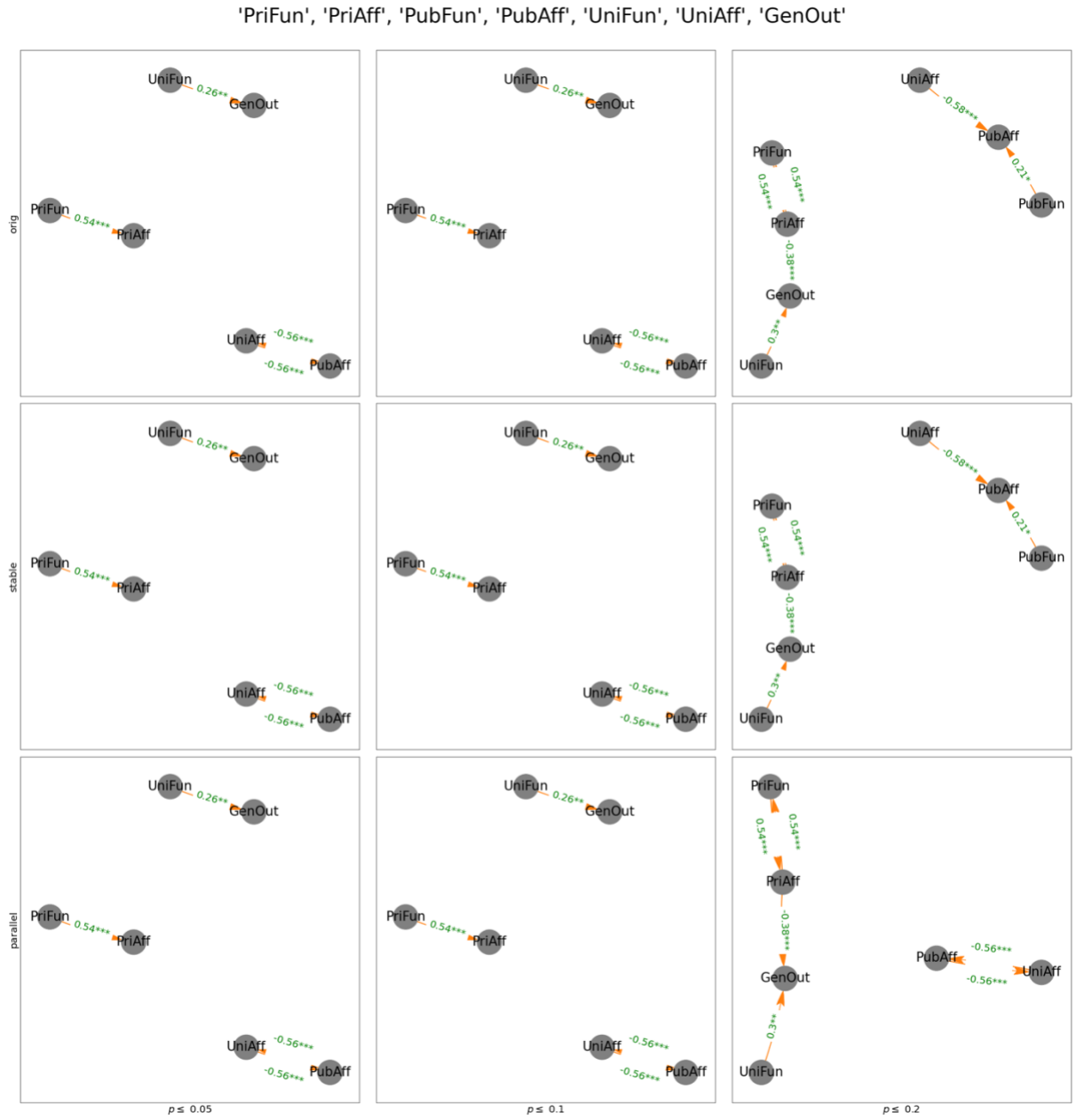

Figure A9. Public funding, public affiliation, private funding, private affiliation, university funding, university affiliation, general outcome prior to 2010.
*, ** and *** denote statistically significant causations at 10%, 5% and 1% respectively

We evaluated the causal link between the researcher's affiliation (public, private, or university), the funding source for the research, and the overall outcome. The results indicated

that the graphs for the 5% and 10% significance level were identical but different from those for the 20% significance. According to the 5% significance, private funding demonstrated a causal relationship with private organizations (a marginal effect of 54%). University affiliation was negatively associated with public affiliation (a marginal effect of 56%), showing that public researchers did not typically collaborate with private firms. Finally, university funding resulted in a positive general outcome (a marginal effect of 26%), which suggested that research conducted before 2010 by universities was more likely to imply that GBH had a negative effect on non-target organisms. These results were completely different from those that came from the whole dataset with the same confidence interval and the same algorithms.

The graphs from the PC and PC Stable produced similar results at the 20% significance. According to the PC and PC Stable algorithms, one cluster of graphs indicated that the general outcome was influenced by university funding (positively by 30%) and private affiliation (negatively by 38%), whereas private affiliation was influenced by private funding (positively by 54 percent). These findings are fairly consistent with the other significance levels of updating links in which university funding is associated with a general outcome and private funding is associated with a private affiliation. A novel element to this is the effect of private affiliation on the overall outcome, which was previously observed in earlier interactions. The other cluster demonstrated that public affiliation was influenced by public funding (positively, by a factor of 21%) and university funding (negatively, by a magnitude of 58 percent).

A.10. Private Funding, Private Affiliation, General Outcome after 2010

The second partition analyzed was for data collected after 2010, which included research completed between 2010 and 2021 that was sampled for the meta-analysis. The DAG findings

for the interaction between private funding, private affiliation, and outcome were consistent across all confidence intervals, as well as for the original PC and stable PC algorithms.

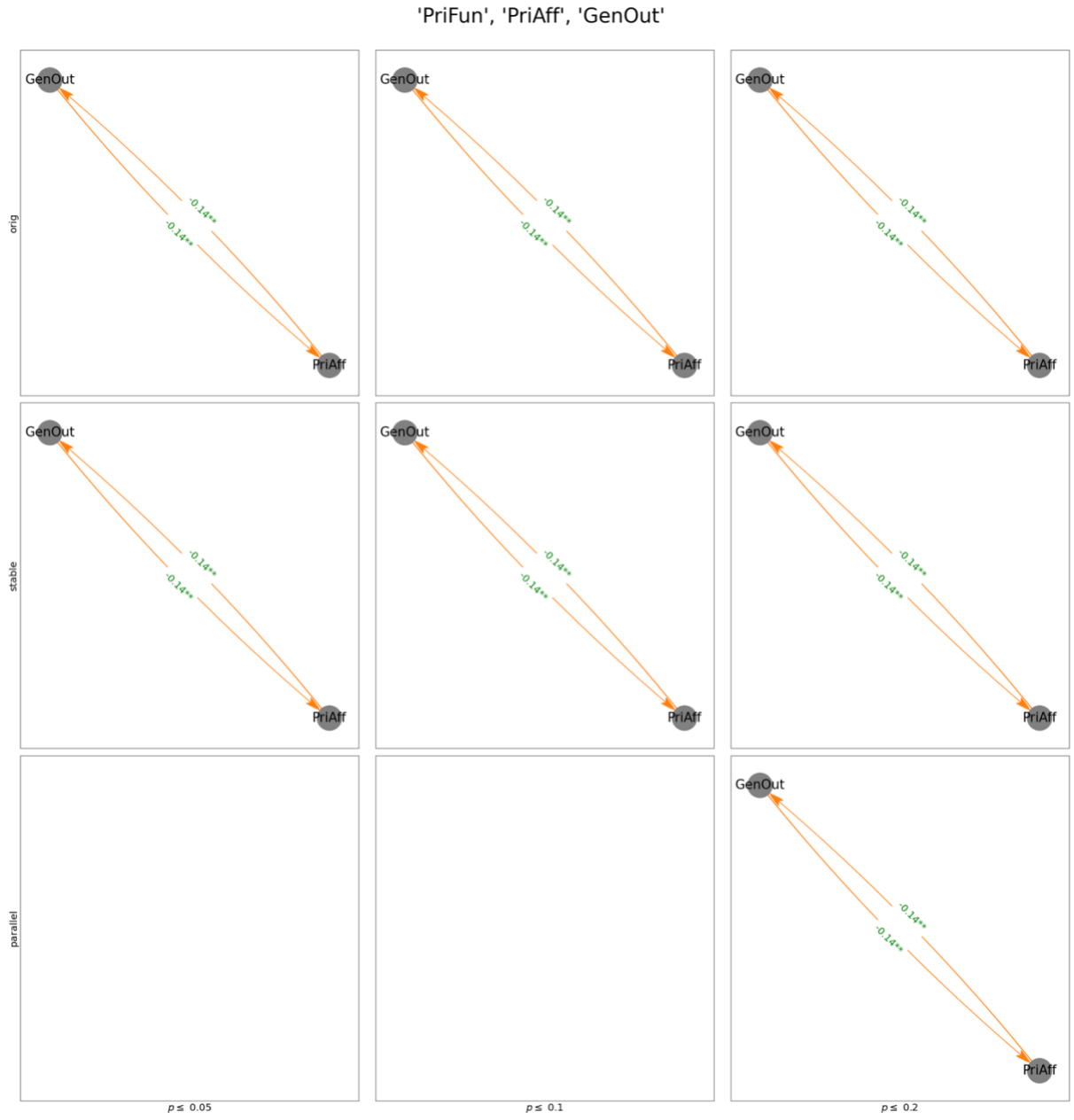

Figure A10. Private funding, private affiliation, general outcome after 2010.
*, ** and *** denote statistically significant causations at 10%, 5% and 1% respectively

However, no relationship was observed for the 5% and 10% significance for parallel PC algorithms. The DAG output for this interaction showed a bidirectional negative causal relationship between private affiliation and general outcome with a marginal impact of 14%.

This can be explained as research undertaken in private organizations is likely to provide results indicating that GBH has no detrimental effect on non-target organisms. This finding can, however, be teased out from the analysis of the complete data set and the data prior to 2010. In the other datasets, there were additional causations, but these did not appear in this.

A.11. Public Funding, Public Affiliation, General Outcome after 2010

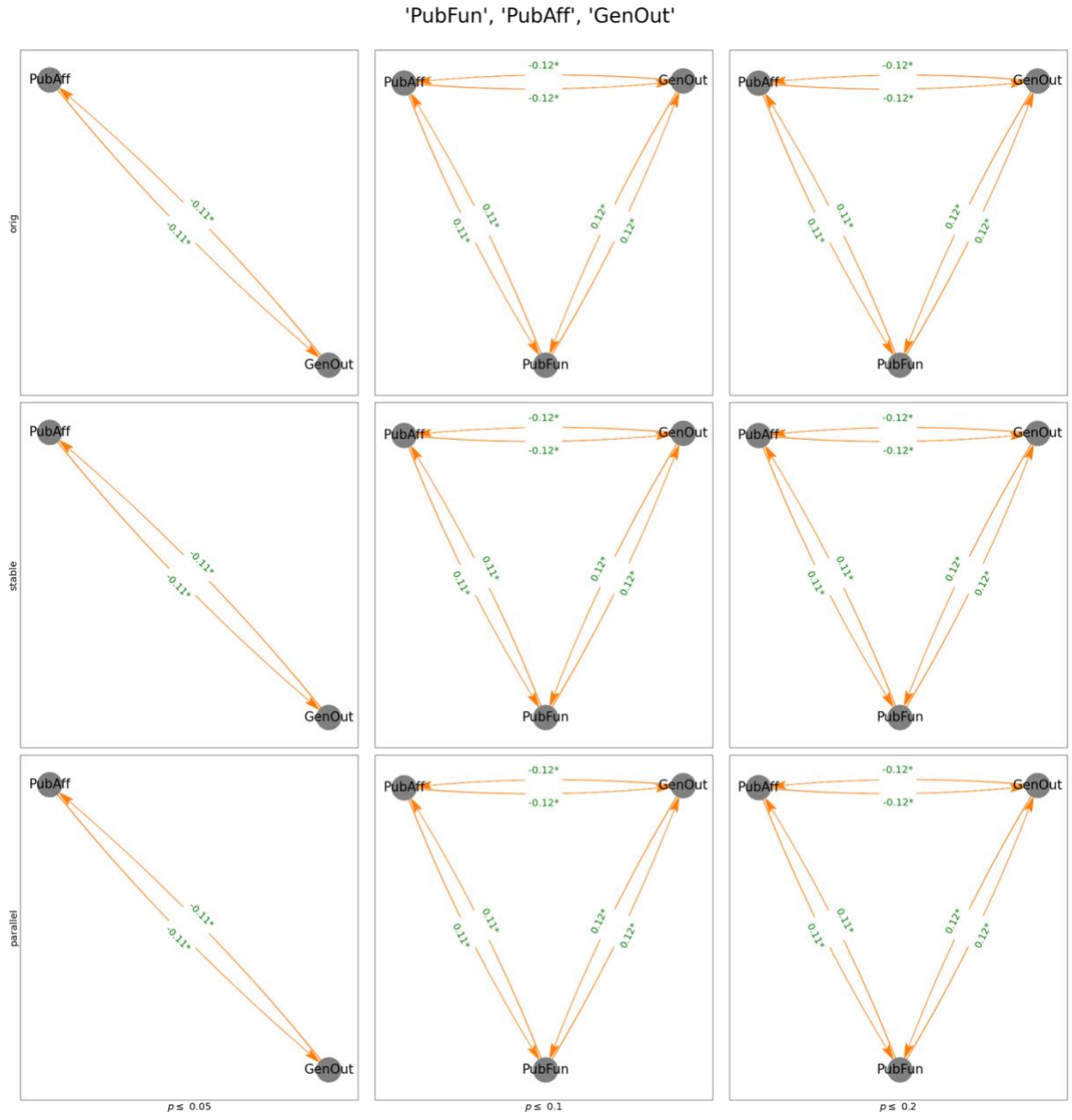

Figure A11. Public funding, public affiliation, general outcome after 2010.
*, ** and *** denote statistically significant causations at 10%, 5% and 1% respectively

When the relationship between public financing, public affiliation, and outcome was examined for data after 2010, the results from all three algorithms were similar, as were the 10% and 20% significance. With a 95% confidence interval, the sole causality discovered was between public affiliation and overall outcome, which had a marginal impact of 11% at the 90% level of confidence. This relationship was also discovered when the complete dataset was analyzed. The DAG results at 10% and 20% significance indicated positive bidirectional causality between public funding and general outcome, as well as between public funding and public affiliation, implying that they are endogenous. With a 90% confidence level in both cases, the magnitudes of the margins were 12% between public financing and result and 11% between public organization and public funding.

Additionally, it was shown that public affiliation had a negative bidirectional relationship with the general outcome, with a marginal effect of 12% at 90% confidence. The magnitude of public funding compared to general outcome is the same as the magnitude of public organization relative to general outcome, implying that they have the same impact and hence cancel out. Similar findings were obtained for the entire dataset; in that case, however, the marginal effect of public funding on the general outcome was greater than the marginal effect of public organizations on the general outcome, implying that public funding influenced the general outcome in ways other than through public organizations. Prior to 2010, the dataset also revealed bidirectional causality between public organizations and public funding. This implies that government funding has been linked to public organizations.

A.12. University Funding, University Affiliation, General Outcome after 2010

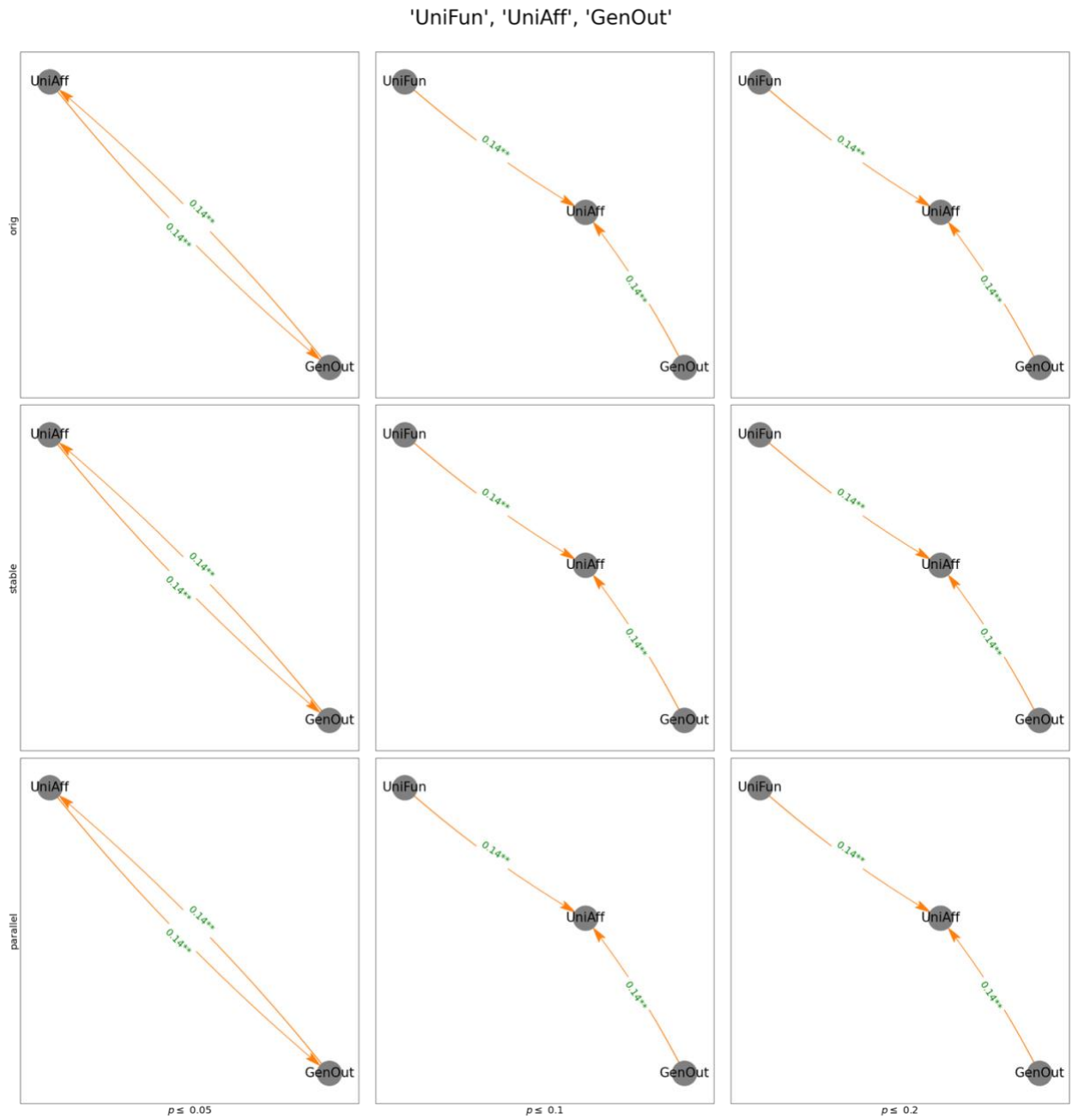

Figure A12. University funding, university affiliation, general outcome after 2010.
*, ** and *** denote statistically significant causations at 10%, 5% and 1% respectively

As was observed for the entire dataset, including data prior to 2010, university affiliation was positively related to overall outcome. This was the sole association discovered in the 5% significance DAG for all algorithms, with a marginal impact of 14% at the 95% confidence interval, which is similar to the magnitude seen in the other dataset. The significance levels of

10% and 20% for all algorithms produced identical DAGs to those generated in the full dataset, with the only difference being that this is unidirectional as opposed to the bidirectional generated in the entire dataset. According to the DAG findings, university funding and general outcomes caused university affiliation with a marginal effect of 14% at the 95% confidence interval for all, and this causation was strictly unidirectional.

A.13. Public Funding, Public Affiliation, Private Funding, Private Affiliation, University Funding, University Affiliation, General Outcome after 2010

The results from graphs of all 3 algorithms with a significance level of 0.05 as well as parallel PC at 10% confidence showed in one cluster generated that private funding and university funding had a negative bidirectional causation with a marginal effect of 16% at 95% confidence for data after 2010. Another cluster generated showed that public affiliation and private affiliation negatively caused university affiliation, which was found when author affiliation interacted with the general outcome.

The results from the original PC and stable PC at 10% significance level 3 separate causations. At the 99% confidence level, public affiliation was found to negatively cause university affiliation with a marginal effect of 54%. Also, general outcome was found to negatively cause private affiliation with a marginal effect of 14% at the 95% confidence level. Private funding and university funding were found to have a bidirectional causal relationship with a marginal effect of 16% at 95% confidence. The results for all 3 algorithms at a 20% significance level yielded the same results where the general outcome was found to cause private affiliation with a marginal effect of 14% at the 95% confidence level.

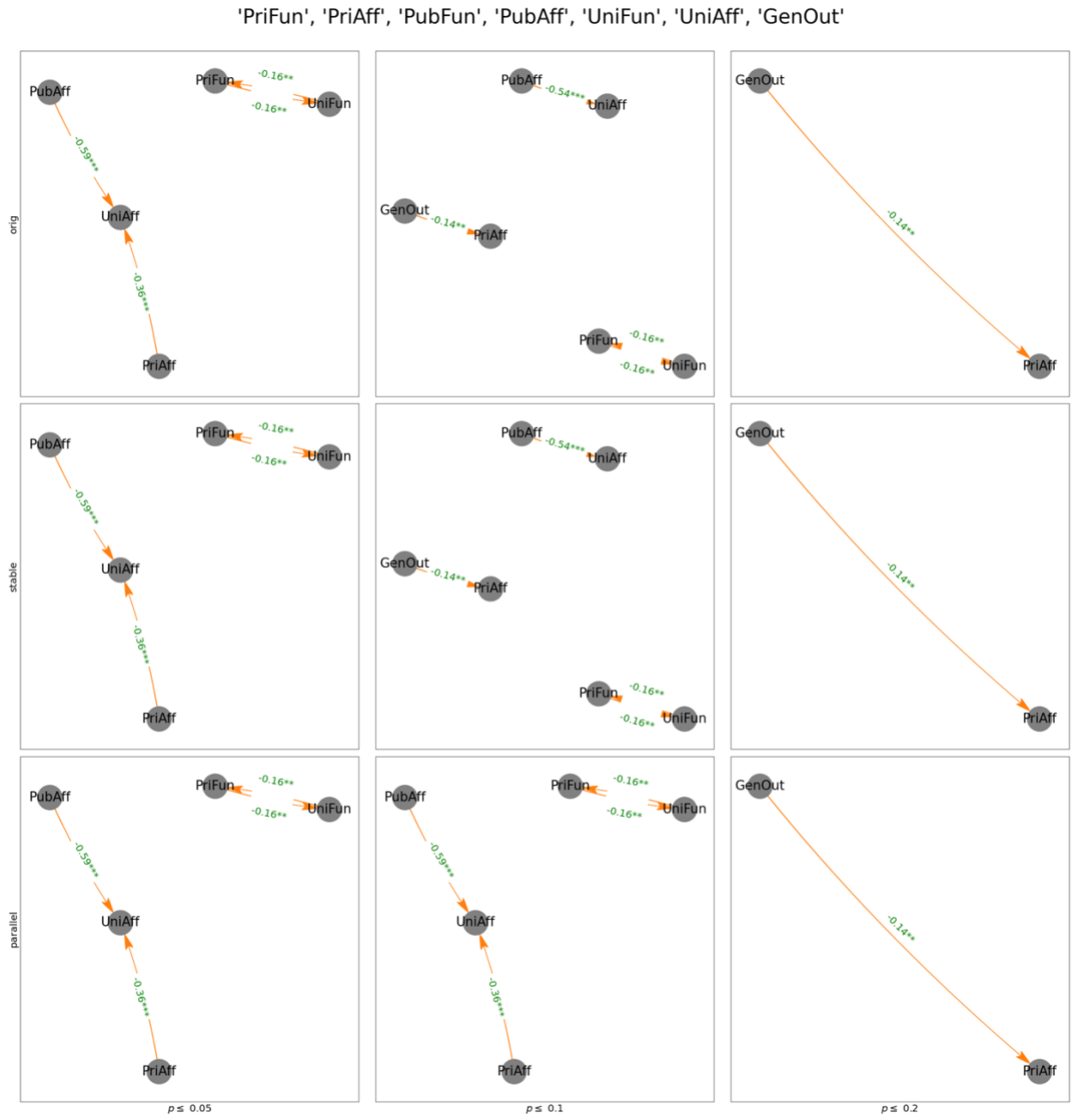

Figure A13. Public funding, public affiliation, private funding, private affiliation, university funding, university affiliation, general outcome after 2010.
*, ** and *** denote statistically significant causations at 10%, 5% and 1% respectively