



**HAL**  
open science

## A brief review on models for birds exposed to chemicals

Dominique Lamonica, Lison Charvy, Dave Kuo, Clémentine Fritsch, Michael Coeurdassier, Philippe Berny, Sandrine Charles

► **To cite this version:**

Dominique Lamonica, Lison Charvy, Dave Kuo, Clémentine Fritsch, Michael Coeurdassier, et al.. A brief review on models for birds exposed to chemicals. 2024. hal-04438562v2

**HAL Id: hal-04438562**

**<https://univ-lyon1.hal.science/hal-04438562v2>**

Preprint submitted on 15 Feb 2024

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial - NoDerivatives 4.0 International License

1 A brief review on models for birds exposed to  
2 chemicals

3 Dr. Dominique LAMONICA<sup>1,2\*</sup>, Mrs. Lison CHARVY<sup>3</sup>, Dr.  
4 Dave KUO<sup>4</sup>, Dr. Clémentine FRITSCH<sup>5</sup>, Dr. Michaël  
5 COEURDASSIER<sup>5</sup>, Prof. Philippe BERNY<sup>6</sup> and Prof.  
6 Sandrine CHARLES<sup>1</sup>

7 <sup>1</sup>University Lyon 1, Laboratory of Biometry and Evolutionary  
8 Biology - UMR CNRS5558, 43 boulevard du 11 novembre 1918,  
9 Villeurbanne Cedex, 69622, France.

10 <sup>2\*</sup>Research Institute for Development, BotAny and Modeling of  
11 Plant Architecture and Vegetation - UMR AMAP, TA A51/PS2,  
12 Montpellier Cedex 05, 34398, France.

13 <sup>3</sup>INSA Lyon, Biosciences department, 20 avenue Albert Einstein,  
14 Villeurbanne, 69100, France.

15 <sup>4</sup>Institute of Environmental Engineering (GIEE), National Taiwan  
16 University, No. 1, Sec. 4, Roosevelt Rd., Taipei, 106, Taiwan.

17 <sup>5</sup>UMR 6249 Chrono-environnement, CNRS - Université de  
18 Franche-Comté, 16 route de Gray, Besançon cedex, 25030, France.

19 <sup>6</sup>UR ICE, VetAgro Sup Campus Vétérinaire de Lyon, 1 Avenue  
20 Bourgelat, Marcy l'étoile, F-69280, France.

21 \*Corresponding author(s). E-mail(s): [dominique.lamonica@ird.fr](mailto:dominique.lamonica@ird.fr);

22 **Abstract**

23 *“A Who’s Who of pesticides is therefore of concern to us all. If we are going to*  
24 *live so intimately with these chemicals eating and drinking them, taking them*  
25 *into the very marrow of our bones - we had better know something about their*  
26 *nature and their power.”* — Rachel Carson, Silent Spring.  
27

28 In her day, Rachel Carson was right: plant protection products  
29 (PPP) like all the other chemical substances that humans increas-  
30 ingly release into the environment without further precaution, are  
31 among our worst enemies today (Bruhl and Zaller, 2019; Naidu  
32 et al, 2021; Tang et al, 2021; Topping et al, 2020). All com-  
33 partments of the biosphere, air, soil and water, are potential  
34 reservoirs within which all species that live there are impaired.  
35 Birds are particularly concerned: PPP are recognized as a fac-  
36 tor in the decline of their abundance and diversity predominantly  
37 in agricultural landscapes. Due to the restrictions on vertebrates  
38 testing, *in silico* based approaches are an ideal choice alterna-  
39 tive given input data are available. This is where the problem  
40 lies as we will illustrate in this paper. We performed an extensive  
41 literature search covering a long period of time, a wide diver-  
42 sity of bird species, a large range of chemical substances and as  
43 many model types as possible to encompass all our future need  
44 to improve environmental risk assessment of chemicals for birds.  
45 In the end, we show that poultry species exposed to pesticides  
46 are the most studied at the individual level with physiologically  
47 based toxicokinetic models. To go beyond, with more species, more  
48 chemical types, over several levels of biological organization, we  
49 show that observed data are crucially missing (Gilbert, 2011).  
50 As a consequence, improving existing models or developing new  
51 ones could be like climbing Everest if no additional data can be  
52 gathered, especially on chemical effects and toxicodynamic aspects.

53 **Keywords:** ecotoxicology, avian species, toxicokinetic-toxicodynamic models,  
54 drug, diet.

## 55 1 Introduction

56 As early as 1962, Rachel Carson warned about the devastating effects of plant  
57 protection products (PPP) on terrestrial vertebrates in her pioneering book  
58 *Silent Spring* (Carson, 1962). Later in 1967, Ratcliffe reported that birds  
59 ingesting the synthetic pesticide DDT (dichloro-diphenyl-trichloroethane) had  
60 a tendency to lay eggs with thin shells that broke prematurely in the nest.  
61 This was confirmed by Cade et al (1971) as resulting in marked population

62 declines, a problem that has driven bald eagles, the national symbol of the  
63 United States, along with peregrine falcons and other bird species, to the  
64 brink of extinction, with populations collapsing by up to 80%. Since then,  
65 all around the world, extensive studies have been carried out to understand  
66 the mechanisms underlying this phenomenon. The results of these studies  
67 are summarized in a recent collective expertise (ESCo, [Pesce et al \(2021\)](#)),  
68 especially chapter 9 ([Mamy et al \(2022\)](#), p623-720) focusing on terrestrial  
69 vertebrates to report on the state-of-the-art about: (i) active substances,  
70 types or families of PPP for which effects on wildlife are proven, probable,  
71 possible or null; (ii) the relationship between the exposure features in different  
72 groups of terrestrial vertebrates and the induced effects; (iii) the main mech-  
73 anisms (in particular direct and indirect ones) inducing the main effects; (iv)  
74 the identification of the most influential environmental factors (agronomic,  
75 ecological...); (iv) the impact of PPP on functions and ecosystem services  
76 provided by terrestrial vertebrates.

77

78 Basically, [Mamy et al \(2022\)](#) identified as highly probable the causal link  
79 between the use of PPP and the decline in invertebrate and bird populations  
80 observed over several decades, particularly in agricultural areas, in interaction  
81 with landscape simplification. Depending on the bird species and their diet,  
82 PPP impacts are mainly the result of either a direct effect (*e.g.*, ingestion  
83 of PPP-treated seeds by granivorous birds) or an indirect effect (*e.g.*, reduc-  
84 tion of food resources due to the decline of prey); see Chapter 9 in [Mamy](#)

85 [et al \(2022\)](#) for more details. Environmental monitoring networks in various  
86 European countries, including France, have revealed a large number of cases  
87 of PPP poisoning of birds in the vicinity of agro-ecosystems. For granivorous  
88 birds, the recorded cases since the beginning of the 2000s are mostly caused  
89 by the ingestion of seeds treated with neonicotinoids ([Bishop et al, 2018](#)),  
90 more specifically imidacloprid ([Rogers et al, 2019](#)). For insectivorous birds,  
91 the impact of PPP is mainly expressed indirectly, through the decline in  
92 food resources. Several studies in Europe have **demonstrated the existence of**  
93 **significant correlations** between the use of PPP and the concomitant decline  
94 in insect communities and bird populations ([Hallmann et al, 2014](#); [Bowler](#)  
95 [et al, 2019](#); [Møller, 2019](#)). **In addition to these correlations, effects through**  
96 **the consumption of contaminated prey have recently been demonstrated by**  
97 **a multi-residue analysis of the diet of nestlings** ([Poisson et al, 2021](#)); these  
98 **effects, which lead to the decline of certain populations, are mainly due to the**  
99 **presence of neonicotinoids in the environment** ([Humann-Guilleminot et al,](#)  
100 [2021](#)). Apart from the lethal effects of PPP, flight efficiency and orientation  
101 of birds may also be impaired in response to exposure. Such sublethal effects  
102 have been observed, for example, in migratory birds stopping over in agricul-  
103 tural areas, thus compromising the smooth running of the critical migration  
104 period ([Eng et al, 2017, 2019](#)).

106 The field of modeling has been particularly prolific in recent years, for example  
107 in the prediction of contaminant transfer based on the physico-chemical char-  
108 acteristics of the substances involved, combined with scenarios incorporating  
109 different types of crops, climate and soil (Servien et al, 2022). But numerous  
110 models have also been developed to better describe how organisms accumulate  
111 the chemicals and how the internal damages translate into effects on their life  
112 history traits (Larras et al, 2022b). Modeling is also repeatedly mentioned as  
113 a potential solution for integrating the processes involved at different spatial  
114 and temporal scales. For example, it is not uncommon in the literature to  
115 find work that combines ecotoxicological models, to describe the impacts of  
116 PPP, with ecological models, which describe the links between organisms and  
117 the functions they ensure within ecosystems. In particular, there are spatially  
118 explicit models that take into account not only the exposure of organisms,  
119 but also the toxic potential of PPP and the adverse effects they have on  
120 demography, while taking into account variability in both the landscape and  
121 exposure (Topping et al, 2005, 2016; Topping and Weyman, 2018; Topping  
122 et al, 2020). Nevertheless, as modeling strongly relies on the collection of  
123 experimental data and the metadata to which they are associated, data avail-  
124 ability is the major constraint to which model building and the testing of  
125 their performances faces, especially at large spatial and temporal scales. All of  
126 this finally prevents a wider use of models in environmental risk assessment.

128 An interesting perspective of the use of population modeling is the possibility  
129 to extrapolate bio-monitoring data related to PPP bioaccumulation or specific  
130 effects in terms of population risk of extinction. Based on a matrix population  
131 model, [Goutte et al \(2018\)](#) provided a nice illustration with the South polar  
132 skua, a large seabird, for which long term demographic monitoring disclosed  
133 a possible effect of an organochlorine insecticide on the breeding success, thus  
134 compromising the population viability. One of the key points of population  
135 models is their ability to support extrapolation from one species to another,  
136 as illustrated for birds by [Etterson et al 2017](#). Such a rapid cross-species  
137 transposition of population models (especially stage-structured ones) benefits  
138 from the recent construction of large ecological databases gathering together  
139 demographic traits particularly helpful in conservation science. For instance,  
140 [De Zwaan et al.](#) have recently compiled a huge data set of alpine breeding  
141 records for 1,310 bird species, representing 12.0% of extant species and cover-  
142 ing all major mountain regions across the five continents, except Antarctica  
143 ([de Zwaan et al, 2022](#)). **Benefiting of such data collections is the condition to**  
144 **support parameter inference for population models, especially when a large**  
145 **number of species is involved. Such data bases are also particularly helpful**  
146 **when ranking species vulnerabilities is required in relationship with the dif-**  
147 **ferent uses of PPP** ([Forbes et al, 2015](#); [Etterson et al, 2017](#)).

148

149 The EU Regulation 1107/2009 defines all requirements before placing PPP on  
150 the market, in association with data requirements from regulations 283/2013

151 and 284/2011. In particular, an assessment is required regarding the risks  
152 for bird reproduction when they are exposed to PPP. In this perspective,  
153 the OECD guideline 206 provides the way data must be collected through  
154 standard toxicity test protocols whereby birds are exposed to the active  
155 substance of interest for a period of 20 weeks. However, the expected expo-  
156 sure period of active substances and their numerous degradation products in  
157 field (as determined by EFSA guidelines), can be much shorter thus creating  
158 disparities between both methodologies. For non-vertebrate species, such an  
159 issue can be overcome by additional testing. However, owing to the need to  
160 avoid vertebrate testing, this option is not valid for birds. Therefore, the use  
161 of *in silico* approaches predicting toxicity endpoints for birds can be helpful  
162 ([European Food Safety Authority et al, 2023](#)). In particular, toxicokinetic  
163 (TK) models, relating the exposure concentration to the fate of chemicals  
164 within an organism, coupled with toxicodynamic (TD) models, that make the  
165 link between cellular, biochemical and physiological damages and individual  
166 effects on life history traits, are potentially useful tools to refine risk assess-  
167 ment of PPP for birds, especially under a regulatory framework where such  
168 models remain still underused.

169

170 EFSA recently formulated recommendations to develop open source generic  
171 physiologically based TK (PBTK) models for a range of relevant species  
172 among which birds play an important role ([European Food Safety Authority  
173 et al, 2023](#)). [Larras et al \(2022a\)](#) also established how huge is the gap between



174 the set of models used in PPP regulatory reports and those existing in the  
175 literature, thus highlighting the need for the implementation of more sophis-  
176 ticated models into PPP regulation. With the idea of describing the whole  
177 cascade of impairments, from the exposure conditions to the apical effects,  
178 PBTKTD models clearly appear as the most appropriate tool to focus with  
179 effects at the individual level in the perspective of moving towards the next  
180 generation risk assessment practice. Nevertheless, accounting for molecular  
181 initiating events (usually based on omic-type data) and the subsequent series  
182 of intermediate steps and key events leading to an adverse outcome is also  
183 of great interest to provide a clear-cut mechanistic representation of critical  
184 toxicological effects; this is what are allowing Adverse Outcome Pathways  
185 (AOP) approaches ([Vinken, 2013](#)). Hence, combining AOP with PBTKTD  
186 models could help in finely refining risk assessment. Similarly, linking individ-  
187 ual effect models such as PBTKTD models with population and community  
188 ones could complement protection schemes including both direct and indirect  
189 effects ([Forbes et al, 2017](#)). One inside the other, PBTKTD models are the  
190 key pillars of a comprehensive approach along the gradient of effects at all  
191 levels of biological organization ([European Food Safety Authority et al, 2023](#)).

192

193 However, as already stated above, moving towards more complex models  
194 necessarily means benefiting of more data. In particular, no generic PBTKTD  
195 models are available for refined environmental risk assessment of birds and  
196 mammals, since data requirements are very high ([Astuto et al, 2022](#)). Here

197 lies the dilemma facing PPP risk assessors for birds, *i.e.* discourage the use  
198 of additional vertebrate testing, while acquiring sufficient and appropriate  
199 data to improve assessment models. Clearly, the way forward seems to be  
200 an intensive search of the literature for information already collected. In this  
201 context, this paper presents a state-of-the-art of the different kinds of models  
202 that have been developed in the last decades to sustain the deciphering of  
203 chemical effects on birds. Notice that we do not detail the different types of  
204 model (done by [Larras et al \(2022b\)](#); [Astuto et al \(2022\)](#)) to focus on where  
205 reusable data feeding these models can be caught up.

206

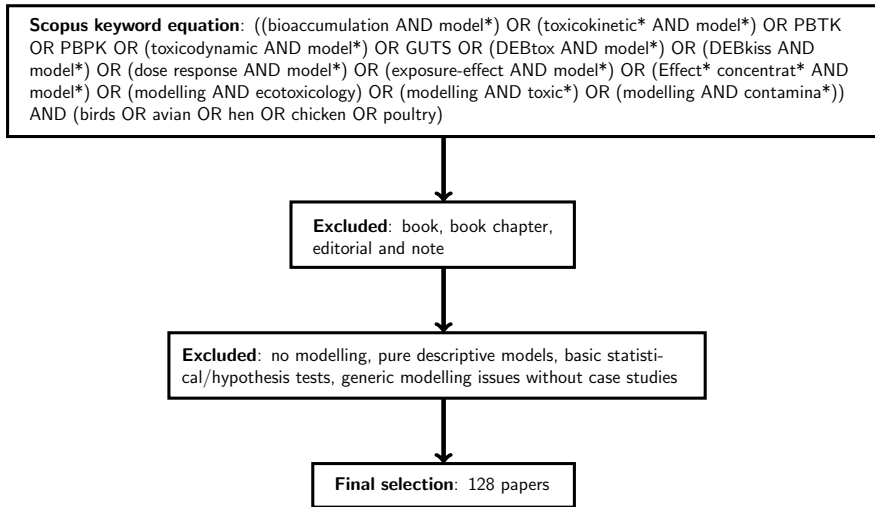
207 After giving full details on the bibliographical methodology we adopted, we  
208 present the general trends that emerge from our corpus of articles. We give a  
209 breakdown of models by type (e.g., TD, food web) and by level of organiza-  
210 tion (e.g., individual, community), before specifically examining bird models  
211 crossing model type with their inputs (e.g., exposure routes) and outputs (e.g.,  
212 measured internal concentration). Then, we conclude in identifying the main  
213 gaps, as well as some ideas for overcoming them, and to go beyond.

## 214 2 Methods

215 Scientific articles were screened within several bibliographic databases includ-  
216 ing Clarivate Web of Science ©, PubMed ([McEntyre and Ostell, 2002](#)),  
217 Google Scholar ([López-Cózar et al, 2019](#)), Scopus ([Baas et al, 2020](#)), and the  
218 co-authors' personal databases (those provided by [Kuo et al \(2022\)](#), > 500

219 entries, and [Mamy et al \(2022\)](#), > 2500 entries). The final paper collection  
220 was achieved in February 2023, covering a period from the end of the seventies  
221 until today.

222  
223 The bibliographic queries were performed following several steps summarized  
224 in [Figure 1](#). Google Scholar was first requested with an initial Scopus keyword  
225 equation (data not shown) providing a preliminary collection of few papers that  
226 were scrutinized through titles and abstracts to refine the final query equation.  
227 Then, the above-mentioned bibliographic databases were all required with the  
228 final Scopus keyword equation ([Figure 1](#)). From there, we excluded references  
229 of books, book chapters, editorials and notes, to only keep peer-reviewed jour-  
230 nal articles. Finally, we excluded all papers not referring to modeling issues. In  
231 particular, we excluded papers without any model, or containing pure descrip-  
232 tive models, such as those with only basic hypothesis testing methods. Purely  
233 general papers without case studies were also removed from our collection.



**Fig. 1** Diagram of the bibliographic method we used to build the final corpus of scientific papers analyzed in this review.

234 Additionally to the terms we used in our query, our paper collection was  
 235 only limited to research and review papers published in peer-reviewed jour-  
 236 nals and written in English. At the end of the process, we had a total  
 237 of 130 papers (97 from the bibliographic databases and 33 from the co-  
 238 authors' personal databases). All these papers have been gathered together  
 239 within a metadata file (in comma separator value format) available at  
 240 <https://doi.org/10.5281/zenodo.7685817>. In addition to the classical fields  
 241 defining a bibliographic reference, this metadata file records information  
 242 about the biological species (wild/domestic, feeding regime, common and  
 243 Latin names), the chemical substances (group, name, CAS number) and/or  
 244 the models (model type, level of biological organization that is concerned)  
 245 that have been used by the authors. The metadata file also inventories the

246 exposure routes and the measured endpoints provided in the papers. In the  
247 end, the metadata file has 130 rows and 59 columns. A critical step in the  
248 assembly of this metadata was the identification of the model type used by  
249 the authors. To proceed, we first separated models processing at the individ-  
250 ual level, that is the most employed. Among them, dose-response models were  
251 easy to classify. For the rest of the papers, a careful check within the different  
252 sections of the papers finally allowed us to clearly identified the type of model.

253

254 The paper collection, no reference being duplicated, was imported into the R  
255 software (R Core Team, 2022) and analyzed to quantify the scientific produc-  
256 tion per year, feeding groups (distinguishing between carnivores, frugivores,  
257 granivores, herbivores, insectivores, omnivores, and piscivores), chemical  
258 groups (according to their usage), level of biological organization (individual,  
259 population community)) and model types (see Table 1 hereafter). **In the end,**  
260 **our paper collection led us to identify the main research tendencies related to**  
261 **the employment of models in support of a better deciphering of the impacts**  
262 **of chemical substances on birds. This also allowed us to highlight advantages**  
263 **and drawbacks of these models.**

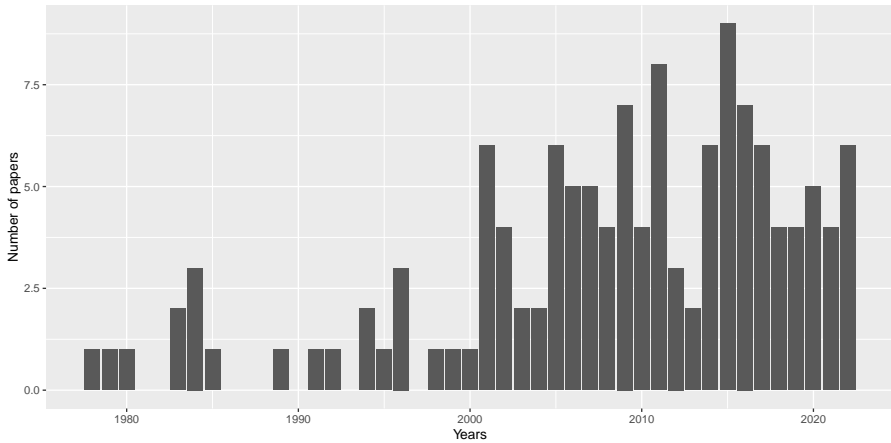
264

265 Additionally to the metadata file, the supplementary material provided at  
266 <https://doi.org/10.5281/zenodo.7685817> contains all resources to identically  
267 reproduce the figures we are presenting below.

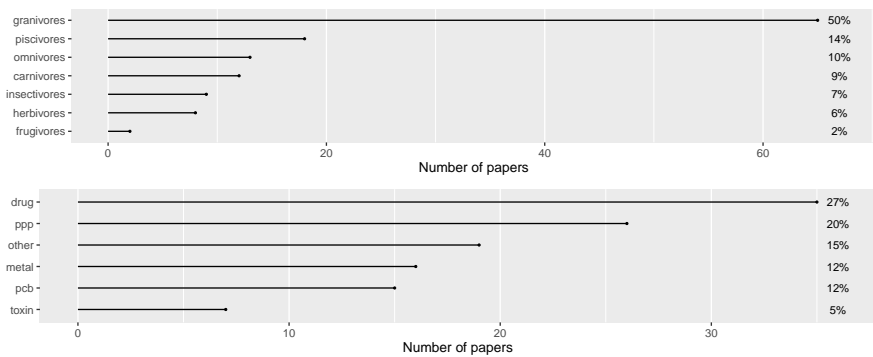
### 3 Results

Without claiming exhaustivity, our collection of papers (fully listed at the end of the manuscript) shows that studies involving models in bird ecotoxicology started to be published during the late seventies, with a slight increase from 2000, then only few papers each year (Figure 2). Half of the 130 papers focused on granivores (namely, seed-eating birds (Anadón et al, 2011; Fournier et al, 2015; Pollet et al, 1985)). Among wild species, groups of carnivores (*i.e.*, predatory birds, such as raptors (Azmanis et al, 2021; Engelman et al, 2012; Rattner et al, 2020)) and piscivores (*i.e.*, birds foraging for and eating fish or other sea life (An et al, 2006; Goutte et al, 2018; Sánchez et al, 2019)) are similarly represented (between 9 and 14 %) (Figure 3, upper panel). A bit less than one third of the papers investigated drugs, while around 20% of them focused on PPP (Figure 3, lower panel). Regarding trace metallic elements, mercury and derivatives have been the most studied (Smith et al, 2009; Nichols et al, 2010; Jackson et al, 2011). Exposure routes, all chemical substances combined, covered the full range of bird feeding regimes via their food sources. Exposure via injection or oral administration were the most widely studied regarding toxicokinetic-toxicodynamic aspects. Last but not least, exposure models describing the contamination routes, dealt with environment (*i.e.*, exposure via air, or not specified), food, or more rarely water *via* drinking (Nelson et al, 1998; Conder et al, 2009; Moore et al, 2018).

290 The salient point, which is not directly visible from Figure 3 but which follows  
291 directly from it, is the total absence of studies that address the effects of PPP  
292 on bird species of interest for the regulatory environmental risk assessment.  
293 For example, European regulations 283/20134 and 284/20135 recommend  
294 determining the acute oral toxicity of an active substance to a quail species  
295 (Japanese quail, *Coturnix coturnix japonica* or bobwhite quail, *Colinus vir-*  
296 *ginianus*), while data on additional species, such as *Serinus canaria*, may be  
297 requested by other legislative frameworks ([European Food Safety Authority](#)  
298 [et al, 2023](#)). These quail and canary species were totally absent from our set of  
299 studies. On the contrary, poultry species are studied a lot, and the most, with  
300 a majority of the related papers employing toxico-/pharmacokinetic (TPK)  
301 models. Laying hens and broiler chicken species were both studied, the latter  
302 being much more used (47 out of 130 papers). Regarding chicken, exposures  
303 to drugs and PPP were the most investigated contaminants, while modeling  
304 speaking, TPK models are almost exclusively used among the 47 papers.



**Fig. 2** Number of papers published per year among our collection of 130 scientific articles.



**Fig. 3** Number of papers per feeding groups (upper panel) and chemical groups (lower panel) among our collection of 130 scientific articles.

305 About 80% of the studies were conducted at the individual level (Table 1, left  
 306 panel). Those papers mainly addressed toxicokinetics or bioaccumulation of  
 307 one or several substances in the organisms, leading to model concentration  
 308 changes over time either in the whole body ([Abou-Donia, 1979](#); [Tarazona et al,](#)



309 2015), or in different organs (Bean et al, 2019; Suknikom et al, 2016), includ-  
310 ing eggs (MacLachlan, 2010; Hekman and Schefferlie, 2011). Toxicokinetic  
311 aspects of drugs in chicken or laying hens were the most frequent combination  
312 (Furusawa et al, 1996; Henri et al, 2017), investigating residues of chemical in  
313 muscles or eggs, which suggested food consumption purpose. Toxicodynamic  
314 and dose-response studies have also been conducted, describing the effect of  
315 a chemical at the individual level, over time or not (Eagles-Smith et al, 2009;  
316 Zhao et al, 2014). However, Toxicodynamic and dose-response studies were  
317 rarer, probably because they would imply experiments with vertebrates that  
318 are subject to restrictions. Another plausible explanation could be a lack  
319 of interest in toxic effects on laboratory species themselves, contrary to the  
320 indirect effects that its diet may have on human health (Rani et al, 2021). In  
321 this perspective, TPK models are the appropriate tools.

322

323 At the population level, several model frameworks have been employed such  
324 as individual-based models (Hallam et al, 1996), matrix demographic models  
325 (Goutte et al, 2018), or Monte Carlo Markov Chain models (Bennett and  
326 Etterson, 2007). Such models describe the effect of a chemical at the popula-  
327 tion level, either by incorporating critical effect concentrations on the chosen  
328 endpoints (*e.g.*, survival, reproduction, behavior) together with an exposure  
329 scenario (Etterson and Bennett, 2013), or by directly negatively impacting

330 one or several vital rates, such as survival rate or reproductive success, com-  
331 pared to a scenario without contamination ([An et al, 2006](#)).

332

333 At higher levels of biological organization and/or with spatially explicit mod-  
334 els, studies are much rarer (less than 5%) (Table 1, right panel). Community  
335 level papers from our collection used food chain models to investigate bioac-  
336 cumulation via two case studies (organochlorine accumulated in Arctic birds  
337 ([Borgå et al, 2004](#)) and polychlorinated biphenyls accumulated in eggs of  
338 San Francisco bay birds ([Gobas and Arnot, 2010](#))). In our database spatially  
339 explicit models were population models including a compartment describing  
340 environmental changes and/or where birds were located in space, allowing to  
341 investigate for example habitat modification impact ([Nacci et al, 2005](#)), feed-  
342 ing habits ([Matsinos and Wolff, 2003](#)), or crop rotation ([Topping et al, 2005](#)).

343

**Table 1** Number (#) of papers per model type (left) and per level of organization (right), among our collection of 130 scientific articles.

Model type	Meaning or Based on	#	Biological level	#
TPK	Toxico-/Pharmaco-Kinetic	89	Individual	104
TD	Toxico-Dynamic	12	Population	22
DR	Dose response	4	Community	2
Energy-based	Dynamic Energy Budget theory	5	Landscape	3
ODE based	Ordinary Differential Equations	11		
IBM	Individuals or Agents	3		
Food web	Multiple trophic interactions	2		
Spatial	Spatially explicit	3		
Exposure	Exposure profile feature	13		
Other	Any other type	6		

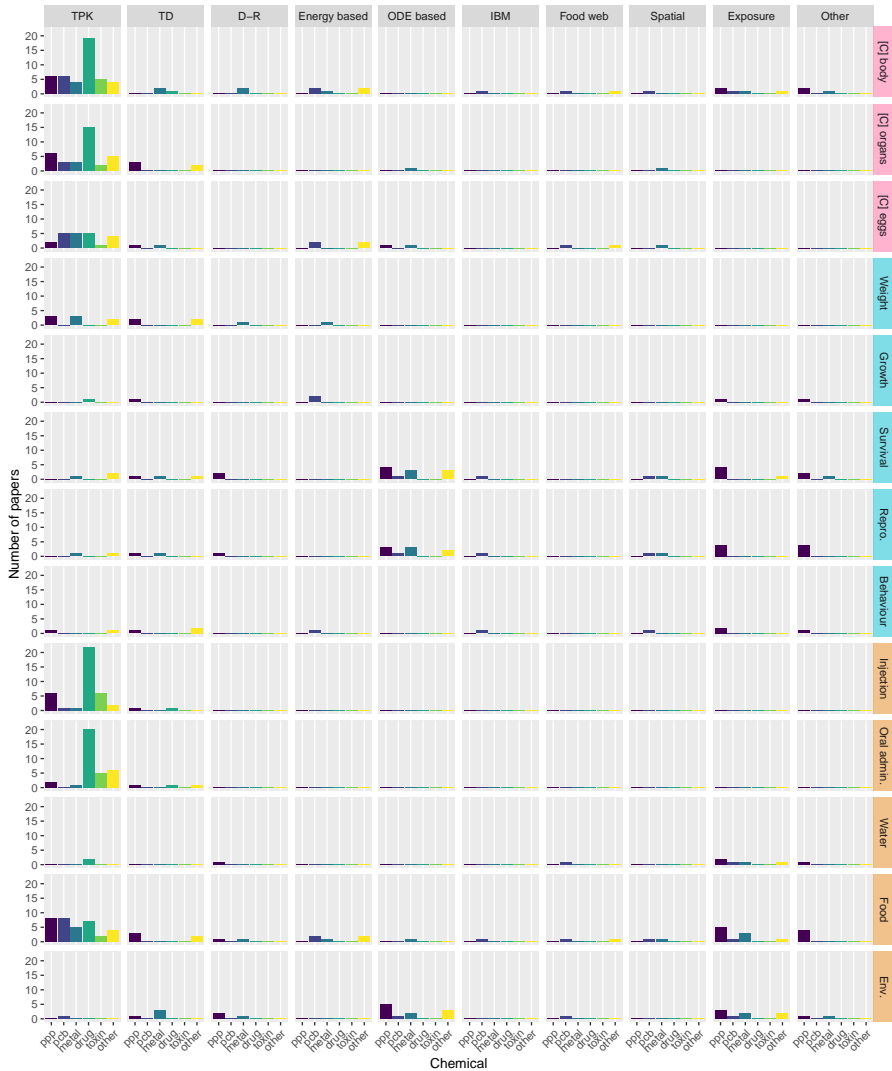
344 By crossing views on our paper collection, classified by both model types  
345 (columns) and either model outputs (measured internal concentration, pink  
346 lines / measured endpoints, blue lines) or model inputs (exposure routes,  
347 orange lines), we finely deciphered what were the main objectives of most  
348 of the studies on birds exposed to chemicals. As shown in Figure 4, most of  
349 the studies employed TPK models to investigate drug effects on birds after  
350 injection or oral administration (Kuo et al, 2022), by measuring the time  
351 course of internal concentrations at the whole organism level (Gögebakan and  
352 Eraslan, 2015), or distinguishing target organs (Yang et al, 2014).

354 Figure 4 (second column and blue lines) also clearly demonstrates that  
355 toxico/pharmaco-dynamics and dose-response analyses are under-represented  
356 (see also Table 1, left panel), which points to a crucial gap in observed data of  
357 chemical effects on bird life history traits. While the lack of toxico/pharmaco-  
358 dynamic models can be understood easily enough (due to their difficult  
359 handling and implementation), it is much more surprising to find so few  
360 studies involving dose-response models, while they are today the basis of the  
361 regulatory environmental risk assessment. Moreover, there are today no gen-  
362 eral accepted methods that are currently available for how to calibrate and  
363 validate toxicokinetic-toxicodynamics (TKTD) models without animal testing  
364 ([European Food Safety Authority et al, 2023](#)). As a consequence, due to the  
365 3R requirements ([European Parliament and European Council, 2010](#)), such a  
366 lack in effect quantifier models prevents to attempt interconnecting individual  
367 and population levels in the perspective of gaining in ecological relevance,  
368 while still including information for which it is easier to obtain experimental  
369 observations. Contamination via food represented the main exposure route  
370 ( $\sim 45\%$ ) within studies covered by our 130 papers (Figure 4, fourth orange  
371 line). For example, Meda *et al.* developed a physiologically based pharma-  
372 cokinetic model to investigate the main factors involved in the transfer of  
373  $\alpha$ -hexabromocyclododecane to broiler meat ([Méda et al, 2020](#)); [Fournier et al](#)  
374 ([2015](#)) assessed the impact of physiological characteristics of laying hen on  
375 the transfer of ingested PCBs to their eggs. Regarding exposure models, they  
376 have been developed to address levels of chemical contamination in the field,

377 mainly for PPP. For example, Moore *et al.* developed probabilistic models to  
378 estimate, during the breeding season and the spring and fall migrations, how  
379 many chlorpyrifos and malathion granules Kirtland's warblers ingest and,  
380 from that, the quantity of pesticide ingested (Moore *et al.*, 2018).

381

382 Among the 130 papers, some studies were generic in scope, but for differ-  
383 ent reasons. A total of 41 papers (31.5%) concerned several biological species  
384 that were simultaneously studied as exposed to a same chemical (Newsted  
385 *et al.*, 2006; Samuels and Ladino, 1984). A total of 45 papers (34.6%) reported  
386 effects of several chemicals on one bird species (Topping *et al.*, 2005; Wayland  
387 *et al.*, 2008). And only 8 papers out the 130 were general reviews covering a  
388 wide spectrum of species-compound combinations (see for example Kuo *et al.*  
389 (2022)). It is worth to note that only two papers dealt with the impacts of  
390 multiple stressors: the first on white-tailed eagle populations (Korsman *et al.*,  
391 2012); the second on the common loon (Nacci *et al.*, 2005). One of the most  
392 striking points of our review is that only 9 papers (~7%) gave access to raw  
393 data, potentially reusable for further studies.



**Fig. 4** Cross-view of the 130 papers analyzed in this review, categorized by model type (columns) and model outputs (measured internal concentration, pink lines, measured endpoints, blue lines) or model inputs (exposure routes, orange lines). At column-line intercepts, histograms show the number of papers as a function of the studied chemical(s).

394 Results displayed in Figure 4 also appeared in a limpид manner within the title-  
 395 based word cloud provided as graphical abstract. This word cloud specifically

396 emphasizes how frequent TPK studies applied to chickens were, as well as that  
397 toxico/pharmaco-kinetic models were equally frequently employed, while no  
398 chemical substances appeared more studied than another one.

## 399 **4 Conclusion**

400 Our bibliographic corpus showed a certain diversity in model types, chemicals,  
401 exposure routes and feeding groups. Nevertheless, we identified a huge gap in  
402 models dealing with chemical effects on birds at the individual level, even if  
403 we found a large collection of papers on toxico/pharmaco-kinetic aspects. This  
404 is far from being a negligible source of information. However, originally inter-  
405 ested in toxicokinetic-toxicodynamic models on birds exposed to PPP, it was  
406 clear that we would have very few previous studies at our disposal on which to  
407 capitalize. Focusing on bird species targeted by the regulatory environmental  
408 risk assessment and their exposure to PPP in addition, we ended up with no  
409 dedicated resources to draw on. Both bad and good news in the end. Indeed,  
410 we had found a new niche in which to innovate and develop new modeling tools  
411 to support next generation risk assessment for birds. In such a perspective, the  
412 key point will undoubtedly be the availability of raw data to build clever and  
413 comprehensible mechanistic effects models, generic enough to be employed for  
414 a wide battery of bird species and chemical compound combinations. Under  
415 the umbrella of Open Science, achieving such dreamed tools, should manda-  
416 torily imply full compliance to the FAIR data principles. To do so, we could  
417 recommend adding non invasive endpoint measurements on birds together with

418 the current practice of TPK studies, or *in vitro* studies that are considered  
419 as a good alternative to *in vivo* testing to better decipher TPK properties.  
420 Such data could advantageously support further development of the TPK part  
421 of TPK-TPD models, tools that now make sense to our community, which  
422 more broadly advocates the need to modernize wildlife risk assessment through  
423 improved collaboration, data sharing, application of standardized exposure  
424 scenarios, better communication of assumptions and uncertainties of models,  
425 and post-regulatory monitoring (Morrissey et al, 2023).

## 426 5 Supplementary Information

427 All supplementary information mentioned in this manuscript is available at  
428 <https://doi.org/10.5281/zenodo.7685817>.

## 429 6 Acknowledgment

430 This work was : (i) part of a tender project financially supported by EFSA  
431 (OC/EFSA/SCER/2021/07); (ii) based on a preliminary work performed by  
432 experts among co-authors within the framework of the collective scientific  
433 assessment commissioned by the French Ministries for Ecology, for Research,  
434 and for Agriculture on the effects of plant protection products on biodiversity  
435 and ecosystem services and published in May 2022; (iii) performed under  
436 the umbrella of the French GDR "Aquatic Ecotoxicology" framework which  
437 aims at fostering stimulating scientific discussions and collaborations for more  
438 integrative approaches in ecotoxicology. The authors would like to thank Dr.



439 Raphaël Pelissier & Dr. Philippe Verley from IRD (UMR AMAP, Montpellier,  
440 France) who supported the participation of Dr. Dominique Lamonica once  
441 she started in her new position as IT engineer in ecology.

442

443 **Ethics approval** Not applicable.

444

445 **Consent to participate** Not applicable.

446

447 **Consent for publication** All authors contributed to and agreed on the final  
448 version of the manuscript.

449

450 **Authors contributions** Dominique Lamonica and Lison Charvy: Paper  
451 collection, Metadata collection and curation. Dominique Lamonica: Metadata  
452 investigation, Methodology, Visualization, Analysis. Dominique Lamonica  
453 and Sandrine Charles: Writing - Original draft preparation. Sandrine Charles:  
454 Investigation, Supervision, Validation, Writing - Reviewing and Editing. Dave  
455 Kuo, Clementine Fritsch, Michaël Coeurdassier and Philippe Berny: Investi-  
456 gation, Reviewing and Editing.

457

458 **Funding** EFSA (OC/EFSA/SCER/2021/07).

459

460 **Competing interests** The authors declare no competing interests.

461

462 **Data, Material and/or Code availability** Data and code are available at  
463 <https://doi.org/10.5281/zenodo.7685817>.

## 464 References

- 465 Astuto MC, Nicola MRD, Tarazona JV, et al (2022) *In Silico* Methods for  
466 Environmental Risk Assessment: Principles, Tiered Approaches, Applica-  
467 tions, and Future Perspectives. In: Benfenati E (ed) *In Silico* Methods for  
468 Predicting Drug Toxicity, Methods in Molecular Biology, vol 2425. Springer  
469 Nature, p 589–636, <https://doi.org/10.1016/B978-0-12-811037-9.00023-0>
- 470 Baas J, Schotten M, Plume A, et al (2020) Scopus as a curated, high-  
471 quality bibliometric data source for academic research in quantitative science  
472 studies. *Quantitative science studies* 1(1):377–386. [https://doi.org/10.1162/](https://doi.org/10.1162/qss_a_00019)  
473 [qss\\_a\\_00019](https://doi.org/10.1162/qss_a_00019)
- 474 Bishop CA, Moran AJ, Toshack MC, et al (2018) Hummingbirds and bumble  
475 bees exposed to neonicotinoid and organophosphate insecticides in the fraser  
476 valley, british columbia, canada. *Environmental toxicology and chemistry*  
477 37(8):2143–2152. <https://doi.org/https://doi.org/10.1002/etc.4174>
- 478 Bowler DE, Heldbjerg H, Fox AD, et al (2019) Long-term declines of European  
479 insectivorous bird populations and potential causes. *Conservation Biology*  
480 33(5):1120–1130. <https://doi.org/10.1111/cobi.13307>

- 481 Bruhl CA, Zaller JG (2019) Biodiversity Decline as a Consequence of  
482 an Inappropriate Environmental Risk Assessment of Pesticides. *Frontiers*  
483 in *Environmental Science* 7:2013–2016. [https://doi.org/10.3389/fenvs.2019.](https://doi.org/10.3389/fenvs.2019.00177)  
484 [00177](https://doi.org/10.3389/fenvs.2019.00177)
- 485 Cade TJ, Lincer JL, White CM, et al (1971) DDE residues and eggshell changes  
486 in Alaskan falcons and hawks. *Science* 172(3986):955–957. [https://doi.org/](https://doi.org/10.1126/science.172.3986.955)  
487 [10.1126/science.172.3986.955](https://doi.org/10.1126/science.172.3986.955)
- 488 Carson R (1962) *Silent Spring*. Fawcett Publications, Inc., Greenwich, Conn.,  
489 [https://doi.org/10.1016/0027-5107\(77\)90059-8](https://doi.org/10.1016/0027-5107(77)90059-8)
- 490 Eng ML, Stutchbury BJ, Morrissey CA (2017) Imidacloprid and chlorpyrifos  
491 insecticides impair migratory ability in a seed-eating songbird. *Scientific*  
492 *Reports* 7(1):1–9. <https://doi.org/10.1038/s41598-017-15446-x>
- 493 Eng ML, Stutchbury BJ, Morrissey CA (2019) A neonicotinoid insecticide  
494 reduces fueling and delays migration in songbirds. *Science* 365(6458):1177–  
495 1180. <https://doi.org/10.1126/science.aaw9419>
- 496 European Food Safety Authority, Aagaard A, Berny P, et al (2023) Peer review  
497 of the pesticide risk assessment of the active substance *Reynoutria sach-*  
498 *linensis* extract. *EFSA Journal* 21(2):7790. [https://doi.org/10.2903/j.efsa.](https://doi.org/10.2903/j.efsa.2023.7790)  
499 [2023.7790](https://doi.org/10.2903/j.efsa.2023.7790)

500 European Parliament, European Council (2010) Directive 2010/63/EU on the  
501 protection of animals used for scientific purposes. Official Journal of the  
502 European Union L 276/33(20.10.2010):33–79

503 Forbes VE, Brain R, Edwards D, et al (2015) Assessing pesticide risks to  
504 threatened and endangered species using population models: Findings and  
505 recommendations from a CropLife America Science Forum. Integrated Envi-  
506 ronmental Assessment and Management 11(3):348–354. [https://doi.org/10.](https://doi.org/10.1002/ieam.1628)  
507 [1002/ieam.1628](https://doi.org/10.1002/ieam.1628)

508 Forbes VE, Salice CJ, Birnir B, et al (2017) A Framework for Predict-  
509 ing Impacts on Ecosystem Services From (Sub)Organismal Responses to  
510 Chemicals. Environmental Toxicology and Chemistry 36(4):845–859. [https:](https://doi.org/10.1002/etc.3720)  
511 [//doi.org/10.1002/etc.3720](https://doi.org/10.1002/etc.3720)

512 Gilbert N (2011) Data gaps threaten chemical safety law. Nature  
513 475(7355):150–151. <https://doi.org/10.1038/475150a>

514 Hallmann CA, Foppen RP, Van Turnhout CA, et al (2014) Declines in insec-  
515 tivorous birds are associated with high neonicotinoid concentrations. Nature  
516 511(7509):341–343. <https://doi.org/10.1038/nature13531>

517 Humann-Guillemot S, Laurent S, Bize P, et al (2021) Contamination by  
518 neonicotinoid insecticides in barn owls (*Tyto alba*) and alpine swifts (*Tachy-*  
519 *marptis melba*). Science of The Total Environment 785:147,403. [https://doi.](https://doi.org/https://doi.org/10.1016/j.scitotenv.2021.147403)  
520 [org/https://doi.org/10.1016/j.scitotenv.2021.147403](https://doi.org/https://doi.org/10.1016/j.scitotenv.2021.147403)

- 521 Larras F, Beaudouin R, Berny P, et al (2022a) A meta-analysis of ecotoxi-  
522 cological models used for plant protection product risk assessment before  
523 their placing on the market. *Science of the Total Environment* p 157003.  
524 <https://doi.org/10.1016/j.scitotenv.2022.157003>
- 525 Larras F, Charles S, Chaumot A, et al (2022b) A critical review of modelling  
526 approaches for environmental risk assessment due to pesticides. *Environ-*  
527 *ment Science and Pollution Research* 29:43,448–43,500. [https://doi.org/10.](https://doi.org/10.1007/s11356-022-19111-3)  
528 [1007/s11356-022-19111-3](https://doi.org/10.1007/s11356-022-19111-3)
- 529 Li L, Li D (2021) Inter-Individual Variability and Non-linear Dose-Response  
530 Relationship in Assessing Human Health Impact From Chemicals in LCA:  
531 Addressing Uncertainties in Exposure and Toxicological Susceptibility.  *Fron-*  
532 *tiers in Sustainability* 2:1–12. <https://doi.org/10.3389/frsus.2021.648138>
- 533 López-Cózar ED, Orduña-Malea E, Martín-Martín A (2019) Google scholar as  
534 a data source for research assessment. In: *Springer handbook of science and*  
535 *technology indicators*. Springer, p 95–127
- 536 Mamy L, Pesce S, Sanchez W, et al (2022) Impacts des produits phytophar-  
537 maceutiques sur la biodiversité et les services écosystémiques. Rapport de  
538 l'expertise scientifique collective. <https://doi.org/10.17180/0gp2-cd65>
- 539 McEntyre J, Ostell J (2002) *The NCBI handbook*. Bethesda (MD): National  
540 Center for Biotechnology Information (US)

- 541 Morrissey C, Fritsch C, Fremlin K, et al (2023) Advancing exposure assessment  
542 approaches to improve wildlife risk assessment. *Integrated Environmental*  
543 *Assessment and Management* 00:1–25. <https://doi.org/10.1002/ieam.4743>
- 544 Møller AP (2019) Parallel declines in abundance of insects and insectivorous  
545 birds in denmark over 22 years. *Ecology and Evolution* 9(11):6581–6587.  
546 <https://doi.org/https://doi.org/10.1002/ece3.5236>
- 547 Naidu R, Biswas B, Willett IR, et al (2021) Chemical pollution: A growing  
548 peril and potential catastrophic risk to humanity. *Environment International*  
549 156:106,616. <https://doi.org/10.1016/j.envint.2021.106616>
- 550 Pesce S, Mamy L, Achard AI, et al (2021) Collective scientific assessment as  
551 a relevant tool to inform public debate and policy-making : an illustration  
552 about the effects of plant protection products on biodiversity and ecosystem  
553 services. *Environmental Science and Pollution Research* 28:38,448–38,454.  
554 <https://doi.org/10.1007/s11356-021-14863-w>
- 555 Poisson MC, Garrett DR, Sigouin A, et al (2021) Assessing pesticides exposure  
556 effects on the reproductive performance of a declining aerial insectivore. *Eco-*  
557 *logical Applications* 31(7):e02,415. [https://doi.org/https://doi.org/10.1002/](https://doi.org/https://doi.org/10.1002/eap.2415)  
558 [eap.2415](https://doi.org/https://doi.org/10.1002/eap.2415)
- 559 R Core Team (2022) R: A Language and Environment for Statistical Com-  
560 puting. R Foundation for Statistical Computing, Vienna, Austria, URL  
561 <https://www.R-project.org/>

- 562 Rani L, Thapa K, Kanojia N, et al (2021) An extensive review on the conse-  
563 quences of chemical pesticides on human health and environment. *Journal*  
564 *of Cleaner Production* 283:124,657. [https://doi.org/10.1016/j.jclepro.2020.](https://doi.org/10.1016/j.jclepro.2020.124657)  
565 [124657](https://doi.org/10.1016/j.jclepro.2020.124657)
- 566 Ratcliffe D (1967) Decrease in Eggshell Weight in Certain Birds of Prey. *Nature*  
567 215(8):208–210
- 568 Rogers KH, McMillin S, Olstad KJ, et al (2019) Imidacloprid Poisoning of  
569 Songbirds Following a Drench Application of Trees in a Residential Neigh-  
570 borhood in California, USA. *Environmental Toxicology and Chemistry*  
571 38:1724–1727. <https://doi.org/10.1002/etc.4473>
- 572 Servien R, Latrille E, Patureau D, et al (2022) Machine learning models based  
573 on molecular descriptors to predict human and environmental toxicological  
574 factors in continental freshwater. *Peer Community In Ecotoxicology and*  
575 *Environmental Chemistry* 2:e15
- 576 Tang FH, Lenzen M, McBratney A, et al (2021) Risk of pesticide pollution at  
577 the global scale. *Nature Geoscience* 14(4):206–210. [https://doi.org/10.1038/](https://doi.org/10.1038/s41561-021-00712-5)  
578 [s41561-021-00712-5](https://doi.org/10.1038/s41561-021-00712-5)
- 579 Topping CJ, Weyman GS (2018) Rabbit population landscape-scale simulation  
580 to investigate the relevance of using rabbits in regulatory environmental risk  
581 assessment. *Environmental Modeling and Assessment* 23:415–457

582 Topping CJ, Dalby L, Skov F (2016) Landscape structure and management  
583 alter the outcome of a pesticide ERA: Evaluating impacts of endocrine  
584 disruption using the ALMaSS European Brown Hare model. *Science of the*  
585 *Total Environment* 541:1477–1488. [https://doi.org/10.1016/j.scitotenv.](https://doi.org/10.1016/j.scitotenv.2015.10.042)  
586 [2015.10.042](https://doi.org/10.1016/j.scitotenv.2015.10.042)

587 Topping CJ, Aldrich A, Berny P (2020) Overhaul environmental risk assess-  
588 ment for pesticides. *Science* 367(6476):360–363. [https://doi.org/10.1126/](https://doi.org/10.1126/science.aay1144)  
589 [science.aay1144](https://doi.org/10.1126/science.aay1144)

590 Vinken M (2013) The adverse outcome pathway concept: A pragmatic tool in  
591 toxicology. <https://doi.org/10.1016/j.tox.2013.08.011>

592 de Zwaan DR, Scridel D, Altamirano TA, et al (2022) GABB: A global dataset  
593 of alpine breeding birds and their ecological traits. *Scientific Data* 9:627.  
594 <https://doi.org/10.1038/s41597-022-01723-6>

## 595 **Bibliographic corpus of the review**

596 Abou-Donia MB (1979) Pharmacokinetics and metabolism of a topically  
597 applied dose of O-4-bromo-2,5-dichlorophenyl O-methyl phenylphospho-  
598 nothioate in hens. *Toxicology and Applied Pharmacology* 51(2):311–328.  
599 [https://doi.org/10.1016/0041-008X\(79\)90474-5](https://doi.org/10.1016/0041-008X(79)90474-5)



- 600 Ackerman JT, Eagles-Smith Ca, Heinz G (2014) Mercury in San Francisco  
601 Bay-Delta Birds: Trophic Pathways, Bioaccumulation and Ecotoxicologi-  
602 cal Risk to Avian Reproduction. U.S. Geological Survey Open-File Report  
603 2014-1251, <https://doi.org/10.3133/ofr20141251>, URL [http://dx.doi.org/](http://dx.doi.org/10.3133/ofr20141251)  
604 [10.3133/ofr20141251](http://dx.doi.org/10.3133/ofr20141251)
- 605 Ahrens FA, Dyer DC, Lloyd WE (1980) Mirex kinetics in chickens. Journal  
606 of Toxicology and Environmental Health 6(4):835–842. [https://doi.org/10.](https://doi.org/10.1080/15287398009529901)  
607 [1080/15287398009529901](https://doi.org/10.1080/15287398009529901)
- 608 An W, Hu JY, Yao F (2006) A method of assessing ecological risk  
609 to night heron, *Nycticorax nycticorax*, population persistence from  
610 dichlorodiphenyltrichloroethane exposure. Environmental Toxicology and  
611 Chemistry 25(1):281–286. <https://doi.org/10.1897/05-043R.1>
- 612 Anadón A, Bringas P, Martínez-Larranaga MR, et al (1994a) Bioavailability,  
613 pharmacokinetics and residues of chloramphenicol in the chicken. Journal of  
614 Veterinary Pharmacology and Therapeutics 23:52–58
- 615 Anadón A, Martínez-Larranaga MR, Diaz MJ, et al (1994b) Pharmacokinetics  
616 of doxycycline in broiler chickens. Avian Pathology 23(1):79–90. [https://](https://doi.org/10.1080/03079459408418976)  
617 [doi.org/10.1080/03079459408418976](https://doi.org/10.1080/03079459408418976)
- 618 Anadón A, Martínez-Larranaga MR, Diaz MJ, et al (1996) Pharmacokinetics  
619 of amoxicillin in broiler chickens. Avian Pathology 25(3):449–458. [https:](https://doi.org/10.1080/03079459608419154)  
620 [//doi.org/10.1080/03079459608419154](https://doi.org/10.1080/03079459608419154)

- 621 Anadón A, Martínez-Larrañaga MR, Iturbe J, et al (2001) Pharmacokinetics  
622 and residues of ciprofloxacin and its metabolites in broiler chickens.  
623 *Research in Veterinary Science* 71(2):101–109. [https://doi.org/10.1053/rvsc.](https://doi.org/10.1053/rvsc.2001.0494)  
624 [2001.0494](https://doi.org/10.1053/rvsc.2001.0494)
- 625 Anadón A, Martínez MA, Martínez M, et al (2008a) Oral bioavailability,  
626 tissue distribution and depletion of flumequine in the food producing ani-  
627 mal, chicken for fattening. *Food and Chemical Toxicology* 46(2):662–670.  
628 <https://doi.org/10.1016/j.fct.2007.09.086>
- 629 Anadón A, Martínez MA, Martínez M, et al (2008b) Plasma and tissue  
630 depletion of florfenicol and florfenicol-amine in chickens. *Journal of Agricultural and Food Chemistry* 56(22):11,049–11,056. [https://doi.org/10.1021/](https://doi.org/10.1021/jf802138y)  
631 [jf802138y](https://doi.org/10.1021/jf802138y)
- 633 Anadón A, Suárez FH, Martínez MA, et al (2011) Plasma disposition and  
634 tissue depletion of difloxacin and its metabolite sarafloxacin in the food  
635 producing animals, chickens for fattening. *Food and Chemical Toxicology*  
636 49(2):441–449. <https://doi.org/10.1016/j.fct.2010.11.021>
- 637 Antonissen G, De Baere S, Novak B, et al (2020) Toxicokinetics of hydrolyzed  
638 fumonisin B1 after single oral or intravenous bolus to broiler chickens fed a  
639 control or a fumonisins-contaminated diet. *Toxins* 12(6):1–13. [https://doi.](https://doi.org/10.3390/toxins12060413)  
640 [org/10.3390/toxins12060413](https://doi.org/10.3390/toxins12060413)

- 641 Ares J (2003) Time and space issues in ecotoxicology: Population models,  
642 landscape pattern analysis, and long-range environmental chemistry. *Envi-*  
643 *ronmental Toxicology and Chemistry* 22(5):945–957. [https://doi.org/10.](https://doi.org/10.1002/etc.5620220501)  
644 [1002/etc.5620220501](https://doi.org/10.1002/etc.5620220501)
- 645 Azmanis P, Pappalardo L, Sara ZA, et al (2021) Disposition of posaconazole  
646 after single oral administration in large falcons (*Falco spp*): Effect of meal  
647 and dosage and a non-compartmental model to predict effective dosage.  
648 *Medical Mycology* 59(9):901–908. <https://doi.org/10.1093/mmy/myab019>
- 649 Baier V, Paini A, Schaller S, et al (????) *Environment International* 169. [https:](https://doi.org/10.1016/j.envint.2022.107547)  
650 [//doi.org/10.1016/j.envint.2022.107547](https://doi.org/10.1016/j.envint.2022.107547)
- 651 Bakir A, O'Connor IA, Rowland SJ, et al (2016) Relative importance of  
652 microplastics as a pathway for the transfer of hydrophobic organic chemi-  
653 cals to marine life. *Environmental Pollution* 219:56–65. [https://doi.org/10.](https://doi.org/10.1016/j.envpol.2016.09.046)  
654 [1016/j.envpol.2016.09.046](https://doi.org/10.1016/j.envpol.2016.09.046)
- 655 Bean TG, Gross MS, Karouna-Renier NK, et al (2019) Toxicokinetics of  
656 Imidacloprid-Coated Wheat Seeds in Japanese Quail (*Coturnix japonica*)  
657 and an Evaluation of Hazard. *Environmental Science and Technology*  
658 53(7):3888–3897. <https://doi.org/10.1021/acs.est.8b07062>
- 659 Benlashehr I, Repussard C, Jouglar JY, et al (2011) Toxicokinetics of fumonisin  
660 B2 in ducks and turkeys. *Poultry Science* 90(8):1671–1675. [https://doi.org/](https://doi.org/10.3382/ps.2011-01434)  
661 [10.3382/ps.2011-01434](https://doi.org/10.3382/ps.2011-01434)

- 662 Bennett RS, Etterson MA (2007) Incorporating Results of Avian Toxicity Tests  
663 into a Model of Annual Reproductive Success. *Integrated Environmental*  
664 *Assessment and Management* 3(4):498–507
- 665 Bistoletti M, Alvarez L, Lanusse C, et al (2013) Disposition kinetics of alben-  
666 dazole and metabolites in laying hens. *Journal of Veterinary Pharmacology*  
667 *and Therapeutics* 36(2):161–168. [https://doi.org/10.1111/j.1365-2885.2012.](https://doi.org/10.1111/j.1365-2885.2012.01401.x)  
668 [01401.x](https://doi.org/10.1111/j.1365-2885.2012.01401.x)
- 669 Borgå K, Fisk AT, Hoekstra PF, et al (2004) Biological and chemical fac-  
670 tors of importance in the bioaccumulation and trophic transfer of persistent  
671 organochlorine contaminants in arctic marine food webs. *Environmental*  
672 *Toxicology and Chemistry* 23(10):2367–2385
- 673 Broekaert N, Devreese M, De Mil T, et al (2015) Oral Bioavailability,  
674 Hydrolysis, and Comparative Toxicokinetics of 3-Acetyldeoxynivalenol and  
675 15-Acetyldeoxynivalenol in Broiler Chickens and Pigs. *Journal of Agricul-*  
676 *tural and Food Chemistry* 63(39):8734–8742. [https://doi.org/10.1021/acs.](https://doi.org/10.1021/acs.jafc.5b03270)  
677 [jafc.5b03270](https://doi.org/10.1021/acs.jafc.5b03270)
- 678 Broekaert N, Devreese M, De Boevre M, et al (2017) T-2 Toxin-3 $\alpha$ -glucoside in  
679 Broiler Chickens: Toxicokinetics, Absolute Oral Bioavailability, and *In vivo*  
680 Hydrolysis. *Journal of Agricultural and Food Chemistry* 65(23):4797–4803.  
681 <https://doi.org/10.1021/acs.jafc.7b00698>

- 682 Bush PB, Tanner M, Kiker JT, et al (1978) Tissue residue studies on toxaphene  
683 in broiler chickens. *Journal of Agricultural and Food Chemistry* 26(1):126–  
684 130. <https://doi.org/10.1021/jf60215a064>
- 685 Capolongo F, Santi A, Tomasi L, et al (2002) Residues of oxytetracycline and  
686 its 4'-epimer in edible tissues from turkeys. *Journal of AOAC International*  
687 85(1):8–14. <https://doi.org/10.1093/jaoac/85.1.8>
- 688 Conder JM, Sorensen MT, Leitman P, et al (2009) Avian ecological risk  
689 potential in an urbanized estuary: Lower Hackensack River, New Jersey,  
690 U.S.A. *Science of the Total Environment* 407(3):1035–1047. [https://doi.org/](https://doi.org/10.1016/j.scitotenv.2008.09.043)  
691 [10.1016/j.scitotenv.2008.09.043](https://doi.org/10.1016/j.scitotenv.2008.09.043)
- 692 Cornejo J, Lapierre L, Iragüen D, et al (2012) Study of enrofloxacin and  
693 flumequine residues depletion in eggs of laying hens after oral administra-  
694 tion. *Journal of Veterinary Pharmacology and Therapeutics* 35(1):67–72.  
695 <https://doi.org/10.1111/j.1365-2885.2011.01283.x>
- 696 Cortright KA, Wetzlich SE, Craigmill AL (2009) A PBPK model for midazo-  
697 lam in four avian species. *Journal of Veterinary Pharmacology and Thera-  
698 peutics* 32(6):552–565. <https://doi.org/10.1111/j.1365-2885.2009.01073.x>
- 699 Crocker DR, Lawrence AJ (2018) Estimating the potential effects of pesticide  
700 seed treatments on the reproductive success of arable birds. *Ecotoxicology*  
701 and *Environmental Safety* 147:124–131. [https://doi.org/10.1016/j.ecoenv.](https://doi.org/10.1016/j.ecoenv.2017.08.035)  
702 [2017.08.035](https://doi.org/10.1016/j.ecoenv.2017.08.035)

- 703 Dauwe T, Jaspers VL, Covaci A, et al (2006) Accumulation of organochlo-  
704 rines and brominated flame retardants in the eggs and nestlings of great  
705 tits, *Parus major*. Environmental Science and Technology 40(17):5297–5303.  
706 <https://doi.org/10.1021/es060747a>
- 707 Delaski KM, Gehring R, Heffron BT, et al (2017) Plasma Concentrations of  
708 Fentanyl Achieved with Transdermal Application in Chickens. Journal of  
709 Avian Medicine and Surgery 31(1):6–15. <https://doi.org/10.1647/2015-153>
- 710 Drouillard KG, Norstrom RJ (2000) Dietary absorption efficiencies and toxi-  
711 cokinetics of polychlorinated biphenyls in ring doves following exposure to  
712 aroclor® mixtures. Environmental Toxicology and Chemistry 19(11):2707–  
713 2714. <https://doi.org/10.1002/etc.5620191114>
- 714 Drouillard KG, Norstrom RJ (2001) Quantifying maternal and dietary sources  
715 of 2,2',4,4',5,5'Hexachlorobiphenyl deposited in eggs of the ring dove (*Strept-*  
716 *topelia risoria*). Environmental Toxicology and Chemistry 20(3):561–567.  
717 <https://doi.org/10.1002/etc.5620200315>
- 718 Drouillard KG, Norstrom RJ (2003) The influence of diet properties and  
719 feeding rates on PCB toxicokinetics in the ring dove. Archives of Envi-  
720 ronmental Contamination and Toxicology 44(1):97–106. [https://doi.org/10.](https://doi.org/10.1007/s00244-002-1199-y)  
721 [1007/s00244-002-1199-y](https://doi.org/10.1007/s00244-002-1199-y)
- 722 Drouillard KG, Fernie KJ, Smits JE, et al (2001) Bioaccumulation and tox-  
723 icokinetics of 42 polychlorinated biphenyl congeners in American kestrels

724 (*Falco sparverius*). Environmental Toxicology and Chemistry 20(11):2514–  
725 2522. <https://doi.org/10.1002/etc.5620201117>

726 Drouillard KG, Fernie KJ, Letcher RJ, et al (2007) Bioaccumulation and  
727 biotransformation of 61 polychlorinated biphenyl and four polybrominated  
728 diphenyl ether congeners in juvenile American kestrels (*Falco sparverius*).  
729 Environmental Toxicology and Chemistry 26(2):313–324. [https://doi.org/](https://doi.org/10.1897/06-052R.1)  
730 [10.1897/06-052R.1](https://doi.org/10.1897/06-052R.1)

731 Ducrot V, Ashauer R, Bednarska AJ, et al (2016) Using toxicokinetic-  
732 toxicodynamic modeling as an acute risk assessment refinement approach in  
733 vertebrate ecological risk assessment. Integrated Environmental Assessment  
734 and Management 12(1):32–45. <https://doi.org/10.1002/ieam.1641>

735 Eagles-Smith CA, Ackerman JT, Julie YE, et al (2009) Mercury demethylation  
736 in waterbird livers: Dose-response thresholds and differences among species.  
737 Environmental Toxicology and Chemistry 28(3):568–577. [https://doi.org/](https://doi.org/10.1897/08-245.1)  
738 [10.1897/08-245.1](https://doi.org/10.1897/08-245.1)

739 Ehrich M, Correll L, Strait J, et al (1992) Toxicity and toxicokinetics  
740 of carbaryl in chickens and rats:a comparative study. Journal of Toxi-  
741 cology and Environmental Health 36(4):411–423. [https://doi.org/10.1080/](https://doi.org/10.1080/15287399209531648)  
742 [15287399209531648](https://doi.org/10.1080/15287399209531648)

- 743 Engelman CA, Grant WE, Mora MA, et al (2012) Modelling effects of chemical  
744 exposure on birds wintering in agricultural landscapes: The western burrow-  
745 ing owl (*Athene cunicularia hypugaea*) as a case study. *Ecological Modelling*  
746 224(1):90–102. <https://doi.org/10.1016/j.ecolmodel.2011.10.017>
- 747 Eraslan G, Tekeli MY, Karabacak M (2017) Toxicokinetic of cypermethrin in  
748 broiler chickens. *Fresenius Environmental Bulletin* 26(7):4704–4710
- 749 Etterson M, Garber K, Odenkirchen E (2017) Mechanistic modeling of insecti-  
750 cide risks to breeding birds in North American agroecosystems. *Plos One*  
751 12(5):e0176,998. <https://doi.org/10.1371/journal.pone.0176998>
- 752 Etterson MA (2022) Realism, Conservatism, and Tiered Ecological  
753 Risk Assessment. *Ecologies* 3(2):131–144. [https://doi.org/10.3390/](https://doi.org/10.3390/ecologies3020011)  
754 [ecologies3020011](https://doi.org/10.3390/ecologies3020011)
- 755 Etterson MA, Ankley GT (2021) Endogenous Lifecycle Models for Chemical  
756 Risk Assessment. *Environmental Science and Technology* 55(23):15,596–  
757 15,608. <https://doi.org/10.1021/acs.est.1c04791>
- 758 Etterson MA, Bennett RS (2013) Quantifying the effects of pesticide expo-  
759 sure on annual reproductive success of birds. *Integrated environmental*  
760 *assessment and management* 9:590–599. <https://doi.org/10.1002/ieam.1450>



- 761 Fournier A, Feidt C, Dziurla MA, et al (2010) Transfer kinetics to egg yolk and  
762 modeling residue recovered in yolk of readily metabolized molecules: Poly-  
763 cyclic aromatic hydrocarbons orally administered to laying hens. *Chemo-*  
764 *sphere* 78(8):1004–1010. <https://doi.org/10.1016/j.chemosphere.2009.12.008>
- 765 Fournier A, Feidt C, Marchand P, et al (2012) Kinetic study of  $\gamma$ -  
766 hexabromocyclododecane orally given to laying hens (*Gallus domesticus*).  
767 *Environmental Science and Pollution Research* 19(2):440–447. [https://doi.](https://doi.org/10.1007/s11356-011-0573-6)  
768 [org/10.1007/s11356-011-0573-6](https://doi.org/10.1007/s11356-011-0573-6)
- 769 Fournier A, Martin O, Travel A, et al (2015) Modeling PCB transfer into hen  
770 eggs: Influence of physiological characteristics of the animal. *Environmental*  
771 *Toxicology and Chemistry* 34(1):173–183. <https://doi.org/10.1002/etc.2781>
- 772 Fournier F, Karasov WH, Kenow KP, et al (2002) The oral bioavailabil-  
773 ity and toxicokinetics of methylmercury in common loon (*Gavia immer*)  
774 chicks. *Comparative Biochemistry and Physiology - A Molecular and Inte-*  
775 *grative Physiology* 133(3):703–714. [https://doi.org/10.1016/S1095-6433\(02\)](https://doi.org/10.1016/S1095-6433(02)00140-X)  
776 [00140-X](https://doi.org/10.1016/S1095-6433(02)00140-X)
- 777 Furusawa N, Mukai T, Ohori H (1996) Depletion of dietary sulpha-  
778 monomethoxine and sulphadimethoxine from various tissues of laying  
779 hens. *British Poultry Science* 37(2):435–442. [https://doi.org/10.1080/](https://doi.org/10.1080/00071669608417874)  
780 [00071669608417874](https://doi.org/10.1080/00071669608417874)

- 781 García Ovando H, Gorla N, Luders C, et al (1999) Comparative pharmacoki-  
782 netics of enrofloxacin and ciprofloxacin in chickens. *Journal of Veterinary*  
783 *Pharmacology and Therapeutics* 22(3):209–212. [https://doi.org/10.1046/j.](https://doi.org/10.1046/j.1365-2885.1999.00211.x)  
784 [1365-2885.1999.00211.x](https://doi.org/10.1046/j.1365-2885.1999.00211.x)
- 785 Gerletti P, Von Kleist M, Mielke H, et al (2020) Transfer kinetics of fipronil  
786 into chicken (*Gallus gallus domesticus*) eggs. *Computational Toxicology*  
787 15(February):100,131. <https://doi.org/10.1016/j.comtox.2020.100131>
- 788 Gilbert CM, Filippich LJ, McGeary RP, et al (2007) Toxicokinetics of the  
789 active doxorubicin metabolite, doxorubicinol, in sulphur-crested cockatoos  
790 (*Cacatua galerita*). *Research in Veterinary Science* 83(1):123–129. [https://](https://doi.org/10.1016/j.rvsc.2006.11.005)  
791 [doi.org/10.1016/j.rvsc.2006.11.005](https://doi.org/10.1016/j.rvsc.2006.11.005)
- 792 Glaser D, Connolly JP (2002) A model of p,p'-DDE and total PCB bioac-  
793 cumulation in birds from the Southern California Bight. *Continental*  
794 *Shelf Research* 22(6-7):1079–1100. [https://doi.org/10.1016/S0278-4343\(01\)](https://doi.org/10.1016/S0278-4343(01)00119-4)  
795 [00119-4](https://doi.org/10.1016/S0278-4343(01)00119-4)
- 796 Gobas FA, Arnot JA (2010) Food web bioaccumulation model for polychlo-  
797 rinated biphenyls in san francisco bay, California, USA. *Environmental*  
798 *Toxicology and Chemistry* 29(6):1385–1395. [https://doi.org/10.1002/etc.](https://doi.org/10.1002/etc.164)  
799 [164](https://doi.org/10.1002/etc.164)

- 800 Gobas FA, Burkhard LP, Doucette WJ, et al (2016) Review of existing  
801 terrestrial bioaccumulation models and terrestrial bioaccumulation model-  
802 ing needs for organic chemicals. *Integrated Environmental Assessment and*  
803 *Management* 12(1):123–134. <https://doi.org/10.1002/ieam.1690>
- 804 Gögebakan T, Eraslan G (2015) Single-dose toxicokinetics of permethrin in  
805 broiler chickens. *British Poultry Science* 56(5):605–611. <https://doi.org/10.1080/00071668.2015.1085957>
- 806
- 807 Goudah A (2009) Pharmacokinetics and tissue residues of moxifloxacin in  
808 broiler chickens. *British Poultry Science* 50(2):251–258. <https://doi.org/10.1080/00071660802710108>
- 809
- 810 Goutte A, Bustamante P, Barbraud C, et al (2014) Demographic responses  
811 to mercury exposure in two closely related antarctic top predators. *Ecology*  
812 95(4):1075–1086. <https://doi.org/10.1890/13-1229.1>
- 813 Goutte A, Barbraud C, Herzke D, et al (2015) Survival rate and breeding out-  
814 puts in a high Arctic seabird exposed to legacy persistent organic pollutants  
815 and mercury. *Environmental Pollution* 200:1–9. [https://doi.org/10.1016/j. envpol.2015.01.033](https://doi.org/10.1016/j.envpol.2015.01.033)
- 816
- 817 Goutte A, Meillère A, Barbraud C, et al (2018) Demographic, endocrine and  
818 behavioral responses to mirex in the South polar skua. *Science of the Total*  
819 *Environment* 631-632:317–325. <https://doi.org/10.1016/j.scitotenv.2018.02.326>
- 820

- 821 Grabowski T, Pasławska U, Poźniak B, et al (2017) Models describing metron-  
822 idazole pharmacokinetics in relation to hemodynamics in turkeys. *Research*  
823 *in Veterinary Science* 112:167–171. [https://doi.org/10.1016/j.rvsc.2017.03.](https://doi.org/10.1016/j.rvsc.2017.03.014)  
824 [014](https://doi.org/10.1016/j.rvsc.2017.03.014)
- 825 Grant WE, Fraser SO, Isakson KG (1984) Effect of vertebrate pesticides on  
826 non-target wildlife populations: Evaluation through modelling. *Ecological*  
827 *Modelling* 21(1-2):85–108. [https://doi.org/10.1016/0304-3800\(84\)90026-7](https://doi.org/10.1016/0304-3800(84)90026-7)
- 828 Hallam TG, Trawick TL, Wolff WF (1996) Modeling effects of chemicals  
829 on a population: Application to a wading bird nesting colony. *Ecological*  
830 *Modelling* 92(2-3):155–178. [https://doi.org/10.1016/0304-3800\(95\)00204-9](https://doi.org/10.1016/0304-3800(95)00204-9)
- 831 Hamamoto K, Koike R, Machida Y (2000) Bioavailability of amprolium in  
832 fasting and nonfasting chickens after intravenous and oral administration.  
833 *Journal of Veterinary Pharmacology and Therapeutics* 23(1):9–14. <https://doi.org/10.1046/j.1365-2885.2000.00239.x>  
834 [//doi.org/10.1046/j.1365-2885.2000.00239.x](https://doi.org/10.1046/j.1365-2885.2000.00239.x)
- 835 Hassan IZ, Duncan N, Adawaren EO, et al (2018) Could the environmen-  
836 tal toxicity of diclofenac in vultures been predictable if preclinical testing  
837 methodology were applied? *Environmental Toxicology and Pharmacology*  
838 64(July):181–186. <https://doi.org/10.1016/j.etap.2018.10.006>
- 839 Hekman P, Schefferlie GJ (2011) Kinetic modelling and residue depletion of  
840 drugs in eggs. *British Poultry Science* 52(3):376–380. [https://doi.org/10.](https://doi.org/10.1080/00071668.2011.577055)  
841 [1080/00071668.2011.577055](https://doi.org/10.1080/00071668.2011.577055)

- 842 Hendriks AJ, Enserink EL (1996) Modelling response of single-species pop-  
843 ulations to microcontaminants as a function of species size with examples  
844 for waterfleas (*Daphnia magna*) and cormorants (*Phalacrocorax carbo*). Eco-  
845 logical Modelling 88(1-3):247–262. [https://doi.org/10.1016/0304-3800\(95\)](https://doi.org/10.1016/0304-3800(95)00111-5)  
846 [00111-5](https://doi.org/10.1016/0304-3800(95)00111-5)
- 847 Hendriks AJ, Maas-Diepeveen JL, Heugens EH, et al (2005) Meta-analysis  
848 of intrinsic rates of increase and carrying capacity of populations affected  
849 by toxic and other stressors. Environmental Toxicology and Chemistry  
850 24(9):2267–2277. <https://doi.org/10.1897/05-122.1>
- 851 Henri J, Carrez R, Méda B, et al (2017) A physiologically based pharma-  
852 cokinetic model for chickens exposed to feed supplemented with monensin  
853 during their lifetime. Journal of Veterinary Pharmacology and Therapeutics  
854 40(4):370–382. <https://doi.org/10.1111/jvp.12370>
- 855 Herman J, Vermeersch H, Remon JP, et al (1989) Pharmacokinetics and  
856 bioavailability of ronidazole from a prolonged release tablet in the homing  
857 pigeon (*Columba livid*). Journal of Veterinary Pharmacology and Therapeu-  
858 tics 12(1):46–49. <https://doi.org/10.1111/j.1365-2885.1989.tb00640.x>
- 859 Hommen U, Forbes V, Grimm V, et al (2016) How to use mechanistic effect  
860 models in environmental risk assessment of pesticides: Case studies and  
861 recommendations from the SETAC workshop MODELINK. Integrated Envi-  
862 ronmental Assessment and Management 12(1):21–31. [https://doi.org/10.](https://doi.org/10.1007/s11367-015-0361-1)

863 [1002/ieam.1704](#)

864 Hutchinson TH, Madden JC, Naidoo V, et al (2014) Comparative metabolism  
865 as a key driver of wildlife species sensitivity to human and veterinary phar-  
866 maceuticals. *Philosophical Transactions of the Royal Society B: Biological*  
867 *Sciences* 369:1656. <https://doi.org/10.1098/rstb.2013.0583>

868 Hüyük R, Eraslan G (2017) Toxicokinetics of the broad-spectrum pyrethroid  
869 insecticide deltamethrin in broiler chickens. *British Poultry Science* 58:95–  
870 99. <https://doi.org/10.1080/00071668.2016.1211253>

871 Jackson AK, Evers DC, Etterson MA, et al (2011) Mercury exposure affects  
872 the reproductive success of a free-living terrestrial songbird, the carolina  
873 wren (*Thryothorus Ludovicianus*). *Auk* 128(4):759–769. [https://doi.org/10.](https://doi.org/10.1525/auk.2011.11106)  
874 [1525/auk.2011.11106](https://doi.org/10.1525/auk.2011.11106)

875 Karasov WH, Kenow KP, Meyer MW, et al (2007) Bioenergetic and phar-  
876 macokinetic model for exposure of common loon (*Gavia immer*) chicks to  
877 methylmercury. *Environmental Toxicology and Chemistry* 26(4):677–685.  
878 <https://doi.org/10.1897/06-262.1>

879 Kongkapan J, Giorgi M, Poapolathep S, et al (2016) Toxicokinetics and tissue  
880 distribution of nivalenol in broiler chickens. *Toxicon* 111:31–36. [https://doi.](https://doi.org/10.1016/j.toxicon.2015.12.013)  
881 [org/10.1016/j.toxicon.2015.12.013](https://doi.org/10.1016/j.toxicon.2015.12.013)

- 882 Korsman JC, Schipper AM, Lenders HJ, et al (2012) Modelling the  
883 impact of toxic and disturbance stress on white-tailed eagle (*Haliaeetus*  
884 *albicilla*) populations. *Ecotoxicology* 21(1):27–36. [https://doi.org/10.1007/  
885 s10646-011-0760-8](https://doi.org/10.1007/s10646-011-0760-8)
- 886 Kuo DTF, Rattner BA, Martinson SC, et al (2022) A Critical Review of  
887 Bioaccumulation and Biotransformation of Organic Chemicals in Birds.  
888 *Reviews of Environmental Contamination and Toxicology* 260:6–61. [https:  
889 //doi.org/10.1007/s44169-021-00007-1](https://doi.org/10.1007/s44169-021-00007-1)
- 890 Lautz LS, Nebbia C, Hoeks S, et al (2020) An open source physiologically  
891 based kinetic model for the chicken (*Gallus gallus domesticus*): Calibration  
892 and validation for the prediction residues in tissues and eggs. *Environment*  
893 *International* 136:105,488. <https://doi.org/10.1016/j.envint.2020.105488>
- 894 Liu X, Liu C, Wang P, et al (2019) Distribution, metabolism and metabolic  
895 disturbances of alpha-cypermethrin in embryo development, chick growth  
896 and adult hens. *Environmental Pollution* 249:390–397. [https://doi.org/10.  
897 1016/j.envpol.2019.03.017](https://doi.org/10.1016/j.envpol.2019.03.017)
- 898 Lu Z, Xue M, Shen G, et al (2011) Accumulation dynamics of chlordanes and  
899 their enantiomers in cockerels (*Gallus gallus*) after oral exposure. *Environ-*  
900 *mental Science and Technology* 45(18):7928–7935. [https://doi.org/10.1021/  
901 es201629p](https://doi.org/10.1021/es201629p)

- 902 MacLachlan DJ (2010) Physiologically based pharmacokinetic (PBPK) model  
903 for residues of lipophilic pesticides in poultry. *Food Additives and Contam-*  
904 *inants - Part A* 27(3):302–314. <https://doi.org/10.1080/19440040903296683>
- 905 Matsinos YG, Wolff WF (2003) An individual-oriented model for ecological risk  
906 assessment of wading birds. *Ecological Modelling* 170(2-3):471–478. [https://doi.org/10.1016/S0304-3800\(03\)00246-1](https://doi.org/10.1016/S0304-3800(03)00246-1)
- 908 Méda B, Travel A, Guyot Y, et al (2020) A PBPK model to study the  
909 transfer of  $\alpha$ -hexabromocyclododecane ( $\alpha$ -HBCDD) to tissues of fast- and  
910 slow-growing broilers. *Food Additives and Contaminants - Part A Chem-*  
911 *istry, Analysis, Control, Exposure and Risk Assessment* 37(2):316–331.  
912 <https://doi.org/10.1080/19440049.2019.1681596>
- 913 Millot F, Berny P, Decors A, et al (2015) Little field evidence of direct acute  
914 and short-term effects of current pesticides on the grey partridge. *Ecotoxicol-*  
915 *ogy and Environmental Safety* 117:41–61. [https://doi.org/10.1016/j.ecoenv.](https://doi.org/10.1016/j.ecoenv.2015.03.017)  
916 [2015.03.017](https://doi.org/10.1016/j.ecoenv.2015.03.017)
- 917 Monteiro LR, Furness RW (2001) Kinetics, dose-response, and excretion  
918 of methylmercury in free-living adult Cory’s shearwaters. *Environmental*  
919 *Science and Technology* 35(4):739–746. <https://doi.org/10.1021/es000114a>
- 920 Moore DRJ, Fischer D, Teed S, et al (2010) A Probabilistic Risk Assessment  
921 Model for Birds Exposed to Granular Pesticides. *Integrated Environmen-*  
922 *tal Assessment and Management* 6:83–101. [https://doi.org/10.1897/ieam\\_](https://doi.org/10.1897/ieam_)



923 [2009-021.1](#)

924 Moore DRJ, Priest CD, Olson AD, et al (2018) A probabilistic risk assess-  
925 ment for the Kirtland’s warbler potentially exposed to chlorpyrifos and  
926 malathion during the breeding season and migration. *Integrated Envi-  
927 ronmental Assessment and Management* 14(2):252–269. [https://doi.org/10.  
928 1002/ieam.2004](https://doi.org/10.1002/ieam.2004)

929 Nacci D, Pelletier M, Lake J, et al (2005) An approach to predict risks to  
930 wildlife populations from mercury and other stressors. *Ecotoxicology* 14(1-  
931 2):283–293. <https://doi.org/10.1007/s10646-004-6275-9>

932 Nelson YM, Thampy RJ, Motelin GK, et al (1998) Model for trace metal  
933 exposure in filter-feeding flamingos at alkaline Rift Valley Lake, Kenya. *Envi-  
934 ronmental Toxicology and Chemistry* 17(11):2302–2309. [https://doi.org/10.  
935 1897/1551-5028\(1998\)017<2302:MFTMEI>2.3.CO;2](https://doi.org/10.1897/1551-5028(1998)017<2302:MFTMEI>2.3.CO;2)

936 Newsted JL, Beach SA, Gallagher SP, et al (2006) Pharmacokinetics and acute  
937 lethality of perfluorooctanesulfonate (PFOS) to juvenile mallard and north-  
938 ern bobwhite. *Archives of Environmental Contamination and Toxicology*  
939 50(3):411–420. <https://doi.org/10.1007/s00244-005-1137-x>

940 Nichols JW, Larsen CP, McDonald ME, et al (1995) Bioenergetics-Based  
941 Model for Accumulation of Polychlorinated Biphenyls by Nestling Tree  
942 Swallows, *Tachycineta bicolor*. *Environmental Science and Technology*  
943 29(3):604–612

- 944 Nichols JW, Echols KR, Tillitt DE, et al (2004) Bioenergetics-based modeling  
945 of individual PCB congeners in nestling tree swallows from two contami-  
946 nated sites on the Upper Hudson River, New York. *Environmental Science*  
947 *and Technology* 38(23):6234–6239. <https://doi.org/10.1021/es0497734>
- 948 Nichols JW, Bennett RS, Rossmann R, et al (2010) A physiologically based  
949 toxicokinetic model for methylmercury in female American kestrels. *Envi-*  
950 *ronmental Toxicology and Chemistry* 29(8):1854–1867. [https://doi.org/10.](https://doi.org/10.1002/etc.241)  
951 [1002/etc.241](https://doi.org/10.1002/etc.241)
- 952 Norstrom RJ, Clark TP, Enright M, et al (2007) ABAM, a model for bioaccu-  
953 mulation of POPs in birds: Validation for adult herring gulls and their eggs  
954 in Lake Ontario. *Environmental Science and Technology* 41(12):4339–4347.  
955 <https://doi.org/10.1021/es062205z>
- 956 Ohlhoff B, Savvateeva D, Leisner J, et al (2022) Transfer of Non-Dioxin-Like  
957 Polychlorinated Biphenyls (ndl-PCBs) from Feed and Soil into Hen Eggs.  
958 *Journal of Agricultural and Food Chemistry* 70(29):8955–8962. [https://doi.](https://doi.org/10.1021/acs.jafc.2c02243)  
959 [org/10.1021/acs.jafc.2c02243](https://doi.org/10.1021/acs.jafc.2c02243)
- 960 Opdycke JC, Menzer RE, Menzer RE (1984) Pharmacokinetics of difluben-  
961 zuron in two types of chickens. *Journal of Toxicology and Environmental*  
962 *Health* 13(4-6):721–733. <https://doi.org/10.1080/15287398409530534>
- 963 Pan Y, Chang J, Xu P, et al (2022) Twenty-four hours of Thiamethoxam:  
964 *In vivo* and molecular dynamics simulation study on the toxicokinetic and

965 underlying mechanisms in quails (*Coturnix japonica*). Journal of Hazardous  
966 Materials 427(October 2021):128,159. [https://doi.org/10.1016/j.jhazmat.  
967 2021.128159](https://doi.org/10.1016/j.jhazmat.2021.128159)

968 Pant S, Rao GS, Sastry KV, et al (2005) Pharmacokinetics and tissue residues  
969 of pefloxacin and its metabolite norfloxacin in broiler chickens. British  
970 Poultry Science 46(5):615–620. <https://doi.org/10.1080/00071660500255323>

971 Pisani JM, Grant WE, Mora MA (2008) Simulating the impact of  
972 cholinesterase-inhibiting pesticides on non-target wildlife in irrigated  
973 crops. Ecological Modelling 210(1-2):179–192. [https://doi.org/10.1016/j.  
974 ecolmodel.2007.07.017](https://doi.org/10.1016/j.ecolmodel.2007.07.017)

975 Poapolathep S, Klangkaew N, Arreesrisom P, et al (2015) Toxicokinetics and  
976 absolute oral bioavailability of melamine in broiler chickens. Journal of Vet-  
977 erinary Pharmacology and Therapeutics 38(1):101–104. [https://doi.org/10.  
978 1111/jvp.12145](https://doi.org/10.1111/jvp.12145)

979 Pollet RA, Glatz CE, Dyer DC, et al (1983) Pharmacokinetics of chlortetra-  
980 cycline potentiation with citric acid in the chicken. American Journal of  
981 Veterinary Research 44(9):1718–1721

982 Pollet RA, Glatz CE, Dyer DC (1985) The pharmacokinetics of chlortetracy-  
983 cline orally administered to turkeys: Influence of citric acid and *Pasteurella*  
984 *multocida* infection. Journal of Pharmacokinetics and Biopharmaceutics  
985 13(3):243–264. <https://doi.org/10.1007/BF01065655>

- 986 Rattner BA, Horak KE, Lazarus RS, et al (2014) Toxicokinetics and coag-  
987 ulopathy threshold of the rodenticide diphacinone in eastern screech-owls  
988 (*Megascops asio*). Environmental Toxicology and Chemistry 33(1):74–81.  
989 <https://doi.org/10.1002/etc.2390>
- 990 Rattner BA, Volker SF, Lankton JS, et al (2020) Brodifacoum Toxicity in  
991 American Kestrels (*Falco sparverius*) with Evidence of Increased Hazard on  
992 Subsequent Anticoagulant Rodenticide Exposure. Environmental Toxicology  
993 and Chemistry 39(2):468–481. <https://doi.org/10.1002/etc.4629>
- 994 Ratzlaff K, Papich MG, Flammer K (2011) Plasma concentrations of flu-  
995 conazole after a single oral dose and administration in drinking water in  
996 cockatiels (*Nymphicus hollandicus*). Journal of Avian Medicine and Surgery  
997 25(1):23–31. <https://doi.org/10.1647/2009-044.1>
- 998 Roelofs W, Crocker DR, Shore RF, et al (2005) Case study part 2: Probabilistic  
999 modelling of long-term effects of pesticides on individual breeding success in  
1000 birds and mammals. Ecotoxicology 14(8):895–923. [https://doi.org/10.1007/  
1001 s10646-005-0035-3](https://doi.org/10.1007/s10646-005-0035-3)
- 1002 Samuels WB, Ladino A (1984) Calculations of seabird population recov-  
1003 ery from potential oilspills in the mid-atlantic region of the united states.  
1004 Ecological Modelling 21:63–84
- 1005 Sánchez CR, Zalesak S, Pich AA, et al (2019) Population pharmacokinetics  
1006 of itraconazole solution after a single oral administration in captive lesser

- 1007 flamingos (*Phoeniconaias minor*). Journal of Veterinary Pharmacology and  
1008 Therapeutics 42(1):1–6. <https://doi.org/10.1111/jvp.12721>
- 1009 Schefferlie GJ, Hekman P (2016) Prediction of the residue levels of drugs  
1010 in eggs, using physicochemical properties and their influence on passive  
1011 diffusion processes. Journal of Veterinary Pharmacology and Therapeutics  
1012 39(4):381–387. <https://doi.org/10.1111/jvp.12290>
- 1013 Sibly RM, Akcakaya HR, Topping CJ, et al (2005) Population-level assess-  
1014 ment of risks of pesticides to birds and mammals in the UK. Ecotoxicology  
1015 14(8):863–876. <https://doi.org/10.1007/s10646-005-0033-5>
- 1016 Siegel DM, Giri SN (1983) Toxicokinetics, covalent binding and histopatho-  
1017 logical features of [14C]2-chloro-4-acetotoluidide toxicity in the starling  
1018 after intravenous administration. Experimental and Molecular Pathology  
1019 39(2):194–206. [https://doi.org/10.1016/0014-4800\(83\)90051-5](https://doi.org/10.1016/0014-4800(83)90051-5)
- 1020 Smith JT, Walker LA, Shore RF, et al (2009) Do estuaries pose a toxic  
1021 contamination risk for wading birds? Ecotoxicology 18(7):906–917. <https://doi.org/10.1007/s10646-009-0352-z>
- 1023 Suknikom P, Jermnak U, Poapolathep S, et al (2016) Dispositions and tissue  
1024 depletion of melamine in ducks. Journal of Veterinary Pharmacology and  
1025 Therapeutics 39(1):90–94. <https://doi.org/10.1111/jvp.12242>

- 1026 Sullivan JP, Scanlon PF (1991) A comparison between intubation and food  
1027 addition as routes of oral exposure for northern bobwhites to DDT insecticide. *Journal of wildlife diseases* 27(3):435–440. [https://doi.org/10.7589/](https://doi.org/10.7589/0090-3558-27.3.435)  
1028 [0090-3558-27.3.435](https://doi.org/10.7589/0090-3558-27.3.435)
- 1030 Tarazona JV, Rodríguez C, Alonso E, et al (2015) Toxicokinetics of per-  
1031 fluorooctane sulfonate in birds under environmentally realistic exposure  
1032 conditions and development of a kinetic predictive model. *Toxicology Letters*  
1033 232(2):363–368. <https://doi.org/10.1016/j.toxlet.2014.11.022>
- 1034 Tavecchia G, Pradel R, Lebreton JD, et al (2001) The effect of lead exposure  
1035 on survival of adult mallards in the Camargue, southern France. *Journal*  
1036 *of Applied Ecology* 38(6):1197–1207. [https://doi.org/10.1046/j.0021-8901.](https://doi.org/10.1046/j.0021-8901.2001.00684.x)  
1037 [2001.00684.x](https://doi.org/10.1046/j.0021-8901.2001.00684.x)
- 1038 Thompson CV, Firman JW, Goldsmith MR, et al (2021) A Systematic Review  
1039 of Published Physiologically-based Kinetic Models and an Assessment of  
1040 their Chemical Space Coverage. *ATLA Alternatives to Laboratory Animals*  
1041 49(5):197–208. <https://doi.org/10.1177/02611929211060264>
- 1042 Topping CJ, Sibly RM, Akcakaya HR, et al (2005) Risk assessment of UK sky-  
1043 lark populations using life-history and individual-based landscape models.  
1044 *Ecotoxicology* 14(8):925–936. <https://doi.org/10.1007/s10646-005-0027-3>
- 1045 Van Eijkeren JC, Zeilmaker MJ, Kan CA, et al (2006) A toxicokinetic  
1046 model for the carry-over of dioxins and PCBs from feed and soil to eggs.

1047 Food Additives and Contaminants 23(5):509–517. [https://doi.org/10.1080/](https://doi.org/10.1080/02652030500512045)  
1048 [02652030500512045](https://doi.org/10.1080/02652030500512045)

1049 Waegeneers N, De Steur H, De Temmerman L, et al (2009) Transfer of soil  
1050 contaminants to home-produced eggs and preventive measures to reduce  
1051 contamination. *Science of the Total Environment* 407(15):4438–4446. <https://doi.org/10.1016/j.scitotenv.2008.12.041>  
1052 [//doi.org/10.1016/j.scitotenv.2008.12.041](https://doi.org/10.1016/j.scitotenv.2008.12.041)

1053 Wang YS, Li M, Tell LA, et al (2021) Physiological parameter values for physi-  
1054 ologically based pharmacokinetic models in food-producing animals. Part II:  
1055 Chicken and turkey. *Journal of Veterinary Pharmacology and Therapeutics*  
1056 44(4):423–455. <https://doi.org/10.1111/jvp.12931>

1057 Wayland M, Drake KL, Alisauskas RT, et al (2008) Survival rates and  
1058 blood metal concentrations in two species of free-ranging North Ameri-  
1059 can sea ducks. *Environmental Toxicology and Chemistry* 27(3):698–704.  
1060 <https://doi.org/10.1897/07-321.1>

1061 Yang F, Yang Y, Wang L, et al (2014) Estimating marbofloxacin withdrawal  
1062 time in broiler chickens using a population physiologically based pharma-  
1063 cokinetics model. *Journal of Veterinary Pharmacology and Therapeutics*  
1064 37:579–588. <https://doi.org/10.1111/jvp.12137>

1065 Yang F, Sun N, Liu YM, et al (2015) Estimating danofloxacin withdrawal  
1066 time in broiler chickens based on physiologically based pharmacokinetics

- 1067 modeling. *Journal of Veterinary Pharmacology and Therapeutics* 38(2):174–  
1068 182. <https://doi.org/10.1111/jvp.12162>
- 1069 Yuan L, Sun J, Wang R, et al (2011) Pharmacokinetics and bioavailability  
1070 of cefquinome in healthy ducks. *American Journal of Veterinary Research*  
1071 72(1):122–126. <https://doi.org/10.2460/ajvr.72.1.122>
- 1072 Yuan L, Chou WC, Richards ED, et al (2022) A web-based interac-  
1073 tive physiologically based pharmacokinetic (iPBPK) model for meloxi-  
1074 cam in broiler chickens and laying hens. *Food and Chemical Toxicology*  
1075 168(August):113,332. <https://doi.org/10.1016/j.fct.2022.113332>
- 1076 Zeng D, Lin Z, Zeng Z, et al (2019) Assessing Global Human Exposure to  
1077 T-2 Toxin via Poultry Meat Consumption Using a Lifetime Physiologically  
1078 Based Pharmacokinetic Model. *Journal of Agricultural and Food Chemistry*  
1079 67(5):1563–1571. <https://doi.org/10.1021/acs.jafc.8b07133>
- 1080 Zhao DH, Zhou YF, Yu Y, et al (2014) Integration of pharmacokinetic  
1081 and pharmacodynamic indices of valnemulin in broiler chickens after a  
1082 single intravenous and intramuscular administration. *Veterinary Journal*  
1083 201(1):109–115. <https://doi.org/10.1016/j.tvjl.2014.05.010>