Science of the Total Environment 919 (2024) 170816

Contents lists available at ScienceDirect

Science of the Total Environment

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

Pesticide exposure in greenspaces: Comparing field measurement of dermal contamination with values predicted by registration models

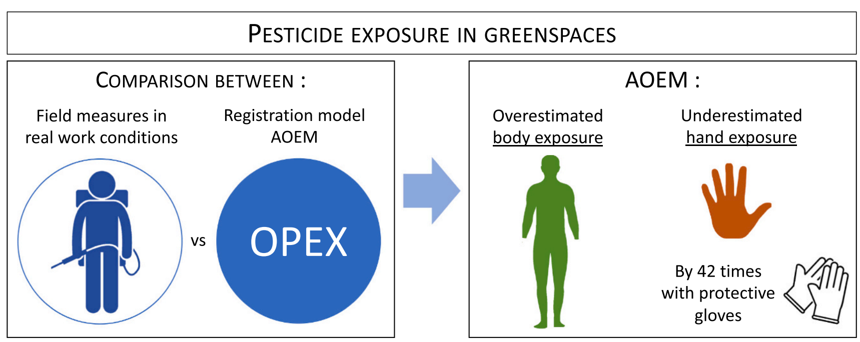
L. de Graaf [a,*], M. Bresson [b,c], M. Boulanger [b,c], M. Bureau [a], Y. Lecluse [b], P. Lebailly [b,c], I. Baldi [a,d]

[a] *Univ. Bordeaux, INSERM, BPH, U1219, F-33000 Bordeaux, France*
[b] *INSERM, UMR1086-Cancers et Préventions, Centre François Baclesse, Caen, France*
[c] *University Caen Normandie, Caen, France*
[d] *Service Santé Travail Environnement, CHU de Bordeaux, F-33000 Bordeaux, France*

HIGHLIGHTS

- The AOEM gave greater overall estimation of dermal exposure than field measures.
- The AOEM underestimates hand exposure, especially when protective gloves are worn.
- The AOEM would benefit from studies conducted in real work conditions in non-agricultural areas.
- Operator's exposure should be estimated with accuracy to ensure proper safety.

GRAPHICAL ABSTRACT



ARTICLE INFO

Editor: Yolanda Picó

Keywords:
Pesticides
Occupational exposure
Exposure model
Non-agricultural areas
Glyphosate

ABSTRACT

Since 2014, the Agricultural Operator Exposure Model (AOEM) has been the harmonised European model used for estimating non-dietary operator exposure to pesticide. It is based on studies conducted by the pesticide companies and it features 13 different crops including non-agricultural areas such as amenity grasslands. The objective of this study was to compare the dermal exposure measured during a field study conducted in a non-agricultural area with the corresponding values estimated by the model AOEM. The non-controlled field study was conducted in France in 2011 and included 24 private and public gardeners who apply glyphosate with knapsack sprayers. Dermal exposure was measured using the whole-body method and cotton gloves. Each measured value had an estimated value given by AOEM and we tested their correlation using linear regression.

The model overestimated body exposure for all observations and there was no correlation between values. However, it underestimated hand exposure by 42 times and it systematically underestimated the exposure when the operators were wearing gloves, especially during the application. The model failed at being conservative regarding hand exposure and highly overestimated the protection afforded by the gloves. At a time of glyphosate renewed approval in Europe, non-controlled field studies conducted by academics are needed to improve AOEM model, especially in the non-agricultural sector. Indeed, among the 34 studies included in the model, none were

* Corresponding author.
E-mail address: lucie.de-graaf@u-bordeaux.fr (L. de Graaf).

https://doi.org/10.1016/j.scitotenv.2024.170816
Received 16 November 2023; Received in revised form 2 February 2024; Accepted 6 February 2024
Available online 10 February 2024

conducted on a non-agricultural area and only four assessed the exposure when using a knapsack sprayer. Moreover, knapsack sprayers being the main equipment used worldwide in both agricultural and non-agricultural settings, it is also crucial to integrate new data specific to this equipment in the model. Operator exposure should be estimated with accuracy in the registration process of pesticides to ensure proper safety as well as in epidemiological studies to improve exposure assessment.

1. Introduction

After >60 years of intensive use, pesticides are posing many issues concerning human health and ecological impacts. To date, exposure to pesticides has mainly been studied in workers because their exposure is higher and easier to characterise than in the general population. Among workers, farmers have received much attention in epidemiological studies on the health impact of pesticides because of the increased risks they represent for chronic diseases such as cancer (including non-Hodgkin's lymphoma, multiple myeloma, prostate cancer, central nervous system tumours, …) (Perrotta et al., 2013; Lewis-Mikhael et al., 2016; Leon et al., 2019), neurological affections like Parkinson's disease (Gunnarsson and Bodin, 2019) and reproductive disorders (Fucic et al., 2021). Although most pesticides are used on crops and livestock, about 10 % are used for non-agricultural purposes (Kristoffersen et al., 2008). These include a wide variety of settings such as public and private greenspaces (gardens, parks, sports fields, campsites), public infrastructure (sidewalks, graveyards, buildings, and surrounding areas), transportation networks (roads, railways, airports) and industrial sites. Although few epidemiological studies have focused exclusively on greenspace workers working in non-agricultural areas, they have shown increased risks for lymphatic and haematopoietic cancer, skin melanoma, central nervous and testicular cancer (Swaen et al., 2004; Hansen et al., 2007; de Graaf et al., 2022a). A recent analysis in the Agrican cohort found a higher prevalence of allergic diseases and depression among greenspace workers and more cancers of the prostate, thyroid, testis and skin melanoma in men and breast cancer in women, in comparison with farmers (de Graaf et al., 2022b).

The most commonly used pesticides for non-agricultural purposes are herbicides (Atwood and Paisley-Jones, 2017). Herbicide sales for agriculture and non-agricultural areas worldwide have reached almost 1.4 million tons, which represents 68 % of all pesticide sales (FAO, 2021) Glyphosate, a non-selective herbicide, is the most widely sold herbicide (Benbrook, 2016). In Europe, it accounts for 33 % of total herbicide sales and it has been estimated that 10 % is used on non-agricultural areas (Suciu et al., 2023; Benbrook, 2016). Its use has drastically increased since the 1970s. For example, non-agricultural use in the US rose 43-fold from 1974 to 2014 (272,000 to 12 million kg of active ingredients sold). In recent years, concerns have increased about the potential health effects of glyphosate. Based on epidemiological and toxicological studies, the International Agency for Research on Cancer (IARC) has classified glyphosate active substance and glyphosate-based herbicides (GBHs) as 'probably carcinogenic to humans' (group 2 A) (International Agency for Research on Cancer, 2017). Workers' exposure to glyphosate has been associated with increased risks of non-Hodgkin's lymphoma and multiple myeloma (Leon et al., 2019; International Agency for Research on Cancer, 2017). However, other agencies such as the European Food Safety Authority (EFSA), in charge of pesticide pure active substance regulatory assessments at the EU levels, did not reach the same conclusion and considered the level of evidence was too limited to classify glyphosate as carcinogenic (EFSA et al., 2023). Unlike IARC, EFSA focused almost exclusively on dietary exposures to pure active substance glyphosate and discounted epidemiological and genotoxicity findings gleaned from studies of formulated GBHs. EFSA's stated reason for doing so is that the presence of coformulants in GHBs likely bias upward estimates of risks arising from dietary exposure to pure substance glyphosate (EFSA, 2015).

Since the 14th of June 2011, pesticide registration has been subject to European legislation (CE) n°1107/2009 (which abrogated the European directives 79/117 CE and 91/414 CE). This regulation applies for active ingredients, synergists, co-formulants and adjuvants. EFSA sets out the scientific framework that pesticide manufacturers must follow for submitting (and resubmitting) an active substance for market authorization. The registrants must provide a complete file presenting a risk assessment regarding human and animal health and the environment, and they must demonstrate that the active substance is safe in light of residues in food. In compliance with the Classification, Labelling and Packaging of Chemicals regulation (CE) n°1272/2008, manufacturers must provide '*clear communication to the users of the intrinsic toxicological potential to hazardous products'*. For each active substance approved, the conditions of applications such as the type of crop on which the active substance can be used, the period of application, the dose(s) and frequency of use, the formulation, etc., have to be specified and approved by Member States.

Operator exposure must be estimated in the formulation-specific risk assessment conducted by Member States. Exposure is predicted thanks to models developed in Europe since the 1990s: the UK Predictive Operator Exposure Model (UK POEM) (Hamey, 1992) and the German Operator Exposure Model (BBA German model) both in 1992, the EURopean Predictive Operator Exposure Model (EUROPOEM) in 2001 (Van Hemmen, 2001), and the Bystanders, Residents, Operators, and WorkerS Exposure models (BROWSE) in 2011 (Doan Ngoc et al., 2011). These models were created using data from a set of exposure studies. Different scenarios are defined according to the type of sprayer and the conditions of applications (environment, direction of the lance, etc.). They were initially designed for agricultural use but have also been used for the non-agricultural sector (Anses, 2012). However, in many cases, the data available in these models were not suitable for this sector.

In France, a task force led by the French agency for food, environmental and occupational health and safety (*Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail* (Anses)) has developed a new model, MODOP-ZNA, that includes five scenarios considered more relevant for non-agricultural uses such as applications with knapsacks/hand-held sprayers, in greenhouses or tunnels and applications on very high crops such as trees (Anses, 2012). The model is based on studies included in existing models such as UK POEM and BBA and on new original unpublished studies conducted by the French worker union for the protection of gardens and public greenspaces (*Union des entreprises pour la Protection des Jardins et des espaces publics,* UPJ).

In 2014, these different models were combined in the first harmonised European model: the Agricultural Operator Exposure Model (AOEM) (EFSA, 2014). This model aims at estimating non-dietary exposure to pesticides in operators (agricultural and non-agricultural workers involved in mixing/loading and spraying pesticides), workers (involved in re-entry tasks following a treatment), residents (anyone living, working, or going to an area adjacent to a treated area) and bystanders (individuals located within or directly adjacent to an area where pesticides have been applied). It features 13 types of crops including non-agricultural areas such as amenity grassland, railway tracks and ornamentals (flowers, trees, shrubs, etc.). The model includes data from 34 published and unpublished studies conducted between 1994 and 2009 by the pesticide companies and provided by the European Crop Protection Association (ECPA) (Großkopf et al., 2013). Only studies with the whole-body dosimetric method conducted under controlled conditions were used (EFSA et al., 2022). None of the 34 studies concerned observations on non-agricultural areas and the studies based on the French model MODOP-ZNA were not included in the European model. Even though exposure studies in the non-agricultural sector are scarce, some studies conducted by academic research teams provide relevant data that could have been incorporated in the model (Freeborg et al., 1985; Johnson et al., 2004; Delhomme et al., 2011; Connolly et al., 2019a). In contrast with studies included in the model, these academic studies were conducted in various non-agricultural settings (urban areas and public and private lawn), in usual work conditions and were using mainly the pad method. Moreover, the academic studies tried more to have various types of farms/cities/and not the biggest ones.

In line with the Pestexpo project, a series of studies begun in the 2000s in France to study farmers' exposure to pesticides under usual work conditions (Baldi et al., 2006, 2012, 2014; Lebailly et al., 2009; Bureau et al., 2022), an exposure study was conducted in 2011 in France among private and public gardeners spraying glyphosate with knapsack sprayers on non-agricultural areas (Boulanger et al., 2023). The objective of the present project was to compare the dermal exposure measured during the exposure study with the corresponding values estimated by the AOEM.

2. Materials and methods

2.1. Field study

2.1.1. Study population

The exposure study was conducted in Calvados (Normandy, France) between March and May 2011 and included 13 private gardeners/landscapers and 11 municipal workers. It is described in detail elsewhere (Boulanger et al., 2023). Briefly, dermal and respiratory exposure to glyphosate during mixing/loading and spraying with a knapsack sprayer was assessed under usual work conditions. All workers were men with a median age of 40 (range from 28 to 47 years old) and with previous experience in spraying pesticides and glyphosate (median experience was 14.5 years, ranging from 20 to 50). They all performed mixing/loading and application tasks and all commercial products used were suspension concentrates. Operators performed a median number of mixing/loading-application cycles of two (from 1 to 8). Treatments were done on hard ground such as cemeteries, sidewalks, roads, embarkments, courtyards and private or public turf.

2.1.2. Individual data collected

A trained field monitor (YL) observed the workers throughout the study and collected data on operators such as sociodemographic characteristics, previous use of glyphosate, years of experience in pesticide use, clothing and usual personal protective equipment (PPE), type of sprayer and age, volume of the tank, type of surface treated, weather conditions, technical problems, etc. Pictures and movies were taken in order to complete data retrospectively.

2.1.3. Pesticide sampling

Dermal exposure was assessed using the whole-body method described by the Organization for Economic Co-operation and Development (OECD) in the Guidance Document for the Conduct of Studies of Occupational Exposure to Pesticides During Agricultural Application (OCDE, 1997). Respiratory exposure was also assessed but for this study, we focused only on dermal exposure as it is the main route of exposure for operators (Adamis et al., 1985; Bonsall, 1985). With the whole-body method, actual exposure (amount of pesticide in contact with the uncovered skin, including the fraction that passes through protective and work clothing) and potential exposure (amount of pesticide in contact with protective equipment, work clothing, and uncovered skin) were assessed. Actual exposure was determined using pre-washed cotton undergarments (long pants and long-sleeve T-shirt) and cotton gloves. The undergarments were worn throughout the day and were removed from the workers at the end of the observation, while cotton gloves were changed between each phase. Pants and T-shirts were analysed separately. Each dosimeter was stored separately to avoid cross-contamination and glyphosate was extracted for its sampling medium and quantified. Total actual dermal exposure (hands plus body exposure) and body exposure were quantified for the whole workday, while hand exposure was also assessed separately at mixing/loading and at application. Potential exposure was measured with a pre-washed cotton coverall. Cotton undergarments and gloves were worn under PPE if used and changed between each phase. Therefore, mixing/loading and applications were assessed separately. However, because the AOEM estimates the actual dermal exposure of operators, we used only the actual measured exposure (undergarments and cotton gloves).

During the field study, a total of four field blank samples were taken. They have been exposed to field ambient conditions, in locations away from the treatment tasks. The field blank samples consisted in two cotton coveralls and two pairs of cotton gloves and they were analysed with the same methods than the field operator dosimeters. The concentrations measured on these samples were very low, attesting of low background contamination (0.02 μg of glyphosate for coveralls and < 0.1 μg for gloves).

2.2. Registration model: AOEM

The AOEM was used to determine the predicted exposure. Initially developed by EFSA as an excel sheet, it has been available online since 2022 (https://r4eu.efsa.europa.eu/app/opex). The data needed for the calculation are the following: i) name of the active substance, brand name and formulation (wettable/soluble powder, wettable/soluble granules, soluble/emulsifiable concentrate or non-soluble granules/fine granules); ii) product category (herbicide or other); iii) concentration of active substance in the product (g/L or g/kg); iv) Acceptable Operator Exposure Level – AOEL (*maximum amount of active substance to which the operator may be exposed without causing any adverse health effects*); v) type of crop treated (13 crops available); vi) maximum rate of products applied (kg/ha or L/ha); vii) scenario application (outdoor or indoor); viii) spraying method (downward or upwards); ix) spraying equipment (sprayers towed by a vehicle, manual hand-held sprayers or knapsack sprayers) and the minimum and maximum volume of water (in litres); and x) type of cultivation (normal or dense).

The parameters entered in the model are summarised in Table 1. For this study, we selected 'amenity grassland and managed amenity turf' as crops. It includes *'semi-natural or planted grassland such as golf course roughs, frequently mown areas, grass grown for turf production, public parks, sports turf, golf greens, tees and fairways'* (EFSA et al., 2022). For this type of 'crop', only the outdoor application scenario, downward spraying and the 'normal' type of cultivation (as opposed to not dense cultivation) can be selected. Knapsack sprayers were selected. The surface treated cannot be changed in the calculator and it was set at 1 ha/day when using a knapsack sprayer on amenity grassland. For operators, exposure duration is set at 8 h by the model. All treatments were done with glyphosate (herbicide) in suspension concentrate (soluble/emulsifiable concentrate) with different commercial products and therefore different concentrations of active substance. We set the AOEL at 0.03 mg/kg of body weight (bw)/day, as proposed for glyphosate in the renewal assessment report filed with EFSA (European Commission, 2021). This value does not influence the results for dermal calculation, but it is required by the calculator to complete the estimation, as the conclusion of the calculation is expressed in % of the AOEL. To calculate the actual dermal exposure and not the absorbed dose, we set the dermal absorption at 100 %. The maximum rate of formulation was calculated as the quantity of active substance applied per hectare divided by the concentration of active substance in the product. The calculator provides exposure levels according to the wearing of PPE for hands, body, head and inhalation for the day and for mixing/loading and application, separately. Three types of PPE are considered in the model: protective gloves, workwear and

Table 1
Parameters entered in AOEM spread.

	Data entered into model	
	Identical for all individuals	**Adjustable**
Name of active substance	Glyphosate	Concentration active substance in product
Formulation	Soluble/emulsifiable concentrate	
Product category	Herbicide	
AOEL	0.3 mg/kg bw/day	
Absorbed dose	100 %[a]	
Type of crop	Amenity grassland	
Scenario application	*Outdoor application*[b]	Maximum rate of product applied
Sprayed method	*Downward spraying*[b]	
Type of cultivation	*Normal*[b]	
Spraying equipment	Knapsack sprayer	Minimum and maximum volume of water
Surface treated	*1 ha*[c]	
	Data predefined by model for operators	
Duration of observation	8 h	
Standard body weight	60 kg	

[a] Set to 100 % to estimate total dermal exposure.
[b] Automatically selected for amenity grassland.
[c] and for knapsack sprayer.

masks (half- or full-face mask particle filters). Workwear consists of long-sleeved shirt and long trousers or coveralls (single layer of work clothing covering arms, body and legs). All exposure levels are expressed as μg/kg bw/day. They are then calculated for each worker by applying their respective body weight and converted into mg/day.

2.3. Statistical analyses

Exposure levels estimated by the AOEM and measured during the field study were expressed in mg/day. The distribution of these variables was non-normal according to the Shapiro-Wilk test, so they were described in terms of median, minimum, maximum and interquartile range. Other quantitative variables such as the concentration of active ingredients in commercial products, dose of products applied per hectare, etc., were also described in terms of median, minimum and maximum. Qualitative data were described in terms of frequency (%). Levels of total, body, and hand daily exposure as well as hand exposure at mixing/loading and at application were compared using the Wilcoxon test. To assess the correlation between measured and estimated exposure, we log-transformed the values and then ran linear regression analyses (*t*-test). Each measured value had an estimated AOEM value and each point of the scatterplot corresponded to one observation day. All statistical analyses were performed using R software (version 1.2.1578) (R Core Team, 2020).

3. Results

3.1. Data used for calculation

In total, 13 different commercial products were used by the workers, with a glyphosate concentration ranging from 240 g/L to 450 g/L (median 360 g/L). The median total amount of glyphosate handled was 180 g (32–720). The tank volume of the knapsack sprayers varied from 12 to 18 L (median 16 L). The median rate of products applied per hectare was 8.22 L/ha (2.50–11.11) and the median rate of active substance applied per hectare was 2.68 L/ha (0.90–5.00). The total duration of the treatment (mixing/loading and application) ranged from 110 to 360 min (median = 210 min). More than half of the workers used at least protective gloves during both phases (n = 15, 62.5 %). Regarding coveralls, 41.6 % and 50.0 % of workers wore them at mixing/loading and application, respectively. Nine subjects (37.5 %) did not use any PPE. In terms of clothing, we observed different scenarios. Most operators did not wear any extra layers of clothes (n = 13, 54.2 %). Five persons wore only a short- or long-sleeved shirt and/or sweater, one wore only trousers and five wore both shirt and trousers. Eight operators wore both a Tyvek® coverall and clothes and seven did not wear any.

3.2. Measured dermal exposure

Actual dermal exposure was estimated by summing the amount of pesticides deposited on the undergarments and the cotton gloves. Because undergarments were not changed between phases, total and actual body exposure could be assessed only for the whole day. However, hand exposure could be assessed for each phase as cotton gloves were changed between mixing/loading and application. Median total daily exposure was 4.57 mg/day of GLY (range from 0.16 to 60.8) and hands accounted for 83.8 % of the total actual exposure (median$n$ = 4.62 mg/day – range from 0.13 to 60.8). Hand exposure was slightly higher during mixing/loading compared to application (respectively 1.95 and 1.35 mg/day of GLY) (Fig. 2). Nevertheless, the difference between the two phases was great when considering the wearing of protective gloves: without gloves, hand exposure was almost seven times higher at mixing/loading than with application (respectively 11.50 and 1.66 mg/day of GLY).

We compared body exposure according to the number of layers of clothing the operators were wearing on the day of the observation (Fig. 1). Four scenarios were possible: i) no extra layer of clothing (n = 7); ii) additional clothing such as T-shirts or shirts and/or pants (n = 5); iii) additional Tyvek® coverall (n = 4) and iv) additional clothing and Tyvek® coverall (n = 8). Interestingly, the lowest levels of exposure were found for operators wearing no extra layer of clothing (median contamination = 0.21 (0.02–0.66) mg/day (p-value = 0.0006) (Wilcoxon test). We also compared overall daily exposure of operators who did not wear any PPE at all phases (N = 9) with operators using the most complete PPE for body and hands available (coveralls and gloves) (N = 7). The median overall daily exposure was respectively 17.21 mg/day of GLY (range from 1.02 to 60.8) and 2.63 mg/day of GLY (range from 0.16 to 43.32).

3.3. Predicted dermal exposure

Median overall daily exposure was estimated at 27.9 mg/day by the AOEM and ranged from 11.8 to 61.1 mg/day. It was higher than exposure measured in the field, but the two distributions overlapped (Fig. 1). The same applied for daily body exposure, which was estimated at 20 mg/day (range from 11.8 to 46.6). Median daily hand exposure was calculated by the AOEM at only 0.11 mg/day, which is 42 times less than in the field. Hands accounted for 26.2 % of total daily exposure in the model versus 83.8 % in the field. Measured and estimated hand exposures were systematically lower when operators wore protective gloves (Fig. 2). However, the protection afforded by the gloves differed between the AOEM and the field study, as well as between phases. When protective gloves were worn, hand exposure decreased by 99.7 % and 63.3 % during mixing/loading and by 93.8 % and 44.0 % during application, respectively, in the model and in the field study. The AOEM underestimated the exposure when protective gloves were used but the distributions overlapped except during application (Fig. 2).

3.4. Relationship between measured and predicted exposure

A positive correlation between measured and calculated exposure was found for overall daily exposure, (r = 0.43, p = 0.04) (Fig. 3). Two values were higher than the estimated value (n° 8 and 22). For body

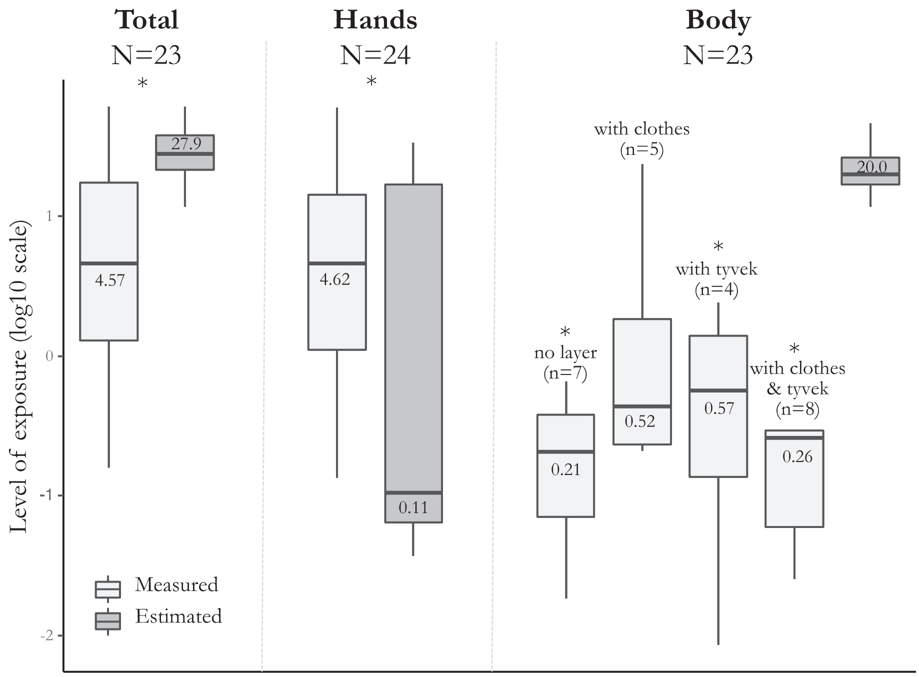


Fig. 1. Measured and estimated daily exposure in total (hands + body), hands only and body only according to number of layers worn by operators (mg/day). * *p*-value <0.05 (Wilcoxon test).

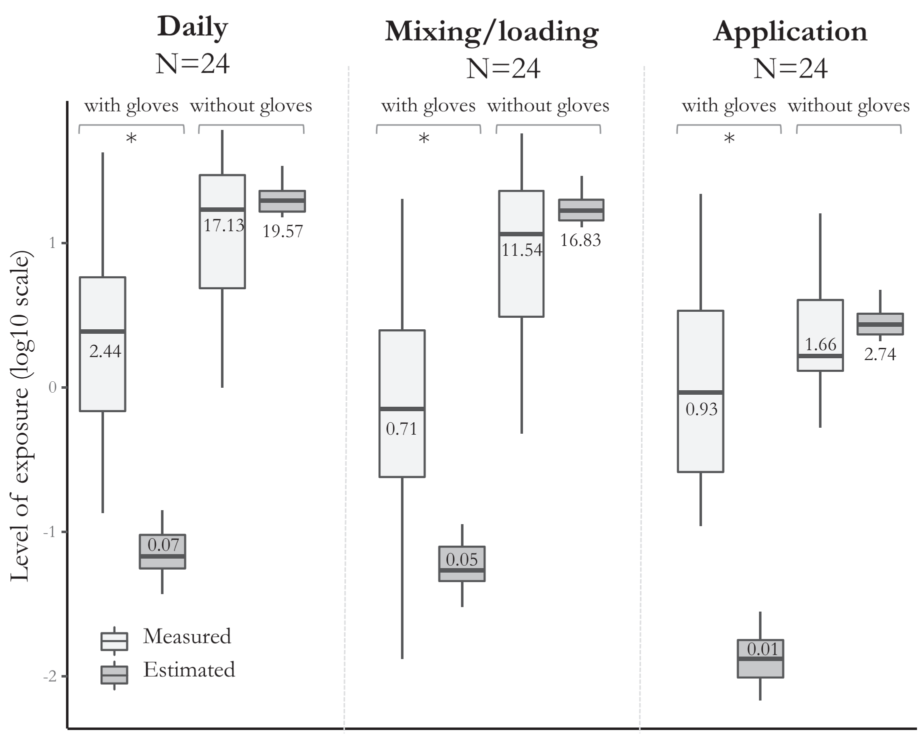


Fig. 2. Measured and estimated hand exposure (daily, at mixing/loading and at application) according to wearing of protective gloves (mg/day). * p-value <0.05 (Wilcoxon test).

exposure, all estimated values were higher than the measures. No correlation between the two was found ($p = 0.39$). ($r = 0.19$, p = 0.39).

Concerning hand exposure, values were distributed in two clouds corresponding to the wearing of gloves: low values when hands were protected and vice-versa. When gloves were worn, measured values were systematically above estimated values (Fig. 4). Measured and estimated values were weakly correlated for daily exposure ($R = 0.45$, $p = 0.03$) and for mixing/loading ($R = 0.48$, $p = 0.02$). No correlation was found for application exposure ($r = 0.11$, $p = 0.61$).

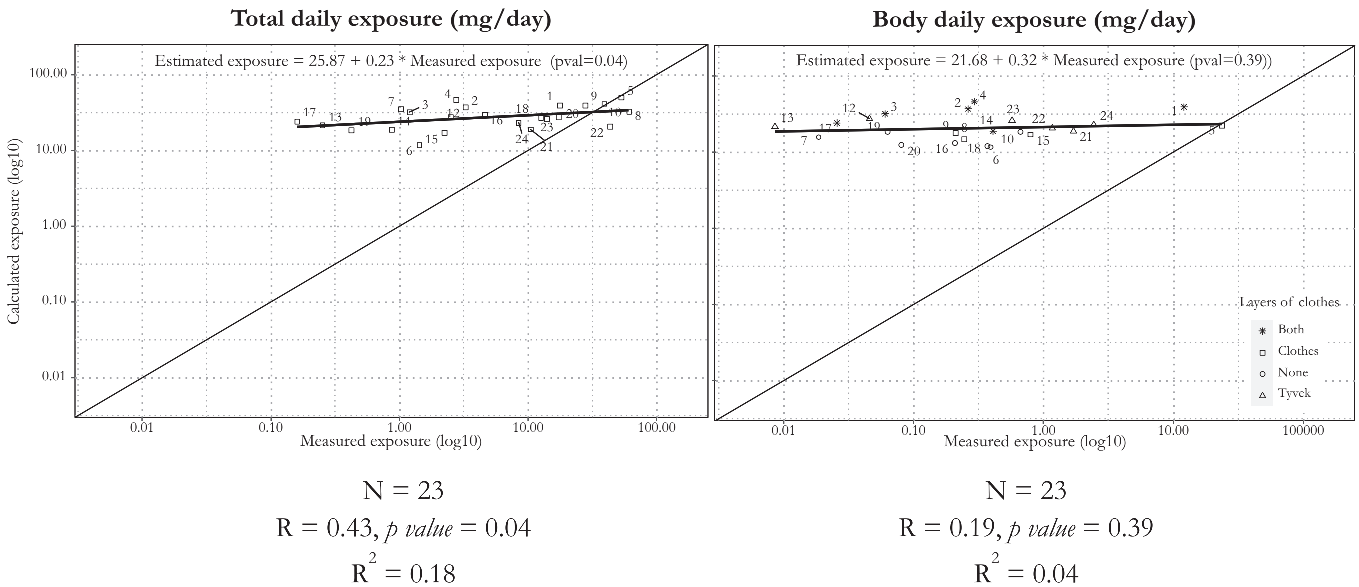


Fig. 3. Linear regression of total daily exposure and body daily exposure (mg/day) measured in field study and estimated in AOEM (n = 23). Each number corresponds to one observation.

4. Discussion

4.1. Main results

Total (body and hands) daily exposure was significantly higher with the AOEM estimation but measured and estimated exposures were not clearly correlated. Hand exposure was systematically underestimated by the AOEM, especially when the operator was wearing protective gloves. It seemed to overestimate the protection afforded by gloves. Body exposure was higher with the model than in the field study and there was no correlation between measured and estimated exposure. Nevertheless, the two distributions overlapped.

4.2. Limitations and strengths

Our field study has some limitations. First, a selection bias cannot be ruled out as participation was voluntary. Even if the communes (French administrative units) were selected after stratification on their size and all the private gardening companies were contacted, subjects were included only if they volunteered. Volunteers may have better work conditions and may be more engaged in prevention, so their exposure levels may have been lower than in the target population. Second, all operators included were all experienced and were not representative of newer applicators or seasonal workers. They may have had better knowledge of safety issues, maintenance of spraying equipment and PPE. However, experienced applicators did not necessarily have lower exposure, as they may have developed bad habits or a certain degree of acceptance of the risk (Salameh et al., 2004). Third, the small number of operators may have led to a lack of variability for some characteristics. For instance, we had different types and combinations of work clothes, yet it was not possible to take this parameter into account in the analyses. Fourth, the presence of a field monitor helps to measure exposure more accurately, but it can also induce changes in an operator's behaviour such as safer work practice and stricter compliance with wearing PPE, thereby leading to lower exposure. However, despite the presence of the monitor, some operators did not wear any PPE. Unlike the studies included in the AOEM, which were carried out in compliance with the principle of 'good agricultural practice' (*see infra*), all observations in this field study were kept in order to be representative of routine work conditions.

With a relative low vapour pressure, the glyphosate is not prompt to volatilise from treated surface, but its presence in the environment is more likely due to the drifting of droplets from spraying. Exposure can therefore occur at distance from where it is sprayed and background exposure cannot be ruled out in our field study. Thus, field blank samples have been taken. In comparison with the median overall body contamination measured (5256 μg of glyphosate), field blank samples had a negligible amount of glyphosate.

To follow EFSA guidelines on the assessment of the exposure of operators to pesticides (Großkopf et al., 2013), actual dermal exposure was measured using the whole-body method. Studies using the pad method were excluded from the model, despite the fact that they are recommended by the OECD, as are those using the whole-body method. In the field study, undergarments could not be changed between phases and body exposure was measured for the entire working day. However, cotton gloves were changed between each phase and hand exposure was assessed separately at mixing/loading and application. The field study data indicate that nearly all the actual exposure came from hand contamination. The use of cotton gloves as dosimeter can overestimate exposure by retaining more pesticides in the fibres than skin (Fenske et al., 1999). Even though the whole-body method has the favour of the regulatory agencies, it can interfere with routine work practice regarding clothing and PPE. Cotton coveralls may be uncomfortable especially in warm conditions, so operators may tend not to wear their usual clothing and/or PPE. The pad method and the whole-body method were compared under standardised conditions and no difference in measured values was observed (Kasiotis et al., 2020).

Some characteristics chosen for the AOEM differed slightly from those of the field study. For example, 'amenity grassland' was taken to be a 'crop' because it was the closest match to the type of surface treated. The term includes lawns, public parks, and sports fields but not hard ground such as cemeteries, sidewalks, roads, and yards. However, 13 out of the 24 operators in the field study sprayed on this type of surface and their median contamination was lower than that of operators who sprayed on greenspaces (3.273 vs 7.180 μg/day of GLY). Nevertheless, the difference was not statistically significant, and it was not considered to be a determinant of exposure. In fact, the type of crop had no impact on the estimation of exposure. For knapsack sprayers, predicted exposure was the same, regardless of the type of crop. Indeed, the AOEM considers that operator exposure is the same, irrespective of applying pesticide on vegetables, ornamentals, or amenity grassland.

In the studies included in AOEM, the area treated with a knapsack

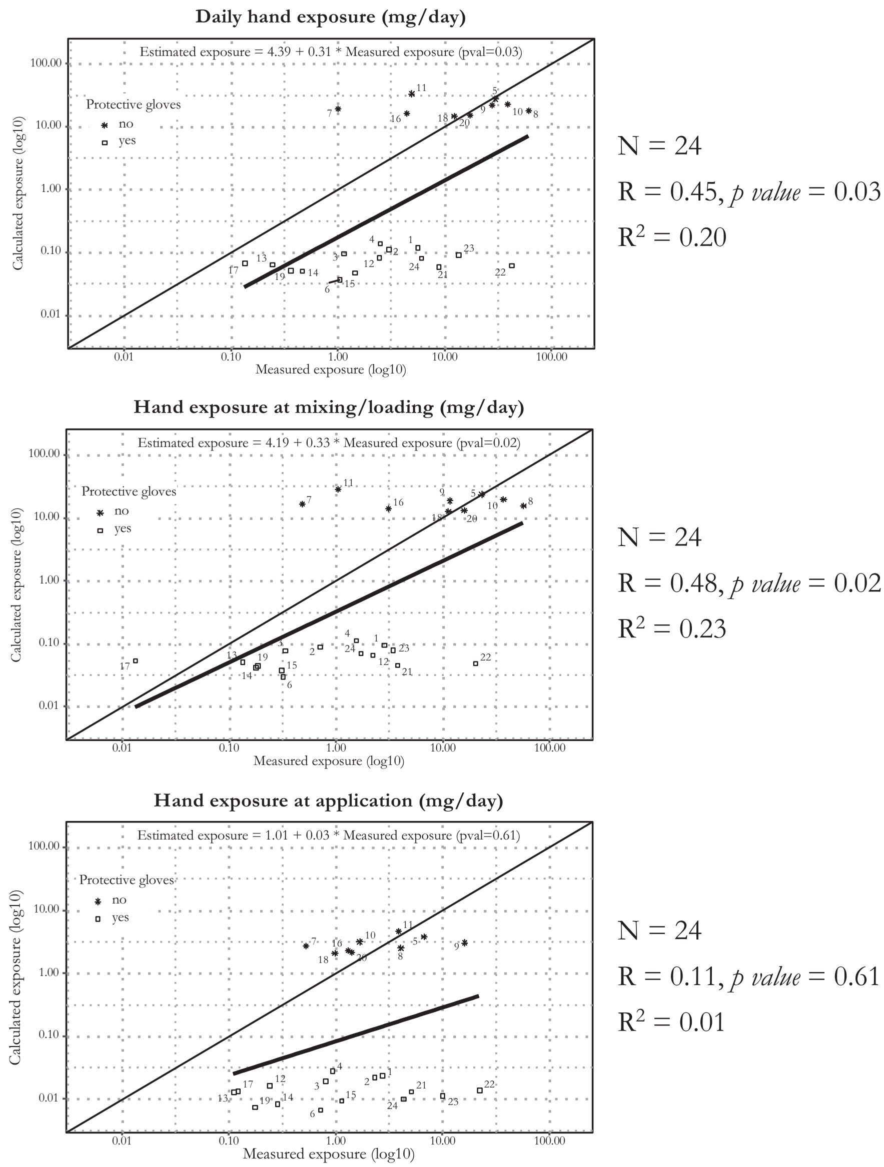


Fig. 4. Linear regression of hand exposure: daily, during mixing/loading and application (mg/day) measured in field study and estimated in AOEM (n = 24). Each number corresponds to one observation.

sprayer ranged from 0.4 to 1.1 ha and the default value was set at 1 ha (10,000 m^2). No studies conducted in non-agricultural areas were included in it (Großkopf et al., 2013), so the estimation of the surface treated is based only on agricultural settings and might not be relevant for amenity grassland. In the field study, this information was available for six operators, the surface ranging from 80 to 2000 m^2 (median = 350 m^2). The AOEM overestimated the surface treated with a knapsack sprayer on non-agricultural areas.

Another difference between the two methods concerns clothing and PPE. In the AOEM, ‘only long-sleeved-shirts or long trousers or coverall’ (single layer of work clothing covering arms, body and legs) were considered, as the studies on which it is based must follow ‘good agricultural practices’, i.e. operators ‘should at least wear workwear irrespective of the actual risk (EFSA et al., 2022). Importantly, coveralls are considered as workwear and not PPE, so it was not possible to differentiate workers who wore only workwear, only coveralls or both. The protection afforded by working clothing or uncertified cotton coveralls is estimated at 90 % in AOEM and at 95 % for protective coveralls. However, some studies have shown that coveralls might in fact increase the exposure because they absorb the product and retain it underneath the coverall (Hardt and Angerer, 2003; Garrigou et al., 2011; Berthet et al., 2014). Given the variety of working conditions and the diversity of active ingredients, formulations and commercial products, the penetration factor is very likely to vary.

4.3. External validity

Very few studies have been conducted with the same objective as ours. The study by Bresson et al. (2022) compared 30 operators’ dermal exposure during the treatment day in the apple-growing industry under real work conditions and using AOEM-predicted values. As in our observations, the AOEM overestimated overall exposure but not in all circumstances. Predicted values of daily and application exposure were higher than measured ones. However, the model underestimated exposure during mixing/loading and especially when protective gloves were worn. As in our study, the AOEM overestimated the protection afforded by gloves. Another study by Abukari (2015) compared predicted exposure using two models (UK-POEM and the German model) with measured results from biological monitoring studies from the open literature (Abukari, 2015). For high crops, predicted values (from both models) were lower than measured ones. For low crops, however, the models performed better with values closer to measured exposure. To ensure operator safety, the AOEM is supposed to be conservative and to overestimate exposure. However, as shown in these studies and ours, the values are not overestimated in all circumstances.

In contrast with the field study, studies included in the AOEM were not conducted under real work conditions, as operators had to follow 'good agricultural practice', i.e. '*practices that address environmental, economic and social sustainability for on–farm processes, and result in safe and quality food and non-food agricultural products*.' (FAO, 2003). This includes a set of behaviours and is considered mandatory in order to ensure the proper safety of workers. There is no official text that describes what 'good agricultural practice' actually is, but instead different guidelines or standards provided by various agencies. It is unclear what practices are considered valid for the model, although one can expect that they entail perfect conditions and proper observance of PPE and equipment. Moreover, observations with 'unusual operator activities' were excluded from the model (Bureau et al., 2022) which might be detached from real life exposure.

The 34 studies included in the AOEM were all conducted by pesticide companies, even though there is some academic data available on the non-agricultural sector. Indeed, we found five studies conducted in this sector (Freeborg et al., 1985; Cowell et al., 1991; Johnson et al., 2004; Delhomme et al., 2011; Connolly et al., 2019b). They were carried out between 1985 and 2019 with sample sizes varying from 4 to 33, making a total number of 84 observations. Four studies assessed dermal contamination using the pad method and one used wipe samples. Studies included in the model were not published and, therefore, unavailable. Only some summaries were accessible (Großkopf et al., 2013) but they provided very little information to fully understand the scope of the study, the exact methodology, the characteristics assessed and the results. There were no studies conducted in non-agricultural areas. In total, there were eight crops included (cereals, olives, citrus, pome, potatoes, sugar beets, grapevine and fallow land/stubble fields) but only four studies assessing the exposure when spraying downward with hand-held sprayers. These four studies involved herbicide treatment (azafenidin, simazine and fluazifop-p-butyl) on grapevines or stubble fields. They were all done with knapsack sprayers, so there was no other type of equipment available for downward treatment in the model. A total of 88 individual values (consisting of 48 mixer/loaders and 49 applicators vs 48 for our field study (24 mixer/loaders and 24 applicators) were incorporated in the model for low crop treatments with hand-held sprayers. Since the knapsack sprayer is the most widely used equipment in agricultural and non-agricultural areas worldwide (Matthews, 2008), the model might be too generic with only four studies involving knapsack sprayers, and it is not likely to capture the heterogeneity and complexity of exposure in various work environments.

On the November 28, 2023, the European Commission has adopted a renewal of the approval of glyphosate for ten years. In 2019, in accordance with the European legislation (CE) n°1107/2009, the *Glyphosate Renewal Group*, a group of eight companies applied for renewed approval. The document was sent to the rapporteur member states (France, Hungary, the Netherlands and Sweden), also known as the *Assessment Group on Glyphosate*, whose task is to produce the renewal assessment report and harmonised classification and labelling report to EFSA and the European Chemicals Agency (ECHA). Based on this report and on an analysis of the current literature, ECHA's committee for hazard assessment concluded that the current harmonised classification of GBH as non-carcinogenic should be retained. EFSA's peer review of the risk assessment '*did not identify any critical area of concern in relation to the risk glyphosate might pose to humans and animals and the environment*' (EFSA, 2023). However, several epidemiologic studies cited in the renewal approval report did highlight some significant associations between glyphosate exposure and some cancers such as NHL (McDuffie et al., 2001; Hardell et al., 2002; De Roos, 2003; Eriksson et al., 2008; Schinasi et al., 2016; Pahwa et al., 2019), multiple myeloma (De Roos et al., 2005) and acute myeloid leukaemia (Andreotti et al., 2018). In the *'Summary of product exposure and risk assessment'* section of the renewed approval report, exposure was predicted using the EFSA calculator. For treatment on invasive species in non-agricultural areas with manual knapsack sprayers, the model predicted a total systemic exposure of 0.003 mg/kg bw/day (without gloves), which is considered safe (9.4 % of AOEL). We tested the model using the same parameters as the one in the report and set the dermal absorption at 100 % in order to be representative of actual dermal exposure (exactly as in this study). Hand exposure with glove protection was still underestimated compared to the field study (0.03 vs 2.44 mg/day). If one considers a dermal absorption of 0.68 % (as suggested in the renewed approval report for glyphosate), this corresponds respectively to 0.01 % and 1 % of the AOEL. However, these Dose-Limiting Toxicity studies were done on pure substance and should be dismissed as they underestimated actual dermal absorption when formulated GBHs fall on skin.

The AOEM would certainly benefit from the addition of other data from field studies that have been conducted in agriculture and non-agricultural areas. Even if studies using the patch method to assess body exposure are not included in the model, one may wonder why data on hand exposure are not included. Indeed, regardless of the methodology used to assess body exposure, hand exposure is still quantified using cotton gloves or hand-washing. Data generated for hand exposure should be included in the AOEM in order to improve predictions.

5. Conclusion

The AOEM gave higher estimations than field measures. However, hand exposure was systematically underestimated when hands were protected by gloves, meaning that the model overestimates the protection that they afford. While the AOEM is a fast and cheap predictive tool compared to laboratory exposure assessment, it is based on a limited number of studies that were carried out exclusively under controlled conditions by the pesticide companies. No studies have been conducted in the non-agricultural area, even though there are some similarities with the agricultural sector regarding the way pesticides are used. Since the knapsack sprayer is the main equipment used in agriculture and non-agricultural areas, having only four studies with this type of equipment included in the model is insufficient. It therefore appears crucial to consider academic studies conducted in real work conditions and to modify the model so that it estimates operator exposure accurately.

CRediT authorship contribution statement

L. de Graaf: Conceptualization, Formal analysis, Methodology, Software, Writing – original draft, Writing – review & editing. **M. Bresson:** Conceptualization, Methodology, Validation. **M. Boulanger:** Data curation, Validation. **M. Bureau:** Validation. **Y. Lecluse:** Validation. **P. Lebailly:** Conceptualization, Methodology, Project administration, Supervision, Validation. **I. Baldi:** Conceptualization, Investigation, Methodology, Project administration, Supervision, Validation.

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.

Data availability

The data that has been used is confidential.

References

Abukari, W., 2015. Pesticides applicator exposure assessment: a comparison between modeling and actual measurement. J. Environ. Earth Sci. 5.

Adamis, Z., Antal, A., Füzesi, I., Molnár, J., Nagy, L., Susán, M., 1985. Occupational exposure to organophosphorus insecticides and synthetic pyrethroid. Int. Arch. Occup. Environ. Health 56, 299–305. https://doi.org/10.1007/BF00405271.
Andreotti, G., Koutros, S., Hofmann, J.N., Sandler, D.P., Lubin, J.H., Lynch, C.F., Lerro, C.C., De Roos, A.J., Parks, C.G., Alavanja, M.C., Silverman, D.T., Beane Freeman, L.E., 2018. Glyphosate use and cancer incidence in the agricultural health study. JNCI J. Natl. Cancer Inst. 110, 509–516. https://doi.org/10.1093/jnci/djx233.
Anses, 2012. Etudes et modèles pouvant être utilisés pour estimer l'exposition des opérateurs lors d'une utilisation d'un produit phytopharmaceutique en zones non agricoles. (Rapport d'expertise collective No. version 2).
Atwood, D., Paisley-Jones, C., 2017. Pesticides Industry Sales and Usage: 2008–2012 Market Estimates, 20460. US Environmental Protection Agency, Washington, DC.
Baldi, I., Lebailly, P., Jean, S., Rougetet, L., Dulaurent, S., Marquet, P., 2006. Pesticide contamination of workers in vineyards in France. J. Expo. Sci. Environ. Epidemiol. 16, 115–124. https://doi.org/10.1038/sj.jea.7500443.
Baldi, I., Lebailly, P., Rondeau, V., Bouchart, V., Blanc-Lapierre, A., Bouvier, G., Canal-Raffin, M., Garrigou, A., 2012. Levels and determinants of pesticide exposure in operators involved in treatment of vineyards: results of the PESTEXPO study. J. Expo. Sci. Environ. Epidemiol. 22, 593–600. https://doi.org/10.1038/jes.2012.82.
Baldi, I., Robert, C., Piantoni, F., Tual, S., Bouvier, G., Lebailly, P., Raherison, C., 2014. Agricultural exposure and asthma risk in the AGRICAN French cohort. Int. J. Hyg. Environ. Health 217, 435–442. https://doi.org/10.1016/j.ijheh.2013.08.006.
Benbrook, C.M., 2016. Trends in glyphosate herbicide use in the United States and globally. Environ. Sci. Eur. 28, 3. https://doi.org/10.1186/s12302-016-0070-0.
Berthet, A., Hopf, N.B., Miles, A., Spring, P., Charrière, N., Garrigou, A., Baldi, I., Vernez, D., 2014. Human skin in vitro permeation of bentazon and isoproturon formulations with or without protective clothing suit. Arch. Toxicol. 88, 77–88. https://doi.org/10.1007/s00204-013-1087-4.
Bonsall, J.L., 1985. Measurement of occupational exposure to pesticides. Taylor Francis, Occupational Hazards of Pesticide Use 13–33.
Boulanger, M., De Graaf, L., Pons, R., Bouchart, V., Bureau, M., Lecluse, Y., Meryet-Figuiere, M., Tual, S., Baldi, I., Lebailly, P., 2023. Herbicide exposure during occupational knapsack spraying in French gardeners and municipal workers. Ann. Work Expo. Health 67, 965–978. https://doi.org/10.1093/annweh/wxad045.
Bresson, M., Bureau, M., Le Goff, J., Lecluse, Y., Robelot, E., Delamare, J., Baldi, I., Lebailly, P., 2022. Pesticide Exposure in Fruit-Growers: Comparing Levels and Determinants Assessed under Usual Conditions of Work (CANEPA Study) with Those Predicted by Registration Process (Agricultural Operator Exposure Model). Int. J. Environ. Res. Public. Health 19, 4611. https://doi.org/10.3390/ijerph19084611.
Bureau, M., Béziat, B., Duporté, G., Bouchart, V., Lecluse, Y., Barron, E., Garrigou, A., Dévier, M.-H., Budzinski, H., Lebailly, P., Baldi, I., 2022. Pesticide exposure of workers in apple growing in France. Int. Arch. Occup. Environ. Health 95, 811–823. https://doi.org/10.1007/s00420-021-01810-y.
Connolly, A., Coggins, M.A., Galea, K.S., Jones, K., Kenny, L., McGowan, P., Basinas, I., 2019a. Evaluating glyphosate exposure routes and their contribution to Total body burden: a study among amenity horticulturalists. Ann. Work Expo. Health 63, 133–147. https://doi.org/10.1093/annweh/wxy104.
Connolly, A., Coggins, M.A., Galea, K.S., Jones, K., Kenny, L., McGowan, P., Basinas, I., 2019b. Evaluating glyphosate exposure routes and their contribution to Total body burden: a study among amenity horticulturalists. Ann. Work Expo. Health 63, 133–147. https://doi.org/10.1093/annweh/wxy104.
Cowell, J.E., Lottman, C.M., Manning, M.J., 1991. Assessment of lawn care worker exposure to dithiopyr. Arch. Environ. Contam. Toxicol. 21, 195–201. https://doi.org/10.1007/bf01055337.
De Roos, A.J., 2003. Integrative assessment of multiple pesticides as risk factors for non-Hodgkin's lymphoma among men. Occup. Environ. Med. 60, 11e–111. https://doi.org/10.1136/oem.60.9.e11.
De Roos, A.J., Blair, A., Rusiecki, J.A., Hoppin, J.A., Svec, M., Dosemeci, M., Sandler, D. P., Alavanja, M.C., 2005. Cancer incidence among glyphosate-exposed pesticide applicators in the agricultural health study. Environ. Health Perspect. 113, 49–54. https://doi.org/10.1289/ehp.7340.
Delhomme, O., Raeppel, C., Briand, O., Millet, M., 2011. Analytical method for assessing potential dermal exposure to pesticides of a non-agricultural occupationally exposed population. Anal. Bioanal. Chem. 399, 1325–1334. https://doi.org/10.1007/s00216-010-4434-9.
Doan Ngoc, K., Steurbaut, W., Spanoghe, P., 2011. Bystanders, residents, operators and workers exposure models for plant protection products (BROWSE). Communications Agric. Appl. Biol. Sci. 76, 960.
EFSA, 2014. Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. EFSA J. https://doi.org/10.2903/j.efsa.2014.3874.
EFSA, 2015. EFSA Explains the Carcinogenicity Assessment of Glyphosate.
EFSA, 2023. Peer Review Report on Glyphosate (AIR V).
EFSA, Charistou, A., Coja, T., Craig, P., Hamey, P., Martin, S., Sanvido, O., Chiusolo, A., Colas, M., Istace, F., 2022. Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment of plant protection products. EFSA J. 20 https://doi.org/10.2903/j.efsa.2022.7032.
EFSA, Álvarez, F., Arena, M., Auteri, D., Binaglia, M., Castoldi, A.F., Chiusolo, A., Crivellente, F., Egsmose, M., Fait, G., Ferilli, F., Gouliarmou, V., Nogareda, L.H., Ippolito, A., Istace, F., Jarrah, S., Kardassi, D., Kienzler, A., Lanzoni, A., Lava, R., Linguadoca, A., Lythgo, C., Mangas, I., Padovani, L., Panzarea, M., Parra Morte, J.M., Rizzuto, S., Romac, A., Rortais, A., Serafimova, R., Sharp, R., Szentes, C., Terron, A., Theobald, A., Tiramani, M., Vianello, G., Villamar-Bouza, L., 2023. Peer review of the pesticide risk assessment of the active substance glyphosate. EFSA J. 21 https://doi.org/10.2903/j.efsa.2023.8164.
Eriksson, M., Hardell, L., Carlberg, M., Åkerman, M., 2008. Pesticide exposure as risk factor for non-Hodgkin lymphoma including histopathological subgroup analysis. Int. J. Cancer 123, 1657–1663. https://doi.org/10.1002/ijc.23589.
European Commission, 2021. Combined draft renewal assessment report prepared according to regulation (EC) N°1107/2009 and proposal for harmonised classification and labelling (CLH report) accordign to regulation (EC) N°1272/2008. Glyphosate. (no. volume 1).
FAO, 2003. Development of a Framework for Good Agricultural Practices (No. Seventeenth Session). Commitee on Agriculture, Rome (Italy).
FAO, 2021. FAOSTAT. URL. https://www.fao.org/faostat/en/#data/RP. accessed 10.9.23.
Fenske, R.A., Simcox, N.J., Camp, J.E., Hines, C.J., 1999. Comparison of three methods for assessment of hand exposure to Azinphos-methyl (Guthion) during apple thinning. Appl. Occup. Environ. Hyg. 14, 618–623. https://doi.org/10.1080/104732299302422.
Freeborg, R.P., Daniel, W.H., Konopinski, V.J., 1985. Applicator exposure to pesticides applied to Turfgrass. ACS Symp. Ser. Dermal Exposure Related to Pesticide Use 273, 287–295.
Fucic, A., Duca, R.C., Galea, K.S., Maric, T., Garcia, K., Bloom, M.S., Andersen, H.R., Vena, J.E., 2021. Reproductive health risks associated with occupational and environmental exposure to pesticides. Int. J. Environ. Res. Public Health 18, 6576. https://doi.org/10.3390/ijerph18126576.
Garrigou, A., Baldi, I., Le Frious, P., Anselm, R., Vallier, M., 2011. Ergonomics contribution to chemical risks prevention: an ergotoxicological investigation of the effectiveness of coverall against plant pest risk in viticulture. Appl. Ergon. 42, 321–330. https://doi.org/10.1016/j.apergo.2010.08.001.
de Graaf, L., Boulanger, M., Bureau, M., Bouvier, G., Meryet-Figuiere, M., Tual, S., Lebailly, P., Baldi, I., 2022a. Occupational pesticide exposure, cancer and chronic neurological disorders: a systematic review of epidemiological studies in greenspace workers. Environ. Res. 203, 111822 https://doi.org/10.1016/j.envres.2021.111822.
de Graaf, L., Talibov, M., Boulanger, M., Bureau, M., Robelot, E., Lebailly, P., Baldi, I., 2022b. Health of greenspace workers: morbidity and mortality data from the AGRICAN cohort. Environ. Res. 212, 113375 https://doi.org/10.1016/j.envres.2022.113375.
Großkopf, C., Martin, S., Mielke, H., 2013. Joint development of a new agricultural operator exposure model. BFR (Wissenschaft).
Gunnarsson, L.-G., Bodin, L., 2019. Occupational exposures and neurodegenerative diseases—a systematic literature review and Meta-analyses. Int. J. Environ. Res. Public Health 16, 337. https://doi.org/10.3390/ijerph16030337.
Hamey, P., 1992. Predictive Operator Exposure Model (POEM): A user's Guide. MAFF Pestic. Saf, Div.
Hansen, E.S., Lander, F., Lauritsen, J.M., 2007. Time trends in cancer risk and pesticide exposure, a long-term follow-up of Danish gardeners. Scand. J. Work Environ. Health 33, 465–469. https://doi.org/10.5271/sjweh.1162.
Hardell, L., Eriksson, M., Nordström, M., 2002. Exposure to pesticides as risk factor for non-Hodgkin's lymphoma and hairy cell leukemia: pooled analysis of two Swedish case-control studies. Leuk. Lymphoma 43, 1043–1049. https://doi.org/10.1080/10428190290021560.
Hardt, J., Angerer, J., 2003. Biological monitoring of workers after the application of insecticidal pyrethroids. Int. Arch. Occup. Environ. Health 76, 492–498. https://doi.org/10.1007/s00420-003-0451-8.
International Agency for Research on Cancer, 2017. Some Organophosphate Insecticides and Herbicides. International Agency for Research on Cancer, Lyon.
Johnson, P.D., Rimmer, D.A., Garrod, A.N.I., Helps, J.E., Mawdsley, C., 2004. Operator exposure when applying amenity herbicides by all-terrain vehicles and controlled droplet applicators. Ann. Occup. Hyg. 49, 25–32. https://doi.org/10.1093/annhyg/meh073.
Kasiotis, K.M., Spaan, S., Tsakirakis, A.N., Franken, R., Chartzala, I., Anastasiadou, P., Machera, K., Rother, D., Roitzsch, M., Poppek, U., Lucadei, G., Baumgärtel, A., Schlüter, U., Gerritsen-Ebben, R.M., 2020. Comparison of measurement methods for dermal exposure to hazardous Chemicals at the Workplace: the SysDEA project. Ann. Work Expo. Health 64, 55–70. https://doi.org/10.1093/annweh/wxz085.
Kristoffersen, P., Rask, A.M., Grundy, A.C., Franzen, I., Kempenaar, C., Raisio, J., Schroeder, H., Spijker, J., Verschwele, A., Zarina, L., 2008. A review of pesticide policies and regulations for urban amenity areas in seven European countries. Weed Res. 48, 201–214. https://doi.org/10.1111/j.1365-3180.2008.00619.x.
Lebailly, P., Bouchard, V., Baldi, I., Lecluse, Y., Heutte, N., Gislard, A., Malas, J.-P., 2009. Exposure to pesticides in open-field farming in France. Ann. Occup. Hyg. 53, 69–81. https://doi.org/10.1093/annhyg/men072.
Leon, M.E., Schinasi, L.H., Lebailly, P., Beane Freeman, L.E., Nordby, K.-C., Ferro, G., Monnereau, A., Brouwer, M., Tual, S., Baldi, I., Kjaerheim, K., Hofmann, J.N., Kristensen, P., Koutros, S., Straif, K., Kromhout, H., Schüz, J., 2019. Pesticide use and risk of non-Hodgkin lymphoid malignancies in agricultural cohorts from France, Norway and the USA: a pooled analysis from the AGRICOH consortium. Int. J. Epidemiol. 48, 1519–1535. https://doi.org/10.1093/ije/dyz017.
Lewis-Mikhael, A.-M., Bueno-Cavanillas, A., Ofir Guiron, T., Olmedo-Requena, R., Delgado-Rodríguez, M., Jiménez-Moleón, J.J., 2016. Occupational exposure to pesticides and prostate cancer: a systematic review and meta-analysis. Occup. Environ. Med. 73, 134–144. https://doi.org/10.1136/oemed-2014-102692.
Matthews, G.A., 2008. Attitudes and behaviours regarding use of crop protection products—a survey of more than 8500 smallholders in 26 countries. Crop Prot. 27, 834–846. https://doi.org/10.1016/j.cropro.2007.10.013.
McDuffie, H.H., Pahwa, P., McLaughlin, J.R., Spinelli, J.J., Fincham, S., Dosman, J.A., Robson, D., Skinnider, L.F., Choi, N.W., 2001. Non-Hodgkin's lymphoma and

specific pesticide exposures inmen: cross-Canada study of pesticides and health. Cancer Epidemiol. Biomark. Prev. 10, 1155–1163.

OCDE, 1997. Guidance document for the conduct of studies of occupational exposure to pesticides during agricultural application. In: Series on Testing and Assessment, 9. Organisation for Economic Co-Operation and Development (OECD), Paris.

Pahwa, M., Beane Freeman, L.E., Spinelli, J.J., Blair, A., McLaughlin, J.R., Zahm, S.H., Cantor, K.P., Weisenburger, D.D., Punam Pahwa, P.P., Dosman, J.A., Demers, P.A., Harris, S.A., 2019. Glyphosate use and associations with non-Hodgkin lymphoma major histological sub-types: findings from the north American pooled project. Scand. J. Work Environ. Health 45, 600–609. https://doi.org/10.5271/sjweh.3830.

Perrotta, C., Kleefeld, S., Staines, A., Tewari, P., De Roos, A.J., Baris, D., Birmann, B., Chiu, B., Cozen, W., Becker, N., Foretova, L., Maynadie, M., Nieters, A., de Sanjose, S., Miligi, L., Seniori Costantini, A., Purdue, M., Spinelli, J., Cocco, P., 2013. Multiple myeloma and occupation: a pooled analysis by the international multiple myeloma consortium. Cancer Epidemiol. 37, 300–305. https://doi.org/10.1016/j.canep.2013.01.008.

R Core Team, 2020. R: A Language and Environment for Statistical Computing.

Salameh, P.R., Baldi, I., Brochard, P., Saleh, B.A., 2004. Pesticides in Lebanon: a knowledge, attitude, and practice study. Environ. Res. 94, 1–6. https://doi.org/10.1016/S0013-9351(03)00092-6.

Schinasi, L.H., Brown, E.E., Camp, N.J., Wang, S.S., Hofmann, J.N., Chiu, B.C., Miligi, L., Beane Freeman, L.E., Sanjose, S., Bernstein, L., Monnereau, A., Clavel, J., Tricot, G. J., Atanackovic, D., Cocco, P., Orsi, L., Dosman, J.A., McLaughlin, J.R., Purdue, M.P., Cozen, W., Spinelli, J.J., Roos, A.J., 2016. Multiple myeloma and family history of lymphohaematopoietic cancers: results from the international multiple myeloma consortium. Br. J. Haematol. 175, 87–101. https://doi.org/10.1111/bjh.14199.

Suciu, N., Russo, E., Calliera, M., Luciani, G.P., Trevisan, M., Capri, E., 2023. Glyphosate, glufosinate ammonium, and AMPA occurrences and sources in groundwater of hilly vineyards. Sci. Total Environ. 866, 161171 https://doi.org/10.1016/j.scitotenv.2022.161171.

Swaen, G.M., van Amelsvoort, L., Slangen, J.J., Mohren, D.C., 2004. Cancer mortality in a cohort of licensed herbicide applicators. Int. Arch. Occup. Environ. Health 77, 293–295. https://doi.org/10.1007/s00420-004-0503-8.

Van Hemmen, J.J., 2001. EUROPOEM, a predictive occupational exposure database for registration purposes of pesticides. Appl. Occup. Environ. Hyg. 16, 246–250. https://doi.org/10.1080/104732201460406.