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The Dermal Advanced REACH Tool (dART): A Bayesian Model for Dermal Exposure Assessment

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Abstract

The dermal Advanced REACH Tool (dART) is a tier 2 exposure model for estimating dermal exposure to the hands (mg min^{-1}) for non-volatile liquid and solid-in-liquid products. The dART builds upon the existing ART framework and describes three mass transport processes (deposition (D_{hands}), direct emission and direct contact (E_{hands}), and contact transfer (T_{hands})) that may each contribute to dermal exposure. The mechanistic model that underpins the dART and calibration of the mechanistic model, such that the dimensionless score that results from encoding contextual information about a task into the determinants of the dART can be converted into a prediction of exposure (mg min^{-1}), have been described in previous work. This paper completes the methodological framework of the dART model through placing the mechanistic model within a wider statistical modelling framework. A mixed-effects model, within a Bayesian framework, is presented for modelling the rate of dermal exposure per minute of activity. The central estimate of exposure for a particular task is provided by a calibrated mechanistic model (and thus based upon contextual information about a task). The model also describes between- and within-worker sources of variability in dermal exposure, with prior distributions for variance components based upon the literature. Estimates of exposure based upon informative prior distributions may be updated using measurement data associated with the task. The dART model is demonstrated using three worked examples, where estimates are initially obtained based upon the prior distributions alone, and then refined through accommodating measurement data on the tasks.

Keywords: Bayesian; dermal exposure; exposure modelling; skin; variability

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What's Important About This Paper?

Many thousands of exposure scenarios need to be assessed under REACH and other legislation. Exposure modelling provides an essential support to this process. There are currently no higher tiered tools available for dermal exposure assessment. The dART is a new generic tier 2 exposure model currently in development for estimating dermal exposures to the hands to low volatile liquid products and solids in liquid.

Introduction

The dermal Advanced REACH Tool (dART) is a new generic tier 2 exposure model for estimating dermal exposures to the hands to low volatile liquid products and solids in liquid. The model is based upon the existing ART (www.advancedreachtool.com) framework (Tielemans *et al.*, 2011) and incorporates elements of the ART model for estimating dermal contamination by aerosol deposition (one of three pathways considered in the model). The mechanistic model of the dART is based upon that of the ART (Fransman *et al.*, 2011) and follows a source–receptor model (Schneider *et al.*, 1999) with principal modifying factors along the source–receptor pathway. A detailed description of the dART mechanistic model is provided in Goede *et al.* (2018, 2019) and the references therein. Calibration of the dART mechanistic model, which is the process of converting the dimensionless score estimated by the dART mechanistic model into an exposure estimate, is described in McNally *et al.* (2019). A tool to implement the theoretical models is currently in development.

The mechanistic model of the dART is a central element of the overall modelling framework. Based upon contextual information about a task, statements about the task can be made, which map onto the underlying determinants of the mechanistic model. Based upon the assignments to model determinants, a dART score is thus obtained (Goede *et al.*, 2019) and this can be converted to an estimate of dermal exposure (mg min^{-1}) based upon the results of calibration (McNally *et al.*, 2019). Furthermore, a (multiplicative) confidence interval about the central estimate of exposure can be estimated.

The calibrated mechanistic model of the dART provides an estimate of average exposures to the hands associated with a task (and uncertainty about this estimate can be quantified), however exposures amongst workers (inter-individual) performing the same task may differ substantially. Furthermore, there may be substantial variability within the repeated exposures of individual workers (Kromhout *et al.*, 2004). A complete modelling framework therefore additionally needs to account for inter- and intra-individual sources of variability.

Various authors (Creeley *et al.*, 2005; Hewett *et al.*, 2006; Ramachandran, 2008) have proposed the use of Bayesian methods so that mathematical models of exposure can be combined with the limited data available from exposure measurements and utilized in risk assessments. A Bayesian framework allows the various disparate sources of information (contextual information related to the task, information on variance components from the literature, and exposure measurements) that are relevant to an exposure scenario to be integrated within a statistically rigorous framework.

In this paper, the technical details of the statistical model that underpins the dART are presented. Following a similar modelling framework to that of the ART (McNally *et al.*, 2014), a Bayesian approach is followed due to the hierarchical model of exposure, the disparate sources of information available and the technical advantages of the approach (a full and complete treatment of uncertainty, the ability to resolve problems that are ill-posed in the classical sense and treatment of censored observations). The model is demonstrated via worked examples which illustrate the entire workflow of the dART, beginning with contextual information about the exposure scenario and ending with a posterior distribution for the exposure distribution after including dermal exposure measurements.

Materials and methods

Exposure model

The underlying statistical model of the dART assumes that every relevant exposure scenario has a distinct exposure distribution that is adequately represented by a lognormal mixed-effects model, with random-effects representing between-worker variability, and a residual error representing within-worker variability. The dependent variable is the rate of deposition of product onto the hands per minute of exposure (derived as mass of product divided by sampling time). For an analyte with a concentration of less than 100%—pure substance—the measurement should be normalized by the fraction of the product-in-use equation (1). This normalization is necessary since the calibrated mechanistic

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model of the dART (see 'Prior specification') predicts the rate of deposition of product—the conversion back from product to analyte is made as the final calculation (see 'Computation').

$$\begin{aligned}\text{Measurement} = {} & \text{weight fraction of analyte}^{-1} \\ & \times \text{mass of analyte} \\ & \times \text{sampling time}^{-1}\end{aligned} \tag{1}$$

The statistical model is written

$$\ln(Y_{ij}) = \mu + w_i + \varepsilon_{ij} \tag{2}$$

$$w_i \sim N(0,\ \sigma_{bw}^2) \tag{3}$$

$$\varepsilon_{ij} \sim N(0,\ \sigma_{ww}^2) \tag{4}$$

In equation (2), Y_{ij} represents the jth dermal exposure measurement on the ith worker, μ represents the mean (natural log) exposure associated with the exposure scenario, w_i represents the worker effect for the ith worker—the tendency for an individual worker performing a task to have exposures that are systematically above or below the average exposure associated with the task, and ε_{ij} represents residual error. Equations (3) and (4) specify that worker effects and residual errors are normally distributed (for a model specified on the log-scale) with standard deviations of σ_{bw} and σ_{ww}, respectively. The model is simpler than that for the ART model (McNally *et al.*, 2014) as between company variability is not modelled: we expand on this aspect of model form in the discussion section.

Prior specification

As noted in the introduction, a Bayesian framework is pursued in this work, consistent with the (inhalation) ART. A joint prior distribution for model parameters is therefore required. Informative prior distributions for the average exposure (μ) and variance components are specified separately, utilizing different information sources.

A Gaussian form equation (5) is adopted for the mean (natural log) exposure.

$$\mu \sim N(\log(\text{CDARTscore}), \sigma_s^2) \tag{5}$$

In equation (5), CDARTscore (calculated through equations (6) and (7)) denotes the estimate of exposure from the calibrated mechanistic model of the dART, which is derived from contextual information about the exposure scenario. Contextual information maps onto the underlying determinants of the dART mechanistic model and dimensionless scores for deposition (D_{hands}), direct emission and direct contact (E_{hands}), and transfer (T_{hands}) (equation (6)) result from application of the scheme described in Goede *et al.* (2019) and the references therein. The parameters α, β_1, and β_2 (Table 1) were estimated during model calibration (McNally *et al.*, 2019) and translate the three dimensionless scores into an estimate of exposure (mg min^{-1}). Uncertainty associated with the mechanistic model prediction is quantified through the standard deviation σ_S (Table 1).

Table 1. Parameters derived from model calibration.

α	β_1	β_2	Glove	σ_s
1.14	87.40	5.02	−5.72	1.08

$$\text{DARTScore} = D_{\text{hands}} + \beta_1 T_{\text{hands}} + \beta_2 E_{\text{hands}} \tag{6}$$

$$\text{CDARTscore} = \alpha \times \text{DARTscore} \tag{7}$$

A published dataset on components of dermal variability (Kromhout *et al.*, 2004) was re-analysed in order to estimate prior distributions for the between- and within-worker variance components. Kromhout *et al.* (2004) studied within- and between-worker variability in dermal exposure to the hands in groups of workers undertaking a particular task at a specific factory. A random-effects analysis of variance model was fitted to thirty such datasets with between- and within-worker variances estimated for each worker group. Summary statistics based on this analysis were reported in Table 5 of Kromhout *et al.* (2004) with detailed results given in Table A1 of appendices. The within- and between-worker variance components (σ_{bw}^2 and σ_{ww}^2, respectively) based upon Table A1 of Kromhout *et al.* (2004) are provided for these 30 worker groups in Table 2—this analysis of variance components was based upon the dependent variable of exposure rate (mg min^{-1}). Also shown in Table 2 are standard deviations (per worker group) which summarize the total variability, where σ_{total} is given by

$$\sigma_{\text{total}} = \sqrt{\sigma_{bw}^2 + \sigma_{ww}^2} \tag{8}$$

Our review of these data led us to conclude that the small datasets and limited repeat sampling of workers for the majority of worker groups led to unreliable estimates of between- and within-worker variance components. Specifically, between-worker variability was estimated as exactly zero for 18 of these 30 worker groups (Table 2). This appears to be as a consequence of how the maximum likelihood algorithm functions for small datasets when there is insufficient information in the data to distinguish between the two sources of variability. We therefore concluded these data were unsuitable for the estimation of prior distributions. However, the estimates of σ_{total} (equation (8)) were judged as being reliable.

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Table 2. Estimates of components of variability in dermal exposure for 30 scenario-in-factory subsets of the Kromhout *et al.* (2004) data.

Scenario	Rate (mg min^{-1})		
	σ^2_{ww}	σ^2_{bw}	σ_{total}
Maintenance/servicing	0.12	0	0.35
Maintenance/servicing	0.37	0.5	0.93
Loading (liquids)	4.29	0	2.07
Filling	0.21	0.53	0.86
Filling	0.33	1.58	1.38
Filling	1.41	0	1.19
Filling	0.03	2.74	1.66
Mixing/diluting	4.58	3.33	2.81
Mixing/diluting	0.72	0	0.85
Wiping	11.3	0	3.36
Wiping	0.19	0.12	0.56
Wiping	0.64	0	0.8
Pouring	2.97	0	1.72
Spreading material	0.12	0	0.35
Rolling	0.37	0	0.61
Rolling	0.42	0	0.65
Brushing	1.14	0.42	1.25
Brushing	0.52	0	0.72
Spray painting	0.7	0.15	0.92
Spray painting	1.06	0	1.03
Spray painting	1.17	0.48	1.28
Galvanizing	0.03	0	0.17
Galvanizing	0.97	0	0.98
Galvanizing	0.47	0	0.69
Galvanizing	1.57	0	1.25
Galvanizing	0.01	0.09	0.32
Grinding	0.95	0.45	1.18
Grinding	0.14	0.17	0.56
Grinding	0.7	0	0.84
Grinding	0.33	0	0.57

An indirect approach to prior specification is pursued in current work. This involves the specification of prior distributions on two functions of σ^2_{bw} and σ^2_{ww}, which can be reliably parameterized, and which subsequently imply prior distributions for σ^2_{bw} and σ^2_{ww}. This modelling approach is compatible (and justified) within a Bayesian approach although not frequently utilized in the occupational hygiene literature.

A prior distribution on σ_{total} was estimated using the calculated values for the Kromhout *et al.* (2004) data (30 data points), and a similar dataset on σ_{total} based upon measurements used in the calibration of the dART mechanistic model (McNally *et al.*, 2019)—a further 38 data points (the numeric values in columns 3 and 4 of Table 3). A log-normal distribution (equation (9)) was found to be an adequate fit to this combined dataset.

$$\sigma_{\text{total}} \sim LN(-0.12, 0.64) \quad (9)$$

A second prior distribution on either σ_{bw} or σ_{ww} or some function of these parameters is required to fully specify a joint prior distribution for σ_{bw} and σ_{ww}. The data on variance components from measurements of inhalation exposures [compiled by Kromhout *et al.* (1993)] and as utilized by McNally *et al.* (2014) were re-analysed to provide this second prior. An analysis of the ratio of between- and within-worker variances in 116 groups of workers led to a log-normal prior distribution (10) for this ratio. Further discussion around the modelling decision to use a dataset on components of variability in inhalation exposure measurements to derive the prior (equation (10)) is provided in the discussion section of this paper.

$$\sigma^2_{bw}/\sigma^2_{ww} \sim LN(-0.92, 1.44) \quad (10)$$

Through equations (9) and (10) marginal distributions for σ^2_{bw} andσ^2_{ww} are defined. Although these do not take the form of recognized probability distributions, these implied prior distributions can be sampled from. An important difference compared with the direct specification of σ^2_{bw} andσ^2_{ww} through independent priors is that through this indirect specification σ^2_{bw} and σ^2_{ww} are strongly correlated.

Computation

In the absence of dermal exposure measurements, estimates of dermal exposure are based upon the prior alone. Samples are drawn from (5), (8), and (9) and summary statistics of interest are calculated for each complete sample from the priors. Central estimates and credible intervals are based upon this sample from the prior. Two quantities of particular interest are the time-weighted average (TWA) and long-term average (LTA) of individual exposure distributions: percentiles from these distributions are calculated from equations (11) and (12), respectively.

$$\text{TWA}_\alpha = \exp(\mu) \times \exp(z_\alpha \times \sqrt{\sigma^2_{bw} + \sigma^2_{ww}}) \quad (11)$$

$$\text{LTA}_\alpha = \exp(\mu + 0.5 \times \sigma^2_{ww}) \times \exp(z_\alpha \times \sqrt{\sigma^2_{bw}}) \quad (12)$$

When measurements on the exposure scenario are available then the joint posterior distribution of model parameters is sampled from and inference is based upon this sample. In the examples presented in 'Worked examples' a Markov Chain Monte Carlo (MCMC) algorithm was coded using the WinBUGS software (Lunn *et al.*, 2009) and the R2WinBugs package for R (R Core

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Table 3. Information on total variability in dermal exposure from for the exposure scenarios analysed in calibration of the dART mechanistic model.

Description	GSD		σ_{total}	
	Over glove	Under glove	Over glove	Under glove
Anti-fouling spraying	1.9	6.9	0.64	1.93
Car body spraying	2.6	NA	0.96	NA
Anti-fouling paint spraying	3.6	NA	1.28	NA
Spray cleaning foam	2.9	NA	1.06	NA
Knapsack motorized spraying	2.2	2.7	0.79	0.99
Knapsack spraying	6.2	NA	1.82	NA
Spraying low pressure lance	NA	2.8	NA	1.03
Spraying high pressure lance	2.6	NA	0.96	NA
Insecticide spraying	5.8	NA	1.76	NA
Boom spraying closed cabin	1.8	NA	0.59	NA
Boom spraying semi-closed cabin	4.8	NA	1.57	NA
Boom spraying closed cabin	1.9	NA	0.64	NA
Boom spraying semi-closed cabin	4.2	NA	1.44	NA
Boom spraying closed cabin	3.5	NA	1.25	NA
Boom spraying semi-closed cabin	5.7	NA	1.74	NA
Boom spraying in orchard cabin	4.5	NA	1.5	NA
Boom spraying in orchard no cabin	NA	NA	NA	NA
Boom spraying in orchard cabin	3.2	NA	1.16	NA
Fogging	NA	5.3	NA	1.67
Dipping activities (timber)	NA	4.2	NA	1.44
Electroplating	NA	NA	NA	NA
Electroplating (KRIOH)	NA	1.8	NA	0.59
Electroplating (KRIOH)	NA	NA	NA	NA
Timber pre-treatment (solvent)	NA	8.8	NA	2.17
Timber pre-treatment (water)	NA	5.2	NA	1.65
AF net deployment (solvent)	NA	1.5	NA	0.41
AF net deployment (water)	NA	1.5	NA	0.41
Forestry: packing and planting	NA	6.2	NA	1.82
Non-professional brush painting	6	11.5	1.79	2.44
Brush and roller painting	NA	10.1	NA	2.31
Opening and closing packaging, cleaning equipment and spreading	10.5	NA	2.35	NA
Car washing	NA	NA	NA	NA
Large-scale surface wiping	1.9	NA	0.64	NA
Loading DEGBE	16.7	NA	2.82	NA
Filling of spray guns	4.6	NA	1.53	NA
Filling DEGBE	3.5	NA	1.25	NA
Filling DEGBE	7.8	NA	2.05	NA
Filling DEGBE	NA	NA	NA	NA
Filling DEGBE	3	NA	1.1	NA
Filling DEGBE	4.4	NA	1.48	NA

Team 2014; Sturtz *et al.*, 2005). Code for the worked examples is supplied in Appendices (available at *Annals of Work Exposures and Health* online).

As discussed in 'Exposure model', the dependent variable in the model is the rate of deposition of product onto the hands per minute of exposure (equation (1)). The total loading onto the hands over a specified duration (such as full shift) is derived by multiplying through by the length of time (minutes) of interest. Similarly, the exposure to a specific analyte within the product is derived by multiplying by the proportion (or weight fraction) of the analyte in the in-use product. Both calculations are demonstrated in examples.

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Worked examples

Spraying of cars

The first example is spraying of cars (activity class 1.1)—one of three exposure scenarios that are reported in Delgado *et al.* (2004). Briefly, the exposure scenario (and associated measurements) relates to the spray painting of cars in repair shops using water-based paints. Spray painting took place in down-flow spray booths. Between 0.38 and 2.4 l of paint were applied during spraying operations with spraying durations of between 6 and 30 min. The scenario began when the trigger of the spray gun was depressed and concluded when the trigger was released: filling of the spray gun and cleaning of spray guns following spray applications were investigated as separate tasks within the study with their own dermal exposure measurements.

This example follows on from Goede *et al.* (2019) where scoring of determinants associated with this scenario is given in detail—the results of these calculations are given here (see Supplementary Material in Goede *et al.*, 2019) for technical detail of determinants and calculations). The calculated scores were of $D_{\text{hands}} = 0.05$, $E_{\text{hands}} = 0.225$, and $T_{\text{hands}} = 0.00075$. The calculated exposure rate is given in (13). Based upon the calibrated mechanistic model the direct emission and direct contact and transfer pathways, accounting for approximately 63% and 36% of the calibrated dART score, respectively, were the important pathways of exposure.

$$\begin{aligned}\text{CDARTscore} = \; & 1.14 \times (0.05 + 87.4 \times 0.00075 \\ & + 5.02 \times 0.225) = 1.49\,\text{mg}\,\text{min}^{-1}\end{aligned} \tag{13}$$

Equation (13) represents the central estimate of the geometric mean (GM); however, a prior distribution representing uncertainty in the estimate of the GM is represented by equation (5) and a density plot of this prior is shown in Fig. 1a. A multiplicative 95% credible interval based upon the prior is of a rate of accumulation of product onto the hands of between 0.18 and 12.4 mg min^{-1}.

Fig. 1b shows the central estimate of the 1st to 99th percentiles for the cumulative distribution of exposure rates (solid red line) and also accounts for between- and within-worker variability (equation (11)). A 95% credible interval for percentiles is indicated by the shaded region.

For this example, the prior to posterior analysis is also demonstrated. In total 29 measurements from 17 workshops, visited during the course of the study, were available. Repeat samples were available on five workers (29 measurements from 24 workers). Cotton sampling gloves were used as the sampling device. Results in Table 2 of Delgado *et al.* (2004) were in units of µg cm^{-2} min^{-1} for both the analyte (aluminium) and product and were provided per glove. A surface area of 410 cm^2 per hand was assumed by Delgado *et al.* (2004). A dataset of 29 measurements for paired (left and right glove) specimens were available. The GM, geometric standard deviation (GSD), and range of measurements for exposure rate to product were 2.33, 2.56, and 0.35–11.02 mg min^{-1}.

As noted in 'Computation', inference is achieved using MCMC. For this example, 20 000 samples of the model parameters were drawn from the posterior with every 20th retained for inference. The GM and the distribution of exposure rates were calculated for each retained sample with summary statistics (presented below) calculated from this retained sample.

Fig. 1c shows the posterior distribution for the GM loading rate and is based upon the calibrated mechanistic model and the 29 measurements. The posterior is indicated by the darker shaded region—the prior is also shown for comparison as the lighter shaded region. The posterior mode and 95% credible interval for the GM were 2.32 and 1.62–3.29 mg min^{-1}, respectively. Fig. 1d shows the posterior distribution (1st to 99th percentiles) for the cumulative distribution of exposure rates. The central estimate is indicated by the dashed red line and a 90% credible interval for percentiles is indicated by the darker shaded region. The solid red line and lighter shaded region correspond to central estimate and credible interval from the prior alone.

The measurements provided high-quality information on both average exposures and on total variability in measurements and consequently summary statistics showed a large reduction in uncertainty compared with the prior. The central estimates changed little from prior to posterior in this example, since the central estimate of the GM provided by the mechanistic model was very close to that estimated from data, however in general use a larger discrepancy between estimates of the GM from prior and from data would be expected.

Inference is for the modelled variable of exposure to product per minute of activity, however calculations based upon the modelled variable can be performed based upon both prior and posterior. Three such calculations are demonstrated in Table 4: the cumulative loading onto the hands (based upon the median sampling time of 16 min); the exposure rate to the measured analyte, aluminium at a concentration of 2%; the loading rate of aluminium per square cm—this final calculation requires information about the exposed area of the hands. In this example, the coding of the mechanistic model (and hence the derived prediction) assumes that one half of a single hand (area of 410/2 = 205 cm^2) was exposed. A central estimate and 95% credible interval for both prior and posterior are given in Table 4 for all three derived variables.

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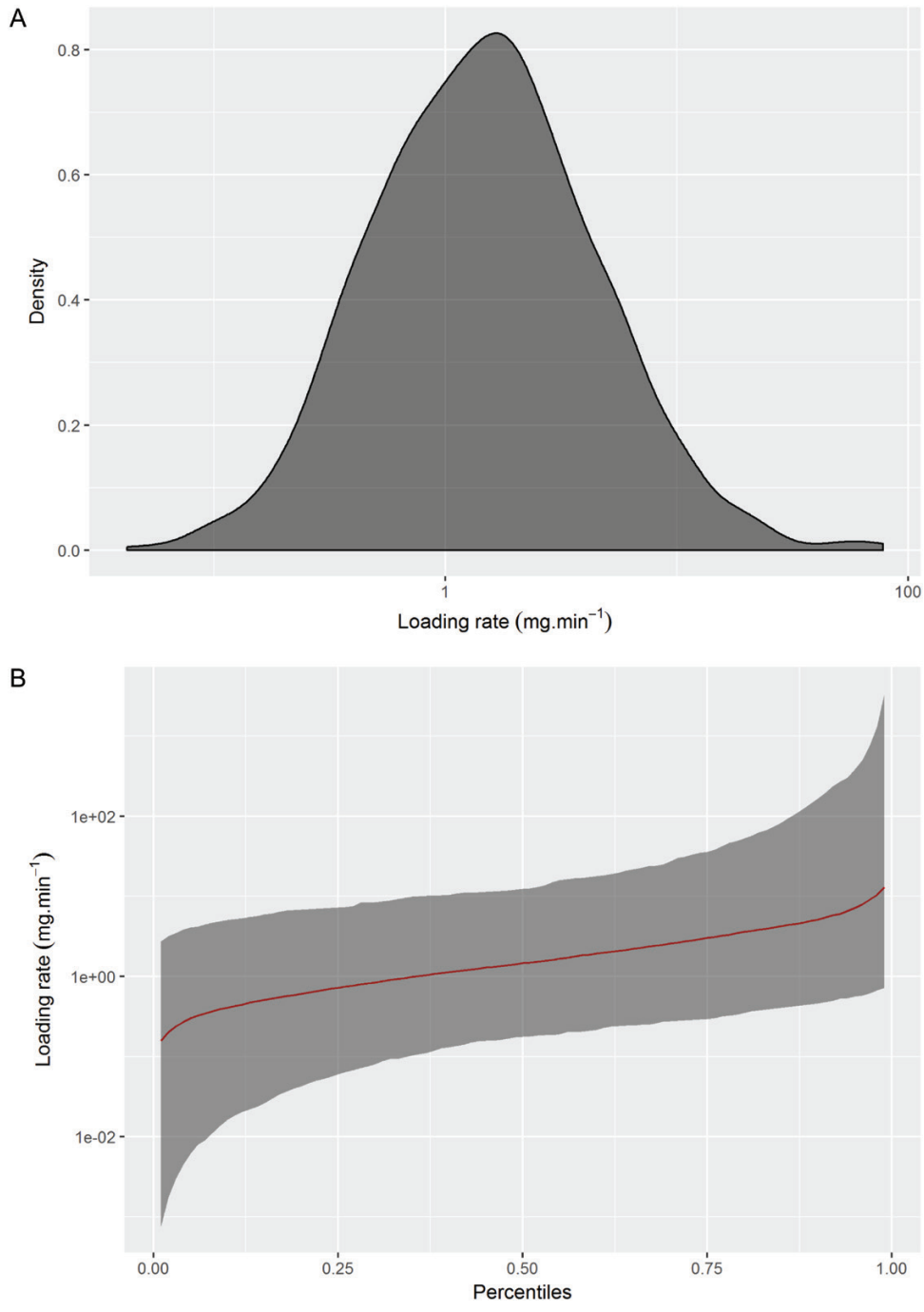

Figure 1. A comparison of the prior and posterior distributions for the GM loading rate and the percentiles of the cumulative distribution of loading rates (mean and 95% credible interval): (a) prior GM loading rate; (b) prior cumulative distribution of loading rates; (c) comparison of prior and posterior GM loading rate—darker shaded region corresponds to posterior; (d) comparison of prior and posterior cumulative distribution of loading rates—darker shading corresponds to posterior 95% credible interval, solid red line denotes prior mean, and dashed red line denotes posterior mean.

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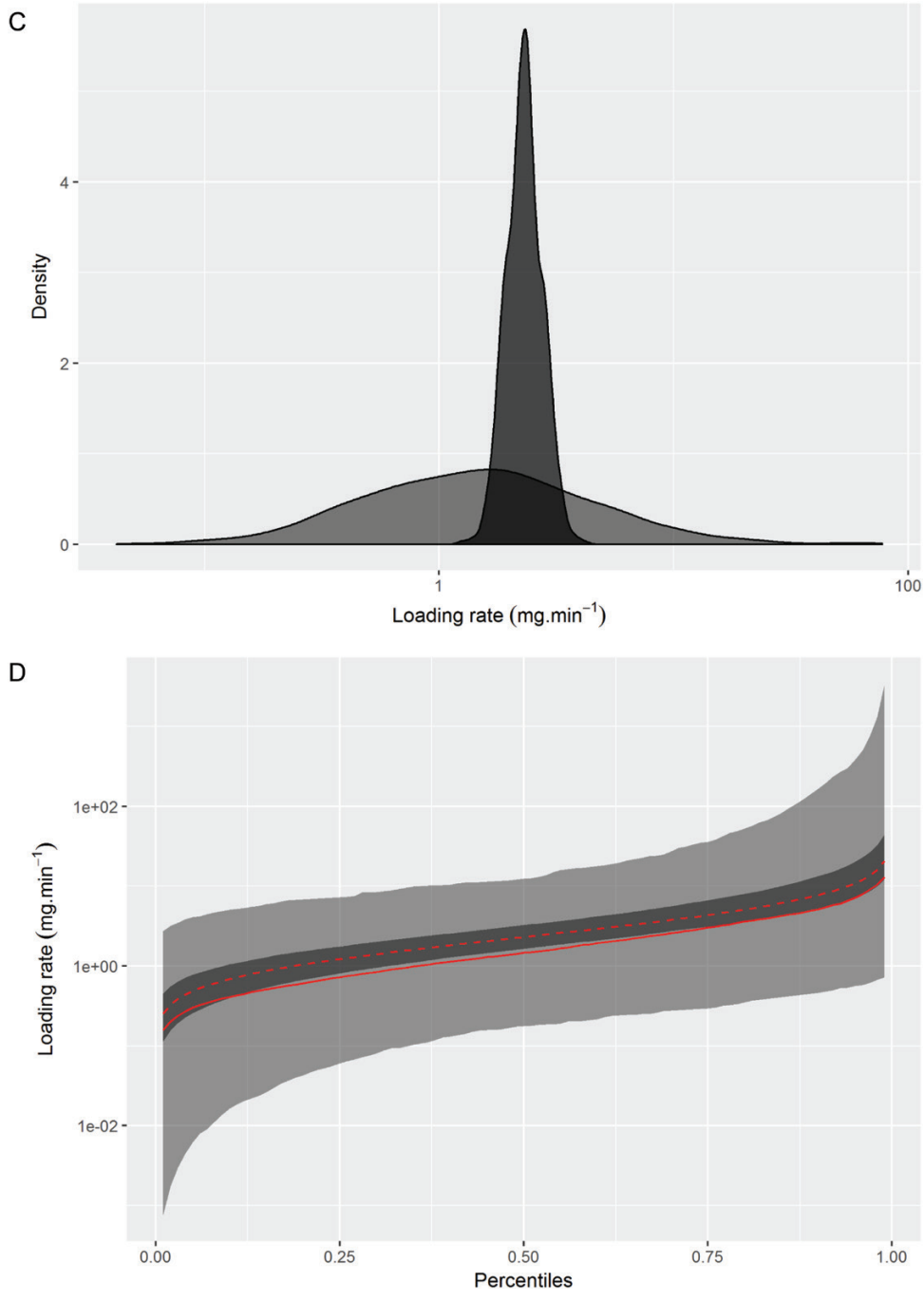

Figure 1. Continued.

Handling immersed objects

The second example is a laboratory exposure scenario taken from the SysDEA study (Franken *et al.*, 2019). Briefly, the exposure scenario required the dipping of cylinders into a bath of low viscosity fluid (activity class 2.1). Fifteen smooth metal cylinders (with diameter and length of approximately 8 and 20 cm, respectively) were (i) each dipped in a low viscosity fluid and hung on a rack; (ii) moved and hung on a second rack following completion of dipping activities; (iii) moved from the

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Table 4. Demonstration of three example calculations for case study 1.

Calculation	Supporting information for calculations	Prior		Posterior	
		GM	95% CI	GM	95% CI
Loading rate per minute product	Product loading rate per minute. Modelled variable. Units of mg min^{-1}.	1.49	0.18, 12.4	2.32	1.62, 3.29
Total product loading	Total product loading during 16 min of exposure. Units of mg.	23.84	2.88, 198.4	37.12	25.92, 52.64
Loading rate per minute analyte	Aluminium, representing 2% of the applied product. Units of mg min^{-1}.	0.030	0.0036, 0.248	0.046	0.032, 0.066
Loading rate per minute analyte per cm^2	Aluminium, representing 2% of the applied product. Surface area of the exposure hand of 205 cm^2. Units of μg cm^{-2} min^{-1}.	0.145	0.018, 1.21	0.224	0.16, 0.32

second rack and placed horizontal on a work surface [a more detailed task description is provided in Franken *et al.* (2019)]. Hands were not immersed during this task. The study took place in a ~39 m^3 room with ~33 air-changes per hour (ACH). The tracer analyte within the dipping fluid was Tinopol SWN at a weight fraction of 0.2% within the product-in-use.

The calculated scores were of $D_{hands} = 0.001$, $T_{hands} = 1.75$, and $E_{hands} = 0.5$. The calculated exposure rate is given in equation (14). Based upon the calibrated mechanistic model the transfer pathway (hand-surface contact) was dominant, accounting for approximately 98.5% of the calibrated dart score.

$$\text{CDARTscore} = 1.14 \times (0.001 + 87.4 \times 1.75 + 5.02 \times 0.5) = 177.23 \ \text{mg min}^{-1} \quad (14)$$

Based upon the prior distributions specified in equations (5), (9), and (10) and the estimate (equation (14)), the prior distribution for the scenario is defined. In this example the GM and the 50th percentile of the LTA distribution are demonstrated, with priors plotted in Fig. 2a and b, respectively. Some summary statistics for the parameters in the prior and calculated variables of interest are given in Table 5.

The experimental study described above was conducted by four volunteers who each undertook four replicates of the task, leading to 16 measurements and good information to distinguish between within- and between-worker sources of variability. Task duration was between 7 and 10 min. The exposure rate to product was derived (based upon measurements of analyte and concentration within the product-in-use), with a GM, GSD, and range of 89.2, 1.44, and 51.4–151.1 mg min^{-1}, respectively. Cotton sampling gloves were used as the sampling device.

For this example, 20 000 samples of the model parameters were drawn from the posterior with every 20th retained for inference. Table 5 provides summary statistics from the posterior distributions of the model parameters and the GM and LTA. Posterior densities of the GM and LTA are shown in Fig. 2c and d, respectively—in both plots the corresponding priors are also show to aid interpretation.

In this case study the prior was clearly consistent with data, however the central estimates of μ and σ_{total} were both reduced in posterior compared with prior, with a large reduction in the uncertainty in both of these parameters (as characterized by the width of the credible intervals). The implied prior distribution of the LTA (Fig. 2b) was particularly wide as a consequence of the significant uncertainty in the two parameters which define variability within the model (Table 5); the posterior of the LTA (Fig. 2d) was significantly narrower.

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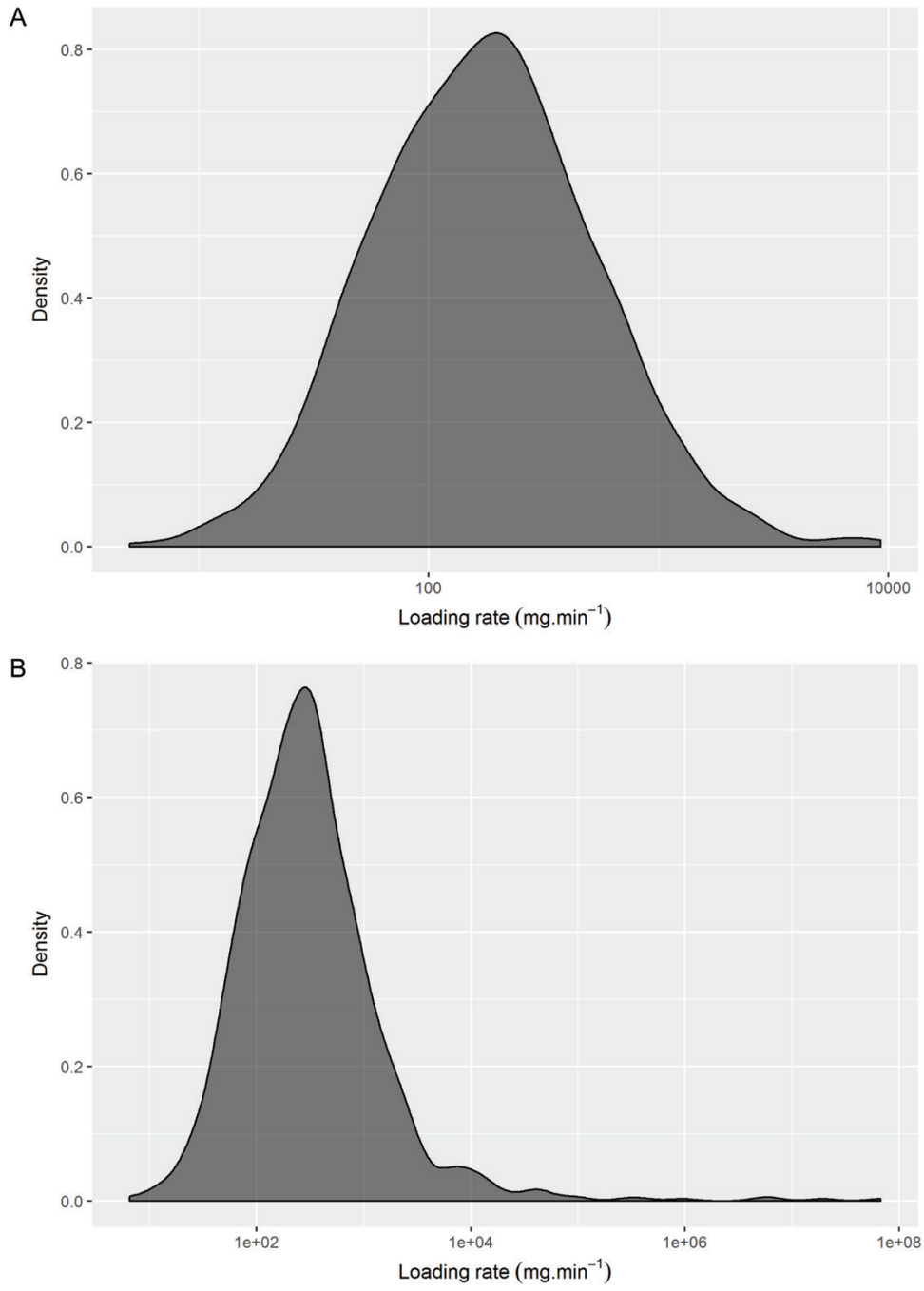

Figure 2. A comparison of the prior and posterior distributions for the GM and LTM loading rates: (a) prior GM loading rate; (b) prior LTM loading rate; (c) comparison of prior and posterior GM loading rate—darker shaded region corresponds to posterior; (d) comparison of prior and posterior LTM loading rate—darker shaded region corresponds to posterior.

Pouring of liquids

The third example is also a laboratory exposure scenario taken from the SysDEA study (Franken *et al.*, 2019). Briefly, the exposure scenario required the pouring of a low volatility liquid (activity class 6.2). Participants' decanted 1 l of a high viscosity liquid from a 5 l bottle into 1 l jug and then carried the filled jug to a workstation and decanted the contents of the jug into an open

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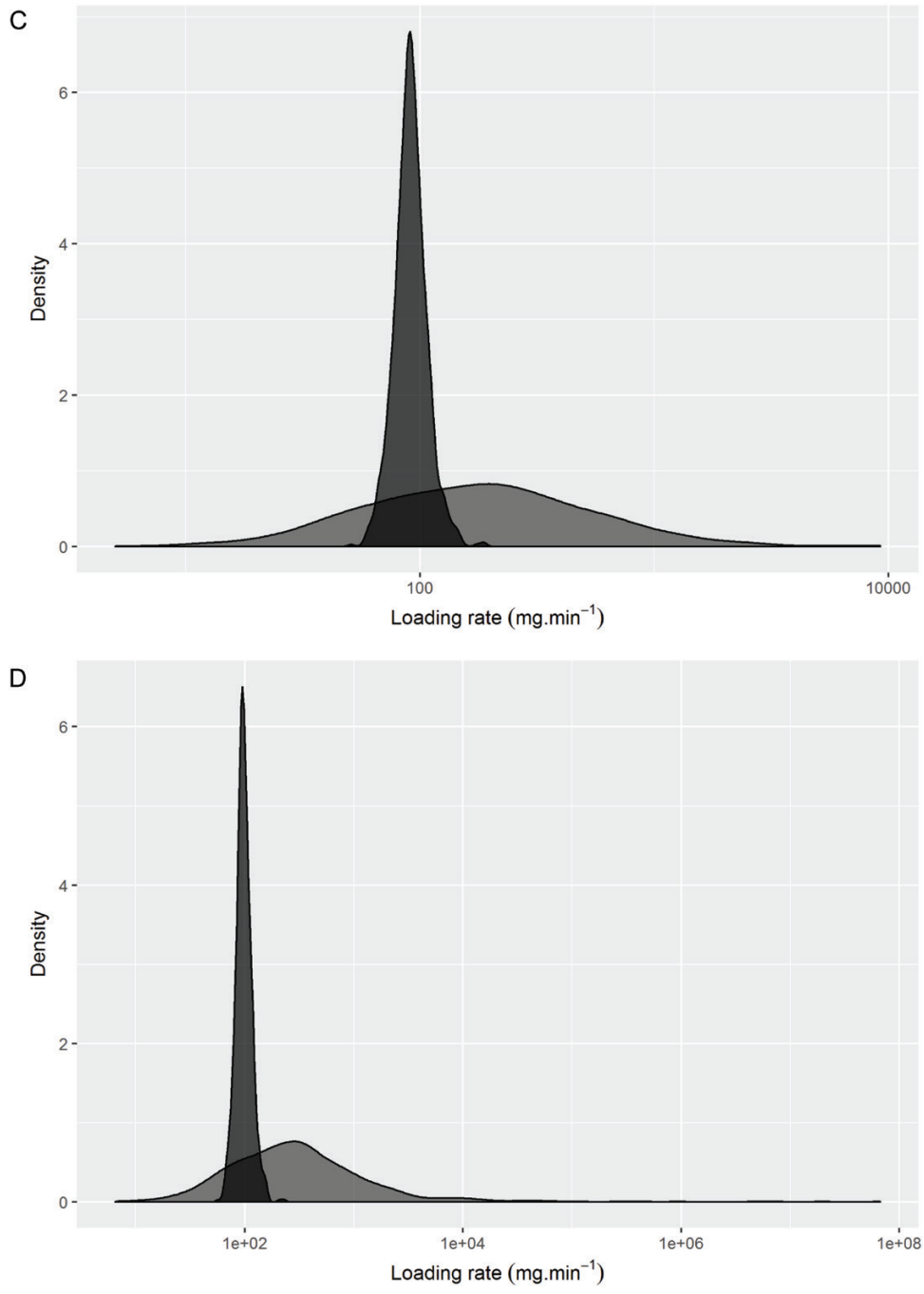

Figure 2. Continued.

receiving container. The task was repeated five times until the bottle had been emptied, and then repeated with a second 5 l bottle, i.e. 10 l of fluid were decanted in total in this exposure scenario (a more detailed task description is provided in Franken *et al.* (2019). The study took place in a ~39 m^3 room with ~33 ACH. The tracer analyte within the dipping fluid was Tinopol SWN at a weight fraction of 0.2% within the product-in-use.

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Table 5. Summary statistics for model parameters and derived variables for case study 2.

Variable	Prior		Posterior	
	Median	95% CI	Median	95% CI
μ	5.16	3.08, 7.29	4.51	4.20, 4.85
σ_{total}	0.86	0.24, 3.32	0.43	0.29, 0.72
$\sigma^2_{bw}/\sigma^2_{ww}$	0.39	0.02, 7.17	0.33	0.03, 3.18
GM	174.3	21.7, 1468.4	90.8	66.6, 127.4
LTA	265.5	27.6, 10 680.5	96.9	70.9, 138.8

The calculated scores for this case study were of $D_{\text{hands}} = 0.009$, $E_{\text{hands}} = 13.5$, and $T_{\text{hands}} = 0.015$. The calculated exposure rate is given in equation (15).

$$\text{CDARTscore} = 1.14 \times (0.009 + 87.4 \times 0.015 + 5.02 \times 13.5) = 78.76\,\text{mg}\,\text{min}^{-1} \quad (15)$$

The direct emission and direct contact accounted for approximately 98% of the calibrated dART score.

In this worked example, calculations of the GM and 90th percentiles of the cumulative distribution of the exposure distribution (corresponding to equation (11) with $z_\alpha = 1.6449$ are demonstrated). Calculations of these summary statistics based upon the prior distribution are given in Fig. 3a and b, with the median and a 95% credible interval indicated in the plot.

The experimental study described above was conducted by four volunteers who each undertook four replicates of the task, leading to 16 measurements and good information to distinguish between within- and between-worker sources of variability. Task duration was between 5 and 7 min. The exposure rate to product was derived (based upon measurements of analyte and concentration within the product-in-use), with a GM, GSD, and range of 17.28, 1.44, and 7.4–32.2 mg min^{-1}, respectively. Handwashing was used as the sampling method.

The prior was sequentially updated, with measurement data from the first volunteer initially utilized (4 measurements), with a further three updates incorporating measurement data from the second (8 measurements), third (12 measurements), and fourth (16 measurements) volunteers. An estimate and 95% credible interval for GM and ninetieth percentiles is shown in Fig. 3a and b for all sets of calculations in addition to those under the prior.

The results indicate that the inclusion of measurement data rapidly corrected the estimates from the prior, with a particularly rapid reduction in uncertainty (represented by the credible interval) even with the inclusion of only four measurements from a single volunteer. There was a further large reduction in uncertainty following the introduction of data from a second volunteer, which provided information with which to update the prior encoding of between-worker variability.

Discussion

In previous work, we presented and calibrated a mechanistic model for dermal exposure to the hands (mg min^{-1}) for exposure scenarios involving the use of low volatile liquid products and solids in liquids (Goede *et al.*, 2019; McNally *et al.*, 2019). Based upon this earlier work a central estimate of the GM with probability bounds could be estimated, using contextual information alone, for supported exposure scenarios. In this paper, a Bayesian mixed-effect model for dermal exposure to the hands (per minute of exposure) has been specified. The central estimate of exposure for a supported exposure scenario is provided by the calibrated mechanistic model. Additionally, between- and within-worker variability are specified, with prior distributions specified based upon data previously published by Kromhout *et al.* (1993, 2004) and McNally *et al.* (2019). Based upon prior alone estimates (with probability bounds) of percentiles of the cumulative distribution of exposures (such as the 90th or 95th percentiles) are now possible (as illustrated in the first and third worked examples). Furthermore, estimation of LTA exposures is possible (as illustrated in the second worked example). Estimates from the prior may be updated using any available measurement data relating to the exposure scenario, as demonstrated in worked examples. The third worked example demonstrates that a rapid reduction in uncertainty results from incorporating measurement data even when few data are available. Whilst inference is for the rate of deposition of product-in-use onto the hands per minute of exposure, exposure to analyte, cumulative loading onto the hands, and exposure to product/analyte per cm^2 can be easily computed. The dART model provides an estimate of the potential dermal exposure. As with the ART, the effect of personal protective equipment (PPE)—in this case protective gloves—is not part of the model. The protective effect of chemical protective PPE gloves can be accounted for through applying established reduction factors, with a factor of 10 or factor of 20 typically applied (TNsG, 2007). However, the appropriate factors may relate to manner of use, glove material, whether gloves are new or used, and whether they are designated as chemical protective (Creely and Cherrie, 2001; Fent *et al.*, 2009; Spaan *et al.*, 2013; Roff, 2015; Marquart

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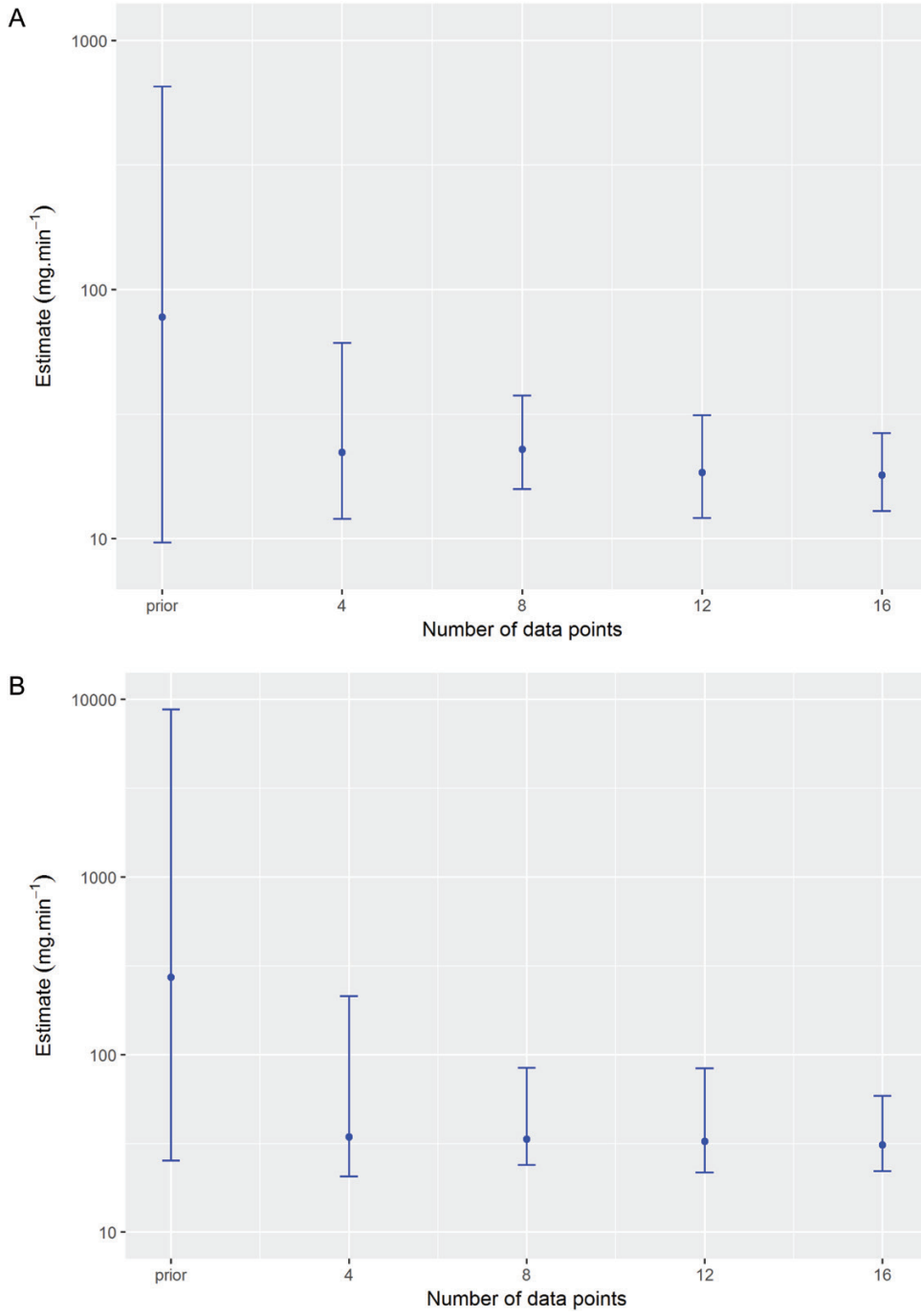

Figure 3. A comparison of the central estimate and a 95% credible interval under the prior and based upon posteriors using 4, 8, 12, and 16 data points: (a) GM; (b) ninetieth percentile.

et al., 2017). A reduction factor can be easily chosen and applied by a user (with appropriate justification).

The dART model builds upon the well-established ART framework, with the ART model providing estimates for the deposition pathway within the dART model. Whilst a similar exposure model may be desirable for consistency, some changes have been made to the form of the statistical model. One important

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simplification of the conceptual model (compared to the ART) is the absence of between company/site variability in equation (2). In their analysis of dermal exposure data, Kromhout *et al.* (2004) reported that between-factory (site) variability (variability across sites carrying out a similar task) was larger than residual (within-worker) variability. This apparent inconsistency with the form of the statistical model of the dART can be reconciled since the mechanistic model of the dART has the ability to distinguish between exposure scenarios with a much finer degree of granularity compared to the factory groups of Kromhout *et al.* (2004). In principle, the ART model can also distinguish between exposure scenarios with a fine degree of granularity, yet between company variability is still accounted for within the exposure model. There are residual differences between companies that are not fully captured by the mechanistic model, however in practical use an exposure scenario may be constructed for the 'average' company associated with the scenario, with small differences in room volume, ventilation, use rate, etc. absorbed into between-company variability; the exposure scenarios included in the exposure measurement database of the ART (Schinkel *et al.*, 2013) are widely defined in this manner. As a consequence of the omission of a between company variance component in the dART statistical model the exposure scenarios are necessarily more tightly defined for dermal exposure. In our experience of coding exposure scenarios for model calibration we found small changes in some determinants such as tool length, degree of automation, frequency of contacts with contaminated surfaces, etc. could make a large difference to scores: a scenario dominated by direct emission in one workplace may have a substantial contribution from contact transfer in other workplaces. Given such differences in the potential for dermal exposure (as estimated by the dART mechanistic model), in what appear to be broadly similar exposure scenarios, we believe this tighter definition of an exposure scenario is necessary in general. Additionally, for many tasks, particularly related to spraying, a between-company component is not applicable since in these exposure scenarios work is undertaken by sole traders and the between company component only makes sense for a nesting of workers-within-company.

A second important difference is in the specification of priors for variance components. For the ART, a database of approximately 20 000 chemical (inhalation) exposures obtained from in excess of 500 groups of workers across a variety of industries [compiled by Kromhout *et al.* (1993)] was used in McNally *et al.* (2014). A statistical analysis of the variance components facilitated the estimation of log-normal prior distributions that quantified the variability in between- and within-worker standard deviations, σ_{bw} and σ_{ww}, respectively. However, the available data on variability in dermal exposures were too weak, due to limited replicates, to allow for identification of the variance components. Therefore, a less direct approach has been used, based upon two steps: (i) specification of a prior for total variability in dermal exposure; (ii) specification of a prior for the ratio of between- to within-worker variation. The second step makes use of the larger volume of data available for variability in inhalation exposures. As noted above, the ART is used directly for providing the deposition score in the dART model and for scenarios where the deposition pathway is dominant this assumption appears reasonable. For exposure scenarios where the direct emission and direct contact and contact transfer pathways are dominant, and where worker behaviour might play an important role, the use of data on inhalation exposures is a potential source of error. However, we note that estimates of the GM and percentiles of the cumulative distribution of exposures are insensitive to this prior. Whilst inference about LTA exposure is sensitive to the prior for the ratio of between- to within-worker variation, our testing indicates that estimates from the prior result in very wide positive skewed distributions for percentiles of the LTA and the true (but unknown) value is likely to lie within this wide distribution. The prior estimates are rapidly refined even with small measurement datasets. Even with relatively poor data available for distinguishing between within- and between-worker variability it is important to include both components within the model, so that the information on these components contained within a given users measurement dataset is properly accounted for. If a suitable dataset is identified, the prior specification will be revised in future work such that within- and between-worker variance components are specified based upon only dermal exposure measurements.

The full Bayesian model of dART has been demonstrated by three diverse case studies, where initial estimates from the prior were updated using measurement data. Measurement data from cotton gloves and handwashing were utilized; the dART will support both of these dermal (hands) sampling methods. In the second and third worked examples, the estimates were dominated by a particular exposure pathway; these cases represent more extreme case studies compared to the calibration dataset (McNally *et al.*, 2019) where typically two pathways contributed to exposures in each scenario. The 'Spraying of cars' and 'Handling immersed objects' scenarios are interesting since they represent a spraying scenario where deposition was unimportant (due to the

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activity taking place in a spray booth) and a dipping scenario where direct emission and direct contact was unimportant (since the task involved careful dipping without splashing and avoided immersion of the hand). Insights about the exposure scenario may be gleaned through the structured assessment of the scenario necessitated by the mechanistic model and a study of the fractions of exposure attributed to different pathways. Thus, the mechanistic model alone offers an improvement in exposure scenario assessment and transparency over other tools for dermal exposure assessment. However, as a consequence of the complexity of the mechanistic model, the process of scoring is not currently a simple process. Both the scenarios used in calibration and the worked examples documented in this paper have required scoring by hand on a determinant-by-determinant basis, with careful assessment, scoring and verification of scores. In principle, a supported dermal exposure scenario requires only a few more user responses compared to the specification of an ART scenario for inhalation (hence deposition), therefore an extension of the existing web-based ART model is desirable. A demo web tool is currently under development. Given a mechanistic model estimate, estimates of all summaries of interest can be obtained through running an R script, and easily updated using measurement data. Once again, in order to reduce the possibility of user input error, it is desirable to fully encompass this facility into a user-friendly software tool.

McNally *et al.* (2019) noted that calibration of the dART required high-quality contextual data on a task so that scoring could be carried out with confidence, and reliable D_{hands}, T_{hands}, and E_{hands} scores compared with measurements on the task through the calibration model. In current work, the dART model has been demonstrated with similar high-quality datasets, where individual determinants could be precisely scored. However, in practical use, conservative assumptions (resulting in a higher dART score) can be made by a user of the tool when contextual data related to some determinants is weak, to ensure that where there is uncertainty, it translates to an over-estimate rather than an under-estimate of dermal exposure. Whilst this suggestion is a practical approach to accommodating imperfect information, this suggested approach would be impractical when the entire task is poorly documented.

Finally, we comment briefly on two outstanding technical issues that require attention prior to the deployment of a finished tool. Firstly, the dART currently has a tendency to over-predict exposure to the hands; this is as a direct consequence of a calibration dataset dominated by measurements from cotton gloves, which due to their capture efficiency have a tendency to over-estimate exposure to the hands. Both the mechanisms of retention and removal of product from the hands, which are particularly important for scenarios where the product loading rate is high, are yet to be coded. A correction will need to be applied both to the mechanistic model of the dART and to any measurement data collected using cotton gloves in order to derive estimates of product loading and retention onto the hands. Conversely, under-estimates of exposure may be obtained from handwashing and also need correcting for. Secondly, the loading capacity of the hands (loading saturation) must also be accounted for in the model to ensure that unrealistically large predictions of dermal exposure, that exceed the capacity of the hands, are not made. Loading saturation of the hands was accounted for in calibration (McNally *et al.*, 2019) through treating measurements as right censored. A similar treatment of measurement data could be applied within the dART model (equation (2)), however an upper bound on the estimate from the mechanistic model is also required to deal with a subset of exposure scenarios, including scenarios involving immersion of the hands, where the retention capacity of the skin is rapidly reached. Downstream calculations such as total loading onto the skin also need adjusting, to ensure that the retention capacity of the hands is not exceeded. Loading rate, task duration, and viscosity of the product-in-use will be important variables that influence the loading of product. It is important that product-in-use feeds into calculations rather than an analyte since the loading rate of product and retention of product are the limiting factors in determining exposures to an analyte of interest—it could result in a considerable over-estimate if a minor fraction analyte was considered. It is our intention to fully account for loading saturation, retention, and removal in future development of a software tool.

Supplementary Data

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

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Conflict of interest

The authors declare no conflict of interest.

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Data availability

The measurement data and R code underlying the worked examples presented in this work are available in online supplementary materials.

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