Science of the Total Environment 829 (2022) 154532

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

A risk ranking of pesticides in Irish drinking water considering chronic health effects

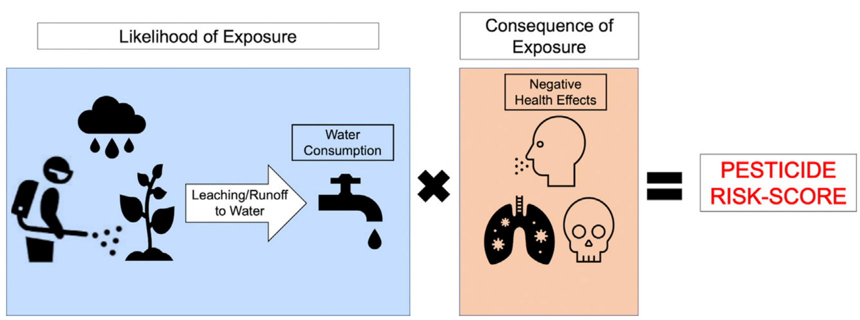
J. Harmon O'Driscoll [a], A. Siggins [b,c], M.G. Healy [b], J. McGinley [b], P.-E. Mellander [c], L. Morrison [d], P.C. Ryan [a,e,*]

[a] Discipline of Civil, Structural and Environmental Engineering, School of Engineering, University College Cork, Cork, Ireland
[b] Civil Engineering and Ryan Institute, National University of Ireland Galway, Galway, Ireland
[c] Teagasc Environmental Research Centre, Johnstown Castle, Co. Wexford, Ireland
[d] Earth and Ocean Sciences, School of Natural Sciences and Ryan Institute, National University of Ireland Galway, Galway, Ireland
[e] Environmental Research Institute, University College Cork, Cork, T23 XE10, Ireland

HIGHLIGHTS

- Ranking scheme for chronic health effects from pesticide exposure was developed.
- Risk scores consider pesticide use, mobility, persistence, and toxicity.
- Existing method was improved by including site data and metabolite risk.
- Sixty-three pesticides used in Ireland were scored and ranked by relative risk.
- Pesticide users can utilise this method to identify high risk pesticides for their sites.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 15 December 2021
Received in revised form 21 February 2022
Accepted 8 March 2022
Available online 15 March 2022

Editor: Yolanda Picó

Keywords:
Pesticides
Metabolites
Risk assessment tool
Drinking water
Human health risk

ABSTRACT

This paper presents a novel scoring system which facilitates a relative ranking of pesticide risk to human health arising from contaminated drinking water. This method was developed to identify risky pesticides to better inform monitoring programmes and risk assessments. Potential risk was assessed considering pesticide use, chronic human health effects and environmental fate. Site-specific soil conditions, such as soil erodibility, hydrologic group, soil depth, clay, sand, silt, and organic carbon content of soil, were incorporated to demonstrate how pesticide fate can be influenced by the areas in which they are used. The indices of quantity of use, consequence and likelihood of exposure, hazard score and quantity-weighted hazard score were used to describe the level of concern that should be attributed to a pesticide. Metabolite toxicity and persistence were also considered in a separate scoring to highlight the contribution metabolites make to overall pesticide risk. This study presents two sets of results for 63 pesticides in an Irish case study, (1) risk scores calculated for the parent compounds only and (2) a combined pesticide-metabolite risk score. In both cases the results are assessed for two locations with differing soil and hydrological properties. The method developed in this paper can be adapted by pesticide users to assess and compare pesticide risk at site level using pesticide hazard scores. Farm advisors, water quality monitors, and catchment managers can apply this method to screen pesticides for human health risk at a regional or national level.

1. Introduction

Pesticides are fundamental in securing food supplies by reducing crop losses through the deterrent, elimination, or regulation of pests, fungi, insects, and weeds (FAO and WHO, 2014; Cerda et al., 2017). However, pesticide use has been found to pose a major threat to the environment

* Corresponding author at: Discipline of Civil, Structural and Environmental Engineering, School of Engineering, University College Cork, Cork, Ireland.
E-mail address: Paraic.ryan@ucc.ie (P.C. Ryan).

http://dx.doi.org/10.1016/j.scitotenv.2022.154532

(Carvalho, 2017), and low but repeated exposure has been linked to several human health disorders (Abreu-Villaça and Levin, 2017; Parker et al., 2017; Wee et al., 2019; Yin et al., 2020; El-Nahhal and El-Nahhal, 2021a). Governmental legislation regulates approval of pesticides on the European market and promotes their sustainable use to reduce overall pesticide risks (European Commission, 2009a, 2009b). Such legislation requires the evaluation and classification of pesticide risk through incremental stages including data collection, priority-setting, risk-assessment, and risk reduction, before official registration for use (Handford et al., 2015; Fargnoli et al., 2019). Priority-setting is a first step in pesticide risk assessment using qualitative or semi-quantitative risk scoring to identify pesticides of concern without the considerable resources and time associated with full risk assessments (Baptista et al., 2012; Reist et al., 2012). This should be carried out at the start of any assessment to screen high risk pesticides and enable efficient allocation of resources for targeted risk-assessments and the implementation of monitoring programmes of high-risk pesticides (Chou et al., 2019; Vryzas et al., 2020).

Earlier efforts to develop risk ranking methods, such as the Treatment Frequency Index (Kudsk, 1989), were based on the quantity of pesticide applied relative to the acceptable dosage. Over the last thirty years, risk ranking has progressed using criteria such as mobility and persistence in the environment, ecotoxicological effects on non-target organisms (Alister and Kogan, 2006), toxic effects on the human population (Gunier et al., 2001; Cha et al., 2014; Choi et al., 2020), or a combination of these criteria (Sugeng et al., 2013; Dabrowski et al., 2014; Kudsk et al., 2018). While such methods may be considered useful, various limitations, such as a reliance on pesticide physio-chemical properties to assess mobility, the use of animal health indicators to represent human health risk and the exclusion of metabolites, reduce their effectiveness and reliability for ranking and comparing pesticide risk. This limits their ability to properly inform future risk assessments or pesticide monitoring programmes.

Understanding pesticide mobility is key in evaluating the likelihood of exposure to pesticides from drinking water. Detailed risk assessments methods and pesticide transport modeling tools used in pesticide registration recognise that site and climatic conditions, soil and hydrologic properties, and agricultural management have considerable effects on pesticide mobility (Sabatier et al., 2014; Bedmar et al., 2017); therefore, these parameters are included in such analysis (Young and Fry, 2014). Despite the recognised need to consider this relationship, existing pesticide prioritization and pesticide risk ranking tools tend to base mobility assessment solely on a pesticide's physio-chemical properties. Most studies use pesticide-specific properties such as half-life and soil adsorption coefficients (Valcke et al., 2005; Yazgan and Tanik, 2005; Sugeng et al., 2013); or physio-chemical based mobility indicators such as the Groundwater Ubiquity Score (GUS) as used by Dabrowski et al. (2014), and the SCI-GROW index as used by Kudsk et al. (2018). This study aims to improve on existing pesticide risk ranking tools by considering both pesticide properties and soil conditions using a more comprehensive mobility indicator, thus demonstrating that more realistic representations of pesticide mobility can be considered in easy-to-use risk screening tools.

The use of various toxicity indicators in literature to represent the human health risks posed by pesticide use presents another significant challenge in scoring pesticide risk. Two commonly used indicators are the reference doses, Lethal Dose (LD_{50}) and Acceptable Daily Intake (ADI), which are used by Alister and Kogan (2006) and Juraske et al. (2007), respectively. These reference doses are based on animal testing and are extrapolated to describe the levels of acceptable exposure to humans. However, neither indicator describes the type of health effect or its severity. An exceedance of the ADI cannot determine if the resulting effect is a minor or major health concern (Bos et al., 2009), and LD_{50} represents the dose that would be fatal to 50% of a population as opposed to providing information about the health effects resulting from pesticide exposure. This study will use an adapted method of ranking pesticide toxicity based on several risk scoring studies (Gunier et al., 2001; Valcke et al., 2005; Sugeng et al., 2013; Dabrowski et al., 2014). Like these studies, the toxicity potential will be scored based on evidence of chronic health effects in place of reference doses that can only suggest a potential harm to human health.

Pesticide risk is dependent on its toxicity and environmental fate, but its metabolites can also contribute to this risk. Once released into the environment, pesticides are liable to breakdown into transformation products known as metabolites (Sinclair et al., 2006), which may move into drinking water sources and expose consumers to both metabolites and their parent compounds. There are growing concerns surrounding metabolites (Hintze et al., 2020) as they tend to be more mobile and persistent, have been detected at higher concentrations (Sinclair et al., 2006; Kameya et al., 2012; Escher et al., 2020) and may be more toxic than parent compounds such as the metabolites of glyphosate, prothioconazole and triclopyr (Fenner et al., 2013; Matsushita et al., 2018). Regulation EC 1107/2009 requires that relevant metabolites be included in assessments of pesticides for registration in the EU (European Commission, 2009b) and as a result models used for pesticide registration and legislation in the EU consider metabolites (Boesten et al., 2014). However, no pesticide risk ranking tools could be identified by the authors that combine metabolite and pesticide risk. This study attempts to combine the direct risk associated with contamination of drinking water due to the use of a pesticide with the indirect risk due to the formation of metabolites in drinking water supplies. This will highlight how some pesticides that are considered “low-risk” may need to be prioritised due to their higher-risk metabolites (Labite and Cummins, 2012).

The aim of this study was to develop an easy-to-use risk screening tool, which builds on existing literature by (1) combining pesticide properties and soil characteristics to give a detailed evaluation of pesticide mobility, (2) assessing the health impacts of pesticides, focusing on evidence of chronic health effects in place of pesticide reference doses, and (3) including the risks associated with a pesticide's metabolites. This tool can then be implemented by pesticide users, farm advisors, and other stakeholders to screen high-risk pesticides at a local level or help catchment managers identify pesticides that may need more detailed assessments. The developed methodology was illustrated by applying it to a specific Irish case study.

2. Materials and methodology

2.1. General approach

The risk associated with pesticide use can be defined as a function of the likelihood of exposure and the consequence of this exposure (FAO, 2018). The framework of the risk ranking comprises of three main stages that (1) calculate the likelihood of exposure score, (2) calculate the consequence of exposure, and (3) incorporate metabolite data, with hazard scores calculated at the end of these steps (Fig. 1). Each stage involves gathering and scoring parameters. The parameters required for user implementation of the risk ranking scheme and sources for these data in the study's case study are provided in the Supplementary Information (SI) Table S1. The likelihood of exposure was evaluated for both groundwater and surface water by scoring the persistence and mobility of each pesticide. These scores were then combined to assess an overall likelihood of exposure score. Users can incorporate the percentage of drinking water drawn from the two different sources into this likelihood of exposure score using a ratio to reflect the local sources of drinking water. The consequence of exposure was calculated as the sum of the potential chronic health effect scores. The likelihood and consequence of exposure scores were then multiplied to calculate a hazard score. Finally, the quantity-weighted hazard was determined by expressing the hazard score as a function of the quantity of use for each pesticide in relation to the overall pesticide use over the period of investigation. This study also attempted to assess the risk from metabolites and consider how this affects their parent compound risk (Stage 3: Fig. 1). This method was applied to an Irish case study with two locations to assess pesticide risk at site-scale and national-scale using Irish quantity data.

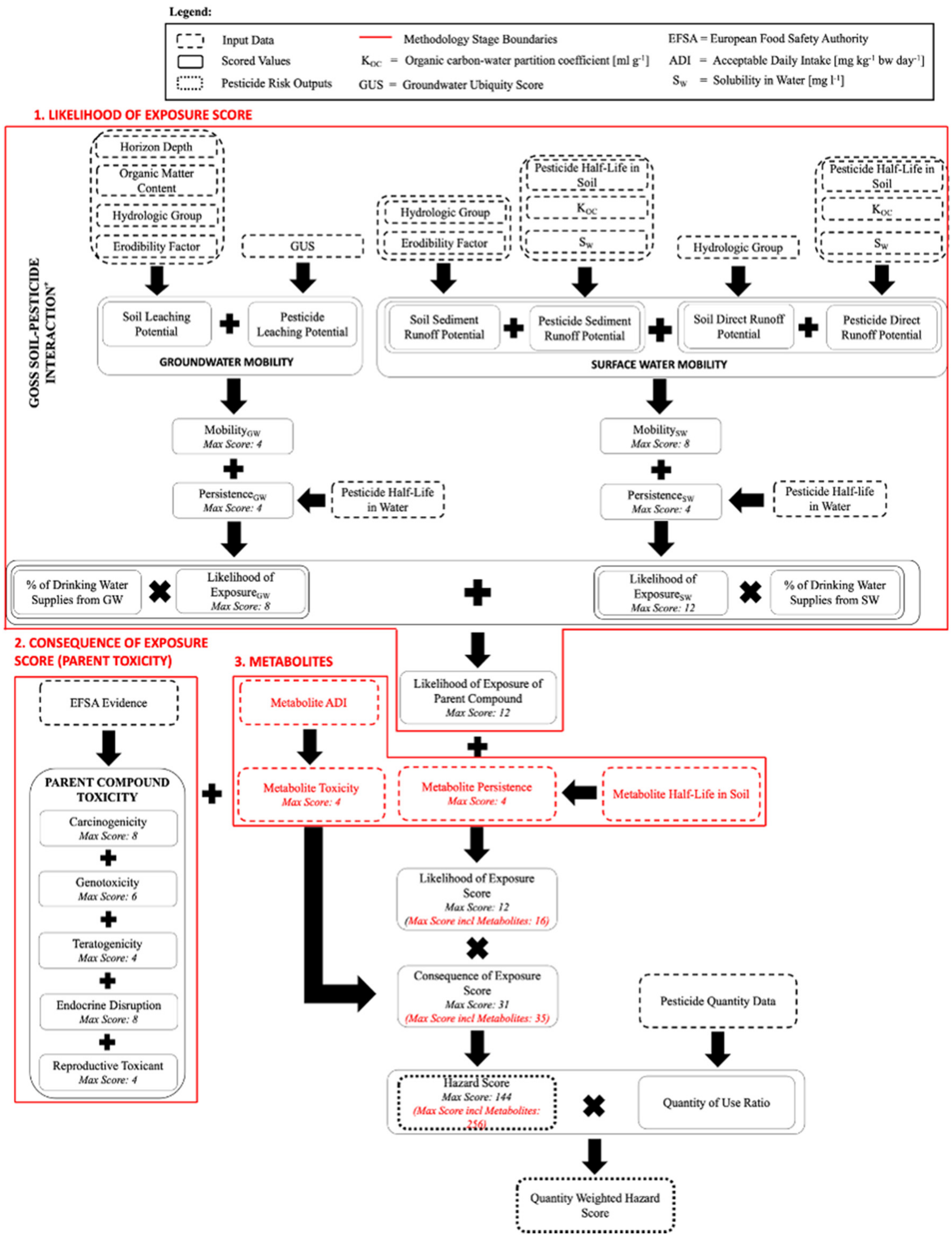


Fig. 1. Methodology framework showing the interaction between Likelihood of Exposure (Stage 1), Consequence of Exposure (Stage 2) and Metabolites (Stage 3). Maximum values given for parameters and risk scores in each stage are discussed in Sections 2.2, 2.3 and 2.4. *: Mobility indicator adapted from Goss (1992).

2.2. Likelihood of exposure

The first stage of the assessment shows how mobility in soil and persistence in water scores are combined to score the likelihood of exposure to water consumers (Stage 1: Fig. 1).

2.2.1. Mobility in soil

Mobility in soil is a key component of pesticide risk as it represents the potential for a pesticide to leave its application site and enter water sources, increasing exposure risk to consumers (Oliver et al., 2016). As both groundwater and surface water can be used for drinking water supplies, the mobility to both sources should be evaluated separately to fully understand the risk associated with pesticide mobility.

Several methods have been used in literature to predict the transport of pesticides (Gurdak, 2014; Perez Lucas et al., 2018; Akay Demir et al., 2019). The Goss method (Goss, 1992) was selected to assess the mobility of pesticides as it considers leaching to groundwater and runoff to surface water in a single indicator. It is relatively simple to use, and the data required to carry out assessment are easily accessible using online pesticide and soil databases or site-based soil tests. The scoring consists of (1) a soil rating for leaching and runoff based on soil characteristics (Table S2), and (2) a pesticide rating for leaching and runoff based on the pesticide parameters (Table S3), combined for a leaching and runoff score for each soil-pesticide interaction. The mobility potential of the soil and pesticide was qualitatively rated using soil properties, such as organic matter content and hydrologic group, etc. and pesticide properties such as half-life (Table 1). Soil-pesticide mobility matrices (Table 2) scored the leaching and runoff potential for each soil-pesticide interaction based on the ratings from Table 1 (Zhang et al., 1997). Separate mobility scores for groundwater ($Mobility_{GW}$) and surface water ($Mobility_{SW}$) were obtained from the combined soil-pesticide mobility matrices in Table 2 as shown in Stage 1 of Fig. 1 and Eqs. (1) and (2):

$$Mobility_{GW}\ Score = Leaching\ Score \tag{1}$$

$$Mobility_{SW}\ Score = Sediment\ Runoff\ Score + Direct\ Runoff\ Score \tag{2}$$

The Goss method used here to score pesticide mobility assesses mobility via leaching, direct runoff, and sediment-based runoff. It is important to note that sediment-sorbed pesticides may not be a priority exposure pathway for many consumers of treated surface water, and therefore readers are advised to consider the relevance of sediment runoff when assessing pesticide mobility.

2.2.2. Persistence in water

Consumers are more likely to be exposed to a persistent substance, allowing for a greater opportunity to cause toxic effects, thus making it a crucial factor in pesticide risk (Valcke et al., 2005). Pesticide persistence in soil and water affect potential for water contamination. Half-life in soil was considered in assessing mobility in soil (Section 2.2.1), so only aqueous persistence was considered herein. Pesticide persistence is influenced by the type of water body they contaminate due to the physical, chemical, and microbial conditions of the different environments. Therefore, pesticide persistence is assessed separately for groundwater and surface water.

Aqueous hydrolysis, the chemical degradation of a pesticide in water, was selected to assess persistence in surface water as it was considered to be the main degradation pathway based on literature (Sinclair et al., 2006; Yang et al., 2017). If a pesticide does not undergo hydrolytic degradation, the water-sediment half-life was used for persistence in surface water (Sinclair et al., 2006). Persistence in groundwater was determined using hydrolysis half-life only as this is considered to be the most relevant degradation process in groundwater (Sinclair et al., 2006; Yang et al., 2017). A nominal half-life of 30 days was used for groundwater persistence if the pesticide does not undergo hydrolytic degradation, as suggested by the European Food Safety Authority (EFSA, 2014). Data can be obtained from the EFSA (2021) or Pesticide Property Database (PPDB) (Lewis et al., 2016) in the case of missing EFSA data and were scored as shown in Table 3. In line with the approach commonly used in literature, a higher score was given in the case of missing data than was given for very low persistence, due to the uncertainty associated with missing data (Valcke et al., 2005; Dabrowski et al., 2014).

As is common practice in literature, the likelihood of exposure for groundwater (LES_{GW}) and surface water (LES_{SW}) was assessed by adding persistence in groundwater and surface water scores were added to their respective mobility scores (Fig. 1 and Eqs. (3) and (4)) (Whiteside et al., 2008; Choi et al., 2020).

$$LES_{GW} = Mobility_{GW} + Persistence_{GW} \tag{3}$$

$$LES_{SW} = Mobility_{SW} + Persistence_{SW} \tag{4}$$

The final likelihood of exposure was obtained by combining groundwater and surface water scores, for a maximum score of 12. The ratio of

Table 2
Soil-pesticide interaction matrix for leaching potential, sediment-phase runoff, and direct runoff.

	Pesticide leaching potential				
Soil leaching potential	Very low	Low	Moderate	High	Reference
Very low	1	1	2	2	Zhang et al., 1997
Low	1	2	2	3	
Moderate	2	2	3	4	
High	2	3	4	4	

	Pesticide sediment runoff potential			
Sediment runoff potential	Low	Moderate	High	Reference
Low	1	2	3	Zhang et al., 1997
Moderate	2	3	4	
High	3	4	4	

	Pesticide direct runoff potential			
Soil direct runoff potential	Low	Moderate	High	Reference
Low	1	2	3	Zhang et al., 1997
Moderate	2	3	4	
High	3	4	4	

Table 1
Goss' criteria for evaluating soil-pesticide mobility potential.

	Transport method	High	Low	Very low	Moderate	References
Soil	Leaching	HG A & OM $\times$ D $\leq$ 30 **OR** HG B & OM $\times$ D $\leq$ 9 & K $\leq$ 0.48 **OR** HG B & OM $\times$ D $\leq$ 15 & K $\leq$ 0.26	HG B & OM $\times$ D $\geq$ 35 & K $\geq$ 0.4 **OR** HG B & OM $\times$ D $\geq$ 45 & K $\geq$ 0.2 **OR** HG C & OM $\times$ D $\leq$ 10 & K $\geq$ 0.28 **OR** HG C & OM $\times$ D $\geq$ 10	HG D	Anything else	Adapted from Goss, 1992
	Runoff (sediment)	HG C & K $\geq$ 0.21 **OR** HG D & K $\geq$ 0.1	HG A **OR** HG B & K $\leq$ 0.1 **OR** HG C & K $\leq$ 0.07 **OR** HG D & K $\geq$ 0.05	–	Anything else	
	Runoff (direct)	HG C **OR** HG D	HG A	–	HG B	
Pesticide	Leaching	GUS > 2.8	0 < GUS < 1.8	GUS < 0	1.8 $\leq$ GUS $\leq$ 2.8	
	Runoff (sediment)	$DT_{50} \geq 40$ & $K_{OC} \geq 1000$ **OR** $DT_{50} \geq 40$ & $K_{OC} \geq 500$ & $S_W \leq 0.5$	$DT_{50} \leq 1$ **OR** $DT_{50} \leq 2$ & $K_{OC} \leq 500$ **OR** $DT_{50} \leq 4$ & $K_{OC} \leq 900$ & $S_w \geq 0.5$ **OR** $DT_{50} \leq 40$ & $K_{OC} \leq 500$ & $S_W \geq$ 0.5	–	Anything else	
	Runoff (direct)	$S_W \geq 1$ & $DT_{50} > 35$ & $K_{OC} < 100{,}000$ **OR** $S_W > 10$ & $DT_{50} < 100$ & $K_{OC} \leq 700$	$K_{OC} \geq 100{,}000$ **OR** $K_{OC} \geq 1000$ & $DT_{50} \leq 1$ **OR** $S_W < 0.5$ & $DT_{50} < 35$	–	Anything else	

HG = soil hydrologic group (USDA, 2009), K = soil K (erodibility) factor [(t ha h)/(ha MJ mm)] (Panagos et al., 2014), OM $\times$ D = soil organic matter content [%] $\times$ horizon 1 depth [cm], GUS = groundwater ubiquity score = $\log(DT_{50}) \times (4-\log(K_{OC}))$ (Gustafson, 1989), DT_{50} = pesticide half-life [days], K_{OC} = pesticide organic carbon adsorption coefficient [ml/g], S_w = pesticide solubility in water [mg/l].

Table 3
Pesticide persistence scoring system.

Half-life	Score	Reference
180 days ≤ DT_{50}	4	Yang et al., 2017
60 days ≤ DT_{50} < 180 days	3	
15 days ≤ DT_{50} < 60 days	2	
No data	1.5	
DT_{50} < 15 days	1	

drinking water from groundwater and surface water was considered to reflect the localised variability in drinking water sources (Eq. (5)). Therefore, users may calculate risk for drinking water contamination sourced from groundwater or surface water only or for both.

$$LES = (LES_{GW} \times \%Drinking\ Water_{GW}) + (LES_{SW} \times \%Drinking\ Water_{SW}) \quad (5)$$

2.3. Consequence of exposure

The consequence of exposure (Stage 2: Fig. 1) was assessed using methods from existing studies (Valcke et al., 2005; Sugeng et al., 2013; Dabrowski et al., 2014). This study builds on these methods by (1) assessing health effects prioritised in Regulation (EC) No. 1107/2009 (European Commission, 2009b), and (2) using EFSA data (EFSA, 2021) to score potential health effects.

In line with existing studies, the health effects were categorised as follows: "Probable", there is significant evidence that the pesticide causes the toxic effect in humans; "Possible" there is limited evidence from animal testing that the pesticide causes the toxic effect in humans; "No data", no studies have been carried out to confirm if the pesticide does or does not cause the toxic effect or the studies that exist are inconclusive; "No", there is definitive evidence that the pesticide does not cause the toxic effect in humans (Valcke et al., 2005; Sugeng et al., 2013; Dabrowski et al., 2014). These categories were then scored for each health effect (Table 4) based on the available evidence of pesticide toxicity (Table S5). Evidence was taken from the EFSA or, in the case of data gaps, from PPDB (Lewis et al., 2016). To account for uncertainty, "No data" was given a higher score than conclusive evidence of no effect ("None") as is done in literature (Gunier et al., 2001; Valcke et al., 2005). The scores were weighted with respect to the perceived severity of the health effect in accordance with the methods used by Valcke et al. (2005) and Dabrowski et al. (2014), therefore carcinogenicity and endocrine disruption were weighted higher than the other health effects.

Table 4
Scoring for chronic health effects.

Health effect	Category	Score	Reference
Carcinogenicity	Probable	8	Valcke et al., 2005
	Possible	6	
	No data	3	
	None	0	
Endocrine disruption	Probable	8	Dabrowski et al., 2014
	Possible	6	
	No data	3	
	None	0	
Genotoxicity	Probable	6	Valcke et al., 2005
	Possible	4	
	No data	2	
	None	0	
Teratogenicity	Probable	4	Valcke et al., 2005
	Possible	2	
	No data	1	
	None	0	
Reproductive toxicant	Probable	4	
	Possible	2	
	No data	1	
	None	0	

It is important to note that pesticides have the potential to cause health effects not included in the study such as cardiotoxicity (El-Nahhal and El-Nahhal, 2021b), respiratory disorders, hepatoxicity, immunotoxicity, etc. (Kalyabina et al., 2021). Pesticide can also be acutely toxic and the level of a pesticide's acute and chronic toxicity can be very different (Damalas and Koutroubas, 2016). Therefore, the acute toxicity classes of the pesticides examined in the case study are included (Table S7b) (WHO, 2019). However, due to the constraints of available toxicological data and the need to maintain a user-friendly risk screening tool, the existing study is limited to health effects that have been prioritised in existing pesticide health risk screening studies (Valcke et al., 2005; Alavanja and Bonner, 2012; Dabrowski et al., 2014) and legislation (European Commission, 2009b).

The final consequence of exposure score (CES) was calculated by summing the toxicity scores for the five chronic health effects to a maximum possible score of 30 (Stage 2: Fig. 1 and Eq. (6)). As some uncertainty is to be expected in the scores due to the exclusion of some potential health effects in this study, an additional score of one was included to avoid giving a pesticide with potentially harmful effects a risk score of zero, as is common practice in literature (Valcke et al., 2005; Dabrowski et al., 2014). Therefore, the final maximum score is 31:

$$CES = Carcinogenicity + Mutagenicity + Teratogenicity + Endocrine\ Disruption + Reproduction\ Toxicant + 1 \quad (6)$$

2.4. Metabolites

Metabolites have properties independent of their parent compounds and should be incorporated into the evaluation of pesticide risk (Labite and Cummins, 2012; Matsushita et al., 2018). Current pesticide risk ranking methods neglect to consider the contribution metabolites make and so this study attempts to address this gap. However, metabolites tend to be less researched than their parent compounds and existing literature is limited (Sinclair et al., 2006; Escher and Fenner, 2011; Zhou et al., 2019). A less detailed evaluation method using only metabolite toxicity and persistence data from EFSA reports or the PPDB (Lewis et al., 2016) was used in the current paper to assess key metabolites. Metabolite data were independently scored and incorporated into pesticide scores to assess combined pesticide-metabolite hazard scores (Stage 3: Fig. 1).

Metabolite toxicity was assessed using the ADI due to a lack of toxicology studies, or if unavailable, the ADI of the parent compound. This approach has been used in existing metabolite only studies, as it is conservatively assumed that the toxicity of the metabolite that have not been studied would be less or equally toxic as the pesticide (Sinclair et al., 2006; Labite and Cummins, 2012). Toxicity was scored based on ADI classifications from literature (Table 5) (Juraske et al., 2007; Chou et al., 2019).

The half-life in soil was used to represent persistence as it is the most researched degradation indicator for metabolites. If this was not available, a very conservative value of 300 days has been suggested by the European Commission (2002). Four classification levels were used to score the persistence of metabolites (Table 5), based on the categories suggested in literature (Valcke et al., 2005).

Metabolite scores were considered in a separate analysis to assess the effects metabolite data has on the overall risk ranking as shown in Fig. 1. The score awarded to the metabolite toxicity was included in the consequence of exposure score, for a maximum consequence of exposure score of 35 (Fig. 1 and Eq. (7)). The score given for the metabolite persistence was included in the likelihood of exposure score for a maximum score of 16 (Fig. 1 and Eq. (8)).

$$Consequence\ of\ Exposure_{MET} = Consequence\ of\ Exposure\ Score + Metabolite\ Toxicity \quad (7)$$

Table 5
Scoring system for key metabolite toxicity and persistence.

Criteria	Measure	Category	Score	Reference
Toxicity	ADI [mg kg^{-1} bw day^{-1}]	≤0.005	4	Juraske et al., 2007
		0.005 ≤ ADI < 0.01	3	
		0.01 ≤ ADI < 0.05	2	
		≥0.05	1	
		No data	1.5	
Persistence	$DT_{50,s}$ [days]	60 ≤ DT_{50}	4	Valcke et al., 2005
		30 ≤ DT_{50} < 60	3	
		15 ≤ DT_{50} < 30	2	
		DT_{50} < 15	1	
		No data	1.5	

$$Likelihood\ of\ Exposure_{MET} = Likelihood\ of\ Exposure\ Score + Metabolite\ Persistence \tag{8}$$

2.5. Hazard score and quantity-weighted hazard score

Hazard scores combine the likelihood of exposure with the effects of this exposure and can represent the relative risk of a pesticide compared to others used in the same area or for the same purpose. In line with methods used in literature, the hazard score is the product of consequence and likelihood of exposure scores (Sugeng et al., 2013; Dabrowski et al., 2014; Choi et al., 2020). However, these studies do not normalise the scores, resulting in the weighting of one parameter. In this study, the consequence of exposure was normalised so both scores contribute equally to the hazard score:

$$Hazard\ Score = \frac{12}{31} Consequence\ of\ Exposure\ Score\ x\ Likelihood\ of\ Exposure\ Score \tag{9}$$

The hazard score of a pesticide may be very high due to its high toxicity and/or exposure potential. Assessing a pesticide's hazard score may help pesticide users select less risky pesticides, specific to their site or purpose, prior to application. On a national or policy level, it is important to also consider the quantity of each pesticide used in a region or country to accurately capture contribution of that pesticide to the national risk profile. For instance, a very harmful pesticide (high hazard score) may be used in a given country in very small quantities, meaning its contribution to overall national pesticide health risk may be minimal. To address this need existing studies have combined consequence of exposure, likelihood of exposure, and a ratio for quantity of use in relation to quantity of overall pesticide use in a country or site to provide a quantity-weighted hazard score as follows (Valcke et al., 2005; Dabrowski et al., 2014):

$$Weighted\ Hazard\ Score = Hazard\ Score \times \frac{Quantity\ of\ Use}{Total\ Annual\ Pesticide\ Use} \tag{10}$$

The same method was used to calculate the risk for all pesticides with the metabolite scores included:

$$Hazard\ Score_{MET} = \frac{16}{35} Consequence\ of\ Expsoure\ Score_{MET} \times Likelihood\ of\ Exposure\ Score_{MET} \tag{11}$$

$$Weighted\ Hazard\ Score_{MET} = Hazard\ Score_{MET} \times \frac{Quantity\ of\ Use}{Total\ Annual\ Pesticide\ Use} \tag{12}$$

The pesticides may then be ranked based on their hazard score and their quantity-weighted hazard score. The pesticide with the highest score, and therefore the greatest perceived risk, was ranked 1.

3. Case study

3.1. Pesticide selection

An Irish case study was used to illustrate how the developed risk ranking method can be used to identify pesticides of concern on site-level and/or national-level. Table S1 shows the sources used the parameter data used in this case study. Irish pesticide usage data were obtained from the Pesticide Usage Reports published by the Irish Department of Agriculture, Food and the Marine (DAFM) for the most recently published years, 2016 and 2017 (DAFM, 2016, 2017). A total of 130 pesticides were used on grassland, fodder, and arable crops over this period. Based on common practice in literature, a minimal quantity of 1000 kg over the study period was selected as the exclusion point, as quantities below this point were subjectively considered too low to be of national importance (Valcke et al., 2005; Dabrowski et al., 2014). Seventy-three pesticides quantities exceeded 1000 kg between 2016 and 2017; however, ten have since been banned and are not included in the assessment. The method described in Section 2 was then applied to the remaining 63 pesticides to rank them by relative risk. Twelve of the sixty-three pesticides analysed do not have any key relevant metabolites according to the EFSA pesticide reports; therefore, only the scores of the remaining 51 pesticides are affected by the inclusion of metabolites.

3.2. Site selection

Pesticide hazard scores were calculated in two sites, selected from the Irish Teagasc Agricultural Catchment Programme (Teagasc, 2017): Cregduff in the west of Ireland (53°36′54.4″N 9°10′44.1″W), a predominately grassland site (92%) with well-draining, shallow brown earth soils on a karst landscape (Mellander et al., 2013); and Dunleer in the East (53°50′08.7″N 6°25′04.1″W), a mixed-use site of 44% grassland, 34% arable land and 22% woodland/other with poorly drained, mixed soils (McDonald et al., 2019). Site data were obtained from the EPA's Irish Soil Information System (EPA, 2021). As information regarding drinking water sources in these sites were unavailable, and to allow this case study to be used as a general guide for methodology implementation, it was nominally assumed that 50% of drinking water was drawn from groundwater and 50% drawn from surface water supplies.

4. Results and discussion

4.1. Quantity, likelihood of exposure and consequence of exposure

The likelihood and consequence of exposure of the 25 most used pesticides in Ireland in the two locations are presented in Figs. 2 and 3, where the size of the bubble is proportional to quantity. Three pesticides, glyphosate, chlormequat chloride and 2-methyl-4-chlorophenoxyacetic acid (MCPA), account for almost 35% of pesticide use in Ireland. If quantity of use was the only measure of risk, these pesticides would be the greatest concern for Ireland. However, as previously discussed, pesticide risk is influenced by the multiple factors such as mobility, persistence, and toxicity, as well as quantity. Therefore, several pesticides in Figs. 2 and 3 can be identified as pesticides of concern due to their high likelihood and/or consequence of exposure scores such as boscalid and mancozeb, despite being used in lower quantities.

In both catchments metamitron is located at the top of Figs. 2 and 3, with the highest likelihood of exposure (8.5 of a maximum of 12) due to its moderate-high runoff potential to surface waters and its very high persistence in both groundwater and surface water. Both prothioconazole and boscalid also have a likelihood of exposure score of 8.5 in Dunleer and a similarly high score of 8 in Cregduff. This suggests the drinking water sources in Cregduff and Dunleer are most likely to be impacted by these mobile and persistent pesticides. Based on Figs. 2 and 3, it can be seen that likelihood of exposure is marginally higher in Dunleer than in Cregduff. Dunleer consists mainly of poorly draining soils and experiences significant loss of pesticides due to surface runoff and a moderate risk for leaching and

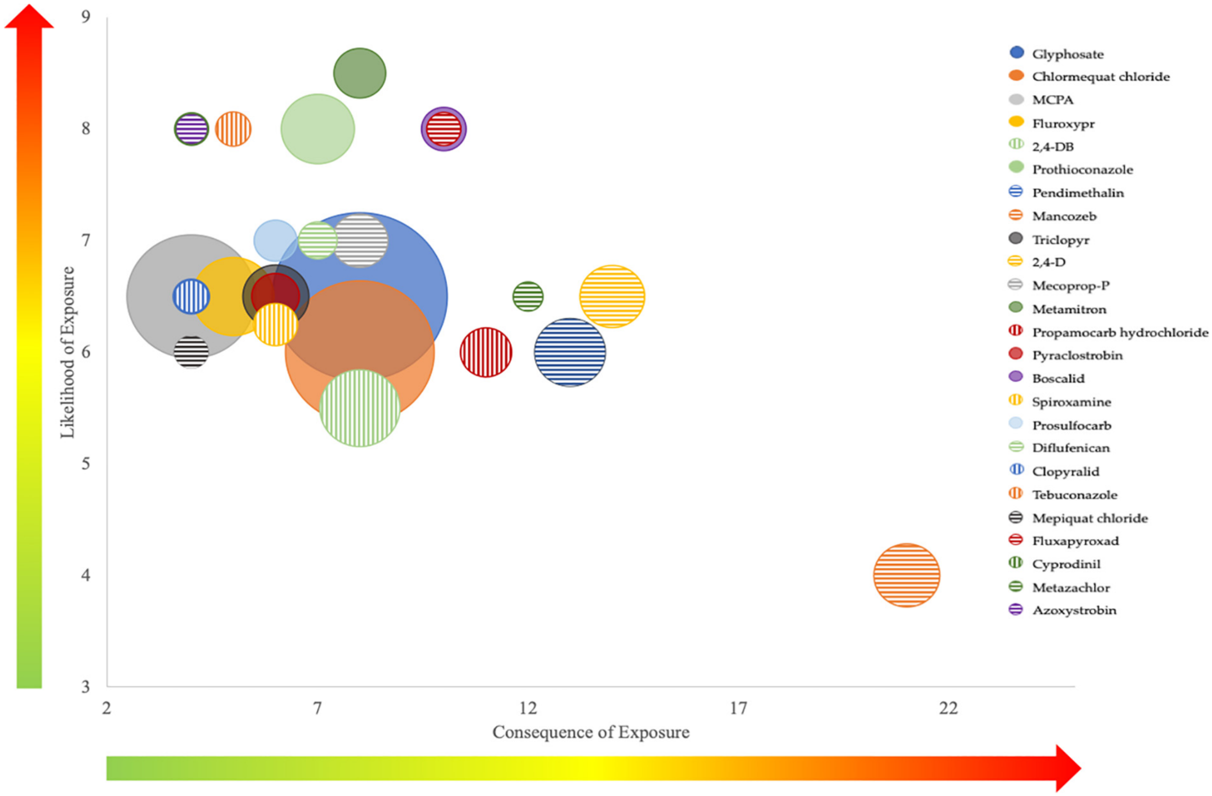


Fig. 2. Likelihood of exposure vs consequence of exposure vs quantity of use in Cregduff catchment for 25 most used pesticides in Ireland. *Area of bubble is proportional to the pesticide's quantity of use (kg).*

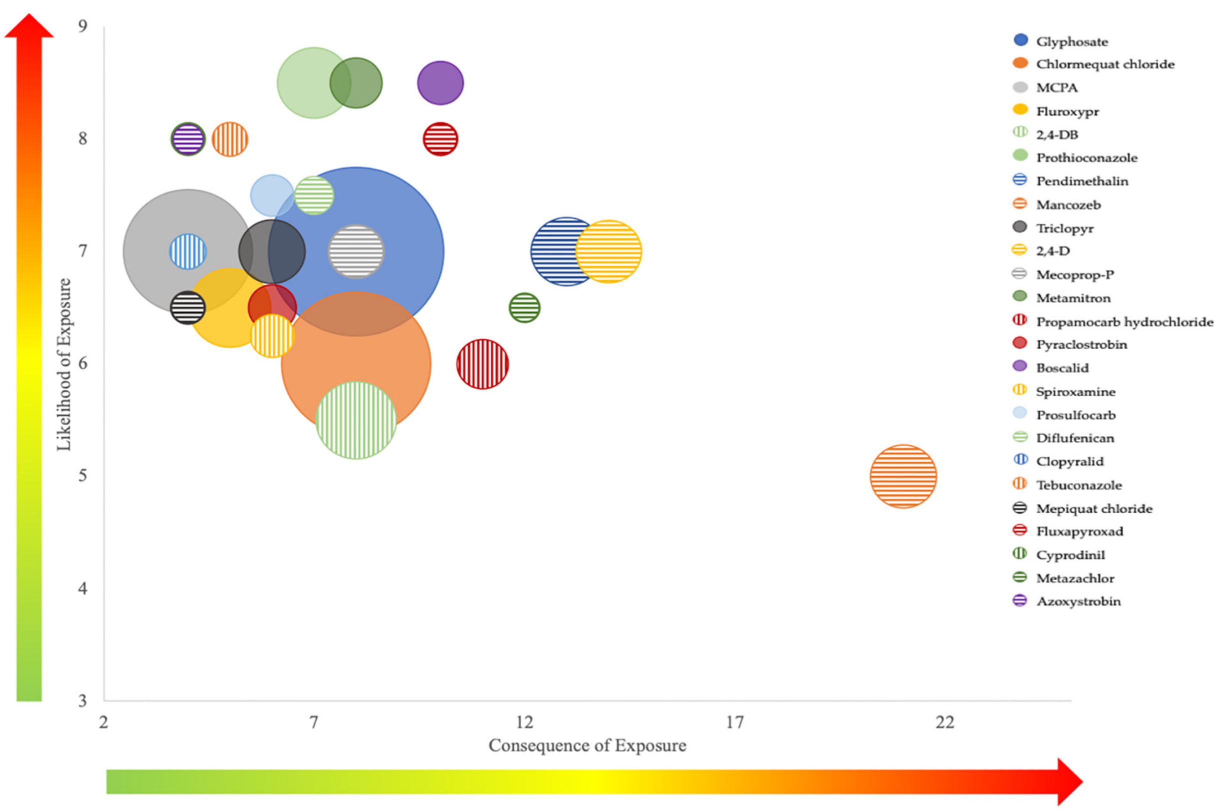


Fig. 3. Likelihood of exposure vs consequence of exposure vs quantity of use in Dunleer catchment for 25 most used pesticides in Ireland. *Area of bubble is proportional to the pesticide's quantity of use (kg).*

sediment runoff compared to low-moderate runoff potential in Cregduff (Table S2). These conditions result in higher pesticide mobility in Dunleer, hence a higher likelihood of exposure score. Therefore, the use of highly mobile pesticides can be considered a higher risk in a site like Dunleer, and a pesticide user may consider using a less mobile pesticide in locations that behave like Dunleer.

The consequence of exposure does not vary between the catchments as it is not dependent on location. Mancozeb is found on the far-right side of Figs. 2 and 3, suggesting a very high consequence of exposure score relative to the pesticides examined in this study. In assessing the consequence of exposure score, five toxicological endpoints from the EFSA were considered and identifying mancozeb as a probable or known carcinogen, teratogen, and endocrine disruptor, hence its high score (Table S6). Many pesticides have been identified as potential toxicants under one or more of the health outcomes examined in this study based on the EFSA reports (Table S6). A significant number of pesticides used in Ireland are potentially toxic to reproductive organs and foetal development, as there is evidence that 54% of pesticides used in Ireland have some kind of teratogenic effects and 24% have some impact on reproductivity.

This study demonstrates how pesticide risk cannot be determined using quantity alone. As illustrated by Figs. 2 and 3, the pesticides of greatest concern result from a combination of quantity, mobility, and toxicity. The hazard scores, calculated in Section 4.2, attempt to numerically represent how this combination varies between pesticides and to identify the pesticides of greatest concern in Irish site.

4.2. Hazard score and quantity-weighted hazard score

Fig. 4 shows the top 30 pesticides hazard scores in Cregduff and Dunleer, and the top 25 quantity-weighted hazard scores in an Irish context. Overall, prochloraz has the greatest hazard score with a score of 52.6 (out of a maximum of 144) in both catchments. Prochloraz's relatively high hazard score is due to the combination of its moderately high consequence of exposure score of 17 (of a maximum of 31) (Table S8), making it the second most toxic pesticide in this study and its high likelihood of exposure score of 8 (out of a maximum of 12) (Table S8). Prochloraz is highly mobile and is extremely persistent in surface water with a half-life of 359 days. Propyzamide has a hazard score of 43.5 (Fig. 4), which is the second highest hazard score overall as it is as mobile as prochloraz but slightly less toxic and persistent (Table S8).

Based on hazard score alone, prochloraz and propyzamide are the pesticides of greatest concern in this study. However, several pesticides have relatively high hazard scores and are used in high quantities. These include mancozeb, 2,4-D and pendimethalin, which have the 3rd, 5th, and 9th highest hazard scores, respectively (Fig. 4). These pesticides are as toxic, if not more in the case of mancozeb, than prochloraz and propyzamide, but are less mobile or persistent (Table S8). However, due to their high hazard scores and large national quantities, these pesticides may require more in-depth risk analysis and monitoring. The hazard scores of the pesticides used the most in Ireland, glyphosate and chlormequat chloride, are ranked in the top half of pesticides examined in this study (23rd of 63 and 28th/30th of 63 respectively); however, their hazard scores are relatively lower than the top ranked pesticides, with glyphosate scoring 21.7 compared to prochloraz's 52.6 in Dunleer (Table S9). Therefore, from their hazard score alone, further assessments may not be required, but incorporation of quantity of usage results in a high quantity-weighted score (Fig. 4: inset), which would identify them as pesticides of concern for Irish drinking water.

As discussed previously, hazard scores are useful to compare the relative risk associated with pesticides at a site-level prior to application to select less risky pesticides. The quantity-weighted hazard score incorporates

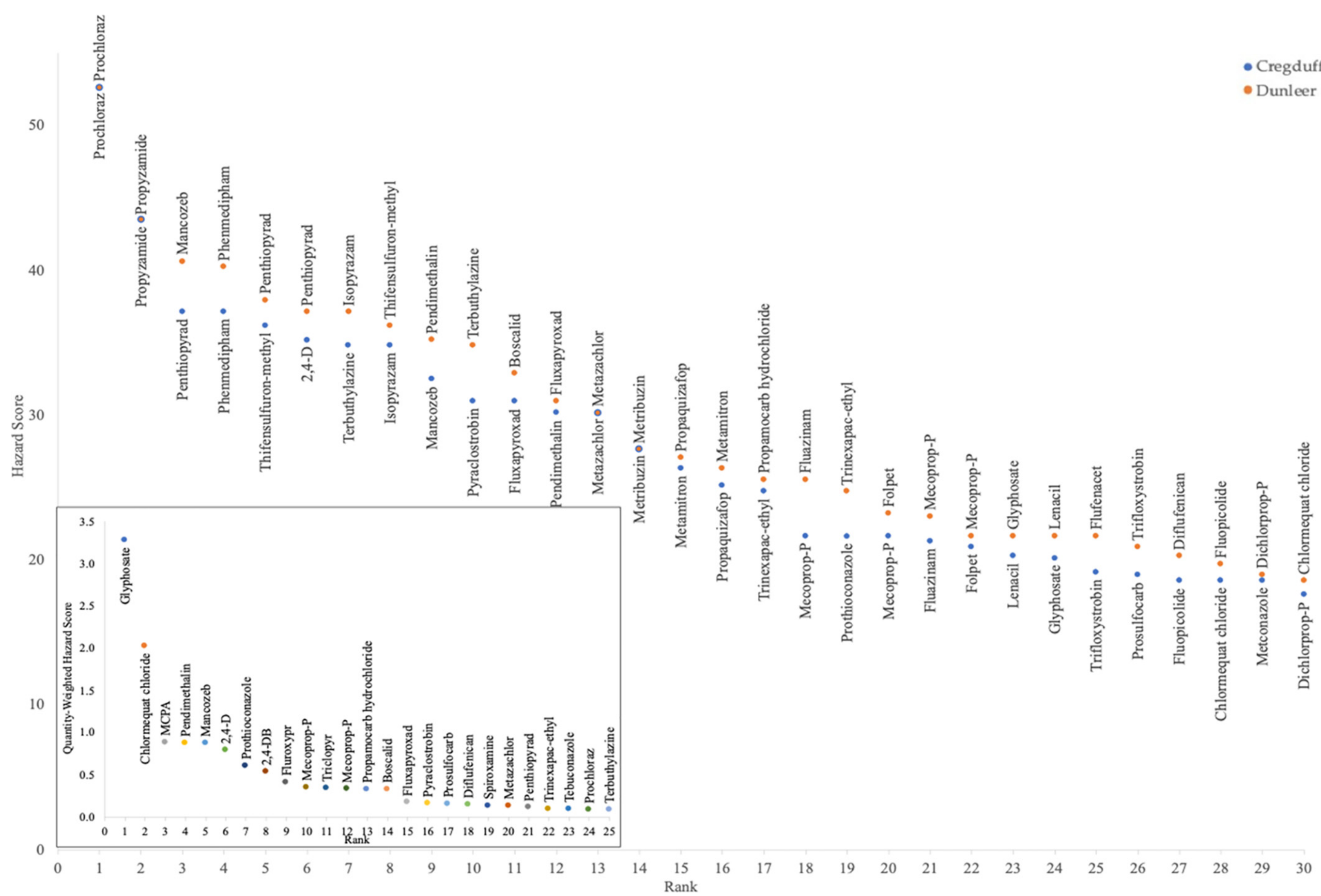


Fig. 4. Top 30 pesticides of concern in Cregduff vs. Dunleer; Top 25 pesticide quantity-weighted hazard score (inset).

pesticide quantity into the calculated hazard score and therefore better represents the regional or national risk-profile from actual pesticide use. The national quantity-weighted hazard scores of pesticides used in Ireland over the study period were calculated using Dunleer as a representative site for Ireland to give a better insight into the national risk profile associated with the various pesticides used on a national scale. This mixed grassland/arable site with mixed soils was selected as it was regarded to be more typical of sites across Ireland. The inset in Fig. 4 shows the top 25 quantity-weighted hazard scores for pesticides used in Ireland.

It is evident that quantity of use has a strong influence on the hazard score as the most used pesticides in Ireland, glyphosate and chlormequat chloride, are the highest ranked pesticides (Fig. 4). The third most used pesticide over the study period MCPA, is ranked 55 of 63 for consequence of exposure (Table S8) and has the 10th lowest hazard score (Table S9). However, it has the third highest quantity-weighted hazard score due to the influence quantity has on the quantity-weighted hazard score. Conversely, prochloraz, is used in relatively low quantities (43rd out of the 63 pesticides) but is ranked second based on toxicity and has the highest hazard score (Tables S8 and S9). Even though prochloraz is used in relatively small quantities (0.2% of total pesticide use; (DAFM, 2016, 2017)), its moderately high quantity-weighted score ranks 24th. Hence highly toxic pesticides should not be discounted as a pesticide of concern, even if used in small quantities, and should be monitored closely to ensure they are not used in quantities that may increase this risk. Pendimethalin and mancozeb can be identified as the pesticides of greatest concern of the 63 examined in this study, as they score highly in all criteria examined, except for likelihood of exposure, and are 4th and 5th highest ranked pesticide respectively based on quantity-weighted hazard score, despite making up only 2% each of overall pesticide use. In the time since this analysis began, approval for mancozeb use in the EU has been withdrawn with a ban on mancozeb use coming into effect at the beginning of 2022 (European Commission, 2020). The upcoming ban on mancozeb confirms the findings of this study, that mancozeb poses a significant risk to Irish drinking water and further monitoring, detailed assessment, or, in this case, a ban is required.

4.3. Metabolites

When metabolite data are included in the assessment, pesticides with key metabolites have increased risk scores. Some do not significantly change such as 2,4-D, as its metabolite is neither toxic nor persistent. Other pesticides experience a notable increase in either their likelihood of exposure score, consequence of exposure score or both, such as boscalid which has a very persistent metabolite, resulting in almost a doubling of its likelihood of exposure and triclopyr which has a very persistent and moderately toxic metabolite (Table S10). What is of most interest is the relative change in these scores and their rankings. Table S10 details the hazard and quantity-weighted scores of pesticides when metabolite data are included and shows how the ranking change when metabolites are considered. Parent compounds that were classified as high concern such as mancozeb and 2,4-D become relatively lower concern when their non-persistent and non-toxic metabolites are considered, with their hazard score dropping from 3rd to 9th and 4th to 10th respectively (Table S10). Others that are not priority pesticides, such as tribenuron-methyl and triclopyr, have much higher ranked hazard scores when metabolites are included, increasing by 12 and 13 places higher respectively (Table S10). Regarding quantity-weighted hazard scores, both triclopyr and boscalid are ranked higher when metabolites are included but metamitron becomes a relatively lesser concern when its metabolite is considered in comparison to other pesticides with more harmful or persistent metabolites (Table S10).

4.4. Sensitivity study

4.4.1. Uncertainty in pesticide and soil data

A sensitivity study was carried out to evaluate how the variability and uncertainty related to pesticide and soil data can affect the output of the risk scoring tool. This was achieved by varying the value of several parameters in turn by a nominal value of 10%, while the values of the other parameters remained constant. The sensitivity study results are presented in Tables S11a, S11b and S12.

The variation in pesticide data (i.e., half-life in groundwater, surface water, and soil, K_{OC} and solubility) had an impact on pesticide mobility (Table S11a) and pesticide persistence, both impacting the hazard score (Table S11b). Due to the banded nature of the scoring used in this methodology, less than half of the pesticides experienced any change when the values for pesticide data were varied. However, any resulting changes to hazard score were notable, with some of the pesticides experiencing up to a 20% change in hazard scores. For example, a reduction in soil half-life resulted in trifloxystrobin's leaching potential to change from low to very low, while its runoff potential reduced from moderate to low (Table S11a), therefore the pesticide is far less mobile resulting in an 18.18% reduction in its hazard score (Table S11b). Both persistence and sorption are key factors in pesticide transport (Kumari and John, 2020) and therefore it is unsurprising that variation in this data would have a strong effect on pesticide risk scores. The variation of pesticide solubility had no impact on pesticide mobility or hazard scores, indicating variability associated with this parameter would not have significant impact on overall risk.

The sensitivity study also examined variability of soil data (i.e. horizon depth, soil organic matter (SOM), clay, sand and silt content) and found that SOM content was the only soil parameter to affect the pesticide mobility and the related hazard scores. A 10% reduction of SOM content led to the sediment runoff potential to change from “Low” to “Moderate”. This parameter is clearly an important source of uncertainty in this study as the majority of resulting pesticide hazard scores increased by 5% or more (Table S12). It is well established that pesticide sorption contributes significantly to pesticide transport as pesticides with high sorption potential tend to be less mobile (Motoki et al., 2014; Kumari and John, 2020) and that there is positive correlation between sorption and SOM content (López-Piñeiro et al., 2013; Dutta et al., 2015). This illustrates the importance of having relevant data, especially related to the organic contents of soil, for locations under assessment as variation in site data influences the results of the tool.

4.4.2. Uncertainty in the scoring system

Scoring systems, similar to that used herein, have been developed and widely used by several authors (Sugeng et al., 2013; Dabrowski et al., 2014; Choi et al., 2020). A contentious point in this scoring method, however, is how missing or inconclusive data are dealt with. It is common in literature to score missing data higher than no/low effects which can lead to the uncertain conservative scoring of non-harmful pesticides or the underestimation of harmful pesticides. As 44 of the pesticides in the case study have missing or inconclusive data for one or more toxicological endpoints, a sensitivity study was carried out to investigate the effects missing toxicology data has on the output of this tool. Missing data were analysed as follows: (1) given the mid-range score for the relevant toxicological effect and (2) scored zero. As expected, the results of this study, presented in Table S13, found that changing the “no data” score has a significant impact on the pesticide hazard scores and their risk ranking. For example, if missing data are assigned a score of zero, the ranking of fluxapyroxad decreases by five as it has missing/inconclusive data for one health concern. Conversely, if missing data are given a mid-range score, fluxapyroxad moves from the 12th highest scored to the 10th most hazardous pesticide in this study for the same reason. Thus, the sensitivity study emphasises the need to continue to develop our understanding of the toxicological effects of pesticides on humans on a global level to improve the understanding and evaluation of pesticide risk.

5. Conclusion

The relative risk of pesticides can be scored and ranked from highest to lowest concern using the method developed and presented in this study. The approach presented allows for the comparison of pesticides based on several criteria: quantity of use, environmental fate, toxicity, overall hazard, and quantity-weighted hazard. The current study has expanded on existing methods to include the effects site data have on pesticide mobility through the use of a more comprehensive mobility indicator and is one of the first pesticide screening tools to address the impact metabolites have on overall pesticide risk pesticide risk. This study emphasises the need for a greater understanding of how metabolites persist in the environment and how they may cause harmful effects on humans. A sensitivity study, carried out to examine the limitations of the methodology, highlights the influence that variability in pesticide data can have on pesticide risks scores and identifies a need for future work pesticide toxicology studies. A simple screening method was developed as the first stage of detailed pesticide risk assessments to identify the main pesticides of concern in a given area. In the context of Irish drinking water, on both a national scale and in two different sites, mancozeb, 2,4-D, pendimethalin and glyphosate are some of the pesticides of greatest concern based on their combined quantity of use, toxicity, and exposure potential. This suggests that monitoring programmes should be considered in areas where these pesticides are used, and detailed risk assessments of these pesticides may be required on a national-scale based on their quantity-weighted hazard scores. This method can easily be adapted by pesticide users to examine the pesticide risk specific to their sites, allowing for the comparison of the relative risk of pesticides they may use and the selection of less risky pesticides. This method also allows risk managers and governmental departments to examine how pesticides may contribute to the health risks of a population on a regional or national-scale using quantity-weighted hazard scores.

CRediT authorship contribution statement

We confirm that all authors listed have contributed significantly to the work presented in this paper.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

This project is funded under the Irish EPA Research Programme 2014-2020 (Project reference number 2019-HW-LS-3). The EPA Research Programme is a Government of Ireland initiative funded by the Department of Communications, Climate Action and Environment. It is administered by the Environmental Protection Agency, which has the statutory function of co-ordinating and promoting environmental research.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2022.154532.

References

Abreu-Villaça, Y., Levin, E.D., 2017. Developmental neurotoxicity of succeeding generations of insecticides. Environ. Int. 99, 55–77.

Akay Demir, A.E., Dilek, F.B., Yetis, U., 2019. A new screening index for pesticides leachability to groundwater. J. Environ. Manag. 231, 1193–1202.

Alavanja, M.C.R., Bonner, M.R., 2012. Occupational pesticide exposures and cancer risk: a review. J. Toxicol. Environ. Health Part B 15, 238–263.

Alister, C., Kogan, M., 2006. ERI: environmental risk index. A simple proposal to select agrochemicals for agricultural use. Crop Prot. 25, 202–211.

Baptista, F.M., Alban, L., Olsen, A.M., Petersen, J.V., Toft, N., 2012. Evaluation of the antibacterial residue surveillance programme in danish pigs using bayesian methods. Prev. Vet. Med. 106, 308–314.

Bedmar, F., Gimenez, D., Costa, J.L., Daniel, P.E., 2017. Persistence of acetochlor, atrazine, and S-metolachlor in surface and subsurface horizons of 2 typic argiudolls under notillage. Environ. Toxicol. Chem. 36, 3065–3073.

Boesten, J.J.T.I., Fischer, R., Gottesbüren, B., Hanze, K., Huber, A., Jarvis, T., Jones, R.L., M, K., Pokludová, M., Remy, B., Sweeney, P., Tiktak, A., Trevisan, M., Vanclooster, M., VAnderborght, J., 2014. Assessing potential for movement of active substances and their metabolites to groundwater in the EU. The Final Report of the Ground Water Work Group of FOCUS (Forum for the Co-ordination of Pesticide Fate Models and Their USe). Version 3.

Bos, P.M.J., Boon, P.E., Voet, H.V.D., Janer, G., Piersma, A.H., Brüschweiler, B.J., Nielsen, E., Slob, W., 2009. A semi-quantitative model for risk appreciation and risk weighing. Food Chem. Toxicol. 47, 2941–2950.

Carvalho, F.P., 2017. Pesticides, environment, and food safety. Food Energy Secur. 6, 48–60.

Cerda, R., Avelino, J., Gary, C., Tixier, P., Lechevallier, E., Allinne, C., 2017. Primary and secondary yield losses caused by pests and diseases: assessment and modeling in coffee. PLoS One 12 e0169133-e0169133.

Cha, E.S., Jeong, M., Lee, W.J., 2014. Agricultural pesticide usage and prioritization in South Korea. J. Agromed. 19, 281–293.

Choi, Y.-H., Kang, M.-S., Da-An, H., Chae, W.-R., Moon, K., 2020. Priority setting for Management of Hazardous Biocides in Korea using chemical ranking and scoring method. Int. J. Environ. Res. Public Health 17, 1970.

Chou, W.C., Tsai, W.R., Chang, H.H., Lu, S.Y., Lin, K.F., Lin, P., 2019. Prioritization of pesticides in crops with a semi-quantitative risk ranking method for Taiwan postmarket monitoring program. J. Food Drug Anal. 27, 347–354.

Dabrowski, J.M., Shadung, J.M., Wepener, V., 2014. Prioritizing agricultural pesticides used in South Africa based on their environmental mobility and potential human health effects. Environ. Int. 62, 31–40.

DAFM, 2016. (Department of Agriculture, Food and the Marine) Pesticide usage in Ireland - 2016 Arable survey report.Available at: https://www.pcs.agriculture.gov.ie/media/pesticides/content/sud/pesticidestatistics/ArableReport2016Final100620.pdf (accessed on 10 September 2021).

DAFM, 2017. (Department of Agriculture, Food and the Marine) Pesticide usage in Ireland - 2017 Grassland and fodder crop survey report.Available at: https://www.pcs.agriculture.gov.ie/media/pesticides/content/sud/pesticidestatistics/2GrasslandReport2017FinalVersion290520.pdf (accessed on: 10 September 2021).

Damalas, C.A., Koutroubas, S.D., 2016. Farmers' exposure to pesticides: toxicity types and ways of prevention. Toxics 4.

Dutta, A., Mandal, A., Manna, S., Singh, S.B., Berns, A.E., Singh, N., 2015. Effect of organic carbon chemistry on sorption of atrazine and metsulfuron-methyl as determined by 13C-NMR and IR spectroscopy. Environ. Monit. Assess. 187, 620.

EFSA, 2014. (European Food Safety Authority), Guidance on the Assessment of Exposure for Operators, Workers, Residents and Bystanders in Risk Assessment for Plant Protection Products, Parma, Italy.

EFSA, 2021. (European food safety Authority) pesticide peer review reports database.Available at: https://www.efsa.europa.eu/en/publications accessed on 17 September 2021.

El-Nahhal, I., El-Nahhal, Y., 2021a. Pesticide residues in drinking water, their potential risk to human health and removal options. J. Environ. Manag. 299, 113611.

El-Nahhal, Y., El-Nahhal, I., 2021b. Cardiotoxicity of some pesticides and their amelioration. Environ. Sci. Pollut. Res. 28, 44726–44754.

EPA, 2021. (Environmental Protection Agency) irish soil information system.Available at: http://gis.teagasc.ie/isis/map.php Accessed on 8/09/21.

Escher, B.I., Fenner, K., 2011. Recent advances in environmental risk assessment of transformation products. Environ. Sci. Technol. 45, 3835–3847.

Escher, B.I., Stapleton, H.M., Schymanski, E.L., 2020. Tracking complex mixtures of chemicals in our changing environment. Science 367, 388.

European Commission, 2002. Guidance Document on Aquatic Ecotoxicology in the Context of the Directive 91/414/EEC, Rev 4 (Final), Brussels, Belgium.

European Commission, 2009a. Directive 2009/128/EC of the European Parliament and the Council of 21 October 2009 establishing a framework for Community action to achieve the sustainable use of pesticides. https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=celex%3A32009L0128.

European Commission, 2009b. Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EC and 91/414/EEC. https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32009R1107.

European Commission, 2020. Commission implementing regulation (EU) 2020/2087 of 14 December 2020 concerning the non-renewal of the approval of the active substance mancozeb, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, amending the Annex to Commission Implementing Regulation (EU) No 540/2011. https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32020R2087&rid=6.

FAO, 2018. (Food and Agricultural Organisation of the United Nations) General guidance on bridging of risk assessments, version 4, FAO Pesticide Registration Toolkit. Available at: https://www.fao.org/fileadmin/user_upload/pesticide_toolkit/pdfs/regsitration_strategies/FAO_Bridging_of_pesticide_risk_assessments.v4.2018.English.pdf.

FAO, WHO, 2014. (Food and Agricultural Organisation of the United Nations and the World Health Organisation) The international code of conduct on pesticide management. Available at: https://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/Code/CODE_2014Sep_ENG.pdf Rome.

Fargnoli, M., Lombardi, M., Puri, D., Casorri, L., Masciarelli, E., Mandić-Rajčević, S., Colosio, C., 2019. The safe use of pesticides: a risk assessment procedure for the enhancement of Occupational Health and Safety (OHS) management. Int. J. Environ. Res. Public Health 16.

Fenner, K., Canonica, S., Wackett, L.P., Elsner, M., 2013. Evaluating pesticide degradation in the environment: blind spots and emerging opportunities. Science 341, 752–758.

Goss, D., 1992. Screening procedure for soils and pesticides for potential water quality impacts. Weed Technol. 6, 701–708.

Gunier, R.B., Harnly, M.E., Reynolds, P., Hertz, A., Von Behren, J., 2001. Agricultural pesticide use of California: pesticide prioritization, use densities, and population distributions for a childhood cancer study. Environ. Health Perspect. 109, 1071–1078.

Gurdak, J., 2014. Groundwater vulnerability. In: Eslamian, S. (Ed.), Handbook of Engineering Hydrology: Environmental Hydrology and Water Management. CRC Press, Taylor and Francis Group, Boca Raton, pp. 145–162.

Gustafson, D., 1989. Groundwater ubiquity score: a simple method for assessing pesticide leachability. Environ. Toxicol. Chem. 8, 339–357.

Handford, C.E., Elliott, C.T., Campbell, K., 2015. A review of the global pesticide legislation and the scale of challenge in reaching the global harmonization of food safety standards. Integr. Environ. Assess. Manag. 11, 525–536.

Hintze, S., Glauser, G., Hunkeler, D., 2020. Influence of surface water – groundwater interactions on the spatial distribution of pesticide metabolites in groundwater. Sci. Total Environ. 733, 139109.

Juraske, R., Antón, A., Castells, F., Huijbregts, M.A.J., 2007. PestScreen: a screening approach for scoring and ranking pesticides by their environmental and toxicological concern. Environ. Int. 33, 886–893.

Kalyabina, V.P., Esimbekova, E.N., Kopylova, K.V., Kratasyuk, V.A., 2021. Pesticides: formulants, distribution pathways and effects on human health – a review. Toxicol. Rep. 8, 1179–1192.

Kameya, T., Saito, M., Kondo, T., Toriumi, W., Fujie, K., Matsushita, T., Takanashi, H., 2012. Detection of fenitrothion and its degradation product 3-methyl-4-nitrophenol in water environment. J. Water Environ. Technol. 10, 427–436.

Kudsk, P., 1989. Experience With Reduced Herbicide Doses in Denmark and the Development of the Concept of Factor-adjusted Doses, pp. 545–554.

Kudsk, P., Jørgensen, L.N., Ørum, J.E., 2018. Pesticide load—a new Danish pesticide risk indicator with multiple applications. Land Use Policy 70, 384–393.

Kumari, D., John, S., 2020. Sorption capacity of pesticides on soil in a predominant apple cultivation area. Soil Sediment Contam. Int. J. 29, 107–119.

Labite, H., Cummins, E., 2012. A quantitative approach for ranking human health risks from pesticides in irish groundwater. Hum. Ecol. Risk Assess. Int. J. 18, 1156–1185.

Lewis, K.A., Tzilivakis, J., Warner, D., Green, A., 2016. PPDB footprint - an international database for pesticide risk assessment and management.Available at:Hum. Ecol. Risk Assess. Int. J. 22, 1050–1064 (accessed on: 1 October 2021) http://sitem.herts.ac.uk/aeru/ppdb/.

López-Piñeiro, A., Peña, D., Albarrán, A., Becerra, D., Sánchez-Llerena, J., 2013. Sorption, leaching and persistence of metribuzin in Mediterranean soils amended with olive mill waste of different degrees of organic matter maturity. J. Environ. Manag. 122, 76–84.

Matsushita, T., Morimoto, A., Kuriyama, T., Matsumoto, E., Matsui, Y., Shirasaki, N., Kondo, T., Takanashi, H., Kameya, T., 2018. Removals of pesticides and pesticide transformation products during drinking water treatment processes and their impact on mutagen formation potential after chlorination. Water Res. 138, 67–76.

McDonald, N.T., Wall, D.P., Mellander, P.E., Buckley, C., Shore, M., Shortle, G., Leach, S., Burgess, E., O'Connell, T., Jordan, P., 2019. Field scale phosphorus balances and legacy soil pressures in mixed-land use catchments. Agric. Ecosyst. Environ. 274, 14–23.

Mellander, P.-E., Jordan, P., Melland, A.R., Murphy, P.N.C., Wall, D.P., Mechan, S., Meehan, R., Kelly, C., Shine, O., Shortle, G., 2013. Quantification of phosphorus transport from a karstic agricultural watershed to emerging spring water. Environ. Sci. Technol. 47, 6111–6119.

Motoki, Y., Iwafune, T., Seike, N., Otani, T., Asano, M., 2014. Effects of organic carbon quality on the sorption behavior of pesticides in japanese soils. J. Pestic. Sci. 39, 105–114.

Oliver, D.P., Kookana, R.S., Anderson, J.S., Umali, B., 2016. Field evaluation of two risk indicators for predicting likelihood of pesticide transport to surface water from two orchards. Sci. Total Environ. 571, 819–825.

Panagos, P., Meusburger, K., Ballabio, C., Borrelli, P., Alewell, C., 2014. Soil erodibility in Europe: a high-resolution dataset based on LUCAS. Sci. Total Environ. 479–480, 189–200.

Parker, A.M., Lester, Y., Spangler, E.K., von Gunten, U., Linden, K.G., 2017. UV/H2O2 advanced oxidation for abatement of organophosphorous pesticides and the effects on various toxicity screening assays. Chemosphere 182, 477–482.

Perez Lucas, G., Vela, N., Aatik, A., Navarro, S., 2018. Environmental Risk of Groundwater Pollution by Pesticide Leaching Through the Soil Profile.

Reist, M., Jemmi, T., Stärk, K.D.C., 2012. Policy-driven development of cost-effective, risk-based surveillance strategies. Prev. Vet. Med. 105, 176–184.

Sabatier, P., Poulenard, J., Fangeta, B., Reyss, J.L., Develle, A.L., Wilhelm, B., Ployon, E., Pignol, C., Naffrechoux, E., Dorioz, J.M., Montuelle, B., Arnaud, F., 2014. Long-term relationships among pesticide applications, mobility, and soil erosion in a vineyard watershed. PNAS 111, 15647–15652.

Sinclair, C.J., Boxall, A.B.A., Parsons, S.A., Thomas, M.R., 2006. Prioritization of pesticide environmental transformation products in drinking water supplies. Environ. Sci. Technol. 40, 7283–7289.

Sugeng, A.J., Beamer, P.I., Lutz, E.A., Rosales, C.B., 2013. Hazard-ranking of agricultural pesticides for chronic health effects in Yuma County, Arizona. Sci. Total Environ. 463–464, 35–41.

Teagasc, 2017. Agricultural catchment programme.Available at: https://www.teagasc.ie/environment/water-quality/agricultural-catchments/catchments/ (accessed 4 October 2021).

USDA, 2009. (United States Department of Agriculture) Chapter 7:hydrologic soil groups.Available online:Part 630 Hydrology, National Engineering Handbook (accessed on 27 January 2021) https://directives.sc.egov.usda.gov/OpenNonWebContent.aspx?content=22526.wba.

Valcke, M., Chaverri, F., Monge, P., Bravo, V., Mergler, D., Partanen, T., Wesseling, C., 2005. Pesticide prioritization for a case-control study on childhood leukemia in Costa Rica: a simple stepwise approach. Environ. Res. 97, 335–347.

Vryzas, Z., Ramwell, C., Sans, C., 2020. Pesticide prioritization approaches and limitations in environmental monitoring studies: from Europe to Latin America and the Caribbean. Environ. Int. 143.

Wee, S.Y., Aris, A.Z., Yusoff, F.M., Praveena, S.M., 2019. Occurrence and risk assessment of multiclass endocrine disrupting compounds in an urban tropical river and a proposed risk management and monitoring framework. Sci. Total Environ. 671, 431–442.

Whiteside, M., Mineau, P., Morrison, C., Knopper, L.D., 2008. Comparison of a score-based approach with risk-based ranking of in-use agricultural pesticides in Canada to aquatic receptors. Integr. Environ. Assess. Manag. 4, 215–236.

WHO, 2019. (World Health Organisation) The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification.

Yang, Y., Lian, X.Y., Jiang, Y.H., Xi, B.D., He, X.S., 2017. Risk-based prioritization method for the classification of groundwater pesticide pollution from agricultural regions. Integr. Environ. Assess. Manag. 13, 1052–1059.

Yazgan, M.S., Tanik, A., 2005. A new approach for calculating the relative risk level of pesticides. Environ. Int. 31, 687–692.

Yin, S., Wei, J., Wei, Y., Jin, L., Wang, L., Zhang, X., Jia, X., Ren, A., 2020. Organochlorine pesticides exposure may disturb homocysteine metabolism in pregnant women. Sci. Total Environ. 708, 135146.

Young, D., Fry, M., 2014. PRZM5 A Model for Predicting Pesticide in Runoff, Erosion, and Leachate: User Manual.

Zhang, M., Geng, S.H.U., Ustin, S.L., Tanji, K.K., 1997. Pesticide occurrence in groundwater in Tulare county, California. Environ. Monit. Assess. 45, 101–127.

Zhou, S., Di Paolo, C., Wu, X., Shao, Y., Seiler, T.-B., Hollert, H., 2019. Optimization of screening-level risk assessment and priority selection of emerging pollutants – the case of pharmaceuticals in european surface waters. Environ. Int. 128, 1–10.