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A screening framework for pesticide substitution in agriculture

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Abstract

Farmers lack science-based tools to flexibly and rapidly identify more sustainable pesticides. To address this gap, we present a screening-level substitution framework to compare and rank pesticides using a consistent set of indicators including registration, pest resistance, human toxicity and aquatic ecotoxicity impact potentials, and market price. Toxicity-related damage costs and application costs were combined with application dosages to yield total costs per pesticide. We applied and tested our framework in a case study on pesticides applied to lettuce in Denmark. Our results indicate that by ranking pesticides within each target class (e.g. fungicides) the most suitable pesticide can be identified based on our set of indicators. As an example, in the insecticide scenario, pymetrozine performs best with total costs of 23 €/ha, while dimethoate and pirimicarb, which are also on the EU candidate substitution list, performed worst. Total costs across considered pesticides range from 23 to 302 €/ha. Our framework constitutes an operational starting point for identifying sustainable pesticides by farmers and other stakeholders and highlights (a) the need to consider various relevant aspects influencing the ranking of pesticides and (b) the importance of combining total cost performance per pesticide unit applied with respective application dosage per hectare as both may vary greatly. Fu-

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ture research should focus on considering additional indicators (e.g. terrestrial ecotoxicity), increasing resistance-related data, and reducing uncertainty that is mainly related to emission and toxicity impact estimates.

Keywords: Substitution scenarios, Decision support, Environmental impacts, Pesticide ranking

1. Introduction

A large variety of chemical pesticide active ingredients (a.i.), hereafter referred to as pesticides, is widely used in agriculture to kill unwanted pests and to improve crop yield. However, pesticide use also causes negative impacts on humans and the environment (Landrigan et al., 2018; Fantke et al., 2012a; Damalas and Eleftherohorinos, 2011; Hou and Wu, 2010). The general public is particularly concerned about long-term effects of pesticides through ingestion of food products and through transfer to the natural environment (EC, 2010). Nevertheless, pesticide use increased dramatically between 1960 and 2000 and is still increasing in most countries (Blair et al., 2014). To date, the worldwide consumption of pesticide is around 3.5 million tons per year spanning a market worth of 45 billion USD (Eyhorn et al., 2015).

To meet local, national, and global sustainable development goals, farmers need to continuously work towards a more sustainable use of pesticides (Lamichane, 2017), which is supported by national and international strategies (EC, 2009; UNEP, 2009). In this context, governments have for years been promoting more sustainable farming practices including integrated pest management (IPM) and organic farming as alternative to conventional farming (Vasileiadis et al., 2017). However, replacing conventional pesticide usage with an IPM-based or organic farming system requires changing the entire farming practice. This includes the use of diverse crop varieties and the reduction of any broad-spectrum pesticides to fight resistance toward chemical pesticides, and comes at the expense of increased workload, costs and education for farmers (Mailly et al., 2017). Hence, in spite of the efforts of promoting alternative practices, applying

chemical pesticides currently remains the dominant pest control mechanism for the majority of farmers worldwide (Vasileiadis et al., 2017).

The variety of pesticides that are available to farmers in the form of different formulation products for agricultural use varies between regions and countries as function of pesticide regulations. A farmer's choice among available pesticides is predominantly driven by the apparent pest(s) and environmental conditions. Pesticide selection is furthermore affected by the farmer's socioeconomic status, knowledge, perceptions and preferences (Damalas and Eleftherohorinos, 2011; Hou and Wu, 2010). Questionnaire studies about farmer preferences in pesticide selection have shown that the most important factor for farmers is pesticide efficacy (Grieshop et al., 1992; Mengistie et al., 2015; Damalas and Koutroubas, 2014), i.e. how effectively pesticides kill the targeted pests. Despite quantifiable consequences for humans and the environment (Kim et al., 2017; Stone et al., 2014; Fantke et al., 2011), potential toxicity-related impacts are ranked low when selecting pesticides compared to other factors, such as availability, personal experience, and user friendliness of pesticide products (Grieshop et al., 1992). Costs of applying pesticides is an additional criterion that is relevant for selecting pesticides, depends on a farmer's income, and is most important for low income farmers (Grieshop et al., 1992; Mengistie et al., 2015; Damalas and Koutroubas, 2014). In this context, a study by Goeb et al. (2016) shows that some farmers believe in a price-quality correlation and tend to buy more expensive pesticides that are believed to perform better. In general, farmers often follow the advice of their retailers for choosing pesticides (Wang et al., 2015). These findings show that costs and impacts on humans and the environment are not consistently used to select pesticides, and several studies conclude that farmers even use banned, restricted and unregistered pesticides (Wang et al., 2015; Thuy et al., 2012), while several countries suffer from continuous overuse of pesticides (Ntow et al., 2006; Damalas and Koutroubas, 2014; Khan et al., 2015; Hou and Wu, 2010). Especially overuse is frequently associated with pesticide resistance (Damalas and Eleftherohorinos, 2011), and can have significant additional adverse effects on ecosystems and human health (Khan et al., 2015).

Overall, there is the need for simple screening-level tools to identify more sustainable pesticides whenever farmers are not able to switch to IPM or organic farming, while still reducing costs and potential health impacts on humans and the environment. Such tool, however, does not exist, considering registration, application costs, resistance, and toxicity-related impacts in a consistent way. Hence, to align farmers' practices with sustainability goals, a screening framework is required that aids farmers and other relevant stakeholders in identifying the most sustainable pesticides under specific conditions. Such a framework must be applicable to a wide range of pesticide-crop combinations and settings. To address this need, it is the aim of the present study to propose a screening framework for designing and evaluating pesticide substitution scenarios. We first present the general framework, discuss the included decision-relevant aspects, and finally apply our framework in a case study on pesticides applied on lettuce in Denmark. We have selected lettuce as example crop, because lettuce is among the most widely produced vegetables in Denmark with 720 hectare harvested and 15450 tonnes produced in 2016 (fao.org/faostat).

2. Methods

<Figure 1>

The overall information flow for designing, implementing and interpreting the pesticide substitution scenarios builds on several steps as shown in Figure 1. Firstly, a scenario is defined including temporal and geographical scope and indicators. Secondly, relevant input data are acquired and preprocessed as input for all indicator scores that are calculated in our models in the third step. Finally, indicator results are structured and pesticides ranked according to all considered indicators.

To compare pesticides that target the same pest, a number of factors needs to be considered. Five relevant indicators were identified, namely the registration status of the pesticide, price (i.e. pesticide application costs), human toxicity

and ecotoxicity potentials of the applied pesticide, and resistance of the target pest(s) toward the applied pesticide. A pesticide is required to be authorised and registered for use on a particular crop in the specific country or region of interest. The price of the pesticide product is crucial and often influences the selection of pesticides. Potential human toxicity and ecotoxicity impacts are important sustainability indicators to evaluate potentially toxic chemicals. Finally, pesticide resistance is an expanding issue (Georghiou, 2012) and an important factor for selecting effective pesticides. To demonstrate how these indicators are applied to define substitution scenarios and select the most viable alternative per scenario in terms of the given indicators, we designed a real-life case study with pesticides applied on lettuce in Denmark. Some of our selected pesticides are already indicated to be candidates for substitution in the EU (EC, 2015).

2.1. Defining substitution scenarios

<Table 1>

In order to define pesticide substitution scenarios, a crop of interest, one or more pests that can potentially damage this crop, and available pesticides that are designed to be effective against these pests need to be identified. For the identified pesticides, information on registration status, application amount, market price, potential toxicity-related impacts, and resistance needs to be collected. Authorisation and registration data are provided by regulatory agencies (e.g. the European Food Safety Authority, EFSA, in Europe). Application amount and market prices are usually found on product labels or in producer application guides. Input data for characterising toxicity impacts are found in databases like the Pesticide Properties Database (Footprint, 2018). Finally, data on resistance are found in individual studies or at databases, such as the Arthropod Pesticide Resistance Database (pesticideresistance.org).

Lettuce, a well known and widely consumed vegetable (Itoiz et al., 2012), was selected as example crop in our case study scenarios with Denmark as ex-

ample country. Our scenarios are defined on a per-hectare basis and with that, our case study reflects average lettuce growth conditions in Denmark. Within Europe, the European Commission authorises pesticides on the background of evaluations from EFSA, while the European Member States regulate which pesticides are formally registered for use on particular crops within their country. A list of pesticides authorised for use on lettuce was collected from EFSA reports published between 2009 and 2017. Common pests targeting lettuce and related pesticides effective against these pests were arranged in a pesticide-pest matrix (Table 1). The sources of reported lettuce pests and respective pesticides originate from Denmark, Australia and USA. The matrix, therefore, represents a global picture for selected common pests in lettuce and applicable pesticides, while it does not provide a comprehensive overview of all potential lettuce pests and related pesticides as our current case study focus is to assess scenarios in Denmark. To develop substitution scenarios for other crops or countries, our matrix would have to be adapted to include the prevalent pests and related available pesticides. In our case study, a single pest within each pesticide target class was selected to be further analysed. Downy mildew (*Bremia lactucae*) was selected as a fungal pest. Danish lettuce farmers have struggled with downy mildew (Henriksen et al., 2003b) and there are several pesticides available that are effective against this fungus. Aphids are a known insect pest in Denmark that attack many crops (Henriksen et al., 2003b), and lettuce aphids (*Nasonovia ribisnigri*) were selected as example insect pest. For evaluating herbicides, we selected annual bluegrass (*Poa annua*) as example weed. The pesticides relevant for inclusion into our case study substitution scenarios for lettuce pests are selected based on the following criteria:

1. The pesticide is currently authorised in the EU and registered for use on lettuce in Denmark;
2. Adequate information is available for the pesticide on all five considered substitution scenario indicators; and
3. The pesticides compared within each target class (e.g. fungicides) can

function as potential alternatives to each other, i.e. being effective against the same pest (to keep the comparison in our case study simple, we compared only pesticides that are applied with the same method e.g. foliar spray).

2.2. Substitution scenario input data

<Table 2>

Input data for our substitution scenarios were collected from different sources and are summarised in Table 2 with a full set of background data provided in the Supplementary material.

Authorisation: Historically, pesticides have been evaluated and approved in different countries for several years. In the EU, the process was harmonised with Directive 91/414/EEC in which it was required that all pesticides have to be approved before they are placed on the market. Today, the pesticide approval and registration process in the EU is controlled by EFSA, the European Commission (EC) and the EU Member States. Pesticide approval is regulated under the framework Regulation (EC) No 1107/2009. Authorisations of uses are then given by the authorities in each Member State. Maximum residue levels (MRLs) for pesticides are set under Regulation (EC) No 396/2005. MRLs are proposed by EFSA, based on which the EC and its Member States decide which MRLs to implement. In summary, pesticide authorisation is granted by the EC after voting among Member States based on an evaluation performed by EFSA. However, the individual Member States are responsible for registering pesticides for use on specific crops via plant protection products entering the national market. Information on registered plant protection products in Denmark can be found on the website of the Danish Environmental Protection Agency (Miljøstyrelsen, 2017). According to Regulation (EC) 1107/2009, pesticide registration includes also so-called bio-pesticides (e.g. ferric phosphate and plant extracts). Bio-pesticides are referred to as low-risk active substances in the legislation, of which currently 28 are approved in the EU.

175 *Application dosage and method:* Recommended usages of a pesticide are re-
 176 ferred to as Good Agricultural Practices (GAPs), differ between Member States,
 177 and are published by EFSA. GAPs include the recommended application dosage
 178 (mass per hectare) applied with a specific method on a crop or crop class to-
 179 gether with other information, such as minimum pre-harvest intervals and ap-
 180 plication counts per season. Data from different EFSA reports on pesticides
 181 applied to lettuce was used to design our scenarios and collect data on appli-
 182 cation methods and dosages. In cases where data originate from more than
 183 one EFSA report, the reported application dosages have been averaged for each
 184 pesticide and then multiplied with the average application count. In the EU,
 185 the application of the most toxic pesticides evaluated in 2009 should be avoided
 186 and substituted according to Regulation (EC) 1107/2009. These pesticides are
 187 marked as a candidate for substitution on the background of their toxic prop-
 188 erties e.g. low Acceptable Daily Intake or endocrine disrupting properties. In
 189 Denmark, one of the features is the taxes on pesticides based on environmental
 190 and health characteristics of the pesticides. Taxes and other instruments are
 191 outlined in the National Action Plan (MEFD, 2017).

192 *Resistance:* Pest resistance towards specific pesticides in lettuce has not been
 193 studied in Denmark according to a report prepared for the Danish EPA (Math-
 194 iassen et al., 2016). In our substitution scenarios (i.e. for comparing pesticides
 195 within the three main target classes with respect to respective pests), the prob-
 196 ability of a pest to develop resistance towards a specific pesticide is therefore
 197 based on studies outside Denmark. To date, information is to a varying degree
 198 available on resistance towards several commonly used pesticides. For some
 199 of our selected pesticides, no studies exist reporting resistance of the selected
 200 pest. In these cases, resistance information is based on data for a similar pest
 201 (another aphid or downy mildew species). Due to differences in reported resis-
 202 tance information, we combined two common methods for classifying resistance
 203 (the fold change in resistance and the percentage of trials showing resistance
 204 versus absolute number of trials showing resistance without giving the overall
 205 number of trials). To combine these types of information, we used a set of

semi-quantitative bins (high, medium, low) to indicate resistance ‘risk’ levels (i.e. high, moderate, or low probability that a pest develops resistance against a pesticide) that were assigned to each pest-pesticide combination in our final scenarios. We adopted the resistance classification from Mazzarri and Georgiou (1995) for low (≤ 5 -fold), moderate (> 5 and ≤ 10 -fold) and high (> 10 -fold) resistance probability. Furthermore, if a pesticide has efficacy above 85%, the resistance level was assigned to be low, and between 50% and 85% resistance probability was considered moderate. Table 3 gives an overview of the data we used for evaluating pest resistance.

<Table 3>

Application costs: Market prices are indicated for existing plant protection products that contain the selected pesticides. One plant protection product was chosen for each pesticide as specified in the Supplementary material. Information on market prices was collected from the official Middeldatabasen website (Middeldatabasen, 2017), which contains information about pesticides used in Denmark, where each plant protection product contains a specific formulation content (i.e. specific content of the active pesticide ingredient per litre of formulation) and recommended treatment rate (i.e. recommended litre per hectare applied to the field). Prices were corrected by the formulation contents provided in the respective EFSA reports and by the kg of actual pesticide active ingredient (a.i.) applied, hence the application cost is given in €/kg a.i.

Human toxicity potential: To characterise human toxicity potentials (expressed as disability-adjusted life years, DALY, per kg pesticide applied) in our substitution scenarios, we applied a mechanistic, screening-level chemical fate, exposure and toxicity assessment model, which is widely accepted and used in life cycle impact assessment and screening-level comparative risk assessment, namely the scientific consensus model USEtox (Rosenbaum et al., 2008; Westh et al., 2015). Characterisation factors for emissions to air and soil as well as residues in lettuce were combined with fractions emitted to air, soil and lettuce, respectively, to obtain related human toxicity potentials (*HTP*), expressed in

237 DALY/kg a.i. applied:

$$HTP_j = CF_{j,air}^h \cdot f_{j,air} + CF_{j,soil}^h \cdot f_{j,soil} + CF_{j,crop}^h \cdot f_{j,crop} \quad (1)$$

238 with CF_j^h as human toxicity characterisation factor [DALY/kg] and f_j as frac-
 239 tion emitted or reaching lettuce [kg/kg] for pesticide j . DALYs have been chosen
 240 as they are widely applied to indicate human health burden (e.g. Forouzanfar
 241 et al. (2016)), and aggregate population-level years of life lost due to premature
 242 death and years lived with a disability into a common metric. For pesticide
 243 emissions, we use widely accepted emission fraction estimates from risk assess-
 244 ment that were adapted to comparative assessments for lettuce and several other
 245 crops (Fantke and Jolliet, 2016). Emission fractions were estimated for lettuce
 246 as 0.05 to air, 0.11 to soil for fungicides and insecticides and 0.8 to soil for
 247 herbicides. Fractions emitted to soil differ for herbicides and other pesticides as
 248 herbicides are generally applied before crop emergence, whereas other pesticides
 249 are usually applied during a later crop growth stage. The fractions of applied
 250 pesticides remaining as residue in lettuce is obtained from (Fantke et al., 2012b).

251 *Ecotoxicity potential:* Characterisation factors representing potential eco-
 252 toxicity related impacts on freshwater aquatic ecosystems are also derived from
 253 USEtox and are expressed as potentially disappeared fraction (PDF) of exposed
 254 species integrated over exposed water volume and time for a chemical unit emis-
 255 sion. As emission compartments, we considered agricultural soil and continental
 256 rural air and subsequent transfer to freshwater, which we again combined with
 257 the default fractions of pesticides emitted to soil and air, respectively, to yield
 258 ecotoxicity potentials (EP), expressed in PDF m³ d/kg a.i. applied:

$$EP_j = CF_{j,air}^e \cdot f_{j,air} + CF_{j,soil}^e \cdot f_{j,soil} \quad (2)$$

259 2.3. Calculating substitution scores

260 Results from all five indicator categories (registration, pest resistance, hu-
 261 man toxicity potential, ecotoxicity potential, and pesticide application costs)
 262 were combined to yield overall indicator scores. As first step, indicator results x
 263 were normalised for each pesticide j to the highest score within each indicator

category i and pesticide target class, with lower normalised scores (N) representing better performances. Normalisation of $i \in \{\text{human toxicity; ecotoxicity; application costs}\}$ was determined as:

$$N_{i,j} = \frac{x_{i,j}}{\max(x_i)}, \quad (3)$$

Normalised scores for resistance were given based on the probability of resistance:

$$N_{\text{resistance}} = \begin{cases} 0\%, & \text{if low} \\ 50\%, & \text{if moderate} \\ 100\%, & \text{if high} \end{cases} \quad (4)$$

Finally, the registration status was normalised by giving a value of 100% if the pesticide was not authorised and registered for use on lettuce in Denmark, and 0% if it was authorised and registered:

$$N_{\text{authorisation}} = \begin{cases} 0\%, & \text{if authorised} \\ 100\%, & \text{if not authorised} \end{cases} \quad (5)$$

As second step, the overall performance for each pesticide j was determined by aggregating the five normalised indicators into a final indicator score (S), where a higher score reflects higher preference for a pesticide in terms of the combination of chosen indicators:

$$S_j = \frac{1}{\sum_{i,j} (N_{i,j})} \quad (6)$$

Individual indicators can have different importance depending on the decision context, which can be addressed by introducing weighting factors. Users might apply distinct weighting factors based on their specific preferences, interests, and perspectives. In our case study, weighting is based on the farmer's perspective as example. Application costs were considered of highest importance from a farmer's perspective with a weighting factor of $\omega = 2$. Resistance was given no weighting (i.e. $\omega = 1$), and if a pesticide is not authorised, the weighted

score will be 0 as the pesticide cannot be used, else $\omega = 1$. Weighting factors for human toxicity and ecotoxicity impacts are based on EU-15 data reported in Stranddorf et al. (2005), calculated from legislation and reduction targets within the EU. The weighting factor for human toxicity was divided between emissions to soil and air with $\omega = 1.23$ for soil, which was used for both soil and crop residues, and with $\omega = 1.06$ for air. For combining both weighting factors, the fractions to crop and soil were used to yield an overall human toxicity weighting factor of 1.22. The ecotoxicity weighting factor for chronic aquatic ecotoxicity was set to $\omega = 1.18$. Weighted final scores are then obtained by combining pesticide-specific normalised scores N with their respective weighting factors ω , where higher scores represent higher preference in terms of the combined and weighted indicators:

$$S_j^{\text{weighted}} = \begin{cases} \frac{1}{\sum_{i,j} (N_{i,j} \cdot \omega_i)}, & \text{if authorised} \\ 0, & \text{if not authorised} \end{cases} \quad (7)$$

2.4. Total costs of pesticides use

Potential impacts that pesticides have on environmental and human health may be converted into damage costs (also referred to as external costs or externalities) expressed in monetary values using valuation factors (VF). For human health impacts, the valuation factor of $VF = 40,000 \text{ €/DALY}$ is based on a contingent valuation study in 9 European countries (Desaigues et al., 2011). Damage costs (DC , €/kg a.i. applied) for each pesticide j were then calculated as:

$$DC_{j,\text{human toxicity}} = HTP_j \cdot VF_{\text{human toxicity}} \quad (8)$$

Calculating damage costs for ecotoxicity impacts requires a conversion of PDF $\text{m}^3 \text{ d}$ into species lost/ha. A valuation factor of $VF = 1.08 \times 10^{11} \text{ €/species}$ is applied based on people's willingness to pay for a species not to go extinct (Itsubo and Inaba, 2010) using a conversion factor of 0.008 €/yen. A species density in European freshwater of 1.18 species/ha (Goedkoop et al., 2009) and a total European freshwater volume of $4.1 \times 10^{13} \text{ m}^3$ (www.usetox.org) were used.

The species lost per hectare over one year was then calculated by multiplying the ecotoxicity characterisation factor with the total amount of freshwater species per hectare. After converting the characterisation factor to species loss per hectare (L), the ecotoxicity damage costs (DC) in €/kg a.i. were calculated for each pesticide j from the application dosage (M , kg/ha) and the valuation factor (VF):

$$DC_{j,ecotoxicity} = \frac{L_j \cdot VF_{ecotoxicity}}{M_j} \quad (9)$$

Often it can be hard to communicate to decision makers a score that consists of several parameters that all have different units. By calculating the ‘total costs’ for each pesticide it is easily communicated which alternative is preferable in terms of the combination of considered indicators. For that, application costs (AC) and damage costs can be aggregated into unit costs (C_{unit} , €/kg a.i.):

$$C_{j,unit} = DC_{j,human\ toxicity} + DC_{j,ecotoxicity} + AC_j \quad (10)$$

Combining unit costs with application dosage (M , kg a.i./ha) then yields total costs (TC , €/ha) per pesticide:

$$TC_j = C_{j,unit} \cdot M_j \quad (11)$$

3. Results an discussion

3.1. Substitution case study results

Unweighted and weighted final indicator scores obtained with Eqs. 6 and 7, respectively, are presented for our case study scenarios in Figure 2. Propamocarb performed best in the fungicide scenario in terms of both unweighted and weighted overall score, mainly due to its relatively low ecotoxicity and human toxicity potentials. Dimethomorph was the second best performing fungicide without weighting, but when introducing weighting factors, fosetyl-Al performed second best due to its low unit application costs. Given uncertainties in the range of two orders of magnitude for the toxicity-related scores, however, a refined analysis with improved toxicity data would be required to underline these

results. For herbicides, our results show relatively small differences between substance scores. In our herbicide scenario, none of the three considered substances is registered for use on lettuce in Denmark and therefore received a scoring of zero when weighted, i.e. none of the listed herbicides is a real option for substitution. In the insecticide scenario, pymetrozine performs best, with a score two times higher than the other insecticides. Dimethoate is the least favourable option, with a score slightly below pirimicarb. The EU lists dimethoate as candidates for substitution, and in Denmark, the substance is no longer registered for use, resulting in a weighted score of zero. Otherwise, our weighting factors have little influence on the ranking of the pesticides.

<Figure 2>

Table 4 shows for our case study scenarios toxicity-related damage costs and overall unit costs aggregating damage costs and application costs per unit mass of pesticide. Ecotoxicity-related damage costs are generally low, reflecting how damages on ecosystems are valued as compared to damages on human health rather than giving a picture of the distribution of impacts. In general for all fungicides except fosetyl-Al and for all herbicides, application costs drive overall unit costs, while for insecticides, human toxicity related damage costs are of similar magnitude as application costs.

<Table 4>

To facilitate an actual comparison of pesticides and identify the most viable substitute per scenario, we are generally interested in combining unit costs with application dosage for each pesticide to yield total pesticide-specific costs on a per hectare basis. Total costs for our case study scenarios are shown in Figure 3 with the z-axis (2nd y-axis on the right side) representing total costs given in €/ha visualised by the diagonal iso-cost lines. The more a pesticide is located at the top-right corner of Figure 3, the higher the related total costs per hectare.

Total costs in the fungicide scenario span over almost one order of magnitude. Low unit costs for fosetyl-Al (best option in the fungicide scenario in Table 4)

are compensated by the high application dosage resulting in relatively high total costs of 151 €/ha compared to the other fungicides. The three herbicides have total costs per hectare of very similar magnitude ranging from 39 €/ha for phenmedipham to 73 €/ha for propyzamide. However, none of them is registered for use on lettuce in Denmark, yielding no suitable substitute but requiring to consider additional options. In the insecticide scenario, dimethoate shows highest total costs of 302 €/ha, due to high damage costs from human toxicity (143 €/kg a.i.) and a relatively high application dosage (2 kg a.i./ha). In this scenario, pymetrozine and acetamiprid perform best with total costs of respectively 23 and 26 €/ha, rendering these pesticides promising substitutes for dimethoate. Overall, our results emphasise that substitution options are constrained by total costs of similar magnitude. An uncertainty analysis of our considered indicators shows that human toxicity potentials contribute with 48% to uncertainty of our total cost results, followed by ecotoxicity and resistance with 35% and 14%, respectively. In contrast, product price and applied pesticide mass only contribute with less than 2% each to uncertainty in cost results. For supporting effective substitution decisions, these uncertainties will have to be minimised based on future research efforts focusing mainly on collecting better input data for estimating human health impacts.

<Figure 3>

3.2. Applicability of our substitution framework

The three considered pesticides that are currently on the EU candidate substitution list were also the worst performing pesticides in our case study, supporting that our substitution framework can help identifying potential candidate pesticides for substitution. Our study provides a platform for farmers, consultants in agricultural service and public authorities to design and evaluate quantitative screening-level pesticide substitution scenarios. Our case study scenarios can be adapted to evaluate other pesticide-crop combinations in Denmark and elsewhere. The presented framework can help making informed decisions

on what pesticide to choose for a specific scenario based on different considered indicators. Weighting factors can be adapted depending on the decision context and based on stakeholders' specific preferences, interests, and perspectives. Additional indicators can moreover be included but should be consistent with the existing set of indicators. In our screening assessment, farmers are currently the only directly affected stakeholders, while for an overall alignment of farming practices with overarching sustainability goals a wider range of stakeholders will have to be considered. While there exist several agricultural insurance systems for farmers in the EU, there is currently no insurance scheme available that focuses on lowering chemical pesticide use. Hence, it is unlikely that such insurance system can act as a substitute for additional pesticide usage.

Our results agree well with findings from other substitution studies for individual aspects considered (e.g. human toxicity), but give an overall different ranking due to differences in the considered indicators. We compared our case study results with results from other screening-level substitution tools (Mghirbi et al., 2017; Juraske et al., 2007). While Mghirbi et al. (2017) included worker and environmental toxicity risk, production costs, yield and direct margin, application method, toxicity from crop residues, and pest resistance were not considered. Juraske et al. (2007) ranked pesticides based on dose, fate, exposure and toxicity impacts, and present results for eight out of twelve pesticides included in our case study. Comparing their results with ours shows that the ranking would match for the considered herbicides and insecticides, but would differ for the considered fungicides. Differences are mainly due to considering resistance and market price in our scenarios, which were not included in earlier studies.

Overall, our screening framework is efficient and applicable as a first step to identify potentially more sustainable alternatives among chemical pesticides. Starting from pesticides available to farmers, relevant substances can be screened with our framework in terms of the considered indicators. Comparing pesticides that are applied via the same methods (e.g. hand sprayer) would yield similar emission distributions regardless of the active substances applied. However,

weather conditions may play an important role and are a relevant aspect that should be considered when more sophisticated frameworks are applied or when entire farming practices are compared.

We reflect the technical rate of substitution via the difference in pesticide application rate, as this information is normalised per unit area of application based on assuming equal pesticide efficacy. By comparing and ranking pesticides based on our normalised scores, our tool helps to uncover potential trade-offs, when e.g. one pesticide has lower application costs per hectare, while showing higher toxicity potentials and related damage costs. Hence, substitution options among pesticides are best represented in our screening framework by aggregating and comparing overall costs for the farmer.

3.3. Limitations and future research needs

Our study has several limitations. In our screening-level substitution framework, human toxicity impacts are extrapolated from animal toxicity data, since for most pesticides epidemiological studies that can be used for comparative purposes are lacking. Ecotoxicity impacts are limited to freshwater ecosystems, while terrestrial and marine ecosystems are currently not included in USEtox but can be relevant for certain pesticides. For example, some neonicotinoid insecticides have shown adverse effects in pollinating insects (Whitehorn et al., 2012), which should be considered in future assessments. Our framework is limited to compare pesticides on the level of individual active ingredients, while often multiple pesticides are combined to target one or more pests. Potential mixture toxicity effects are hence not currently considered in our study and would require to decouple the pesticide function in the overall mixture as well as to consider mode-of-action specific data. Evaluating pest resistance is currently limited to using semi-quantitative information and is not systematically available for all pesticide-crop combinations. In Denmark, there are specific farms with zero pesticide use and to evaluate such farms, a more sophisticated substitution framework is required that can consider zero-pesticide practices. More quantitative resistance data would allow farmers to include this impor-

455 tant aspect in future substitution assessments. Finally, uncertainty in emission
 456 patterns and toxicity characterisation is currently not considered, but can be
 457 high depending on available data and relevant pathways. Indicator-specific un-
 458 certainty information should be included in future substitution scenarios, ac-
 459 counting for differences in data availability and quality.

460 The field of pesticides is in constant development, with new pesticides being
 461 designed and authorised, some existing pesticides being restricted or banned,
 462 and market prices fluctuating over time. Our substitution scenarios there-
 463 fore need to be continuously adapted to consider these developments. In our
 464 screening-level framework, the impact of agricultural policies is only consid-
 465 ered by including the registration status of pesticides, while more sophisticated
 466 frameworks might be able to capture additional policy aspects. One of the
 467 major challenges in our study was selecting data sources and collecting data.
 468 More readily available information on pesticide application, emission distribu-
 469 tion, toxicity characterisation, and pest resistance will simplify the process for
 470 farmers to use our framework. Technological progress in the agricultural sector
 471 will likely increase by 2050 with better crop management, modified crops and
 472 more efficient uptake of pesticides (e.g. Damak et al., 2016). Our substitution
 473 framework together with other tools will help pushing toward better pesticides
 474 management, where farmers yield the same plant protection level at lower costs
 475 as well as lower potential environmental and human toxicity impacts.

476 4. Conclusion

477 We presented and tested an operational framework for farmers to compare
 478 pesticides in agricultural practices using a score based on five indicators to rank
 479 pesticides. Data from EFSA reports helped to define substitution scenarios.
 480 Analysing pesticide resistance required a definition of semi-quantitative classes,
 481 and the registration status of pesticides for use on a specific crop in a certain
 482 country was considered. Our substitution scenarios showed substantial differ-
 483 ences in the scores for insecticides and fungicides. The weighting factors did not

substantially influence the ranking within these scenarios, while differences were mainly driven by varying (eco-)toxicity potentials. Total costs of pesticides, including toxicity-related damage costs, application costs and application amounts were obtained. Although being initially considered for evaluation based on EU authorisation, none of the herbicides included in our case study is actually registered for use on lettuce in Denmark, indicating few options for farmers battling annual bluegrass with chemical pesticides. Several pesticides were identified as potential substitutes for substances on the EU candidate substitution list. Pymetrozine can substitute dimethoate and pirimicarb and phenmedipham or propyzmide can function as a better alternative for pendimethalin. Improving the characterisation of pest resistance and reducing uncertainty in toxicity characterisation is necessary to further improve our substitution framework, while it can already be used for screening pesticides to identify viable and sustainable options.

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Appendix A. Supplementary material

Supplementary material including a list of various pesticide application scenarios summarised in a spreadsheet can be found at

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Table 1: Pesticide-pest matrix for lettuce scenarios in Denmark with pests in columns and pesticides in rows. Pesticides listed as being effective against the listed pest(s) are indicated by 'X'. Grey columns represent the three analysed scenarios with bold 'X' for the considered pesticides.

	Fungal pests				Weeds			Insect pests							
	PBR	GM	SLS	DM	LD	C	PW	AB	AW	BA	FA	L	LA	SW	H
Fungicides	azoxystrobin	X ^a		X ^d	X ^b										
	boscalid	X ^a		X ^a	X ^{a,b}										
	cyprodinil		X ^{a,b}		X ^{a,b}										
	dimethomorph			X ^{a,b}											
	fenamidone ¹			X ^a											
	fluopicolide ¹			X ^a											
	fosetyl-Al			X ^{a,c}											
	iprodione		X ^{a,b}		X ^{a,b}										
	mandipropamid			X ^{a,b}											
metalaxy ¹			X ^a												
propamocarb			X ^{b,c}												
Herbicides	diquat ²					X ^b		X ^a							
	pendimethalin ³						X ^b	X ^b							
	phenmedipham						X ^b	X ^b							
	propyzamide					X ^b		X ^{a,b}							
Insecticides	acetamiprid								X ^a				X ^a		
	dimethoate ³									X ^a			X ^a		
	enamectin benzoate													X ^b	
	imidacloprid ²									X ^a			X ^{a-c}	X ^{a,b}	
	indoxacarb								X ^a	X ^a					X ^b
	methoxyfenozone								X ^a	X ^a					X ^b
	pirimicarb ³											X ^b	X ^{b,c}		
	pymetrozine										X ^a		X ^{a,b}	X ^b	
	spinosad								X ^a	X ^a		X ^a			

Fungal pests: PBR: Phoma basal rot (*Phoma exigua*), GM: Grey mould (*Botrytis cinerea*), SLS: Septoria leaf spot (*Septoria apiicola*), DM: Downy mildew (*Bremia lactucae*), LD: Lettuce drop (*Sclerotinia sclerotiorum*); **weeds:** C: Clovers (*Galium aparine*), PW: Potato weed (*Galinsoga* spp.), AB: Annual bluegrass (*Poa annua*); **insect pests:** AW: Armyworm (*Mythimna unipuncta*), BA: Beet armyworm (*Spodoptera exigua*), FA: Foxglove aphid (*Aulacorthum solani*), L: Leafminers (*Liriomyza sativae*), LA: Lettuce aphid (*Nasonovia ribisnigri*), SW: Silverleaf whitefly (*Bemisia tabaci*), H: Helicoverpa (*Helicoverpa* spp.)

a) (UC IPM, The University of California Agriculture and Natural Resource, 2017), b) (Horticulture Innovation Australia, 2016), c) (Henriksen et al., 2003a), d) (Miljøstyrelsen, 2017). 1) Adequate information not available, 2) Application method seed or soil treatment, 3) Listed as candidates for substitution in the EU (EC, 2015).

Table 2: Input data for all pesticides included in the substitution scenario for lettuce in Denmark.

Pest	Active substance	CAS number	Application method ^(a,b)	Registered for use in DK	Resistance level	Application dosage ^(b) [kg a.i./ha]	Product costs ^(c) [€/kg a.i.]	Ecotoxicity ^(d) [PDF m ³ d/kg a.i.]	Human toxicity ^(d) [DALY/kg a.i.]
Fungi	azoxystrobin	131860-33-8	foliar spray	yes	moderate	0.67	38	1.2×10^3	9.0×10^{-5}
	dimethomorph	110488-70-5	foliar spray	yes	low	0.39	30	8.7	1.2×10^{-4}
	fosetyl-AI	39148-24-8	foliar spray	yes	moderate	9.6	40	0.32	2.9×10^{-4}
	mandipropamid	374726-62-2	foliar spray	yes	low	0.23	26	6.2	7.7×10^{-5}
	propamocarb	24579-73-5	foliar spray	yes	low	2.3	112	1.8×10^{-2}	3.5×10^{-5}
Weeds	pendimethalin	40487-42-1	foliar spray	no	moderate	1.5	52	8.9×10^2	1.1×10^{-6}
	phenmedipham	13684-63-4	foliar spray	no	low	0.59	40	24.1	1.4×10^{-6}
	propyzamide	23950-58-5	foliar spray	no	low	1.5	55	1.1×10^2	3.2×10^{-4}
	acetamiprid	135410-20-7	foliar spray	yes	low	0.11	10	0.58	3.7×10^{-3}
Insects	dimethoate	60-51-5	foliar spray	no	low	2.0	11	74	3.6×10^{-3}
	pirimicarb	23103-98-2	foliar spray	yes	high	0.47	36	2.4	1.4×10^{-3}
	pymetrozine	123312-89-0	foliar spray	yes	low	0.48	11	13	6.7×10^{-4}

a) Application method is either 'manual foliar spray' or 'truck mounted pesticide sprayer' in Denmark.

b) References are given in the supplementary material.

c) Application costs as reported 22-09-2017 in Middeldatabasen (2017) in DKK and converted with a conversion factor of 0.13 DKK/€.

d) Ecotoxicity and human toxicity impacts are calculated with the scientific consensus model USEtox (usetox.org).

Table 3: Overview of information on pest resistance levels for selected pesticides applied on lettuce.

Targeted pest	Pesticide	Resistance level	Remarks	References
Downy mildew (<i>Bremia lactucae</i>)	azoxystrobin	Moderate	No reported resistance for <i>Bremia lactucae</i> , but high resistance reported for similar species (<i>Plasmopara viticola</i> , <i>Phytophthora infestans</i>)	Gisi and Sierotzki (2008)
	dimethomorph	Low	90-95 % efficacy	Cohen et al. (2008)
	fosetyl-Al	Moderate	50% of samples showed insensitivity, 2% resistant sites	Crute (1992); Brown et al. (2004)
	mandipropamid	Low	90-95 % efficacy	Cohen et al. (2008)
	propamocarb	Low	<1% resistant sites	Crute (1992)
Annual bluegrass (<i>Poa annua</i>)	pendimethalin	Moderate	2.3-fold resistance, 9-fold resistance	Isgriigg III et al. (2002); Cuntulle et al. (2009)
	phenmedipham	Low	No studies of reported resistance found	
	propyzamide	Low	>90% efficacy, >87% efficacy	Isgriigg III et al. (2002); Toler et al. (2007)
Lettuce aphid (<i>Nasonovia ribisnigri</i>)	acetamiprid	Low	No cases found for <i>Nasonovia ribisnigri</i> and strong evidence of resistance towards similar pest (<i>Myzus persicae</i>) has not been detected	Agriculture and Horticulture Development Board (2014)
	dimethoate	Low	No resistance	Barber et al. (1999)
	pirimicarb	High	6.6-fold resistance, 62-fold-resistance, 42-fold resistance	Barber et al. (1999); Rufin-gier et al. (1997, 1999)
	pymetrozine	Low	No cases found for <i>Nasonovia ribisnigri</i> and resistance of similar pest (<i>Myzus persicae</i>) unknown	Agriculture and Horticulture Development Board (2014)

Table 4: Human toxicity and ecotoxicity damage costs (DC) and overall costs (C_{unit}) per pesticide unit applied to lettuce in Denmark.

	Active substance	$DC_{\text{human toxicity}}$	$DC_{\text{ecotoxicity}}$	C_{unit}
		[€/kg a.i.]	[€/kg a.i.]	[€/kg a.i.]
Fungi	azoxystrobin	4	0.13	59
	dimethomorph	5	1×10^{-3}	79
	fosetyl-Al	12	3.6×10^{-5}	16
	mandipropamid	3	7×10^{-4}	116
	propamocarb	1	2×10^{-6}	49
Weeds	pendimethalin	0.04	0.1	33
	phenmedipham	0.06	2.8×10^{-3}	66
	propyzamide	13	1.2×10^{-2}	49
Insects	acetamiprid	148	1.2×10^{-4}	231
	dimethoate	143	1.3×10^{-4}	148
	pirimicarb	56	1.1×10^{-4}	129
	pymetrozine	27	1.1×10^{-4}	48

A novel framework for the substitution of agricultural pesticides is presented.

A case study of pesticides applied to lettuce in Denmark was developed.

Results show costs from toxicity related damages and application practice.

Both costs per unit application and application amount per hectare are relevant.