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Original Article

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Evaluating Glyphosate Exposure Routes and Their Contribution to Total Body Burden: A Study Among Amenity Horticulturalists

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Abstract

Objective: To evaluate determinants of dermal and inadvertent ingestion exposure and assess their contribution to total body burden among amenity horticultural users using glyphosate-based pesticide products.

Methods: A dermal and inadvertent ingestion exposure assessment was completed alongside a biomonitoring study among amenity horticultural workers. Linear mixed effect regression models were elaborated to evaluate determinants of exposure and their contribution to total body burden.

Results: A total of 343 wipe and glove samples were collected from 20 workers across 29 work tasks. Geometric mean (GM) glyphosate concentrations of 0.01, 0.04 and 0.05 μg cm^{-2} were obtained on wipes from the workers' perioral region and left and right hands, respectively. For disposable and reusable gloves, respectively, GM glyphosate concentrations of 0.43 and 7.99 μg cm^{-2} were detected. The combined hand and perioral region glyphosate concentrations explained 40% of the variance in the urinary (μg l^{-1}) biomonitoring data.

Conclusion: To the author's knowledge, this is the first study to have investigated both dermal and inadvertent exposure to glyphosate and their contribution to total body burden. Data show the dermal exposure is the prominent route of exposure in comparison to inadvertent ingestion but inadvertent ingestion may contribute to overall body burden. The study also identified potential exposure to non-pesticide users in the workplace and para-occupational exposures.

Keywords: amenity horticulture; dermal exposure; glyphosate; inadvertent ingestion; occupational exposure; pesticides

Introduction

Glyphosate is a broad spectrum post emerging herbicide and is the highest volume herbicide used worldwide, present in >750 products (Guyton *et al.*, 2014). It was classified as a Group 2A—'probably carcinogenic to humans' by the International Agency for Research on Cancer (IARC) (IARC, 2015). Several regulatory bodies and national authorities have challenged the IARC classification (JMPR, 2016; US EPA, 2016; ECHA, 2017; EFSA, 2017). In 2017, the European Commission approved the renewal of the glyphosate licence for 5 years (European Commission, 2018).

Only a few occupational biomonitoring exposure studies involving glyphosate have assessed exposure in the agricultural (Acquavella *et al.*, 2004; Curwin, 2006; Curwin *et al.*, 2007; Mesnage *et al.*, 2012) and horticultural sectors (Lavy *et al.*, 1992; Johnson *et al.*, 2005; Connolly *et al.*, 2017, 2018a). European environmental biomonitoring studies have identified low levels of glyphosate exposure in the general public (Krüger *et al.*, 2014; Conrad *et al.*, 2017; Connolly *et al.*, 2018c). Studies have identified dermal absorption to be the primary route of pesticide exposure, accounting for up to 99.9% of total exposure (Lavy *et al.*, 1992; Tuomainen *et al.*, 2002; Aprea et al., 2005; Flack *et al.*, 2008; Vitali *et al.*, 2009), with inhalation exposure only accounting for ~1% of total exposure (Honeycutt, 1986). Glyphosate is mostly not metabolised in the human body and has an estimated half-life of 33 h, extrapolated from animal toxicological studies (IARC, 2016). However, human studies have estimated the rapid phase half-life as ~between 3 and 20 h (Faniband *et al.*, 2017; Connolly *et al.*, 2018b). An *in vitro* study using human skin and *in vivo* studies involving rhesus monkeys estimate the percutaneous absorption of glyphosate as <2% of the administered dose (Wester *et al.*, 1991) but it is still considered the main route of exposure. Inhalation exposure is considered a minor glyphosate exposure route by comparison (Jauhiainen *et al.*, 1991; Johnson *et al.*, 2005; IARC, 2016).

A study of UK local authority horticultural workers using glyphosate based products found a potential for both inhalation and dermal exposure. Workers applied pesticides using controlled droplet applicators and all-terrain vehicles with front mounted spray bars. Glyphosate concentrations were detected on cotton gloves worn inside the worker protective gloves and on worker socks and body patches (inside and outside of clothing). The study suggests that human behaviour (operator attitude and work practices) along with personal protective equipment (PPE) practices, including the re-use of PPE, and contact with contaminated work surfaces may be important determinants for pesticide exposure (Johnson *et al.*, 2005).

Similarly, Lavy *et al.* (1992) highlights the importance of the dermal exposure pathway in their glyphosate exposure assessment study among tree nursery workers. Dermal patch samples, water hand rinses along with urine samples were collected and analysed for glyphosate. Hand washes and cotton gauze patches, both over and under the clothing of workers, had detectable glyphosate concentrations. However, the urine samples were all non-detectable for glyphosate, which could be a result of the analytical detection limit (10 μg l^{-1}).

Other occupational exposure studies among agricultural users have identified PPE use as an important determinant of pesticide exposure (Acquavella *et al.*, 2004) and also highlighted the potential for take-home pesticide pathways (Curwin *et al.*, 2007). Curwin (2006) in their study of multiple pesticides (including glyphosate) exposures among farm and non-farm families in Iowa collected dust and wipe samples from potentially contaminated surfaces within participants' homes and vehicles. Although the majority of farmers in the study had not applied glyphosate-based products before sampling, glyphosate was detected in dust samples taken from in their homes. All the wipe samples were non-detectable for glyphosate concentrations, which the authors attribute to the use of inappropriate sample media. A slight positive association was observed between spouse urinary concentrations and home dust concentrations, as well as the farmer's urinary glyphosate concentrations correlating with their spouse and children's urinary concentrations. Although limited by sample size, the study highlights the potential for para-occupational exposures via clothing and footwear of pesticide users (Curwin, 2006; Curwin *et al.*, 2007). Glyphosate exposure studies have collected dermal and urinary samples (Lavy *et al.*, 1992; Curwin *et al.*, 2007) but due to the analytical methods adopted, the contribution of the dermal pathway to glyphosate total body burden has not been investigated.

Inadvertent ingestion has also been identified as a potential pesticide exposure route (Garrod *et al.*, 1999; Cattani *et al.*, 2001; Cherrie *et al.*, 2006) but only limited data is available on this pathway (Freeman *et al.*, 2005; Christopher, 2008).

Inadvertent ingestion can occur by the clearance of inhaled aerosol particles, ingestion of contaminated food/drink, transfer of contaminants from hand/object into the mouth or to the perioral region and then into the mouth (Christopher *et al.*, 2007). Approximately 16% of the UK working population is estimated to be exposed to hazardous materials via this exposure route (Cherrie *et al.*, 2006). Inadvertent ingestion has been identified as a potential exposure route to metals in an occupational setting and for pesticides among children due to residential pesticide use (Freeman *et al.*, 2005; Gorman Ng *et al.*, 2016, 2017). Only one study has estimated inadvertent ingestion of pesticides, including glyphosate-based products, among occupational users. Inadvertent ingestion exposure was estimated by collecting and analysing samples including worker hands and perioral wipes and saliva samples. Surface wipe samples of spraying vehicles were also collected and analysed (Christopher, 2008). Previous work on inadvertent ingestion of metals in occupational settings have identified exposure time, activities performed between worker tasks, use of PPE, frequency of hand to mouth contact and personal habits, for example smoking or nail biting, as determinants of inadvertent ingestion exposure (Gorman Ng *et al.*, 2016, 2017). There are no approved methods for assessing exposure by inadvertent ingestion, although the adoption of good hygiene practices is recommended as a suitable control (ECB, 2003). Nevertheless, good hygiene practices may not be a sufficient control measure, given its association with human behaviours (Cherrie *et al.*, 2006).

To the authors' knowledge, no previous exposure studies have investigated, both, dermal and inadvertent ingestion exposure to pesticides or their contribution to total body burden. The authors of this current study conducted a glyphosate urinary biomonitoring study among amenity horticulturists using glyphosate-based pesticide products (Connolly *et al.*, 2018a). Parallel to the biomonitoring study, dermal and inadvertent ingestion exposure assessments were performed by collecting and analysing worker glove samples, worker hand and face wipes, as well as wipes from potentially contaminated work surfaces.

The objective of the present analyses was to evaluate the potential determinants of dermal and inadvertent ingestion for glyphosate exposure among this occupational group. The study evaluated the cumulative contribution of the dermal and inadvertent ingestion exposure pathways to the total body burden of glyphosate.

Materials and methods

Site description and study population

Exposure assessments were conducted at sites managed by the Irish Commissioner for Public Works (OPW) from September 2016 to September 2017. The worker recruitment strategy has been previously described (Connolly *et al.*, 2018a). Briefly, workers were grouped into three similar exposure groups (SEGs): manual knapsack, pressurised lance and controlled droplet applicator, based on the applicator used to apply glyphosate-based pesticide products. The manual knapsack applicator SEG (typical capacity of 10–15 l), is carried as a knapsack with the pesticide product being applied with a handheld lance. The pressurised lance SEG applied the pesticide product using a handheld lance connected to a motorised knapsack. The controlled droplet applicator SEG, similar to the manual knapsack, but with a capacity 5 l, is purchased with a pre-mixed solution (eliminating the mixing and loading task) and has an adaptable applicator that can increase the droplet size, thus reducing the spray drift.

Study participants were recruited via oral presentation and circulated project information leaflets. Participation was voluntary and all participants gave informed consent. Ethics approval for this project was received from the National University of Ireland, Galway Research Ethics Committee (Ref: 16 July 2019) on the 5th September 2016.

Sampling methods

Biomonitoring samples

A biomonitoring study involving the collection of individual full urinary void spot samples was completed and previously been reported (Connolly *et al.*, 2018a). A minimum of three urine samples were collected from each participant: a sample before the task began, within 1 h of task completion and the following first morning void. For 59% (n = 17) of tasks, participants gave samples for each void over the exposure assessment period (pre-task to the following first morning void). Urine samples were analysed separately for glyphosate, so the sample with the highest glyphosate concentration could be identified for each task. The urine sample with the highest glyphosate concentration measured during the sampling period was selected and referred to as the peak urinary sample for that participant (Supplementary Material at *Annals of Occupational Hygiene* online).

Dermal and inadvertent ingestion sampling strategy

Wipe samples of the hands, perioral region and of potentially contaminated work surfaces (pesticide product container, worker mobile phones and steering wheels of work vehicles) were collected. Wipe sampling was conducted using Ghost Wipes™, pre-packaged polyvinyl alcohol wipes wetted with deionised water by the manufacturer. Dermal and perioral wipe samples were collected from the workers before and after the sampling task. Pre-work task wipe samples were required to evaluate whether detectable data collected post-task was as a result of the observed pesticide application task. Workers' glove and surface wipe samples were collected after the pesticide application tasks. The researcher wore disposable nitrile gloves for collecting samples and changed these gloves with each sample obtained. An appropriate number of Ghost Wipes™ and glove field blanks were also collected.

Following sampling, wipes were placed in 100 ml plastic pots and appropriately labelled. Samples were extracted and aliquots were frozen to −18°C within 24 h of collection, shipped and chemical analysis completed at the Health and Safety Executive's Laboratory, Buxton, UK.

Dermal sampling

Hand wipes were collected, using two wipes per hand, following protocols used in a previous study (Galea *et al.* 2018). The front of the hand was wiped with five strokes from the base of the hand to the top of the palm and then five strokes across the palm, starting from the base of the palm of the small finger. The wipe was folded in half and the same sequence repeated on the back of the hand. The wipes were then folded once more and each individual finger was wiped, starting at the small finger to the thumb, going between the fingers and including the finger web areas. Followed by the tips of each finger wiped in a circular motion. The same procedure was completed again with a second wipe and repeated for both hands. Dermal wipe samples were collected from the hands when workers removed their gloves, either during the task (i.e. lunch break) or after the pesticide application task.

Glove contamination samples

PPE use varied from disposable to reusable chemical resistant nitrile gloves as per company policy. After the work task, disposable glove samples were collected for glyphosate analysis, while only some participants provided their reusable gloves for analysis. Worker gloves were collected after the pesticide application tasks or within the task if gloves were changed during the pesticide task. At the end of the pesticide application task, dermal wipe samples were collected of each hand after the gloves were removed.

Inadvertent ingestion sampling

Perioral wipes were collected starting from the upper lip area and wiped in a clockwise motion around the upper lip and philtrum area and down around to the mentolabial fold to the edge of the mouth of the lower lip area. The wipe was folded in half and similarly wiped in an anti-clockwise direction, starting at the lower lip area and finishing at the upper lip area. One wipe was used for the perioral region.

An inadvertent ingestion observational study was also conducted. The frequency of worker contacts per task, (which in the current study included all surfaces contacted by the worker), frequency of worker hand to mouth contacts, contacts with the body and surrounding area (i.e. potentially contaminated surfaces) were recorded using protocols and a template from previous studies (Christopher *et al.*, 2007; Gorman Ng *et al.*, 2016). The frequency of contacts was recorded during only the pesticide task. Worker contacts pre- and post-work task or during work breaks were not recorded.

Potentially contaminated work surface sampling

Potentially contaminated work surfaces were wiped using one Ghost Wipe™, according to an object-specific sampling protocol developed within the study. Specifically, mobile phones were first wiped on the front of the phone, from the top to the bottom of the screen in one stroke. The wipe was folded in half and wiped on the back from top to bottom in one stroke. Finally, the wipe was folded once more and the edge of the phone was wiped, starting at the top right hand corner and completing the full edge in a clockwise motion.

Similarly, work vehicle steering wheel wipe samples were wiped from the top of the steering wheel in a clockwise direction, then folded it in half and repeated in an anti-clockwise direction. The wipe was folded once more and the centre of the wheel was wiped in a clockwise direction and the spokes were wiped from the edge to the base of the steering wheel.

Pesticide product containers were wiped from top to bottom for the full width of the container. The bottom of the container was wiped from right to left in one stroke. The wipe was folded and the top of the container was wiped in a clockwise motion. The container handle and surrounding area were wiped from top to bottom afterwards. The wipe was folded once more and the area around the lid was wiped, and then the lid itself, in a clockwise motion.

Chemical analysis

Wipe samples from the hands and perioral region, as well as the disposable glove samples, were placed into a 100 ml plastic pot and extracted by adding 50 ml of deionised water, shaken vigorously for 30 s, then placed on the Denley Spriamax 5 roller mixer for an hour. A 20 ml aliquot was transferred to a labelled Sterilin™ pot for storage and transport before analysis. Glyphosate was extracted from large reusable gloves at the laboratory. One glove was placed into a grip seal bag with 100 ml deionised water. Bags were placed on a gyratory rocker for 1 h with bags being turned over at 30 min. The liquid contents were then transferred to Sterilin™ pots for storage before analysis. The solubility of glyphosate in water (11.6 g L^{-1} at 25°C) made it an appropriate extraction solvent (IARC, 2016).

All samples were prepared and analysed for glyphosate following analytical methods previously described (Connolly *et al.*, 2017) with some minor alterations. In brief, glyphosate was extracted from dermal wipe, surface wipe and glove extracted water samples (100 µl diluted with 900 µl deionised water) using strong anion exchange solid phase extraction eluting into 10% formic acid in methanol. The eluent was evaporated under a stream of nitrogen and reconstituted in 200 µl of 0.1% formic acid. Quantitative analysis was performed by liquid chromatography tandem mass spectrometry. Chromatographic separation was achieved on a Zorbax XDB-C8, 150 x 4.6 mm, 5 µm (Agilent, Stockport, UK) column with mobile phases of 0.1% formic acid and acetonitrile with a gradient elution. The method was linear over the range 1–1000 µg l^{-1} and the LOQ was 1 µg l^{-1} and the LOD was 0.5 µg l^{-1}. Where results exceeded the top of the linear range (1000 µg l^{-1}) the samples were repeated with dilutions. The method was reproducible with an intra assay CV of 2.9% (n = 12) and an inter assay CV of 4.2% (n = 42, over four runs).

Data processing and analysis

All 23 wipe field blanks had non-detectable glyphosate concentrations. Seventeen glove field blanks were collected from the sites (as some workers used reusable gloves), six having non-detectable glyphosate concentrations, whereas detectable levels were found in the remainder. For each task with detectable glyphosate levels found on the blank glove, each glove sample within that task was field blank corrected. All the samples were corrected for the sample volume and for the surface area wiped. Though samples were not corrected for recovery efficiencies, the mean recovery percentage for plastic containers, disposable chemical resistant nitrile gloves and mobile phones, spike at 20 µg, was 122, 104 and 125%, respectively. Ghost wipes have a mean recovery for three samples spiked at 200 µg of 106%. Similar results were found in Curwin *et al.* (2005) for recovery efficiencies of Sof-Wick sponges of 90–100%.

The average hand surface area measurements were assigned according to published US EPA guidance (US EPA, 2011). The glove adjustments were assigned in the same manner as the surface area for hands. This assumes a 1070 cm^{-2} for both male hands, or 535 cm^{-2} surface per hand and 890 cm^{-2} for both female hands, or 445 cm^{-2} per hand. Average surface area measurements for the perioral region were assigned as 40 cm^{-2} (Gorman Ng, 2013).

Surface area calculations for the steering wheel were assigned as 1100 cm^{-2} surface area, according to a previously published study (Lu *et al.*, 2000). An average mobile phone surface area of 202 cm^{-2} was calculated using the physical phone dimension measurements, based on the phone type sampled. Similarly, for the product containers, an average surface area value of 2300 cm^{-2} was calculated.

Statistical analysis

Before the conducting statistical analysis, all concentration levels below the LOQ were imputed, in SAS v 9.4 (SAS Institute, North Carolina, USA). A single random imputation method based on maximum likelihood estimation was used (Lubin *et al.*, 2004). The remainder of the statistical analysis was performed using Stata Statistical Software 15 (StataCorp, 2015).

The data were log normally distributed and thus all statistical analysis was performed with log transformed exposure concentrations. Summary and descriptive analysis was performed on the work demographics and glyphosate concentrations levels for the combined dataset and by SEG. The results for the potentially contaminated surfaces are only shown for the combined dataset.

Pearson's correlation coefficients were estimated to evaluate relationships between glyphosate concentrations on the right and left hand, the dominant hand and both hands combined. Similar tests were performed on the glove data.

A linear mixed effect regression model was elaborated based on exposure determinants for inadvertent ingestion previously identified and evaluated in regression analysis against measurements of metals (Gorman Ng *et al.*, 2017). In this model, the hand contamination and the frequency of contacts per task were entered as fixed effects whereas the worker's id was entered as a random effect to account for correlations between repeated measurements from the same worker. This model had some differences to Gorman Ng *et al.*, 2017 model, including that respiratory protective equipment (RPE) was not considered as it was used by all workers participating in the study and that we used frequency of contacts per task, not just hand to perioral/oral contacts per task. Further models using a forward model built approach were elaborated to examine the robustness of the derived model as well as to identify determinants for inadvertent ingestion and dermal exposure and their relative contribution to overall body burden. In these models, parameters were entered sequentially based on their level of significance and kept within the model if they had a statistical significance of ($P < 0.1$).

Results

Demographic and working characteristics

Details on demographics and work characteristics have been previously published (Connolly *et al.*, 2018a). Briefly, 20 amenity horticulturists who applied glyphosate-based pesticide products as part of their daily duties participated in the study (18 males and 2 females), grouped in 3 SEGs as previously described. The pesticide task duration ranged from approximately a half hour to 6 hours. Work tasks involving the manual knapsack, controlled droplet applicator and the pressurised applicator were, on average, ~3, 3½ and 6 h, respectively.

Good worker compliance with PPE use was observed, with workers using PPE for most of the work tasks sampled; gloves, Tyvek suits and RPE were used for 29 (100%), 26 (90%) and 28 (97%) of the observed tasks, respectively.

Levels of glyphosate concentrations on wipes, gloves and contaminated surfaces

A total of 343 wipe and glove samples across 29 work tasks were collected and analysed for glyphosate. A minimum of seven sets of wipe samples were collected for each task sampled. A sample set consists of a blank wipe, perioral sample and each hand sample (two wipes per hand), before and after each work task.

Glyphosate concentration data for perioral and hand wipes (µg cm^{-2}), collected pre and post the work tasks are presented in Table 1 for overall samples and per SEG. Table 2 details the glyphosate concentration data for the disposable and reusable gloves samples. Seventeen pairs of disposable gloves and seven pairs of reusable gloves were analysed in this study. For three of the work tasks analysed, workers wore disposable gloves over a pair of reusable gloves and gave both sets of gloves for analysis. For eight of the tasks, the workers refused to give their gloves.

On some occasions, additional dermal and gloves samples were collected for workers who took a break during the pesticide application task. For three of the work tasks, dermal wipe samples were collected from three participants before taking a break and the glyphosate concentrations for the perioral and both hands (combined) ranged from 0.01 to 0.15 and 0.002 to 0.41 µg cm^{-2}, respectively. Similarly, three participants provided their disposable gloves during the break for five of the work tasks, which included two of these participants giving samples on two consecutive days and found glyphosate concentrations that ranged from 1.27 to 20.89 µg cm^{-2}. As concentrations were similar to the post-work task samples and due to the limited sample numbers, this data were not included in further analysis. The additional samples collected could only have had a negligible effect on the post-work task samples due to similar detection levels. The assumption would be that workers would wash hands and dispose of contaminated work gloves before their break, removing the contaminant, thus no accumulation of glyphosate concentration occurs on the post-work task samples.

Wipe samples data from pesticide product containers (n = 21), work vehicle steering wheels (n = 10) and participant's personal mobile phones (n = 18) are presented in Table 3.

Differences in exposure levels across SEGs, sampling and working parameters

Disposable worker gloves had the highest glyphosate concentrations, followed by worker hands (post-work task). Glyphosate concentrations were lowest on perioral wipes (Fig. 1a). The highest glyphosate concentrations were detected on wipe samples collected from the pesticide product containers, followed by much lower levels on the work vehicle steering wheel. The lowest concentrations were detected on the worker mobile phones (Fig. 1b). Three of the participants in this study had their mobile phone wiped on two separate occasions, and on both occasions, glyphosate concentrations were detected.

A strong positive relationship was found between urinary glyphosate concentrations (µg l^{-1}) and glyphosate wipe concentrations (µg cm^{-2}) on the worker perioral wipe samples (Fig. 2a). Similarly, perioral region and worker hands glyphosate concentrations (µg cm^{-2}) correlated positively and strongly (Fig. 2b).

Elaborated linear mixed effect regression models are presented in Table 4. The model evaluating previously documented determinants of inadvertent ingestion exposure Gorman Ng *et al.* (2017), explained 45% of the variability for the glyphosate concentrations found on the perioral region. In this model (Model 1), an

Table 1. Glyphosate wipe concentration data (µg cm^{-2}) for pre- and post-work task perioral and hand (left and right) measurements. Results are presented as for the overall sample and per similar exposure group concerned.

Variable	*k*	*N*	<LOQ *N* (%)	GM	GSD	Min	Max	<LOQ *N* (%)	GM	GSD	Min	Max
Combined SEGs				Pre-work task samples					Post-work task samples			
Perioral	20	29	11 (38%)	2.1×10^{-03}	12.93	8.2×10^{-06}	0.15	6 (21%)	0.01	9.05	1.7×10^{-04}	0.40
Hand left	20	29	0	6.1×10^{-03}	8.77	9.4×10^{-05}	0.31	0	0.04	9.21	4.7×10^{-04}	2.56
Hand right	20	29	0	6.5×10^{-03}	9.09	9.4×10^{-05}	0.22	0	0.05	8.73	2.8×10^{-04}	2.04
Manual knapsack				Pre-work task samples					Post-work task samples			
Perioral	10	12	6 (50 %)	1.1×10^{-03}	21.30	8.2×10^{-06}	0.15	4 (33%)	0.01	11.30	1.7×10^{-04}	0.23
Hand left	10	12	0	2.2×10^{-03}	8.47	9.4×10^{-05}	0.07	0	0.01	4.64	4.7×10^{-04}	0.08
Hand right	10	12	0	2.7×10^{-03}	11.00	9.4×10^{-05}	0.14	0	0.01	5.26	2.8×10^{-04}	0.09
Pressurised lance				Pre-work task samples					Post-work task samples			
Perioral	6	10	2 (20 %)	3.9×10^{-03}	8.56	5.8×10^{-05}	0.05	0	0.04	4.68	2.5×10^{-03}	0.40
Hand left	6	10	0	2.2×10^{-02}	10.01	3.7×10^{-04}	0.31	0	0.19	9.17	2.6×10^{-03}	2.56
Hand right	6	10	0	1.8×10^{-02}	10.62	4.7×10^{-04}	0.22	0	0.21	7.41	3.7×10^{-03}	2.04
Controlled droplet				Pre-work task samples					Post-work task samples			
Perioral	5	7	3 (43 %)	2.6×10^{-03}	9.44	1.1×10^{-04}	0.03	2 (29%)	0.01	8.34	6.0×10^{-04}	0.10
Hand left	5	7	0	5.9×10^{-03}	2.39	2.4×10^{-03}	0.03	0	0.04	5.89	3.5×10^{-03}	0.50
Hand right	5	7	0	6.8×10^{-03}	2.09	3.0×10^{-03}	0.02	0	0.06	5.73	7.9×10^{-03}	0.85

k is the number of participants in the group. *N* is the number of samples (one sample per task) in the group. Number of samples below the limit of quantification (<LOQ) (1 µg l^{-1}) by number (*N*) and percentage (%). GM is the geometric mean, GSD the geometric standard deviation and the range (min–max).

Table 2. Glyphosate wipe concentration data (µg cm^{-2}) for the post-work task glove samples. Results are presented for the overall sample and per similar exposure group concerned.

Variable	*k*	*N*	GM	GSD	Min	Max	*k*	*N*	GM	GSD	Min	Max
Combined SEGs			Post-work task disposable gloves						Post-work task reusable gloves			
Glove left	12	17	0.18	6.14	3.9×10^{-03}	2.78	6	6	4.49	4.68	0.81	58.87
Glove right	12	17	0.20	6.96	2.4×10^{-03}	10.62	6	6	4.52	4.43	0.73	66.27
Glove both	12	17	0.43	5.67	0.02	13.41	6	7	7.99	4.14	1.53	125.1
Manual knapsack			Post-work task disposable gloves						Post-work task reusable gloves			
Glove left	7	8	0.06	5.39	3.9×10^{-03}	0.63	1	1	—	—	6.11	6.11
Glove right	7	8	0.07	6.56	2.4×10^{-03}	0.49	1	1	—	—	6.43	6.43
Glove both	7	8	0.15	4.46	0.02	1.12	1	1	—	—	12.54	12.54
Pressurised lance			Post-work task disposable gloves						Post-work task reusable gloves			
Glove left	3	4	0.39	2.42	0.19	1.23	2	2	—	—	6.64	58.87
Glove right	3	4	0.36	1.44	0.26	0.58	2	2	—	—	6.11	66.27
Glove both	3	4	0.80	1.94	0.46	1.76	2	2	—	—	12.74	125.1
Controlled droplet			Post-work task disposable gloves						Post-work task reusable gloves			
Glove left	3	5	0.55	5.83	0.04	2.78	2	3	1.51	1.75	0.81	2.39
Glove right	3	5	0.75	7.29	0.05	10.62	2	3	1.49	1.86	0.73	2.17
Glove both	3	5	1.35	6.76	0.09	13.41	3	4	3.19	1.64	1.53	4.56

k is the number of participants in the group. *N* is the number of samples (one sample per task) in the group. There was no samples in this table that were below the limit of quantification (<LOQ) (1 µg l^{-1}). GM is the geometric mean, GSD the geometric standard deviation and the range (min–max).

Table 3. Glyphosate concentration data (µg cm⁻²) for wipe samples collected from work surfaces. Sampling from those was performed post-work task completion and results are presented as geometric mean (GM), geometric standard deviation (GSD) and range (min–max) for the overall sample.

Variables	*k*	*N*	<LOQ*N* (%)	GM	GSD	Min	Max
Combined SEGs							
Product container	15	21	0	2.06	7.48	0.01	27.7
Steering wheel	7	10	0	0.06	2.44	0.02	0.27
Mobile	15	18	2 (11%)	0.004	6.50	1.0×10^{-4}	0.12

k is the number of participants in the group. *N* is the number of samples (one sample per task) in the group. Samples that are below the limit of quantification (<LOQ) (1 µg l⁻¹) by number (*N*) and percentage (%). GM is the geometric mean, GSD the geometric standard deviation and the range (min–max).

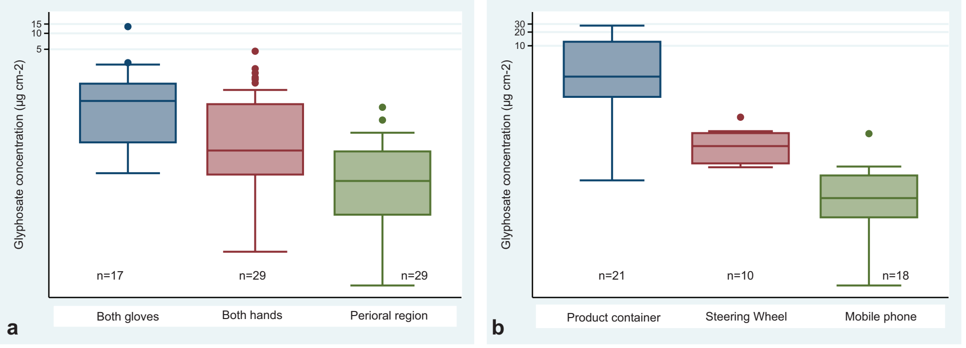

Figure 1. Boxplot showing the post-work task glyphosate concentrations for (a) disposable gloves, the workers hands (under the glove) and the perioral region and (b) for potentially contaminated work surfaces, pesticide product containers, the steering wheel of work vehicles and participants mobile phone (µg cm⁻²). The box is the 25th to the 75th percentile, the line within the box is the median and the whiskers the lower and the upper adjacent values. Single points indicate outliers. *n is the number of samples. Reusable gloves were not included in the boxplot (a) due to the low number of samples. Mean measured concentrations were statistically different between all types of samples (*t*-tests; $P < 0.001$).

increase in the frequency of contacts per task and post-task hand contamination was significantly associated with an increased in perioral glyphosate concentrations.

Forward building of the same model on the basis of improvement of the fit parameters resulted with the same parameters being included alongside sampling time. The effects for hand contamination and frequency of contacts per task were comparable to those of the Model 1, whereas perioral concentrations also increased with increasing sampling time ($\beta = 0.01$; $P < 0.08$). This model explained ~50% of the total variability in perioral glyphosate concentrations.

The forward built model examining determinants of participants hand contamination (Model 2) comprised of the task sampling time, the age of the participant and the SEG and explained 62% of the total variability of glyphosate concentrations measured on the hands.

To identify the relative contribution of the routes of exposure to the total uptake of glyphosate, a separate model was forward built using the log-transformed results of the biomonitoring exposure measurements as the dependent covariate. The final elaborated model comprised of only the combined hand and perioral region glyphosate concentration (Table 5). Overall, the model explained 40% of the total variance in urinary concentrations. The hands and perioral data were not entered as separate covariates in the model, as they were highly correlated ($r = 0.64$; $P < 0.001$).

Discussion

This study provides occupational glyphosate exposure data for dermal and inadvertent ingestion routes for amenity horticulturists and evaluates these exposure routes' contribution to total body burden. The biomonitoring data and related methodology have been previously published (Connolly *et al.*, 2018a).

There have been few dermal exposure studies reported for glyphosate (Lavy *et al.*, 1992; Johnson *et al.*, 2005; Curwin, 2006). Methodologies used to

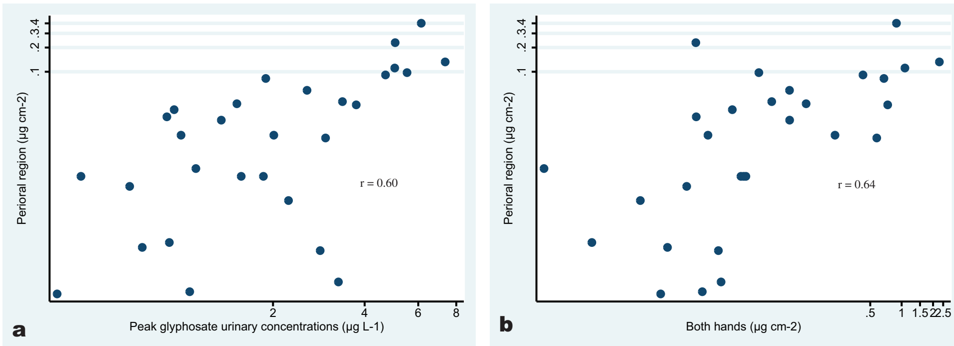

Figure 2. Scatter graph showing moderate relationships between glyphosate perioral glyphosate wipe contamination levels (µg cm^{-2}) and (a) peak urinary glyphosate concentrations (µg l^{-1}) and (b) both hands glyphosate surface loading contamination levels after a pesticide application task (µg cm^{-2}).

Table 4. Mixed effect models with participants identification number included in the models as a random effect. Model 1 results are describing the effects of hand contamination and the frequency of contacts per task on glyphosate concentrations measured on the perioral region. Model 2 results describe the effects of sampling time, the age of the workers and work task characteristic on glyphosate surface loading concentrations measured on the hands. Measurements are given as on the log-transformed glyphosate concentrations per surface area (µg cm^{-2}) and were taken from 20 workers over 29 pesticide application tasks.

Covariate	Model 1			Model 2		
	β	SE	*P*	β	SE	*P*
Intercept	–3.91	0.70	0.00	–10.05	1.67	0.00
Glyphosate conc. of both hands, post-work task (µg cm^{-2})	0.56	0.16	0.00			
Sampling time of the work task (mins)				0.01	0.003	0.01
Total frequency of contacts per task	0.02	0.01	0.02			
Age of the participant (years)				0.12	0.04	0.00
Similar exposure groups						
Pressurised lance				1.41	0.67	0.04
Controlled droplet applicator				0.69	0.67	0.30
Manual knapsack				Ref	—	—
Between variance (naive model)		1.18 (2.32)			0.00 (3.94)	
Within variance (naive model)		1.55 (2.62)			1.85 (0.97)	
Total variance explained		45%			62%	

β, regression coefficient for log-transformed exposure data; SE, standard error. The naive model is the results from the model without the inclusion of any fixed effects.

collect and analyse samples were different to the current study, therefore comparisons between studies should be considered with caution.

In the current study, arithmetic mean (range) glyphosate concentrations of 2708 (3.0–21 845) µg wipe^{-1} and 2797 (5.0–27 354) µg wipe^{-1}, (right and left hand, respectively) were found on worker hand wipe samples collected after the pesticide application task. Glyphosate concentration levels of 41 (<LOQ–321) µg wipe^{-1} were detected on wipes collected from the perioral region. Values reported for hand wipes in this study are higher than those found for agricultural pesticide users 647 (83–2081) µg (Christopher, 2008). However, the perioral glyphosate concentrations are within a range of that reported in Christopher (2008), with an arithmetic mean and range of 39.5 (2.6–91) µg. Christopher (2008) also detected glyphosate in worker saliva samples with an arithmetic mean and range of 140 (56–440) ng,

Table 5. Mixed effect model describing the effects of glyphosate concentration of the combined hands and the perioral region on the log-transformed glyphosate concentrations (µg l^{-1}) measured of 20 workers over 29 pesticide application tasks. Mixed models build with participants identification number as a random effect.

Covariate	β	SE	*P*
Intercept	1.20	0.19	0.00
Ln concentrations in hand and perioral region surfaces	0.26	0.06	0.00
Between variance (naive model)		0.15 (0.36)	
Within variance (naive model)		0.22 (0.27)	
Total variance explained		40%	

β, regression coefficient for log-transformed exposure data; SE, standard error. The naive model is the results from the model without the inclusion of any fixed effects.

which could suggest comparable inadvertent ingestion levels for the current study workers.

The current study results are an order of magnitude higher than glyphosate concentrations reported among forestry workers in nurseries, that is average (range) of 210 (0–1080) µg hand^{-1} wash (Lavy *et al.*, 1992). However, different sample collection methods were adopted among the studies and so it is difficult to compare results. In the current study, glyphosate was detected in all the pre- and post-work task hand wipe samples, as well as on the post-work task glove samples. Only 11 (38%) of the pre-work task and 6 (21%) post-work task perioral wipes had non-detectable glyphosate concentrations. For a third of work tasks sampled (n = 10), workers had started the pesticide task prior to the collection of pre-work task samples. Detectable glyphosate concentrations were also found on 11 (65%) of the blank gloves samples, collected from PPE field stores. Field observations suggest that cross contamination may occur when storing new gloves in close proximity of the pesticide chemical storage area or when handling unused gloves with contaminated hands.

The majority of workers were not face fit tested for RPE and workers regularly adjusted the half-face tight fitting RPE during work tasks, which may cause contamination through transfer from worker gloves or hands to the perioral region. Ensuring that all workers are face fit tested could reduce both the need for adjustment and risk of contamination.

Strong positive associations were found between left and right hands, and between the dominant hand, the individual hands and the combination of both hands. Between SEGs, similar glyphosate concentrations were detected on perioral wipes, with the highest geometric mean (GM) and maximum value found in the pressurised lance SEG. This was the only SEG with the highest glyphosate urinary concentrations and no post-work task perioral wipe samples below the limit of detection (Connolly *et al.*, 2018a).

Within SEGs, similar glyphosate wipe concentrations were found on both the right and left hands in the manual knapsack group and the pressurised lance applicator. Johnson *et al.* (2005) reported that UK local authority workers using controlled droplet applicators had low levels of inhalation exposure and higher levels of dermal exposure, which was found on the hands inside the worker gloves, socks and body patches. In the current study, glyphosate concentrations on reusable gloves were two orders of magnitudes higher than those on disposable gloves. These data present a strong argument to encourage the use of disposable gloves and their replacements after every work task.

As expected, of all the potentially contaminated work surfaces sampled in this study (n = 49), highest glyphosate concentrations were detected on the pesticide product containers. Typically these amenity horticultural workers use a 5 l pesticide product container multiple times before its disposal. Volumes of ~100–150 ml of pesticide concentrate are required per knapsack application. This pertains that a pesticide product container can be handled up to 50 times by the worker before disposal, which emphases that workers should always don gloves when handling pesticide containers to prevent personal contamination.

Glyphosate was also detectable on all wipes from work vehicle steering wheels (n = 21), with a mean and range of 1928 (478–5984) µg wipe^{-1} (unadjusted values). These included small tractors and vehicles (e.g. vans, cars) used to transport equipment to and around field sites. Participating workers drove the work vehicle, on some occasions to travel to multiple sites within a day, and performed the required pesticide application tasks. The presence of pesticide residues on the steering wheel wipes is of concern as it indicates that the wheels can be a source of exposure for other workers, who may not use pesticides but drive the vehicles, as observed in the field. Christopher (2008) collected surface wipe samples from inside (steering wheel, door bar and key ignition) and outside (door handle, hopper and valve handle) the cab of the pesticide application vehicles and reported an arithmetic mean and range of 480 (4–2900) µg, which were in order of magnitude lower than values reported in this study for steering wheel wipes. A study of take-home exposures found no detectable glyphosate concentrations on the steering wheel samples taken from farm or the non-farm families but the authors attributed this difference to the sampling media used (Curwin, 2006). In a take-home exposure pathway study of organophosphate pesticides the vehicles used to travel to work were sampled (using cotton gauze pads). Low level exposures (range 0–0.03 µg cm^{-2}) were found, with a frequency of detection ranging from 7 to 11%, suggesting the vehicles as a potential pathway for take-home pesticide exposures (Lu *et al.*, 2000).

Only two (11%) of the mobile phone samples had non-detectable glyphosate concentrations. Most mobile phones were personal use phones, highlighting an opportunity for para-occupational exposure among residents living with an occupational pesticide user (Food Standards Agency, 2018).

All the workers who participated in this study wore gloves when applying pesticides. Gloves were used throughout the task however it was observed that on a number of occasions workers would remove their gloves for various reasons (e.g. checking mobile phones, to drive work vehicles, when going on a break, etc.). All had detectable glyphosate concentrations on their hands. Field observations suggest that poor glove doffing procedures or removing gloves during the work task (e.g. answering the phone, adjusting facemasks) may be responsible for hand contamination. Donning and doffing of gloves was a probable source for hand contamination, also found in a study of workers spraying pesticides on olive trees (Aprea *et al.*, 2005). Glyphosate hand wipe concentrations were positively correlated with perioral concentration levels, suggesting that workers inadvertently transfer contaminants from their hands to their face.

Glyphosate perioral concentrations were also positively correlated with the peak glyphosate urinary concentration values. It could, therefore, be inferred that worker's hands inadvertently contaminated the perioral region, resulting in glyphosate uptake due to inadvertent ingestion or via dermal absorption around the perioral region, or both.

An evaluation of known determinants of inadvertent ingestion exposure as documented on previous analysis applying linear regression analysis on measurements of metals (Gorman Ng *et al.*, 2017), were included in the current study. Differences in considered determinants at our start model (Model 1) with this earlier evaluation included the absence of control for respiratory PPE usage by participants and the use of frequency of contacts per task, not just hand to perioral/oral contacts per task, within our study. Glyphosate concentrations on the worker hands and the frequency of contacts per task were significant determinants of inadvertent ingestion, explaining up to 45% of the variability on perioral region contamination (Table 4). In Gorman Ng *et al.* (2017), only the frequency of hand to mouth contact per hour was included, which was not statistically significantly associated with contamination on the perioral region. We observed similar effects (i.e. no association) when only the hand to mouth contacts were included in the model. This discrepancy with our results could suggest that recording the frequency of worker hand to mouth contact alone is not sufficient, as the worker must touch potentially contaminated surfaces and then transfer contaminates to the perioral region to cause increased exposure levels. It could also indicate that the level of contaminate on the worker's hands is the main driver for perioral exposure rather than the frequency of contacts being a significant determinant of exposure.

Inclusion of additional determinants on the forward selection process increased model performance in terms of variability explained for the model with perioral contamination as the dependent variable. Use of disposable gloves appeared to also improve the model but it was not statistically significant and correlated with sampling time ($r = -0.58$, $P < 0.01$), therefore it was not included in the final models. Further research with studies with larger sample sizes are required to verify the differences observed in measured concentrations between the use of reusable and disposable gloves. The glyphosate hand contamination could explain approximately 38% of the variability of the perioral contamination alone, showing that the perioral region contamination, available for inadvertent ingestion, is probably mostly transferred from the hands.

Model 2 suggests the pesticide task time period (sampling time), the participant's age and the SEG to be important determinants of hand contamination. However, Bonferroni ad hoc tests suggested no statistical significant geometric mean level differences between SEGs, likely due to small sample size. Sampling time alone explained 37% of variance, while an increasing worker age was also associated with increase hand glyphosate contamination. The results indicate that workers may benefit from regular refresher training to promote a safety culture when using pesticides.

Hand and perioral glyphosate concentrations are important determinants of total glyphosate body burden (glyphosate urinary concentrations), explaining 40% of variance in the urine data (Table 5). Unfortunately, as their concentrations correlated strongly, discriminating the individual contribution for each route to the total body burden was not possible. However, hand glyphosate concentrations alone explained approximately one third of the variance in the glyphosate urine concentrations, which would indicate that dermal exposure is the predominant route but that inadvertent ingestion may contribute to overall body burden since the presence of glyphosate contamination in the perioral region may result in ingestion and/or dermal absorption.

A limitation of this study was that only hand wipe samples were taken for the dermal exposure and inhalation samples were not taken in this study. However, it is important to consider that pesticide exposure studies have found the highest contamination levels on the hands (Tuomainen *et al.*, 2002, Vidal *et al.*, 2002; Lebailly *et al.*, 2009; Flores *et al.*, 2011, Garzia *et al.*, 2018) and inhalation exposure to be a minor route of exposure (Honeycutt, 1986; Jauhiainen *et al.*, 1991; Johnson *et al.*, 2005). Concentrations for hand and glove measurements were calculated using standard values for the surface area as recommended by the US EPA guidance (US EPA, 2011). The authors assumed that the contamination occurs primarily on the outer surface of the glove. However, in reality, actual surface contamination will depend on the exact hand size of every participant, whereas contamination on the glove itself may occur both inside and outside of the gloves. Nevertheless, the use of standardised measurement values when estimating exposure assists with comparisons within and between studies. In addition, some of the participants started the work task before monitoring began. Although this has no influence on the dermal exposure assessments measurements as samples were taken before and after the work task but it could potentially impact on the urinary concentrations which may not accurately reflect the full day's exposure. One may also argue that the precision of peak urinary concentration estimates used within our analysis may be dependent on the number of samples available for participants. However, we found no statistically significant differences in peak urinary concentrations between participants that gave the minimum three samples required versus those that exceeded this number (Connolly *et al.*, 2018a).

Conclusions

This is the first exposure assessment study that evaluated the total uptake of glyphosate, in parallel with dermal and inadvertent exposure routes, by collecting urine, wipes and glove samples.

The results show dermal to be a prominent route of exposure but support inadvertent ingestion potential contribution to the total body burden among this worker group. This study also identified a potential for the spread of contamination among non-pesticide users in the workforce and para-occupational exposures. Study results also showed that PPE practice is an important determinant of both inadvertent ingestion and dermal exposure. An implementation of PPE management and work practices policies for pesticide use could potentially reduce both occupational exposures and para-occupational exposures.

This study's exposure characterisation of pesticide users among this occupational group provides information that could be used for risk characterisation for regulatory risk assessments. It could also inform workplace risk mitigation measures that could reduce exposures, information that is useful for health and safety management, occupational hygienists, risk management and policy makers.

Supplementary Material

Supplementary data are available at *Annals of Work Exposures and Health* online.

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Conflict of Interest

The authors of the manuscript declare no conflict of interest.

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