



**HAL**  
open science

# Modélisation mathématique de la peste porcine africaine à l'interface entre élevages de cochons et sangliers : implications pour la lutte

Brandon Hayes

## ► To cite this version:

Brandon Hayes. Modélisation mathématique de la peste porcine africaine à l'interface entre élevages de cochons et sangliers : implications pour la lutte. Agricultural sciences. Université de Rennes, 2022. English. NNT : 2022REN1B072 . tel-04090824

**HAL Id: tel-04090824**

**<https://theses.hal.science/tel-04090824>**

Submitted on 6 May 2023

**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.

# THESE DE DOCTORAT DE

L'UNIVERSITE DE RENNES 1

ECOLE DOCTORALE N° 600

*Ecole doctorale Ecologie, Géosciences, Agronomie et Alimentation*

Spécialité : Statistiques/Modélisation en écologie, géosciences, agronomie et alimentation

Par

**Brandon H HAYES**

## **Mathematical modelling of African swine fever at the domestic-wildlife interface: Implications for control**

Thèse présentée et soutenue à l'Ecole Nationale Vétérinaire de Toulouse, le 14 Décembre 2022

Unité de recherche : Épidémiologie, santé et bien-être (EPISABE), ANSES, Ploufragan-Plouzané-Niort ; Interactions Hôtes-Agents Pathogènes (IHAP) INRAE-ENVT (UMR 1225), Toulouse

### **Rapporteurs avant soutenance :**

Pauline EZANNO Directrice de recherche, INRAE

Carola SAUTER-LOUIS Directeur adjoint Institut d'épidémiologie, Friedrich-Loeffler-Institut

### **Composition du Jury :**

Président : Emmanuelle GILOT-FROMONT Professeure d'épidémiologie, VetAgro Sup

Examineurs : Pauline EZANNO Directrice de recherche, INRAE

Ferran JORI Vétérinaire épidémiologiste, CIRAD

Carola SAUTER-LOUIS Directrice adjoint Institut d'épidémiologie, Friedrich-Loeffler-Institut

Mathieu ANDRAUD Chargé de recherche, ANSES

Dir. de thèse : Nicolas ROSE

Chef d'unité Epidémiologie, Santé et Bien-être & Directeur adjoint du laboratoire, ANSES

Co-dir. de thèse : Timothée VERGNE

Maître de conférences en santé publique vétérinaire, ENVT







## Acknowledgements

This work could not have been completed without the support and guidance from many mentors, colleagues, friends, family, and benefactors throughout this journey. First and foremost, thank you to my advisors Timothée Vergne, Mathieu Andraud, and Nicolas Rose. Your support, encouragement, perpetual availability, commitment to my development, warmth, dedication, and hospitality—especially through the difficulty of multiple Covid-19 quarantines—was paramount to my success. Thank you as well to the members of my thesis committee—Gaël Beaunée, Stéphanie Desvaux, Benoît Durand, and Vladimir Grosbois—for your expertise and insight into developing my research questions, and refining my approaches so that I could discover the answers. My brother Bradley Hayes, along with his family Liz Dressler and F.D.T. Hayes, thank you for your inspiration and boundless humor that only family can provide, you make the distance between France and Colorado a lot less far. Steve, Ruth, Jim, Kathy, Sue, and Amir, thank you for your enthusiasm, interest, love and undying support in my endeavors; I could not have hoped for a more encouraging family. Debapriyo Chakraborty and Shreejata Gupta, you are inspirational as both scientists and scholars. Thank you for such close friendship and support during difficult times of shared isolation and uncertainty, and inspiring me to always reach higher in my academic and personal pursuits. My colleagues Mattias Delpont, Claire Guinat, Sebastien Lambert, Jeremy Lesueur, Jun-sik Lim, Sebastian Moya Duran, and Luis Salazar, thank you for your collegiality and camaraderie; you brought life to the laboratory and helped to create the most pleasant of research environments. Sarah Marchand and the incredibly-talented Toulouse musician community, thank you for providing an outlet away from the laboratory and fostering an always-enjoyable shared creative space; it's been a pleasure to perform with you all. AJ, Natalie, Quinn, Olivia, Laura, Alvaro, Artie and Rose Cahill, and Beverly Suarez, thank you for your support from back home in New York, and for always keeping a place for me no matter where in the world I am. Daniella, Kai, and the Altit family, thank you for your support, essential contributions, and lovely shabbat dinners during the last final push of thesis writing. Neil Vora and Louis DelGiudice, thank you for your mentorship, your guidance in my personal and professional development, and for countless letters of recommendation; I would not have arrived at this point in my career without your support. Lastly, to my original public health and epidemiology mentors—Helen Engelke, Malika Kachani, Suzie Kovacs, and Peggy Schmidt—thank you for helping set me on this career path many years ago; you are the reason this journey began.

Many thanks to INAPORC and Agreenium for providing funding for this research, to the Romanian veterinary authorities and specifically Christian Mortasivu for their expertise and local insight, and to the INRAE MIGALE bioinformatics facility for providing essential computing resources.



## R | Résumé substantiel

### R.1 Introduction à la peste porcine africaine

La peste porcine africaine (PPA) est une fièvre hémorragique virale dévastatrice du porc, dont le taux de mortalité chez *Sus scrofa* (porcs domestiques et sangliers) approche les 100 % pour certains génotypes (Blome et al., 2013). C'est une maladie réglementée à déclaration obligatoire, impactant les marchés économiques de la filière porcine à toutes les échelles (WOAH, 2021). Les mesures de surveillance et de contrôle sont définies par la législation européenne, auxquelles peuvent s'ajouter des mesures locales dans les zones (pays) infectées. En 2007, le virus de la peste porcine africaine, enzootique en Afrique subsaharienne, a été introduit sur le continent Européen et s'est depuis propagé dans le monde entier, décimant les populations porcines en Europe, en Asie, en Océanie et aux Caraïbes. En l'absence de vaccin ou de traitement, et compte tenu de la transmission du virus entre les porcs domestiques et les sangliers, la PPA est l'une des maladies infectieuses les plus difficiles à contrôler.

La PPA est l'une des maladies les plus lourdes de conséquences pour les porcs domestiques. Elle est donc inscrite sur la liste des maladies à déclaration obligatoire de l'Organisation Mondiale de la Santé Animale (WOAH, 2021). Partout où son émergence est reconnue, cette fièvre hémorragique est socioéconomiquement dévastatrice pour les exploitations individuelles et les pays touchés (Dixon et al., 2020). En Roumanie, l'indemnisation des agriculteurs pour leurs pertes a coûté au gouvernement plus de €121 millions (Euromeat News, 2021). Au Vietnam, les foyers de 2019 ont été estimés à une perte de revenu national comprise entre US\$880 millions et US\$4,4 milliards (Nguyen-Thi et al., 2021). Si l'on tient compte des pertes initiales dues à la maladie et à l'abattage, ainsi que de la réorientation des ressources pour reconstituer le cheptel reproducteur national, les pertes dues aux foyers en Chine et en Asie du Sud-Est ont été estimées entre US\$55 et US\$130 milliards (Weaver & Habib, 2020). Dans l'Union européenne, on estime que les pays possédant des troupeaux porcins industrialisés (comme le Danemark) pourraient subir des pertes totales (coûts directs et pertes à l'exportation) allant jusqu'à €520 millions par épizootie (Halasa, Bøtner, et al., 2016a). Au-delà des pertes purement économiques, les effets psychosociaux du dépeuplement massif nécessaire des troupeaux infectés sont tout aussi graves. Des cas d'épuisement émotionnel et d'angoisse mentale ont été signalés chez les éleveurs, leurs familles et les agents de santé animale (Baysinger & Kogan, 2022). Enfin, les modèles de projection prévoient que le prix mondial du porc - la viande la plus consommée dans le monde—augmentera jusqu'à 85 %, ce qui aura des répercussions directes sur la sécurité alimentaire mondiale (Mason-D'Croz et al., 2020). La lutte contre la panzootie de la PPA est donc une priorité mondiale.



Seuls deux pays (sur les 45 qui ont connu des foyers jusqu'à présent) ont réussi à contrôler l'épizootie et à retrouver le statut de pays indemne de PPA, la République Tchèque et la Belgique. Ces deux pays y sont parvenus en utilisant des stratégies de contrôle codifiées qui comprennent l'établissement de zones spéciales de surveillance intensive par la construction de clôtures autour des cas détectés chez les sangliers, l'abattage des troupeaux de porcs domestiques affectés et à risque d'infection, la restriction des mouvements de cochons et de produits d'origine porcine, l'abattage des sangliers par des chasses ciblées et silencieuses, et la surveillance active et l'élimination des carcasses de sangliers infectieux (EFSA et al., 2021). La dynamique des épizooties de PPA en cours varie géographiquement, certains pays ne connaissant que des cas chez les sangliers, tandis que d'autres connaissent des épidémies dans les compartiments domestique et sauvage (WOAH, 2022d).

## R.2 Introduction à la modélisation mathématique

Les modèles mathématiques ont fait leurs preuves dans l'aide à la décision en matière d'épizootie. Les premiers modèles, au début du XXe siècle, reposaient sur des équations différentielles pour expliquer les fluctuations de la dynamique des populations (Brauer, 2017). Dans ces modèles, une population est divisée en compartiments en fonction de son état de santé, les plus simples étant les modèles à deux compartiments : ceux qui sont sensibles à la maladie (dans le compartiment S) et ceux qui sont infectieux (dans le compartiment I) (Brauer, 2017). Les modèles ultérieurs ont commencé à prendre en compte des statuts épidémiologiques supplémentaires, comme les états correspondant à la latence (E ; état durant lequel un individu est infecté mais n'est pas encore infectieux) les états de guérison (R, état dans lequel les individus ne sont plus infectieux et développent une immunité). Avec le développement des capacités mathématiques et informatiques, il est aujourd'hui possible de prendre en compte les spécificités liées aux connaissances sur la population hôte, le pathogène et leurs interactions. Il reste néanmoins important de bien identifier les objectifs du projet afin de développer le modèle pouvant y répondre sans ajouter une complexité inutile.

À l'aube du XXIe siècle, des modèles plus sophistiqués ont été capables de représenter les individus des populations, en tenant compte des relations temporelles et spatiales entre les agents du modèle. Ici, la somme des interactions individuelles a permis d'élucider la dynamique des populations. Les premiers modèles de ce type ont été appelés modèles d'automates cellulaires, où une trame de cellules représente une population, chaque cellule représentant un individu ou un groupe (Di Stefano et al., 2000; Rousseau et al., 1997). Les mouvements entre les individus peuvent être explicitement représentés, permettant de suivre la progression de chaque individu au sein du modèle. Ces modèles permettent de prendre en compte des caractéristiques individuelles au niveaux démographique et comportemental (White et al., 2007). Des modèles de métapopulation ont également été développés pour tenir compte des groupes d'hôtes partageant des caractéristiques similaires avec des interactions

entre groupes. La métapopulation peut inclure différents types d'hôtes par exemple, ou des groupes différents en réponse aux infections. Ici, la transmission de la maladie entre les sous-populations tient compte à la fois des taux de déplacement et des changements dans les populations (Brauer, 2017; van den Driessche, 2008). Avec l'augmentation de la puissance de calcul, la complexité des modèles basés sur les individus pourra également croître, ce qui permettra de réaliser des simulations d'épidémies prenant en compte des différences à haute résolution entre les agents du modèle, telles que la susceptibilité et l'infectiosité.

La compréhension de la dynamique de transmission de la tuberculose bovine, de l'encéphalopathie spongiforme bovine et de la fièvre aphteuse a été améliorée par l'utilisation de modèles mathématiques. Lors de l'épidémie de la fièvre aphteuse de 2001 au Royaume-Uni, les modèles ont été utilisés pour informer les stratégies de contrôle et fournir une aide à la décision en temps réel (Keeling, 2005). A propos de la tuberculose bovine, les modèles mathématiques ont mis en évidence les taux de propagation entre les populations réservoirs de blaireaux et hôtes et de bovins, afin d'éclairer les stratégies de contrôle d'une population pour en protéger une autre (Donnelly & Nouvellet, 2013; Donnelly & Hone, 2010). Enfin, les modèles mathématiques ont été nécessaires pour estimer l'incidence stratifiée par âge chez les bovins et déterminer l'impact des politiques d'abattage visant à contrôler la crise de l'ESB (« maladie de la vache folle ») du XXe siècle. En prédisant les voies de transmission et le temps jusqu'à l'extinction de la maladie, des stratégies de contrôle ont pu être conçues (R. M. Anderson et al., 1996).

### R.3 Revue systématique des modèles mathématiques de la peste porcine africaine

Pour concevoir des stratégies efficaces de prévention, de surveillance et d'intervention contre la PPA, il faut comprendre la dynamique de la transmission du virus, qui peut souvent être élucidée à l'aide de modèles mécanistes. Afin d'examiner les hypothèses sur la transmission et les objectifs des modèles mécanistes de la PPA, une revue systématique de la littérature scientifique a été réalisée. Les articles ont été examinés en fonction de multiples caractéristiques épidémiologiques et de modèles, la filiation entre les modèles étant déterminée par la création d'un arbre joint par le voisinage à l'aide d'un logiciel phylogénétique.

Trente-quatre articles ont été retenus, avec quatre objectifs principaux de modélisation identifiés : estimation des paramètres de transmission (11 études), évaluation des déterminants de la transmission (7), examen des conséquences d'épidémies hypothétiques (5), évaluation des stratégies de contrôle alternatives (11). Des modèles sont développés à différentes échelles dépendant de leurs objectifs : population (17), métapopulation (5) ou individu (12). Les représentations aux échelles populationnelle et métapopulationnelle étant principalement utilisées dans les modèles focalisés

spécifiquement sur la transmission du virus chez les porcs domestiques. Les modèles individu-centrés étant principalement utilisés chez les sangliers. La majorité des modèles (25) ont été paramétrés sur des données expérimentales ou de terrain pour des isolats de génotype II qui circulent actuellement en Europe et en Asie.

Les paramètres de transmission estimés dans les articles variaient considérablement selon les souches de VPPA, les lieux et l'échelle de transmission. Les incertitudes sur les paramètres épidémiologiques et écologiques ont généralement été prises en compte pour évaluer l'impact des valeurs des paramètres sur la trajectoire d'infection modélisée. À ce jour, presque tous les modèles n'intègrent qu'un seul type d'hôte les porcs domestiques ou les sangliers, malgré le fait qu'il soit prouvé que les événements de transmission interspécifique jouent un rôle important dans les épidémies de PPA. Par conséquent, il est crucial de développer des modèles intégrant de telles voies de transmission, de manière à quantifier la contribution relative de ces deux populations dans le maintien de la circulation virale. L'efficacité d'un grand nombre de stratégies de contrôle a été évaluée, mais il s'agissait toujours d'interventions guidé par la législation de l'UE et définies *a priori*. En outre, les stratégies de contrôle ont été examinées en concurrence les unes avec les autres, ce qui est opposé à la façon dont elles seraient réellement mises en œuvre de manière synergique. Bien que la comparaison des stratégies soit bénéfique pour identifier l'ordre d'efficacité des méthodes de lutte, cette structure ne détermine pas nécessairement la combinaison la plus efficace de toutes les stratégies disponibles. Pour que les modèles de lutte contre la PPA puissent soutenir efficacement la prise de décision dans la lutte contre le virus au niveau mondial, ces limites de modélisation doivent être abordées.

#### R.4 Revue systématique de la modélisation mathématique à l'interface domestique-faune sauvage

Dans le domaine de la modélisation mathématique des maladies épizootiques, le développement de modèles à l'interface domestique-faune sauvage présente un ensemble unique de défis. En effet, des articles entiers ont été écrits sur les défis inhérents (Buhnerkempe et al., 2015; Roberts et al., 2021). La simple estimation de la transmission entre espèces est une tâche lourde, car il est difficile de définir ce qui constitue un contact épidémiologiquement pertinent (Buhnerkempe et al., 2015). Les contacts forcés en laboratoire sont différents de ceux qui ont lieu dans des circonstances naturelles, et l'observation des contacts naturels pour déduire les paramètres du modèle est une tâche écologique difficile (Buhnerkempe et al., 2015). En outre, les événements de transmission sont rarement observés, mais leur fréquence doit être indirectement déduite, afin d'informer les moyens de transmission de la maladie dans la population non-réservoir. Une deuxième revue de la littérature a été réalisée afin d'éclairer le développement de notre modèle de la PPA à l'interface domestique-

faune sauvage. Nous avons cherché à examiner les moyens de représentation des espèces animales domestiques et sauvages dans les études épidémiologiques à l'interface élevage-faune, et à identifier les facteurs de transmission utilisés dans les modèles.

Trente-cinq articles ont été retenus. De multiples cadres de modèles étaient représentés à l'échelle de l'individu (15), de la population (12), ou utilisant des approches de type automates cellulaires (3), modèles écologiques (2), modèles de réseau (2) et un modèle de métapopulation. Les objectifs de ces modèles peuvent être résumés comme suit : évaluer les stratégies de contrôle (17), la dynamique de la transmission (8) ou les deux (2), estimer les paramètres (4) et établir des preuves de concept pour de nouvelles méthodologies (4). Les espèces domestiques ont été représentées par des emplacements ponctuels, des rasters de distribution de la densité, des nœuds de réseau du type d'hôte ou, pour les modèles basés sur la population, des variables individuelles reflétant le nombre d'animaux dans un compartiment donné à un moment donné. Les hôtes sauvages ont été principalement représentés par des rasters de domaines vitaux représentant l'habitabilité en fonction de données géographiques. Des nœuds de réseau, des données historiques de présence ou des paramètres individuels d'abondance d'hôtes (pour les modèles basés sur la population) ont également été utilisés.

Les taux de transmission sont le moyen le plus courant de quantifier la transmission de la maladie entre les hôtes domestiques et sauvages, de manière unidirectionnelle ou bidirectionnelle. Bien que rencontrées moins fréquemment, des probabilités de transmission, ont néanmoins été utilisées, essentiellement lorsque des données permettant de spécifier le taux de contacts inter-espèces étaient disponibles. La majorité des modèles ont simulé la transmission directe de l'infection, bien que la transmission indirecte (par exemple via un environnement partagé ou des insectes vecteurs) ait également été prise en compte dans quelques modèles.

La contribution relative des espèces impliquées dans la propagation de l'épizootie n'a été déterminée que dans deux modèles, où les données historiques sur les cas et les mouvements ont été utilisées pour déterminer le potentiel de transmission intra-hôte et, à partir de là, le risque de transmission inter-hôte.

Après avoir exploré les multiples façons dont la transmission des maladies infectieuses entre les espèces domestiques et sauvages a été modélisée mécaniquement, nous avons pu appliquer les résultats - en particulier en ce qui concerne les échelles et les modalités de représentation des populations, les voies de transmission, et la contribution relatives des deux espèces - pour informer le développement d'un modèle de transmission de la PPA à cette interface.

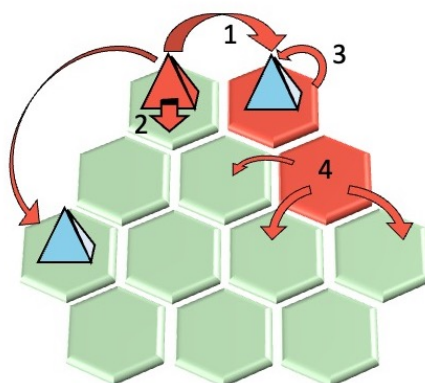
## R.5 Modélisation de la transmission de la peste porcine africaine à l'interface des porcs domestiques et des sangliers en Roumanie

Depuis 2018, la Roumanie fait face à une épizootie de PPA d'une ampleur sans précédent, affectant à la fois les sangliers sauvages et les porcs domestiques. La compréhension de la dynamique de transmission est nécessaire pour concevoir des mesures de contrôle sur mesure, adaptées aux spécificités de l'élevage de porcs domestiques au regard des aspects socio-économiques. L'omniprésence de l'élevage de porcs de basse-cour dans les villages - la majorité des familles ayant un ou plusieurs porcs élevés dans des élevages de basse-cour à faible biosécurité - fournit un environnement très propice à la transmission entre cochons et sangliers. Afin de reproduire la dynamique spatio-temporelle en Roumanie, d'estimer la contribution relative des élevages de porcs domestiques et des sangliers à la propagation de l'épizootie, et d'évaluer l'impact des différents types d'unités hôtes (c'est-à-dire les zones forestières et non forestières pour les sangliers, les villages et les sites industriels pour les élevages de porcs domestiques), un modèle mécaniste de transmission spatialisé et multi-hôtes a été construit.

Dans le cadre de cette thèse, nous avons travaillé sur la région du sud-est de la Roumanie où la propagation initiale de l'épizootie a été observée au cours du deuxième semestre 2018. Les données épidémiologiques pour l'ensemble des cas, dans les élevages de porcs domestiques et dans la faune sauvage, ont été utilisées pour la calibration du modèle : dates et géolocalisations des notifications et espèces impliquées. La construction du modèle repose sur l'utilisation de données géographiques l'identification et la géolocalisation des villages (unité administrative), la géolocalisation des élevages de porcs industriels et la couverture végétale comme proxy de la distribution de la population de sangliers. La population de porcs domestiques a été représentée à l'échelle du village, pour les élevages de basse-cour, ou de l'élevage, pour les sites industriels avec des niveaux de biosécurité respectifs faible et fort. L'abondance des troupeaux de sangliers a été modélisée via l'adéquation de l'habitat en utilisant une trame hexagonale de couverture du paysage en cellules de 25 km<sup>2</sup>, dont la taille correspond aux domaines vitaux estimés des sangliers. L'intersection de cette grille avec les données issues de l'imagerie satellite CORINE Land Cover, a permis d'évaluer l'habitabilité de chaque cellule en fonction de sa couverture forestière.

Le modèle d'interaction entre les animaux d'élevage et la faune sauvage est un modèle hybride qui a été construit en superposant un modèle individuel d'unités de porcs domestiques (villages ou sites industriels) à un modèle d'automates cellulaires pour la population de sangliers, et en permettant à l'infection de se produire à la fois dans et entre les couches (Fig. R.1). Les modèles épidémiologiques consistent en des combinaisons de quatre états pour chaque unité épidémiologique : sensible (S),

infectieux non détecté ( $I_u$ ), infectieux détecté ( $I_d$ ) et rétabli ( $R$ ). Les unités de porcs domestiques ne peuvent être infectées qu'une fois, l'état  $R$  représentant (de manière plus réaliste pour un virus comme le VPPA) le dépeuplement de l'unité épidémiologique. Les cellules de sangliers sont continuellement infectieuses jusqu'à la fin de la période d'étude, représentant la persistance du virus dans la population de sangliers et dans l'environnement. Pour pouvoir identifier la contribution des différentes voies de transmission, quatre taux de transmission, définis comme les taux auxquels un agent sensible acquiert une infection à partir d'un agent infecté par unité de temps, ont été considérés : d'un troupeau (villageois ou industriel) à un autre troupeau, d'une cellule à une autre cellule, d'une cellule à un troupeau à l'intérieur de la cellule, d'un troupeau à la cellule qui le contient. Les taux de transmission ont été introduits dans des équations de force d'infection - le cumul des pressions infectieuses individuelles exercées par tous les individus infectieux sur l'individu sensible - pour déterminer la probabilité de transition de l'état sensible à l'état infectieux non détecté. D'autres transitions d'état ont été modélisées de manière stochastique.



**Fig. R.1** | Représentation des unités de porcs domestiques (pyramides) et des cellules de sangliers (cellules matricielles hexagonales) dans le paysage modèle. Les unités infectées sont en rouge. Les flèches correspondent aux pressions d'infection exercées par et sur chaque unité du modèle : (1) unités de porcs domestiques sur d'autres unités de porcs domestiques, (2) unités de porcs domestiques sur la cellule de sanglier qui les contient, (3) cellules de sanglier sur les unités de porcs domestiques au sein de la cellule, et (4) cellules de sanglier sur d'autres cellules de sanglier.

Les valeurs des paramètres ont été définies par une combinaison de revues de la littérature, des méthodes d'inférence bayésiennes et de calibration manuelle aux données observées. Ainsi, le modèle développé a pu être ajusté aux trajectoires épizootiques observées en Roumanie parmi les

unités de porcs domestiques et les cellules de sangliers sauvages. La contribution relative des compartiments domestiques et sauvages a ensuite pu être évaluée. Parmi les unités de porcs domestiques, nous avons estimé qu'une médiane de 94 % des infections (intervalle de crédibilité à 95 % : 75,6-96,3 %) provenaient d'autres troupeaux de porcs, tandis que 5,17 % (IC 95 % : 2,88-20,6 %) provenaient de sangliers. Inversement, parmi les cellules de sangliers, 57,8 % des infections (IC 95 % : 38,5-86,8 %) provenaient d'autres cellules de sangliers, tandis que 40,9 % (IC 95 % : 9,48-59,6 %) provenaient d'unités de porcs domestiques.

Ce modèle mécaniste a ensuite été utilisé pour explorer *in silico* l'impact de stratégies de contrôle alternatives, si elles avaient été mises en œuvre dès le début de l'épizootie.

#### R.6 Évaluation de stratégies de gestion alternatives contre la peste porcine africaine dans un système multi-hôte

Les stratégies de contrôle observées, à savoir la surveillance passive des troupeaux de porcs domestiques, la mise en place d'une surveillance active des troupeaux de porcs domestiques par l'établissement de zones de surveillance de 10 km autour des cas détectés, l'abattage des troupeaux infectés dans un village, et la surveillance active des sangliers (recherche de carcasse et chasse), ont été incluses dans la paramétrisation de notre modèle. Nous avons d'abord effectué une analyse d'incertitude, où nous avons évalué la réponse du modèle à la perturbation de paramètres spécifiques. Par la suite, des scénarios alternatifs ont été examinés en simulant une variété de stratégies de contrôle.

Une analyse d'incertitude a été effectuée sur deux paramètres clés : le paramètre régissant la décroissance exponentielle de la transmission en fonction de la distance entre deux élevages ( $\delta$ ) et l'augmentation relative du taux de détection des cas parmi les unités de porcs domestiques qui se produit dans les zones de surveillance. Quatre valeurs du paramètre  $\delta$ , avec une gamme de variation inférieure à 20 % par rapport à la valeur initiale, ont été testées. L'effet de la zone de surveillance - initialement fixée à 50 % et représentant l'efficacité des activités sur le terrain sur la détection des cas - a été examiné dans des scénarios où elle n'avait aucun effet ou augmentait le taux de détection relatif de 25 % et 75 %. Les stratégies de contrôle alternatives ont été choisies pour envisager des améliorations soit dans la détection des cas, soit dans la prévention des cas et sont résumées dans le tableau R1.

Tableau R1 | Synthèse des stratégies de contrôle évaluées

Stratégie de lutte	Méthode d'évaluation
Autres tailles de zones de surveillance	Ajuster la taille de la zone de surveillance
Améliorer la surveillance passive des unités de porcs domestiques	Réduire la durée moyenne de la période infectieuse non détectée
Abattage à l'échelle du village dès la détection d'un cas	Forcer une durée moyenne de la période infectieuse d'une semaine dans tous les troupeaux.
Abattage préventif des unités de porcs domestiques en cas de détection d'un cas de sanglier à proximité.	Les unités de porcs domestiques dans une cellule infectieuse détectée passent automatiquement à l'état R dès la détection de la cellule.
Assainissement de l'environnement par l'élimination des carcasses de sangliers	Les cellules retournent à l'état sensible après la période spécifiée de détection de l'infection.

L'impact des paramètres de l'analyse d'incertitude et des stratégies de contrôle alternatives a été évalué en comparant leurs effets moyens sur la taille totale de l'épizootie et la contribution relative des hôtes à la propagation de l'épizootie.

Le kernel de transmission—la décroissance exponentielle de la force de transmission selon la distance—a eu un effet profond sur la taille de l'épizootie parmi les unités de porcs domestiques, avec une différence moyenne de taille d'épizootie de 30 % (l'écart : 25-36 %) pour  $\delta = 0.24$ . Comme on pouvait s'y attendre, l'augmentation du kernel de transmission (de 0,2 à 0,22 ou 0,24) a entraîné une diminution du nombre de cas, réduisant les champs d'interaction des élevages infectés. Le choix du kernel de transmission a également eu un effet sur la contribution relative de chaque hôte à la transmission, bien que limité : l'augmentation de 10% du paramètre du kernel de transmission a entraîné une diminution moyenne de 3,9 % de la transmission relative des troupeaux de porcs domestiques aux cellules de sangliers.

Les résultats de la simulation d'épizootie étaient également sensibles au taux d'augmentation supposé de la détection des cas dans une zone de surveillance. Pour chaque augmentation de 25 % du taux de détection relatif dans une zone de surveillance, on a observé une diminution moyenne de 89 cas d'unités de porcs domestiques. L'augmentation du taux de détection des élevages dans les zones de surveillance a également entraîné une diminution des cas de cellules de sangliers, avec une moyenne de 23 cas de moins par augmentation de 25 % du taux de détection.

La taille des zones de surveillance a eu un effet significatif sur la taille globale de l'épizootie, tant pour les unités de porcs domestiques que pour les cellules de sangliers. Chaque augmentation de 5 km de la taille de la zone de surveillance a entraîné une réduction moyenne de 50 unités de porcs domestiques et de 14 cellules de sangliers infectées (soit 350 km<sup>2</sup> supplémentaires exempts de PPA). La fréquence relative de la transmission entre les compartiments a également été affectée par la taille



de la zone de surveillance. Pour chaque augmentation de 5 km de la taille de la zone de surveillance, une diminution de 2,6 % de la transmission relative des unités de porcs domestiques aux cellules de sangliers a été observée.

La réduction de la période de non détection de 3 semaines à 2,5 ou 2 semaines a entraîné de faibles changements dans la taille finale de l'épizootie. Avec une période infectieuse non détectée de 2,5 semaines, une médiane de 48 troupeaux et 12 cellules de plus ont échappé à l'infection. L'augmentation du taux de détection passive parmi les troupeaux de porcs domestiques était aussi associée à une diminution de la contribution relative des unités de porcs domestiques à l'infection des cellules de sangliers.

Lors de l'examen des stratégies d'abattage, on a considéré à la fois l'abattage préventif d'un village en cas de détection d'un cas dans un troupeau de sangliers voisin et l'abattage complet d'un village en cas de détection d'un cas dans un troupeau de basse-cour du village. L'abattage préventif a permis de réduire la taille médiane de l'épizootie dans les troupeaux de porcs domestiques de 16 % (n = 69) pour atteindre 369 infections. De plus, une médiane de 9 cas de moins (n = 95) parmi les cellules de sangliers a été observée avec cette stratégie. Lorsque l'abattage à l'échelle du village en réponse à un cas de porc domestique a été utilisé, la taille médiane de l'épizootie a été réduite de plus de 33 %.

La dernière stratégie de contrôle examinée était l'effet de l'élimination des carcasses et de la décontamination de l'environnement. Une différence faible mais présente dans la contribution entre les hôtes a été notée, l'élimination des carcasses pendant 8 ou 6 semaines ayant entraîné de légères diminutions de la transmission des cellules de sangliers aux unités de porcs domestiques, passant d'une médiane de base de 5,17 % des événements de transmission à 4,42 % ou 4,19 %, respectivement.

Les ajustements du kernel de transmission—conséquences des restriction potentielles des échanges commerciaux et de la limitation des déplacements entre les villages—ainsi que l'augmentation de l'efficacité des zones de surveillance (notamment par l'augmentation de la main-d'œuvre disponible et des mesures de surveillance intra-villageoise) et l'abattage à l'échelle du village lors de la détection des cas ont eu les effets les plus importants sur la limitation de l'ampleur de l'épizootie. Malgré cela, la diminution des cas provenant de porcs domestiques est compensée dans une certaine mesure par une augmentation relative des cas provenant de sangliers. Les futures étapes de la recherche, dans lesquelles des algorithmes d'optimisation sont appliqués aux six stratégies explorées ici, pourraient permettre de mieux comprendre quelles stratégies sont les mieux utilisées en combinaison.

## Discussion et conclusions

En utilisant un nouveau modèle créé spécifiquement pour notre question de recherche, nous avons réussi à générer une estimation de la contribution relative des hôtes domestiques et sauvages à la propagation épizootique du VPPA en Roumanie. Après avoir identifié les contributions relatives des hôtes, nous avons pu aborder la deuxième question de recherche : élucider les effets des stratégies de contrôle dans un compartiment sur la dynamique globale du système. D'autres stratégies couramment employées, telles que l'installation de clôtures et l'augmentation de la pression de chasse des sangliers, n'ont pas pu être incluses dans notre modèle, mais les versions futures devraient prendre en compte ces ajouts. De plus, avant d'utiliser notre modèle pour formuler des recommandations politiques, il faudrait inclure un module économique qui quantifie les coûts et les bénéfices anticipés des stratégies de contrôle alternatives. Bien que des modèles de simulation de plus en plus réalistes puissent jouer un rôle de plus en plus important dans les processus de décision des décideurs, une collaboration multisectorielle entre épidémiologistes, vétérinaires, virologistes, écologues, économistes, éleveurs de porcs, décideurs, et modélisateurs sera essentielle pour maintenir une approche inclusive de la modélisation de la PPA. S'assurer que toutes les parties ont des objectifs alignés concernant la définition et les objectifs de la lutte contre la PPA facilitera une approche unifiée pour faire face à cette panzootie porcine mondiale, et les modèles mathématiques pourront continuer à apporter leur soutien.



# Table of Contents

<b>Acknowledgements</b> .....	<b>1</b>
<b>Résumé substantiel</b> .....	<b>3</b>
<b>Table of Contents</b> .....	<b>15</b>
<b>Acronyms and abbreviations</b> .....	<b>17</b>
<b>List of figures</b> .....	<b>19</b>
<b>List of tables</b> .....	<b>21</b>
<b>§ I   Introduction to African swine fever and epizootic modelling</b> .....	<b>23</b>
1   <i>Epidemiology of African swine fever</i> .....	25
1.1 African swine fever epizootics—A history of escape .....	25
1.2 An African swine fever panzootic—Georgia 2007/01 .....	28
1.3 African swine fever virus and its hosts .....	30
1.4 African swine fever transmission .....	32
1.5 African swine fever control .....	34
1.6 African Swine Fever impact.....	36
2   <i>Mathematical modelling of epizootic disease</i> .....	39
2.1 A concise history of mathematical modelling .....	39
2.2 The proven utility of epizootic mathematical modelling .....	41
<b>§ II   Systematic reviews of mathematical modelling</b> .....	<b>45</b>
3   <i>Mathematical modelling of African swine fever: A systematic review</i> .....	47
3.1 Introduction .....	47
3.2 Material and methods.....	47
3.3 (Results) Included publications and epidemiological characteristics.....	49
3.4 (Results) Model objectives and filiation .....	51
3.5 (Results) Model insights and assumptions .....	60
3.6 Discussion.....	66
3.7 Conclusions .....	69
4   <i>Systematic review of mathematical modelling at the domestic-wildlife interface</i> .....	73
4.1 Introduction .....	73
4.2 Materials and Methods.....	74
4.3 Results .....	75
4.4 Discussion.....	83

4.5 Conclusions .....	85
<b>§ III   Evaluating control strategies against African swine fever transmission at the domestic-wildlife interface.....</b>	<b>87</b>
5   <i>Modelling African swine fever transmission at the interface of domestic pigs and wild boar in Romania</i> .....	89
5.1 Introduction .....	89
5.2 Materials and methods .....	91
5.3 Results .....	102
5.4 Discussion.....	112
5.5 Conclusions .....	119
6   <i>Assessing alternative management strategies against African swine fever in a multi-host system.....</i>	121
6.1 Introduction .....	121
6.2 Materials and Methods .....	122
6.3 Results .....	123
6.4 Discussion.....	129
6.5 Conclusions .....	138
<b>§ IV   Overall discussion and conclusion .....</b>	<b>141</b>
7   <i>Discussion.....</i>	143
7.1 Thesis aims and accomplishments .....	143
7.2 Impact: Our contribution to the ASF modelling body .....	145
7.3 Future directions .....	148
7.4 Reflections.....	153
8   <i>General conclusions .....</i>	157
<b>§ V   Bibliography .....</b>	<b>159</b>
9   <i>Bibliography.....</i>	159

## Acronyms and abbreviations

ABC-SMC	Approximate Bayesian computation - sequential Monte Carlo
ABM	Agent-based model
ANSVSA	Autoritatea Națională Sanitară Veterinară și pentru Siguranța Alimentelor (Romanian National Veterinary Sanitary and Food Safety Authority)
ANCPI	Agencia Naional de Cadastru i Publicitate Imobiliara (Romanian National Agency for Mapping and Real Estate)
APMC	Adaptive population Monte Carlo
ASF	African swine fever
ASFV	African swine fever virus
BSE	Bovine spongiform encephalopathy
bTB	Bovine tuberculosis
$d_{50}$	The distance at which the transmission kernel is reduced by 50%
EFSA	European Food Safety Authority
EU	European Union
FAO	Food and Agricultural Organization of the United Nations
FMD	Foot-and-mouth disease
HDI	Highest Density Interval
HIV	Human immunodeficiency virus
IBM	Individual-based model
PBCM	Population-based compartmental model
$R_0$	Basic reproduction number
$R_E$	Effective reproduction number
S-I <sub>u</sub> -I <sub>d</sub>	Susceptible-Infectious (undetected)-Infectious (detected)
S-I <sub>u</sub> -I <sub>d</sub> -R	Susceptible-Infectious (undetected)-Infectious (detected)-Recovered
S-I <sub>u</sub> -I <sub>d</sub> -R-S	Susceptible-Infectious (undetected)-Infectious (detected)-Recovered-Susceptible
S-I <sub>u</sub> -I <sub>d</sub> -S	Susceptible-Infectious (undetected)-Infectious (detected)-Susceptible
SEIR	Susceptible-Exposed-Infected-Recovered
SIR	Susceptible-Infected-Recovered
SIS	Susceptible-Infected-Susceptible
USA	United States of America
WOAH	World Organization for Animal Health (formerly OIE)



## List of figures

<b>FIG. 1.1</b>   WORLD MAP OF ASF CASES. ....	26
<b>FIG. 1.2</b>   TIMELINE OF THE ASFV GENOTYPE II PANZOOTIC BY HOST OF DISEASE INTRODUCTION, 2007-2022. ....	27
<b>FIG. 3.1</b>   PRISMA FLOW DIAGRAM FOR ARTICLE SELECTION. ....	50
<b>FIG. 3.2</b>   PUBLICATIONS BY YEAR SUBSET BY HOST .....	51
<b>FIG. 3.3</b>   FILIATION TREE OF INCLUDED ARTICLES ON MECHANISTIC MODELLING OF ASF. ....	56
<b>FIG. 4.1</b>   PRISMA FLOW DIAGRAM FOR ARTICLE SELECTION. ....	75
<b>FIG. 4.2</b>   FREQUENCY OF REPRESENTED DOMESTIC SPECIES IN INCLUDED MODELS .....	76
<b>FIG. 4.3</b>   PUBLICATIONS BY YEAR SUBSET BY MODEL OBJECTIVE .....	78
<b>FIG. 5.1</b>   SPATIOTEMPORAL CLUSTERS OF ASF IN ROMANIA, JUNE 2018 – AUGUST 2019. ....	90
<b>FIG. 5.2</b>   EXPANDED MAP OF SOUTHEASTERN COUNTIES IN ROMANIA. ....	92
<b>FIG. 5.3</b>   VISUALIZATION OF FOREST-COVERAGE HABITAT-RASTER GENERATION FROM CORINE LANDCOVER DATA. ....	93
<b>FIG. 5.4</b>   REPRESENTATION OF MODELLED SPACE. ....	95
<b>FIG. 5.5</b>   FLOW DIAGRAM OF INFECTION STATES FOR MODEL UNITS OF THE FINAL SELECTED MODEL ( $SI_{ub}R-SI_{ub}$ ). ....	96
<b>FIG. 5.6</b>   SPATIAL VISUALIZATION OF QUARTERLY DISTRIBUTION OF OBSERVED CASES. ....	104
<b>FIG. 5.7</b>   ASF WEEKLY INCIDENCE FOR JUNE 2018 THROUGH DECEMBER 2018. ....	105
<b>FIG. 5.8</b>   QUARTERLY INFECTIOUS PERIODS BY EPIDEMIOLOGICAL UNIT. ....	105
<b>FIG. 5.9</b>   MEAN SQUARED ERROR (MSE) FOR INFECTION-STATE MODEL VARIANTS. ....	106
<b>FIG. 5.10</b>   POSTERIOR PROBABILITY COMPARISON FOR MODELS OF FIRST AND SECOND ORDER ADJACENCY TRANSMISSION. ....	107
<b>FIG. 5.11</b>   EPIDEMIOLOGIC FREQUENCY TRAJECTORIES OF SIMULATED EPIZOOTICS. ....	110
<b>FIG. 5.12</b>   EPIZOOTIC SIZES ACROSS SIMULATIONS BY HOST. ....	111
<b>FIG. 5.13</b>   RELATIVE CONTRIBUTION OF DOMESTIC PIG UNITS AND WILD BOAR CELLS TO EPIZOOTIC PROPAGATION. ....	111
<b>FIG. 5.14</b>   SPATIAL VISUALIZATION OF PROPORTION OF INFECTIONS PER UNIT. ....	112
<b>FIG. 6.1</b>   TRANSMISSION KERNEL DISTANCE EFFECT BY KERNEL VALUE. ....	124
<b>FIG. 6.2</b>   SENSITIVITY OF FINAL EPIZOOTIC SIZE TO THE TRANSMISSION KERNEL BY HOST. ....	126
<b>FIG. 6.3</b>   SENSITIVITY OF THE RELATIVE TRANSMISSION FREQUENCY BETWEEN HOSTS TO ALTERNATIVE TRANSMISSION KERNELS. ....	126
<b>FIG. 6.4</b>   SENSITIVITY OF FINAL EPIZOOTIC SIZE TO THE RELATIVE INCREASE IN DETECTION WITHIN SURVEILLANCE ZONES. ....	127
<b>FIG. 6.5</b>   SENSITIVITY OF THE RELATIVE TRANSMISSION FREQUENCY BETWEEN HOSTS TO INCREASES IN THE DETECTION RATE WITHIN SURVEILLANCE ZONES. ....	127
<b>FIG. 6.6</b>   EFFECT OF SURVEILLANCE ZONE SIZE ON FINAL EPIZOOTIC SIZE. ....	130
<b>FIG. 6.7</b>   EFFECT OF SURVEILLANCE ZONE SIZE ON RELATIVE TRANSMISSION FREQUENCY BETWEEN HOSTS. ....	130
<b>FIG. 6.8</b>   EFFECT OF REDUCING THE UNDETECTED INFECTIOUS PERIOD ON FINAL EPIZOOTIC SIZE BY HOST. ....	131
<b>FIG. 6.9</b>   EFFECT OF REDUCING THE UNDETECTED INFECTIOUS PERIOD ON RELATIVE TRANSMISSION FREQUENCY BETWEEN HOSTS. ....	131
<b>FIG. 6.10</b>   EFFECT OF CULLING STRATEGIES ON FINAL EPIZOOTIC SIZE. ....	132
<b>FIG. 6.11</b>   EFFECT OF CULLING STRATEGIES ON THE RELATIVE TRANSMISSION FREQUENCY BETWEEN HOSTS. ....	132
<b>FIG. 6.12</b>   EFFECT OF CARCASS REMOVAL ON FINAL EPIZOOTIC SIZE. ....	133
<b>FIG. 6.13</b>   EFFECT OF CARCASS REMOVAL ON THE RELATIVE TRANSMISSION FREQUENCY BETWEEN HOSTS. ....	133





## List of tables

<b>TABLE 3.1</b>   EPIDEMIOLOGICAL CHARACTERISTICS OF ARTICLES .....	52
<b>TABLE 3.2</b>   MODEL CHARACTERISTICS OF ARTICLES .....	57
<b>TABLE 3.3</b>   PARAMETER RESULTS .....	58
<b>TABLE 3.4</b>   PARAMETER ASSUMPTIONS .....	61
<b>TABLE 4.1</b>   EPIDEMIOLOGICAL CHARACTERISTICS OF THE 35 ARTICLES INCLUDED IN THE REVIEW .....	77
<b>TABLE 4.2</b>   MODEL CHARACTERISTICS OF ARTICLES .....	81
<b>TABLE 5.1</b>   PARAMETER VALUES .....	101
<b>TABLE 5.2</b>   PARAMETER CALIBRATION RESULTS. ....	108
<b>TABLE 6.1</b>   SUMMARY OF ASSESSED CONTROL STRATEGIES .....	123
<b>TABLE 6.2</b>   TRANSMISSION KERNEL DISTANCE FUNCTION.....	124



## § I | Introduction to African swine fever and epizootic modelling

In 2007, African swine fever virus (ASFV) genotype II—one of the 24 genotypes of ASFV circulating in Africa—escaped from its native home range in the southeastern part of the continent. Entering Eurasia through the Caucasus region, sustained ASFV transmission has since resulted in a panzootic of unprecedented scale. With nations across four continents outside of Africa afflicted (Asia, Europe, North America, and Oceania), this fatal and untreatable disease of pigs is decimating the global swine industry. Improving prevention and management strategies is paramount to controlling the disease and halting further spread.

Mathematical models have been used to inform disease management strategies since their inception one century prior (Kermack *et al.*, 1927). They have a proven track record of confronting infectious disease outbreaks; facilitating the design, improvement, and optimization of control strategies. Using equations to mechanistically describe transmission processes, they have been applied to numerous infectious disease scenarios among both human and animal populations. With the advent of modern computing capabilities, increasingly complex models have been able to be employed. Progressing from the original deterministic explanations for otherwise complex phenomena, modern epidemiological models capture the stochastic dynamics observed in epidemics. Through the discovery of transmission parameters that enable the reproduction and simulation of an epidemic, alternative control strategies can be evaluated to improve future outbreak responses. Similarly, mathematical modelling holds promise for addressing the areas of need for the current ASF panzootic. In this section, we will first synthesise the current knowledge we have on ASF and then describe the history and utility of mathematical modelling of epizootic diseases.



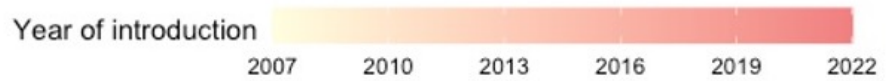
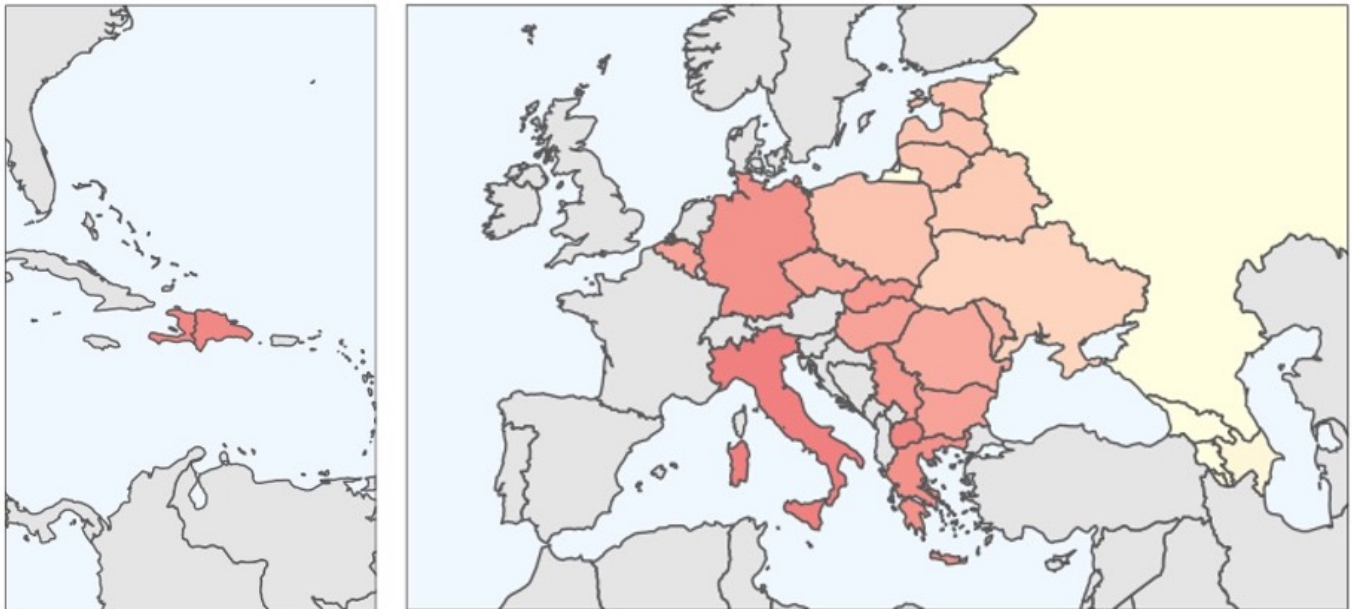
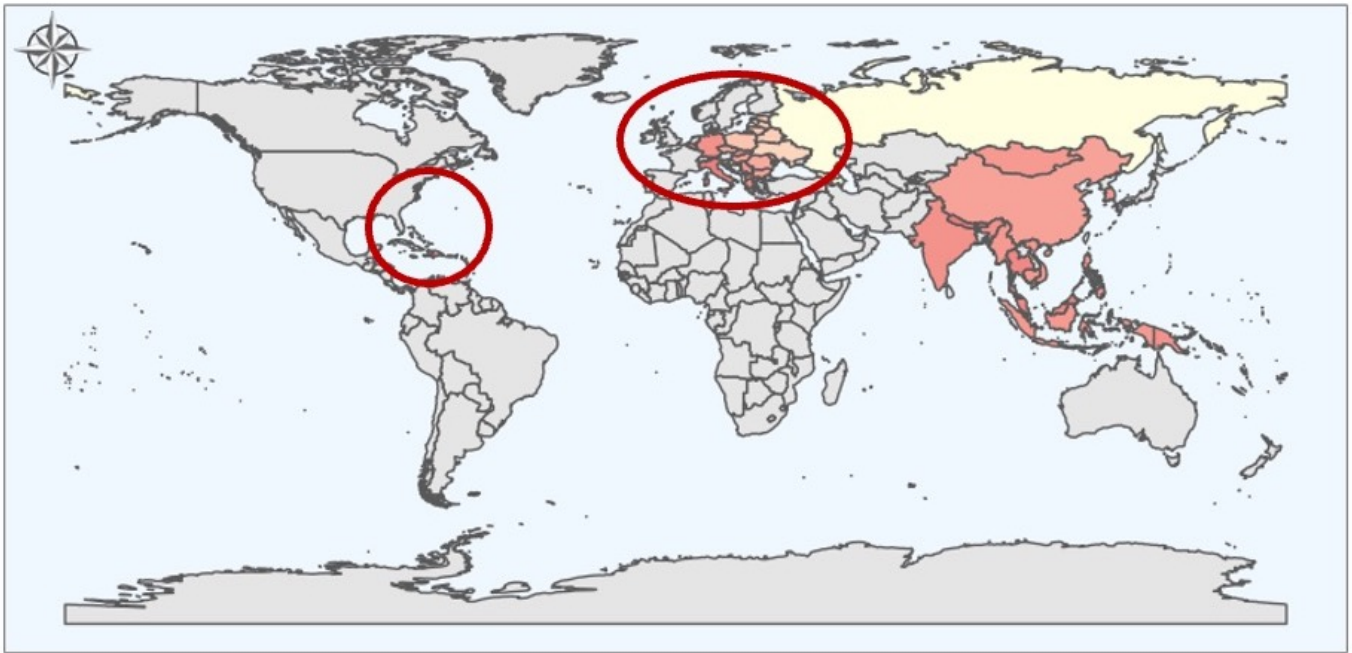
## 1 | Epidemiology of African swine fever

### 1.1 African swine fever epizootics—A history of escape

Enzootic throughout sub-Saharan Africa, eponymously-named African swine fever virus (ASFV) has escaped from its home continent multiple times since its discovery last century. The first escape from Africa occurred into Europe in 1957 when ASFV genotype I was detected in Portugal. Believed to have originated from infected airline food waste being fed to pigs near Lisbon airport (Van Schepen & Kunesh, 1981; Costard *et al.*, 2009; Boinas *et al.*, 2011; Danzetta *et al.*, 2020), the virus spread across and beyond the Iberian Peninsula, with European nations experiencing multiple small epizootics over the subsequent 30 years (Cwynar *et al.*, 2019; Dixon *et al.*, 2020). These outbreaks in France (1964, 1967, 1974), Italy (1967, 1969, 1993), Malta (1978), Belgium (1985), and the Netherlands (1986) were able to be brought under control through combinations of domestic pig depopulation and wild boar hunting measures, with the island of Sardinia the sole exception to ASF eradication where it is still enzootic (Costard *et al.*, 2009; Cwynar *et al.*, 2019; Mazur-Panasiuk *et al.*, 2019). Even Spain and Portugal, where ASF had become enzootic via the local *O. erraticus* tick population, achieved a return to ASF-free status by 1995 through a comprehensive eradication program targeting infected herds and *Ornithodoros* reservoirs (Arias & Sánchez-Vizcaíno, 2002; Boinas *et al.*, 2011; Danzetta *et al.*, 2020).

Following European invasion ASFV continued to spread through trade and transit networks, reaching several Caribbean nations (Cuba in 1971, Dominican Republic in 1978, Haiti in 1979) as well as Brazil (1978) prior to being eradicated within a few years in each country (Costard *et al.*, 2009; Lyra, 2006; Simeón-Negrín & Frías-Lepoureau, 2002; P. Wilkinson, 1989). The second introduction into the European continent occurred in 2007, where investigations indicated that transport ships out of southeast Africa arriving at the port of Poti on the Black Sea sold contaminated meat products that were later fed to pigs (Rowlands *et al.*, 2008; Gogin *et al.*, 2013; Cwynar *et al.*, 2019; Beltrán-Alcrudo *et al.*, 2008). Genotyping, revealing the isolated virus to be consistent with ASFV genotype II, suggested an origination of Mozambique, Zambia, or Madagascar (Rowlands *et al.*, 2008).

What began as a single viral incursion, however, has since grown into a porcine panzootic of unprecedented scale (Fig. 1.1, Fig. 1.2). Following dissemination across Georgia—where over 80,000 pigs died from disease or were culled—ASF spread through the Caucasus region into Armenia, Azerbaijan, and the Russian Federation (Gogin *et al.*, 2013; Cwynar *et al.*, 2019; Rowlands *et al.*, 2008). Ukraine and Belarus began reporting cases in 2012 and 2013, respectively, and then in 2014 ASF entered into the European Union (EU) via the Baltic States and Poland (Cwynar *et al.*, 2019; Dixon *et al.*, 2020). Cases have since been identified in 12 EU Member States, with nine—Bulgaria, Estonia,



**Fig. 1.1** | World map of ASF cases. Expanded greater European continent and part of North America by year of first domestic pig or wild boar case for the current ASFV genotype II panzootic. ASF spread can be seen from its 2007 entrance in the Caucasus up through recent cases in western Europe, East Asia, and the Caribbean.

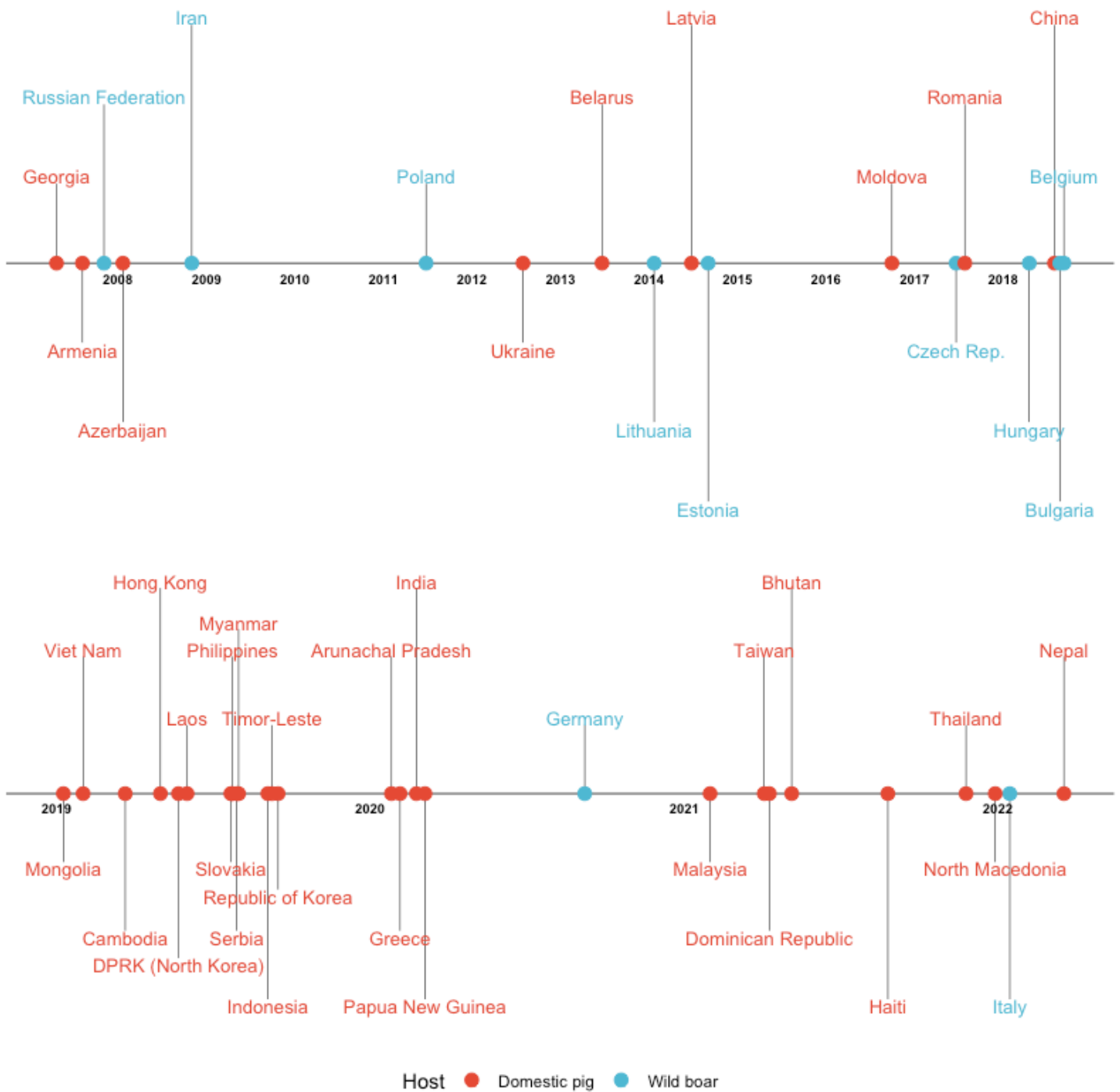


Fig. 1.2 | Timeline of the ASFV genotype II panzootic by host of disease introduction, 2007-2022.



Germany, Hungary, Latvia, Lithuania, Poland, Romania, and Slovakia—still facing epizootics as of the end of 2021 (EFSA *et al.*, 2022).

The ASF Georgia 2007/01 panzootic became acutely worse in 2018 when China, home to half of the global swine population, reported its first case in its northeastern provinces (Dixon *et al.*, 2020). As the epizootic grew, cases spread both south throughout China as well as into Mongolia, and a year later in 2019 were reported in Vietnam (Mighell & Ward, 2021). The same year, ASF was reported in Cambodia in April and in Hong Kong and the Democratic People’s Republic of Korea in May, and by the end of 2019, cases had also been reported in Laos, the Philippines, Myanmar, Indonesia, Timor-Leste, and the Republic of Korea (Mighell & Ward, 2021). Following both genotype and serotype characterization of ASFV strains from China and Vietnam, molecular evidence revealed high homology between viruses in Asia and Europe—indicating that the cases in Asia are likely a continuation of spread of the original Georgia 2007/01 strain (Ge *et al.*, 2018; Le *et al.*, 2019; Mighell & Ward, 2021). Of note, ASFV genotype I has recently been detected in China, too. Though molecularly similar to genotype I isolates from Portugal in the 1960s, a source of invasion has yet to be elucidated (Sun *et al.*, 2021).

Outside of the Eurasian continent, ASFV Georgia 2007/01 managed to access the Caribbean islands as well, where in 2021 cases were reported in the Dominican Republic and Haiti (USDA, APHIS, 2021). Following its escape, ASF has now been reported in 35 countries across 5 world regions (Africa, the Americas, Asia, Europe, and Oceania) (WOAH, 2022b).

## 1.2 An African swine fever panzootic—Georgia 2007/01

The current panzootic strain—ASFV genotype II Georgia 2007/01—has managed to spread around the world, and with effective vaccine and treatment strategies still lacking, its control and eradication has proven exceedingly difficult (Turlewicz-Podbielska *et al.*, 2021). The majority of circulating Georgia 2007/01 isolates are highly-virulent, although a variant with reduced virulence was identified among wild boar in Estonia (Dixon *et al.*, 2020; Zani *et al.*, 2018).

ASF transmission pathways have been seen to vary between epizootic areas. Some nations have experienced cases predominantly or exclusively among wild boar, as is the case in the Baltic states and South Korea (and with Italy and Germany recently increasing the list) (DEFRA, 2021; Jo & Gortázar, 2021; Lim *et al.*, 2021; Van Goethem, 2021). Other countries, like China, the Russian Federation, or Romania—where there exists a preponderance of low-biosecurity backyard pig farms—have experienced cases among both domestic pigs and wild boar, with likely spillover between these domestic and wild compartments (Andraud *et al.*, 2021; Gogin *et al.*, 2013; Mighell & Ward, 2021). In

the Russian Federation, both spillover from wild boar into domestic pig populations, as well as spillback following human activity around improper domestic pig carcass disposal, had been noted (Sauter-Louis, Conraths, *et al.*, 2021). Nonuniform surveillance between affected areas complicates assessment of these pathways, however. In most of Asia there is a paucity of reported cases among wild boar, despite much evidence suggesting that wild boar densities in some regions are similar to eastern Europe. Coupled with the wide distribution of observed domestic pig cases, regular spillback to the wild compartment of ASF is strongly suspected (Vergne *et al.*, 2020).

Human activities have been historically seen as the primary driver of transmission between domestic pigs, and have been suspected for the majority of the recent introductions in western Europe such as in Belgium and Germany (Chenais *et al.*, 2019). Even after control measures are put into place, complex social factors—including factors associated with farmer livelihood (such as inadequate compensation to culling mandates) and personal relationships (distrust of authorities)—can lead to breakdowns in containment, underground markets, and further transmission; as has been seen in the Caucasus region (Chenais *et al.*, 2019; Gulenkin *et al.*, 2011).

Among wild boar, it was initially hypothesized that without the presence of a domestic pig reservoir—due to the high virulence of the Georgia 2007/01 ASFV strain—the disease would be self-limiting among wild populations (Chenais *et al.*, 2019; Schulz *et al.*, 2019). This was proven false as northern countries (i.e. Poland and the Baltic states) saw ASF become established at low prevalences within wild populations, following initial infection and subsequent population decrease (Chenais *et al.*, 2019; Schulz *et al.*, 2019). The effect of wild boar density on ASFV transmission remains uncertain, being that no population density threshold has been able to be defined that would arrest disease spread (EFSA *et al.*, 2018; Schulz *et al.*, 2019). While the transmission velocity among wild boar appears to be slow in heavily affected areas (estimated at 2-5 km/month), long range jumps in ASFV—most likely associated with human-mediated activities related to the feeding of contaminated products—have been observed to and within multiple countries, including the Czech Republic, Poland, Hungary and Belgium (Chenais *et al.*, 2019; DEFRA, 2017; EFSA *et al.*, 2017).

Additional transmission pathways of concern for the current panzootic include the role of both arthropod reservoirs and insect vectors. While the current ASF incursion has not yet reached the Iberian Peninsula, *O. erraticus* is known to be capable of harboring and transmitting ASFV. However, experimental studies on transmission dynamics within this species suggest they are likely incapable of sustaining circulation of the current Georgia 2007/01 ASFV strain (Boinas *et al.*, 2011; Pereira de Oliveira *et al.*, 2019; Vergne *et al.*, 2021). In the Baltic nations, an observed seasonality of domestic pig outbreaks corresponded with the seasonal presence of hematophagous insects. Though this

strongly suggested a potential role in ASFV transmission, when such flies were collected from infected farms in Lithuania they tested negative for ASFV (EFSA *et al.*, 2020; Guinat, Gogin, *et al.*, 2016).

Despite the aggressive global spread of ASF, there is hope for once again achieving control. Though ASF is a highly contagious disease—as has been exemplified through numerous transmission experiments of multiple strains (Ferreira *et al.*, 2013; Gallardo *et al.*, 2017; Guinat, Gubbins, *et al.*, 2016; Olesen *et al.*, 2017; Thomson *et al.*, 1980)—field observations and an experiment of the current panzootic strain suggest that, contextually, contagiousness in the field may be far less than laboratory-observed contagiousness (Chenais *et al.*, 2019). On some farms, field investigations revealed only a few ill or dead animals at time of suspicion, with other animals testing negative for ASFV in spite of direct contact (via a shared pen) for over a week (Chenais *et al.*, 2019; Nurmoja *et al.*, 2020; Oļševskis *et al.*, 2016). Further, as evidenced in a transmission experiment, only the weakest wild boar (two animals with a runted appearance) became infected from inoculation—the other animals only later becoming infected following direct contact with the carcasses of the originally infected animals (Chenais *et al.*, 2019; Pietschmann *et al.*, 2015). Coupled with a case report on transmission within a large commercial farm, where excess mortality was not observed for over a month, evidence suggests that the initial mortality—and consequent rate of transmission—may be low (Chenais *et al.*, 2019; Lamberg *et al.*, 2020).

Available control strategies have already demonstrated their effectiveness, with Belgium and the Czech Republic having been declared free of ASF (and Estonia, having achieved ASF-free status among its domestic pigs, soon to be as well) (EFSA *et al.*, 2021). Until a vaccine becomes available, further improvements of existing control strategies (especially regarding wild boar), leading to better and more cost-effective surveillance, prevention, and responses to ASF incursions, will be the next hurdle towards stopping this panzootic.

### 1.3 African swine fever virus and its hosts

The disease of African swine fever is a consequence of infection by the sole viral member of the genus *Asfivirus*, of the *Asfarviridae* family: African swine fever virus (ASFV) (Alonso *et al.*, 2018; Dixon *et al.*, 2020). First identified in Kenya in 1921, ASFV is a large, double-stranded DNA virus native to sub-Saharan Africa with over 24 different genotypes having since been discovered (as defined by the C-terminal end of the p72 protein) (Dixon *et al.*, 2020; Eustace Montgomery, 1921; Njau *et al.*, 2021). These different genotypes do not intrinsically suggest differing pathogenicities between ASF viruses, but are a reflection of the genetic diversity that results from the ancient sylvatic cycle that maintains the virus in the wild (Dixon *et al.*, 2020).

All members of the *Suidae* family are susceptible to ASFV infection, though the clinical presentation of disease of a hemorrhagic fever is restricted to members of *Sus scrofa* (domestic pigs and wild boar) (Blome *et al.*, 2013; Dixon *et al.*, 2020). Generally classified as of high, moderate, or low virulence (Pan & Hess, 1984), different strains of ASFV result in peracute, acute, subacute, or (disputedly) chronic forms of ASF (Sánchez-Vizcaíno *et al.*, 2015). Observed with highly-virulent strains, peracute and acute (the most common) forms of disease result in death within four or eight days post-infection, respectively, while less virulent strains yield a subacute presentation and may not be fatal until 20 days following infection (Sánchez-Vizcaíno *et al.*, 2015).

A chronic carrier form of ASFV among domestic pigs has been historically suggested, based on serological evidence and as observed in Spain, Portugal and the Dominican Republic (as cited in Sánchez-Vizcaíno *et al.*, 2015). In the 1960s, low-virulent isolates of ASFV were used in live-attenuated vaccination studies in the Iberian Peninsula, and it is hypothesized that these isolates resulted in the natural evolution of a chronic carrier state among the local population (Costard *et al.*, 2013; Sánchez-Vizcaíno *et al.*, 2015). Affected pigs were observed to have visible cutaneous lesions and other clinical signs, however, and would not be considered asymptomatic carriers (Sanchez-Botija, 1982; Sánchez-Vizcaíno *et al.*, 2015). A recent review has indicated that, epidemiologically, such a chronic carrier state among otherwise healthy pigs is an unlikely reality (Ståhl *et al.*, 2019).

Eurasian wild boar, known to also be highly susceptible to ASF, have conversely been detected to have antibodies to ASFV in the absence of clinical signs (Jori & Bastos, 2009; Pérez *et al.*, 1998). Historically ASFV has been seen to fade-out from wild boar populations, however, without the availability of re-infection from free-range domestic pig herds (Jori & Bastos, 2009; Pérez *et al.*, 1998). With such seropositivity among wild boar having been tied to regions with infected free-range domestic pigs, wild boar have historically not been considered a major reservoir in the absence of their infected co-host (Jori & Bastos, 2009; Laddomada *et al.*, 1994). In contrast, self-sustainability of the current panzootic strain of ASFV genotype II in wild boar populations in the absence of domestic pig cases appears to be the rule rather than the exception (Sauter-Louis, Conraths, *et al.*, 2021).

The other African *Suidae* genera of *Phacochoerus* (warthogs), *Potamochoerus* (bushpigs and red river hogs) and *Hylochoerus* (giant forest hogs) exhibit a natural resistance to clinical disease (Blome *et al.*, 2013; Jori & Bastos, 2009; WOA, 2021). Through experimentation, however, these species have been proven to be capable of acting as infectious hosts (E. C. Anderson *et al.*, 1998; Jori & Bastos, 2009; Oura *et al.*, 1998; Thomson *et al.*, 1980). While both warthogs and bushpigs are found throughout eastern and southern Africa, and while both their ecological ranges are in accord with observed distributions of ASFV, due to the greater numbers, more uniform distribution, and greater rates of

infection observed, warthogs are agreed to be the primary wildlife reservoir (Costard *et al.*, 2013; De Tray, 1957; Plowright *et al.*, 1969; Thomson, 1985).

The resistance to clinical disease among warthogs enables ASFV to persist in a sylvatic cycle with soft ticks of the *Ornithodoros* genus (Jori & Bastos, 2009; Sánchez-Vizcaíno *et al.*, 2015; Wade *et al.*, 2019). Multiple *Ornithodoros* spp. are capable of harboring live ASFV for years (EFSA Panel on Animal Health and Welfare, 2010; Frant *et al.*, 2017). These soft ticks are predominantly found throughout Africa, though they have also been identified on the European continent in Spain, Portugal, Italy, southern Greece, and Turkey (Frant *et al.*, 2017). *O. moubata*, synonymous with the *O. porcinus* designation that originally described the original reservoir species in 1962, serves as the primary arthropod host for maintaining this sylvatic cycle (Frant *et al.*, 2017; Jori & Bastos, 2009; Roger *et al.*, 2001; Walton, 1962). Distributed throughout southern and eastern Africa, this tick species is conspicuously absent from West Africa, where such a sylvatic cycle has yet to be revealed (Jori & Bastos, 2009).

*Ornithodoros* spp. are also responsible for a transmission cycle among domestic pigs in ASFV-enzootic regions, with *O. erraticus*—present in Northern Africa and Mediterranean regions—being the originally identified vector and reservoir of ASFV in the Iberian Peninsula (Costard *et al.*, 2013; Sanchez-Botija, 1963; Sánchez-Vizcaíno *et al.*, 2015; Wade *et al.*, 2019). Transmission experiments have shown *O. erraticus* to be capable of harboring viable ASFV for a minimum of two years (Boinas *et al.*, 2011). With the ability of individuals to survive up to five years without feeding and having life spans of 15 – 20 years, these ticks have played essential roles in the maintenance of ASF in formerly enzootic regions (Danzetta *et al.*, 2020).

#### 1.4 African swine fever transmission

ASFV is able to be transmitted both within and between hosts while being maintained in its environment. In addition to the aforementioned sylvatic and tick-domestic-pig cycles, transmission has also been recorded in an exclusively domestic cycle (either solely among domestic pigs or also involving pig products) and recently as well as between wild boar and their environment in a wild boar-habitat cycle (Chenais *et al.*, 2019; Costard *et al.*, 2013).

Domestic pig herds are susceptible to both direct and indirect ASFV transmission (WOAH, 2019c). Multiple experimental and observational studies, across different genotypes and for both moderate- and high-virulence strains, have revealed effective transmission between pigs (Ferreira *et al.*, 2013; Guinat, Gogin, *et al.*, 2016; Guinat, Gubbins, *et al.*, 2016). Whether separated or in direct contact, experiments have shown infection occurring within 9 to 15 days, respectively, following exposure of susceptible pigs (Gallardo *et al.*, 2015; Greig, 1972; Guinat *et al.*, 2014; Guinat, Gogin, *et al.*, 2016;

Howey *et al.*, 2013). With live virus able to survive in all porcine secretions and excretions, direct transmission to susceptible animals is possible over multiple weeks (Costard *et al.*, 2013; Pensaert, 1989).

Indirect ASFV transmission via swill feed and fomites has also been demonstrated by many studies (Guinat, Gogin, *et al.*, 2016; Mazur-Panasiuk *et al.*, 2019). ASFV is capable of surviving for months in both animal tissues and meat products (McKercher *et al.*, 1978, 1987; Mebus *et al.*, 1993, 1997). The practice of swill feeding—though illegal in many places—is still common in backyard and traditional production systems, and because of the hardiness of ASFV serves as another source of potential contamination (European Commission, 2020; Kagira *et al.*, 2010; Phengsavanh *et al.*, 2010). Even basic feed ingredients, when contaminated with ASFV, can serve as an effective conduit for over 30 days (Dee *et al.*, 2018; Mazur-Panasiuk *et al.*, 2019). Recent experiments have shown drinking water to be highly infectious too, and capable of hosting viable virus for almost two months at room temperature (Niederwerder *et al.*, 2019; Sindryakova *et al.*, 2016). Fomites, such as clothing and farm or hunting equipment, have yet to be demonstrated as sources of infection; however, given the long environmental persistence of ASFV in the blood and excretions of infected animals, this route cannot be excluded (Guinat, Gogin, *et al.*, 2016).

ASFV transmission among wild boar is known to occur through both direct horizontal transmission and multiple indirect environmental pathways (FAO, 2019). Existing in matriarchal social groups with a mean four to five individuals per group, horizontal transmission is able to occur between individuals through typical interactions (FAO, 2019; Maselli *et al.*, 2014; Rosell *et al.*, 2004). Environmentally, transmission can come from contact with normal excretions of feces and urine, contact with infectious carcasses, and contact with hunter remnants (i.e. offal, blood, and infected meat) leftover from the field dressing of infected animals (FAO, 2019).

Carcasses especially have been identified to play a pivotal role in ASFV transmission, maintaining the wild boar-habitat cycle (Chenais *et al.*, 2019; FAO, 2009). The stability of ASFV enables to remain viable in carcasses for months—years if the carcasses are frozen—and carcasses are able to persist in the environment for weeks, where they have been observed to be frequently contacted by wild boar (FAO, 2019; Fischer *et al.*, 2020; Probst *et al.*, 2017; Sánchez-Vizcaíno *et al.*, 2009). In addition to the carcasses, the soil beneath the carcass is able to be contaminated is likely also capable of serving as an effective source of transmission for weeks after contamination (Probst *et al.*, 2019).

Transmission between domestic pigs and wild boar has been demonstrated experimentally and is also strongly suspected from field observations. Controlled experiments have revealed ASFV can be transmitted between hosts via both direct and indirect contact (Pietschmann *et al.*, 2015). In the field,

though a phylogenetic connection has not yet to be made, outbreak investigations have revealed strong spatiotemporal associations between cases among wild boar and domestic pigs (Gogin *et al.*, 2013; Vergne *et al.*, 2017). Habitat encroachment and low biosecurity create an environment favorable to interactions between domestic pigs and wild boar, which is then facilitated by their shared preference for crop raiding, the sexual attraction towards domestic sows by wild males, and food availability on farms (Dixon *et al.*, 2020). Additionally, poor biosecurity from improper handling of hunted wild boar offal can serve as an effective transmission route between wild and domestic hosts (Dixon *et al.*, 2020).

Whereas only *Ornithodoros* spp. soft ticks have been identified as an arthropod reservoir (i.e. where internal replication of ASFV can occur), multiple past and recent studies—in Africa, Europe, and Asia—have demonstrated the ability of hematophagous insects to potentially act as mechanical vectors (Mellor *et al.*, 1987; Baldacchino *et al.*, 2013; Yoon *et al.*, 2021). *Stomoxys* spp. (stable flies), *Culicoides* spp. (biting midges), and *Haematopinus suis* (swine lice) have been shown to have a possible role in mechanical transmission of ASFV (Balmoş *et al.*, 2021; Hess *et al.*, 1987; Sanchez Botija & Badiola, 1966; Yoon *et al.*, 2021).

### 1.5 African swine fever control

Without an available vaccine, control strategies against ASF are a direct reflection of these understood transmission dynamics. Though recent advances show promise for the successful development of an ASFV vaccine, historically many factors hindered its development. Intrinsic to ASFV, the genome has considerable variability between the 24 identified genotypes, impeding the development of a single overarching ASF vaccine (Malogolovkin *et al.*, 2015). Further, with multiple genes encoding immune-modulating proteins, the virus is exceptionally adept at evading the host immune response (Dixon *et al.*, 2013). From a vaccinology perspective, both live-attenuated and inactivated vaccines have been unsuccessful in their development. Inactivated vaccines that only induce humoral and not cellular immunity—even in high doses—have not proved effective at conferring protection (Cadenas-Fernández *et al.*, 2021; Takamatsu *et al.*, 2013). Conversely, live-attenuated vaccines, while able to provide protection, carry multiple side-effects and safety risks—including potential for persistent viremia and the reversion to a chronic carrier state of vaccinated animals, as occurred in Spain in the 1960s (Muñoz-Pérez *et al.*, 2021; Revilla *et al.*, 2018). Currently, without a means of large-scale production (due to the lack of a cell line allowing for replication of vaccine-candidate ASFV strains) or of differentiating vaccinated from infected animals, vaccination cannot be considered as an available management strategy (Gavier-Widén *et al.*, 2020; Rock, 2017; Sánchez *et al.*, 2019). However, should a vaccine become available, both the vaccination route and the targeted hosts should be identified.

Oral vaccination appears as a potential lead among wild boar (Barasona et al., 2019). Another option would be the vaccination of domestic pig herds to reach a herd immunity, reducing the risk of transmission and related consequences on-farm, between-farm and potentially into wild boar populations. For a clear identification of the optimal vaccination strategies, it appears essential to evaluate and quantify the relative role of domestic pigs and the wild boar compartment in the transmission process for ASFV, prior to finalizing and commercializing a vaccine.

Among EU Member States, ASF control measures among domestic pigs are designed to eradicate disease while halting its spread and minimizing disruption to supply chains. Following the same principles for other transboundary animal diseases, these strategies consist of whole or partial herd culling, movement controls, contact tracing (of both animals and animal products), the establishment of surveillance and protection zones, and compensation to affected farmers (Busch *et al.*, 2021; European Commission, 2014). Within these zones, pig holdings are recommended to be closely monitored for clinical signs of ASF (sudden mortality events, evidence of hemorrhagic syndromes) both ante-mortem and post-mortem (European Commission, 2014). Veterinary inspection is a critical component of ASF identification, with veterinary consult recommended both if there is suspicion of ASF from clinical signs, or if pigs are slaughtered for home consumption and would otherwise bypass normal detection chains (European Commission, 2014). Strict biosecurity of affected areas is mandated, including controlled disposal of carcasses, closer surveillance of live pig markets, enforcement of swill feeding prohibitions, and environmental sanitation including applications of tick control where relevant (European Commission, 2014, 2020).

Management strategies in wild boar vary between affected areas depending on the epizootic situation and phase of incursion. After the epizootic peak it may be relevant to decrease wild boar density, as implementation of a wait-and-see period in the core infected zone—in order to prevent further ASF spread through movement of wild boars triggered by hunting actions—is a critical component of strategy. Initially, strategies reflected this: through conventional approaches of feeding bans and targeted hunting of reproductive females, as alternative strategies of mass depopulation were considered impractical and, politically, unpalatable (Lange, 2015; Sauter-Louis, Conraths, *et al.*, 2021). Within surveillance zones, testing of all hunted or found-dead wild boar was mandated. Alternative strategies of erecting fences or mobile barriers, as well as active carcass surveillance and disposal, had also been employed to varying degrees of success (Jo & Gortázar, 2021; Lange, 2015). In South Korea in 2019, the use of fences to delineate infected zones followed by silent culling (and along with natural mortality from ASF), resulted in almost complete elimination of wild boar and ASF cases in these areas (though incidentally, carcass removal may have contributed to ASF spread outside of this area) (Jo & Gortázar, 2021). Following establishment of an additional zone type—“zones blanches”, that



delineates ASF-free areas that are adjacent to areas with positive wild boar cases—the institution of mass silent culling of wild boar in these high-risk fenced areas had successfully contributed to re-achievement of ASF-free status of both the Czech Republic and Belgium (EFSA *et al.*, 2021).

#### 1.6 African Swine Fever impact

African swine fever (ASF) is one of the highest consequence diseases of domestic pigs, and is accordingly listed as a notifiable disease by the World Organization for Animal Health (WOAH, 2021). With a case-fatality rate approaching 100% for highly-virulent strains and severe trade restrictions wherever its emergence is recognized, this hemorrhagic fever is socioeconomically devastating to both individual farms and affected countries (Blome *et al.*, 2013; Dixon *et al.*, 2020; FAO, 2009). For a smallholder farrow-to-finish individual farm of 122 sows in Africa, an ASF outbreak was estimated to potentially cause losses of up to US\$1,000,000 over a three-year period, if the outbreak occurred in the first year (Fasina *et al.*, 2012). These losses were estimated to consist of half of the first year's total outputs, lost inputs in the first year including feed, veterinary services, labor, herd renewal, and transport, plus lost potential finished pigs from subsequent years. On the national scale, the effects are over a thousandfold more: in Vietnam, the outbreaks in the year 2019 alone were estimated to cause between US\$880 million and US\$4.4 billion in losses to national income (covering the whole swine supply chain for swine-derived products) due to reductions in the values of swine farm output (Nguyen-Thi *et al.*, 2021).

Among the global leaders in pork production—China, the European Union (EU), and the United States of America (USA)—economic models have painted even more shocking scenarios. Direct losses from the outbreaks in China and Southeast Asia have been estimated to be between US\$55 and US\$130 billion, accounting for both initial losses to disease and culling as well as the redirection of resources to restore the national breeding herd (Weaver & Habib, 2020). In the European Union, individual countries such as Denmark could experience total losses (both direct costs and export losses) of up to €520 million per epizootic (Halasa, Bøtner, *et al.*, 2016a). In the USA, should an ASF incursion occur and be controlled within 2 years (allowing the country to then re-enter the export market), it has been estimated that revenue losses to the pork industry over that time would be approximately US\$15 billion (Carriquiry *et al.*, 2021). Should ASF become enzootic among wild boar in America, however, industry losses over a 10-year period would total US\$50 billion in addition to the loss of an estimated 140,000 jobs (Carriquiry *et al.*, 2021).

The devastation wrought by ASF crosses many scales and disciplines. In addition to the socioeconomic toll, the psychosocial effects—though not yet assessed explicitly for ASF and a pertinent area for current research—are just as severe. Whole-herd depopulation is the sole reactive control method

approved in both Europe and the United States (Council of the European Union, 2002; USDA, APHIS, 2020). The psychological toll of mass depopulation has been previously evaluated for past epizootics of foot-and-mouth disease and Ovine Johne's disease, and studies consistently reveal the presence of severe emotional distress and mental anguish among farmers and their families (Hall *et al.*, 2004; Mort *et al.*, 2005). Animal health workers involved in such culling duties are subject to experiencing negative mental health outcomes, and public opinion sours when light is shed on production systems for massive culling. Mass swine depopulations during the COVID-19 epidemic (secondary to infrastructure breakdowns) were revealed to have resulted in emotional exhaustion, loss of job satisfaction, and depersonalization among the involved veterinary officers (Baysinger & Kogan, 2022).

The consequences of ASF are not just limited to the immediate stakeholders in animal production either. In addition to the direct effects of ASF outbreaks to individuals, agribusiness, and nations, projection models predict the global price of pork—the most widely consumed meat in the world—to increase by 17–85% (FAO, 2014; Mason-D'Croz *et al.*, 2020). Such repercussions will have direct strain on global food security, with the decline in available calories putting millions more people at risk of hunger (Mason-D'Croz *et al.*, 2020). Following the emergence of ASF, national markets for pig and pork products were highly disturbed with limitations or outright bans on external exportation to the EU. However, the majority of initial case detections for the current ASF panzootic were observed in wild boar. Therefore, to reduce the economic consequences of ASFV introduction to previously ASF-free countries, regionalization and/or segmentation between hosts was implemented to avoid the loss of ASF-free status for an entire nation (Gordejo, 2021). Both the domestic and wild compartments have to be jointly considered to evaluate the global economic impact of ASF and implemented or potential control measures.

Confronting the ASF panzootic—among both domestic pigs and wild boar—is a global priority.

### Box 1.1 | Chapter 1 key points

- ASF is one of the highest consequence diseases of domestic pigs and a panzootic of international concern.
- In its home range of sub-Saharan Africa, ASF remains endemic via a sylvatic cycle involving warthogs and *Ornithodoros* ticks.
- Evidence indicates the current panzootic started from the illegal sale of shipping waste — contaminated with ASFV genotype II—that was then used as swill feed for pigs.
- In prior invasions of ASFV outside of Africa, ASF has faded-out among wild boar following the control of domestic pig infections. In the current panzootic, however, we are seeing maintenance of the disease in Europe and Asia via both a domestic cycle among pig herds and a separate wild boar-habitat cycle.
- Human activities are the primary driver of infections between domestic pig herds.
- ASFV can persist in the environment for months, and contaminated wild boar carcasses play a crucial role in maintaining the wild boar-habitat cycle in affected areas
- In regions with a preponderance of low-biosecurity backyard farms, spillover between domestic pig herds and wild boar is also believed to contribute to the epizootic propagation.
- Control strategies, designed to interrupt these drivers of transmission, consist among domestic pigs of whole-herd culling, movement restrictions, contact tracing, and establishing surveillance zones. Among wild boar, carcass identification and disposal appear to be a key component for achieving local control.

## 2 | Mathematical modelling of epizootic disease

### 2.1 A concise history of mathematical modelling

Designing effective prevention, surveillance, and intervention strategies requires the understanding of transmission dynamics, and these dynamics can often be unraveled through the employ of mechanistic mathematical models (Keeling and Rohani, 2008). The original mathematical disease models were all deterministic population-based models, commonly referred to as compartmental models (Brauer, 2017). In these models, a population is divided into compartments by health state, the simplest being two-compartment models of those who are susceptible to disease (in the  $S$  compartment) and those who are infectious (in the  $I$  compartment)—yielding an  $SI$  model (Brauer, 2017). Relying on differential equations to explain system dynamics, and stemming from W.H. Hamer’s 1906 postulate that disease transmission is dependent on the number of both infectious and susceptible individuals—and can be described through a mass action law—the Kermick-McKendrick model is credited as one of these first compartmental epidemic models (Brauer, 2017; Hamer, 1906; Kermack *et al.*, 1927; Wilson & Burke, 1942). With these models, the basic reproduction number of an infectious disease (defined as the average number of secondary cases arising from an average primary case in a fully susceptible population, denoted as  $R_0$ , and first coined in the 1950s by George Macdonald) was able to be calculated, allowing one to determine if—whether the  $R_0$  value is above or below 1—an epidemic trajectory would trend towards an endemic equilibrium or disease-free equilibrium (Brauer, 2017; Keeling & Rohani, 2008; Macdonald, 1957). Stochasticity was later incorporated through the development of chain-binomial models, the most famous being the Reed-Frost model (Brauer, 2017; Keeling & Rohani, 2008).

Throughout the twentieth century, digital computing capabilities first developed and then rapidly advanced, and with them came the ability for increasingly complex models. Though classic population-based (compartmental) models (PBM) of epidemics continued to grow through the consideration of additional population states— $SIR$  to include those recovered from disease,  $SEIR$  to account for those in the exposed (and thus latent) state,  $SIS$  to consider re-susceptibility, and many more—these models remained incapable of capturing important spatial dynamics and individual contact processes repeatedly observed in epidemics (Di Stefano *et al.*, 2000; Perez & Dragicevic, 2009).

Advances in network theory among stochastic models—originating from the mid-twentieth century theories of Erdős & Rényi (1959) on graphs—led to the adaptation and use of the network models found in the social sciences (Brauer, 2017; Keeling & Eames, 2005). This allowed for the consideration of disease spread via individual and social group connectivity, originally finding utility for describing sexually-transmitted infections in the 1980s and 1990s (Keeling & Eames, 2005; Klodahl, 1985;

Kretzschmar *et al.*, 1996; Mollison, 1977). These models were then adapted into the epizootic modelling arena, being—to the best of my knowledge—first used to reconstruct transmission trees of FMD following the 2001 outbreak in the UK (Haydon *et al.*, 2003; Keeling & Eames, 2005).

At the turn of the twenty-first century, cellular automata models were adapted for epidemiological study (Di Stefano *et al.*, 2000; Rousseau *et al.*, 1997). Developed in the 1940s by Stanislaw Ulam and John Von Neumann as a means of exploring crystal growth and self-replicating systems, cellular automata models consist of a lattice of cells, each containing a single bit of data whose value is computed at discrete time steps based on local neighborhood interactions (Cosentino *et al.*, 2013; Wolfram & Gad-el-Hak, 2003). In cellular automata disease models, individual cells advance through a sequence of infection states (Rousseau *et al.*, 1997; Wolfram, 1984). Interactions occur within a cell's immediate neighborhood, allowing simple local rules (such as probability of infection) to lead to the emergence of complex epidemic dynamics (Di Stefano *et al.*, 2000; Rousseau *et al.*, 1997; Wolfram, 1984). Though movement is not explicitly simulated, local spatial dynamics of disease spread are able to be evaluated through this framework via the assumption of each cell representing an individual or group of individuals (White *et al.*, 2007).

An extension of PBMs, metapopulation (or patch-based) models allowed further incorporation of spatial heterogeneity, though under a different set of rules than cellular automata. In the simplest metapopulation model form, infectives in one patch can simply transmit disease to susceptibles in either their patch or another patches (van den Driessche, 2008). A second more complex type of metapopulation model explicitly provides a framework for connecting multiple subpopulations within a population via movement between subpopulations (Arino & van den Driessche, 2003a, 2003b; Brauer, 2017). In these metapopulation models, both rates of travel and changes in populations are accounted for, and will include different reproduction numbers ( $R_0$ ) within patches as well as between patches (Brauer, 2017; van den Driessche, 2008).

Individual-based models (IBMs, and synonymous with agent-based models (ABMs)) were first explored for deciphering within-host viral and immunological dynamics in the early 2000s, for pathogens like influenza A and human immunodeficiency virus (HIV) (Bauer *et al.*, 2009; Beauchemin *et al.*, 2005; Castiglione, 2009; Zorzenon dos Santos & Coutinho, 2001). Later, with increases in computation capabilities, came their use in epidemiology for simulating complex interactions between individuals. Under the same cellular automata premises of a simple pre-programmed set of rules guiding behavior, and complex behaviors emerging from simple system interactions, IBM agents are additionally programmed with movement parameters allowing for the tracking of contacts between simulated individuals within the system, in addition to the individual transitions of an agent through disease states (Perez & Dragicevic, 2009; Wolfram, 1984). As computational power grows the

complexity of IBMs will be able to grow as well, allowing for epidemic simulations that consider high-resolution differences between model agents, such as individually variable susceptibility and infectivity (Brauer, 2017).

Despite the proliferation of individual-based epidemic models following their debut, no standard methodology for describing these models exists, which has led to irregularities and inconsistencies among model descriptions (Orbann *et al.*, 2017). Though protocols have been proposed for describing model structures in a standardized way, they are not specific to disease modelling nor are they consistently followed (Grimm *et al.*, 2006; Orbann *et al.*, 2017). In the following reviews of mathematical modelling articles, the model classifications used are those that have been reported by the authors and model developers.

## 2.2 The proven utility of epizootic mathematical modelling

Mathematical models have a proven track-record, not just for confronting epidemics of public health interest but also against notable epizootics. Understandings of the transmission dynamics of bovine tuberculosis (bTB), bovine spongiform encephalopathy (BSE), and foot-and-mouth disease (FMD) outbreaks have all been improved through investigation with mathematical models.

One of the first times models were used during an epizootic for decision support was during the 2001 FMD outbreak in the UK (Keeling, 2005). Multiple models were parameterized and evaluated, ranging from deterministic population-based compartmental models (Ferguson *et al.*, 2001) to spatially-explicit (Keeling *et al.*, 2001) and complex individual-based (Morris *et al.*, 2001) simulations. The results of these different models, highly congruent in their predictions despite their different methodologies, played important roles in informing strategy (Keeling, 2005), albeit not without significant political strife (Kitching *et al.*, 2006). The lessons learned from this epizootic, as a case study of the use of modelling in real-time decision support, have since been explored repeatedly (Green & Medley, 2002; Kao, 2002; Keeling, 2005; Tildesley *et al.*, 2008) and will continue to provide further insight into the capabilities and limitations of the modelling toolset.

Bovine TB, one of the most important livestock diseases globally, affects countries across six continents and was even once described as “the greatest challenge [...] facing New Zealand science” (Barlow, 1994; Coleman & Cooke, 2001; WOA, 2019b). In England, considerable debate occurred over the culling strategies against wild badgers for controlling bTB epizootics in cattle: some stakeholders declared badgers played no role in transmission to cattle, whereas others emphatically stated that the majority of cases were due to badger transmission (Donnelly & Nouvellet, 2013). Through dynamical modelling, the association of bTB between badgers and cattle, along with the

contribution of badgers to maintaining outbreaks among cattle, was able to be elucidated (Donnelly & Nouvellet, 2013; Donnelly & Hone, 2010). Though the lively debate continued (and continues) on which management strategies are appropriate, the insight from these models provided valuable evidence on inter-species transmission.

During the “mad cow disease” crisis of the late 1980s and 1990s, mathematical models were necessary for estimating age-stratified incidence in cattle and ascertaining the impacts of culling policies (R. M. Anderson *et al.*, 1996; Ferguson *et al.*, 1998). As there was no *in vivo* test for detecting infection, the back-calculation methods used in these models (considering the incubation period alongside trends in incidence) enabled the determination of BSE incidence trajectories. This information was able to inform control strategies going forward, predicting transmission routes and time until disease fade-out (R. M. Anderson *et al.*, 1996).

### Box 2.1 | Chapter 2 key points

- Mathematical models have been successfully applied to many epizootic diseases.
- The first mathematical models of disease were compartmental population-based models, compartmentalizing the entire population by infection state and using differential equations to explain the dynamics between the states.
- Contact-network based models, adapted from the social sciences, were incorporated into the field the late 20<sup>th</sup> century to explain frequency-based transmission dynamics as seen with sexually transmitted infections.
- Only in the 21<sup>st</sup> century has disease modelling progressed to mechanistically consider spatial effects via the adaptation of cellular automata, metapopulation, and individual-based models.
- Famous epizootics of BTB, BSE, and FMD have all benefited from investigation with mathematical models, elucidating crucial information for predicting epidemic trajectories and informing control strategies.





## § II | Systematic reviews of mathematical modelling

Mathematical modelling of infectious diseases at the domestic-wildlife interface is a unique subset of mechanistic modelling. Requiring cross-disciplinary competence in infectious disease epidemiology, domestic animal health and livestock production, and wildlife ecology, these models seek to unravel the complex mechanisms behind both disease transmission between ecosystems and disease emergence in novel ecosystems.

Transmission of disease is the product of multiple factors between an infectious and susceptible host, accounting for the pathogen population, pathogen dynamics, host immunology, host behavior, and environmental influences (Grassly & Fraser, 2008). Mathematical models couple these biological mechanisms to the epidemic dynamics that emerge in a population (Grassly & Fraser, 2008). In disease modelling, these myriad and complex host factors often get reduced into a single parameter to quantify the transmission probability of a disease given infectious-susceptible contact. Multiplying this parameter by the contact rate between hosts yields the transmission rate— $\beta$  (beta)—and is central to mathematically describing the transmission of an infectious agent among a population (Craft, 2015; Keeling & Rohani, 2008; Vynnycky & White, 2010). This transmission rate parameter, therefore, represents the information that encompasses all the aforementioned facets of disease transmission between two hosts.

Global and local drivers of transmission—resulting in ever-increasing interaction between wildlife and livestock—are investigated through these models. Livestock production systems constitute the largest use of land in the world, and increasing global food demand invariably result in the expansion of these systems (Jori, Hernandez-Jover, *et al.*, 2021). The consequent deforestation that makes room for these enterprises results in the juxtaposition of livestock with wildlife, increasing the areas of interaction between the two (Jones *et al.*, 2013; Jori, Hernandez-Jover, *et al.*, 2021).

Climate change has had profound effects at both global and local scales. Large-scale shifts in vector distributions have resulted in outbreaks of diseases that were formerly confined to tropical regions, as seen with bluetongue virus (Jacquot *et al.*, 2017; Jori, Hernandez-Jover, *et al.*, 2021). Locally, water scarcity in arid and semi-arid regions has resulted in mixed congregations around available water sources for pastoral livestock and wildlife (Jori, Hernandez-Jover, *et al.*, 2021).

In the majority of rural communities, backyard farming and small-scale animal production systems constitute the primary livelihoods and food sources (Committee on Considerations for the Future of Animal Science Research *et al.*, 2015). These low-biosecurity operations permit regular contact between livestock and wildlife, and have often been central to outbreaks of diseases shared at this

interface—including ASF, CSF, FMD, brucellosis, and rabies (Jori, Hernandez-Jover, *et al.*, 2021; WOA, 2022c). Improved animal welfare in high-income countries has also resulted in increases in the number of outdoor and open-air production systems, which also puts livestock at higher risk of wildlife contacts (Jori, Hernandez-Jover, *et al.*, 2021). The livestock-wildlife interface acts as an important area of infectious disease propagation, and mathematical models are able to investigate and quantify the involved dynamics, helping to improve our understanding of these drivers of transmission and contribute to the conception of holistic control strategies.

With mathematical models able to elucidate disease dynamics, unravel disease transmission properties, and improve disease management strategies, they hold promise for helping to confront the current African swine fever panzootic. Through systematically reviewing the literature of ASF mechanistic modelling, we will be able to identify previously described parameters, elucidate effective methods for mathematically investigating ASF epizootics, and identify gaps in the knowledge body that would benefit from further investigation. Here, a systematic review of the literature was conducted to see the state of the art regarding ASF modelling in both wild and domestic compartments, identifying all published articles of mathematical modelling of African swine fever. This review was subsequently published in *Preventive Veterinary Medicine* (Hayes *et al.*, 2021). Following this review, as mechanistic models of ASF at the domestic-wildlife interface were lacking, a review of mechanistic models at the domestic-wildlife interface was conducted to inform potential methodologies that could be used in the development of our own model of ASF transmission at the domestic-wildlife interface, including how to represent the interactions between the domestic and the wild compartments.

### 3 | Mathematical modelling of African swine fever: A systematic review

*This chapter is derived from the publication in Preventive Veterinary Medicine (Hayes et al., 2021)*

#### 3.1 Introduction

Designing effective prevention, surveillance, and intervention strategies against African swine fever (ASF)—one of the highest consequence diseases of domestic pigs—requires understanding of the virus' transmission dynamics. These dynamics can often be unraveled through the use of mechanistic modelling (Keeling and Rohani, 2008). Mechanistic models have been successfully applied to many epizootic incursions including foot-and-mouth disease (FMD) (Pomeroy *et al.*, 2017), classical swine fever (CSF) (Backer *et al.*, 2009), and bluetongue (Courtejoie *et al.*, 2018), to assess vaccination strategies, design and evaluate targeted and alternative control strategies, and elucidate epidemiological parameters, respectively.

Only following the incursion of ASF into the Eurasian continent did mechanistic models of ASF begin to be explored, as identified in a literature review of modelling viral swine diseases (Andraud and Rose, 2020). In order to identify gaps in specific ASF modelling strategies with regard to its present epidemiology, through examining the assumptions on transmission and objectives of the mechanistic models of ASF, a systematic review of the scientific literature was conducted.

#### 3.2 Material and methods

##### *3.2.1 Literature search*

The systematic review was performed in accordance with PRISMA guidelines (Liberati *et al.*, 2009). The search query was constructed to identify all publications on ASF in any species that incorporated the use of mechanistic models. No restrictions were imposed on publication language (other than through the use of English search terminology), study location, or publication date. Eight target publications on mathematical modelling of ASF, selected through author familiarity of the subject and diverse among animal host and literature type (black and white literature and grey literature), were identified to calibrate the literature search. The literature search was conducted initially on January 31, 2020 through terms agreed upon by all researchers in the following Boolean query: “*African swine fever*” AND *model\** AND (*math\** OR *mechani\** OR *determin\** OR *stochast\** OR *dynam\** OR *spat\** OR *distrib\** OR *simulat\** OR *comput\** OR *compart\** OR *tempor\**). Terms were searched in the fields title and abstract, title abstract and subject, or title and topic, for Medline, CAB Abstracts, and Web of Science, respectively. The search was repeated prior to publication (January 18, 2021) to capture all relevant articles through December 31, 2020. Of note, as articles ahead of print were included in this

review at time of its publication, their cited dates have been updated following their publication which has resulted in included articles with dates beyond December 31, 2020. Additionally, as the previous systematic review was conducted after this one, one additional ASF modelling article that was published recently (Yoo *et al.*, 2021) was not included in this study.

### 3.2.2 Study Selection

Inclusion criteria for the articles were the topic of African swine fever and reference to a mechanistic model either directly or indirectly (e.g. through mention of a specific type of model). Exclusion criteria were more exhaustive and consisted of the following: non-population models (e.g. within-host), virological and genomic models, non-suid models (e.g. models exclusively of the arthropod vector), and non-mechanistic models (e.g. statistical or purely economic models).

Primary screening of title and abstract was performed by two authors. Kappa scores ( $\kappa$ ) were calculated to determine interrater reliability. Discussion among authors occurred until a consensus on qualifying studies was reached. Full-text articles were subsequently assessed for eligibility with all the above criteria plus the additional inclusion criteria of containing an explicit process of infection and not being a duplication of published results, and cross-validated by other authors. Snowball sampling was used to identify any remaining mechanistic modelling articles. Specific screening questions are available online as supplementary material.

### 3.2.3 Data collection process

Table shells were created to capture study design and model properties. Publication information (authors, year), ASF outbreak data (host, ASFV strain (genotype and isolate), location of study), research methodology (data collection method, study direction (ex-post or ex-ante)), model components (framework, temporality, spatiality, infection states), model descriptors (transmission scale, basic epidemiological unit, model objective), and model parameter assumptions were all recorded.

### 3.2.4 Filiation tree construction

To assess model filiation, a distance-based phylogenetic tree of the selected studies was constructed. This was performed via the neighbor-joining method of tree construction using Molecular Evolutionary Genetics Analysis (MEGA) software (Kumar *et al.*, 2018). This methodology was chosen as it produces a parsimonious tree based on minimum-evolution criterion (Pardi & Gascuel, 2016; Saitou & Nei, 1987). Full characteristics of all models were assessed (Supplementary Material, Table A), and cross-correlation between those characteristics resulted in the selection of four main

variables: host (domestic pig, wild boar, or both), data collection methodology (experimental, observational, or simulation), model framework (PBM, IBM, or metapopulation), and model objective (estimating parameters, assessing alternative control strategies, assessing determinants of transmission, or examining consequences of hypothetical outbreaks). Vectors of each model were constructed by dummifying selected model components by their subcategory and then calculating pairwise differences between all model pairings. The corresponding values formed a distance matrix that was then used for analysis.

### 3.3 (Results) Included publications and epidemiological characteristics

#### 3.3.1 Publications

A total of 351 articles were identified across all databases (Fig. 3.1). Following removal of duplicate references, 171 records remained for primary screening. Out of these, 36 full-text articles were determined to qualify for secondary screening. With  $\kappa = 0.65$ , the reviewers were determined to be in substantial agreement (Landis & Koch, 1977). Four articles were excluded in secondary screening. Two additional studies were identified through snowball sampling resulting in 34 articles for review. A marked increase in the number of mechanistic modelling publications occurred in the most recent year of review (Fig. 3.2). Closely split between models among domestic pigs and wild boar (referred to as “pigs” and “boar” in tables and figures), 2020 saw a doubling in the number of publications (10) compared to previous most-published years.

#### 3.3.2 Epidemiological characteristics

Out of 34 mechanistic modelling studies on ASF, 20 modelled disease dynamics specifically in domestic pigs, 12 modelled disease dynamics specifically in wild boar, and two included transmission between wild and domestic hosts (Table 3.1). The majority of studies (25) were parameterized to the genotype II strains currently circulating in Europe (i.e. Georgia 2007/01, Armenia 2008), including the first mechanistic model of ASF (Gulenkin *et al.*, 2011) and all but one of the wild boar models.

Different strains were considered depending on their geographical spread. Genotype I dynamics were modelled both in Sardinia where it is enzootic (Loi *et al.*, 2020; Mur *et al.*, 2018), and in an experimental study with the Malta 1978 and Netherlands 1986 isolates (Ferreira *et al.*, 2013). Genotype IX was modelled in its home range of Eastern Africa both ex-post to a historical outbreak (Barongo *et al.*, 2015) as well as via a simulation for assessing control measures (Barongo *et al.*, 2016). Genotype II strains were examined ex-post among domestic pigs to historical outbreaks in the Russian Federation (Guinat *et al.*, 2018; Gulenkin *et al.*, 2011), via transmission experiments in domestic pigs

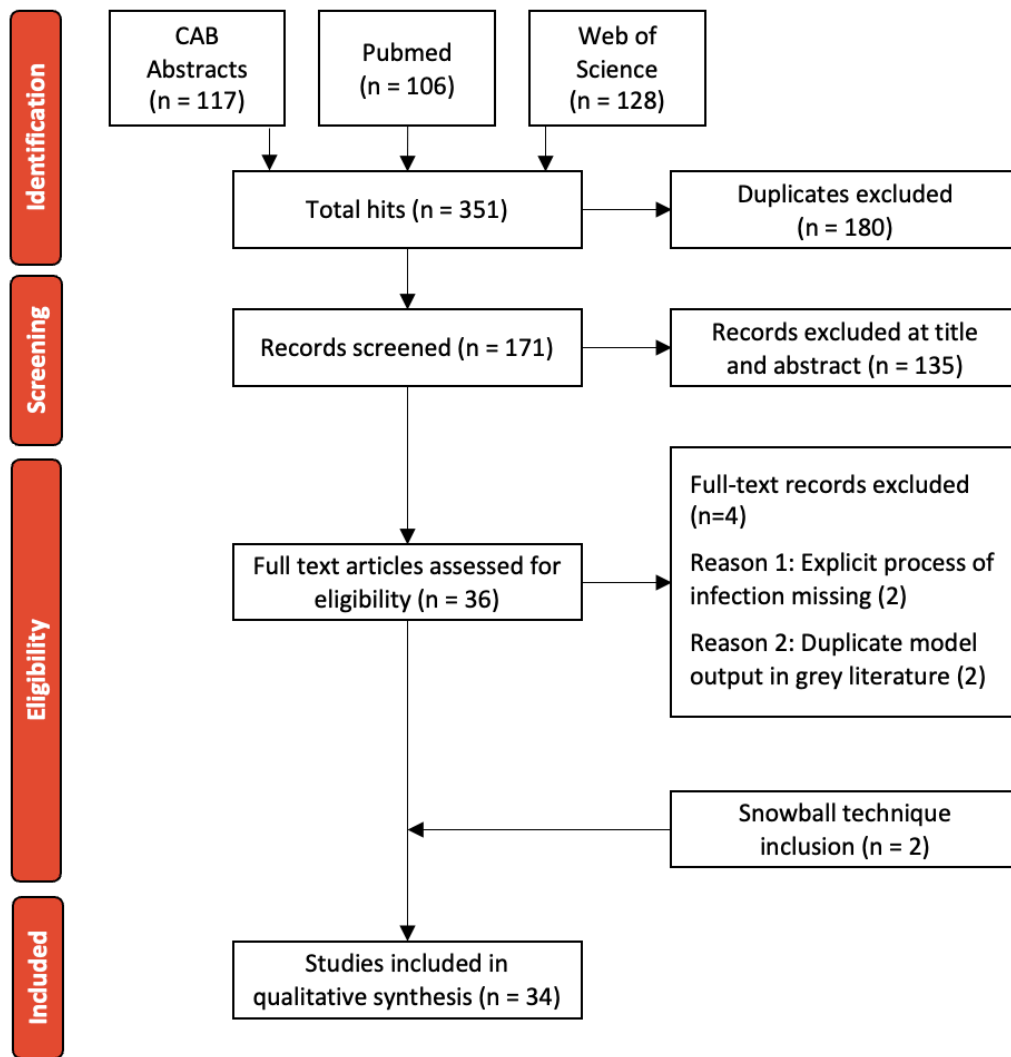


Fig. 3.1 | PRISMA flow diagram for article selection.

(Guinat, Gubbins, *et al.*, 2016; Hu *et al.*, 2017; Nielsen *et al.*, 2017) or between both domestic pigs and wild boar (Pietschmann *et al.*, 2015), and through a multitude of in-silico simulations of both domestic pigs (Andraud *et al.*, 2019; Faverjon *et al.*, 2021; Halasa, Boklund, *et al.*, 2016; Halasa, Bøtner, *et al.*, 2016a, 2016b; Halasa *et al.*, 2018; Lee *et al.*, 2021; Vergne *et al.*, 2021) and wild boar herds (Croft *et al.*, 2020; Gervasi *et al.*, 2019; Halasa *et al.*, 2019; Lange, 2015; Lange *et al.*, 2018; Lange & Thulke, 2015; O'Neill *et al.*, 2020; Pepin *et al.*, 2020; Taylor *et al.*, 2021; Thulke & Lange, 2017). One model of ASF spread, which was focused on spread due to wild boar dispersion, considered the influence of transmission from outdoor free-range domestic pigs (Taylor *et al.*, 2021).

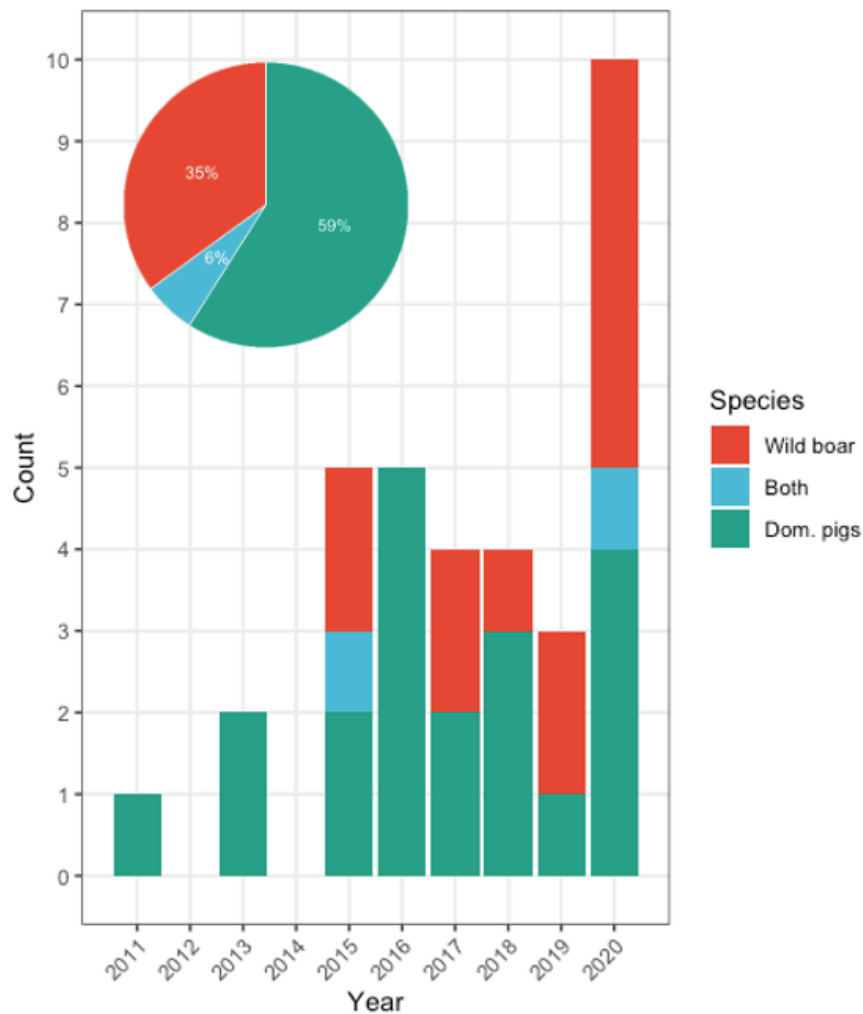


Fig. 3.2 | Publications by year subset by host

The term “herd” was chosen to refer to an animal collective and will be used for the remainder of this article, with it being interchangeable with the terms farm (Gulenkin *et al.*, 2011; Mur *et al.*, 2018; Nigsch *et al.*, 2013), production unit (Halasa, Boklund, *et al.*, 2016), and parish (Barongo *et al.*, 2016). Further, for the purpose of standardization of terms for model comparison, sub-population groups of wild boar (known as sounders) are herein referred to as herds as well.

### 3.4 (Results) Model objectives and filiation

#### 3.4.1 Model objectives

Four main modelling objectives were identified: Estimating parameters (11), assessing determinants of transmission (7), examining consequences of hypothetical outbreaks (5), and assessing alternative control strategies (11) (Table 3.2).



**Table 3.1** | Epidemiological characteristics of articles

Reference	Host	ASFV isolate	ASFV genotype	Location	Data collection method
<b>Gulenkin <i>et al.</i>, 2011</b>	Pig	Georgia 2007/1	Genotype II	Russian Federation	Observational
<b>Ferreira <i>et al.</i>, 2013</b>	Pig	Malta 1978 Netherlands 1986	Genotype I	Laboratory	Experimental
<b>Nigsch <i>et al.</i>, 2013</b>	Pig	-	-	European Union	Simulation
<b>Barongo <i>et al.</i>, 2015</b>	Pig	-	Genotype IX	Uganda	Observational
<b>Costard <i>et al.</i>, 2015</b>	Pig	-	-	Non-specific	Simulation
<b>Barongo <i>et al.</i>, 2016</b>	Pig	-	-	Eastern Africa	Simulation
<b>Guinat, Gubbins, <i>et al.</i>, 2016</b>	Pig	Georgia 2007/1	Genotype II	Laboratory	Experimental
<b>Halasa, Boklund, <i>et al.</i>, 2016</b>	Pig	Georgia 2007/1	Genotype II	Non-specific	Simulation
<b>Halasa, Bøtner, <i>et al.</i>, 2016a</b>	Pig	Georgia 2007/1	Genotype II	Denmark	Simulation
<b>Halasa, Bøtner, <i>et al.</i>, 2016b</b>	Pig	Georgia 2007/1	Genotype II	Denmark	Simulation
<b>Hu <i>et al.</i>, 2017</b>	Pig	Georgia 2007/1	Genotype II	Laboratory	Experimental
<b>Nielsen <i>et al.</i>, 2017</b>	Pig	Georgia 2007/1	Genotype II	Laboratory	Experimental
<b>Guinat <i>et al.</i>, 2018</b>	Pig	Georgia 2007/1	Genotype II	Russian Federation	Observational
<b>Halasa <i>et al.</i>, 2018</b>	Pig	Georgia 2007/1	Genotype II	Denmark	Simulation
<b>Mur <i>et al.</i>, 2018</b>	Pig	-	Genotype I	Sardinia	Simulation
<b>Andraud <i>et al.</i>, 2019</b>	Pig	Georgia 2007/1	Genotype II	France	Simulation
<b>Faverjon <i>et al.</i>, 2021</b>	Pig	Georgia 2007/1	Genotype II	Laboratory	Simulation
<b>Lee <i>et al.</i>, 2021</b>	Pig	Georgia 2007/1	Genotype II	Vietnam	Simulation
<b>Shi <i>et al.</i>, 2020</b>	Pig	-	-	Laboratory	Simulation
<b>Vergne <i>et al.</i>, 2021</b>	Pig	Georgia 2007/1	Genotype II	Non-specific	Simulation
<b>Pietschmann <i>et al.</i>, 2015</b>	Pig, Boar	Armenia 2008	Genotype II	Laboratory	Experimental
<b>Taylor <i>et al.</i>, 2021</b>	Pig, Boar	Georgia 2007/1	Genotype II	Europe	Simulation
<b>Lange, 2015</b>	Boar	Georgia 2007/1	Genotype II	Non-specific	Simulation
<b>Lange and Thulke, 2015</b>	Boar	Georgia 2007/1	Genotype II	Non-specific	Simulation
<b>Lange and Thulke, 2017</b>	Boar	Georgia 2007/1	Genotype II	Baltic region	Observational
<b>Thulke and Lange, 2017</b>	Boar	Georgia 2007/1	Genotype II	Baltic region	Simulation
<b>Lange <i>et al.</i>, 2018</b>	Boar	Georgia 2007/1	Genotype II	Baltic region	Simulation
<b>Gervasi <i>et al.</i>, 2019</b>	Boar	Georgia 2007/1	Genotype II	Non-specific	Simulation
<b>Halasa <i>et al.</i>, 2019</b>	Boar	Georgia 2007/1	Genotype II	Denmark	Simulation
<b>Croft <i>et al.</i>, 2020</b>	Boar	Georgia 2007/1	Genotype II	England	Simulation
<b>Loi <i>et al.</i>, 2020</b>	Boar	-	Genotype I	Sardinia	Observational
<b>O'Neill <i>et al.</i>, 2020</b>	Boar	Georgia 2007/1	Genotype II	Spain, Estonia	Simulation
<b>Pepin <i>et al.</i>, 2020</b>	Boar	Georgia 2007/1	Genotype II	Poland	Simulation
<b>Yang <i>et al.</i>, 2021</b>	Boar	-	-	United States of America	Simulation

The majority of domestic pig models—including the first two ASF models (Ferreira *et al.*, 2013; Gulenkin *et al.*, 2011)—and three of the wild boar models (Lange & Thulke, 2017; Loi *et al.*, 2020; Pietschmann *et al.*, 2015) focused on estimating various transmission parameters using either experiment-based or field-observation data. The predominant parameters calculated were the transmission coefficient  $\beta$  (which determines the rate of new infections per unit time, via the product of the contact rate and transmission probability) and the basic reproduction ratio  $R_0$  (the average number of secondary cases produced by one infectious individual in a fully susceptible population) (Table 3.3) (R. M. Anderson & May, 1992; Keeling & Rohani, 2008).  $\beta$ 's ranged from 0.0059 herds per infected herd per month for between herd transmission of genotype IX (Barongo *et al.*, 2015) to 2.79 (95% CI 1.57, 4.95) pigs per day for within-pen transmission of the Malta 1978 isolate (Ferreira *et al.*, 2013).  $R_0$  values ranged from 0.5 (95% CI 0.1, 1.3) for indirect transmission of the Armenia 2008 isolate between boar and pigs (Pietschmann *et al.*, 2015) to 18.0 (95% CI 6.90, 46.9) for transmission of the Malta 1978 isolate between domestic pigs (Ferreira *et al.*, 2013). Among the wild boar models, Pietschmann *et al.* (2015) used the Armenia 2008 isolate to calculate  $R_0$  among wild boar and between boars and pigs in a laboratory setting, Lange & Thulke (2017) trained an artificial neural network on spatiotemporally-explicit case notification data to determine the probability of carcass-mediated and direct transmission between boar herds, and Loi *et al.* (2020) estimated both the basic and effective reproduction numbers ( $R_0$  and  $R_e$ , respectively) in Sardinia through historical hunting data coupled with virological and serological testing data. Lastly, via estimating  $R_0$  and the disease-free equilibrium for varying parameter sets, one recent model examined the mathematical theorems behind the differential equations used in many ASF models to determine if integer or fractional order systems better describe ASF epizootic dynamics (Shi *et al.*, 2020).

Seven simulation models were used to disentangle determinants of transmission of ASF. Of the four models in domestic pigs, the first model by Nigsch *et al.* (2013) simulated international trade patterns to determine the EU member nations most susceptible to importation and exportation of ASF. Halasa, Boklund, *et al.* (2016) simulated ASFV transmission within a pig herd to examine the influences of dead animal residues and herd size, and Mur *et al.* (2018) simulated ASFV transmission between pig herds in Sardinia to determine the influence of farm and contact type. Lastly among pigs, Vergne *et al.* (2021) looked at the influence of the feeding behavior of *Stomoxys* flies on ASFV transmission in a simulated outdoor farm. Halasa *et al.* (2019) examined the transmission pathway of ASFV in wild boar among varying population densities. This past year Pepin *et al.* (2020) modelled the contribution of carcass-based transmission to the on-going outbreak in boar in Eastern Europe, while O'Neill *et al.* (2020) looked at the influence of host and environmental factors on ASFV persistence in scenarios of contrasting environmental conditions.

Assessing alternative control strategies via simulations was the most frequent objective among wild boar studies (Gervasi *et al.*, 2019; Lange, 2015; Lange *et al.*, 2018; Lange & Thulke, 2015; Thulke & Lange, 2017). The strategies examined consisted of combinations of mobile barriers, depopulation, feeding bans, intensified and targeted hunting, carcass removal, and variations in active and passive surveillance. Taylor *et al.* (2021) focused on varying intensities of carcass removal, hunting, and fencing for interrupting ASF spread due only to wild boar movements. In domestic pigs, control strategies that were assessed consisted of improving the sensitivity of detection of ASF by farmers (Costard *et al.*, 2015), enhancing biosecurity (Barongo *et al.*, 2016), theoretical vaccination (Barongo *et al.*, 2016), and instituting EU-legislated and nationally-legislated (Danish) control measures in combination with alternative methods (Halasa, Bøtner, *et al.*, 2016b). These codified measures simulated by Halasa, Bøtner, *et al.* (2016b) encompassed a nationwide shutdown of swine movements, culling of infected herds, implementation of both movement restriction and enhanced surveillance zones, contact tracing, and pre-emptive depopulation of neighboring herds. Most recently, Faverjon *et al.* (2021) quantified the mortality thresholds that permit the best balance between rapid detection of ASF while minimizing false alarms within domestic pig herds, and Lee *et al.* (2021) modelled ASF in Vietnam to determine the efficacy of movement restrictions of varying intensities.

Five models assessed the consequences of hypothetical outbreaks, with four focusing on the Georgia 2007/01 strain. Three models examined ASF within industrialized swine populations, with transmission through both Danish (Halasa, Bøtner, *et al.*, 2016a; Halasa *et al.*, 2018) and French (Andraud *et al.*, 2019) swine systems simulated. Croft *et al.* (2020) examined the outcome of natural circulation of ASF in an isolated boar population in an English forest, and Yang *et al.* (2021) applied ASF parameters to their network model of wild boar to determine its spread in the United States.

#### 3.4.2 Filiation tree and model characteristics

The generation of the neighbor-joined filiation tree allowed for the identification of three clusters of models: models used for parameter estimations, simulation models in domestic pigs, and individual-based models (Fig. 3.3). The individual-based simulation models (with the exceptions of Gervasi *et al.* (2019) and Yang *et al.* (2021)) grouped at the bottom of the tree, the domestic pig simulation models clustered in the middle (with the exception of O'Neill *et al.* (2020) focused on wild boar), and the parameter estimation models clustered in the top-most group.

The parameter estimation cluster, internally parsed by data collection methodology, consisted mostly of stochastic, non-spatial population-based models that derived parameters for within-herd (including within and between pen) transmission between pigs (Ferreira *et al.*, 2013; Guinat *et al.*, 2018; Guinat,

Gubbins, *et al.*, 2016; Hu *et al.*, 2017; Nielsen *et al.*, 2017) (Table 3.2). Gulenkin *et al.* (2011) and Barongo *et al.* (2015) calculated ASF parameters for transmission between herds, and Loi *et al.* (2020) estimated transmission parameters between wild boar. Seven of the nine models focused on the currently-circulating genotype II strain. Though the Shi *et al.* (2020) model also estimated parameters, due to its simulation methodology it was clustered with the rest of the domestic pig simulations.

Five population-based models were used to simulate within-herd transmission in domestic pigs (Barongo *et al.*, 2016; Faverjon *et al.*, 2021; Halasa, Boklund, *et al.*, 2016; Shi *et al.*, 2020; Vergne *et al.*, 2021), and one did so for wild boar (O'Neill *et al.*, 2020), though capturing between-herd transmission dynamics saw the use of stochastic, temporally discrete, spatially-explicit metapopulation models (Andraud *et al.*, 2019; Halasa, Bøtner, *et al.*, 2016a, 2016b; Halasa *et al.*, 2018; Mur *et al.*, 2018). Two named metapopulation models were represented: the Denmark Technical University - Davis Animal Disease Simulation - African Swine Fever (DTU-DADS-ASF) model (Andraud *et al.*, 2019; Halasa, Bøtner, *et al.*, 2016a, 2016b; Halasa *et al.*, 2018) and the Between Farm Animal Spatial Transmission (Be-FAST) model (Mur *et al.*, 2018). Both the Be-FAST and DTU-DADS-ASF models were updates of previously published models. The Be-FAST model, originally designed to simulate CSF spread within and between farms, was adapted for the ASF situation in Sardinia. The DTU-DADS-ASF model, an extension of the existing DTU-DADS model originally designed for the spread of foot-and-mouth disease in pigs, was constructed through inserting the within-herd model sensitive to unit size (from Halasa, Boklund, *et al.* (2016)) into the existing DTU-DADS model. This new model, reflecting an industrialized swine population, simulated epidemiological and economic outcomes of an outbreak (Halasa, Bøtner, *et al.*, 2016a) and was later used to assess alternative control strategies (Halasa, Bøtner, *et al.*, 2016b). This model was further refined to exemplify the Danish and French swine populations, where the consequences of hypothetical outbreaks were assessed (Andraud *et al.*, 2019; Halasa *et al.*, 2018).

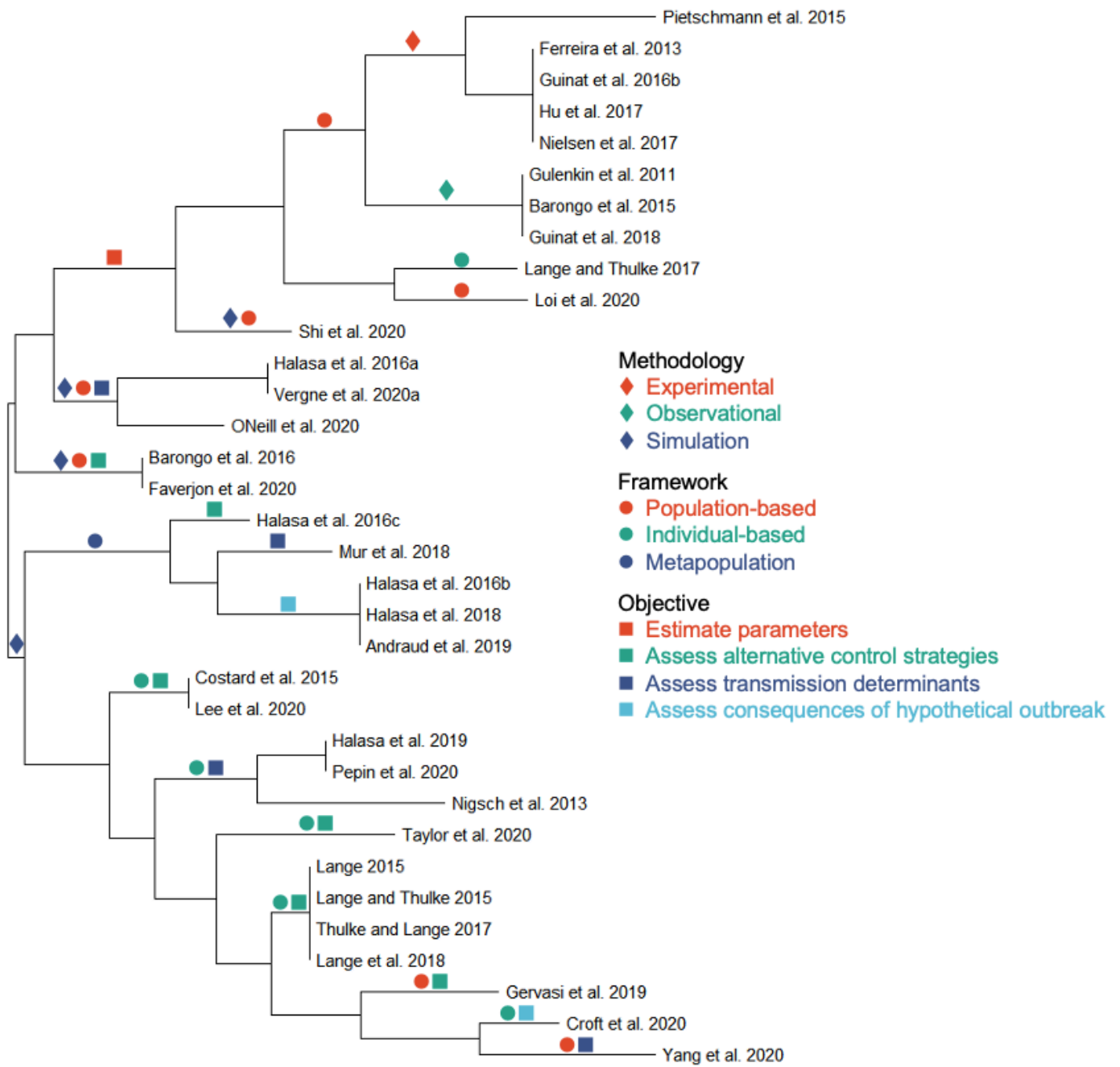


Fig. 3.3 | Filiation tree of included articles on mechanistic modelling of ASF.

**Table 3.2** | Model characteristics of articles

Reference	Host	Framework	Time	Space	Model Objective
<i>Gulenkin et al., 2011</i>	Pig	PBM	Continuous	No	Estimate parameters
<i>Ferreira et al., 2013</i>	Pig	PBM	Discrete	No	Estimate parameters
<i>Nigsch et al., 2013</i>	Pig	IBM	Discrete	Movement	Assess transmission determinants
<i>Barongo et al., 2015</i>	Pig	PBM	Continuous	No	Estimate parameters
<i>Costard et al., 2015</i>	Pig	IBM	Discrete	No	Assess alt. control strategies
<i>Barongo et al., 2016</i>	Pig	PBM	Continuous	No	Assess alt. control strategies
<i>Guinat, Gubbins, et al., 2016</i>	Pig	PBM	Discrete	No	Estimate parameters
<i>Halasa, Boklund, et al., 2016</i>	Pig	PBM	Discrete	No	Assess transmission determinants
<i>Halasa, Bøtner, et al., 2016a</i>	Pig	Meta-population	Discrete	Movement and distance	Assess consequences of outbreak
<i>Halasa, Bøtner, et al., 2016b</i>	Pig	Meta-population	Discrete	Movement and distance	Assess alt. control strategies
<i>Hu et al., 2017</i>	Pig	PBM	Continuous	No	Estimate parameters
<i>Nielsen et al., 2017</i>	Pig	PBM	Discrete	No	Estimate parameters
<i>Guinat et al., 2018</i>	Pig	PBM	Continuous	No	Estimate parameters
<i>Halasa et al., 2018</i>	Pig	Meta-population	Discrete	Movement and distance	Assess consequences of outbreak
<i>Mur et al., 2018</i>	Pig	Meta-population	Discrete	Movement and distance	Assess transmission determinants
<i>Andraud et al., 2019</i>	Pig	Meta-population	Discrete	Movement and distance	Assess consequences of outbreak
<i>Faverjon et al., 2021</i>	Pig	PBM	Discrete	Distance	Assess alt. control strategies
<i>Lee et al., 2021</i>	Pig	IBM	Discrete	Movement	Assess alt. control strategies
<i>Shi et al., 2020</i>	Pig	PBM	Continuous	No	Estimate parameters
<i>Vergne et al., 2021</i>	Pig	PBM	Continuous	No	Assess transmission determinants
<i>Pietschmann et al., 2015</i>	Pig, Boar	PBM	Discrete	No	Estimate parameters
<i>Taylor et al., 2021</i>	Pig, Boar	IBM	Discrete	Movement	Assess alt. control strategies
<i>Lange, 2015</i>	Boar	IBM	Discrete	Movement	Assess alt. control strategies
<i>Lange and Thulke, 2015</i>	Boar	IBM	Discrete	Movement	Assess alt. control strategies
<i>Lange and Thulke, 2017</i>	Boar	IBM	Discrete	Movement	Estimate parameters
<i>Thulke and Lange, 2017</i>	Boar	IBM	Discrete	Movement	Assess alt. control strategies
<i>Lange et al., 2018</i>	Boar	IBM	Discrete	Movement	Assess alt. control strategies
<i>Gervasi et al., 2019</i>	Boar	PBM	Discrete	No	Assess alt. control strategies
<i>Halasa et al., 2019</i>	Boar	IBM	Discrete	Movement	Assess transmission determinants
<i>Croft et al., 2020</i>	Boar	IBM	Discrete	Movement	Assess consequences of outbreak
<i>Loi et al., 2020</i>	Boar	PBM	Continuous	No	Estimate parameters
<i>O'Neill et al., 2020</i>	Boar	PBM	Continuous	No	Assess transmission determinants
<i>Pepin et al., 2020</i>	Boar	IBM	Continuous	Movement	Assess transmission determinants
<i>Yang et al., 2021</i>	Boar	PBM	Continuous	No	Assess consequences of outbreak

**Table 3.3** | Parameter results

ASFV Strain	Host	Basic epidemiological unit	Scale of transmission	Assumed latent period (days)	Assumed infectious period (days)	$\beta$	$R_0$	Reference
<b>Genotype I</b>	Boar	Individual	Within population	3.57 days	5 - 7	0.5	1.124 (95% CI 1.103–1.145) - 1.170 (1.009–1.332)	Loi <i>et al.</i> , 2020
<b>Malta 1978</b>	Pig	Individual	Within pen	4 ± 0.8 (low dose) 5 ± 1.4 (high dose)	Min: 7.0 ± 2.9 Max: 33.6 ± 22.5	2.79 (95% CI 1.57, 4.95)	Min infectious period: 18.0 (95% CI 6.90, 46.9) Max infectious period: 62.3 (95% CI 6.91, 562)	Ferreira <i>et al.</i> , 2013
<b>Netherlands 1986</b>	Pig	Individual	Within pen	5 ± 0.5	Min: 5.9 ± 2.6 Max: 19.9 ± 20.2	0.92 (95% CI 0.44, 1.92)	Min infectious period: 4.92 (95% CI 1.45, 16.6) Max infectious period: 9.75 (95% CI 0.76, 125)	Ferreira <i>et al.</i> , 2013
<b>Georgia 2007/1</b>	Pig	Individual	Within pen	4	Min: 4.5 ± 0.75 days Max: 8.5 ± 2.75 days	0.62 (95% CI 0.32, 0.91)	Min infectious period: 2.71 (95% CI 1.32, 4.56) Max infectious period: 4.99 (95% CI 1.36, 10.13)	Guinat, Gubbins, <i>et al.</i> , 2016
	Pig	Individual	Within pen	Gamma(mean, shape) mean ~ Gamma(4.5, 10) shape ~ Gamma(10, 2)	Gamma(mean, shape) mean ~ Gamma(10,6.0) shape ~ Gamma(19.3, 2)	2.62 (95% HPDI 0.96, 5.61)	24.1 (95% HPDI 7.34, 54.2)	Hu <i>et al.</i> , 2017
	Pig	Individual	Within pen	3 - 5	4.5 ± 0.75	1.00 (95% CI 0.56, 1.69)	(not reported)	Nielsen <i>et al.</i> , 2017
	Pig	Individual	Between pen	4	Min: 4.5 ± 0.75 days Max: 8.5 ± 2.75 days	0.38 (95% CI 0.06, 0.70)	Min infectious period: 1.66 (95% CI 0.28, 3.31) Max infectious period: 3.07 (95% CI 0.37, 6.97)	Guinat, Gubbins, <i>et al.</i> , 2016
	Pig	Individual	Between pen	Gamma(mean, shape) mean ~ Gamma(4.5, 10) shape ~ Gamma(10, 2)	Gamma(mean, shape) mean ~ Gamma(10,6.0) shape ~ Gamma(19.3, 2)	0.99 (95% HPDI 0.31, 1.98)	9.17 (95% HPDI 2.67, 19.2)	Hu <i>et al.</i> , 2017
	Pig	Individual	Between pen	3 - 5	4.5 ± 0.75	0.46 (95% CI 0.16, 1.06)	(not reported)	Nielsen <i>et al.</i> , 2017
	Pig	Individual	Within herd	-	1 - 5	(not reported)	8-11	Gulenkin <i>et al.</i> , 2011
	Pig	Individual	Within herd	Gamma(mean, shape) mean ~ Gamma(6.25, 10) shape ~ Gamma(19.39, 5)	Gamma(mean, shape) mean ~ Gamma(9.12, 10) shape ~ Gamma(22.20, 5)	0.7 (95% HPDI 0.3, 1.6) - 2.2 (95% HPDI 0.5, 5.3)	4.4 (95% CrI 2.0, 13.4) - 17.3 (3.5, 45.5)	Guinat <i>et al.</i> , 2018
	Pig	Herd	Between herd	-	1 - 5	(not reported)	2-3	Gulenkin <i>et al.</i> , 2011
<b>Armenia 2008</b>	Boar	Individual	Within pen	4	2 - 9	(not reported)	6.1 (95% CI 0.6, 14.5)	Pietschmann <i>et al.</i> , 2015
	Pig, Boar	Individual	Within pen	4	2 - 9	(not reported)	5.0 (95% CI 1.4, 10.7)	Pietschmann <i>et al.</i> , 2015
	Pig, Boar	Individual	Between pen	4	2 - 9	(not reported)	0.5 (95% CI 0.1, 1.3)	Pietschmann <i>et al.</i> , 2015
<b>Genotype IX</b>	Pig	Herd	Between herd	-	1 month	1,77	1.77 (95% CI 1.74, 1.81)	Barongo <i>et al.</i> , 2015
	Pig	Herd	Between herd	-	1 month	0,0059	1.58 (range not reported)	Barongo <i>et al.</i> , 2015
	Pig	Herd	Between herd	-	1 month	1,90	1.90 (95% CI 1.87, 1.94)	Barongo <i>et al.</i> , 2015
<b>Not specified</b>	Pig	Herd	Within population	2.86 - 8.33 days	1.25 – 100	0.001 – 0.3	0.8043 – 3.7695	Shi <i>et al.</i> , 2020

Both the DTU-DADS-ASF and the Be-FAST models relied on simulated live-animal movements and kernel-based distances to model susceptible-infectious contacts between herds. In the DTU-DADS-ASF model, movements (including both animal movements between herds and indirect contacts such as abattoir movements and contact with vehicles and animal health workers) were simulated through series of transmission probabilities parameterized to historical movement frequency data in the represented location (Denmark or France). Distance-based probabilities between herds were used to model local spread. The Be-FAST model also considered direct and indirect contact between herds, using a metapopulation framework to model trade networks and indirect means of spread (Ivorra *et al.*, 2014). Whereas the Be-FAST model used SI infection states within herds, the DTU-DADS-ASF simulation used a modified SEIR model with the infectious state split into sub-clinical and clinical states.

Stochastic, discrete, spatially-explicit individual-based models, mostly focused on assessing alternative control strategies, were the predominant approaches to modelling ASF in wild boar, with the exceptions of Croft *et al.* (2020) who used a deterministic approach and Gervasi *et al.* (2019) and Yang *et al.* (2021) who used deterministic non-spatial population-based models. Of the spatially-explicit individual-based models, unlike in the domestic pig metapopulation models, disease spread was simulated exclusively through movement-based algorithms. For the ASF Wild Boar model (Lange, 2015; Lange *et al.*, 2018; Lange & Thulke, 2015; Thulke & Lange, 2017), the model replicated from it (Halasa *et al.*, 2019), and the model by Pepin *et al.* (2020), this was accomplished using a rasterized spatial habitat grid. In order to avoid raster-associated bias in their model, Croft *et al.* (2020) elected against a grid-based landscape, instead using a mosaic of irregular polygons scaled to the average wild boar herd range. In all these models, individual animal movements occurred via dispersal and orientation probabilities of each individual animal, followed by upper-bounded number of dispersal steps that could be taken. Unlike domestic pig simulations or the Halasa *et al.* (2019) and Pepin *et al.* (2020) wild boar simulations, the ASF Wild Boar individual-based models (Lange, 2015; Lange *et al.*, 2018; Lange & Thulke, 2015; Thulke & Lange, 2017), and Croft *et al.* (2020) used weekly not daily time steps in their process scheduling.

Three domestic pig models used individual-based frameworks as well, to examine routes of ASF transmission between EU Member States (Nigsch *et al.*, 2013), the efficacy of movement-restriction control measures (Lee *et al.*, 2021), and to assess controlling the silent release of ASF from farms (Costard *et al.*, 2015). For evaluating transmission determinants in the EU, Interspread Plus—a proprietary software program that allows for modelling a variety of animal diseases—used movement-based algorithms to simulate disease spread between herds but did not account for



distance-based transmission routes. It was used to model the transmission of ASF both within and between countries. Both pig movements between farms as well as indirect contacts within-country were modelled, followed by simulated export movements. A similar stochastic, discrete, spatially-explicit state-transition model was adapted to the swine network in Vietnam by Lee *et al.* (2021)—the North American Animal Disease Spread Model (NAADSM). Here, farm-type-dependent contact probabilities and rates simulated animal trade movements. To ascertain the risk of ASF spread secondary to an emergency sell-off of pigs, Costard *et al.* (2015) developed their own individual-based model. Here, ASF transmission was stochastically simulated within a herd and then coupled to data on the behavior of farmers to determine the risk of ASF spread outside the affected herd.

### 3.5 (Results) Model insights and assumptions

#### 3.5.1 Model parameters

ASF transmission parameters, estimated from models with both individuals and herds acting as the basic epidemiological unit (depending on the study), were often used to parameterize future models—though a variety of other parameter data sources were identified as well (Table 3.4). This resulted in a range of values being used for ASFV's infectious period, incubation period (the time between infection and clinical signs), and latent period (classically considered as the time between infection and infectiousness, though in (Costard *et al.*, 2015) this was defined as infectious without clinical signs) across all models. When ASF data was unavailable, certain parameters had to be adapted from other disease models. Transmission probabilities for pig movements (Nigsch *et al.*, 2013), indirect contacts (Andraud *et al.*, 2019; Halasa, Boklund, *et al.*, 2016; Halasa, Bøtner, *et al.*, 2016a, 2016b; Halasa *et al.*, 2018; Mur *et al.*, 2018; Nigsch *et al.*, 2013), and local spread (Andraud *et al.*, 2019; Halasa, Boklund, *et al.*, 2016; Halasa, Bøtner, *et al.*, 2016a, 2016b; Halasa *et al.*, 2018; Mur *et al.*, 2018) were adapted from CSF studies, as was the range for  $R_0$  in Costard *et al.* (2015). When alternative control strategies were evaluated, some parameters that determined the probability of success of a control measure and the time required for its implementation were adapted from CSF or FMD studies as well (Andraud *et al.*, 2019; Halasa, Bøtner, *et al.*, 2016a, 2016b; Halasa *et al.*, 2018).

Limited field data for wild boar resulted in the evolution of many assumptions as new information was discovered. Carcass-based transmission was modelled through direct transmission within and between groups first as sex-dependent (Lange & Thulke, 2015), then neither age nor sex-dependent (Lange, 2015; Lange & Thulke, 2017), and then as age-dependent (Lange *et al.*, 2018). Infection probability per carcass was originally parameterized at 20% according to the best-fit model that

**Table 3.4 | Parameter assumptions**

(a) Average ASFV infectious period duration

Reference	Host	Value	Source
Gulenkin <i>et al.</i> , 2011	Pigs	1-5 days	FAO, 2009
Barongo <i>et al.</i> , 2015	Pigs	1 month	Ferreira <i>et al.</i> , 2013
Guinat, Gubbins, <i>et al.</i> , 2016	Pigs	Min: 3 - 6 days Max: 3 - 14 days	Gabriel <i>et al.</i> , 2011; Blome <i>et al.</i> , 2012, 2013
Hu <i>et al.</i> , 2017	Pigs	Gamma(mean (days), shape) mean ~ Gamma(10,6.0) shape ~ Gamma(19.3, 2)	Ferreira <i>et al.</i> , 2013
Nielsen <i>et al.</i> , 2017	Pigs	4.5 ± 0.75 days	Guinat <i>et al.</i> , 2014
Guinat <i>et al.</i> , 2018	Pigs	Gamma(mean (days), shape) mean ~ Gamma(9.12, 10) shape ~ Gamma(22.20, 5)	Guinat, Gubbins, <i>et al.</i> , 2016; Gulenkin <i>et al.</i> , 2011; Hu <i>et al.</i> , 2017
Lange, 2015; Lange and Thulke, 2015, 2017; Thulke and Lange, 2017; Lange <i>et al.</i> , 2018	Boar	1 week	Blome <i>et al.</i> , 2012
Halasa <i>et al.</i> , 2019	Boar	PERT(1, 5, 7) days	Olesen <i>et al.</i> , 2017
Faverjon <i>et al.</i> , 2021	Pig	Uniform (3, 5.5)	Guinat, Gogin, <i>et al.</i> , 2016; Guinat, Gubbins, <i>et al.</i> , 2016
Lee <i>et al.</i> , 2021	Pig	4-52 weeks	assumed
Loi <i>et al.</i> , 2020	Boar	5-7 days	Blome <i>et al.</i> , 2012; Gabriel <i>et al.</i> , 2011; Guinat, Gubbins, <i>et al.</i> , 2016
O'Neill <i>et al.</i> , 2020	Boar	Live boar: 5 days Carcasses: 8 weeks	Gallardo <i>et al.</i> , 2015 Carrasco García, 2016; Probst <i>et al.</i> , 2017
Pepin <i>et al.</i> , 2020	Pig, Boar	Poisson(5 days)	Blome <i>et al.</i> , 2012; Gallardo <i>et al.</i> , 2017
Taylor <i>et al.</i> , 2021	Boar	Live boar: PERT(3, 6, 10) days Carcasses: PERT(15, 26, 124) days	Gabriel <i>et al.</i> , 2011; Guinat <i>et al.</i> , 2014 Morley, 1993; Olesen <i>et al.</i> , 2018; Probst <i>et al.</i> , 2017; Chenais <i>et al.</i> , 2019
Vergne <i>et al.</i> , 2021	Pig	PERT(3, 7, 14) days	Guinat, Gubbins, <i>et al.</i> , 2016
Yang <i>et al.</i> , 2021	Boar	5 days	Davies <i>et al.</i> , 2017

(b) Beta

Reference	Host	Value	Source
Barongo <i>et al.</i> , 2016	Pigs	PERT(0.2, 0.3, 0.5)	Ferreira <i>et al.</i> , 2013
Halasa, Boklund, <i>et al.</i> , 2016	Pigs	0.30 or 0.60	Guinat, Gubbins, <i>et al.</i> , 2016
Hu <i>et al.</i> , 2017	Pigs	Gamma(2,2)	Gulenkin <i>et al.</i> , 2011
Guinat <i>et al.</i> , 2018	Pigs	Gamma(2, 2)	Guinat, Gubbins, <i>et al.</i> , 2016; Gulenkin <i>et al.</i> , 2011; Hu <i>et al.</i> , 2017
Halasa, Bøtner, <i>et al.</i> , 2016a, 2016b; Halasa <i>et al.</i> , 2018	Pigs	Nuclear, production: PERT(0.14, 0.38, 0.8); Boar, backyard, quarantine, hobby: PERT(0.36, 0.60, 0.93)	Guinat, Gubbins, <i>et al.</i> , 2016
Mur <i>et al.</i> , 2018	Pigs	Industrial, closed, semi-free: 1.42, Family: 1.85	Gulenkin <i>et al.</i> , 2011
Andraud <i>et al.</i> , 2019	Pigs	Within herd: PERT(0.6, 1, 1.5)	Halasa <i>et al.</i> , 2016b
Faverjon <i>et al.</i> , 2021	Pig	Within pen: Truncated normal(min, mean, max, sd)(0, 0.6, 14.3, 0.4) Between pen: Truncated normal(0, 0.3, 14.3, 0.2) Between room: Truncated normal(0, 0.01, 0.1, 0.05)	Ferreira <i>et al.</i> , 2013; Guinat, Gogin, <i>et al.</i> , 2016; Guinat, Gubbins, <i>et al.</i> , 2016 Assumed

<b>Lee et al., 2021</b>	Pig	Direct contact, indirect contact between small and medium farms: 0.6 Indirect contact to large farms: 0.006	Guinat, Gubbins, et al., 2016
<b>Shi et al., 2020</b>	Pig	0.001 - 0.3	Ferreira et al., 2013
<b>Taylor et al., 2021</b>	Boar	Wild boar to pig: Uniform(0, 0.167) Wild boar to wild boar: PERT(0, 0.167, 0.3) Dead wild boar to wild boar: Uniform(0, 0.167)	Pietschmann et al., 2015 and assumed
<b>Vergne et al., 2021</b>	Pig	PERT(0.2, 0.4, 0.6)	Guinat, Gubbins, et al., 2016

### (c) Average ASFV incubation period duration

Reference	Host	Value	Source
<b>Gulenkin et al., 2011</b>	Pigs	15 days	WOAH, 2008
<b>Nigsch et al., 2013</b>	Pigs	PERT(3, 5, 13) days	FAO, 2009, Depner personal communication
<b>Barongo et al., 2015</b>	Pigs	5-15 days	Sanchez-Vizcaino et al., 2015
<b>Costard et al., 2015</b>	Pigs	Weibull(shape, scale) 2+ (Weibull (1.092, 4.197 (median 5, range 2-19) days	Plowright et al., 1994; Arias and Sanchez-Vizcaino, 2002; Penrith et al., 2004; Sanchez-Vizcaino, 2012
<b>Mur et al., 2018</b>	Pigs	Poisson(8)	Ferreira et al., 2013; WOA, 2014
<b>Faverjon et al., 2021</b>	Pig	Gamma(shape, scale) (13.299, 0.3384482)	Ferreira et al., 2012, 2013; Guinat, Gogin, et al., 2016; Guinat, Gubbins, et al., 2016
<b>Pepin et al., 2020</b>	Boar	Poisson(4) days	Blome et al., 2012; Gallardo et al., 2017

### (d) Average ASFV latent period duration

Reference	Host	Value	Source
<b>Nigsch et al., 2013</b>	Pigs	1-2 days	FAO, 2009
<b>Costard et al., 2015</b>	Pigs	Uniform(1,2) days	Arias and Sanchez-Vizcaino, 2002; Plowright et al., 1994
<b>Pietschmann et al., 2015</b>	Both	4 days	Assumed
<b>Guinat, Gubbins, et al., 2016</b>	Pigs	2-5 days	Assumed
<b>Barongo et al., 2016</b>	Pigs	PERT(2.86, 4, 8.3) days	WOAH, 2008; FAO, 2008, 2009
<b>Hu et al., 2017</b>	Pigs	Gamma(mean (days), shape) mean ~ Gamma(4.5, 10) shape ~ Gamma(10, 2)	Ferreira et al., 2013
<b>Nielsen et al., 2017</b>	Pigs	3-5 days	Guinat et al., 2014
<b>Guinat et al., 2018</b>	Pigs	Gamma(mean (days), shape) mean ~ Gamma(6.25, 10) shape ~ Gamma(19.39, 5)	Guinat, Gubbins, et al., 2016; Gulenkin et al., 2011; Hu et al., 2017
<b>Mur et al., 2018</b>	Pigs	Poisson(2)	Ferreira et al., 2013; WOA, 2014
<b>Halasa et al., 2019</b>	Boar	PERT(1, 5, 9) days	Olesen et al., 2017
<b>Loi et al., 2020</b>	Boar	3.57 days	Blome et al., 2012; Gabriel et al., 2011; Guinat, Gubbins, et al., 2016
<b>Shi et al., 2020</b>	Pig	2.86 - 8.33 days	Barongo et al., 2016
<b>Vergne et al., 2021</b>	Pig	PERT(3,4,5) days	Guinat, Gubbins, et al., 2016
<b>Yang et al., 2021</b>	Boar	4 days	Barongo et al., 2016

explained the observed data (Lange & Thulke, 2015). Camera trapping data from Probst *et al.* (2017) and the results of Lange & Thulke (2017) resulted in this parameter being refined to 2–5% in the subsequent model by Lange *et al.* (2018). The assumed live infectious periods in the wild boar models were predominantly 5–7 days (Halasa *et al.*, 2019; Lange, 2015; Lange *et al.*, 2018; Lange & Thulke, 2015, 2017; Loi *et al.*, 2020; O’Neill *et al.*, 2020; Pepin *et al.*, 2020; Taylor *et al.*, 2021; Thulke & Lange, 2017), however greater variation was seen among the assumed carcass infectious periods.

In the ASF Wild Boar models, carcass persistence—synonymous with carcass infectivity—was originally statically modelled at 8 weeks (Lange & Thulke, 2015). However, after disease spread was observed and a model was fit, the spread was best explained using a 6-week carcass persistence time (Lange, 2015). Carcass persistence time was further revised to 4 weeks in Lange & Thulke (2017) and Thulke & Lange (2017) (and similarly used in Halasa *et al.* (2019) in line with field research on vertebrate scavenging behavior from Ray *et al.* (2014)). The carcass persistence parameter was then further revised to reflect a seasonally-dependent variability in Lange *et al.* (2018), with persistence times ranging from 4 weeks in the summer to 12 weeks in the winter, in accordance with seasonal differences observed in field research (Ray *et al.*, 2014). This seasonal variability in carcass persistence was also assumed in Pepin *et al.* (2020). In the later wild boar models, O’Neill *et al.* (2020) assumed a static carcass infectivity time of 8 weeks, and Taylor *et al.* (2021) used a PERT distribution of parameters 2, 4, and 18 weeks (specifically: 15, 26, and 124 days), with the latter model also accounting for the probability of carcass removal during the period.

The first wild boar individual-based models (Lange, 2015; Lange & Thulke, 2015) used a 4 km<sup>2</sup> geographical unit, corresponding to the home range of a wild boar herd, in accordance with ecological data from radio-tracking sessions from Spitz & Janeau (1990) and Leaper *et al.* (1999). At this unit size there may be some interactions between neighboring herds, though as boar prefer to stay within their home range and interact with their groupmates, long distance movements are consequently mostly related to dispersal of juveniles. The geographical raster was later increased to units of 9 km<sup>2</sup> (Lange *et al.*, 2018; Lange & Thulke, 2017; Thulke & Lange, 2017) to avoid perfect overlap between the study area and voxel size used in the model (Lange & Thulke, 2017), as necessary for the model objective. The wild boar individual-based model by Halasa *et al.* (2019), replicated from Lange (2015) and Lange & Thulke (2017), again used 4 km<sup>2</sup> units. The more recent boar models increase the geographical unit size, with Pepin *et al.* (2020) using 25 km<sup>2</sup> grid cells, and Taylor *et al.* (2021) applying 100 km<sup>2</sup> cells over the Polish landscape.

Lastly, the timing of viral release varied across the wild boar individual-based models as well. In order to allow population dynamics to become established, virus release was originally set for the first week

of the 4<sup>th</sup> year of simulation run and to 10 hosts in Lange & Thulke (2015). This parameter was adjusted to the beginning of June of the 5<sup>th</sup> year of simulation (corresponding to the dispersal period for juveniles) and for 25 hosts (Lange, 2015). The next model iterations (Lange & Thulke, 2017; Thulke & Lange, 2017) simulated ASFV release at the end of June of the 4<sup>th</sup> year of simulation and to 10 hosts, and the following model (Lange *et al.*, 2018) released the infection at the end of June of the 6<sup>th</sup> year of simulation to 5 hosts. The model described in Halasa *et al.* (2019) allowed one year for population dynamics to emerge (as evidenced by the dramatic increase in groups in the population graph prior to stabilization), with virus release occurring at the beginning of the second year and to only one random boar. There is no mention of the wild boar population stabilizing before virus introduction. Conversely, Pepin *et al.* (2020) used a 10-year burn-in period for population dynamics to stabilize prior to ASF release.

### 3.5.2 Transmission determinant assessment

Halasa, Boklund, *et al.* (2016) revealed that ASFV's path of transmission through a domestic pig herd is influenced by subclinical animal infectiousness, dead animal residues, and herd size. For spread between pig herds, for the enzootic situation in Sardinia where free-roaming unregistered pigs (known as *brado*) complicate eradication efforts, Mur *et al.* (2018) identified local spread through fomites as the primary transmission route. Brado and wild boar were indicated to play central roles in the occurrence of ASF cases, reinforcing the importance of herd biosecurity in interrupting transmission. On the international scale, it was demonstrated that limited transmission of ASF between EU member nations would occur through swine trade networks prior to disease detection, reinforcing the importance of surveillance measures (Nigsch *et al.*, 2013). Factors influencing the path of transmission of ASFV were also assessed for wild boar in Denmark, where the model showed that the density, size, and location and dispersion of a boar population will affect transmission and circulation of ASF (Halasa *et al.*, 2019). The importance of carcass-based transmission was quantified in Pepin *et al.* (2020), where it was inferred over half of the transmission events were from infected carcass contact. When observed dynamics of ASF in boar in Europe were modelled—specifically to capture the troughs and peaks of infection and population densities—differences in temperature and scavenger abundance were shown to impact carcass degradation affecting outbreak severity, reinforcing the role of carcasses in epizootic maintenance (O'Neill *et al.*, 2020).

One model explored the role of insect vectors in contributing to disease spread (Vergne *et al.*, 2021), demonstrating that only a small percentage of ASFV transmission events would be due to stable flies, assuming an average abundance of flies (measured once previously as 3-7 flies per pig). However, as vector abundance increased ten- and twenty-fold, the percentage of transmission due to the insects

increased dramatically as well. Transmission was also highly sensitive to blood-meal regurgitation quantity and ASFV infectious dose, indicating areas of necessary further study.

### *3.5.3 Alternative control strategy assessment and prediction of consequences of hypothetical outbreaks*

When control strategies were compared and the consequences of outbreaks assessed, Costard *et al.* (2015) showed that increasing farmers' awareness of and sensitivity of detection to ASF will not reduce the risk of silent release through emergency sales. Barongo *et al.* (2016) demonstrated that, in a free-range pig population, rapid biosecurity escalation (within 2 weeks of outbreak onset) would significantly decrease the burden of disease. Halasa, Bøtner, *et al.* (2016b) showed that, for industrialized European swine populations, including virological and serological testing of up to five dead animals per herd per week within the perimeter of an outbreak, in addition to established national and EU measures, provided the most effective control strategy. When the consequence of using shorter durations of control zones was assessed, the model predicted such a reduction would greatly reduce economic losses without jeopardizing worsening transmission (Halasa *et al.*, 2018). Conversely, increasing the size of the area under surveillance would offset the increased incurred cost through shortening the epizootic's duration (Halasa *et al.*, 2018). For arresting ASF spread in Vietnam, movement restrictions were used as the control method and it was shown they would have to interdict at least half of all pig movements to be effective. This was problematic as many traders were identified to specifically avoid quarantine checkpoints and sell pigs through illegal means (Lee *et al.*, 2021).

Models that assessed the consequences of hypothetical outbreaks did so for specific industrialized (Danish and French) swine populations and two independent populations of wild boar. The simulations of ASFV spread in the domestic pig compartment only predicted short and small epizootics (mean duration of less than one month) in both Denmark and France, with disease spread primarily driven by animal movements and often contained upon implementation of the codified national and EU control strategies (Andraud *et al.*, 2019; Halasa, Bøtner, *et al.*, 2016a). As the epizootic could fade out in the inciting herd, some (14.4% of epizootics originating in nucleus herds, 12.1% from sow herds) were predicted to never be detected. Further, the initial outbreak was predicted to have the highest economic cost—more-so than any subsequent outbreaks—due primarily to the ensuing trade restrictions that dwarf the direct costs (Halasa, Bøtner, *et al.*, 2016a). In France, due to the pyramidal structure of the swine production system, variation was seen dependent upon the index herd's location in the production pyramid (Andraud *et al.*, 2019). Geographic dispersal of ASF cases was highly dependent on the density of herds where the outbreak initialized, with cases spreading up to 800 km from herds in low-density areas. If ASF spread originated from free-range pig herds, as

opposed to the top of the production pyramid, it was predicted to potentially affect up to 15 herds. Similar to the results of the assessment of transmission determinants by Mur *et al.* (2018), local transmission appeared to be the driving route. Among wild boar models, the consequences of concern were the outcome of natural circulation of ASFV in a closed population, where any outbreak was determined to be self-limiting (Croft *et al.*, 2020), and the impact of baiting on disease establishment, where through modelling changes in  $R_0$  it was seen that such practice would relatively increase the risk of an ASF epizootic taking hold (Yang *et al.*, 2021).

Wild boar simulations demonstrated the importance of long-term sustained control efforts (i.e. over many generations of wild boar), as the scale of depopulation required for a more rapid solution would likely be untenable (Lange, 2015). As the simulation model parameters were refined with updated evidence, delayed carcass removal (two or more weeks postmortem) was shown to have no effect on curtailing ASF spread; only carcass removal within 1 week (an impractical assumption, given current reported carcass removal rates) was shown to have a positive effect (Thulke & Lange, 2017). This conclusion was expanded in Lange *et al.* (2018), where successful carcass removal within a core area was shown to reduce the required hunting intensity. A distinction between control methods required for scenarios of focal introduction as opposed to spread from adjacent enzootic areas was identified as well: in the case of focal introduction, due to the small size of the affected area, it's possible that a high carcass removal rate could achieve control without the need for intensive hunting (Lange *et al.*, 2018). When surveillance methods were compared, passive surveillance —assuming a 50% carcass detection rate—was shown to be more effective than active surveillance at detecting ASF cases in a small population, however active surveillance was better when both disease prevalence and population density were low (<1.5% prevalence, < 0.1 boar/km<sup>2</sup>) and the hunting rate was over 60% (Gervasi *et al.*, 2019). When transmission from free-range, outdoor pigs was factored into the spread of ASF from wild boar dispersion, hunting was shown to reduce the number of new cases but not the size of the area at risk, and conversely fencing reduced the size of the region at risk of ASF but not the number of cases (Taylor *et al.*, 2021).

### 3.6 Discussion

Mechanistic modelling has been a valuable tool for deriving infection parameters, unraveling routes of transmission, assessing alternative control strategies, and determining the consequences of hypothetical outbreaks of ASF. However, despite all that has been elucidated, there is still much research to be done. Existing ASF models are limited in the contexts of their application, their means of evaluating control strategies, and the lack of a bridge between domestic and wild compartments, and attention should be given to resolving these shortcomings.

ASF simulation models, either in domestic pigs or wild boar, have been applied only to a limited number of contexts, despite the epizootic risk faced by all European countries and the insights one could get from mechanistic models to anticipate virus emergence. Simulations of ASF outbreaks in domestic pigs, for the current epizootic of the circulating Georgia 2007/01 isolate, have been published only for two European (Denmark and France) and one Asian (Vietnam) nation. Many differences exist between countries in terms of the type of production system, the distribution of farm types, and the source-nation of imported pigs, preventing the extrapolation of results from one nation to another. Similarly, the presence and distribution of, and control mandates against, wild boar are not uniform between areas, precluding extrapolation of model results outside the area of study. Though the general utility of different control strategies has been indicated, real-world data on wild boar abundance, as difficult as it may be to assess, is needed to facilitate parameterization of these models to real-world scenarios. When the wild boar individual-based models were applied to real-world locations, they were run only at low-population scales: in Denmark where there exists a legal mandate for their elimination, in the Baltic nations but only in the area of the international border, a forest in England, and part of Poland. Of the five-year period in which wild boar models were published, almost half of such publications occurred in the most recent year, 2020. Whereas earlier wild boar models were constructed by only one group, the diversity among the 2020 models is a promising trend in the direction of ASF ecological modelling. However, as the number of individuals being modelled grows the required computing time grows cubically (Keeling & Rohani, 2008), so insightful as these individual-based models may be, presently they may be too computationally expensive to adapt to larger populations in other scenarios or scales.

All models that assess control strategies assume the employed strategies will remain constant over the period of implementation. Due to the evolving nature of epizootics, this is unlikely to reflect real-world conditions. Future models may consider including temporal components to the control strategies, both through parsing by specific pre-defined time points (e.g. optimal control strategies to be used before and after  $R_0$  becomes less than 1), as well as via objective functions to identify when is the best time to implement certain strategies (especially with regards to types of surveillance).

Accounting for limitations in the surveillance data used to fit mechanistic models (such as imperfect case detection and delays in reporting) is an important consideration in model development. For instance, many models rely on pig mortality thresholds for detecting ASF, though ASFV could circulate in a herd for almost a month prior to it being detected through such criteria (Guinat *et al.*, 2018). The DTU-DADS-ASF simulation factored in a parameter to account for delays during contact tracing, though detection delays due to imperfect herd-level surveillance (such as from small changes in



mortality) was not simulated. Among wild boar, passive carcass detection and under-reporting was a common limitation, as such detection was both seasonally variable and irregular. Taylor *et al.* (2021) accounted for this through including an “under-reporting factor” in their parameters, while Pepin *et al.* (2020) fit parameters for this uncertainty using approximate Bayesian computation, though the influence of a lack of negative surveillance data was identified in their analysis. Similarly, when parameters were estimated among wild boar in Sardinia, both non-uniform sampling and a lack of passive surveillance samples were identified as limitations. Though no adjustments were made to address them, the large quantity of data potentially offset the bias, as suggested by the authors. Refining this uncertainty through field studies of wild boar could benefit future models and is worthy of investigation.

Resolving structural uncertainty is another on-going gap in ASF modelling that requires improvement. This uncertainty is demonstrated in multiple ways, such as through the range of values among parameter assumptions and the various routes of transmission (and corresponding scale) that are modelled: where specific routes of indirect transmission may be parameterized in one model another will group all such routes under a single local transmission parameter. Quantifying the contribution of individual indirect routes of transmission to ASF spread is one of many areas for refinement through further research. Whereas uncertainty is a quality inherent to all models, studies have shown that this can be minimized through ensemble modelling, where the results of multiple models are aggregated to generate a common final output. Combinations of models providing the best predictions was demonstrated through the results of the *RAPIDD Ebola forecasting challenge* competition: among a variety of individual- and population-based, stochastic and deterministic, mechanistic and semi-mechanistic models, ensemble predictions routinely performed better than any individual model (Viboud *et al.*, 2018). A similar modelling challenge on ASF was launched in 2020, involving several modelling teams. Though still a work-in-progress, it is anticipated that this exercise will be able to provide similar assessments among ASF models, potentially reinforcing the importance of utilizing synthesized results (INRAE, 2020).

Prior to 2020, there was a noticeable lack of diversity among the existing models. Though the proliferation of models last year helped to offset this imbalance, still over one-third (5/14) of the domestic pig simulations are derived from the DTU-DADS-ASF (and component precursor by Halasa, Boklund, *et al.* (2016)) model. Similarly, prior to 2020 all but one of the wild boar models were derived from Lange and Thulke’s ASF Wild Boar model, and Croft *et al.* (2020) used epidemiological parameters from Lange and Thulke’s model as well. The influx of recent wild boar models by Croft *et al.* (2020), O’Neill *et al.* (2020), and Pepin *et al.* (2020) provided contrasting simulations of wild boar and carcass-

based transmission in different outbreak scenarios, helping to diversify the field. This diversity aids in reinforcing the shared conclusions among the different models, such as the importance of combining targeted hunts or culls with active carcass removal to achieve outbreak control while avoiding eradication of the wild boar population (Lange, 2015; O'Neill *et al.*, 2020).

Only one simulation model considered transmission between domestic pigs and wild boar despite differences in the observed transmission pathways between countries. While the individual-based wild boar models not accounting for transmission with domestic pigs may be sufficient for areas with ASF dissemination exclusively in the wildlife compartment, areas where spillover—however intermittently—likely occurs will require models that address this aspect. The one simulation that did consider this inter-compartment transmission relied on contact parameters derived for a free-range savannah-like outdoor farm not typically representative of European swine operations (though the authors accounted for this by assuming such contact as an upper-limit). While this model by Taylor *et al.* (2021) is a critical step towards a unified ASF model of both domestic pig and wild boar transmission, it also indicates the need to better define the parameters informing wild boar and domestic pig contact risks and rates through further research. Simulation models of hypothetical outbreaks and alternative control strategies that link the domestic and wildlife compartments are critical for informing decision-making. Just as this has been done for multiple other animal diseases such as Aujeszky's disease and hepatitis E (Charrier *et al.*, 2018), foot-and-mouth disease (M. Ward *et al.*, 2015), and bovine tuberculosis (Brooks-Pollock & Wood, 2015), this should be a priority for all nations at risk of ASF importation.

While mathematical models can provide many insights into disease control, they are far from the only tool available. Recent ASF outbreaks have been successfully controlled without the use of mathematical models, such as in the Czech Republic and Belgium. Multisectoral collaboration between epidemiologists, veterinarians, virologists, ecologists, field-work studies, and expert opinion plays an integral role in ASF control. From model building to outcome validation and decision analysis, experts from these fields should be included to maintain an inclusive multi-faceted approach to ASF modelling.

### 3.7 Conclusions

With outbreaks across 18 European and 12 Asian nations (as of publication in June 2021), ASF has become established as an urgent threat to the global swine industry (ProMED-mail, 2020; Taylor *et al.*, 2021). Mechanistic models have shown much potential for helping to confront this epizootic, however, more modelling studies using empirical data derived from real epizootics are needed,

especially for generating better estimates of transmission parameters. As these parameters are integral to designing calibrated intervention plans (such as identifying optimal protection and surveillance zones, or (when available) the fraction of necessary vaccination coverage), and since these parameters have been seen to vary between individual ASF outbreaks, extrapolation of parameters between independent outbreak scenarios is precarious at best. Deriving parameters from Georgia 2007/01 genotype II historical outbreaks beyond the two examinations of the past Russian Federation epizootic (Guinat *et al.*, 2018; Gulenkin *et al.*, 2011) is critical for further refining models to combat the on-going ASF panzootic. Limitations of surveillance systems in obtaining accurate data are an active impediment. Though this is being overcome through more complex modelling and inference techniques (e.g. approximate Bayesian computation), existing labour and workforce limitations hinder field data collection.

Prior to this past year, there was a need to diversify modelling approaches through developing additional frameworks (as almost half of the studies at the time stemmed from one of either two models: DTU-DADS-ASF (Halasa, Bøtner, *et al.*, 2016a) and ASF Wild Boar (Lange & Thulke, 2015), however the large influx of modelling teams in 2020 seeking to address ASF unknowns is a promising direction for the field that will probably be reinforced due to the ASF modelling challenge. In addition, current evidence indicates that spillover events between domestic pigs and wild boar play an important role in ASF outbreaks, and this transmission should be a component of models going forward. Finally, to date, only codified, hypothetical and *a priori* defined interventions were compared. Therefore, moving from intervention comparison to identifying optimized control strategies is critical. Doing so will enable policy-makers to identify the ideal course of action rather than a relatively better option among pre-determined routes. From a decision point of view, while we promote models to support policy, policy-makers should consider several models together. As ensemble modelling studies have not been performed yet, we recommend using existing models as decision guides only for the specific scenarios modelled. Due to the uncertainty of even basic parameters, and as evidenced in the sensitivity analyses of different models, we do not encourage extrapolating results to non-modelled scenarios (e.g. across national borders). The current modelling body provides excellent insight for addressing ASF transmission at a multitude of scales, and these studies should be referenced as such when forming policy decisions on that level by considering all associated models (i.e. for addressing ASF in Sardinia considering the results of both Mur *et al.* (2018) and Loi *et al.* (2019), or when deciding on intra-herd strategy considering the results of Costard *et al.* (2015), Faverjon *et al.* (2021), Halasa, Boklund, *et al.* (2016), and Vergne *et al.* (2021). For ASF modellers, until uncertain parameters are further refined, we hope our consolidation of parameter assumptions and results will facilitate parameter selection for future models. Addressing all these modelling hurdles is expected to

generate more appropriate information, for policy-makers and modellers to contribute to the control of ASF both locally and globally.

### Box 3.1 | Chapter 3 key points

- Almost 75% of ASF mechanistic models are tailored to the currently-panzootic genotype II strain.
- Models almost exclusively focused on either domestic pigs or wild boar independently, with only 2 articles (at the time of publication) examining between-host transmission.
- Better estimates of multiple transmission parameters are needed, as these parameters can vary considerably between outbreaks.
- Spillover events between domestic pigs and wild boar are suspected to play a crucial role in some regions, and need to be considered in future models.
- Only *a priori* defined interventions have been assessed, and future models would benefit from identifying optimised control strategies.
- The current modelling body provides excellent insight for addressing ASF transmission at a multitude of scales, and these studies should be referenced as such when forming policy decisions on the level appropriate to the model.

### 4.1 Introduction

Within the realm of mathematical modelling of epizootic diseases, developing models at the domestic-wildlife interface carries its own unique set of challenges. Indeed, entire articles have been written on the inherent challenges (Buhnerkempe *et al.*, 2015; Roberts *et al.*, 2021). Simply estimating transmission between species is a burdensome task, as there exists difficulty even in defining what constitutes an epidemiologically-relevant contact (Buhnerkempe *et al.*, 2015). Laboratory-based forced contact is different than that experienced under natural circumstances, and observing natural contacts to infer model parameters is a challenging ecological task (Buhnerkempe *et al.*, 2015). Further, spillover events are rarely observed but their frequency must be indirectly inferred, so as to inform the means of disease transmission in the non-reservoir population (Roberts *et al.*, 2021).

Transmission drivers have been well studied among human and domestic animal populations, however among wildlife species the resolution of such datasets is relatively poor (Huyvaert *et al.*, 2018; McCallum, 2016). Wildlife characteristics ranging from descriptions of movement patterns and contact networks to simply quantifications of host population size are less certain (Cowled & Garner, 2008; Craft, 2015; Cross *et al.*, 2012; Huyvaert *et al.*, 2018; Russell *et al.*, 2017). The difficulty of observing wildlife species further affects the ability to obtain accurate measurements of disease frequency due to biases among sampled and non-sampled subsets of wildlife populations (Gilbert *et al.*, 2013; Huyvaert *et al.*, 2018). These uncertainties inherently affect the ability to quantify a disease's transmission potential among this population, and are compounded when an attempt is made to reduce all these factors to a transmission probability.

Modelling disease transmission between species, therefore, is a complex equation system involving multiple distinct host and pathogen factors that must be captured in each state-transition process. Within these mathematical models, both the wild and domestic species must be accurately represented and the driver of transmission between species must be explicitly described. This literature review aims to examine the means of representation of livestock and wildlife species in epidemiological studies at the livestock-wildlife interface, and identify the drivers of transmission used in the models.

## 4.2 Materials and Methods

The literature search was conducted via the PubMed and Web of Science databases on 21 June 2022 and performed in accordance with PRISMA guidelines (Liberati *et al.*, 2009). Constructed to capture all articles of mechanistic modelling that accounted for transmission between major livestock species and wildlife, the search—within keywords, title, and abstract—was comprised of the following query: *(livestock OR cattle OR swine OR pig OR sheep OR goat) AND (wildlife OR "wild boar" OR buffalo OR bison OR deer OR elk) AND transmission AND (simulation OR mathematical OR stochastic OR estimation OR inference) AND model*). The search was restricted to mammalian species as the methods and models used for non-mammalian epizootic disease of major concern, notably highly-pathogenic avian influenza, were thought to be less applicable to informing ASF modelling methods between domestic pigs and wild boar. No date limitation was specified, and the English language was indirectly specified through search terminology.

A total of 455 articles were retrieved (PubMed N=263, Web of Sciences N=192) (Fig. 4.1). Following removal of duplicates (N=85), 370 articles were considered for preliminary title and abstract screening. All original research describing mechanistic models between mammalian wildlife and livestock were included.

Preliminary review resulted in the exclusion of 320 articles. There were articles that only considered a single species (N=127), did not include interaction between livestock and mammalian (i.e. non-avian) wildlife (N=39), were an exclusively within-host study (i.e. molecular, microbiological, immunological, or genomic model) (N=29), were of phylogenetic or phylodynamic models (n=13), focused on purely statistical models (i.e. risk factor analysis, quantitative risk analysis) (N=52), were of economic or decision-analysis models (N=7), were a review or editorial (N=20), or were non-modelling studies such as experiments or field studies (N=41).

Of the 42 articles that qualified for full-text review, eight articles were excluded following full-text assessment for not mechanistically modelling transmission at the livestock-wildlife interface (Barron *et al.*, 2015; Byrom *et al.*, 2015; Marion *et al.*, 2008; Mateus-Anzola *et al.*, 2019; Moreno-Torres *et al.*, 2017; Mur *et al.*, 2018; Santos *et al.*, 2020; Smith, 2006). The one calibration article not identified in the initial search was subsequently added, yielding 35 articles for data extraction. Author, date, domestic and wildlife species, disease, location, model framework, method of domestic and wildlife representation, driver of transmission between species, type of transmission between species (direct or indirect), direction of transmission, and model were extracted.

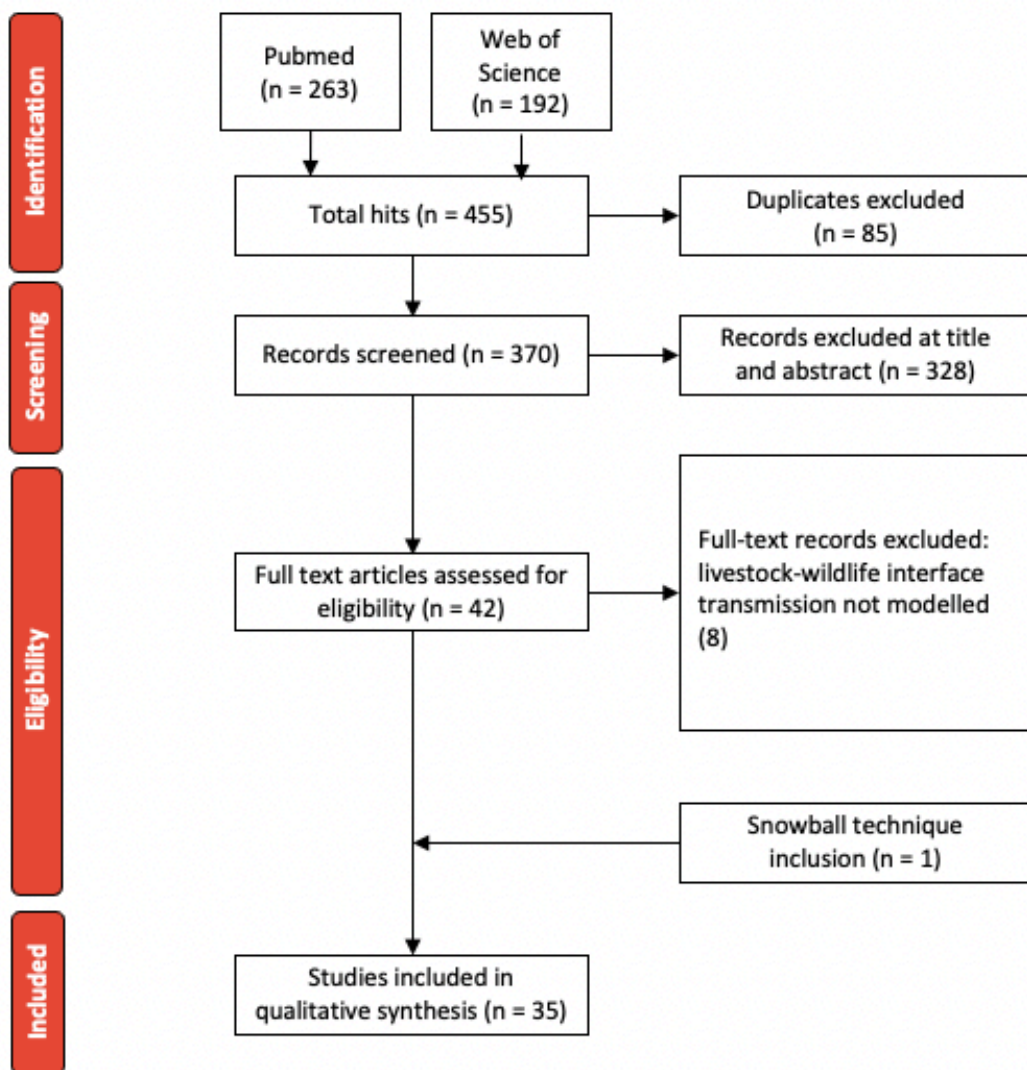


Fig. 4.1 | PRISMA flow diagram for article selection

## 4.3 Results

### 4.3.1 Epidemiological characteristics

Publication dates ranged from 2001 to 2021. Cattle were the predominant domestic species represented—either alone (N=18) or in combination with other livestock (goats pigs and sheep, goats and sheep, or solely sheep) (N=3)—and bovine tuberculosis (bTB) was the most frequently modelled disease (N=11) (Table 4.1). Pigs, sheep, and goats were less frequently represented (Fig. 4.2). Among explicitly modelled wildlife, wild boar (N=8), badgers (N=7), and deer (N=4) were most commonly represented with one model including both wild boar and deer. Further included wildlife were bharal, buffalo, saiga antelopes, cats, stray dogs, impala, zebra, and wildebeest (Table 4.1).



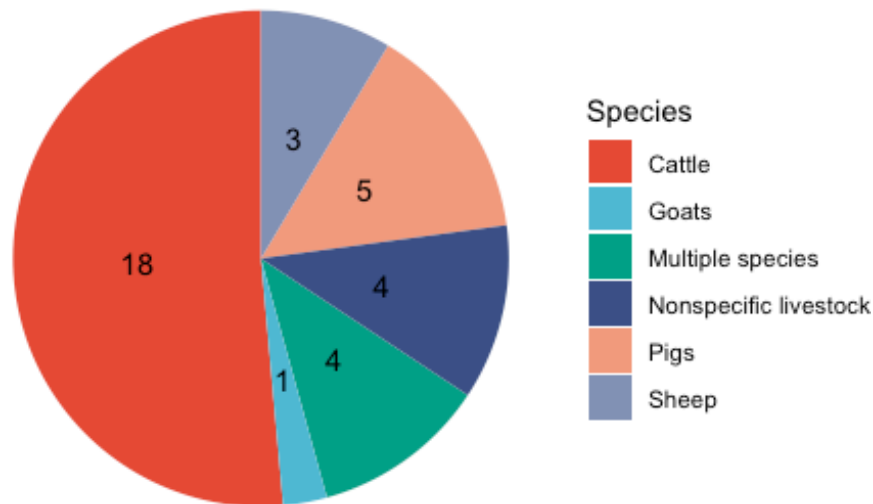


Fig. 4.2 | Frequency of represented domestic species in included models

Viral, bacterial, and parasitic diseases were represented among the models. In addition to bTB, foot-and-mouth disease (FMD) (N=5), African swine fever (ASF) (N=3), trypanosomiasis (N=3), brucellosis (N=2), and nematodiasis (N=2) were represented more than once, with babesiosis, classical swine fever, echinococcosis, louping ill, toxoplasmosis, and trichostrongylosis each represented a single time (Table 4.1). Of the locations explicitly modelled, the United Kingdom (UK) and United States of America (USA) were represented the most frequently (N=7 and N=6, respectively) though a total of 15 different countries across Africa, Europe, North America, and Oceania were represented among the studies (Table 4.1).

#### 4.3.2 Model frameworks, objectives, and representation of hosts

Five model frameworks were represented in the included articles: individual-based models (N=15), population-based models (N=12), cellular automata models (N=3), ecological models (N=2), network models (N=2), and metapopulation models (N=1) (Table 4.2). Among these models, the primary objectives were to assess control strategies (N=17), assess transmission dynamics (N=8), or assess both (N=2), though estimating parameters (N=4) and evaluating methodologies for proof-of-concepts (N=4) were also represented (Fig. 4.3).

**Table 4.1** | Epidemiological characteristics of the 35 articles included in the review

Reference	Domestic species	Wildlife species	Disease	Location
<b>Agudelo et al., 2021</b>	Cattle	Deer	Babesiosis	USA
<b>Birch et al., 2018</b>	Cattle	Badgers	bTB	UK
<b>Boklund et al., 2008</b>	Pigs	Wild boar	CSF	Denmark
<b>Bouchez-Zacria et al., 2018</b>	Cattle	Badgers	bTB	France
<b>Cosgrove et al., 2018</b>	Cattle	Deer	bTB	USA
<b>Doran et al., 2005</b>	Cattle, sheep	Wild boar	FMD	Australia
<b>Greenman et al., 2008</b>	Nonspecific livestock	Nonspecific wildlife	bTB	Nonspecific
<b>Hargrove et al., 2012</b>	Cattle	Nonspecific wildlife	Trypanosomiasis	Uganda
<b>Kajunguri et al., 2014</b>	Cattle	Nonspecific wildlife	Trypanosomiasis	Nonspecific
<b>Khanyari et al., 2021</b>	Goats, sheep	Bharal	Nematodiasis	India
<b>Laffan et al., 2011</b>	Cattle	Wild boar	FMD	USA
<b>Lintott et al., 2013</b>	Nonspecific livestock	Nonspecific wildlife	Nonspecific	Nonspecific
<b>Manlove et al., 2019</b>	Nonspecific livestock	Nonspecific wildlife	Nonspecific	Nonspecific
<b>Marion et al., 2008</b>	Cattle	Nonspecific wildlife	Nonspecific	Nonspecific
<b>Mateus-Pinilla et al., 2002</b>	Pigs	Cats	Toxoplasmosis	Nonspecific
<b>Morgan et al., 2007</b>	Sheep	Saiga antelopes	Trichostrongylosis	Kazakhstan
<b>Nyerere et al., 2020</b>	Nonspecific livestock	Nonspecific wildlife	Brucellosis	Nonspecific
<b>O'Hare et al., 2014</b>	Cattle	Badgers	bTB	UK
<b>Odeniran et al., 2020</b>	Cattle, goats, sheep	Nonspecific wildlife	Trypanosomiasis	West Africa
<b>Phepa et al., 2016</b>	Cattle	Buffalo	bTB	South Africa
<b>Pietschmann et al., 2015</b>	Pigs	Wild boar	ASF	Nonspecific
<b>Pineda-Krch et al., 2010</b>	Cattle, goats, pigs, sheep	Wild boar	FMD	USA
<b>Porter et al., 2011</b>	Sheep	Deer	Louping ill	UK
<b>Ramsey et al., 2016</b>	Cattle	Deer	bTB	USA
<b>Rong et al., 2021</b>	Sheep	Stray dogs	Echinococcosis	China
<b>Roy et al., 2011</b>	Cattle	Nonspecific wildlife	Brucellosis	Sub-Saharan Africa
<b>Smith, Cheeseman, Clifton-Hadley, et al., 2001</b>	Cattle	Badgers	bTB	UK
<b>Smith, Cheeseman, Wilkinson, et al., 2001</b>	Cattle	Badgers	bTB	UK
<b>Smith et al., 2016</b>	Cattle	Badgers	bTB	UK
<b>Taylor et al., 2021</b>	Pigs	Wild boar	ASF	Europe
<b>Walker et al., 2018</b>	Goats	Impala, zebra, wildebeest	Nematodiasis	Bostwana
<b>Ward et al., 2015</b>	Cattle	Wild boar	FMD	Australia
<b>Ward et al., 2011</b>	Cattle	Wild boar, deer	FMD	USA
<b>Wilkinson et al., 2004</b>	Cattle	Badgers	bTB	UK
<b>Yoo et al., 2021</b>	Pigs	Wild boar	ASF	Republic of Korea

IBMs, mostly focused on bTB though also used for ASF, babesiosis, CSF, FMD, and trypanosomiasis, took a variety of approaches in representing their hosts, with rasters being the most common epidemiological unit for both domestic and wildlife species. The raster definition for livestock relied on combinations of farm locations, livestock density, and pasture area (Agudelo et al., 2021; Cosgrove et al., 2018; Ramsey et al., 2016; Taylor et al., 2021), as well as farm type (Smith et al., 2016) or host

presence (Manlove *et al.*, 2019) to provide the raster data. Point locations of herds were also used (Boklund *et al.*, 2008; Pineda-Krch *et al.*, 2010; M. Ward *et al.*, 2015; Yoo *et al.*, 2021), as was a patch lattice (Marion *et al.*, 2008) or, in the case of the vector-borne disease trypanosomiasis, a single parameter representing host abundance. Wildlife rasters used either habitat (Agudelo *et al.*, 2021; Boklund *et al.*, 2008; Cosgrove *et al.*, 2018; Ramsey *et al.*, 2016; Taylor *et al.*, 2021), population density (Pineda-Krch *et al.*, 2010), territories (Smith *et al.*, 2016), presence (Manlove *et al.*, 2019), or—in the case of badgers where exact locations of setts were known—contiguous social groups (Smith, Cheeseman, Clifton-Hadley, *et al.*, 2001; Smith, Cheeseman, Wilkinson, *et al.*, 2001; D. Wilkinson *et al.*, 2004). When a raster was not used, either historical presence data (Marion *et al.*, 2008), point-locations of herds (M. Ward *et al.*, 2015) or cases (Yoo *et al.*, 2021), or a single parameter of wildlife abundance (Odeniran *et al.*, 2020) was used to represent wildlife.

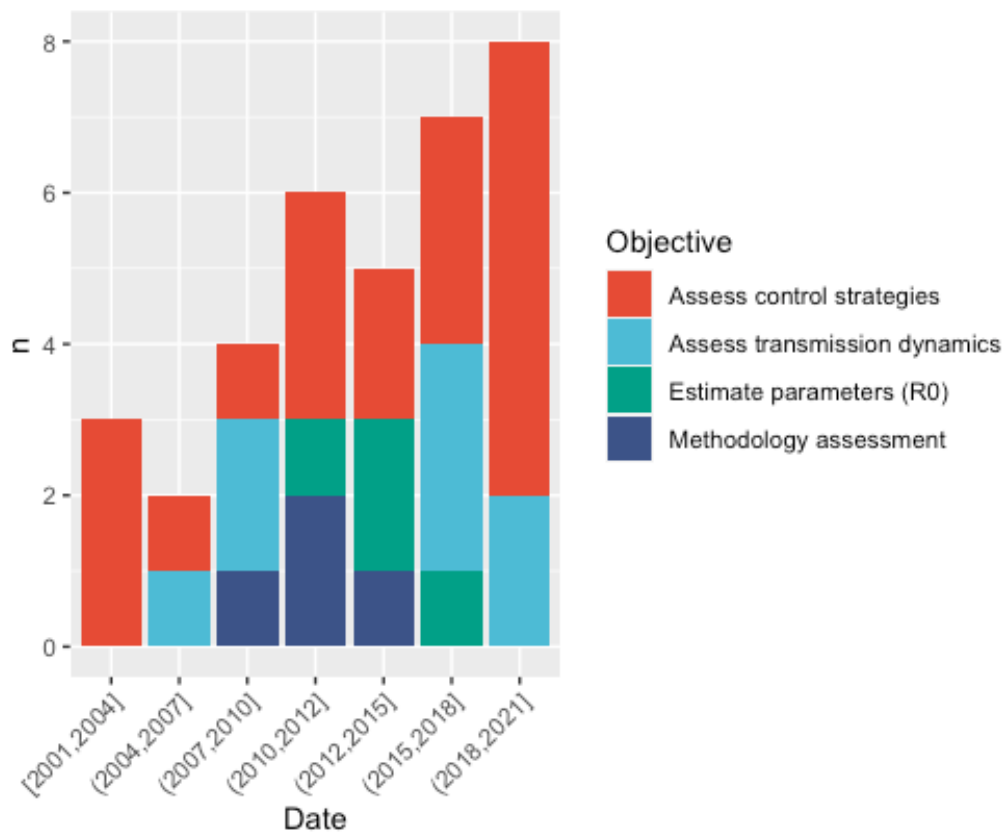


Fig. 4.3 | Publications by year subset by model objective

Population-based frameworks were used for a variety of diseases, including ASF, brucellosis, bTB, echinococcosis, louping ill, toxoplasmosis, trichostrongylosis, and trypanosomiasis. These models represented domestic and wildlife species through parameters quantifying host abundance, though

population density (Greenman & Hoyle, 2008) was also used in one model. Cellular automata models were used to model FMD in Australia and the USA (Doran & Laffan, 2005; Laffan *et al.*, 2011; M. P. Ward *et al.*, 2011). A density distribution over a cellular lattice (Doran & Laffan, 2005; Laffan *et al.*, 2011) or a raster of herds (M. P. Ward *et al.*, 2011) was used to represent domestic species, while wildlife species were represented via seasonal habitat or land cover density over a cellular lattice (Doran & Laffan, 2005; Laffan *et al.*, 2011) or habitat raster (M. P. Ward *et al.*, 2011). Direct, bi-directional disease transmission between wildlife and livestock was simulated through transmission probability (Doran & Laffan, 2005), with Laffan *et al.* (2011) and Ward *et al.* (2011) including contact rate as a transmission driver. These models were used to assess transmission dynamics (Doran & Laffan, 2005) but also for proof-of-concept to examine the methodology of the approach (Laffan *et al.*, 2011; M. P. Ward *et al.*, 2011).

Two models, examining nematodiasis in Botswana and India with climate as the driving force for pasture infectivity, used host density distributions for representing the livestock and wildlife (Khanyari *et al.*, 2021; Walker *et al.*, 2018). Whereas Walker and collaborators modelled unidirectional transmission from wildlife to livestock, Khanyari *et al.* included bidirectional disease transmission, both for the purposes of assessing control strategies (Khanyari *et al.*, 2021; Walker *et al.*, 2018). These ecological models modelled indirect transmission, using climate-driven pasture infectivity as the driver of transmission.

Network models were used to simulate bTB (Bouchez-Zacria *et al.*, 2018) and brucellosis (Roy *et al.*, 2011) transmission. In the model of bTB, network nodes were used to represent pastures of domestic hosts and home ranges of wild hosts, while in the brucellosis model network nodes represented herd type (for domestic species) with an additional node to represent the reservoir wildlife species.

A metapopulation approach was used in one model, where point locations of farms were used to represent domestic herds and wildlife was represented via a farm-specific force of infection parameter (Birch *et al.*, 2018).

#### 4.3.3 Drivers of disease transmission

The models in this review examined transmission in all directions, with unidirectional transmission from wildlife to livestock (N=16) or bidirectional transmission between wildlife and livestock (N=16) being the most frequent type (Table 4.2). One model examined unidirectional disease transmission from livestock to wildlife (Taylor *et al.*, 2021), and two models looked at transmission of disease between both wildlife and livestock to humans (Hargrove *et al.*, 2012; Kajunguri *et al.*, 2014).

Transmission rate parameters, used in IBMs, PBMs, network models, and the metapopulation model, were the most frequent means of simulating disease transmission between domestic and wildlife hosts (N=13) for models of ASF, brucellosis, bTB, echinococcosis, louping ill, and trypanosomiasis. When used in IBMs, the transmission rate was responsible for dictating infection between wildlife and livestock hosts, either directly between hosts or, as in Odeniran *et al.* (2020), indirectly from wildlife to vector and vector to livestock (or vice versa). PBMs captured livestock-wildlife transmission through specific transmission rates such as a density-dependent transmission rate (Greenman & Hoyle, 2008), environmental transmission rate (Nyerere *et al.*, 2020; Rong *et al.*, 2021), all-encompassing external transmission rate (O'Hare *et al.*, 2014), or, when a vector-borne disease was modelled, a life-stage-specific transmission rate of the tick vector (Porter *et al.*, 2011). In the metapopulation model of Birch *et al.* (2018), the transmission rate was a parameter unique to each farm that drove transmission from each farm's local reservoir.

Transmission probabilities, either alone (N=8) or in combination with contact rate parameters (N=4), were also often used to drive disease transmission in IBMs, cellular automata, PBMs, and network models. Direct and indirect transmission between hosts and from wildlife to livestock, as well as in the one model focused on livestock to wildlife transmission (Taylor *et al.*, 2021) relied on such probabilities. Alternatively, contact rate and pathogen prevalence drove transmission in Manlove *et al.* (2019), host and environment contact rates were used to determine interhost transmission in a PBM for bTB (Phepa *et al.*, 2016) and contact probability drove transmission in a network model of bTB (Bouchez-Zacria *et al.*, 2018).

Other drivers of transmission between host species included the sharing of pasture (Agudelo *et al.*, 2021), the proportion of blood meals from each host species (Hargrove *et al.*, 2012; Kajunguri *et al.*, 2014), and climate-driven pasture infectivity (Khanyari *et al.*, 2021; Walker *et al.*, 2018). Additionally, one IBM considered the risk of indirect transmission from feces on shared state-space (Marion *et al.*, 2008), and a PBM inferred inter-species transmission for one host through examining model output involving both hosts and then through the exclusion of one host (Morgan *et al.*, 2007).

Table 4.2 | Model characteristics of articles

Reference	Model framework	Domestic representation	Wild representation	Transmission driver	Transmission type	Transmission direction	Objective
<b>Agudelo et al., 2021</b>	IBM	Raster (habitat)	Raster (habitat)	Shared pasture	Indirect	Wildlife <> Livestock	Assess control strategies
<b>Birch et al., 2018</b>	Meta-population	Point locations (herd)	Parameter (farm-specific FoI)	Transmission rate	Direct	Wildlife > Livestock	Assess transmission dynamics
<b>Boklund et al., 2008</b>	IBM	Point locations (herd)	Raster (habitat)	Contact rate, transmission probability	Direct	Wildlife <> Livestock	Assess transmission dynamics and control strategies
<b>Bouchez-Zacria et al., 2018</b>	Network	Network nodes (pastures)	Network nodes (home ranges)	Contact probability	Direct	Wildlife > Livestock	Assess transmission dynamics
<b>Cosgrove et al., 2018</b>	IBM	Raster (farm locations, pasture area, density)	Raster (habitat)	Transmission rate	Direct	Wildlife > Livestock	Assess transmission dynamics
<b>Doran et al., 2005</b>	Cellular automata	Cellular lattice (density distribution)	Cellular lattice (habitat)	Transmission probability	Direct	Wildlife <> Livestock	Assess transmission dynamics
<b>Greenman et al., 2008</b>	PBM	Parameter (host density)	Parameter (host density)	Transmission rate	Direct	Wildlife > Livestock	Methodology assessment (proof of concept)
<b>Hargrove et al., 2012</b>	PBM	Parameter (host abundance)	Parameter (host abundance)	Host blood meal	Indirect	Livestock+wildlife > Human	Assess control strategies
<b>Kajunguri et al., 2014</b>	PBM	Parameter (host abundance)	Parameter (host abundance)	Host blood meal	Indirect	Livestock+wildlife > Human	Assess control strategies
<b>Khanyari et al., 2021</b>	Ecological	Spatial density distribution	Density distribution	Pasture infectivity	Indirect	Wildlife <> Livestock	Assess control strategies
<b>Laffan et al., 2011</b>	Cellular automata	Cellular lattice (density distribution)	Cellular lattice (land cover)	Contact rate, transmission probability	Direct	Wildlife <> Livestock	Methodology assessment (proof of concept)
<b>Lintott et al., 2013</b>	PBM	Parameter (host abundance)	Parameter (host abundance)	Transmission rate	Direct	Wildlife <> Livestock	Methodology assessment (proof of concept)
<b>Manlove et al., 2019</b>	IBM	Raster (presence)	Raster (presence)	Contact rate, pathogen prevalence	Direct	Wildlife <> Livestock	Assess control strategies
<b>Marion et al., 2008</b>	IBM	Patch lattice	Historical presence	Shared state-space risk	Indirect	Wildlife > Livestock	Assess transmission dynamics
<b>Mateus-Pinilla et al., 2002</b>	PBM	Parameter (host abundance)	Parameter (host abundance)	Transmission probability	Indirect	Wildlife > Livestock	Assess control strategies
<b>Morgan et al., 2007</b>	PBM	Parameter (host abundance)	Parameter (host abundance)	Qualitatively inferred	Indirect	Wildlife <> Livestock	Assess transmission dynamics
<b>Nyerere et al., 2020</b>	PBM	Parameter (host abundance)	Parameter (host abundance)	Transmission rate	Indirect	Wildlife <> Livestock	Assess transmission dynamics
<b>O'Hare et al., 2014</b>	PBM	Parameter (host abundance)	Parameter (host abundance)	Transmission rate	Indirect	Wildlife > Livestock	Estimate parameters (R0)
<b>Odeniran et al., 2020</b>	IBM	Parameter (host abundance)	Parameter (host abundance)	Transmission rate	Indirect	Wildlife <> Livestock	Assess control strategies

<b>Phepa et al., 2016</b>	PBM	Parameter (host abundance)	Parameter (host abundance)	Contact rate	Direct and indirect	Wildlife <> Livestock	Estimate parameters (R0)
<b>Pietschmann et al., 2015</b>	PBM	Parameter (host abundance)	Parameter (host abundance)	Transmission rate	Direct and indirect	Wildlife <> Livestock	Estimate parameters (R0)
<b>Pineda-Krch et al., 2010</b>	IBM	Point locations (herd)	Raster (density)	Contact rate, transmission probability	Direct and indirect	Wildlife > Livestock	Assess transmission dynamics and control strategies
<b>Porter et al., 2011</b>	PBM	Parameter (host abundance)	Parameter (host abundance)	Transmission rate	Indirect	Wildlife > Livestock	Estimate parameters (R0)
<b>Ramsey et al., 2016</b>	IBM	Raster (farm location, density)	Raster (habitat potential)	Transmission rate	Direct	Wildlife > Livestock	Assess control strategies
<b>Rong et al., 2021</b>	PBM	Parameter (host abundance)	Parameter (host abundance)	Transmission rate	Direct and indirect	Wildlife <> Livestock	Assess control strategies
<b>Roy et al., 2011</b>	Network	Network nodes (herd type)	Network node (static reservoir)	Transmission rate	Direct	Wildlife > Livestock	Assess control strategies
<b>Smith, Cheeseman, Clifton-Hadley, et al., 2001</b>	IBM	Raster (herd)	Raster (contiguous social groups)	Transmission probability	Direct	Wildlife > Livestock	Assess control strategies
<b>Smith, Cheeseman, Wilkinson, et al., 2001</b>	IBM	Raster (herd)	Raster (contiguous social groups)	Transmission probability	Direct	Wildlife > Livestock	Assess control strategies
<b>Smith et al., 2016</b>	IBM	Raster (farm type)	Raster (home ranges)	Transmission rate	Direct	Wildlife <> Livestock	Assess control strategies
<b>Taylor et al., 2021</b>	IBM	Raster (density)	Raster (abundance and habitat suitability)	Transmission probability	Direct	Wildlife > Livestock	Assess control strategies
<b>Walker et al., 2018</b>	Ecological	Spatial density distribution	Density distribution	Pasture infectivity	Indirect	Wildlife > Livestock	Assess control strategies
<b>Ward et al., 2015</b>	IBM	Point locations (herds)	Point locations (herds)	Transmission probability	Direct	Wildlife <> Livestock	Assess control strategies
<b>Ward et al., 2011</b>	Cellular automata	Raster (herds)	Raster (habitat)	Contact rate, transmission probability	Direct	Wildlife <> Livestock	Methodology assessment (proof of concept)
<b>Wilkinson et al., 2004</b>	IBM	Raster (herds)	Raster (contiguous social groups)	Transmission probability	Direct	Wildlife > Livestock	Assess control strategies
<b>Yoo et al., 2021</b>	IBM	Point locations (herds)	Case locations	Transmission probability	Direct	Wildlife > Livestock	Assess transmission dynamics

#### 4.4 Discussion

Modelling disease transmission between wild and domestic species requires accurate representation of both distinct populations—often with drastically differing population dynamics—and drivers of transmission. These choices of methodology will be a reflection of both the research question being addressed by the model and the availability of data, as for example is the case of evaluating wild boar densities in France where even despite having some information, such densities are difficult to assess. Domestic species were able to be defined through explicit herd locations, and further delineated by additional parameters of herd density, defined pasture area, habitat and abundance. In contrast, wildlife species were often modeled through variables of habitat potential, density distribution, or population abundance. Only in a few models of badgers were the exact burrow locations known, but even then only the underground dens were identified and surrounding home ranges still had to be inferred (Smith, Cheeseman, Clifton-Hadley, *et al.*, 2001; Smith, Cheeseman, Wilkinson, *et al.*, 2001; D. Wilkinson *et al.*, 2004). Cost-benefit analysis of choosing a paradigm to represent a system is important to consider, especially with regards to increasing model complexity and underlying assumptions. Though a model should be a realistic representation, deciding on the degree of realism required—and keeping in mind that models are only synthetic representations of a phenomenon—is part of the art of model selection. The parsimony principle should always be kept in mind, especially in situations involving wildlife where parameters are difficult to document or require a high level of data for inference.

Habitability is often used as a proxy to represent wild host populations, as was the case in eight models (Agudelo *et al.*, 2021; Boklund *et al.*, 2008; Cosgrove *et al.*, 2018; Doran & Laffan, 2005; Laffan *et al.*, 2011; Ramsey *et al.*, 2016; Taylor *et al.*, 2021; M. P. Ward *et al.*, 2011). Defining such suitability can involve the incorporation of landcover maps, abundance data from hunting records, expert opinion, and previously-published species distribution models. In the context of models examined in this review, species distribution is a means to the end for representing disease transmission through multiple populations, and assessing control strategies against such disease was the primary objective among all these models. Owing to limitations of computational capabilities, simplifications of a species' true distribution is necessary. Combined with data limitations among wildlife species, this will invariably result in wildlife disease transmission models that contain more uncertainties than those of domestic animal species (McCallum, 2016). Though there are innate assumptions that may not be fully accurate when using habitat suitability to represent wildlife presence in disease transmission models at the livestock-wildlife interface, for the given modelling objectives these assumptions are acceptable. While sensitivity analyses within the selected articles focused on model parameters (e.g.



transmission detection and contact rates, mortality, and initial infection location) and not the representation of the distribution of wildlife, Birch *et al.* (2018) did assess the sensitivity of their model to the number of environmental reservoirs—identifying that that parameter was more constrained than that of the environment-to-livestock transmission rate.

In modelling infectious diseases, the transmission driver is the parameter(s) that links the representative agents of the domestic and wildlife hosts. The transmission rate was the primary parameter used to drive infection between species—and only in one model was the livestock-wildlife transmission rate assumed from available data (Nyerere *et al.*, 2020)—whereas other models used contact rate and/or transmission probability to produce infection. Though contact rate is a much more observable phenomenon compared to disease transmission rate, using contact rates still required estimation or assumption of the probability of transmission given contact. Methods of estimation of these parameters differed per study (and is beyond the scope of this review), however the commonality exists that quantification of this parameter through either estimation or calibration from data is necessary.

Included studies that focused on control strategy assessments invariably quantified the number of infected herds, as explicitly stated in Pineda-Krch *et al.* (2010), Ramsey *et al.* (2016), and Smith *et al.* (2001, 2016), but certain methodologies precluded the ability to determine the relative contribution of species to overall spread. For instance, when foot-and-mouth disease was investigated among feral pigs and livestock, a single-layer cellular automata model was used (Doran & Laffan, 2005). Therefore, multiple species had to be mutated into a composite herd that varied based on a species-specific infectivity parameter (depending on the type and number of each specie). Though effective at discerning the overall epizootic spatio-temporal pattern, such a method did not allow for the disentangling of individual species' contribution. The relative contribution of involved species to epizootic propagation was only ascertained in two models (Birch *et al.*, 2018; Yoo *et al.*, 2021). For bTB, Birch *et al.* (2018) determined the range for the rate of infections originating from environmental reservoirs, and from there were able to elucidate the rate of infection from other cattle. For ASF, vehicle movement data was able to be used in concert with wild boar case data to determine the relative contribution to infection risk experienced by a farm for each potential source (Yoo *et al.*, 2021).

Having explored the myriad ways in which infectious disease transmission between domestic and wildlife species has been mechanistically modelled, we can now apply the results—specifically regarding domestic and wild representation, the transmission driver and type, and transmission direction—to inform our own development an ASF model at this interface. For domestic pigs, an

individual-based approach using either herd point locations or a raster (depending on the availability of density data) for herds is an established method for capturing infection spatio-temporal dynamics (see Table 4.2). To represent the wild boar component, cellular automata models, as used in Doran & Laffan (2005), Laffan *et al.* (2011), and Ward *et al.* (2015), have the advantage of being artificial life models that account for spatial relationships while avoiding the additional complexity and computational requirements of IBMs (that would arise from the need to program individual wild boar with individual movement parameters). Raster cells, used in lieu of distinct individuals, can be parameterized with vegetation and landcover data as in Doran & Laffan (2005), to further inform wildlife habitability. With limited data on contact probabilities between domestic pigs and wild boar (as evidenced in the systematic review of ASF models), direct virus transmission from domestic pigs to wild boar and from wild boar to domestic pigs can be modelled by estimating transmission rates, as done in multiple models here (see Table 4.2).

#### 4.5 Conclusions

Multi-host pathogens that affect both livestock and wildlife can cause severe harm to individual farmers, economies, and the environment (Craft, 2015). Controlling diseases at this interface is a critical step towards improving both livestock and wildlife health, and mechanistic models are becoming increasingly used to explore the strategies needed to confront these diseases. Developing models that include transmission between livestock and wildlife species is an exceptional challenge however, with these hurdles already having been investigated in a recent review (Huyvaert *et al.*, 2018). Only 12 diseases at this interface have benefited from the utility of mathematical modelling, despite prior studies of Europe and the United States revealing a far greater number of diseases shared between livestock and wildlife (Gortázar *et al.*, 2007; Jori, Hernandez-Jover, *et al.*, 2021; Miller *et al.*, 2013). Transmission rates between species, including contact rates and transmission probability, are key parameters needed for these models, and continued research into both these values and means of estimation of these values is needed. As computing capabilities increase, the resolution of the models and data used in these models will be able to increase as well, with a potential goal being the linking of modern complex ecological models with the depth of dynamics responsible for pathogen transmission. Mechanistic mathematical models have provided important insights into the dynamics of and control strategies against diseases shared between livestock and wildlife, and will continue to serve as an important tool in the fight against infectious disease.

#### Box 4.1 | Chapter 4 key points

- In mechanistic models, disease transmission is modelled via the transmission rate parameter  $\beta$  which accounts for both the contact rate between hosts and the transmission probability of a disease given infectious-susceptible contact.
- The majority of models were designed to evaluate control strategies while accounting for the presence of wildlife reservoirs, however just exploring the dynamics at the interface was also a common objective.
- Bovine tuberculosis and foot-and-mouth disease were the most represented diseases, with 3 articles examining African swine fever.
- Population-based models relied on parameters of overall host abundance to represent hosts.
- In spatially-explicit (i.e. non-population based) models, livestock were able to be represented through herd locations or density distributions, whereas wildlife was modelled indirectly through rasters of habitat suitability.
- Transmission was modelled predominantly as an overall transmission rate from livestock to wildlife or wildlife to livestock, though some models relied on contact rates, transmission probability, or pathogen prevalence.
- Over 90% of models examined wildlife-to-livestock transmission (either unidirectionally or in-concert with livestock-to-wildlife transmission). Only one model focused exclusively on livestock-to-wildlife transmission.
- Only two models explicitly determined the relative role of different species in overall epizootic propagation.
- Combining an individual-based model for domestic pig herds along with a cellular automata model for wild boar can be an approach to use in the conception of our ASF domestic-wildlife transmission model.

## § III | Evaluating control strategies against African swine fever transmission at the domestic-wildlife interface

Having systematically explored the ASF mathematical modelling body without discovering any models that fully capture the observed dynamics of transmission between the domestic and wildlife compartments for ASF, we undertook the challenge of constructing a model for this task. A two-step process, the first action was model construction (Chapter 5), followed by assessing intervention strategies (Chapter 6). Data from the on-going ASF epizootic in Romania, where spillover transmission between the domestic and wildlife compartments is suspected to be commonplace due to the prevalence of low-biosecurity backyard farms, were explored to inform model conception, construction and parameterization, and then a combination of manual and algorithmic model fitting strategies (i.e. literature review, approximate Bayesian computation, and fine tuning) were used to inform parameter values. The model output was evaluated by epizootic size and trajectory, and allowed us to determine the relative contribution of the domestic and wild compartments to the overall epizootic.

Part of a larger project to evaluate the interspecific effectiveness of interventions, a main goal of this research is to create an adaptable model that can be applied to areas in France that are rich in free-range swine holdings. Given the recent history of human-mediated ASF introductions into neighbouring western European nations of Germany and Belgium, and with ASF-positive wild boar detected in northwestern Italy earlier this year, it is likely only a matter of time until ASFV reaches the French border or jumps into her interior (WOAH, 2022a). The resilience of the French commercial farm network to ASF has already been explored (Andraud *et al.*, 2019), so here we would consider transmission among free-range herds while also accounting for expected transmission from and among wild boar. Though the model parameters that define the rates and distances of transmission will likely differ between the area of model development (Romania) and the end-objective nation of its application (France), the underlying dynamics governing contacts and transmission between wild and domestic hosts will remain the same. Through accounting for this yet-to-be mechanistically modelled transmission, our model will be another step forward towards a more complete picture of ASFV transmission dynamics.



## 5 | Modelling African swine fever transmission at the interface of domestic pigs and wild boar in Romania

### 5.1 Introduction

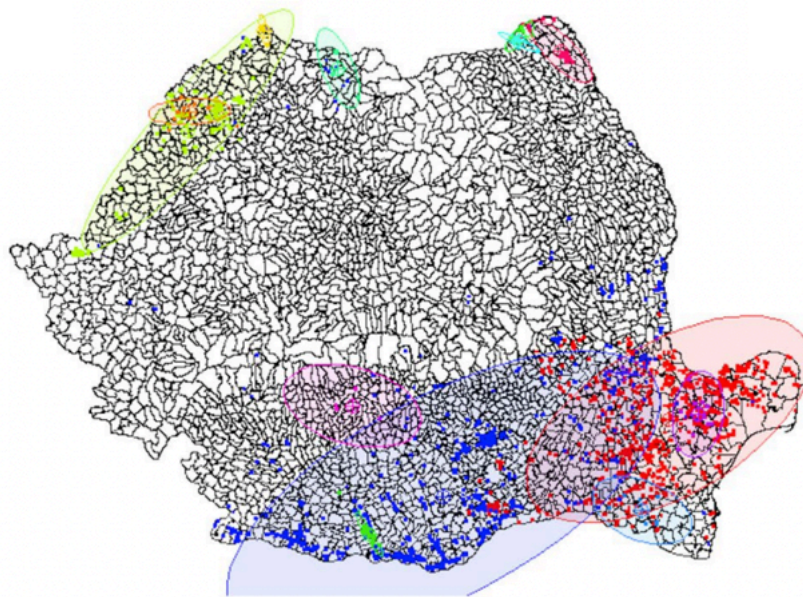
Since the introduction of the current panzootic strain into the European Union (EU) in 2014, cases have been identified in 12 EU Member States, with 10 nations still facing epizootics as of the end of 2021 (EFSA *et al.*, 2021; Van Goethem, 2021). ASF introduction and transmission pathways vary between epizootic areas, with some nations (e.g. the Baltic states) experiencing cases predominantly or exclusively among wild boar, and others (such as Romania) seeing cases mostly among domestic pigs with likely spillover to wild boar (Chenais *et al.*, 2019; DEFRA, 2021). As interrupting disease transmission is reliant on control strategies targeting these pathways, understanding the dynamics unique to each epizootic provides the best chance of achieving epizootic control (Keeling & Rohani, 2008).

As of August 2022, two nations have been successful at eradicating ASF following declared outbreaks for the current panzootic: Belgium and the Czech Republic. Unlike other countries, however, both of these nations had unique features in addition to the use of progressively-adapted zoning measures that facilitated such an achievement. First, both Belgium and the Czech Republic were confronting focal introductions—with the first reported case hundreds of kilometers from previously-reported extranational cases (as cited in Sauter-Louis *et al.* (2021))—and all subsequent cases were clustered around the index case (Sauter-Louis, Schulz, *et al.*, 2021). In the Czech Republic, the cases were in a highly fragmented landscape that aided confinement and depopulation of the local wild boar population. In Belgium, the observed cases were in an area with only one pig herd which was stamped out, greatly limiting the risk of spillover between domestic and wild hosts. In contrast, Romania—like Germany—is suspected to face constant infection pressure along its border, and control strategies accounting for such introduction routes are needed.

Mechanistic models, which allow the quantification of transmission parameters, the prediction of epizootic trajectories and the evaluation of the effectiveness of control strategies, are a proven way of confronting epizootics. However, as identified in our systematic review of mechanistic models of ASF (see chapter 4), current models do not account for spillover events between domestic pigs and wild boar, despite these events being suspected to play an important role in the propagation of some ASF epizootics (Hayes *et al.*, 2021). It was concluded that, in addition to needing more modelling studies using empirical data derived from real epizootics, transmission between domestic pig farms and wild boar should be a component of future models (Hayes *et al.*, 2021)

Since 2018, Romania has been facing an epizootic of unprecedented scale, affecting both wild boars and domestic pigs (DEFRA, 2021), and is considered as one of the EU countries most severely affected by ASF. Genotyping has confirmed that the ASFV strain circulating in Romania is of genotype II and identical to isolates from EU member states (Lithuania and Poland) and Caucasus nations (Ungur *et al.*, 2021). Understanding the transmission dynamics is necessary to design tailored control measures, adapted to the specificities of domestic pig rearing in regards of societal and economical aspects. The ubiquity of backyard pig farming in villages—with the majority of families having one or more pigs kept in low-biosecurity backyard holdings—provides an environment highly amenable to between-host transmission (Andraud *et al.*, 2021).

Prior epizootic analysis revealed three large clusters of cases in two temporally distinct waves (Fig. 5.1) (Andraud *et al.*, 2021). The first large epizootic wave was witnessed throughout the southeast of Romania—having initiated in Tulcea County—and persisted despite strong interventions by the authorities. Further, when explanatory variables were assessed, they were not consistent between waves and clusters suggesting the effect of additional mechanisms.



**Fig. 5.1** | Spatiotemporal clusters of ASF in Romania, June 2018 – August 2019. First wave in red (10/06/2018 – 14/05/2019), second waves in light green and blue (30/10/2018 – 28/08/2019, 26/04/2019 – 31/08/2019) (Andraud *et al.*, 2021)

To reproduce the spatiotemporal dynamics in Romania, quantifying the duration of the observed states, estimating the relative contribution of domestic pig farms and wild boar to epizootic propagation, and assessing the impact of different host unit types (i.e. forested and non-forested areas for wild boar, villages and industrial sites for domestic pig farms), a multihost spatiotemporal mechanistic simulation model was constructed.

## 5.2 Materials and methods

### 5.2.1 Data

Four datasets were used in the construction and calibration of the model: case records, village spatial distribution, industrial swine herd locations, and wild boar distribution using landcover as a proxy. Case records, which include the date of occurrence, coordinates, type of host (swine or wild boar) and associated farm type (backyard or industrial) were retrieved from WOA's Animal Disease Information System database for the period from initial case detection (10 June 2018) to the end of the first year (31 Dec 2018) (<https://wahis.woah.org/>) (WOAH, 2022a). Cases were restricted to the southeastern region of Romania where the initial epizootic spread was witnessed—the counties of Braila, Calarasi, Constanta, Galati, Ialomita, and Tulcea (Fig. 5.2).

The at-risk population of domestic pigs was distributed across either low-biosecurity (villages) or high-biosecurity (industrial) epidemiological units. As individual backyard herd locations were not able to be explicitly located, and per conclusions from field investigations that recommended counting outbreaks in the form of infected and cleared villages, backyard cases were aggregated to the level of the village (see the procedure in 5.2.2), where each village acted as a single epidemiological unit (Rose & Boisseleau, 2018). Based on the epidemiological data and preventive culling operations in surveillance zones, this approximation is unlikely to bias our conclusions. Village spatial data was retrieved from the Romanian National Agency for Mapping and Real Estate (ANCP) (<https://www.ancpi.ro/>), providing a total of 986 villages in the six counties (Romanian ministry of development, public works, and administration, 2021). Village locations were then represented by the centroid of each village. Industrial sites ( $n = 55$ ) were also represented by their point coordinates, whose locations were retrieved from county-level data available through the county-level directorates of the National Sanitary Veterinary and Food Safety Authority (ANSVSA).

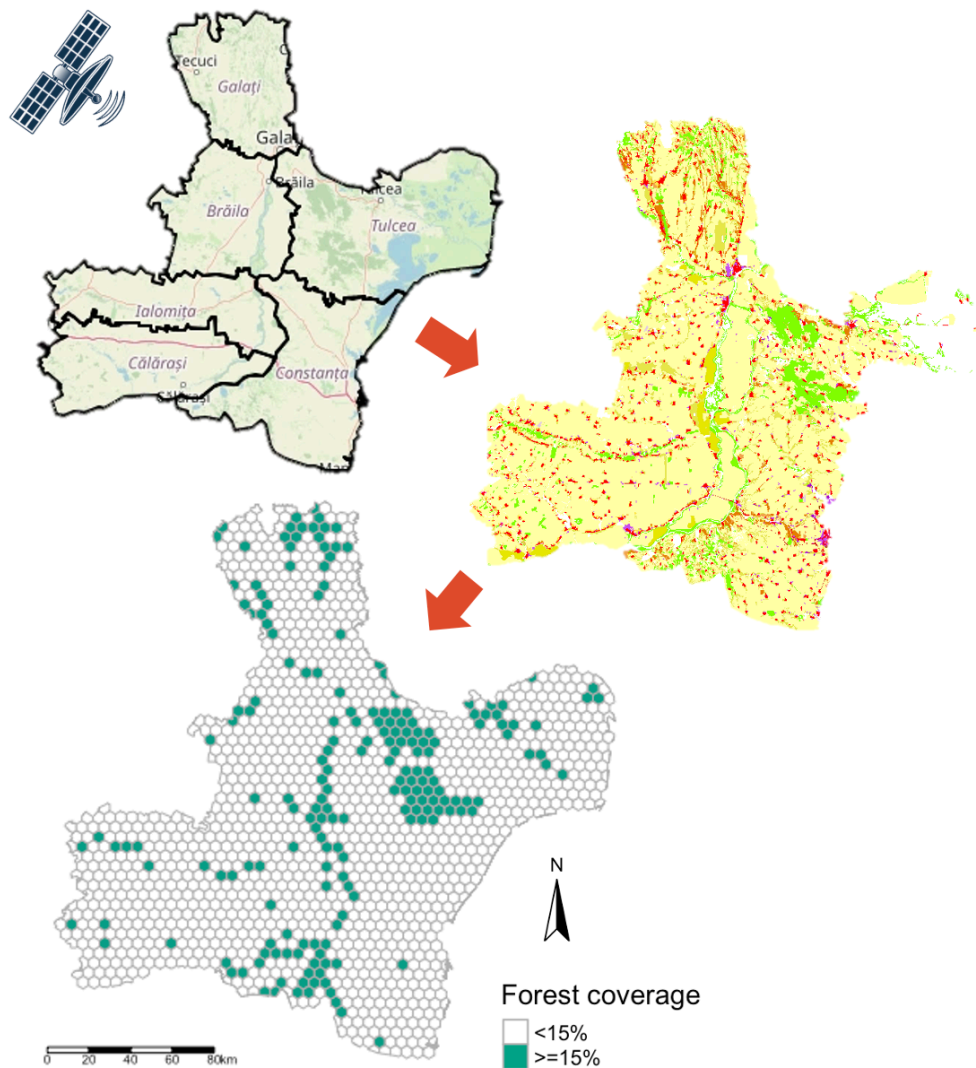




**Fig. 5.2** | Expanded map of southeastern counties in Romania. Expanded counties highlighted in tan, where initial epizootic spread was witnessed and our model is focused.

The abundance of wild boar herds was modelled via habitat suitability using a hexagonal raster of landscape coverage, as inspired by Vergne *et al.* (2016). CORINE Land Cover imagery (© European Union, Copernicus Land Monitoring Service 2021, European Environment Agency) was rasterized into 25 km<sup>2</sup> cells (n=1376), sized in accordance with estimated wild boar home ranges, and the percent of forest coverage was calculated per cell (Janoska *et al.*, 2018). Using results from wild boar distribution studies by Alexander *et al.* (2016) and the ENETWILD consortium (2019), a forest coverage threshold of 15% was selected to define suitable habitat for the cells, associated with a greater abundance of wild boar (Fig. 5.3).

Per Romanian regulation and in accordance with EU directives, following the detection of an infected pig, the affected herd is culled, movement restrictions of people, animals and products are enacted, and a 10 km surveillance zone is established around the culled herd which is kept in place for 4 weeks (ANSVSA, 2019; C. Mortasivu, personal communication, 2021). If no additional infectious units are



**Fig. 5.3** | Visualization of forest-coverage habitat-raster generation from CORINE landcover data.

detected during this period, the surveillance zone is then removed. While an industrial site will be culled in entirety, backyard farms within a village are considered individually and neighboring backyard herds to the infected herd are not automatically culled, allowing several backyard farms being reported successively over periods of several days or weeks.

### 5.2.2 Descriptive preliminary epizootic analysis

The epizootic was first analyzed spatially and temporally by host (domestic pig or wild boar) and domestic pig herd type (village or industrial site). Raw case data was spatially and temporally

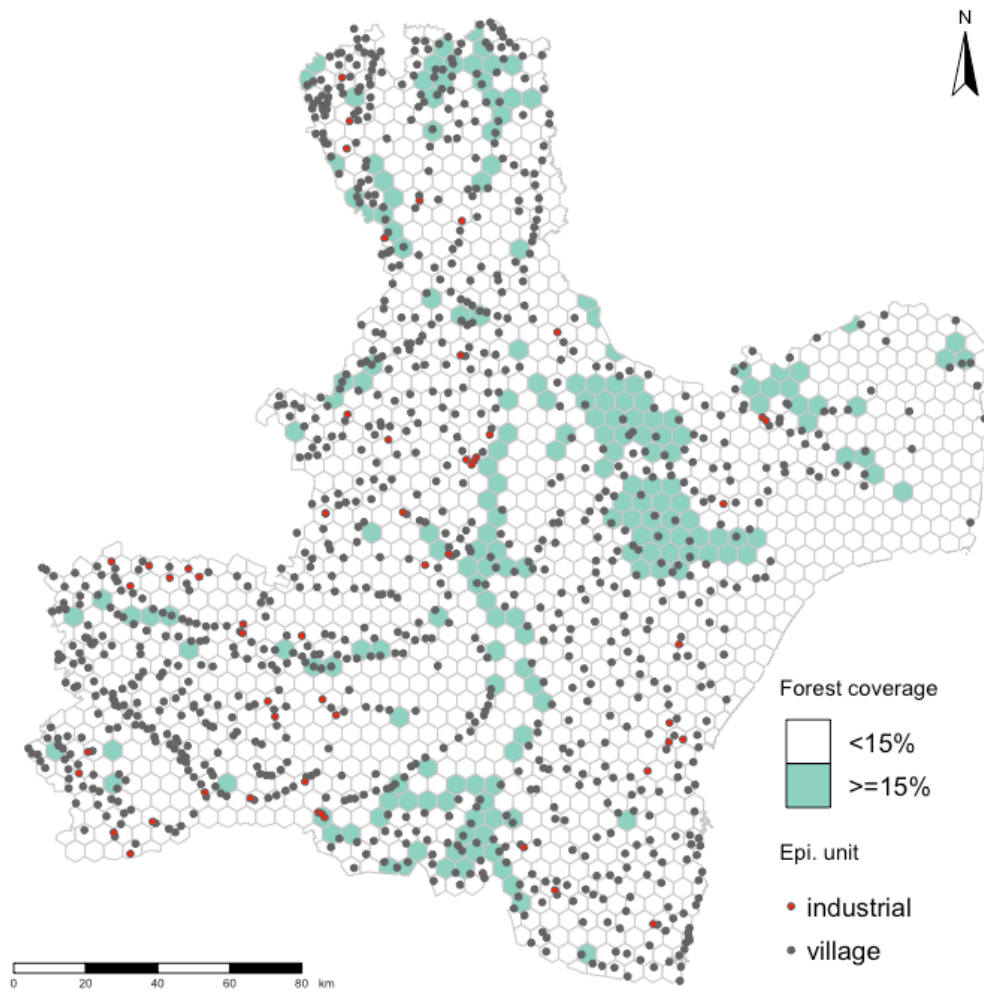
aggregated to reflect the epidemiological units (village, industrial farm, or habitat cell) and time scale (weekly) of the model. Temporally, cases were aggregated to the ISO-standard week. Based on expert opinion solicited from local veterinary officials, villages were defined as continuously infectious as long as successive outbreaks were declared less than two weeks apart. While the observed control strategies result in an internal diversity within the epidemiological unit of the village, this facet was addressed through considering the infectious status of a village en-masse from first to last case detection per outbreak. Epidemiological units were examined through frequency measurements to inform model development.

### 5.2.3 Model development

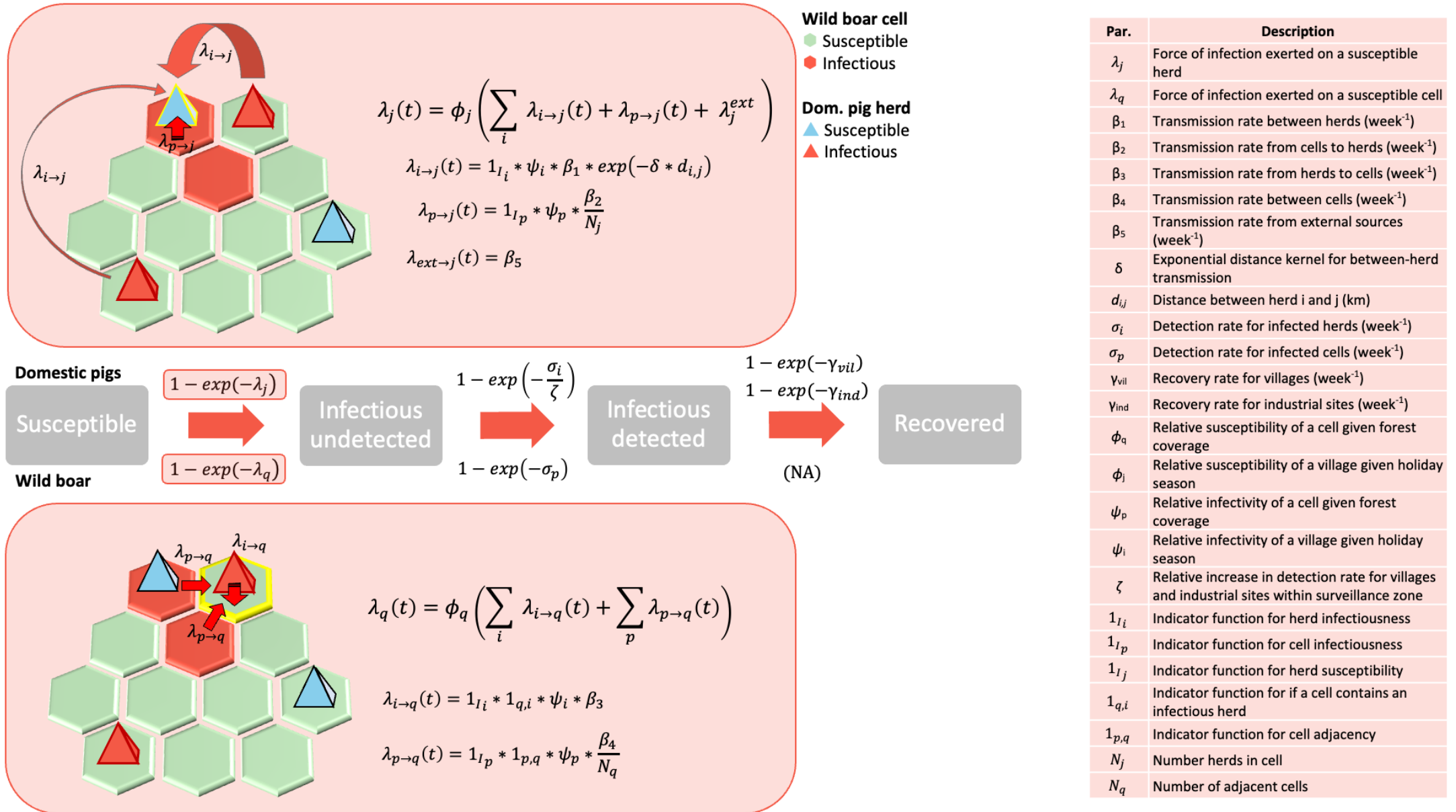
The domestic-wildlife interaction model is a hybrid model that was constructed through layering an individual-based model of domestic pig units over a cellular automata model of wild boar cells (represented via home ranges), and allowing for infection to occur both within and between layers (Fig. 5.4). The infection models consisted of combinations of four states for each epidemiological unit to transit through—susceptible (S), infectious undetected ( $I_u$ ), infectious detected ( $I_d$ ), and recovered (R) (Fig. 5.5).

Two models were tested for each component, leading to four model combinations. Villages and industrial sites were considered to either become perpetually recovered or, following a two-week refractory period, re-susceptible to infection. Wild boar cells were considered to either be continuously infectious until the end of the study period or able to become re-susceptible following their infectious period. When combined, this yielded models of  $S I_u I_d R$ - $S I_u I_d$ ,  $S I_u I_d R S$ - $S I_u I_d$ ,  $S I_u I_d R$ - $S I_u I_d S$ , and  $S I_u I_d R S$ - $S I_u I_d S$  state combinations. Infectious periods were calculated per county from observed data for each of the epidemiological unit classes. Model selection among infection state combinations was performed through calculating the mean squared error (MSE) of median weekly incidence and cumulative incidence for domestic pig units and for wild boar cells, respectively, for each model component.

To further inform transmission dynamics among wild boar cells, having assumed home range size, cell-to-cell transmission of both first-order and second-order adjacency was modelled. Long range wild boar dispersal beyond the assumed 25 km<sup>2</sup> home range can occur secondary to hunting pressure and has been observed to be up to a mean of 45 km from the origin (Casas-Díaz *et al.*, 2013; Jori, Massei, *et al.*, 2021). Following model selection among the four infection state combinations, one hundred simulations were performed with both first and second order adjacency transmission. Differences in



**Fig. 5.4** | Representation of modelled space. All three epidemiological units are displayed: village and industrial site point locations (as navy and red dots), and wild boar habitat cells (from a hexagonal raster) delineated by forest coverage percentage.



**Fig. 5.5** | Flow diagram of infection states for model units of the final selected model (SI<sub>u</sub>IdR-SI<sub>u</sub>Id). In each schematic representation, the unit experiencing the surrounding forces of infection is highlighted in yellow. State-transition formulae for domestic pig units and wild boar cells (above and below transition arrows, respectively) refer to the probabilities of transition per time step (in fraction of a week) and not rates.

modelled dynamics were determined through comparing posterior probabilities by calculating the 95% Highest Density Intervals (HDIs). This analysis was conducted through the BEST package in R (Kruschke & Meredith, 2021).

To be able to identify the contribution of the different transmission routes, four transmission rates, defined as the rates at which a susceptible agent acquires infection from an infected agent per unit time, were considered: from a herd (village or industrial) to another herd, from a cell to another cell, from a cell to a herd within the cell, from a herd to the cell that contains it. The transmission rates were fed into force of infection equations—the cumulation of individual infectious pressures exerted by all infectious individuals onto the susceptible individual—which were influenced from those derived by Andronico *et al.* (2019).

At time  $t$ , the force of infection experienced by a susceptible herd  $j$  located in cell  $p$ , was given as the sum of all forces of infection ( $\lambda$ ) exerted by infected herds  $i$  and cell  $p$ , plus an external force of infection to capture all other forces of infection not explicitly represented (including long-distance trade among the commercial network and reintroduction pressures from neighboring infected countries), modified by the relative susceptibility of the herd ( $\phi_j$ ), as illustrated in Eq. 1:

$$\lambda_j(t) = \phi_j * (\sum_i \lambda_{i \rightarrow j}(t) + \lambda_{p \rightarrow j}(t) + \lambda_{ext \rightarrow j}) \quad [1]$$

Relative susceptibility (as a proxy for biosecurity level) was dependent on farm type (equal to 1 for villages and  $\phi_{ind}$  (range 0 – 1) for industrial sites) and model time period (equal to 1 for villages prior to the holiday slaughter period that occurs in the last weeks of the year, and  $\phi_{vil}$  for villages during these final weeks).

Between-herd transmission was assumed to be density-dependent, with  $\lambda_{i \rightarrow j}$  of the form:

$$\lambda_{i \rightarrow j}(t) = 1_{I_i}(t) * \psi_i * \beta_1 * \exp(-\delta * d_{i,j}) \quad [2]$$

where  $\psi_i$  represents the relative infectivity of herd  $i$  dependent on farm type (equal to 1 for villages and  $\psi_{ind}$  (range 0 – 1) for industrial sites, assuming that industrial sites are less infectious than villages) and model time period (equal to 1 for villages prior to the last quarter, and  $\psi_{vil}$  for villages during the holiday slaughter period, assuming that infectiousness decreases during December when pigs are slaughtered for holiday consumption among families),  $\beta_1$  is the between-herd transmission rate,  $\delta$  is the transmission kernel parameter defining the exponentially-distributed effect of distance on the force of infection for between-herd transmission,  $d_{i,j}$  represents the Euclidian distance between herds  $i$  and  $j$ , and  $1_{I_i}$  is the indicator function equal to 1 if herd  $i$  is infectious at time  $t$  and 0 otherwise.

Transmission from infected cell  $p$  to susceptible herd  $j$  was assumed to be frequency-dependent, and took the form given in Eq. 3:

$$\lambda_{p \rightarrow j}(t) = 1_{I_p}(t) * \psi_p * \frac{\beta_2}{N_j} \quad [3]$$

where  $\psi_p$  is the relative infectivity of the cell (1 if equal or above the forest coverage threshold,  $\psi_{\text{cell}}$  otherwise, assuming that infectivity is decreased if there is inadequate habitat quality for wild boar),  $\beta_2$  is the cell-to-herd transmission rate,  $N_j$  is the number of herds within the infectious cell, and  $1_{I_p}$  is the indicator function equal to 1 if cell  $p$  is infectious at time and 0 otherwise.

All other sources of transmission that were not explicitly modelled were captured through a constant external force of infection parameter representing the mean of those forces. This parameter was given by Eq. 4:

$$\lambda_{\text{ext} \rightarrow j} = \beta_5 \quad [4]$$

And is equal to  $\beta_5$ , the transmission rate from external sources.

The force of infection experienced by a susceptible cell  $q$ , was given as the sum of all forces of infection exerted by infected herds located within that cell and by adjacent infected cells, modified by the relative susceptibility of the cell ( $\phi_q$ , assuming that the susceptibility of a cell decreases if there is inadequate forest coverage). Relative susceptibility of a cell was dependent on percent forest coverage of the cell (equal to 1 for cells with forest coverage equal or above the threshold of 15% and  $\phi_{\text{cell}}$  (range 0 – 1) for cells with inadequate forest coverage), and is illustrated in Eq. 5:

$$\lambda_q(t) = \phi_q (\sum_i \lambda_{i \rightarrow q}(t) + \sum_p \lambda_{p \rightarrow q}(t)) \quad [5]$$

where  $i$  represents infected herds located within cell  $q$  and  $p$  represents infected cells adjacent to cell  $q$ .

Transmission from an infected herd to a susceptible cell was assumed to be density-dependent, and took the form of Eq. 6:

$$\lambda_{i \rightarrow q}(t) = 1_{I_i}(t) * 1_{q,i} * \psi_i * \beta_3 \quad [6]$$

with indicator function  $1_{q,i}$  to indicate if cell  $q$  contains herd  $i$ , and  $\beta_3$  being the herd-to-cell transmission rate, and  $1_{I_i}$  being the indicator function defined as in Eq. 2. Lastly, transmission from an infected cell  $p$  to susceptible cell  $q$  was limited to second-order adjacency—meaning an infected

cell can infect either its immediate neighbors or the neighbors of its neighbors—was assumed to be frequency-dependent, and took the form in Eq. 7:

$$\lambda_{p \rightarrow q}(t) = 1_{I_p}(t) * 1_{p,q} * \psi_p * \frac{\beta_4}{N_q} \quad [7]$$

with the indicator function  $1_{p,q}$  to indicate adjacency, the cell-to-cell transmission rate  $\beta_4$ , and the number of adjacent cells  $N_q$ . The external force of infection was calculated the same as for herds. Models with first-order-only adjacency were also developed and assessed.

Transitions between states S-I<sub>v</sub>-I<sub>d</sub>-R were stochastically modelled, and based on a tau-leap algorithm (Keeling and Rohani, 2011). For the transition between susceptible and infectious states, each susceptible unit was potentially infected according to a Poisson distribution with the corresponding force of infection as the rate, defined as  $p_{inf} = 1 - \exp(-\lambda_j)$ . Through the assumption that the frequency of transitions occurring in a single time-step (set at 1/10<sup>th</sup> of a week in our model) follows a Poisson distribution, any events occurring during a shared time step are independent of one another and do not affect the rates of change (Keeling & Rohani, 2008). From there, the probability of no infection events occurring was able to be calculated to additionally obtain the probability of remaining susceptible, as a herd escaping from infection remains susceptible. Occurrence of and source of infection was then identified through stochastic selection among the possible sources while accounting for their relative contribution to the force of infection.

The probability of passive detection of infection (I<sub>v</sub>-I<sub>d</sub> state transition) was considered as an exponentially-distributed function of the detection rate  $\sigma$ , with a probability of detection at a given time step defined as  $p_{det} = 1 - \exp(-\sigma)$ . Among infected domestic pig units (both villages and industrial sites), the detection rate was modified by parameter  $\zeta$  ( $\zeta \in ]0,1[$ ), which was a multiplicative term to account for an increase of the detection rate within a surveillance zone at that time step.

Assuming that all infections among domestic pig units were eventually detected, the probability of recovery from infection for villages and industrial sites ( $p_{rec}$ ) was governed by the exponentially-distributed recovery rate gamma, defined as:  $p_{rec} = 1 - \exp(-\gamma)$ .

Simulations were initialized via the infection of two cells in Tulcea County several weeks (to be calibrated) prior to the first case detection in the epizootic data; these cells being the two cells which contained the first detected wild boar cases in Romania, as reported on 12 June and 16 June 2018.



#### 5.2.4 Parameterization

Of the 18 parameters in the model, seven were able to be fully or partially informed from available data in the literature: the weekly transmission rates between hosts  $\beta_1$ – $\beta_4$ , the exponential transmission kernel parameter for between-herd transmission  $\delta$ , and the weekly detection rates of infected herds  $\sigma_i$  and infected cells after the first detection  $\sigma_{p_{pre}}$  (Table 5.1). The transmission rate ranges were extrapolated from daily transmission probabilities (Lee *et al.*, 2021), contact rates (Shi *et al.*, 2020), or both (Taylor *et al.*, 2021). The detection rate was estimated at 1/3 weeks<sup>-1</sup> for domestic pig herds, based on results by (Guinat *et al.*, 2018). For cells, the detection rate was further partitioned into the pre-first detection and post-first detection rates, with the latter set to 1/8 weeks<sup>-1</sup> based on estimates for a large wild boar population from (Gervasi *et al.*, 2019), and the former according to the best fitting model that explained the observed data. The transmission kernel was informed through a model of the 1997-1998 classical swine fever epizootic in the Netherlands, where  $d_{50}$ —the distance at which the kernel is reduced by 50%—was assumed to be 1 km. Given the increased tenacity of ASF compared to CSF (Schulz *et al.*, 2017), a stronger transmission kernel was targeted for our model. Other ASF models (like Mur *et al.* (2018)) used a transmission kernel truncated at 2 km, however the mean nearest-neighbor distance in our model was 3.23 km (95% confidence interval 3.13–3.34), with only 23% of herds less than 2 km from each other. Using the mean nearest neighbor as a  $d_{50}$  target yielded a transmission kernel of approximately 0.214, which was further refined to 0.2.

Two parameters were elucidated from the observed data (the village and industrial site recovery rates  $\gamma_{vil}$  and  $\gamma_{ind}$ ), where the mean infectious periods that were calculated during preliminary epizootic analysis were used to parameterize the temporally-forced spatially-dependent recovery rates for villages and industrial sites.

#### 5.2.5 Model calibration and algorithmic model fitting methodologies

Parameter values were first informed by the experimental and observational data available in the oeuvre of ASF mathematical modelling. Calibration was then able to be performed on a reduced set of 13 parameters through iteration of potential parameter values.

Algorithmic parameter inference was then attempted through approximate Bayesian computation (ABC) standard rejection methodology (Toni *et al.*, 2009). Uniform distributions were used as prior distributions for the estimated model parameters. Summary statistics for rejection reflected the spatial and temporal distribution of detected outbreaks, using quarterly incidence per county for villages and industrial sites, and cumulative quarterly incidence per county for wild boar cells, for a

**Table 5.1** | Parameter values

Parameter	Description	Model value	Source value	Source
$\beta_1$	Transmission rate between herds (week <sup>-1</sup> )	To be estimated	0.007 – 2.1 <sup>a</sup>	Shi <i>et al.</i> (2020) vis-à-vis Ferreira <i>et al.</i> (2013)
$\beta_2$	Transmission rate from cells to herds (week <sup>-1</sup> )	To be estimated	0 – 0.312 <sup>a</sup>	Taylor <i>et al.</i> (2021) vis-à-vis Kukielka <i>et al.</i> (2013) and Pietschmann <i>et al.</i> (2015)
$\beta_3$	Transmission rate from herds to cells (week <sup>-1</sup> )	To be estimated	0 – 0.312 <sup>a</sup>	Taylor <i>et al.</i> (2021) vis-à-vis Kukielka <i>et al.</i> (2013) and Pietschmann <i>et al.</i> (2015), and then fit to model
$\beta_4$	Transmission rate between cells (week <sup>-1</sup> )	To be estimated	0 – 1.32 <sup>a</sup>	Taylor <i>et al.</i> (2021) vis-à-vis Kukielka <i>et al.</i> (2013) and Pietschmann <i>et al.</i> (2015)
$\beta_5$	Transmission rate from external sources (week <sup>-1</sup> )	To be estimated	-	According to best fit model from manual calibration
$\delta$	Exponential transmission kernel for between-herd transmission	0.2	0.69 <sup>b</sup>	EFSA Panel on Animal Health and Welfare (EFSA AHAW Panel) <i>et al.</i> , 2021 vis a vis Backer <i>et al.</i> (2009) <sup>c</sup>
$\sigma_i$	Detection rate for infected herds (week <sup>-1</sup> )	0.33	0.25 – 0.5 <sup>a</sup>	Guinat <i>et al.</i> (2018)
$\sigma_{p_{pre}}$	Detection rate for infected cells prior to first detection (week <sup>-1</sup> )	To be estimated	-	According to best fit model from manual calibration
$\sigma_{p_{post}}$	Detection rate for infected cells after first detection (week <sup>-1</sup> )	0.125	0.125 – 0.225 <sup>a</sup>	Gervasi <i>et al.</i> (2019)
$\gamma_{vil}$	Recovery rate for villages (week <sup>-1</sup> )	Mean: 0.599	-	Estimated from observed data
$\gamma_{ind}$	Recovery rate for industrial sites (week <sup>-1</sup> )	Mean: 0.784 Range: 0.5-1	-	Estimated from observed data

<sup>a</sup> translated into weekly rate

<sup>b</sup> estimated from source value given  $d_{50}$  (the distance at which transmission is reduced by 50%) is 1 km

<sup>c</sup> value for classical swine fever

total of 72 summary statistics. The sum of the absolute difference between the observed and the simulated sets of summary statistics was used for calculating the overall distance between a given simulation and the observed epizootic data. One hundred thousand (100,000) simulations were conducted, with the top 0.1% of the smallest distance conserved for inference.

Finally, parameter inference was performed through an ABC sequential Monte Carlo (ABC-SMC) variant—adaptive population Monte Carlo (APMC) (Lenormand *et al.*, 2012). Sequential ABC methods guide the selection of parameter values (particles) through the comparison of summary statistics that describe the observed and simulated data. APMC includes a weighted particle filtering methodology combined with an algorithm for auto-determining the rejection tolerance level after each generation of particle selection, to aid in convergence to the final parameter distributions. The same spatiotemporal summary statistics were used as from the simple rejection methodology for villages

and industrial sites, though for wild boar cells quarterly incidence per county was used in lieu of cumulative quarterly incidence per county.

Relying on non-informative priors, particles to comprise the initial parameter sets of the estimated model parameters were drawn from uniform distributions. Following a round of 1000 model simulations, weights were applied to each particle based on the resulting distance between simulated and observed summary statistics. The best-fitting fifty percent of particles were retained, and another 500 particles were computed. This process repeated itself until the proportion of newly generated particles that satisfied the preset final tolerance limit (set at 0.05) was reached. The tolerance level specifies the acceptable distance of a particle from the data, and through this algorithm a decreasing sequence of tolerance levels are used which directs particle sampling towards a high-likelihood parameter space, thus avoiding unnecessary time spent throughout the entire parameter field. At this limit, additional simulations would have limited effect on the final posterior distributions.

Data compilation, model implementation, and analysis were performed in R statistical software, version 4.1.3 “One Push-Up” (R Core Team, 2022).

### 5.3 Results

#### *5.3.1 Descriptive epizootic analysis*

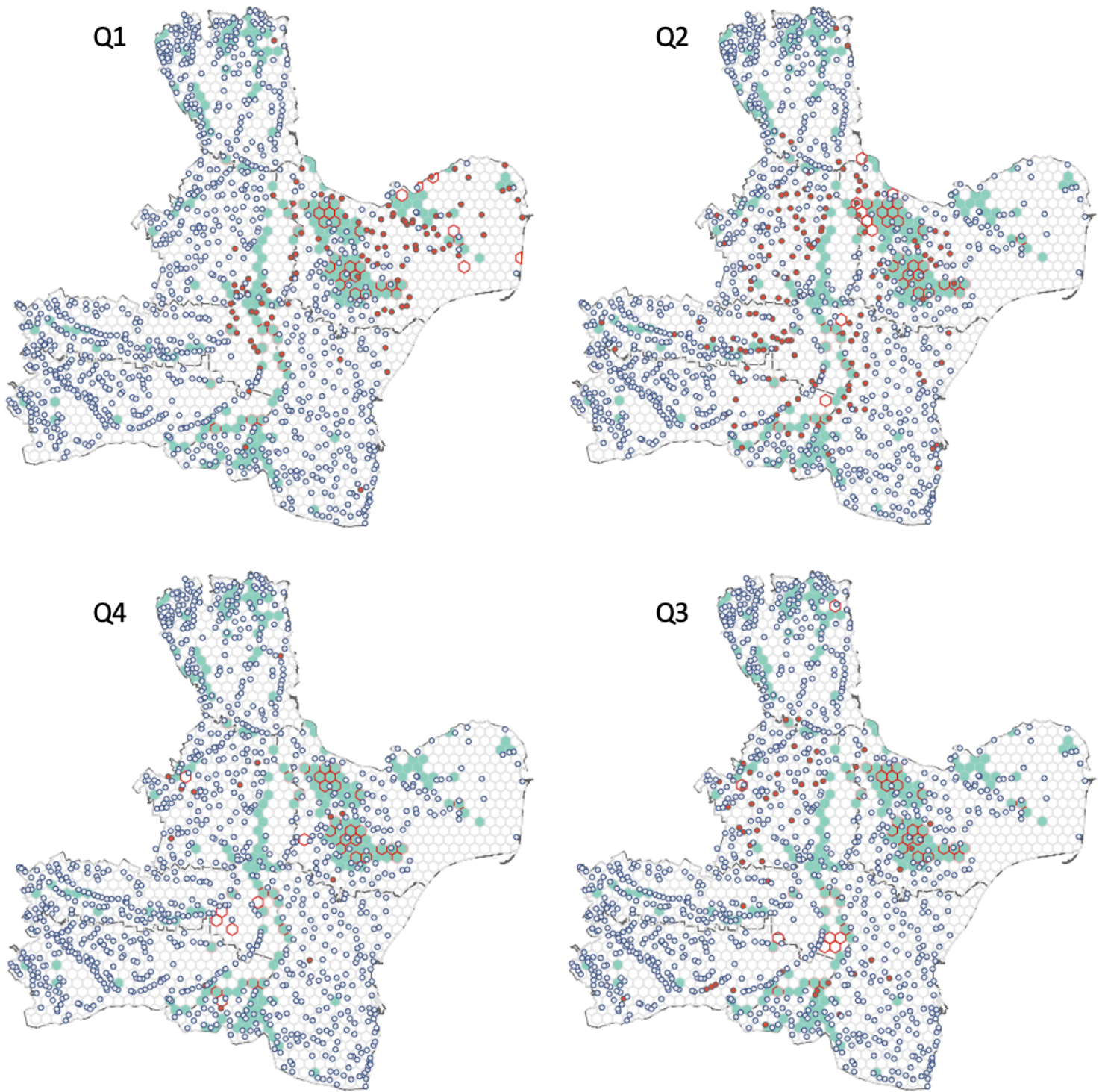
A total of 1128 cases were reported over the study period, distributed across the six counties. The vast majority of cases were seen among backyard farms in villages (n=1001), along with 17 cases among industrial sites and 110 among wild boar. These cases were aggregated epidemiological unit into 393 outbreaks. Two-hundred and sixty-six (266) villages (representing 27% of villages in the studied area) experienced outbreaks as did 15 industrial sites (27% of total number of industrial sites). Two industrial sites in Tulcea were classified as having two outbreaks (one and two weeks apart, respectively). These outbreaks likely belonged to two other small industrial sites or type-A holdings (that is, small scale producers with special trade allowances) that were not captured during the retrieval of site coordinates during model construction, but who exist in close proximity to the larger operations to whom the cases were algorithmically assigned. This misclassification is not expected to bias model outputs. Among wild boar, 109 out of 110 cases were identified on hunting grounds (with one case location not stated). Found carcasses comprised 63% (n=69) of wild boar cases, while 29% (n=32) were among wild boar killed during hunting (8% of cases did not provide a means of capture). Only 5% (n=65) of cells contained wild boar cases, with only 33% (n=36) of wild boar cases discovered

in cells with forest coverage above the 15% habitat threshold (Fig. 5.6). Note that these highly forested cells represent only 14% (n=197) of the cells of the study region.

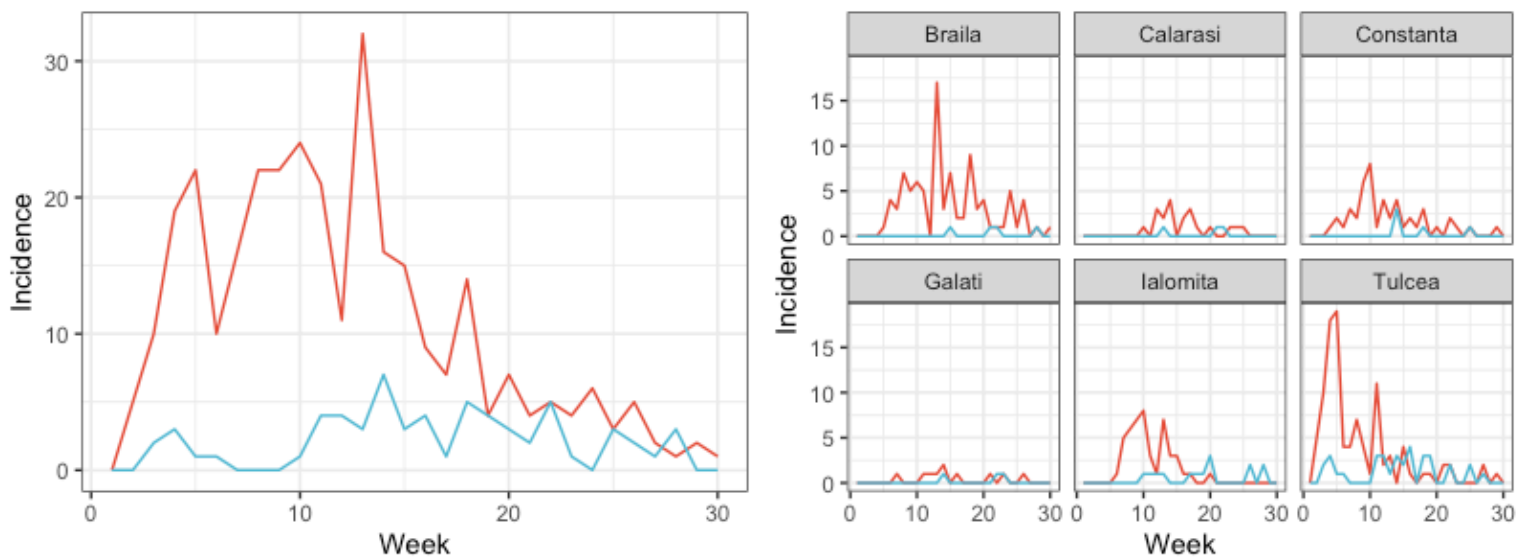
The observed epizootic curve exhibited an initial spike followed by gradual fade-out among infected villages, contrasting sharply to the paucity of cases detected among cells (Fig. 5.7). The average infectious period—calculated as the time in weeks between the first and last case in an outbreak, with an outbreak defined as a group of cases with less than two weeks between each case—varied temporally and, for villages, also by county, with a mean overall infectious period of 1.67 weeks. Partitioned quarterly, both villages and industrial sites experienced decreases in their infectious periods after the first quarter (Fig. 5.8). Villages experienced subsequent quarterly decreases, with variation evident between counties.

### 5.3.2 Model selection

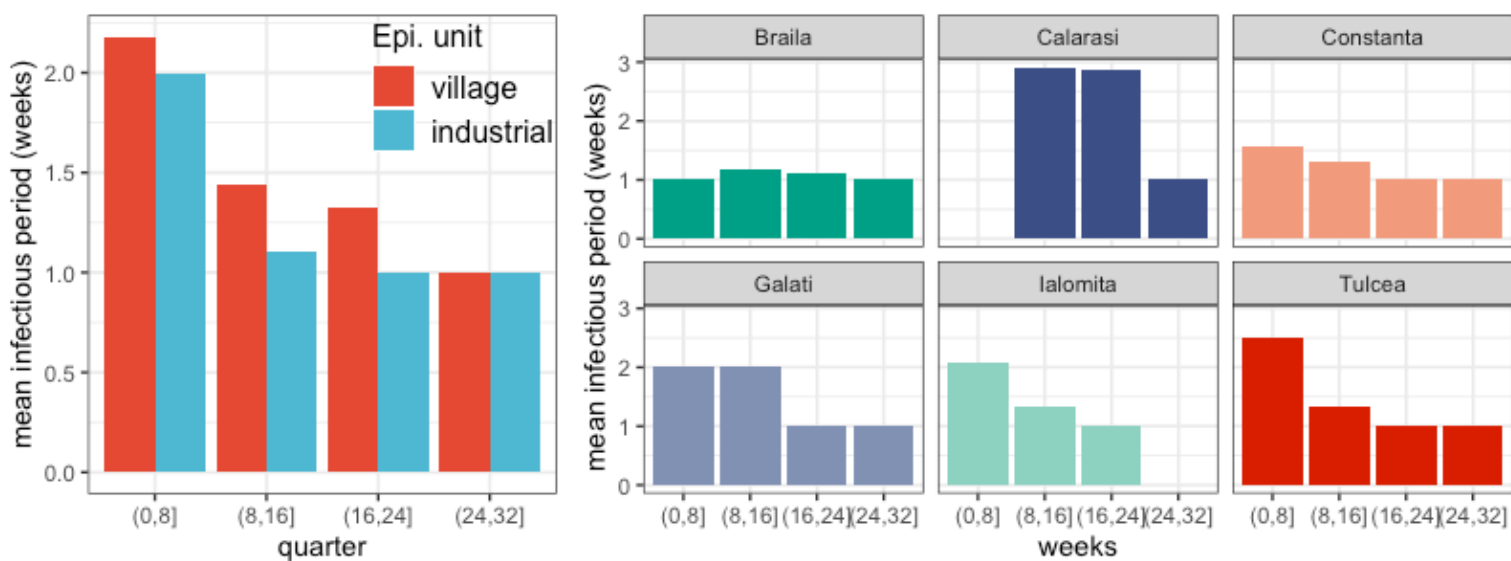
Two sets of infection states—with or without re-susceptibility—were considered for each host unit in model development. With domestic pig units experiencing either  $SI_{u|d}R$  or  $SI_{u|d}RS$  states and cells experiencing either  $SI_{u|d}$  or  $SI_{u|d}S$  states, the assessed model infection state combinations yielded  $SI_{u|d}R-SI_{u|d}$ ,  $SI_{u|d}R-SI_{u|d}S$ ,  $SI_{u|d}RS-SI_{u|d}$ , and  $SI_{u|d}RS-SI_{u|d}S$  models. Following parameterization of each model variant via ABC-SMC, the total MSE of the median weekly incidence for domestic pig units and median weekly cumulative incidence for wild boar cells was calculated (Fig. 5.9). The  $SI_{u|d}R-SI_{u|d}$  and  $SI_{u|d}RS-SI_{u|d}$  models (i.e. those without re-susceptibility among wild boar cells) had the lowest MSE (271.1 and 239.1, respectively). The goodness of fit for domestic pig units and wild boar cells were then examined independently. The  $SI_{u|d}R-SI_{u|d}$  model better approximated the observed data among domestic pigs, as a worse MSE was seen when reinfections were considered (47.3 for  $SI_{u|d}R$  compared to 70.84 for  $SI_{u|d}RS$ ). Reinfection events, having occurred in 40 (15%) of villages, were few and augmentation of the domestic pig model through considering reinfection was not supported by the data. The  $SI_{u|d}R-SI_{u|d}$  model was selected as the final model for further analysis.



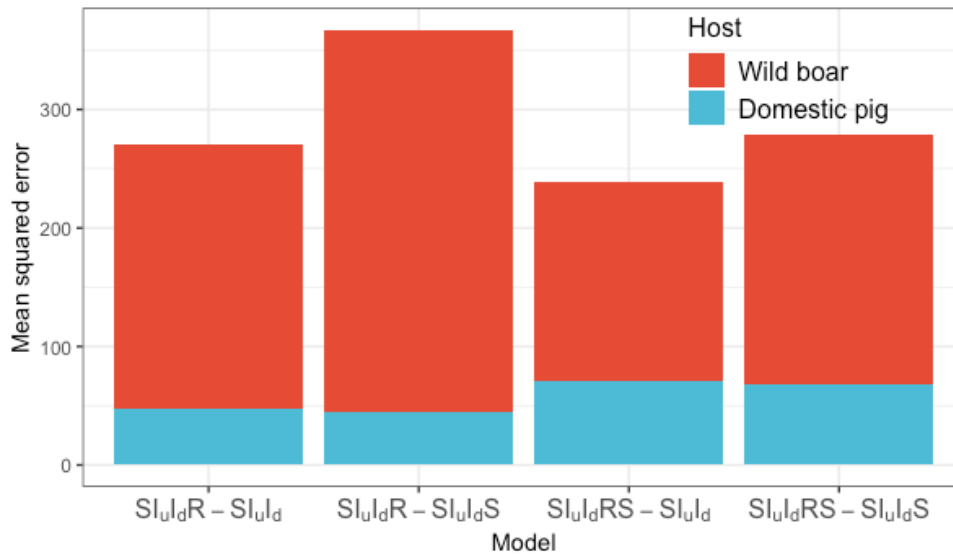
**Fig. 5.6** | Spatial visualization of quarterly distribution of observed cases. Cases shown for both villages and wild boar cells aggregated to 8-week periods. The distribution of infected villages (filled red dots) and infected wild boar cells (hexagons outlined in red) is visualized against the distribution of never-infected villages (blue circles) and cells with suitable habitat (forest coverage equal or above 15%, green-filled hexagons).



**Fig. 5.7** | ASF weekly incidence for June 2018 through December 2018. Incidence displayed both en-masse and faceted by county. Incidence refers to newly detected cases among domestic pig epidemiological units (villages and industrial sites) or wild boar cells.

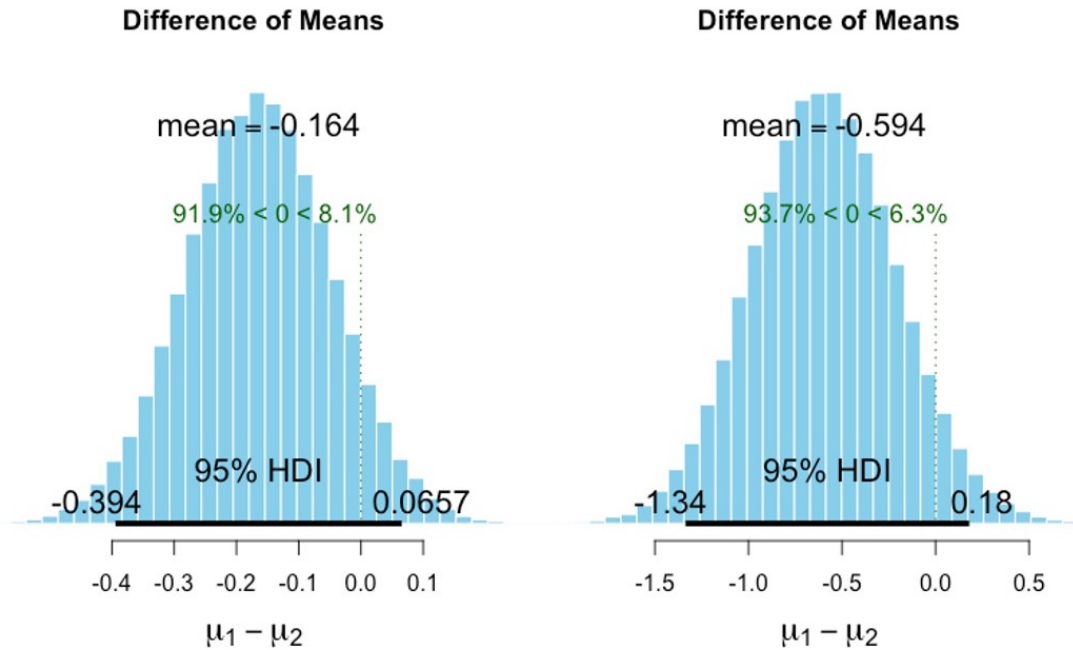


**Fig. 5.8** | Quarterly infectious periods by epidemiological unit. Mean infectious periods for villages and industrial sites are displayed en-aggregate (left). Mean infectious periods for villages were faceted by county (right).



**Fig. 5.9** | Mean squared error (MSE) for infection-state model variants. Median weekly incidence for domestic pig units and cumulative incidence for wild boar cells was used to calculate the MSE for all infection-state model variants. Two models were tested for each component, yielding four model combinations. Domestic pig units (villages and industrial sites) were modelled through either SI<sub>uId</sub>R or SI<sub>uId</sub>RS states, and wild boar cells were modeled with SI<sub>uId</sub> or SI<sub>uId</sub>S infection states.

The SI<sub>uId</sub>R-SI<sub>uId</sub> model was also evaluated with cell-to-cell transmission of both first-order and second-order adjacency, to see if such transmission assumptions affected the outcome. Both models produced nearly identical results, with differences in the mean weekly incidence of cells and villages of 0.164 and 0.594 cases, respectively (Fig. 5.10). With the observed posterior probabilities both including 0 within their 95% HDIs, the null hypothesis of a difference between means was rejected, indicating there is no significant difference between the effect of first-order and second-order cell-to-cell transmission adjacency. Thusly, to account for long-range dispersal, second-order adjacency was chosen as the preferred transmission method.



**Fig. 5.10** | Posterior probability comparison for models of first and second order adjacency transmission. Here the difference in mean weekly incidence of cells (left) and villages (right) between models using first-order adjacency and second-order adjacency transmission between cells. As the 95% HDIs (thick black lines) include 0, we cannot conclude that differences exist in weekly incidence among either cells or villages between the two models.

### 5.3.3 Model calibration and epizootic simulation

In addition to fine-tuning, model calibration was attempted through both ABC simple rejection as well as ABC-SMC methodology. As these automated methods have yet to be successful at finding the parameters, only the results from the manual fitting will be presented here.

Calibration focused on a reduced set of 13 parameters, consisting of the weekly transmission rates between hosts (including external sources)  $\beta_1 - \beta_5$ , the detection rate for infected cells prior to the first detection  $\sigma_{p_{pre}}$ , relative susceptibility  $\phi$  and infectivity  $\psi$  of epidemiologic unit subtypes (i.e. cells with or without adequate forest coverage, industrial site or village domestic pig units, and villages before or during the holiday slaughter period), and the relative increase in the detection rate for villages and industrial sites within a surveillance zone  $\zeta$  (Table 5.2).



Additionally, certain parameters were able to be excluded from the final model. When parameterization was performed through ABC-SMC methodology, though it was not successful at calibrating all parameters, the relative susceptibility and infectivity for industrial sites— $\phi_{ind}$  and  $\psi_{ind}$ —demonstrated minimal convergence, indicating a large plasticity in their possible values. This was not surprising given that only 5% of herds (55/1041) were industrial sites. It was concluded, based on the current data availability, that these parameters could not be accurately estimated and were thusly excluded from the model.

**Table 5.2** | Parameter calibration results. Values derived by either fine-tuning of literature-derived values, from the best fit model after manual calibration, or from tentative results from ABC-SMC calibration.

Parameter	Description	Model value	Source value	Source
$\beta_1$	Transmission rate between herds (week <sup>-1</sup> )	0.16	0.007 – 2.1 <sup>a</sup>	Shi <i>et al.</i> (2020) vis-à-vis Ferreira <i>et al.</i> (2013)
$\beta_2$	Transmission rate from cells to herds (week <sup>-1</sup> )	0.3	0 – 0.312 <sup>a</sup>	Taylor <i>et al.</i> (2021) vis-à-vis Kukielka <i>et al.</i> (2013) and Pietschmann <i>et al.</i> (2015)
$\beta_3$	Transmission rate from herds to cells (week <sup>-1</sup> )	0.8	0 – 0.312 <sup>a</sup>	Taylor <i>et al.</i> (2021) vis-à-vis Kukielka <i>et al.</i> (2013) and Pietschmann <i>et al.</i> (2015), and then fit to model
$\beta_4$	Transmission rate between cells (week <sup>-1</sup> )	0.4	0 – 1.32 <sup>a</sup>	Taylor <i>et al.</i> (2021) vis-à-vis Kukielka <i>et al.</i> (2013) and Pietschmann <i>et al.</i> (2015)
$\beta_5$	Transmission rate from external sources (week <sup>-1</sup> )	0.0001	-	According to best fit model from manual calibration
$\sigma_{p_{pre}}$	Detection rate for infected cells prior to first detection (week <sup>-1</sup> )	0.067	-	According to best fit model from manual calibration
$\varphi_{cell}$	Relative susceptibility of cells given forest coverage	0.1	-	According to best fit model from manual calibration
$\varphi_{ind}$	Relative susceptibility of industrial sites	1	-	According to tentative ABC-SMC calibration
$\varphi_{vil}$	Relative susceptibility of villages given holiday season	0.05	-	According to best fit model from manual calibration
$\psi_{cell}$	Relative infectivity of cells given forest coverage	0.1	-	According to best fit model from manual calibration
$\psi_{ind}$	Relative infectivity of industrial sites	1	-	According to best fit model from ABC-SMC calibration
$\psi_{vil}$	Relative infectivity of villages given holiday season	0.05	-	According to best fit model from manual calibration
$\zeta$	Relative increase in detection rate for villages and industrial sites within surveillance zone	0.5	-	Assumed

<sup>a</sup> translated into weekly rate

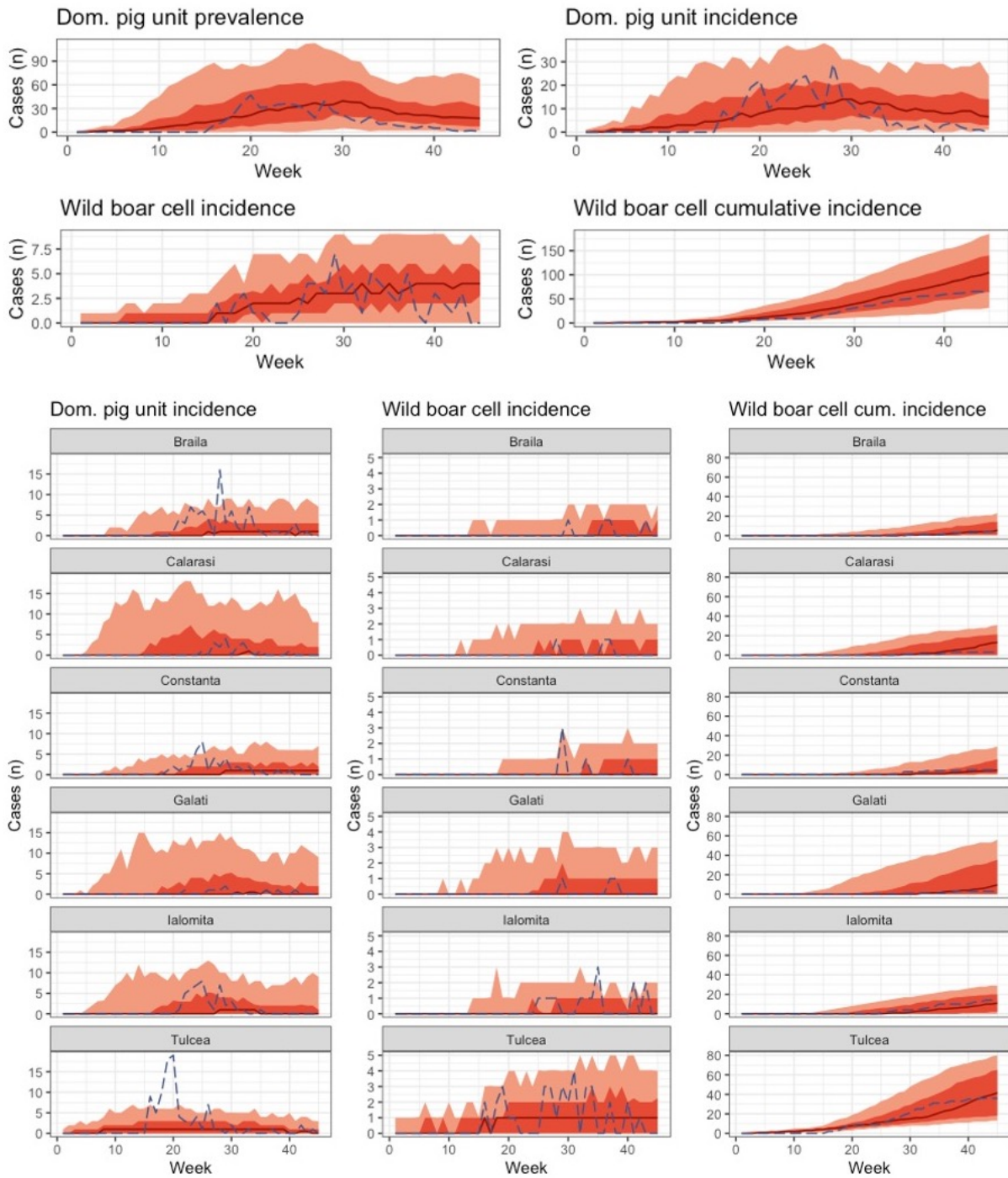
Following parameterization, the observed epizootic trajectory—both prevalence and incidence—was able to be captured spatially and temporally when evaluated over the entire study area (Fig. 5.11). When faceted by county, spatial differences became apparent (Fig. 5.11). In some counties the simulations did not fully capture the weekly variation in incidence. This was most pronounced among villages in Braila and Tulcea counties, and among wild boar in Ialomita County, with observed case spikes being (slightly) outside the predicted 90% credible interval ranges. Given the relatively small size of the detected epizootic among wild boar, it was not unexpected that the spike in detected cases in the observed data in one of six counties (Ialomita) was not captured. As wild boar cells were considered persistently infectious in the model, their cumulative incidence was considered a better measure. When viewed by cumulative incidence, the incongruence in weekly wild boar incidence was lost and the model again succeeded in its epizootic representation, both en-masse and by county.

#### *5.3.4 Elucidating host contribution to epizootic propagation*

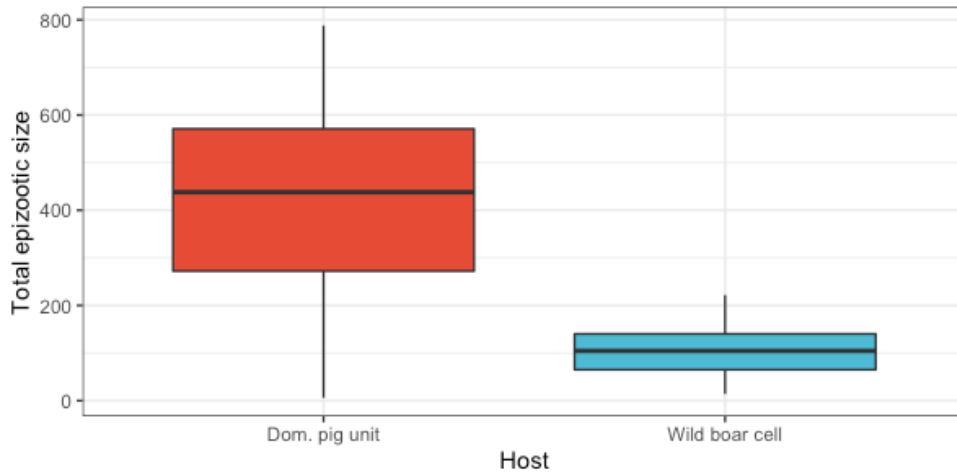
Using the fitted model that captured the observed epizootic trajectory, the contribution of different epidemiological units was able to be elucidated. Overall, a median of 441 domestic pig units (416 villages and 25 industrial sites) were infected per simulation, along with 104 wild boar cells (Fig. 5.12).

Among domestic pig units, a median of 94% of infections (95% credible interval: 75.6–96.3%) came from other pig herds while 5.17% (95% credible interval: 2.88–20.6%) came from wild boar (Fig. 5.13). Conversely, among wild boar cells, 57.8% of infections (95% credible interval: 38.5–86.8%) came from other wild boar cells while 40.9% (95% credible interval: 9.48–59.6%) came from domestic pig units. The external force of infection, representing the mean of all additional forces of infection not otherwise captured, accounted for very few infections across all simulations for both domestic pig units (0.817%, 95% credible interval 0.0761–3.47%) and wild boar cells (0.964%, 95% credible interval 0–5.83). Given the sizes of the simulated epizootics, this translates to, at most, 16 infections among domestic pig units and six infections among cells.

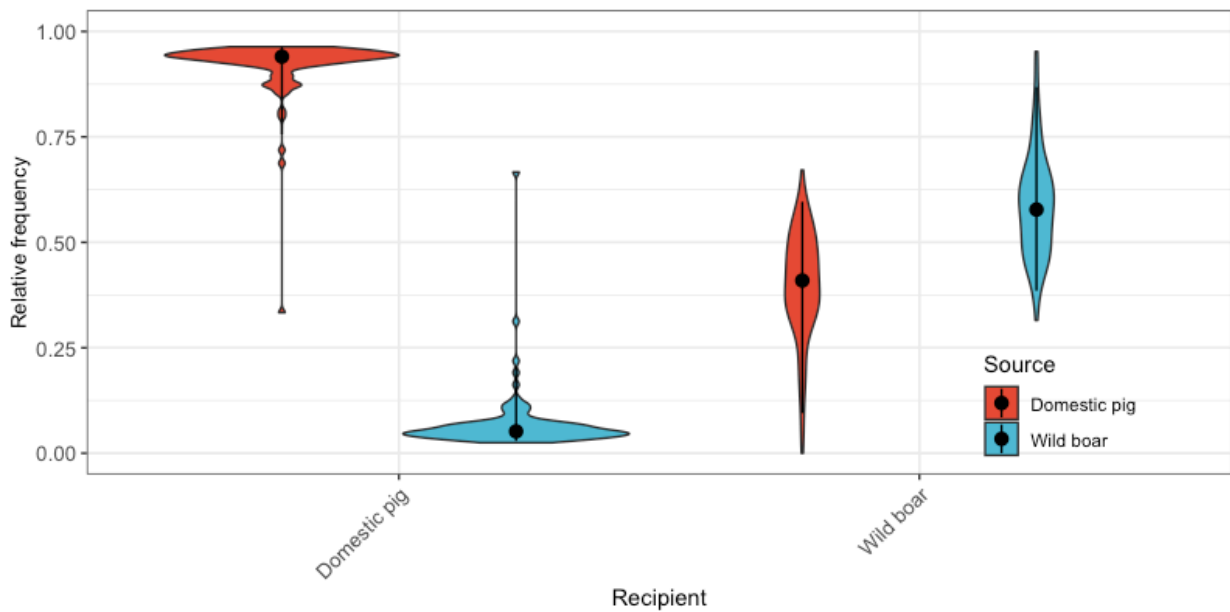
In the observed data, almost all detected wild boar cases were either in or immediately adjacent to forested cells. Similar patterns were observed when the simulated data was examined spatially, with herds experiencing higher proportions of infections when either in or adjacent to cells with sufficient forest coverage (Fig. 5.14(a)). Similarly, the infected cells are almost exclusively those with sufficient forest coverage, with only a few frequently infected cells in Calarasi County below the habitat threshold (Fig. 5.14(b)). The increased density of villages that can be seen in the southwestern and northern-most counties certainly also contributes to the increased frequency of infections experienced by those herds.



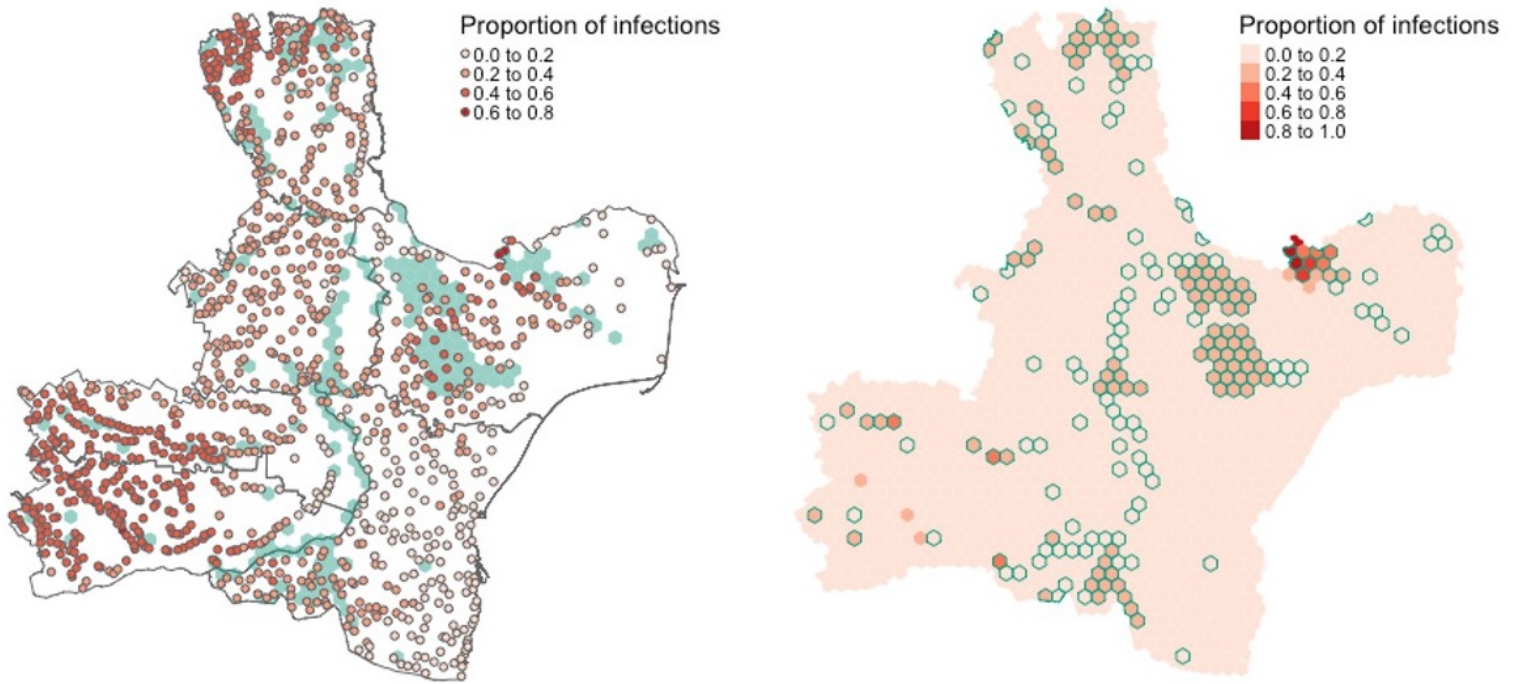
**Fig. 5.11** | Epidemiologic frequency trajectories of simulated epizootics. Trajectories shown for both domestic pig units and wild boar cells overall (top plots) and faceted by county (bottom vertical plots). The pale red ribbon indicates the 90% credible interval—that is, a 90% probability the true epizootic estimate lies within this region—while the red ribbon indicates the 50% credible interval, the dark red line the simulated median, and the dashed navy line the observed data.



**Fig. 5.12** | Epizootic sizes across simulations by host. Median, interquartile range (IQR), maximum and minimum values are reported over 100 simulations. Median case counts for domestic pig units were 438 (IQR: 272; 571) and for cells 104 (IQR: 65; 140).



**Fig. 5.13** | Relative contribution of domestic pig units and wild boar cells to epizootic propagation. Results shown for each host in the manually calibrated  $SI_{u,d}R-SI_{u,d}$  model over 100 simulations. For each recipient (as indicated on the x-axis), the y-axis indicates the relative frequency for the given source of infection, with the width of the violin plot demonstrating the frequency of the value. The black dot inside the violin plots indicates median value with the bar indicating the 95% credible interval. For domestic pig units, a median of 94% (95% CI 75.6–96.3) of infections can from other domestic pig herds, while 5.17% (95% CI 2.88–20.6%) came from wild boar cells. Among wild boar cells, 40.9% (95% CI 9.48–59.6%) of infections came from pig units, while 57.8% (95% CI 38.5–86.8%) came from other cells.



**Fig. 5.14** | Spatial visualization of proportion of infections per unit. Proportions given for results across 100 simulations in the  $SI_{Ud}R-SI_{Ud}$  model for (a) domestic pig units and (b) wild boar cells. Green patches (a) and green hexagon outlines (b) represent sufficiently forested areas. Herds and cells are shaded on a red scale based on the proportion of infections experienced by the unit across the simulations.

#### 5.4 Discussion

A mechanistic model of ASFV transmission that simulates transmission both within and between domestic pig and wild boar hosts was constructed and parameterized using data from an on-going epizootic. Our analysis focused on the initial 30 weeks of the epizootic, a period where the initialization and subsequent augmentation of control strategies led to non-uniform application of control measures both temporally over the study period and spatially between counties. These differences were accounted for in the modeled transmission dynamics, and to do so our model included both spatial-dependence (by county) and seasonal-forcing (by quarterly period) of infectious period parameters in an attempt to reflect the varied and changing control pressures. The final result was a model where the general trends observed in the epizootic period were able to be captured through stochastic simulation.

Our model was created through combining an individual-based model of domestic pig units and a cellular automata model for wild boar habitat. Independently, similar models had been successfully used to investigate single-host epizootic dynamics for ASF among domestic pig units in Sardinia, Denmark, and France (Andraud *et al.*, 2019; Halasa, Bøtner, *et al.*, 2016a, 2016b; Mur *et al.*, 2018), as well as at the domestic-wildlife interface for bTB among cattle and badgers in the UK (Birch *et al.*, 2018), and cellular automata models succeeded in representing wild species to investigate host dynamics between cattle and wildlife for FMD (Doran & Laffan, 2005; Laffan *et al.*, 2011; M. P. Ward *et al.*, 2011). Through overlaying these two model types and considering separate transmission rate parameters to govern ASFV transmission between model layers, a multihost model was able to be constructed.

In our cellular automata model, habitat suitability was used a proxy variable for wild boar presence. Habitat suitability models, where the suitability of a location is based on observed environmental relationships, are already extensively used in the field of ecology (Guisan *et al.*, 2017; Rowden *et al.*, 2017). They are, however, not without a few key assumptions: that the species-environment relationship is already at equilibrium, and the data of the environmental variable being used is at an appropriate resolution to capture the species' niche (Guisan *et al.*, 2017). In the ecological context, these models are used for environmental protection, resource management, conservation planning, and invasive species management, where the species ecology is a fundamental focus of the research (Naqibzadeh *et al.*, 2021; Song *et al.*, 2013). In contrast to current epidemiological models—that mostly focus on but a single habitat layer like forest or agricultural coverage—ecological models tend to use advanced methods to merge multiple layers as friction models. Additionally, temporal changes in individual landscape variables, as is the case with seasonal land-use in agriculture or forestry exploitation on forest distributions, are important considerations in species representation. As was the case with ASF, recent research revealed that artificial landscape fragmentation was efficient at slowing the spread of ASF among wild boar (Salazar *et al.*, 2022). Future ASF models at the domestic-wildlife interface may want to consider these more advanced ecological models for accurately representing wildlife hosts—especially across seasons and at larger time scales than our model—however the additional costs in complexity and computing time would have to be accounted for.

#### 5.4.1 Model selection

In our final model we assumed that both villages and industrial sites were able to become fully recovered and not experience reinfection. Though reinfections (defined as outbreaks more than 2 weeks apart within the same village) were documented in 15% of villages, both models that

considered this additional route of transmission ( $SI_{u,d}RS-SI_{u,d}$  and  $SI_{u,d}RS-SI_{u,d}S$ ) did not fit the observed data well.

As our model did not include internal infection dynamics within each village, many of the nuances that would contribute to reinfection—including the neighbors of ASF-infected farms slaughtering and storing their pigs prior to investigation to avoid culling of their herds (as reported by local investigators), as well as the continued practice of swill feeding (Boklund *et al.*, 2020)—were likely unable to be captured through a single village-wide parameter to account for this force of infection. Conversely, the limited duration of the study period also is likely to have precluded full capture of suspected reinfection events. Though the absence of a reinfection mechanism is not representative of the observed data, the overall significance of this assumption was considered low given the low percentage of villages affected by this class of transmission.

In contrast, wild boar cells were assumed to remain perpetually infectious once infected. Recent research has shown environmental eradication to be highly improbable unless more than 50% of all infectious carcasses are discovered (Gervasi & Guberti, 2022). As wild boar surveillance was imperfect during this initial epizootic period, it is unlikely that more than half of all infectious carcasses were discovered. This is commensurate with the results of model selection, where the lowest MSE values were among the models that considered perpetual environmental contamination.

#### 5.4.2 Parameter estimation

Model parameterization was based on literature, when values were available, or through calibration from observed epizootic data. Transmission rates were disentangled depending on the source and recipient hosts. This allowed us to quantify explicitly the relative contribution of each epidemiological unit. The weekly transmission rates differed for each type of transmission, with herd-to-herd transmission having the lowest transmission rate ( $\beta_1 = 0.16 \text{ week}^{-1}$ ), followed by herd-to-cell transmission ( $\beta_2 = 0.3 \text{ week}^{-1}$ ) and cell-to-cell transmission ( $\beta_3 = 0.4 \text{ week}^{-1}$ ), and lastly cell-to-herd transmission with the highest rate ( $\beta_4 = 0.8 \text{ week}^{-1}$ ). The variation in these parameters indicates the differences in influence on epizootic propagation of each type of transmission, with similar rates of transmission to susceptible wild boar cells from both domestic pig units and other wild boar cells. However, as the observed number of wild boar cases to which the model was fitted is very likely an underestimation of the true case count (with the true wild boar case count likely being even greater than that of domestic pigs), the estimated transmission rates fitted to imperfect surveillance data may be biased. Examining additional time periods of the Romanian epizootic, after the initial phase in 2018

and when consistent surveillance efforts were established, could help to further clarify estimated transmission rates.

The fitted values for two parameters—the weekly transmission rate from herds to cells, and the transmission kernel—were tuned through manual iteration using the values published in the literature as a starting reference. Given the difference of scale between the model of Taylor *et al.* (2021) and our own model (the former using grid cells of 100 km<sup>2</sup> compared to our 25 km<sup>2</sup>), it is not unexpected that our rate for a smaller area would differ, in this case being lower than their estimated rate. Additionally, the transmission rates between herds and cells, from Taylor *et al.* (2021), were based on a study of contact of wild boar with free-roaming farms in Spain, which may not be representative of the contact rate between Romanian backyard herds and wild boar in Romania (Kukielka *et al.*, 2013).

Our choice of transmission kernel purposely excludes long distance transmission, here defined as transmission over 20 km. While other ASF mechanistic models used transmission kernels that assumed maximum local transmission distances of 2 km (Andraud *et al.*, 2019; Halasa, Bøtner, *et al.*, 2016a, 2016b; Ivorra *et al.*, 2014; Mur *et al.*, 2018), these models accounted for non-local transmission through network movements—and in the cases of Andraud *et al.* (2019), and Halasa, Bøtner, *et al.* (2016a, 2016b) were also tailored to industrialized populations. Without considering industrial networks, and to capture non-reported pig movements between villages which principally occur at a small scale, our maximum distance and associated kernel were adjusted accordingly. While our assumptions may be realistic regarding local spread between villages, this is unlikely the case among industrial sites where transport distances of pigs can be many times greater. However, industrial sites are limited in number in our area of geographic interest and are principally large integrative herds that may play only a minor role in transmission to backyard herds, infection transmission among the transit network is not being modelled, and the external force of infection exists to capture these long-distance jumps in transmission that are otherwise extremely difficult to model mechanistically in the absence of movement records.

As the final parameters for the model were tuned manually, they were dependent on the assumptions for other parameters that were not able to be deduced from the literature or observed data. The effects of these parameters, modifying relative infectivity and susceptibility for the influence of forest coverage on wild boar habitat and for the holiday slaughter season on villages, were influential on both model fit and relative host transmission. The final values for the influence of forest coverage on transmission were 10%, indicating habitat-poor cells would have to be 90% less susceptible and infective than cells with adequate forest coverage to explain the observed dynamics from the chosen parameters. Additionally, the final values for the relative infectivity and susceptibility during the



holiday slaughter season—to account for decreases in the overall domestic pig population from the mass cull along with changes in trade and sales—were estimated at 5%. A 95% decrease in infectivity and susceptibility is a massive dynamic change, however it was also the level of change in transmission needed to facilitate extinguishing the epizootic in the simulations. Local customs play heavily into the ASF scenario being modelled, and the winter holiday slaughtering of pigs likely acted as a strong external influence on ASF infection and propagation at the village level (C. Mortasivu, personal communication, 2021). Indeed, half of the total annual slaughter of pigs in the country occurs in the month of December (Bergevoet *et al.*, 2020). Research into the social dynamics around pig farming during this time period would help to further clarify the accuracy of this fitted value. Further, our model was focused leading up to this time period but not proceeding beyond as the transmission dynamics will have inevitably changed following such a mass culling. As the subsequent epizootic wave in 2019 was initiated at a similar period, it's possible that this temporal consistency is associated with this annual social dynamic, though further investigation is required to confirm this hypothesis.

The inability of the algorithmic parameter estimation methods (rejection ABC and ABC-SMC) to find the model parameters is likely a result of the high-dimensionality of the parameter set. Though multiple levels of rejection tolerance were explored along with variations in the resolution of the summary statistics (including at one point trying 810 summary statistics to capture weekly incidence per county per epidemiological unit), the observed epizootic trajectory was not able to be replicated via these methods. This was not unexpected given the complexity of our model, and additional methods of algorithmic model fitting will continue to be explored. Obtaining model parameters through an algorithmic method, which can then be compared to our present parameters, will be beneficial for further informing the robustness of our representation of the explored Romanian ASF epizootic as well as contribute to the greater parameterization of ASF dynamics.

#### *5.4.3 Relative host contribution*

Figure 5.13 demonstrates the median frequency and 95% credible intervals of transmission sources for domestic pig units and wild boar cells. The majority of domestic pig herd infections came from other nearby herds, but a median of 5% (95% credible interval 2.88–20.6) of domestic pig herd infections were shown to be due to wild boar. Among wild boar, between compartment transmission was much more pronounced. Though again the majority of infections came from transmission from nearby cells as would be expected, roughly 40% of infections came from domestic pig units. Such

transmission is accordant with previous understandings of ASF epidemiology<sup>1</sup> that transmission from infected domestic pig units is essential for maintaining circulation within the wild boar population (Jori & Bastos, 2009). Granted, the dynamics seen with the current genotype II epizootic reveal the ability of the virus to persist environmentally without repeated re-introduction events (FAO, 2019), previous observations (in Sardinia and Spain with genotype I) indicated that ASFV dissipates from wild boar hosts without continual reinfection from domestic pigs (Laddomada *et al.*, 1994). Frequent transmission from the domestic compartment would then be expected to maintain such wild circulation, as is seen in our model. Further, these relative numbers could reflect the limited capacity of habitat-poor cells to host infection, as roughly half (53%,  $n = 708$ ) of the 1347 cells contained domestic pig units, and of those only 104 also had adequate forest coverage.

Low-density enzooticity and ASFV propagation has been observed and attributed to combinations of ASFV environmental stability, carcass-mediated transmission, and wild boar behavior, though viral shedding from persistently-infectious survivors has also been proposed (Gervasi & Guberti, 2021). When ASF enters the local wild boar population, a large and rapid decrease in population (approximately 85% of all individuals) is first observed (Morelle *et al.*, 2020). Following this population crash ASF can become enzootic with a low prevalence—as currently is seen in northern Europe—and continue to be transmitted through direct and carcass-based transmission (Gervasi & Guberti, 2022). A similar population crash could be expected with the introduction of ASFV into the wild boar-dense regions of Romania, which would then require frequent transmission from domestic pig herds to result in the observed dissemination of cases in our area of study. Underreporting among wild boar cases is a known limitation of the surveillance efforts during the six-month period of our investigation, however, and further informed surveillance will allow a greater understanding of wild boar case distribution and spatial correlations.

Spatial distribution of wild boar cases was congruent between the observed data and simulations, with wild boar cells experiencing higher proportions of infections when either in or adjacent to cells with sufficient forest coverage. However, disparities between which villages were infected in the simulations compared to those infected in the observed data were observed, especially towards the northern and southwestern periphery of our study area. The use of a uniform transmission kernel across the region despite differences in village density between counties is suspected to play a role, as the villages infected in these areas appear to be much more tightly clustered than in other regions.

---

<sup>1</sup> A term coined by the United States Geological Survey in 2002 to describe the identification of the environmental factors that affect the disease status of living organisms (Bizouarn, 2016; Susser & Susser, 1996; United States Geological Survey (USGS), 2002)).

This discrepancy will need to be explored in future iterations of this work. Further, future models should consider including an additional habitat type of forested-adjacent cells, and then investigate the forest coverage that optimally captures detected cases (minimising false positives and maximising true negatives).

Putting our results in perspective, another recent model out of the Republic of Korea that examined their 2019 outbreak had shown that six of the 14 farms infected with ASF had roughly a 60% risk of the main source of infection being wild boar (yielding a frequency of infection for between-host transmission of 0.26) (Yoo *et al.*, 2021). Though our estimated between-host transmission is less than theirs, the low relative susceptibility and infectivity of unsuitable habitat cells from our assumed model parameters strongly biases the ability of these units to infect and become infected. Accordingly, this limits the interpretation of the modelled relative contribution of domestic pigs and wild boar to epizootic propagation for each host, and the contributions of wild boar to epizootic propagation should be viewed as a minimum value in each compartment (as any increase in habitat suitability will only further increase the observed transmission).

A limitation of this study is the inability to—so far—parameterize our model algorithmically. Though multiple ABC methods were attempted, the high dimensionality of the parameter set precluded the elucidation of the internal model parameters. Continued exploration of available fitting strategies will provide further insight into pathways to overcome the current methodological hurdle.

Though our model has its limitations, these are not gaps in the greater ASF modelling field. Our model does not account for individual wild boar dynamics, but modelling these dynamics is computationally expensive, and we want our model to be able to be used for policy support in real time. Further, these dynamics have already been thoroughly investigated (Lange *et al.*, 2018; Lange & Thulke, 2015, 2017; Salazar *et al.*, 2022; Thulke & Lange, 2017). Neither does our model mechanistically model long-distance transmission among wild boar. Though we assumed second-order neighbour transmission, it has been shown that ASF transmission among wild boar to adjacent habitats rapidly decreases with distance (Han *et al.*, 2022). Further investigation into wild boar ecology in the study region will help to reduce the assumptions in home range size and transmission distance. Lastly, our model does not consider transmission along commercial transit network. This type of transmission was already assessed for nations with highly-industrialized swine operations—revealing that such network transmission would be limited with any incursion rapidly controlled—though obtaining such network data for Romania would prove extremely informative (Andraud *et al.*, 2021; Halasa, Bøtner, *et al.*, 2016a, 2016b; Halasa *et al.*, 2018).

## 5.5 Conclusions

Here we developed a mechanistic model of ASF that is able to disentangle sources of transmission, allows for the assessment of observed epizootic dynamics, and will be able to be used to explore alternative control strategies (i.e. modifying culling rates or improving case detection). Further, our model can be adapted to other areas based on different geographies and/or policies, and runs quickly enabling its use in real time (a single simulation on a commercially-available computer takes (on average) less than 12 seconds).

Parameter calibration resulted in a model that captured the majority of the observed epizootic dynamics, and through fitting the model to data of an on-going epizootic, we were able to estimate the relative contribution of different transmission routes to observed epizootic spread. With a mechanistic model now parameterized to the epizootic under study, alternative control strategies are now able to be explored to ascertain the relative outcomes they may have on the epizootic dynamics in comparison to the strategy enacted.

### Box 5.1 | Chapter 5 key points

- A mechanistic model of ASF transmission that includes the domestic-wildlife interface was constructed through combining a metapopulation model of domestic pig herds with a cellular automata model of wild boar groups.
- Domestic pig herds were represented as either low-biosecurity backyard herds or high-biosecurity industrial sites. Backyard herds were aggregated to the village scale, allowing us to consider the infection status of the village en-masse for modelling ASFV transmission.
- Wild boar units were represented via hexagonal raster cells sized to their estimated home range, with abundance potential a function of forest coverage per cell.
- Final model parameterization was achieved through a combination of literature review, observed epidemic analysis, and manual iteration.
- The high-dimensionality of the model has—so far—precluded algorithmic Bayesian methods from ascertaining the fitted parameter sets.
- Among domestic pig herds, 95% of cases came from other domestic pig herds with only 5% coming from wild boar. However, among wild boar, 40% of the cases were revealed to originate from contact with domestic pig herds.
- With this model, we are now able to explore the effects of alternative control strategies.

## 6 | Assessing alternative management strategies against African swine fever in a multi-host system

### 6.1 Introduction

The current ASF panzootic is an unprecedented international issue in animal health, and controlling it is recognized as a high priority for the EU (European Commission, 2020). The measures encoded in EU legislation are in accord with WOAHA international standards and are to be applied anywhere ASF is suspected or confirmed (Gavinelli *et al.*, 2020). For domestic pigs, such measures consist of stamping out affected farms, establishing protection and surveillance zones around affected premises to enable targeted disinfection, movement restrictions, and active surveillance measures, and animal and animal product contact tracing (Council of the European Union, 2002). For wild boar, the European Commission on wildlife management recommends also establishing core infected and surrounding surveillance zones in which active carcass search and removal, installation of fences, and intensive wild boar depopulation are considered (FAO, 2019).

Romania, currently classified alongside Sardinia with the highest levels of regulation, faces the most severe trade restrictions and control measures (Animal Health Advisory Committee (AHAC), 2021; European Commission, 2022). However, disparities in the understanding of ASF management recommendations among villagers and small-scale farmers greatly complicates the ideal enforcement of recommended measures (C. Mortasivu, personal communication, 2021). Indeed, rare reports of farmers not receiving compensation for their losses exacerbates distrust (Rose & Boisseleau, 2018). These behaviors hinder the effectiveness of trade restrictions and stamping out procedures (Chenais *et al.*, 2019)—resulting in culling of only an affected farm rather than all neighboring farms, for instance—and the result is the observed trajectory of the epizootic as illustrated in the previous chapter.

As seen in section 2 (chapters 3 and 4), assessing control strategies was the predominant objective of models at the domestic-wildlife interface and of models of ASF. Similarly, after parameterizing our model to the on-going epizootic in Romania and successfully capturing the overall spatial and temporal dynamics of the observed outbreaks, alternative control scenarios can now be explored. The objective of this chapter is to evaluate the hypothetical joint effects in domestic and wildlife compartments of what could have happened with alternative management strategies than those enacted at the onset of the epizootic.

## 6.2 Materials and Methods

### *6.2.1 Mechanistic model of ASF transmission in Romania*

We used the model that was presented in the previous chapter to further explore alternative control strategies. The details of our spatiotemporal stochastic simulation model, using villages to represent aggregated backyard pig farms, directly representing industrial sites, and using habitat-suitability raster cells to represent wild boar locations, are fully described in the previous chapter (Chapter 5). Parameters were informed through a combination of literature review, observed data, and fine tuning to fit the model to the observed spatiotemporal epizootic trends. Observed control strategies—consisting of passive surveillance of domestic pig herds, active surveillance of domestic pig herds through the establishment of 10 km surveillance zones around detected cases, culling of infected herds within a village but not of the entire village, and active surveillance of wild boar—were included in the parameterization. Having parameterized the model to this initial period of the Romanian epizootic, alternative scenarios could now be simulated through both assessing the sensitivity of the model to the perturbation of specific parameters, as well as by simulating novel control strategies.

### *6.2.2 Uncertainty analysis*

An uncertainty analysis was performed on two key assumed parameters delta ( $\delta$ ) and zeta ( $\zeta$ ): respectively, the transmission kernel and the relative increase in the case detection rate among domestic pig units that occurs in surveillance zones. Our baseline transmission kernel parameter of  $\delta = 0.2$  results in a  $d_{50}$  (the distance at which the transmission kernel is reduced by 50%) of 3.47 km, with a transmission rate of less than a 5% of its baseline value after 15 km and a minimum transmission rate of 1.8% at the truncated maximum distance of 20 km. Four additional kernels ( $\delta = 0.16, 0.18, 0.22, 0.24$ ) around our baseline kernel were evaluated. The effect of the surveillance zone—that is, the relative increase in detection rate of ASF cases for units in the surveillance zone compared to those outside the zone as given by our parameter zeta—was initially set at 50% and represents the effectiveness of the field activities on case detection. To evaluate the effect of this parameter, simulations were also conducted with surveillance zones having no effect, as well as increasing the relative detection rate by 25%, 50% (baseline), and 75%. Average parameter effects on total epizootic size and relative contribution of hosts to epizootic propagation were evaluated for each perturbed parameter.

### 6.2.3 Control strategy assessment

Alternative control strategies were chosen to consider improvements in either case detection or case prevention, being evaluated through the end effects on total epizootic size and relative host contribution (Table 6.1). First, we evaluated alternative surveillance zone sizes of 5, 15, and 20 km in addition to the baseline 10 km zone. Next, we examined improving passive surveillance among domestic pig units through reducing the average duration of the undetected infectious period from three weeks to either two and a half or two weeks. Alternative culling strategies were selected to evaluate village-wide culling upon case detection (through forcing an average duration of the infectious period of one week across all herds), as well as pre-emptive village-wide culling upon detection of wild boar cases in a shared cell. Lastly, given the importance of carcass persistence and environmental contamination on contributing to epizootic propagation among wild boar, the effects of achieving carcass clearance within six and eight weeks after detection were assessed, in which cells were able to return to a susceptible state following carcass removal.

**Table 6.1** | Summary of assessed control strategies

<b>Control strategy</b>	<b>Method of evaluation</b>
Alternative surveillance zone sizes	Adjust surveillance zone size
Improving passive surveillance of domestic pig units	Reduce the average duration of the undetected infectious period
Village-wide culling upon case detection	Forcing an average duration of the infectious period of one week across all herds
Pre-emptive culling of domestic pig units upon nearby wild boar case detection	Domestic pig units in an infectious-detected cell automatically transit to the R state upon cell detection
Environmental sanitation through wild boar carcass clearance	Cells return to the susceptible state after specified infectious-detected period

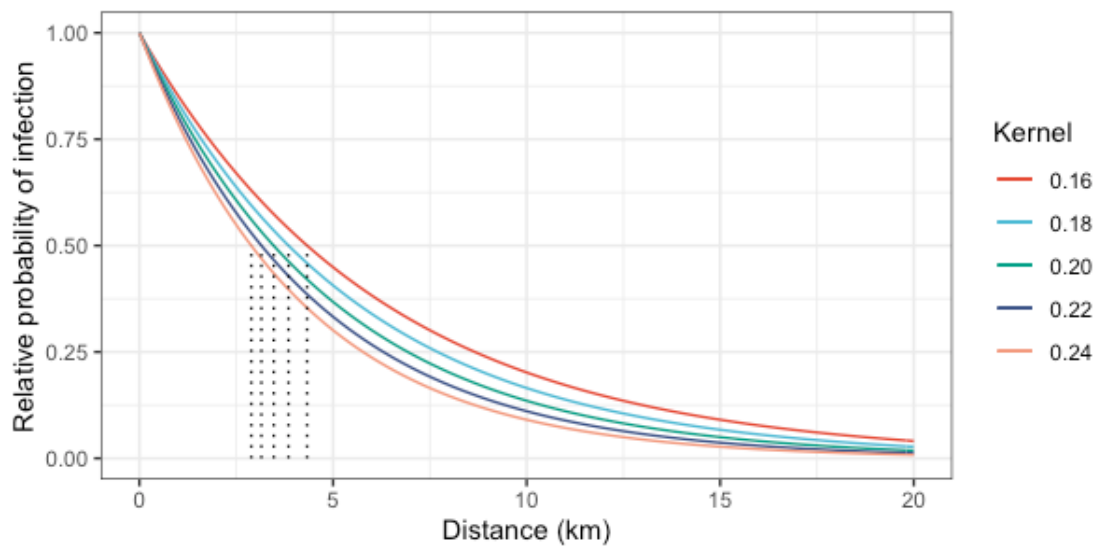
## 6.3 Results

### 6.3.1 Uncertainty analysis

Model uncertainty to the transmission kernel was assessed through exploring alternative values 20% above and below the baseline value (Fig. 6.1). This yielded an explored  $d_{50}$  range of 2.89 – 4.33 km (Table 6.2). By increasing the transmission kernel and thereby modifying the rate of exponential decay,



we are able to change the weight of local transmission at small distances that can reflect differences in contact patterns among villages.



**Fig. 6.1** | Transmission kernel distance effect by kernel value. Kernels were truncated for a maximum transmission distance of 20 km. Dotted x-intercepts represent corresponding  $d_{50}$  distances for each kernel parameter value (see Table 6.1).

**Table 6.2** | Transmission kernel distance function

Kernel parameter value	$d_{50}$ (km)	$d_5$ (km)	Transmission probability at 20 km
0.16	4.33	18.8	0.041
0.18	3.85	16.7	0.027
0.20	3.47	15.0	0.018
0.22	3.15	13.7	0.012
0.24	2.89	12.5	0.008

$d_{50}$  Distance where transmission probability is 50% of baseline

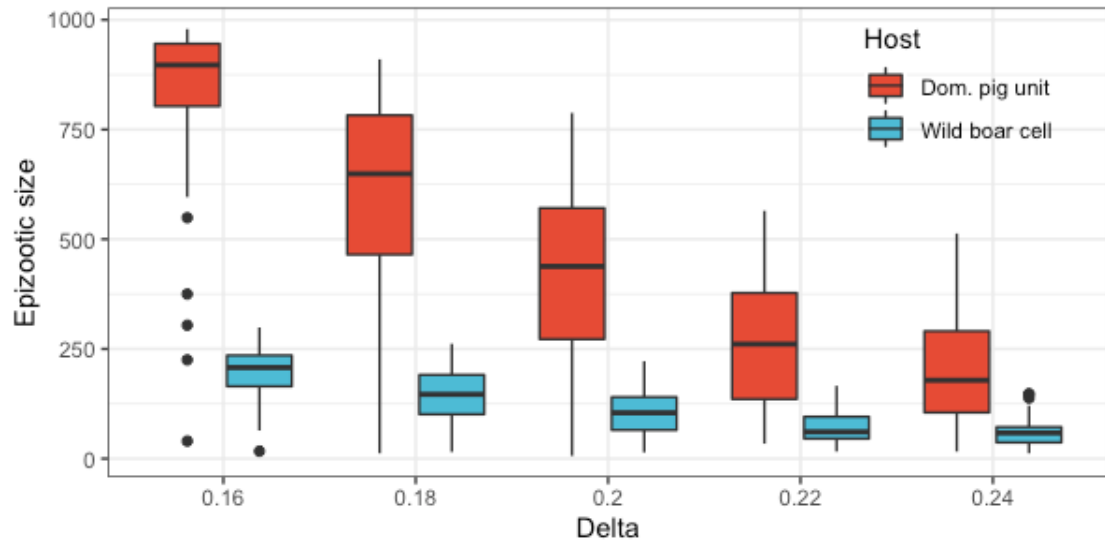
$d_5$  Distance where transmission probability is 5% of baseline

The transmission kernel had a profound effect on epizootic size, with a mean difference in epizootic size of 30% (range: 25–36%) observed between alternative consecutive kernels (e.g.  $\delta = 0.2$  and 0.22) among domestic pig units (Fig. 6.2). As would be expected, increases in the transmission kernel parameter value (from 0.2 to 0.22 or 0.24) led to fewer cases. Changing the transmission kernel by

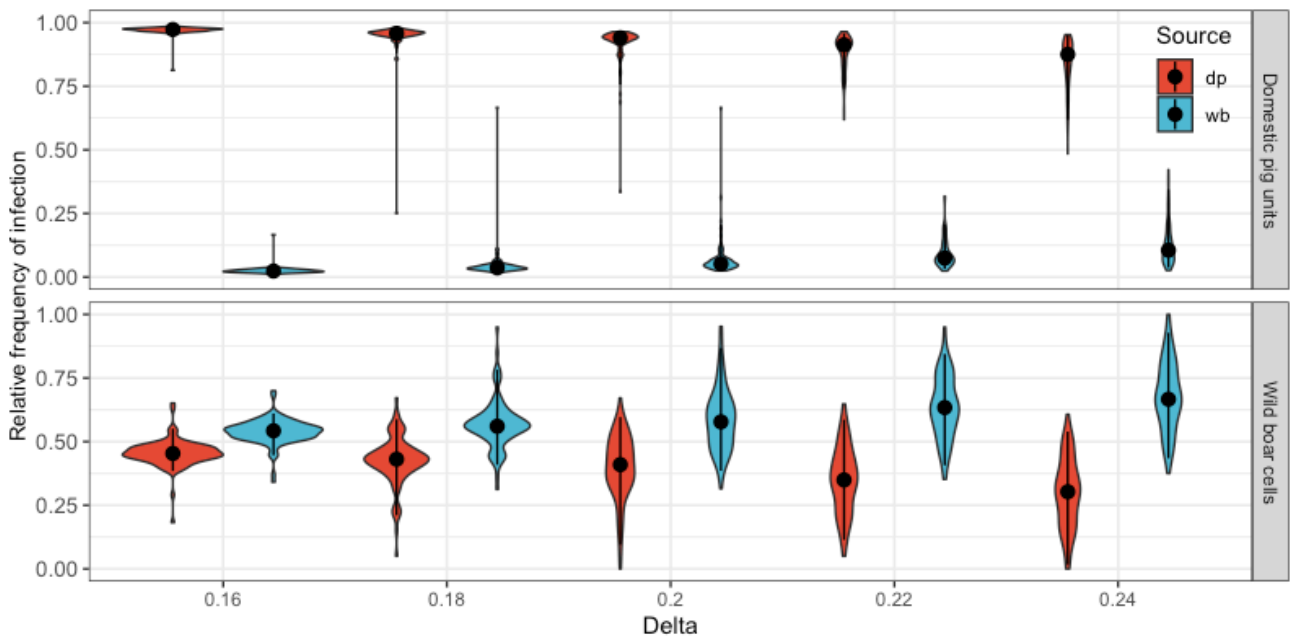
10% from  $\delta = 0.2$  to  $\delta = 0.22$  reduced the median total epizootic size among domestic pig units by 177 outbreaks: from 438 (IQR: 272; 571) to 261 (IQR: 136; 378) outbreaks, while further changing it from 0.22 to 0.24 showed diminishing returns, reducing median epizootic size by only 83 outbreaks. Further, with almost 40% of wild boar cell infections predicted to come from domestic pig units in the baseline model (see chapter 5), increases in the transmission kernel also reduced epizootic size among wild boar cells. Increasing the transmission kernel from 0.2 to 0.22 resulted in a median of 43 fewer infected wild boar cells (the equivalent of an additional 1075 km<sup>2</sup> free of ASF, given our cell size of 25 km<sup>2</sup>). Conversely, when the transmission kernel was decreased from  $\delta = 0.20$  to  $\delta = 0.18$ , an additional 211 outbreaks among domestic pig units were observed (a 48% increase), along with 42 additional wild boar cell infections.

The choice of transmission kernel additionally had effects on the relative contribution of each host to transmission. As the transmission kernel value increased (thusly increasing the effect of distance on mitigating transmission), relative decreases in transmission from domestic pig units and increases in transmission from wild boar cells occur among both domestic pig units and wild boar cells (Fig. 6.3). Increases in the transmission kernel resulted in a mean decrease of 3.9% between examined kernels in the relative transmission from domestic pig herds to wild boar cells.

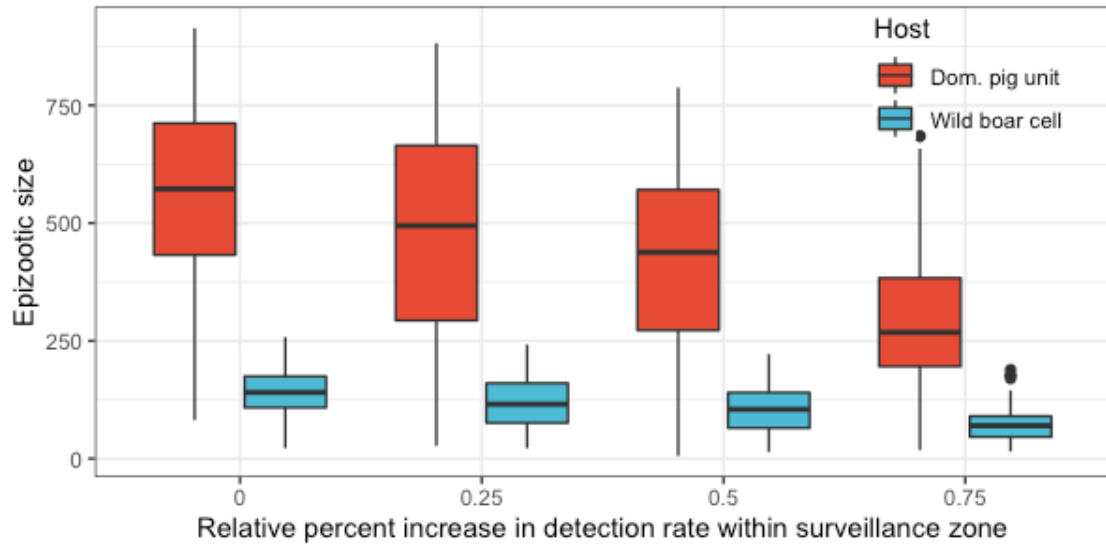
Epizootic simulation output was also sensitive to the rate of assumed increase in case detection that occurs within a surveillance zone. For each 25% increase in the relative detection rate within a surveillance zone, a mean of 89 fewer domestic pig unit cases were seen (Fig. 6.4). Increasing the relative detection rate in surveillance zones also resulted in fewer wild boar cell cases, with a mean of 23 fewer cases per 25% increase in relative detection rate. Between compartments, as detection within surveillance zones became more effective, significantly smaller proportions of cases among wild boar were seen to come from domestic pigs (Fig. 6.5). At a 50% increase in detection rate in surveillance zones, approximately 40% of cases among wild boar come from domestic pigs, while at 75%, approximately 32% of cases do. This translates into almost half as many cases coming from domestic pigs to wild boar (42 compared to 22 cases), almost an additional 500 km<sup>2</sup> area free of ASF.



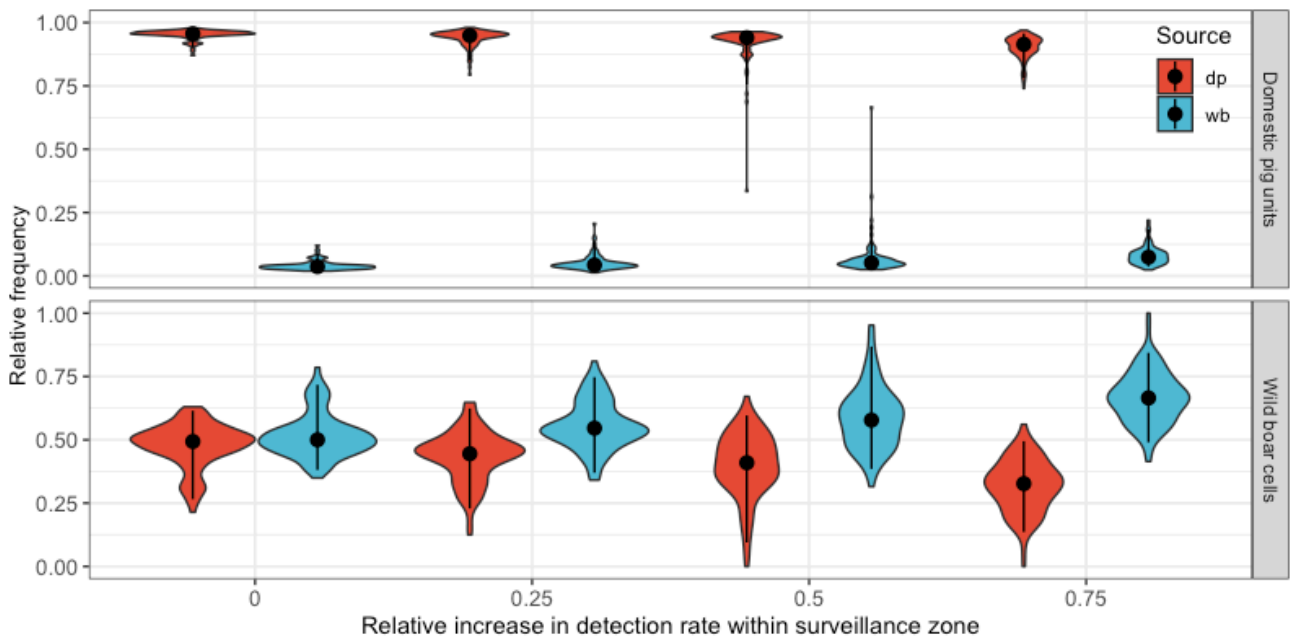
**Fig. 6.2** | Sensitivity of final epizootic size to the transmission kernel by host. X-axis transmission kernel values represent  $d_{50}$  distances (that is, the distance at which transmission decreases by 50%) of 4.33, 3.85, 3.47, 3.15, and 2.89 km, respectively, from left to right. Boxplots represent median, interquartile range (IQR), maximum and minimum values of epizootic size across 100 simulations per kernel value.



**Fig. 6.3** | Sensitivity of the relative transmission frequency between hosts to alternative transmission kernels. Results faceted by source of infection (dp: domestic pig units, wb: wild boar cells). Increases in the transmission kernel result in relatively fewer cases among from domestic pig units to both other domestic pig units as well as wild boar cells.



**Fig. 6.4** | Sensitivity of final epizootic size to the relative increase in detection within surveillance zones. Boxplots represent median, interquartile range (IQR), maximum and minimum values of epizootic size across 100 simulations per kernel value. Zero (0) indicates the surveillance zone has no effect on case detection.



**Fig. 6.5** | Sensitivity of the relative transmission frequency between hosts to increases in the detection rate within surveillance zones. Results faceted by source of infection (dp: domestic pig units, wb: wild boar cells). Zero (0) indicates the surveillance zone has no effect on case detection.

### 6.3.2 Control strategy assessment

The size of the surveillance zones was found to have a significant effect on overall epizootic size, for both domestic pig units and wild boar cells (Fig. 6.6). Each 5 km increase in surveillance zone size resulted in a mean of 50 fewer infected domestic pig units and 14 fewer infected wild boar cells (translating as additional 350 km<sup>2</sup> free of ASF). Compared to the baseline strategy of a 10 km surveillance zone, a 15 km zone reduces the median epizootic size among domestic pig units by 11.6%, while doubling the surveillance zone diameter to 20 km decreased the epizootic size by 20.5%. Conversely, shrinking the surveillance zone to 5 km results in a 12.8% increase in epizootic size. Similar percentage changes were seen among wild boar cells (i.e. 13% reduction in wild boar cell infections with the 15 km surveillance zone, and 12% increase in wild boar cases with the 5 km surveillance zone). The relative frequency of transmission between compartments was affected by surveillance zone size as well. For each 5 km increase in surveillance zone size, a 2.6% decrease in relative transmission from domestic pig units to wild boar cells was observed (Fig. 6.7). Relative transmission rates to domestic pig units were only minimally affected (less than 1% difference in relative transmission rates to domestic pig units between different surveillance zone sizes).

Reducing the undetected infectious period from 3 weeks to 2.5 or 2 weeks resulted in small changes to final epizootic size (Fig. 6.8). At an undetected period of 2.5 weeks, a median of 48 fewer herds (n = 390) and 12 fewer cells (n = 92) were infected. A further decrease in the undetected infectious period resulted in diminishing returns, with an additional 20 less herds (n = 370) and 5 fewer cells (n = 87) infected. Increases in the passive detection rate among domestic pig herds corresponded to decreases in the relative contribution of domestic pig units to wild boar cell infection (Fig. 6.9). Compared to a baseline of 40.9%, at an undetected infectious period of 2.5 weeks there was a median of 38.1% wild boar cell infections from domestic pig units, and at 2 weeks the median was 36.8%. Among domestic pig units, decreasing the undetected infectious period resulted in small decreases in the contribution of domestic herds to other domestic pig unit infections, from a baseline of 94% to 93% and 92.4%, respectively.

When culling strategies were examined, both preventive culling of a village upon case detection in a nearby wild boar herd, and full culling of a village upon case detection in a backyard herd in the village, were considered (Fig. 6.10). Preventive culling reduced the median epizootic size among domestic pig herds by 16% (n = 69) to 369 infections. Additionally, a median of 9 fewer cases (n = 95) among wild boar cells were observed with this strategy. When village-wide culling in response to a domestic pig case was used, the median epizootic size was reduced by over 33%. There were 146 fewer outbreaks among domestic pig units (n = 292, IQR: 198; 411) as compared to the baseline (n = 438, IQR: 272;

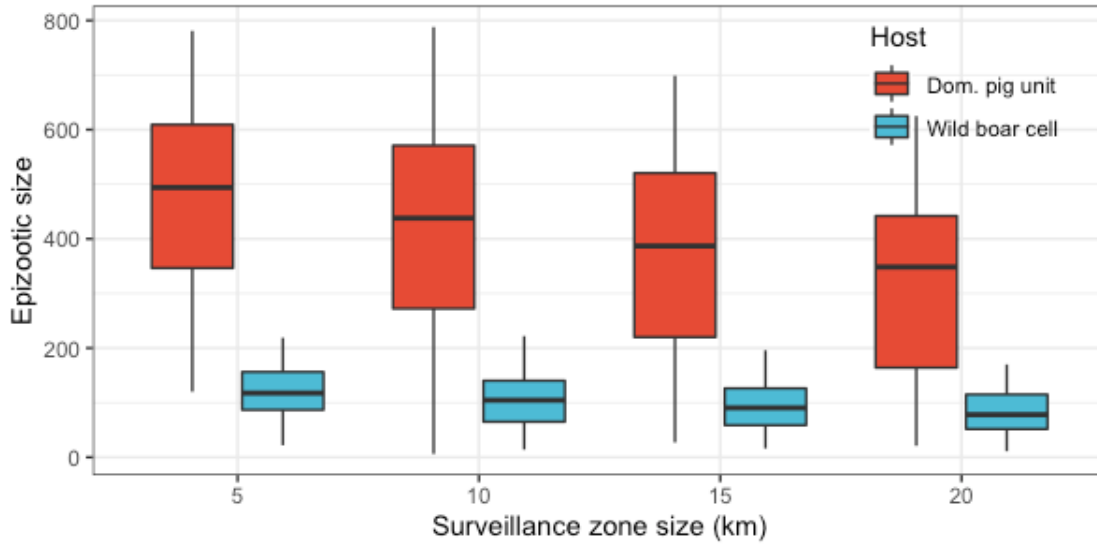
571) and 40 fewer cases among wild boar cells ( $n = 64$ , IQR: 40; 94). Alternative culling strategies had minimal effect on the relative contribution of each host to the overall epizootic (Fig. 6.11).

The final control strategy examined was the effect of carcass clearance and environmental decontamination. Whether all carcasses were removed within 8 weeks or 6 weeks of detection within a 25 km<sup>2</sup> area, minimal improvement in epizootic size was observed (Fig. 6.12). A small but present difference in contribution between hosts was noted. Carcass removal over 8 or 6 weeks resulted in slight decreases in transmission from wild boar cells to domestic pig units, from a baseline median of 5.17% of transmission events to 4.42% or 4.19%, respectively (Fig. 6.13). Conversely, carcass removal increased the relative contribution of domestic pig units to overall wild boar cell infections, from the baseline of 40.9% up to 46.9% and 48.2% for clearance times of 8 and 6 weeks, respectively.

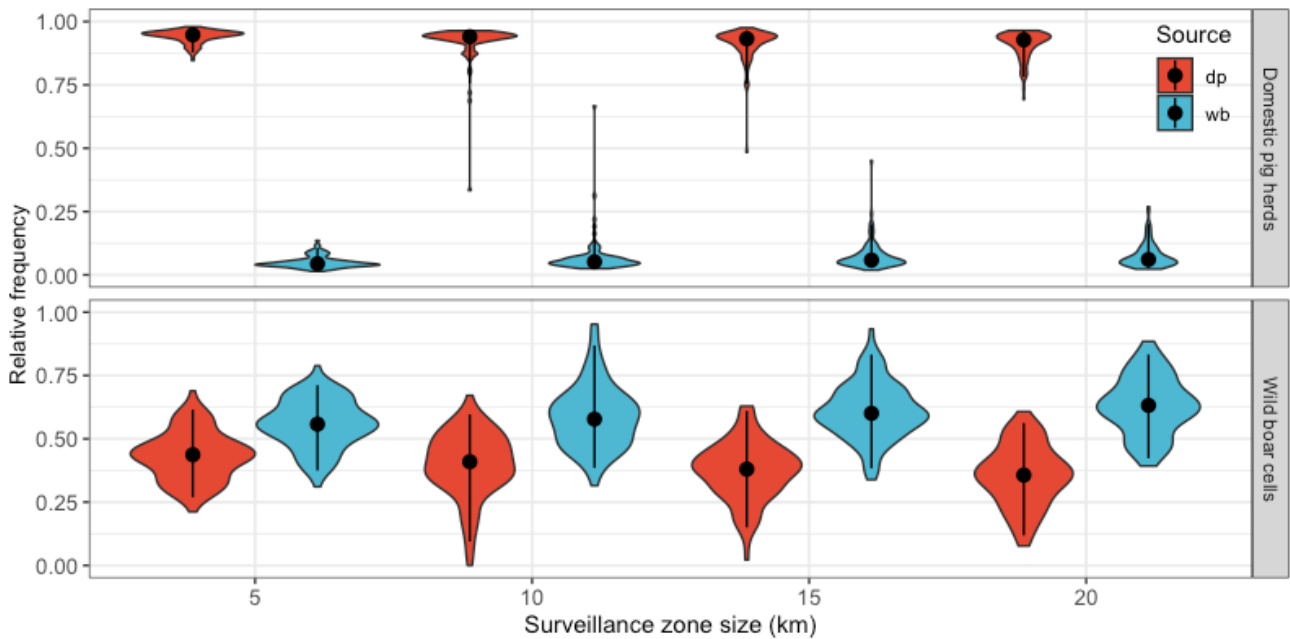
#### 6.4 Discussion

Here we were able to both examine the behaviour of the model according to different ranges of values of choice uncertain parameters (the transmission kernel  $\delta$  and surveillance zone detection rate modifier  $\zeta$ ), as well as evaluate the impact of alternative control strategies had they been employed at the onset of the observed epizootic.

The transmission kernel predicts the relative rate of transmission as a function of the distance of the susceptible herd from an infectious herd. In the absence of data of the commercial network in Romania, the rate of transmission between herds was weighed by a transmission kernel—as done in multiple previous ASF modelling studies (Andraud *et al.*, 2019; Halasa, Bøtner, *et al.*, 2016a, 2016b; Ivorra *et al.*, 2014; Mur *et al.*, 2018). An exponential decay was assumed—the rate of which was calibrated to 0.2—and the transmission was limited to a radius of 20 km from infected premises. Previous ASF models have used single transmission kernels to inform local farm-to-farm transmission defined as transmission under 2 km (Andraud *et al.*, 2019; Halasa, Bøtner, *et al.*, 2016a, 2016b; Ivorra *et al.*, 2014; Mur *et al.*, 2018). Though our assumed maximum local distance is ten times this amount, with domestic pig units aggregated to and defined at the village scale, our definition of local transmission also scales to locally between villages. An uncertainty analysis nevertheless revealed a high sensitivity of model outcomes on the exponential decay parameter value. Therefore, field studies defining the social and commercial networks of farmers that exist between villages could validate or further inform our assumptions on local transmission between villages.



**Fig. 6.6** | Effect of surveillance zone size on final epizootic size. Boxplots represent median, interquartile range (IQR), maximum and minimum values of epizootic size across 100 simulations per kernel value.



**Fig. 6.7** | Effect of surveillance zone size on relative transmission frequency between hosts. Results faceted by source of infection (dp: domestic pigs, wb: wild boar). Increases in surveillance zone size affected transmission dynamics to wild boar cells, but had minimal effect on relative transmission rates to domestic pig units.

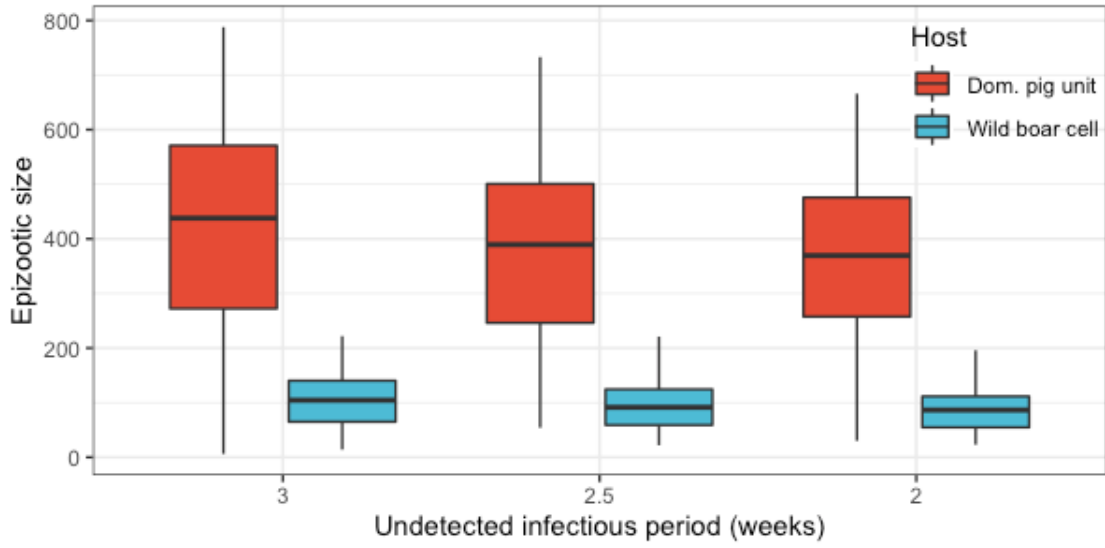


Fig. 6.8 | Effect of reducing the undetected infectious period on final epizootic size by host.

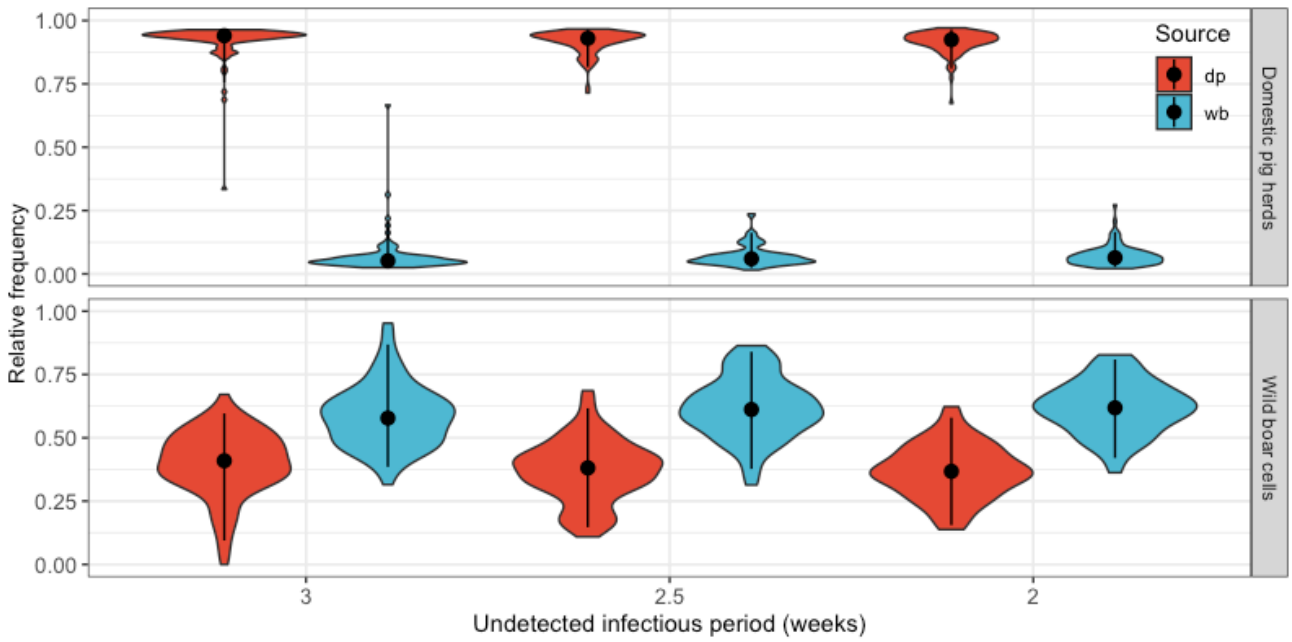
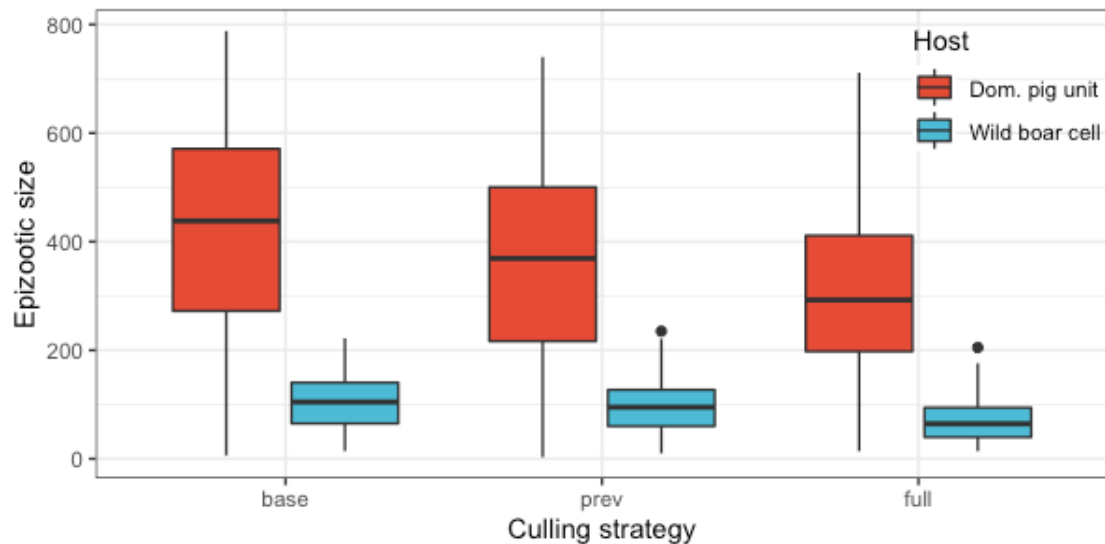
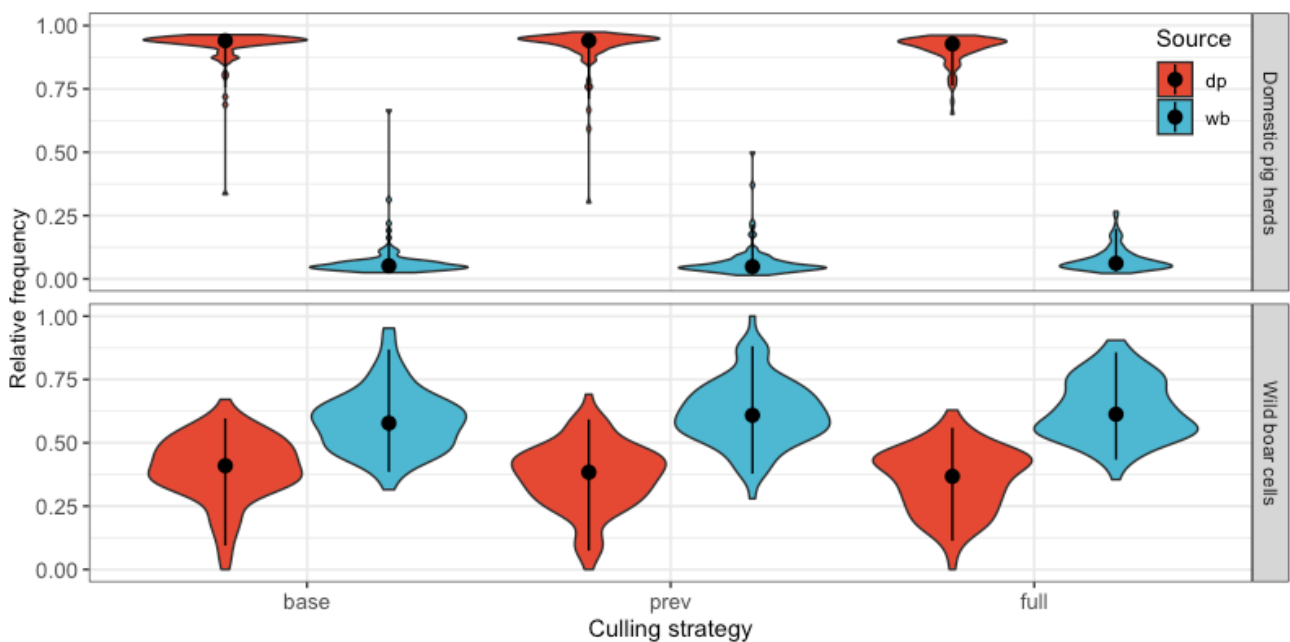


Fig. 6.9 | Effect of reducing the undetected infectious period on relative transmission frequency between hosts. Results faceted by source of infection (dp: domestic pigs, wb: wild boar).

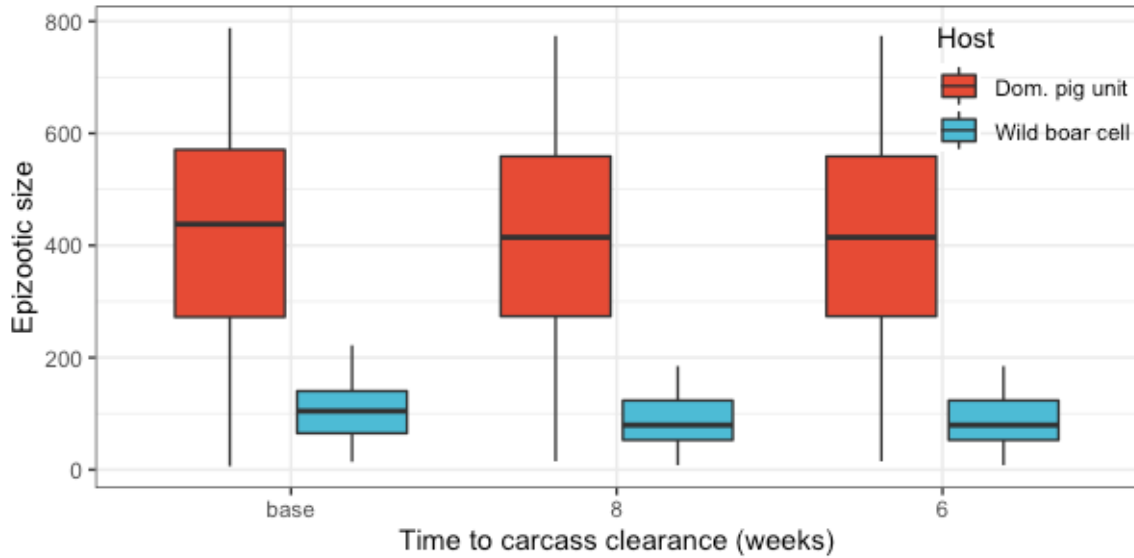




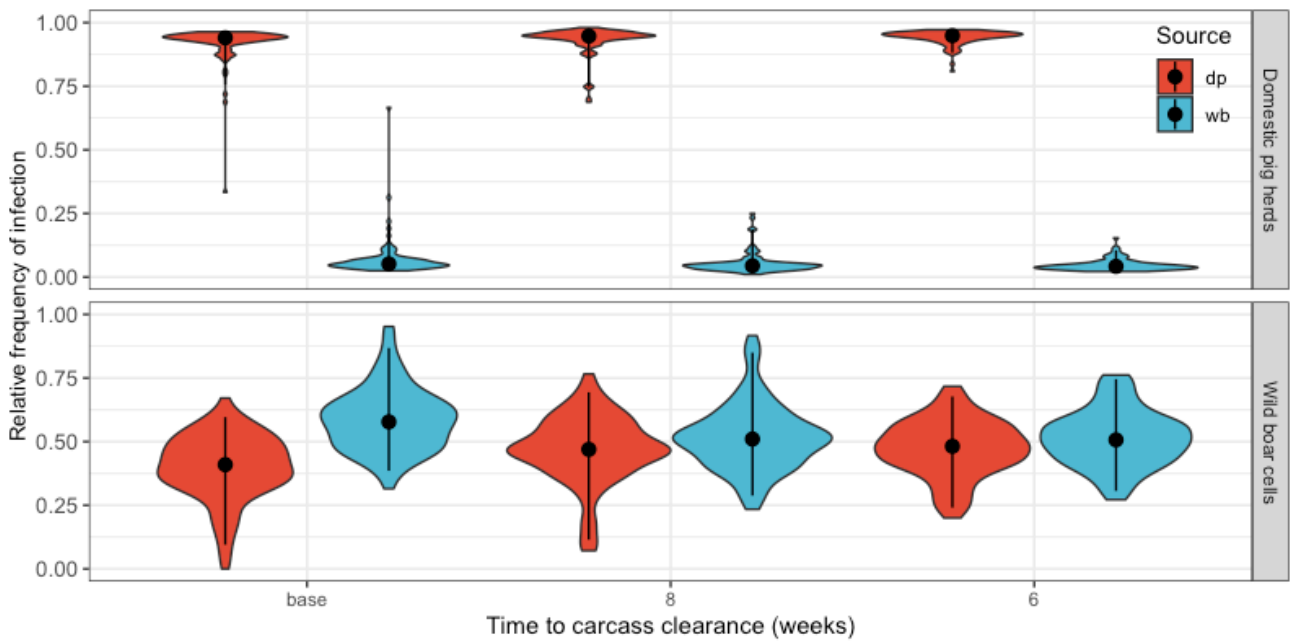
**Fig. 6.10** | Effect of culling strategies on final epizootic size. In comparison to the baseline culling strategy (“base”) of only individual farms being culled leading to a range of infectious periods among villages, village-wide culling upon case detection in a village (“full”) was compared in addition to preventive culling upon wild boar case detection (“prev”). Significant difference was seen between the baseline and the full culling strategy, but not between the baseline and preventive culling strategy.



**Fig. 6.11** | Effect of culling strategies on the relative transmission frequency between hosts. Results faceted by source of infection (dp: domestic pigs, wb: wild boar). Minimal difference was observed in the relative host contribution between the baseline culling strategy of only individual farms being culled (“base”) and alternative strategies of village-wide culling upon case detection in a village (“full”) and preventive culling upon wild boar case detection (“prev”).



**Fig. 6.12** | Effect of carcass removal on final epizootic size. “Base” indicates the baseline scenario of persistent infection without environmental sanitation, while 8 and 6 refer to scenarios in which all carcasses are removed within 8 and 6 weeks, respectively.



**Fig. 6.13** | Effect of carcass removal on the relative transmission frequency between hosts. Results faceted by source of infection (dp: domestic pigs, wb: wild boar). “Base” indicates the baseline scenario of persistent infection without environmental sanitation, while 8 and 6 refer to scenarios in which all carcasses are removed within 8 and 6 weeks, respectively.

Altering the shape of the transmission kernel was seen to have large effects on the final epizootic size, and could be considered to reflect changes in contact patterns between pig holders. As evidenced from multiple investigations into the spread of ASF in spite of strict quarantine and movement restrictions, illegal movements of infected swill feed has been shown to be responsible for almost all (about 97% of) introductions of ASFV into naïve herds (Khomenko *et al.*, 2013). Intervention strategies that target changes in this parameter, such as educational initiatives to improve locals knowledge of these consequences of illegal movements and swill feeding, should be a priority. Even with the inevitable illegal movements, reducing the  $d_{50}$  distance by small amounts was seen to have profound effects. Additionally, as village spatial distribution varies between counties, considering county-specific measures, especially as related to movement controls and surveillance zones could provide cost savings as well. For instance, Tulcea County is comprised of 140 villages spread over 8467 km<sup>2</sup>, in contrast to Galati County which contains 186 villages in almost half the area (4462 km<sup>2</sup>).

Increasing the transmission kernel results in less weight given to local transmission at small distances, thereby reducing final epizootic size in both the domestic and wild compartments. However, amplification of the relative number of cases derived from wild boar cells for both domestic pigs and wild boar recipients was also observed. Therefore, the overall reduction in total case counts was offset, to a certain degree, through continued transmission to domestic pigs from the wild compartment. As camera trapping research has shown frequent and direct interaction between free-ranging domestic pigs and wild boar, it is not unexpected that reductions in cases from one compartment could be offset by increases in cases from the other (Cadenas-Fernández *et al.*, 2019). Management strategies should therefore consider accounting for both domestic and wildlife transmission to avoid such counteraction of intervention efficacy.

Previous assessment on the radii of surveillance zones found that, at the codified 10 km, there is less than a 0.2% probability of ASF transmission beyond that limit (EFSA Panel on Animal Health and Welfare (EFSA AHAW Panel) *et al.*, 2021). However, it is equally stated that such a probability does not include transmission risks due to wild boar, and so we felt it important to assess this parameter in our model that accounts for this transmission. Doubling the surveillance zone size from 10 km to 20 km resulted in almost 100 fewer infected villages, however increasing it by 50% to 15 km did not result in significant difference for any of the units. Interestingly this finding is congruent with both results for industrialized swine populations, where Halasa *et al.* (2018) also did not predict improvements in epizootic control when the surveillance zone was increased from 10 to 15 km, and from results from the ASF Modelling Challenge where a team also did not find a 5 km surveillance zone increase to reduce the number of cases (Dankwa *et al.*, 2022). Conversely, decreasing the surveillance zone size

from 10 km to 5 km did not result in a statistically significant change in the overall size of the epizootic either. However, our model is at the scale of the village where there may not be much difference in the number of villages at 5 km intervals, as compared to the number of individual farms. Additionally, in our model the surveillance zone only affected case detection rates, whereas in the legislation there are additional protective regulations including movement restrictions and disinfection protocols of transportation (Council of the European Union, 2002). It is therefore possible that accounting for these additional interventions within a surveillance zone would increase the simulated impact from changes to surveillance zone size. Even if a significant impact was observed, recommending such changes be made in the field would require considerable additional considerations, accounting for both workforce and laboratory diagnostic capabilities.

The relative effect of the surveillance zones, indicating the effectiveness of the field activities around case detection, had an important influence on final epizootic size. Activities within the surveillance zone consist of taking a census of all pig holdings, enforcing movement prohibitions of pigs and pig products, cleansing and disinfection protocols, and clinical and laboratory examination of all pigs (Council of the European Union, 2002). Our model, occurring at the scale of the village, considers the combined effect of all these undertakings. Surveillance zone activities have been shown to be already highly effective at identifying cases and preventing further spread of ASF (EFSA Panel on Animal Health and Welfare (EFSA AHAW Panel) *et al.*, 2021). An economic analysis on the costs of providing the necessary veterinary and para-veterinary services within the surveillance zones will help to determine if the impact of even more effective surveillance zones is worth the price.

Reducing the undetected infectious period—through improved case reporting—did not have a significant effect on final epizootic size in our model. As we are considering the whole village rather than individual farms, it is possible that the average undetected infectious period is greater than our assumed 3 weeks, and a significant difference could be seen in the case of decreases from a larger period. Also, as long as control strategies are applied unevenly between counties, it is also likely that this period varies between counties, in which case targeting this parameter may result in county-specific improvements in epizootic size. The risk of silent transmission of ASF due to individual farmer behavior during emergency sales has also been shown to be high, which would also suggest that the degree of ASF spread occurring during this period is high enough that more drastic decreases in the undetected infectious period are needed (Costard *et al.*, 2015). Through providing educational opportunities that lead to better awareness of symptoms and risks, pig holders could be more sensitive to the risk of transmission to others, and could react more rapidly. Indeed, the observed data

displays a progressive decrease in the calculated infectious periods, that could be attributable to increasing awareness over the course of the epizootic.

Village-wide culling had the most pronounced effect on final epizootic size, resulting in a median of 146 fewer outbreaks among villages per epizootic scenario. Unfortunately, preventive culling actions of even just neighboring herds within a village were reported to be difficult to justify to small-scale Romanian farmers, and possibly led to illegal movement activities (Rose & Boisseleau, 2018). In contrast, during the ASF outbreak in the Republic of Korea in September 2019, preventive culling of all swine herds within a 3 km radius of an infected herd was successfully instituted, resulting in complete outbreak control in under 4 weeks (Kim *et al.*, 2021). There are likely multiple cultural, social, and political factors behind these differences in the acceptance of such a strategy, and decision makers would benefit from further social science research to elucidate such factors for facilitating epizootic control. Village-specific parameters (e.g. population) and within-village dynamics were not accounted for in our model though, and would be important factors to consider prior to recommending such large-scale culling based on our results. However, accounting for within-village transmission dynamics would require actual geolocation of domestic pig holdings—which is currently lacking—and obtaining such census data should be a consideration among Romanian stakeholders. Regardless, the large effect of this increase in the recovery rate on the final epizootic cannot be ignored and should be a focus of additional research.

Our model did not reveal preventive culling of villages upon nearby case detection in wild boar to have a significant effect on final epizootic size. Indeed, in our simulations wild boar were responsible for only a small fraction of cases among domestic pigs, and domestic pig units (namely villages) comprised the majority of cases of the overall epizootic. However, field research has shown wildlife contact to be an important contributor to cases among domestic pigs. Phylogenetic results in Poland had shown that while separate genetically-distinct ASFV incursions were responsible for clusters of outbreaks, within those clusters wild boar were suspected to be responsible for transmission to domestic pig herds (Śmietanka *et al.*, 2016). In Estonia, direct contact with wild boar was suspected to be the inciting cause of outbreaks on two out of 28 investigated farms (European Food Safety Authority (EFSA) *et al.*, 2018). Beyond only direct transmission, a scoping review of articles on wild-domestic ASFV transmission concluded that when such between-host transmission occurs, indirect routes may in fact be more common (Brookes *et al.*, 2021). Our results contrast to those of one of the models out of the ASF Modelling Challenge, where preventive culling of domestic pig herds nearby to detected wild boar cases resulted in a decrease of almost 20% in the final number of infected pig herds (Dankwa *et al.*, 2022). Acceptance of such a strategy by farmers could be difficult without targeted educational

programs, however, and as highlighted by Dankwa *et al.* (2022), the cost-benefit ratio of such a strategy would have to be established given the presumed substantial costs.

Carcass removal did not have an effect on final epizootic size (given the small proportion of cases among domestic pigs due to wild boar, and that the epizootic is mostly among domestic pig herds, this is again not unexpected), but did result in relative decreases in transmission from wild boar cells. Carcass removal has been shown to be a critical supportive intervention against ASF, especially when instituted during epizootic onset—as seen in the successful eradication of ASF in both Belgium and the Czech Republic (EFSA *et al.*, 2021; Van Goethem, 2021; WOA, 2019a). Maintaining good relationships with the hunting community is essential for successful passive and active surveillance, especially as passive surveillance is the most likely means of detecting ASF in wild boar (EFSA *et al.*, 2018). Assistance for decreasing the workload and costs bestowed unto hunters, along with knowledge of their important role in reducing infection pressures, were identified as important factors for fostering hunter participation in anti-ASF efforts (in Latvia) (Urner *et al.*, 2021). Passive surveillance of wild boar cells is accounted for through two parameters, split by prior to first case detection and following first case detection. Modifying the pre-first case detection rate for infected cells ( $\sigma_{pre}$ ) could be a means to examine the results improving hunter participation in passive surveillance efforts. Future iterations of this model should consider such examination.

When wild boar behavior towards carcasses was evaluated through field experiments, direct contact of a carcass by a wild boar occurred on average 15 days (range: 1-32) after the carcass was placed (Probst *et al.*, 2017). Consequently, for carcass removal to have an effect on curbing ASF transmission, both detection and removal would be expected to have to occur within 2 – 4 weeks. In our Romanian model, given our estimated transmission rate among wild boar, even with an average of 8 weeks for wild boar case detection and assuming an additional 6 weeks for carcass clearance, a beneficial effect was observed with environmental sanitation.

Previous study indicated at least 50% of carcasses must be removed for this strategy to have an effect, so it can be assumed that, in our model, sanitation of an infected cell would be defined as the capture of at least 50% of the carcasses in a 25 km<sup>2</sup> area (Gervasi & Guberti, 2022). While this could be perceived as an unrealistic task (given that carcass removal efforts in Latvia were estimated to detect less than 0.5 carcasses / 100 km<sup>2</sup>), our model assumes a uniform landscape (outside of forest coverage) that is free from any fragmentation within each cell. Rivers, highways, commercial infrastructure and other geological features— which has been shown to affect transmission dynamics—can all contribute to such landscape division thus limiting the overall area to search for carcasses (Salazar *et al.*, 2022).

Economic considerations will play a pivotal role in the decision processes behind the selection and enactment of control strategies. The associated costs of implementation for increasing checkpoints to curtail movements between villages and industrial sites, as well as to consider increasing surveillance zone effectiveness, must be determined before policy recommendations can be made.

## 6.5 Conclusions

Achieving control of an ASF outbreak is a complex task, involving coordinated efforts between stakeholders from veterinary services, animal agriculture, conservation and hunting groups, law enforcement, and government, among others. Multiple alternative control strategies were explored, including altering the effect of distance on transmission between herds, the surveillance zone size, the efficacy of the surveillance zones, the detection rates among domestic pig units, preventive or extended culling, and wild boar carcass removal. Adjustments in the transmission kernel—through restricting trade and limiting movement between villages—along with increases in the efficacy of surveillance zones (such as through increases in the available workforce and intra-village surveillance measures) and village-wide culling upon case detection had the most profound effects on limiting the scale of the epizootic. Even so, the decreases in cases arising from domestic pig sources are offset to a degree by relatively more cases arising from wild boar. Future research steps in which optimization algorithms are applied to the six strategies explored here could yield further insight into which strategies are best used in-concert. Achieving epizootic control requires the consideration of the effects of management decisions both within and between ecological compartments, and as long as backyard farms continue to be a source of infection for wild boar—and to a lesser extent vice-versa—attaining full epizootic control is far but from assured.

### Box 6.1 | Chapter 6 key points

- Multiple alternative control strategies were explored, including altering the effect of distance on transmission between herds, the surveillance zone size, the efficacy of the surveillance zones, the detection rates among domestic pig herds, preventive or extended culling, and wild boar carcass removal.
- Epidemic size was able to be best limited through altering the transmission kernel (via changing contact patterns among villages, as would occur through restricting trade and limiting movement), increasing the efficacy of surveillance zones (by increasing the available workforce and intra-village surveillance measures), and instituting village-wide culling upon case detection.
- The least beneficial interventions were carcass removal and increasing the surveillance zone size.
- Decreases in final epidemic size are best seen with control measures targeting domestic pig herds (expectedly as they constitute the majority of cases), however decreases in cases from domestic pig sources are offset to a degree by relatively more cases arising from wild boar.
- As long as domestic pig herds continue to be a source of infection for wild boar, and vice versa, total ASF eradication will be an untenable objective.





## § IV | Overall discussion and conclusion

In this overall discussion chapter, we first synthesized what we intended to do and then took some perspective by examining our methods and findings in light of other ASF models. After summarizing the approach to and outcomes of the PhD project, we examined the impact of our work, and what we have contributed to the greater ASF modelling body. Potential future directions are then investigated, for both other scenarios where our model can be applied as well as what else would be beneficial to include in future iterations of our work. Lastly, we reflect on all that has been accomplished. From such a perspective we can consider what would be done differently if this project was again started anew, and how our research can be extended for continued and improved utility.



### 7.1 Thesis aims and accomplishments

African swine fever—with its devastating effects on swine production, farmer livelihood, animal welfare, and biodiversity loss—is recognized as one of the most severe diseases of swine (FAO, 2012; WOA, 2019c). What started as a focal incursion at a port on the eastern Black Sea coast has since grown into a multi-continent panzootic (WOA, 2019c). As of July 2022, 45 countries across Africa, the Americas, Asia, Europe, and Oceania have reported ASF in the past two years (WOA, 2022d). Affected nations have experienced variable outbreak dynamics, with some seeing ASF cases only among wild boar or domestic pigs, and others confronting both epizootic spread among domestic pig herds as well as enzootic establishment among wild boar populations (WOA, 2022d). In these areas where transmission was suspected to occur between both the wild and domestic compartments, as in Romania, quantifying the transmission dynamics of ASFV at the domestic-wildlife interface would be an important step to improving the management of ASF. Therefore, we sought to answer the question: To what extent does ASFV transmission between domestic pigs and wild boar, in areas of low-biosecurity backyard farming, contribute to total ASF spread? By elucidating this quantity, we could then answer the question: how do control strategies targeting one compartment affect the transmission dynamics in the other compartment?

Mathematical models have a proven history of elucidating transmission dynamics, and have recently been used to inform the risk of infection between species for some epizootics, as for bTB in the UK and ASF in South Korea (Birch *et al.*, 2018; Yoo *et al.*, 2021). However, no mechanistic model existed that quantified ASFV transmission at the domestic-wildlife interface (Chapter 3). Therefore, to improve the understanding of how ASFV circulates at the interface between domestic and wild hosts, to elucidate the relative host contributions to these dynamics, and to understand how control strategies enacted in one compartment can affect the transmission dynamics in the other compartment, we designed, constructed, and then parameterized an ASF model at the domestic-wildlife interface to the on-going epizootic in Romania (Chapters 5 and 6).

Through using a novel model created specifically for our research question, we were able to succeed in generating an estimate of the relative contribution of domestic and wild hosts to ASFV epizootic spread in Romania. Only one other recent ASF model has quantified the relative contributions of domestic and wild hosts to ASF spread, and did so in-concert with detailed between-herd vehicle movement data to account for and determine herd-to-herd transmission probabilities (Yoo *et al.*, 2021). Without the availability of data on between-farm or between-village pig movements, we had

to infer herd-to-herd contact rates and did so through an exponentially-distributed transmission kernel. In both cases, human-mediated transmission was suspected to be the primary means of spread among domestic pig herds, and accounting for this mode of transmission was necessary in order to then ascertain the contribution of wild boar to domestic pig herd infections (Andraud *et al.*, 2021).

Domestic and wild hosts in our model were aggregated representations of the real-world hosts, and so our results reflect the relative contributions of each host at the given level of representation. With wild boar represented through wild boar habitat cells, our interface transmission results indicate the estimated percentage of domestic pig unit infections attributable to 25 km<sup>2</sup> infected areas of wild boar habitat (not to be confused for domestic pig infections from individual wild boar). Equally, our results indicate the percentage of infections of 25 km<sup>2</sup> wild boar habitat cells that would be attributable to individual domestic pig units. Thereby, more specifically we answered the question: What is relative contribution of infected wild boar habitat and ASF-infected villages and industrial sites to overall epizootic propagation? An alternative modelling approach using an individual-based model of wild boar, such as that used by Dankwa *et al.* (2022) in the ASF Modelling Challenge, could potentially have helped refine the results to elucidate the contribution of individual wild boar (and not just boar-occupied habitat), however their model did not include a means of disentangling sources of infection. Further, an individual-based approach would have been extremely parameter intensive. As our focus was on the epizootic dynamics, by reducing the description of the host population to polygons and ignoring the population dynamics, we were able to reduce unnecessary complexity. Our estimates, though a proxy for rates of ASF transmission between backyard domestic pig herds and wild boar, are nevertheless an important step towards elucidating the true relative infection contributions between hosts to a multihost epidemic using mathematical modelling.

Following disentanglement of the relative host contributions, we were able to approach the second research question regarding elucidation of the effects of control strategies in one compartment on the epizootic dynamics of the other compartment. Through examining alternative surveillance zone sizes, improvements in passive surveillance of domestic pig units, village-wide culling upon case detection, pre-emptive culling of domestic pig units upon nearby wild boar case detection, and environmental sanitation through wild boar carcass clearance, we were able to observe the sometimes subtle, sometimes substantial, alterations in epizootic size and relative host contributions for each compartment. The included strategies were based on what was observed in the Romanian environment. Other commonly employed strategies such as fencing and increasing wild boar hunting pressure were not included in our model, as fencing was out of the Romanian context and though hunting pressure was certainly increased there was no data to inform on that point. However, these

strategies have been recently explored in other models (Picault *et al.*, 2022; Ezanno *et al.*, 2022). Dankwa *et al.* (2022) was able to show that increased hunting pressure with fencing had a more pronounced benefit to reducing both wild boar and domestic pig herd cases over the longer term. However, as this model does not allow for the determination of the source of infection of an infected model unit, we can only conclude overall benefits to the modelled epizootic trajectory. A following step for our model's control strategy assessments would be to include such fencing and hunting abilities, and then observe the effects on relative transmission.

Box 7.1 provides a synthesis of the approach we used to address the research questions and describes the main outcomes of the project.

## 7.2 Impact: Our contribution to the ASF modelling body

With the recent close of the ASF Modelling Challenge, there are now at least six multihost models of ASF that account for domestic-wildlife transmission (Ezanno *et al.*, 2022). Taylor *et al.* (2021) (prior to the ASF Modelling Challenge) developed a model of ASF spread across the European continent that included transmission from free-range, outdoor pigs to wild boar, and examined hunting and fencing effects. Yoo *et al.* (2021), through an ex-post model, elucidated which farms in the 2019 South Korean ASF incursion were likely infected by wild boar. Whereas between-host transmission in Taylor *et al.* (2021) was unidirectional from domestic pigs to wild boar, Yoo *et al.* (2021) utilized unidirectional transmission from wild boar to domestic pigs. Following the publication of the first ASF Modelling Challenge models, bidirectional transmission was now included in the modelling body through the works of Beaunée *et al.* (2022) and Han & Vignes (2022) (pre-publication, as referenced by Ezanno *et al.* (2022)). The model by Dankwa *et al.* (2022) considered unidirectional transmission from wild boar to domestic pigs, while Muñoz *et al.* (2022) did not include mechanistic transmission between hosts but, similar to Yoo *et al.* (2021) modelled the risk of pig farm infection from wild boar case data.

### Box 7.1 | Synthesis of the approach to, and outcomes of, the PhD

- African swine fever is a devastating disease whose outbreaks have grave impacts on all levels of the pig farming industry—from psychosocial distress and livelihood losses to the individual small-scale farmer up through decreases in the national income of affected countries from lost export markets.
- Elucidating the dynamics of how ASF transmits among hosts, both within and between domestic and wildlife compartments, can be accomplished through mathematical models.
- Through a systematic review of the mathematical modelling literature on ASF, we found that none of the existing models accounted for transmission at the domestic-wildlife interface.
- To fill this gap in the ASF modelling body, we developed spatio-temporal, multi-host, stochastic mechanistic simulation model of ASF transmission. Domestic pig herds were represented as either backyard farms at the level of the village or as industrial operations using point locations, while wild boar were represented through a habitat raster of cells using forest coverage as a proxy variable for abundance.
- Using a combination of literature review, approximate Bayesian computation, and manual tuning, the model was able to be parameterized to the on-going epizootic in Romania. Transmission rates (among other parameters) were estimated between domestic pig units (0.16 herds per weeks), from domestic pig units to wild boar cells (0.3 cells per weeks), from cells to domestic pig units (0.8 herds per week), and from cells to cells (0.4 cells per weeks).
- Through capturing the observed epizootic trajectories, our model estimated that approximately 5% of domestic pig unit infections were coming from infected wild boar cells, and 40% of wild boar cell infections were coming from domestic pig units.
- With the observed dynamics replicated, we were then able to explore alternative control strategies: alternative surveillance zone sizes, improving passive surveillance of domestic pig units, village-wide culling upon case detection, pre-emptive culling of domestic pig units upon nearby wild boar case detection, and environmental sanitation through wild boar carcass clearance.
- Village-wide culling (as opposed to single-herd culling) was determined to be the most effective strategy for reducing overall epizootic size, however economic analyses (including cost-benefit analysis) will need to be included to practically inform control strategy decision-making.
- Instituting wild boar carcass removal did not greatly affect overall epizootic size, however it did reduce the relative contribution of transmission from wild boar cells.

Our model, while sharing certain characteristics with these models (such as means of wildlife representation (Beaunée *et al.* (2022)) or explored alternative control strategies related to culling and surveillance zone size (Picault *et al.*, 2022)), stands out by allowing the quantification of the relative contribution of the domestic and wildlife compartments to overall epizootic spread. This information can be used by policy makers to inform resource allocation, as knowing the relative role of a host in a multihost outbreak can assist with targeting of control strategies. Here in Romania, it was estimated that 40% of wild boar cell infections came from domestic pig herds and 5% of domestic pig herds were infected by wild boar cells. While these quantities would ideally be further informed by phylogenetic field studies, the non-zero numbers indicate the need for strategies to address transmission in both compartments. Further, our model showed that for many alternative control strategies, decreases in transmission from one compartment will be offset by relative increases in transmission from the other compartment. With the panzootic genotype II strain of ASF being capable of sustaining itself within a wild boar population outside of domestic pig reinfection (Sauter-Louis, Conraths, *et al.*, 2021), mitigating transmission between host compartments will likely be a critical aspect of achieving full epizootic control in Romania (and any other area rich in backyard swine farming).

Another unique aspect of our model was its full development and parameterization to an on-going epizootic. To our knowledge, this is the first time such a feat was accomplished with a multi-host animal health model (see Chapter 4). This suggests that this methodological approach, combining individual-based and cellular automata models to consider wildlife-livestock transmission, can be developed at a pace sufficient to inform active epizootic scenarios. The use of mathematical modelling to inform decision-making has become standard practice for public health (Kretzschmar, 2020), and with sufficient resource availability it can become an important tool in veterinary public health and outbreak response too.

Through the rapid deployment of a model of an ongoing outbreak, real-time policy support for animal health stakeholders can be a reality. However, our model will still require additional refinement prior to recommending its use for policy support. Foremost, field research that estimates the relative transmission rates between hosts will be essential for validating the predictions of our model. A retrospective analysis of animal movements could help to highlight the main drivers. Additionally, our model only evaluates epidemiological outcomes. The inclusion of economic modules that quantify direct and indirect epizootic costs, along with the costs for the proposed control strategies, will be important for justifying recommendations from model outputs (Barratt *et al.*, 2019). Lastly, our model focuses on epizootic onset, a period whose dynamics are invariably different than those of other epizootic phases (Nunes *et al.*, 2020). To use the model in the present phase of the epizootic,



recalibration to the infected areas and infection patterns would be necessary, though very challenging, to capture the present dynamics. If these aspects of our model are able to be addressed, then we believe its current version will be sufficient for providing decision support to policy makers. Additional refinements, such as including within-village transmission or modelling individual backyard herds rather than entire villages, while potentially beneficial, will come at the expense of computational time and could negate the potential for real-time support (indeed, a backyard-herd model at our current scale will have thousands of additional units).

### 7.3 Future directions

More than just adapting our model to other phases of the Romanian epizootic, our model can be adapted to other countries as well. Such adaptation has been done successfully for other models, including the 2001 UK FMD model by Keeling *et al.* (2001) that was adapted to Denmark (Tildesley & Keeling, 2008), and the DTU-DADS-ASF model by Halasa *et al.* (2016) that was adapted to industrial swine populations in both Denmark (Halasa *et al.*, 2018) and France (Andraud *et al.*, 2019). This endeavor benefits both the modeller and the user. The modeller is able to make wider improvements to their model based on new data availability in the country other than its origin, and for the country of adoption, the existing dynamics in the model can aid local epidemiologists in considering alternative transmission processes that may not yet have been assessed (Dubé *et al.*, 2011). In our case, for adapting our ASF model to France, this could include incorporating swine network movement data that was either not available or not accessible in Romania, along with multiple subtypes of industrial swine operations. However, given that any incursion into the industrial sector has been shown to be detected rapidly with limited spread, the additional computing power, run time and data collection requirements may not outweigh the benefits of a unified model (Andraud *et al.*, 2019, 2022).

As our model did not use an existing modelling platform (e.g. InterSpread Plus, SimInf, or NAADSM) for its development, its translation to another context will require multiple technical and conceptual steps (Harvey *et al.*, 2007; Stevenson *et al.*, 2013; Widgren *et al.*, 2019). Technically, all the relationship matrices including the artificial landscape raster, forest coverage indicators, and distances between domestic pig herd locations will need to be regenerated. More difficult, however, is the conceptual translation. In our model we represent backyard herds through their aggregation to the scale of a village. If we were to adapt our model for the production systems in France that would be-at risk of spillover transmission, we would need to consider a different epidemiological unit for domestic pig herds. Realistically, we would adapt our model units from backyard herds to free-range pig production sites. The economic activity in free-range farms can rival that of traditional industrial operations, and differing greatly in the level of biosecurity per site (i.e. whether the outdoors space is an entire open

pasture or just a yard open to the barn door) (Delsart *et al.*, 2020). The model could then be parameterized by the relative level of biosecurity that would be expected for different free-range herd types, and simulated ASF transmission could be explored. Geographically, we would want to select an area in France with a high density of wild boars together with a known important population of outdoor farms. However, with ASF present in Italy, the southeast of France would be a location to consider investigating the consequences of cross-border introduction and subsequent spread. Results of such simulations could inform stakeholders on the risk of introduction into the domestic compartments, and with the addition of an economic module, could help decide whether preventive culling of herds in the areas surrounding wild boar cases is an option. Alternatively, we could assume an ASF introduction scenario similar to that which occurred in Belgium (a single human-mediated event resulting in infection among wild boar) in a low-density area of pig farms (Claeys & Heymans, 2020). Lastly, we would need to add additional control measures to our model to reflect those that would be employed in the country of adoption.

Fences are a primary management strategy against wild boar (FAO, 2019), and representing this strategy would be necessary for adapting our model to France. Though fencing is an important component of the recommended EU ASF control strategy (European Commission, 2020), there is little literature on its effectiveness (Laguna *et al.*, 2022), though more studies are now examining this method (Han *et al.*, 2022). Both the type of fencing to be used and the objective of the fencing (i.e. exclusion or containment) would need to be known to include this strategy accurately. Multiple types of fencing are available, including both single and double-fencing, electric, and chemical. Chemical fencing—as attempted in Lithuania—had not succeeded in preventing ASF entrance into the country (EFSA *et al.*, 2018). Conversely, in the Czech Republic, a combination of electric and chemical (odour) fencing was constructed around the area of ASF incursion, contributing to the successful elimination of ASF (though not without a few cases detected outside of the fenced area) (EFSA *et al.*, 2018; WOA, 2019a). Additionally, as the incursion occurred in a mostly-urbanized area, existing landscape fragmentation played a key role in limiting transmission and facilitating enclosure of the cases. For adapting our model to an incursion in France by imported wild boar, reactionary fencing around the infected area could be included with our current model structure, though timing of installation would also have to be incorporated.

In the Czech Republic, a 32 km fence was erected around the infected area (EFSA *et al.*, 2018). In our model, wild boar are represented through 25 km<sup>2</sup> hexagonal cells. Fencing around a wild boar cell following detection could be worked into the current model—and would translate as erecting an 18.6 km fence per hexagon—though to make such control simulation realistic we would need to account

for landscape characteristics. For this distance, rapid fencing around one or even two wild boar cells in our model can be considered feasible, based on actions in the Czech Republic. However, as the size of the fenced area scales upward, workforce capabilities will need to be considered to accurately model construction time. Additionally, barriers like lakes, motorways, and unnavigable terrain play an important role in limiting wild animal movements, as was seen in the 2002 outbreak of classical swine fever in France (Pol *et al.*, 2008) and recently for ASF in South Korea (Han *et al.*, 2022). Incorporating these features alongside artificial barriers will be necessary to best model the efficacy of barrier strategies, as recently performed for both French border and internal regions (Salazar *et al.*, 2022). Following these modifications, in addition to the previously recommended inclusion of an economic module for, at minimum, producing a cost-benefit analysis of control strategies, our model could be considered for policy recommendation here in France.

Through having an array of available control strategies represented in our model, it can potentially be used to attempt a control strategy optimization, an approach yet to be done in the ASF modelling field. All previous models of ASF that assessed control strategies did so through comparing a finite set of *a priori* defined interventions, and many control strategies were examined in competition with each other, which is opposed to how they would be actually implemented. For instance, the efficacy of active and passive surveillance for wild boar was considered independently and without the influence of the other in Gervasi *et al.* (2019), when in reality such methods would likely be implemented simultaneously. While comparing strategies is beneficial for identifying a rank-order efficacy of control methods, this structure does not necessarily determine the most effective combination of all available strategies. Future models should be built to identify the optimal contributions of each control method for achieving specific outcomes (e.g. elimination of ASF cases, or minimizing overall economic impact). This can be achieved by using an objective function where the function inputs are the parameters defining the control strategies (e.g. size and duration of the surveillance zones, preventive culling around infected premises, or active detection rate of cases among domestic pigs or wild boar) and the function output is a measure of the epizootic impact (e.g. epidemic size, duration, total cost of the epizootic) (Moore *et al.*, 2010; Rushton *et al.*, 1999). Optimization algorithms can then be used to examine the space of the input parameter values to find which ones minimize the function output (Hauser & McCarthy, 2009; Moore *et al.*, 2010). It is expected that such modelling output will generate more precise information to policy-makers for designing beneficial control strategies.

Economic considerations play a critical role in the adoption of control strategies, with cost-benefit analyses being the standard financial tool for such evaluation (Fasina *et al.*, 2012). However, while cost-benefit analyses can inform control programs or provide “simple” cost estimates for a given

disease (simple meaning they only account for immediate proximal effects, even if the analyses include the complex costs of depopulation, sanitation and repopulation, as done in Halasa, Bøtner, *et al.* (2016a)), they are indeed not adequate to truly guide economic decisions (McInerney *et al.*, 1992). Costs to an individual farmer do not account for the complex longer-term, downstream impacts of disease occurrence, including market shifts, changes in trade relationships, and redistributions in the food processing industry (McInerney *et al.*, 1992). Even with regionalization measures to delineate either risk or presence of ASF and among whom (wild boar or both domestic pigs and wild boar) (Gordejo, 2021), economic effects can be expected from cases among wild boar as well.

Modern economic frameworks account for multiple facets in determining a disease's impact, with the first such framework developed by McInerney *et al.* (1992). Here, he considered both output losses after occurrence of a disease, as well as necessary costs for treatment and preventing reoccurrence. The framework developed by Rushton (2009) to evaluate the overall disease impact further refines direct costs as both visible and invisible losses—such as for culled animals and discarded animal products, and changes in herd management, respectively—as well as considers indirect costs—split into additional costs related to control strategies, and foregone revenue related to trade restrictions and loss of market access (Knight-Jones & Rushton, 2013). Whereas our model could potentially include an economic component for visible direct losses if the necessary expense data was accessible, to capture the economic impact of ASF in Romania or in any other setting, the indirect costs would need to be included as well. Invisible direct losses, such as changes in animal growth or fertility issues, are less applicable to non-chronic conditions however, and likely do not play a significant role in ASF impact. Additionally, economic impacts can vary depending on the stakeholder, such as if the state compensates some but not all of the direct losses experienced by a farmer. Therein, both the state suffers a form of direct loss through providing compensation, but the farmers do as well from receiving inadequate compensation. Trade restrictions will have stakeholder-specific effects too, depending if the perspective is from a farmer, a production organization, a consumer, or the state. Therefore, when an economic module is eventually included in our model, it will be necessary to clearly define the point of view being adopted for defining costs.

A recent scoping review revealed that, as of 2022, there were only six studies which examined the economic impacts of ASF; with both of the only two retrospective studies examining ASF in Nigeria (Casal *et al.*, 2022). Economic analyses of hypothetical outbreaks in industrialized populations have shown that direct losses pale in comparison to losses from exports (at the national level, in Denmark) (Halasa, Bøtner, *et al.*, 2016a). Comparatively, among epizootics in areas with a predominance of smallholder farmers—as in the Philippines and Vietnam—the majority of costs are directly associated

with affected farms and the implementation of control measures (Casal *et al.*, 2022). In Romania, the majority of direct economic losses to farmers are estimated to have come from movements bans on commercial farms, with total losses per sow per affected farm of €250, on average (Bergevoet *et al.*, 2020). A survey of seven Romanian industrial farms indicated roughly 766000 pigs were killed because of overpopulation, with over 7500 sold below normal value (Bergevoet *et al.*, 2020). It is claimed that compensating farmers for these losses as of 2021 has cost the Romanian government over €121 million (Euromeat News, 2021).

To truly ascertain the economic impact of ASF in Romania, in addition to the direct losses that have been partially quantified above, indirect costs will have to be considered as well. Indirect costs are notoriously difficult to estimate, however (Barratt *et al.*, 2019). Among control costs, the surveillance costs per backyard herd and industrial site (including additional workforce, sampling costs, and laboratory costs), costs of culling for backyard herds and industrial sites, and costs for the authorities to enforce movement restrictions would be necessary to obtain. Additionally, for wild boar, the costs of erecting fencing, searching for wild boar carcasses, and providing hunting incentives would also need to be included. Foregone revenue, the primary means of loss among industrialized swine populations, would need to be accounted for among Romania commercial producers (Halasa, Bøtner, *et al.*, 2016a). The lack of export ability will need to be quantified at an industry level, as will the downstream effects of loss of market access. Being barred from desirable trade market hinders the development of commercial farming, and excess swine and swine products sold domestically will drive prices down for consumers at the expense of the producers, which will also need to be accounted for (Knight-Jones & Rushton, 2013). This is an on-going issue in China, where pork prices first hit record highs in 2019 (Beek, 2019), but then inventory liquidation by small and medium producers flooded the market and subsequently prices plummeted (Pig333, 2021). Indeed, the price for live hogs fell by almost 65%. Recent economic assessment of ASF outbreaks China, accounting for losses across all sectors of industry as many are tangentially related to agriculture, has put the total economic losses for a one-year period beginning from August 2018 at almost 1% (0.78%) of China's gross domestic product—an absolutely staggering number (You *et al.*, 2021). Non-agriculture sectors that are linked to the pig production market—such as the medical sector for its reliance on pigs for medications like insulin and heparin—will also need to be factored into economic impact analyses (Barratt *et al.*, 2019). Lastly, should Romania eliminate ASF and achieve ASF-free status again, economics models will have to include the on-going costs of import controls and wildlife surveillance to prevent further incursions (Knight-Jones & Rushton, 2013). Considering all these cost aspects would facilitate a holistic economic assessment of the Romanian situation, which could help guide the Romanian authorities in their own decision processes. Further, the complexity involved in this type of analysis highlights the need for

multidisciplinary collaboration between veterinary epidemiologists and animal health economists, especially in response to the current ASF crisis.

#### 7.4 Reflections

“Self-reflection is the school of wisdom”, wrote the 17<sup>th</sup> century Spanish writer Baltasar Gracián. Similarly, we must reflect upon the past three years of research into mathematical modelling of ASF, in order to better understand not only what was done, but where to and how else to go forward. Here we developed and parameterized a discrete stochastic spatio-temporal mechanistic model of ASF for estimating disease spillover between wild and domestic hosts. There are other means to achieve similar epizootic insights, with phylodynamic approaches—where phylogenetics is coupled with epidemiological data— demonstrating particular promise at elucidating transmission parameters and quantifying spillover events (Guinat *et al.*, 2021). However, choosing to use such methods could be dependent on viral genetic characteristics, and ASFV, being a very large double-stranded DNA virus, may currently limit successes of this approach. Deciding upon whole genome or single-gene approaches, along with identifying if genetic variability can be captured with just a small number of sequences among outbreaks, are current hurdles with such an approach (Fiori *et al.*, 2021; Frias-De-Diego *et al.*, 2021). Indeed, mechanistic approaches are “especially useful in systems where spillover events are infrequent, rarely observed, or hard to differentiate from within-species transmission events” (Cross *et al.*, 2019). However, while our methodology had its benefits, by developing a stochastic model we were reliant on Bayesian methods to estimate our parameters. Likelihoods in our stochastic model, with its high dimensionality, would have been intractable (Stocks *et al.*, 2018). A deterministic approach was considered, however deterministic models inherently assume no randomness in transmission, with all variability in the observed data accounted for as noise (Stocks *et al.*, 2017, 2018). Given the uncertainty in negative parts of our surveillance data, partially-observed Markov process (POMP) models for modelling transmission were considered. However, methods for extending their benefit from strictly time-series data to spatio-temporal data were not yet developed (the R package SpatPOMP for such spatio-temporal POMP inference has only just been developed this previous year (Asfaw *et al.*, 2021)). In the end, our stochastic spatio-temporal hybrid IBM-cellular automata formulation was chosen.

Juxtaposed to alternative model solutions, we are also able to reflect on alternative data scenarios. Indeed, the benefit of transit network data and herd-level coordinate data would have enabled additional levels of detail to be included, that could have resulted in improved representation of the on-the-ground dynamics. Even aggregated backyard herd data (consisting of the number and sizes of herds per village, without explicit location coordinates) could have facilitated further differentiation

between villages. Accessing swine movement data and representing the trade network could make our model more realistic, however network-driven transmission is not the main route for ASF spread in our modelled region, and network topology can have large impacts on transmission dynamics and is outside the scope of this thesis (Shirley & Rushton, 2005). Often, a few individuals (or herds) can be responsible for a large number of contacts (Keeling & Eames, 2005), as was recently determined among French swine herd trading partnerships (Hammami *et al.*, 2022). Lastly—and most importantly regarding the incorporation or exclusion of network transmission—our objective was to ascertain the relative contribution of the wild and domestic compartments to overall ASF spread. Incorporating network transmission would likely have small if any impact on the relative contribution of the different transmission routes, which was relatively well captured through a transmission kernel. That being said, a spatial index would be beneficial to determine the dispersal of ASF spread in regards to the observed data.

Lastly, human behavior plays a central role in diseases transmission (Ferguson, 2007). In Romania, an audit by the European Commission indicated that, among backyard farmers, high levels of non-compliance were observed with regards to requirements for pig identification, registration and movement notifications (European Commission, 2018). Though this precluded the ability to perform contact tracing, permanent road checkpoints were established and hundreds of fines were issued to individuals illegally transporting animals (European Commission, 2018). Still, these illegal transports enabled backyard pigs to enter the national market, and disseminate ASFV across the national landscape (European Commission, 2018). Additionally, though County Prefects were given the ability to mandate preventive culling, strong resistance from backyard farmers beyond the immediate neighbors of an affected farm hindered the ability to enforce such actions (European Commission, 2018; C. Mortasivu, personal communication, 2021). During the epizootic at the end of 2018, a substantial number of animals were illegally moved or slaughtered (Bergeroet *et al.*, 2020). Additionally, farmers were suspected to pre-emptively slaughter their pigs and then freeze the contaminated meat, resulting in the resurgence of ASF many months later in previously recovered villages after when such meat would have been thawed and consumed (C. Mortasivu, personal communication, 2021). While an economic epidemiological approach may capture some of these actions—under the assumption of rational behavior of all individuals—incorporating theories of human behavior from psychological and sociological perspectives will be necessary to capture the complexity of behavioral responses (Bedson *et al.*, 2021). Some behaviors have already been evaluated in ASF models, such as that related to ASF dissemination from emergency pig sales (Costard *et al.*, 2015). In our model, behaviors could potentially be incorporated at the level of the village, to account for reactions to risk communication and community engagement (RCCE) (Bedson *et al.*, 2021).

Here, villages that are exposed to an ASF prevention messaging may be less susceptible to infection, though could potentially also become more infectious in the case of circulating undetected infections (as shown by Costard *et al.* (2015)). Fear of ASF infection in response to infections in nearby villages—that could result in pig movements or pre-emptive slaughter—could also be included in our model. To model trade modulation without a transit network, the kernel function could be modified from the current exponential one to a Gaussian or other alternative formulation, as previously done in HPAI risk assessment (Boender *et al.*, 2007). A knowledge, attitudes, and practices survey of farmers in Ukraine recently elucidated relationships between knowledge gaps in ASF and risky behavioral practices, and also highlighted important regional differences in the areas studied (Muñoz-Gómez *et al.*, 2021). Similarly, further study into the social and behavioral responses of Romanian backyard farmers to ASF would provide data that could be incorporated into future models.

Though much has been done in the conception, development, and application of our model, there is much room for further growth. My recommendation for the first extension of this work would be to represent within-village dynamics. Representing all herds individually would be the ideal solution, but the data does not exist and with over one million herds known to have illegal status (neither reported nor geolocalized), complete geolocalization is but a pipe dream. Alternatively, designing a within-village module that captures the behaviors related to emergency culling, carcass freezing, and carcass thawing, while using a demographic or size-based proxy to estimate the number of backyard herds per village would be a possibility. A more realistic extension would be to refine the wild boar model component, as that is an area of much uncertainty. If forest coverage is to continue to serve as a proxy variable for wild boar abundance, considering an additional cell type of forest-adjacent cells (that are less infectious than adequately-covered cells but not as much as other cells) may better-capture the observed wild boar case data, and should be explored. In addition to better representation of wild boar abundance, wild boar control strategies need to be expanded if we are to better explore the dynamics of control strategies across compartments. Currently, we are only able to account for perfect carcass clearance of a cell. Including fencing and hunting strategies in addition to varying levels of carcass retrieval would allow extension of our model to both other epizootic phases in Romania as well as other environments. The Republic of Korea would be one such environment—and in fact an ideal setting for this—due to the presence of small-holder pig farming, the availability of detailed surveillance data, and the availability of published studies of prior ASF incursions for comparison (Han *et al.*, 2022; Lim *et al.*, 2021; Yoo *et al.*, 2021). Examination of the domestic-wildlife interface dynamic there, through transposition of this model, could serve as such an opportunity to both make these model improvements as well as attempt additional parameterization strategies.



### Box 7.2 | Chapter 7 Key points

- Our model is unique from other ASF models that include the domestic-wildlife interface through mechanistically allowing the quantification of the relative contribution of the domestic and wildlife compartments to overall epizootic spread.
- In addition to including more control strategies such as hunting and fencing, it is recommended that future model versions include an economic module that quantifies direct and indirect epizootic costs, including the costs for implementing the proposed control strategies.
- Accounting for market shifts, changes in trade relationships, and redistributions in the food processing industry is necessary to truly capture the economic effects of an epizootic.
- Representing within-village dynamics would be another important extension of this work, and can be accomplished through a module that captures the behaviors related to emergency culling, carcass freezing, and carcass thawing.
- Forest-adjacent cells—that are less infectious than adequately-covered cells but not as much as other cells—should be considered as a way to potentially better-capture the observed wild boar case data.
- Through including fencing and hunting strategies along with varying levels of carcass retrieval, our model could be extended to other environments. Due to the presence of small-holder pig farming, the availability of detailed surveillance data, and the availability of published studies of prior ASF incursions for comparison, The Republic of Korea would be an ideal country to consider for future developments of this work.

In Romania, where the ASF epizootic is entrenched in both the domestic and wild compartments, novel strategies accounting for transmission between domestic pigs and wild boar, or updated control objectives that consider low level of circulation in the wild compartment, may be necessary. To consider control strategies at the domestic-wildlife interface, additional levels of cooperation among stakeholders will be necessary, as management in one compartment will affect disease dynamics—and correspondingly necessary response measures—in the complimentary compartment. Though some ASF outbreaks have been successfully controlled, the countries that have so far achieved eradication—the Czech Republic and Belgium (and also Greece but from only one case among domestic pigs)—were confronting epizootics exclusively in the wild compartment (Van Goethem, 2021), halting ASFV circulation through near-depopulation of domestic pigs in the areas with wild boar cases (WOAH, 2019a) and aggressive silent culling of wild boar within the first few months of detection in high risk areas (EFSA *et al.*, 2021). These two scenarios seem to be the exception, however, as many other countries with ASF in the wild compartment (e.g. Hungary, Bulgaria, and the Baltic states), did not succeed at achieving control, and it is currently enzootic in that compartment (EFSA *et al.*, 2022). As evidenced in the annual epidemiological analyses of EU Member States by EFSA, successful eradication of ASF enzooticity via wild boar is a “challenging, often unsuccessful task” (EFSA *et al.*, 2022; Gervasi & Guberti, 2022). Among domestic pig farms, recent (within the past year) increasing spread of ASF has been witnessed in both EU Member States (Slovakia, Poland and Romania) and South East Asia (Thailand, Hong Kong, and Malaysia) (DEFRA, 2022; EFSA *et al.*, 2022). Continued improvements in existing management strategies to get ahead of these epizootics is needed, and mathematical models—having a proven track record—can help guide such developments.

There is still much research to be done, as evidenced by the fact that in only the year-and-a-half since the publication of our systematic review, 15 new ASF modelling studies have entered the research sphere (as of 5 August 2022 as indexed via Pubmed). Of note, the creation of economic models that account for costs to both producers and state governments are needed so as to be included in control strategy optimization schemes, to truly allow an algorithmically-optimized approach to ASF management. While ASF has been successfully eradicated from some EU Member States through existing codified strategies, the continued transcontinental spread paints an uncertain future for achieving complete panzootic control. Indeed, current objectives targeting ASF eradication may not be feasible, tenable, cost-effective, or even optimal for some or many of the multitude of nations affected (especially outside of the EU). As the current genotype II strain demonstrates its ability to become entrenched among wild boar populations, and with export losses responsible for the majority

of the economic impact of ASF on a country, a refocus of strategies that account for a nation's net-export profits against the costs of aggressive control measures may be necessary.

Though increasingly realistic simulation models have the potential to play ever-greater roles in the decision processes of policymakers, multisectoral collaboration between epidemiologists, veterinarians, virologists, ecologists, swine farmers, policymakers, and modellers will be essential to maintain an inclusive approach to ASF modelling. Ensuring all parties have aligned objectives against ASF will facilitate a unified approach to confronting this global porcine panzootic, and mathematical models will continue to be able lend their support.

## § V | Bibliography

### 9 | Bibliography

- Agudelo, M. S., Grant, W. E., & Wang, H.-H. (2021). Effects of white-tailed deer habitat use preferences on southern cattle fever tick eradication: Simulating impact on “pasture vacation” strategies. *Parasites & Vectors*, *14*(1), 102. <https://doi.org/10.1186/s13071-021-04590-z>
- Alexander, N. S., Massei, G., & Wint, W. (2016). The European Distribution of *Sus Scrofa*. Model Outputs from the Project Described within the Poster – Where are All the Boars? An Attempt to Gain a Continental Perspective. *Open Health Data*, *4*(1), Article 1. <https://doi.org/10.5334/ohd.24>
- Alonso, C., Borca, M., Dixon, L., Revilla, Y., Rodriguez, F., Escribano, J. M., & ICTV Report ConsortiumYR 2018. (2018). ICTV Virus Taxonomy Profile: Asfarviridae. *Journal of General Virology*, *99*(5), 613–614. <https://doi.org/10.1099/jgv.0.001049>
- Anderson, E. C., Hutchings, G. H., Mukarati, N., & Wilkinson, P. J. (1998). African swine fever virus infection of the bushpig (*Potamochoerus porcus*) and its significance in the epidemiology of the disease. *Veterinary Microbiology*, *62*(1), 1–15. [https://doi.org/10.1016/S0378-1135\(98\)00187-4](https://doi.org/10.1016/S0378-1135(98)00187-4)
- Anderson, R. M., Donnelly, C. A., Ferguson, N. M., Woolhouse, M. E. J., Watt, C. J., Udy, H. J., MaWhinney, S., Dunstan, S. P., Southwood, T. R. E., Wilesmith, J. W., Ryan, J. B. M., Hoinville, L. J., Hillerton, J. E., Austin, A. R., & Wells, G. a. H. (1996). Transmission dynamics and epidemiology of BSE in British cattle. *Nature*, *382*(6594), Article 6594. <https://doi.org/10.1038/382779a0>
- Anderson, R. M., & May, R. M. (1992). *Infectious Diseases of Humans: Dynamics and Control*. OUP Oxford.
- Andraud, M., Bougeard, S., Chesnoiu, T., & Rose, N. (2021). Spatiotemporal clustering and Random Forest models to identify risk factors of African swine fever outbreak in Romania in 2018–2019. *Scientific Reports*, *11*(1), Article 1. <https://doi.org/10.1038/s41598-021-81329-x>
- Andraud, M., Halasa, T., Boklund, A., & Rose, N. (2019). Threat to the French Swine Industry of African Swine Fever: Surveillance, Spread, and Control Perspectives. *Frontiers in Veterinary Science*, *6*, 248. <https://doi.org/10.3389/fvets.2019.00248>
- Andraud, M., Hammami, P., H Hayes, B., A Galvis, J., Vergne, T., Machado, G., & Rose, N. (2022). Modelling African swine fever virus spread in pigs using time-respective network data: Scientific support for decision makers. *Transboundary and Emerging Diseases*, *69*(5), e2132–e2144. <https://doi.org/10.1111/tbed.14550>

- Andronico, A., Courcoul, A., Bronner, A., Scoizec, A., Lebouquin-Leneveu, S., Guinat, C., Paul, M. C., Durand, B., & Cauchemez, S. (2019). Highly pathogenic avian influenza H5N8 in south-west France 2016–2017: A modeling study of control strategies. *Epidemics*, *28*, 100340. <https://doi.org/10.1016/j.epidem.2019.03.006>
- Animal Health Advisory Committee (AHAC). (2021, March 26). *Special control measures for ASF from 21 April 2021*. European Commission Sante G2.
- ANSVSA. (2019, October 24). *Epidemiological Situation of ASF in Romania*. SCOPAFF.
- Arias, M., & Sánchez-Vizcaíno, J. M. (2002). African Swine Fever. In *Trends in Emerging Viral Infections of Swine* (pp. 119–124). John Wiley & Sons, Ltd. <https://doi.org/10.1002/9780470376812.ch4a>
- Arino, J., & van den Driessche, P. (2003a). The Basic Reproduction Number in a Multi-city Compartmental Epidemic Model. In L. Benvenuti, A. De Santis, & L. Farina (Eds.), *Positive Systems* (pp. 135–142). Springer. [https://doi.org/10.1007/978-3-540-44928-7\\_19](https://doi.org/10.1007/978-3-540-44928-7_19)
- Arino, J., & van den Driessche, P. (2003b). A multi-city epidemic model. *Mathematical Population Studies*, *10*(3), 175–193. <https://doi.org/10.1080/08898480306720>
- Asfaw, K., Park, J., Ho, A., King, A. A., & Ionides, E. (2021). *Partially observed Markov processes with spatial structure via the R package spatPomp* (arXiv:2101.01157). arXiv. <https://doi.org/10.48550/arXiv.2101.01157>
- Backer, J. A., Hagens, T. J., van Roermund, H. J. W., & de Jong, M. C. M. (2009). Modelling the effectiveness and risks of vaccination strategies to control classical swine fever epidemics. *Journal of The Royal Society Interface*, *6*(39), 849–861. <https://doi.org/10.1098/rsif.2008.0408>
- Baldacchino, F., Muenworn, V., Desquesnes, M., Desoli, F., Charoenviriyaphap, T., & Duvallet, G. (2013). Transmission of pathogens by Stomoxys flies (Diptera, Muscidae): A review. *Parasite (Paris, France)*, *20*, 26. <https://doi.org/10.1051/parasite/2013026>
- Balmoş, O., Supeanu, A., Tamba, P., Cazan, C., Ionică, A., Ungur, A., Motiu, M., Manita, F., Ancuceanu, B., Bărbuceanu, F., & Mihalca, A. (2021). Entomological survey to study the possible involvement of arthropod vectors in the transmission of African swine fever virus in Romania. *EFSA Supporting Publications*, *18*(3), 6460E. <https://doi.org/10.2903/sp.efsa.2021.EN-6460>
- Barasona, J. A., Gallardo, C., Cadenas-Fernández, E., Jurado, C., Rivera, B., Rodríguez-Bertos, A., Arias, M., & Sánchez-Vizcaíno, J. M. (2019). First Oral Vaccination of Eurasian Wild Boar Against African Swine Fever Virus Genotype II. *Frontiers in Veterinary Science*, *6*, 137. <https://doi.org/10.3389/fvets.2019.00137>
- Barlow, N. D. (1994). Bovine tuberculosis in New Zealand: Epidemiology and models. *Trends in Microbiology*, *2*(4), 119–124. [https://doi.org/10.1016/0966-842x\(94\)90598-3](https://doi.org/10.1016/0966-842x(94)90598-3)

- Barongo, M. B., Bishop, R. P., Fèvre, E. M., Knobel, D. L., & Ssematimba, A. (2016). A Mathematical Model that Simulates Control Options for African Swine Fever Virus (ASFV). *PLOS ONE*, *11*(7), e0158658. <https://doi.org/10.1371/journal.pone.0158658>
- Barongo, M. B., Ståhl, K., Bett, B., Bishop, R. P., Fèvre, E. M., Aliro, T., Okoth, E., Masembe, C., Knobel, D., & Ssematimba, A. (2015). Estimating the Basic Reproductive Number (R0) for African Swine Fever Virus (ASFV) Transmission between Pig Herds in Uganda. *PLOS ONE*, *10*(5), e0125842. <https://doi.org/10.1371/journal.pone.0125842>
- Barratt, A. S., Rich, K. M., Eze, J. I., Porphyre, T., Gunn, G. J., & Stott, A. W. (2019). Framework for Estimating Indirect Costs in Animal Health Using Time Series Analysis. *Frontiers in Veterinary Science*, *6*. <https://www.frontiersin.org/articles/10.3389/fvets.2019.00190>
- Barron, M. C., Tompkins, D. M., Ramsey, D. S. L., & Bosson, M. A. J. (2015). The role of multiple wildlife hosts in the persistence and spread of bovine tuberculosis in New Zealand. *New Zealand Veterinary Journal*, *63 Suppl 1*(sup1), 68–76. <https://doi.org/10.1080/00480169.2014.968229>
- Bauer, A. L., Beauchemin, C. A. A., & Perelson, A. S. (2009). Agent-based modeling of host–pathogen systems: The successes and challenges. *Information Sciences*, *179*(10), 1379–1389. <https://doi.org/10.1016/j.ins.2008.11.012>
- Baysinger, A., & Kogan, L. R. (2022). Mental Health Impact of Mass Depopulation of Swine on Veterinarians During COVID-19 Infrastructure Breakdown. *Frontiers in Veterinary Science*, *9*. <https://www.frontiersin.org/articles/10.3389/fvets.2022.842585>
- Beauchemin, C., Samuel, J., & Tuszynski, J. (2005). A simple cellular automaton model for influenza A viral infections. *Journal of Theoretical Biology*, *232*(2), 223–234. <https://doi.org/10.1016/j.jtbi.2004.08.001>
- Beaunée, G., Deslandes, F., & Vergu, E. (2022). Inferring A.S.F. transmission in domestic pigs and wild boars using a paired model iterative approach. *Epidemics*.
- Bedson, J., Skrip, L. A., Pedi, D., Abramowitz, S., Carter, S., Jalloh, M. F., Funk, S., Gobat, N., Giles-Vernick, T., Chowell, G., de Almeida, J. R., Elessawi, R., Scarpino, S. V., Hammond, R. A., Briand, S., Epstein, J. M., Hébert-Dufresne, L., & Althouse, B. M. (2021). A review and agenda for integrated disease models including social and behavioural factors. *Nature Human Behaviour*, *5*(7), 834–846. <https://doi.org/10.1038/s41562-021-01136-2>
- Beek, V. ter. (2019, September 2). *ASF China: Pork prices soar as future effects become clear*. Pig Progress. <https://www.pigprogress.net/health-nutrition/asf-china-pork-prices-soar-as-future-effects-become-clear/>
- Beltrán-Alcrudo, D., Lubroth, J., Depner, K., & De La Rocque, S. (2008). *African swine fever in the Caucasus* (EMPRES WATCH, p. 8). FAO. <https://www.fao.org/3/aj214e/aj214e.pdf>

- Bergevoet, R. H. M., Hoste, R., Verweij-Novikova, I., Jongeneel, R. A., Gonzalez Martinez, A., & Hennen, W. H. G. J. (2020). *Future of pig production in Romania: Options for governmental policy*. Wageningen Economic Research. [https://scholar.google.com/scholar\\_lookup?title=Future+of+pig+production+in+Romania+%3A+Options+for+governmental+policy&author=Bergevoet%2C+R.H.M.&publication\\_year=2020](https://scholar.google.com/scholar_lookup?title=Future+of+pig+production+in+Romania+%3A+Options+for+governmental+policy&author=Bergevoet%2C+R.H.M.&publication_year=2020)
- Birch, C. P. D., Goddard, A., & Tearne, O. (2018). A new bovine tuberculosis model for England and Wales (BoTMEW) to simulate epidemiology, surveillance and control. *BMC Veterinary Research*, *14*(1), 273. <https://doi.org/10.1186/s12917-018-1595-9>
- Bizouarn, P. (2016). L'éco-épidémiologie—Vers une épidémiologie de la complexité. *médecine/sciences*, *32*(5), Article 5. <https://doi.org/10.1051/medsci/20163205018>
- Blome, S., Gabriel, C., & Beer, M. (2013). Pathogenesis of African swine fever in domestic pigs and European wild boar. *Virus Research*, *173*(1), 122–130. <https://doi.org/10.1016/j.virusres.2012.10.026>
- Blome, S., Gabriel, C., Dietze, K., Breithaupt, A., & Beer, M. (2012). High virulence of African swine fever virus caucasus isolate in European wild boars of all ages. *Emerging Infectious Diseases*, *18*(4), 708. <https://doi.org/10.3201/eid1804.111813>
- Boender, G. J., Hagenaars, T. J., Bouma, A., Nodelijk, G., Elbers, A. R. W., Jong, M. C. M. de, & Boven, M. van. (2007). Risk Maps for the Spread of Highly Pathogenic Avian Influenza in Poultry. *PLOS Computational Biology*, *3*(4), e71. <https://doi.org/10.1371/journal.pcbi.0030071>
- Boinas, F. S., Wilson, A. J., Hutchings, G. H., Martins, C., & Dixon, L. J. (2011). The persistence of African swine fever virus in field-infected *Ornithodoros erraticus* during the ASF endemic period in Portugal. *PloS One*, *6*(5), e20383. <https://doi.org/10.1371/journal.pone.0020383>
- Boklund, A., Dhollander, S., Chesnoiu Vasile, T., Abrahantes, J. C., Bøtner, A., Gogin, A., Gonzalez Villeta, L. C., Gortázar, C., More, S. J., Papanikolaou, A., Roberts, H., Stegeman, A., Ståhl, K., Thulke, H. H., Viltrop, A., Van der Stede, Y., & Mortensen, S. (2020). Risk factors for African swine fever incursion in Romanian domestic farms during 2019. *Scientific Reports*, *10*(1), 10215. <https://doi.org/10.1038/s41598-020-66381-3>
- Boklund, A., Goldbach, S. G., Uttenthal, A., & Alban, L. (2008). Simulating the spread of classical swine fever virus between a hypothetical wild-boar population and domestic pig herds in Denmark. *Preventive Veterinary Medicine*, *85*(3–4), 187–206. <https://doi.org/10.1016/j.prevetmed.2008.01.012>
- Bouchez-Zacria, M., Courcoul, A., & Durand, B. (2018). The Distribution of Bovine Tuberculosis in Cattle Farms Is Linked to Cattle Trade and Badger-Mediated Contact Networks in South-Western

- France, 2007-2015. *Frontiers in Veterinary Science*, 5, 173. <https://doi.org/10.3389/fvets.2018.00173>
- Brauer, F. (2017). Mathematical epidemiology: Past, present, and future. *Infectious Disease Modelling*, 2(2), 113–127. <https://doi.org/10.1016/j.idm.2017.02.001>
- Brookes, V. J., Barrett, T. E., Ward, M. P., Roby, J. A., Hernandez-Jover, M., Cross, E. M., Donnelly, C. M., Barnes, T. S., Wilson, C. S., & Khalfan, S. (2021). A scoping review of African swine fever virus spread between domestic and free-living pigs. *Transboundary and Emerging Diseases*, 68(5), 2643–2656. <https://doi.org/10.1111/tbed.13993>
- Brooks-Pollock, E., & Wood, J. L. N. (2015). Eliminating bovine tuberculosis in cattle and badgers: Insight from a dynamic model. *Proceedings of the Royal Society B: Biological Sciences*, 282(1808), 20150374. <https://doi.org/10.1098/rspb.2015.0374>
- Buhnerkempe, M. G., Roberts, M. G., Dobson, A. P., Heesterbeek, H., Hudson, P. J., & Lloyd-Smith, J. O. (2015). Eight challenges in modelling disease ecology in multi-host, multi-agent systems. *Epidemics*, 10, 26–30. <https://doi.org/10.1016/j.epidem.2014.10.001>
- Busch, F., Haumont, C., Penrith, M.-L., Laddomada, A., Dietze, K., Globig, A., Guberti, V., Zani, L., & Depner, K. (2021). Evidence-Based African Swine Fever Policies: Do We Address Virus and Host Adequately? *Frontiers in Veterinary Science*, 8. <https://www.frontiersin.org/articles/10.3389/fvets.2021.637487>
- Byrom, A. E., Anderson, D. P., Coleman, M., Thomson, C., Cross, M. L., & Pech, R. P. (2015). Assessing Movements of Brushtail Possums (*Trichosurus vulpecula*) in Relation to Depopulated Buffer Zones for the Management of Wildlife Tuberculosis in New Zealand. *PloS One*, 10(12), e0145636. <https://doi.org/10.1371/journal.pone.0145636>
- Cadenas-Fernández, E., Sánchez-Vizcaíno, J. M., Pintore, A., Denurra, D., Cherchi, M., Jurado, C., Vicente, J., & Barasona, J. A. (2019). Free-Ranging Pig and Wild Boar Interactions in an Endemic Area of African Swine Fever. *Frontiers in Veterinary Science*, 6, 376. <https://doi.org/10.3389/fvets.2019.00376>
- Cadenas-Fernández, E., Sánchez-Vizcaíno, J. M., van den Born, E., Kosowska, A., van Kilsdonk, E., Fernández-Pacheco, P., Gallardo, C., Arias, M., & Barasona, J. A. (2021). High Doses of Inactivated African Swine Fever Virus Are Safe, but Do Not Confer Protection against a Virulent Challenge. *Vaccines*, 9(3), 242. <https://doi.org/10.3390/vaccines9030242>
- Carriquiry, M. A., Elobeid, A. E., Hayes, D. J., & Swenson, D. A. (2021). *Impacts of An African Swine Fever Outbreak in the United States: Implications on National and Iowa Agriculture*. Agricultural & Applied Economics Association Annual Meeting.



[https://ageconsearch.umn.edu/record/312921/files/Abstracts\\_21\\_07\\_02\\_14\\_43\\_15\\_42\\_\\_179\\_26\\_209\\_123\\_0.pdf](https://ageconsearch.umn.edu/record/312921/files/Abstracts_21_07_02_14_43_15_42__179_26_209_123_0.pdf)

- Casal, J., Tago, D., Pineda, P., Tabakovski, B., Santos, I., Benigno, C., Huynh, T., Ciaravino, G., & Beltran-Alcrudo, D. (2022). Evaluation of the economic impact of classical and African swine fever epidemics using OutCosT, a new spreadsheet-based tool. *Transboundary and Emerging Diseases*, *n/a(n/a)*. <https://doi.org/10.1111/tbed.14590>
- Casas-Díaz, E., Closa-Sebastià, F., Peris, A., Miño, A., Torrentó, J., Casanovas, R., Marco, I., Lavin, S., Fernández-Llario, P., & Serrano, E. (2013). Recorded dispersal of wild boar (*Sus scrofa*) in Northeast Spain: Implications for disease-monitoring programs. *Wildlife Biology in Practice*, *9*, 19–26. <https://doi.org/10.2461/wbp.2013.ibeun.3>
- Castiglione, F. (2009). Agent Based Modeling and Simulation, Introduction to. In R. A. Meyers (Ed.), *Encyclopedia of Complexity and Systems Science* (pp. 197–200). Springer New York. [https://doi.org/10.1007/978-0-387-30440-3\\_13](https://doi.org/10.1007/978-0-387-30440-3_13)
- Charrier, F., Rossi, S., Jori, F., Maestrini, O., Richomme, C., Casabianca, F., Ducrot, C., Jouve, J., Pavio, N., & Le Potier, M.-F. (2018). Aujeszky's Disease and Hepatitis E Viruses Transmission between Domestic Pigs and Wild Boars in Corsica: Evaluating the Importance of Wild/Domestic Interactions and the Efficacy of Management Measures. *Frontiers in Veterinary Science*, *5*. <https://www.frontiersin.org/articles/10.3389/fvets.2018.00001>
- Chenais, E., Depner, K., Guberti, V., Dietze, K., Viltrop, A., & Ståhl, K. (2019). Epidemiological considerations on African swine fever in Europe 2014–2018. *Porcine Health Management*, *5*(1), 6. <https://doi.org/10.1186/s40813-018-0109-2>
- Claeys, H., & Heymans, J.-F. (2020). *Self-declaration of Belgium's African swine fever-free status in all swine species* (Declaration). WOA. [https://www.woah.org/fileadmin/Home/eng/Animal\\_Health\\_in\\_the\\_World/docs/pdf/Self-declarations/2020\\_12\\_Belgium\\_ASF\\_self-declaration\\_ENG.pdf](https://www.woah.org/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/Self-declarations/2020_12_Belgium_ASF_self-declaration_ENG.pdf)
- Coleman, J. D., & Cooke, M. M. (2001). Mycobacterium bovis infection in wildlife in New Zealand. *Tuberculosis (Edinburgh, Scotland)*, *81*(3), 191–202. <https://doi.org/10.1054/tube.2001.0291>
- Committee on Considerations for the Future of Animal Science Research, Program, S. and T. for S., Affairs, P. and G., Resources, B. on A. and N., Sciences, D. on E. and L., & Council, N. R. (2015). Global Considerations for Animal Agriculture Research. In *Critical Role of Animal Science Research in Food Security and Sustainability*. National Academies Press (US). <https://www.ncbi.nlm.nih.gov/books/NBK285723/>

- Cosentino, C., Vescio, B., & Amato, F. (2013). Cellular Automata. In W. Dubitzky, O. Wolkenhauer, K.-H. Cho, & H. Yokota (Eds.), *Encyclopedia of Systems Biology* (pp. 381–385). Springer. [https://doi.org/10.1007/978-1-4419-9863-7\\_989](https://doi.org/10.1007/978-1-4419-9863-7_989)
- Cosgrove, M. K., O'Brien, D. J., & Ramsey, D. S. L. (2018). Baiting and Feeding Revisited: Modeling Factors Influencing Transmission of Tuberculosis Among Deer and to Cattle. *Frontiers in Veterinary Science*, *5*, 306. <https://doi.org/10.3389/fvets.2018.00306>
- Costard, S., Mur, L., Lubroth, J., Sanchez-Vizcaino, J. M., & Pfeiffer, D. U. (2013). Epidemiology of African swine fever virus. *Virus Research*, *173*(1), 191–197. <https://doi.org/10.1016/j.virusres.2012.10.030>
- Costard, S., Wieland, B., de Glanville, W., Jori, F., Rowlands, R., Vosloo, W., Roger, F., Pfeiffer, D. U., & Dixon, L. K. (2009). African swine fever: How can global spread be prevented? *Philosophical Transactions of the Royal Society B: Biological Sciences*, *364*(1530), 2683–2696. <https://doi.org/10.1098/rstb.2009.0098>
- Costard, S., Zagmutt, F. J., Porphyre, T., & Pfeiffer, D. U. (2015). Small-scale pig farmers' behavior, silent release of African swine fever virus and consequences for disease spread. *Scientific Reports*, *5*(1), Article 1. <https://doi.org/10.1038/srep17074>
- Council of the European Union. (2002). Council Directive 2002/60/EC of 27 June 2002 laying down specific provisions for the control of African swine fever and amending Directive 92/119/EEC as regards Teschen disease and African swine fever. *Off. J. Eur. Union L*, *192*, 27–46.
- Cowled, B., & Garner, G. (2008). A review of geospatial and ecological factors affecting disease spread in wild pigs: Considerations for models of foot-and-mouth disease spread. *PREVENTIVE VETERINARY MEDICINE*, *87*(3–4), 197–212. <https://doi.org/10.1016/j.prevetmed.2008.03.012>
- Craft, M. E. (2015). Infectious disease transmission and contact networks in wildlife and livestock. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *370*(1669), 20140107. <https://doi.org/10.1098/rstb.2014.0107>
- Croft, S., Massei, G., Smith, G. C., Fouracre, D., & Aegerter, J. N. (2020). Modelling Spatial and Temporal Patterns of African Swine Fever in an Isolated Wild Boar Population to Support Decision-Making. *Frontiers in Veterinary Science*, *7*. <https://www.frontiersin.org/articles/10.3389/fvets.2020.00154>
- Cross, P. C., Creech, T. G., Ebinger, M. R., Heisey, D. M., Irvine, K. M., & Creel, S. (2012). Wildlife contact analysis: Emerging methods, questions, and challenges. *Behavioral Ecology and Sociobiology*, *66*(10), 1437–1447. <https://doi.org/10.1007/s00265-012-1376-6>
- Cross, P. C., Prosser, D. J., Ramey, A. M., Hanks, E. M., & Pepin, K. M. (2019). Confronting models with data: The challenges of estimating disease spillover. *Philosophical Transactions of the Royal*

- Society of London. Series B, Biological Sciences*, 374(1782), 20180435.  
<https://doi.org/10.1098/rstb.2018.0435>
- Cwynar, P., Stojkov, J., & Wlazlak, K. (2019). African Swine Fever Status in Europe. *Viruses*, 11(4), Article 4. <https://doi.org/10.3390/v11040310>
- Dankwa, E. A., Lambert, S., Hayes, S., Thompson, R. N., & Donnelly, C. A. (2022). Stochastic modelling of African swine fever in wild boar and domestic pigs: Epidemic forecasting and comparison of disease management strategies. *Epidemics*, 40, 100622. <https://doi.org/10.1016/j.epidem.2022.100622>
- Danzetta, M. L., Marenzoni, M. L., Iannetti, S., Tizzani, P., Calistri, P., & Feliziani, F. (2020). African Swine Fever: Lessons to Learn From Past Eradication Experiences. A Systematic Review. *Frontiers in Veterinary Science*, 7. <https://www.frontiersin.org/article/10.3389/fvets.2020.00296>
- De Tray, D. E. (1957). African swine fever in wart hogs (*Phacochoerus aethiopicus*). *Journal of the American Veterinary Medical Association*, 130(12), 537–540.
- Dee, S. A., Bauermann, F. V., Niederwerder, M. C., Singrey, A., Clement, T., de Lima, M., Long, C., Patterson, G., Sheahan, M. A., Stoian, A. M. M., Petrovan, V., Jones, C. K., De Jong, J., Ji, J., Spronk, G. D., Minion, L., Christopher-Hennings, J., Zimmerman, J. J., Rowland, R. R. R., ... Diel, D. G. (2018). Survival of viral pathogens in animal feed ingredients under transboundary shipping models. *PLoS One*, 13(3), e0194509. <https://doi.org/10.1371/journal.pone.0194509>
- DEFRA. (2017). *African Swine Fever in the Czech Republic* (African Swine Fever in Pigs in Central and Eastern Europe, p. 3) [Preliminary Outbreak Assessment]. [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/623618/asf-czech-republic.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/623618/asf-czech-republic.pdf)
- DEFRA. (2021). *African swine fever in Eastern Europe and Germany* (Updated Outbreak Assessment No. 23; Advice Services - International Disease Monitoring).
- DEFRA. (2022). *Updated Outbreak Assessment #23* (No. 23; p. 5).
- Delsart, M., Pol, F., Dufour, B., Rose, N., & Fablet, C. (2020). Pig Farming in Alternative Systems: Strengths and Challenges in Terms of Animal Welfare, Biosecurity, Animal Health and Pork Safety. *Agriculture*, 10(7), 261. <https://doi.org/10.3390/agriculture10070261>
- Di Stefano, B., Fuks, H., & Lawniczak, A. T. (2000). Object-oriented implementation of CA/LGCA modelling applied to the spread of epidemics. *2000 Canadian Conference on Electrical and Computer Engineering. Conference Proceedings. Navigating to a New Era (Cat. No.00TH8492)*, 1, 26–31 vol.1. <https://doi.org/10.1109/CCECE.2000.849664>

- Dixon, L. K., Chapman, D. A. G., Netherton, C. L., & Upton, C. (2013). African swine fever virus replication and genomics. *Virus Research*, 173(1), 3–14. <https://doi.org/10.1016/j.virusres.2012.10.020>
- Dixon, L. K., Stahl, K., Jori, F., Vial, L., & Pfeiffer, D. U. (2020). African Swine Fever Epidemiology and Control. *Annual Review of Animal Biosciences*, 8, 221–246. <https://doi.org/10.1146/annurev-animal-021419-083741>
- Donnelly, C. A., & Nouvellet, P. (2013). The contribution of badgers to confirmed tuberculosis in cattle in high-incidence areas in England. *PLoS Currents*, 5, ecurrents.outbreaks.097a904d3f3619db2fe78d24bc776098. <https://doi.org/10.1371/currents.outbreaks.097a904d3f3619db2fe78d24bc776098>
- Donnelly, C. A., & Hone, J. (2010). Is There an Association between Levels of Bovine Tuberculosis in Cattle Herds and Badgers? *Statistical Communications in Infectious Diseases*, 2. <https://doi.org/10.2202/1948-4690.1000>
- Doran, R. J., & Laffan, S. W. (2005). Simulating the spatial dynamics of foot and mouth disease outbreaks in feral pigs and livestock in Queensland, Australia, using a susceptible-infected-recovered cellular automata model. *Preventive Veterinary Medicine*, 70(1–2), 133–152. <https://doi.org/10.1016/j.prevetmed.2005.03.002>
- Dubé, C., Sánchez, J., & Reeves, A. (2011). Adapting existing models of highly contagious diseases to countries other than their country of origin. *Revue Scientifique et Technique (International Office of Epizootics)*, 30, 581–589. <https://doi.org/10.20506/rst.30.2.2061>
- EFSA, Anette, B., Anette, B., Theodora, C. V., Klaus, D., Daniel, D., Vittorio, G., Georgina, H., Daniela, K., Annick, L., Aleksandra, M., Simon, M., Edvins, O., Sasa, O., Helen, R., Mihaela, S., Karl, S., Hans-Hermann, T., Grigaliuniene, V., ... Christian, G. S. (2020). Epidemiological analyses of African swine fever in the European Union (November 2018 to October 2019). *EFSA Journal*, 18(1), e05996. <https://doi.org/10.2903/j.efsa.2020.5996>
- EFSA, Baños, J. V., Boklund, A., Gogin, A., Gortázar, C., Guberti, V., Helyes, G., Kantere, M., Korytarova, D., Linden, A., Masiulis, M., Miteva, A., Neghirla, I., Ojševiskis, E., Ostojic, S., Petr, S., Staubach, C., Thulke, H.-H., Viltrop, A., ... Ståhl, K. (2022). Epidemiological analyses of African swine fever in the European Union (September 2020 to August 2021). *EFSA Journal*, 20(5), e07290. <https://doi.org/10.2903/j.efsa.2022.7290>
- EFSA, Depner, K., Gortazar, C., Guberti, V., Masiulis, M., More, S., Ojševiskis, E., Thulke, H.-H., Viltrop, A., Woźniakowski, G., Cortiñas Abrahantes, J., Gogin, A., Verdonck, F., & Dhollander, S. (2017). Epidemiological analyses of African swine fever in the Baltic States and Poland. *EFSA Journal*, 15(11), e05068. <https://doi.org/10.2903/j.efsa.2017.5068>

- EFSA, Desmecht, D., Gerbier, G., Gortázar Schmidt, C., Grigaliuniene, V., Helyes, G., Kantere, M., Korytarova, D., Linden, A., Miteva, A., Neghirla, I., Olsevskis, E., Ostojic, S., Petit, T., Staubach, C., Thulke, H.-H., Viltrop, A., Richard, W., Wozniakowski, G., ... Ståhl, K. (2021). Epidemiological analysis of African swine fever in the European Union (September 2019 to August 2020). *EFSA Journal*, *19*(5), e06572. <https://doi.org/10.2903/j.efsa.2021.6572>
- EFSA, More, S., Miranda, M. A., Bicout, D., Bøtner, A., Butterworth, A., Calistri, P., Edwards, S., Garin-Bastuji, B., Good, M., Michel, V., Raj, M., Nielsen, S. S., Sihvonen, L., Spoolder, H., Stegeman, J. A., Velarde, A., Willeberg, P., Winckler, C., ... Gortázar Schmidt, C. (2018). African swine fever in wild boar. *EFSA Journal. European Food Safety Authority*, *16*(7), e05344. <https://doi.org/10.2903/j.efsa.2018.5344>
- EFSA Panel on Animal Health and Welfare. (2010). Scientific Opinion on the Role of Tick Vectors in the Epidemiology of Crimean-Congo Hemorrhagic Fever and African Swine Fever in Eurasia. *EFSA Journal*, *8*(8), 1703. <https://doi.org/10.2903/j.efsa.2010.1703>
- EFSA Panel on Animal Health and Welfare (EFSA AHAW Panel), Nielsen, S. S., Alvarez, J., Bicout, D. J., Calistri, P., Depner, K., Drewe, J. A., Garin-Bastuji, B., Gonzales Rojas, J. L., Gortázar Schmidt, C., Herskin, M., Michel, V., Miranda Chueca, M. Á., Pasquali, P., Roberts, H. C., Sihvonen, L. H., Spoolder, H., Ståhl, K., Velarde, A., ... Aznar, I. (2021). Scientific Opinion on the assessment of the control measures of the category A diseases of Animal Health Law: African Swine Fever. *EFSA Journal*, *19*(1), e06402. <https://doi.org/10.2903/j.efsa.2021.6402>
- ENETWILD-consortium, Acevedo, P., Croft, S., Smith, G., & Vicente, J. (2019). ENETwild modelling of wild boar distribution and abundance: Initial model output based on hunting data and update of occurrence-based models. *EFSA Supporting Publications*, *16*(5), 1629E. <https://doi.org/10.2903/sp.efsa.2019.EN-1629>
- Erdős, P., & Rényi, A. (1959). On random graphs I. *Publicationes Mathematicae (Debrecen)*, *6*, 290–297.
- EuroMeat News. (2021, April 13). *ASF crisis in Romania to keep the pig farming under pressure*. EuroMeatNews. <https://euromeatnews.com/Article-ASF-crisis-in-Romania-to-keep-the-pig-farming-under-pressure/4603>
- European Commission. (2014). *Guidelines on surveillance and control of African swine fever in feral pigs and preventive measures for pig holdings (SANCO/7138/2013)*. Health And Consumers Directorate-General.
- European Commission. (2018). *Final report of an audit carried out in Romania from 17 October 2018 to 25 October 2018 in order to evaluate the implementation of animal health controls in*

- relation to African swine fever* (DG(SANTE) 2018-6700). Directorate-General for health and food safety.
- European Commission. (2020). *Strategic approach to the management of African Swine Fever for the EU* (SANTE/7113/2015 – Rev 12). Directorate-General for health and food safety.
- European Commission. (2022). *EU ASF zoning measures* [Map].
- European Food Safety Authority (EFSA), Boklund, A., Cay, B., Depner, K., Földi, Z., Guberti, V., Masiulis, M., Miteva, A., More, S., Olsevskis, E., Šatrán, P., Spiridon, M., Stahl, K., Thulke, H.-H., Viltrop, A., Wozniakowski, G., Broglia, A., Cortinas Abrahantes, J., Dhollander, S., ... Gortázar, C. (2018). Epidemiological analyses of African swine fever in the European Union (November 2017 until November 2018). *EFSA Journal. European Food Safety Authority*, 16(11), e05494. <https://doi.org/10.2903/j.efsa.2018.5494>
- Eustace Montgomery, R. (1921). On A Form of Swine Fever Occurring in British East Africa (Kenya Colony). *Journal of Comparative Pathology and Therapeutics*, 34, 159–191. [https://doi.org/10.1016/S0368-1742\(21\)80031-4](https://doi.org/10.1016/S0368-1742(21)80031-4)
- Ezanno, P., Picault, S., Bareille, S., Beaunée, G., Boender, G. J., Dankwa, E. A., Deslandes, F., Donnelly, C. A., Hagensars, T. J., Hayes, S., Jori, F., Lambert, S., Mancini, M., Munoz, F., Pleydell, D. R. J., Thompson, R. N., Vergu, E., Vignes, M., & Vergne, T. (2022). The African swine fever modelling challenge: Model comparison and lessons learnt. *Epidemics*, 40, 100615. <https://doi.org/10.1016/j.epidem.2022.100615>
- FAO. (2009). Preparation of African swine fever contingency plans. In M.-L. Penrith, V. Guberti, K. Depner, & J. Lubroth, *FAO Animal Production and Health manual* (p. 86). FAO. <https://www.fao.org/documents/card/66/c/d91e4185-2270-559c-9539-76db35b85d66>
- FAO. (2012). *Threat of African Swine Fever spread in Eastern Europe: Urgent need for international collaboration*. <https://www.fao.org/europe/events/detail-events/en/c/272989/>
- FAO. (2014). *Sources of Meat*. FAO. [https://www.fao.org/ag/againfo/themes/en/meat/backgr\\_sources.html](https://www.fao.org/ag/againfo/themes/en/meat/backgr_sources.html)
- FAO. (2019). African swine fever in wild boar: Ecology and biosecurity. In V. Guberti, S. Khomenko, M. Masiulis, & S. Kerba, *FAO Animal Production and Health Manual*. FAO, OIE and EC. <https://doi.org/10.4060/CA5987EN>
- Fasina, F. O., Lazarus, D. D., Spencer, B. T., Makinde, A. A., & Bastos, A. D. S. (2012). Cost implications of African swine fever in smallholder farrow-to-finish units: Economic benefits of disease prevention through biosecurity. *Transboundary and Emerging Diseases*, 59(3), 244–255. <https://doi.org/10.1111/j.1865-1682.2011.01261.x>

- Faverjon, C., Meyer, A., Howden, K., Long, K., Peters, L., & Cameron, A. (2021). Risk-based early detection system of African Swine Fever using mortality thresholds. *Transboundary and Emerging Diseases*, *68*(3), 1151–1161. <https://doi.org/10.1111/tbed.13765>
- Ferguson, N. M., (2007). Capturing human behaviour. *Nature*, *446*(7137), Article 7137. <https://doi.org/10.1038/446733a>
- Ferguson, N. M., Donnelly, C. A., & Anderson, R. M. (2001). The foot-and-mouth epidemic in Great Britain: Pattern of spread and impact of interventions. *Science (New York, N.Y.)*, *292*(5519), 1155–1160. <https://doi.org/10.1126/science.1061020>
- Ferguson, N. M., Ghani, A. C., Donnelly, C. A., Denny, G. O., & Anderson, R. M. (1998). BSE in Northern Ireland: Epidemiological patterns past, present and future. *Proceedings of the Royal Society of London. Series B: Biological Sciences*, *265*(1396), 545–554. <https://doi.org/10.1098/rspb.1998.0329>
- Ferreira, H. C. de C., Backer, J. A., Weesendorp, E., Klinkenberg, D., Stegeman, J. A., & Loeffen, W. L. A. (2013). Transmission rate of African swine fever virus under experimental conditions. *Veterinary Microbiology*, *165*(3), 296–304. <https://doi.org/10.1016/j.vetmic.2013.03.026>
- Ferreira, H. C. de C., Weesendorp, E., Elbers, A. R. W., Bouma, A., Quak, S., Stegeman, J. A., & Loeffen, W. L. A. (2012). African swine fever virus excretion patterns in persistently infected animals: A quantitative approach. *Veterinary Microbiology*, *160*(3), 327–340. <https://doi.org/10.1016/j.vetmic.2012.06.025>
- Fiori, M. S., Sanna, D., Scarpa, F., Floris, M., Di Nardo, A., Ferretti, L., Loi, F., Cappai, S., Sechi, A. M., Angioi, P. P., Zinellu, S., Sirica, R., Evangelista, E., Casu, M., Franzoni, G., Oggiano, A., & Dei Giudici, S. (2021). A Deeper Insight into Evolutionary Patterns and Phylogenetic History of ASFV Epidemics in Sardinia (Italy) through Extensive Genomic Sequencing. *Viruses*, *13*(10), 1994. <https://doi.org/10.3390/v13101994>
- Fischer, M., Hühr, J., Blome, S., Conraths, F. J., & Probst, C. (2020). Stability of African Swine Fever Virus in Carcasses of Domestic Pigs and Wild Boar Experimentally Infected with the ASFV “Estonia 2014” Isolate. *Viruses*, *12*(10), 1118. <https://doi.org/10.3390/v12101118>
- Frant, M., Woźniakowski, G., & Pejsak, Z. (2017). African Swine Fever (ASF) and Ticks. No Risk of Tick-mediated ASF Spread in Poland and Baltic States. *Journal of Veterinary Research*, *61*(4), 375–380. <https://doi.org/10.1515/jvetres-2017-0055>
- Frias-De-Diego, A., Jara, M., Pecoraro, B. M., & Crisci, E. (2021). Whole Genome or Single Genes? A Phylodynamic and Bibliometric Analysis of PRRSV. *Frontiers in Veterinary Science*, *8*. <https://www.frontiersin.org/articles/10.3389/fvets.2021.658512>

- Gabriel, C., Blome, S., Malogolovkin, A., Parilov, S., Kolbasov, D., Teifke, J. P., & Beer, M. (2011). Characterization of African swine fever virus Caucasus isolate in European wild boars. *Emerging Infectious Diseases*, *17*(12), 2342–2345. <https://doi.org/10.3201/eid1712.110430>
- Gallardo, C., Soler, A., Nieto, R., Cano, C., Pelayo, V., Sánchez, M. A., Pridotkas, G., Fernandez-Pinero, J., Briones, V., & Arias, M. (2017). Experimental Infection of Domestic Pigs with African Swine Fever Virus Lithuania 2014 Genotype II Field Isolate. *Transboundary and Emerging Diseases*, *64*(1), 300–304. <https://doi.org/10.1111/tbed.12346>
- Gallardo, C., Soler, A., Nieto, R., Sánchez, M. A., Martins, C., Pelayo, V., Carrascosa, A., Revilla, Y., Simón, A., Briones, V., Sánchez-Vizcaíno, J. M., & Arias, M. (2015). Experimental Transmission of African Swine Fever (ASF) Low Virulent Isolate NH/P68 by Surviving Pigs. *Transboundary and Emerging Diseases*, *62*(6), 612–622. <https://doi.org/10.1111/tbed.12431>
- Gavier-Widén, D., Ståhl, K., & Dixon, L. (2020). No hasty solutions for African swine fever. *Science (New York, N.Y.)*, *367*(6478), 622–624. <https://doi.org/10.1126/science.aaz8590>
- Gavinelli, A., Forcella, S., & Van Goethem, B. (2020). *WOAH Bulletin: Prevention and control measures for ASF*. <https://bulletin.woah.org/?panorama=02-2-5-2020-1-ec>
- Ge, S., Li, J., Fan, X., Liu, F., Li, L., Wang, Q., Ren, W., Bao, J., Liu, C., Wang, H., Liu, Y., Zhang, Y., Xu, T., Wu, X., & Wang, Z. (2018). Molecular Characterization of African Swine Fever Virus, China, 2018. *Emerging Infectious Diseases*, *24*(11), 2131–2133. <https://doi.org/10.3201/eid2411.181274>
- Gervasi, V., & Guberti, V. (2021). African swine fever endemic persistence in wild boar populations: Key mechanisms explored through modelling. *Transboundary and Emerging Diseases*, *68*(5), 2812–2825. <https://doi.org/10.1111/tbed.14194>
- Gervasi, V., & Guberti, V. (2022). Combining hunting and intensive carcass removal to eradicate African swine fever from wild boar populations. *Preventive Veterinary Medicine*, *203*, 105633. <https://doi.org/10.1016/j.prevetmed.2022.105633>
- Gervasi, V., Marcon, A., Bellini, S., & Guberti, V. (2019). Evaluation of the Efficiency of Active and Passive Surveillance in the Detection of African Swine Fever in Wild Boar. *Veterinary Sciences*, *7*(1), E5. <https://doi.org/10.3390/vetsci7010005>
- Gilbert, A. T., Fooks, A. R., Hayman, D. T. S., Horton, D. L., Müller, T., Plowright, R., Peel, A. J., Bowen, R., Wood, J. L. N., Mills, J., Cunningham, A. A., & Rupprecht, C. E. (2013). Deciphering serology to understand the ecology of infectious diseases in wildlife. *EcoHealth*, *10*(3), 298–313. <https://doi.org/10.1007/s10393-013-0856-0>



- Gogin, A., Gerasimov, V., Malogolovkin, A., & Kolbasov, D. (2013). African swine fever in the North Caucasus region and the Russian Federation in years 2007–2012. *Virus Research*, 173(1), 198–203. <https://doi.org/10.1016/j.virusres.2012.12.007>
- Gordejo, F. R. (2021, March 23). *African swine fever: Tools to ensure safe trade*. Thematic session on African swine fever, WTO/SPS committee, DG Sante, European Commission.
- Gortázar, C., Ferroglio, E., Höfle, U., Frölich, K., & Vicente, J. (2007). Diseases shared between wildlife and livestock: A European perspective. *European Journal of Wildlife Research*, 53(4), 241. <https://doi.org/10.1007/s10344-007-0098-y>
- Grassly, N. C., & Fraser, C. (2008). Mathematical models of infectious disease transmission. *Nature Reviews Microbiology*, 6(6), Article 6. <https://doi.org/10.1038/nrmicro1845>
- Green, L. E., & Medley, G. F. (2002). Mathematical modelling of the foot and mouth disease epidemic of 2001: Strengths and weaknesses. *Research in Veterinary Science*, 73(3), 201–205. [https://doi.org/10.1016/s0034-5288\(02\)00106-6](https://doi.org/10.1016/s0034-5288(02)00106-6)
- Greenman, J. V., & Hoyle, A. S. (2008). Exclusion of generalist pathogens in multihost communities. *The American Naturalist*, 172(4), 576–584. <https://doi.org/10.1086/590967>
- Greig, A. (1972). Pathogenesis of African swine fever in pigs naturally exposed to the disease. *Journal of Comparative Pathology*, 82(1), 73–79. [https://doi.org/10.1016/0021-9975\(72\)90028-x](https://doi.org/10.1016/0021-9975(72)90028-x)
- Grimm, V., Berger, U., Bastiansen, F., Eliassen, S., Ginot, V., Giske, J., Goss-Custard, J., Grand, T., Heinz, S. K., Huse, G., Huth, A., Jepsen, J. U., Jørgensen, C., Mooij, W. M., Müller, B., Pe'er, G., Piou, C., Railsback, S. F., Robbins, A. M., ... DeAngelis, D. L. (2006). A standard protocol for describing individual-based and agent-based models. *Ecological Modelling*, 198(1), 115–126. <https://doi.org/10.1016/j.ecolmodel.2006.04.023>
- Guinat, C., Gogin, A., Blome, S., Keil, G., Pollin, R., Pfeiffer, D. U., & Dixon, L. (2016). Transmission routes of African swine fever virus to domestic pigs: Current knowledge and future research directions. *The Veterinary Record*, 178(11), 262–267. <https://doi.org/10.1136/vr.103593>
- Guinat, C., Gubbins, S., Vergne, T., Gonzales, J. L., Dixon, L., & Pfeiffer, D. U. (2016). Experimental pig-to-pig transmission dynamics for African swine fever virus, Georgia 2007/1 strain. *Epidemiology & Infection*, 144(1), 25–34. <https://doi.org/10.1017/S0950268815000862>
- Guinat, C., Porphyre, T., Gogin, A., Dixon, L., Pfeiffer, D. U., & Gubbins, S. (2018). Inferring within-herd transmission parameters for African swine fever virus using mortality data from outbreaks in the Russian Federation. *Transboundary and Emerging Diseases*, 65(2), e264–e271. <https://doi.org/10.1111/tbed.12748>
- Guinat, C., Reis, A. L., Netherton, C. L., Goatley, L., Pfeiffer, D. U., & Dixon, L. (2014). Dynamics of African swine fever virus shedding and excretion in domestic pigs infected by intramuscular

- inoculation and contact transmission. *Veterinary Research*, 45(1), 93. <https://doi.org/10.1186/s13567-014-0093-8>
- Guinat, C., Vergne, T., Kocher, A., Chakraborty, D., Paul, M. C., Ducatez, M., & Stadler, T. (2021). What can phylodynamics bring to animal health research? *Trends in Ecology & Evolution*, 36(9), 837–847. <https://doi.org/10.1016/j.tree.2021.04.013>
- Guisan, A., Zimmermann, N. E., & Thuiller, W. (Eds.). (2017). Assumptions Behind Habitat Suitability Models. In *Habitat Suitability and Distribution Models: With Applications in R* (pp. 52–58). Cambridge University Press. <https://doi.org/10.1017/9781139028271.009>
- Gulenkin, V. M., Korennoy, F. I., Karaulov, A. K., & Dudnikov, S. A. (2011). Cartographical analysis of African swine fever outbreaks in the territory of the Russian Federation and computer modeling of the basic reproduction ratio. *Preventive Veterinary Medicine*, 102(3), 167–174. <https://doi.org/10.1016/j.prevetmed.2011.07.004>
- Halasa, T., Boklund, A., Bøtner, A., Mortensen, S., & Kjær, L. J. (2019). Simulation of transmission and persistence of African swine fever in wild boar in Denmark. *Preventive Veterinary Medicine*, 167, 68–79. <https://doi.org/10.1016/j.prevetmed.2019.03.028>
- Halasa, T., Boklund, A., Bøtner, A., Toft, N., & Thulke, H.-H. (2016). Simulation of Spread of African Swine Fever, Including the Effects of Residues from Dead Animals. *Frontiers in Veterinary Science*, 3. <https://www.frontiersin.org/articles/10.3389/fvets.2016.00006>
- Halasa, T., Bøtner, A., Mortensen, S., Christensen, H., Toft, N., & Boklund, A. (2016a). Simulating the epidemiological and economic effects of an African swine fever epidemic in industrialized swine populations. *Veterinary Microbiology*, 193, 7–16. <https://doi.org/10.1016/j.vetmic.2016.08.004>
- Halasa, T., Bøtner, A., Mortensen, S., Christensen, H., Toft, N., & Boklund, A. (2016b). Control of African swine fever epidemics in industrialized swine populations. *Veterinary Microbiology*, 197, 142–150. <https://doi.org/10.1016/j.vetmic.2016.11.023>
- Halasa, T., Bøtner, A., Mortensen, S., Christensen, H., Wulff, S. B., & Boklund, A. (2018). Modeling the Effects of Duration and Size of the Control Zones on the Consequences of a Hypothetical African Swine Fever Epidemic in Denmark. *Frontiers in Veterinary Science*, 5, 49. <https://doi.org/10.3389/fvets.2018.00049>
- Hall, M. J., Ng, A., Ursano, R. J., Holloway, H., Fullerton, C., & Casper, J. (2004). Psychological impact of the animal-human bond in disaster preparedness and response. *Journal of Psychiatric Practice*, 10(6), 368–374. <https://doi.org/10.1097/00131746-200411000-00005>
- Hamer, W. H. (1906). Epidemic diseases in England—The evidence of variability and of persistence. *The Lancet*, 167, 733–738.

- Hammami, P., Widgren, S., Grosbois, V., Apolloni, A., Rose, N., & Andraud, M. (2022). Complex network analysis to understand trading partnership in French swine production. *PLOS ONE*, *17*(4), e0266457. <https://doi.org/10.1371/journal.pone.0266457>
- Han, J. H., & Vignes, M. (2022). A stochastic compartmental grid-based model for the Merry Island 2020 ASF outbreak Challenge. *Epidemics*.
- Han, J.-H., Yoo, D.-S., Pak, S.-I., & Kim, E.-T. (2022). Understanding the transmission of African swine fever in wild boars of South Korea: A simulation study for parameter estimation. *Transboundary and Emerging Diseases*, *69*(4), e1101–e1112. <https://doi.org/10.1111/tbed.14403>
- Hargrove, J. W., Ouifki, R., Kajunguri, D., Vale, G. A., & Torr, S. J. (2012). Modeling the control of trypanosomiasis using trypanocides or insecticide-treated livestock. *PLoS Neglected Tropical Diseases*, *6*(5), e1615. <https://doi.org/10.1371/journal.pntd.0001615>
- Harvey, N., Reeves, A., Schoenbaum, M. A., Zagmutt-Vergara, F. J., Dubé, C., Hill, A. E., Corso, B. A., McNab, W. B., Cartwright, C. I., & Salman, M. D. (2007). The North American Animal Disease Spread Model: A simulation model to assist decision making in evaluating animal disease incursions. *Preventive Veterinary Medicine*, *82*(3–4), 176–197. <https://doi.org/10.1016/j.prevetmed.2007.05.019>
- Hauser, C. E., & McCarthy, M. A. (2009). Streamlining ‘search and destroy’: Cost-effective surveillance for invasive species management. *Ecology Letters*, *12*(7), 683–692. <https://doi.org/10.1111/j.1461-0248.2009.01323.x>
- Haydon, D. T., Chase–Topping, M., Shaw, D. J., Matthews, L., Friar, J. K., Wilesmith, J., & Woolhouse, M. E. J. (2003). The construction and analysis of epidemic trees with reference to the 2001 UK foot–and–mouth outbreak. *Proceedings of the Royal Society of London. Series B: Biological Sciences*, *270*(1511), 121–127. <https://doi.org/10.1098/rspb.2002.2191>
- Hayes, B. H., Andraud, M., Salazar, L. G., Rose, N., & Vergne, T. (2021). Mechanistic modelling of African swine fever: A systematic review. *Preventive Veterinary Medicine*, *191*, 105358. <https://doi.org/10.1016/j.prevetmed.2021.105358>
- Hess, W. R., Endris, R. G., Haslett, T. M., Monahan, M. J., & McCoy, J. P. (1987). Potential arthropod vectors of African swine fever virus in North America and the Caribbean basin. *Veterinary Parasitology*, *26*(1–2), 145–155. [https://doi.org/10.1016/0304-4017\(87\)90084-7](https://doi.org/10.1016/0304-4017(87)90084-7)
- Howey, E. B., O’Donnell, V., de Carvalho Ferreira, H. C., Borca, M. V., & Arzt, J. (2013). Pathogenesis of highly virulent African swine fever virus in domestic pigs exposed via intraoropharyngeal, intranasopharyngeal, and intramuscular inoculation, and by direct contact with infected pigs. *Virus Research*, *178*(2), 328–339. <https://doi.org/10.1016/j.virusres.2013.09.024>

- Hu, B., Gonzales, J. L., & Gubbins, S. (2017). Bayesian inference of epidemiological parameters from transmission experiments. *Scientific Reports*, 7(1), Article 1. <https://doi.org/10.1038/s41598-017-17174-8>
- Huyvaert, K. P., Russell, R. E., Patyk, K. A., Craft, M. E., Cross, P. C., Garner, M. G., Martin, M. K., Nol, P., & Walsh, D. P. (2018). Challenges and Opportunities Developing Mathematical Models of Shared Pathogens of Domestic and Wild Animals. *Veterinary Sciences*, 5(4), E92. <https://doi.org/10.3390/vetsci5040092>
- INRAE. (2020). *ASF Challenge*. <https://www6.inrae.fr/asfchallenge/>
- Ivorra, B., Martínez-López, B., Sánchez-Vizcaíno, J. M., & Ramos, Á. M. (2014). Mathematical formulation and validation of the Be-FAST model for Classical Swine Fever Virus spread between and within farms. *Annals of Operations Research*, 219(1), 25–47. <https://doi.org/10.1007/s10479-012-1257-4>
- Jacquot, M., Nomikou, K., Palmarini, M., Mertens, P., & Biek, R. (2017). Bluetongue virus spread in Europe is a consequence of climatic, landscape and vertebrate host factors as revealed by phylogeographic inference. *Proceedings. Biological Sciences*, 284(1864), 20170919. <https://doi.org/10.1098/rspb.2017.0919>
- Janoska, F., Farkas, A., Marosan, M., & Fodor, J.-T. (2018). Wild Boar (*Sus scrofa*) Home Range and Habitat Use in Two Romanian Habitats. *Acta Silvatica et Lignaria Hungarica*, 14, 51–63. <https://doi.org/10.2478/aslh-2018-0003>
- Jo, Y.-S., & Gortázar, C. (2021). African Swine Fever in wild boar: Assessing interventions in South Korea. *Transboundary and Emerging Diseases*, 68(5), 2878–2889. <https://doi.org/10.1111/tbed.14106>
- Jones, B. A., Grace, D., Kock, R., Alonso, S., Rushton, J., Said, M. Y., McKeever, D., Mutua, F., Young, J., McDermott, J., & Pfeiffer, D. U. (2013). Zoonosis emergence linked to agricultural intensification and environmental change. *Proceedings of the National Academy of Sciences of the United States of America*, 110(21), 8399–8404. <https://doi.org/10.1073/pnas.1208059110>
- Jori, F., & Bastos, A. D. S. (2009). Role of Wild Suids in the Epidemiology of African Swine Fever. *EcoHealth*, 6(2), 296–310. <https://doi.org/10.1007/s10393-009-0248-7>
- Jori, F., Hernandez-Jover, M., Magouras, I., Dürr, S., & Brookes, V. J. (2021). Wildlife–livestock interactions in animal production systems: What are the biosecurity and health implications? *Animal Frontiers: The Review Magazine of Animal Agriculture*, 11(5), 8–19. <https://doi.org/10.1093/af/vfab045>

- Jori, F., Massei, G., Licoppe, A., Ruiz-Fons, F., Linden, A., Václavek, P., Chenais, E., & Rosell, C. (2021). Management of wild boar populations in the European Union before and during the ASF crisis. In *Understanding and combatting African Swine Fever: A European perspective*. [https://doi.org/10.3920/978-90-8686-910-7\\_8](https://doi.org/10.3920/978-90-8686-910-7_8)
- Kagira, J. M., Kanyari, P. W. N., Maingi, N., Githigia, S. M., Ng'ang'a, J. C., & Karuga, J. W. (2010). Characteristics of the smallholder free-range pig production system in western Kenya. *Tropical Animal Health and Production*, *42*(5), 865–873. <https://doi.org/10.1007/s11250-009-9500-y>
- Kajunguri, D., Hargrove, J. W., Ouifki, R., Mugisha, J. Y. T., Coleman, P. G., & Welburn, S. C. (2014). Modelling the use of insecticide-treated cattle to control tsetse and *Trypanosoma brucei rhodesiense* in a multi-host population. *Bulletin of Mathematical Biology*, *76*(3), 673–696. <https://doi.org/10.1007/s11538-014-9938-6>
- Kao, R. (2002). The role of mathematical modelling in the control of the 2001 FMD epidemic in the UK. *Trends in Microbiology*, *10*, 279–286. [https://doi.org/10.1016/S0966-842X\(02\)02371-5](https://doi.org/10.1016/S0966-842X(02)02371-5)
- Keeling, M. J. (2005). Models of foot-and-mouth disease. *Proceedings of the Royal Society B: Biological Sciences*, *272*(1569), 1195–1202. <https://doi.org/10.1098/rspb.2004.3046>
- Keeling, M. J., & Eames, K. T. D. (2005). Networks and epidemic models. *Journal of The Royal Society Interface*, *2*(4), 295–307. <https://doi.org/10.1098/rsif.2005.0051>
- Keeling, M. J., & Rohani, P. (2008). *Modeling Infectious Diseases in Humans and Animals*. Princeton University Press. <https://doi.org/10.2307/j.ctvc4gk0>
- Keeling, M. J., Woolhouse, M. E. J., Shaw, D. J., Matthews, L., Chase-Topping, M., Haydon, D. T., Cornell, S. J., Kappey, J., Wilesmith, J., & Grenfell, B. T. (2001). Dynamics of the 2001 UK Foot and Mouth Epidemic: Stochastic Dispersal in a Heterogeneous Landscape. *Science*, *294*(5543), 813–817. <https://doi.org/10.1126/science.1065973>
- Kermack, W. O., McKendrick, A. G., & Walker, G. T. (1927). A contribution to the mathematical theory of epidemics. *Proceedings of the Royal Society of London. Series A, Containing Papers of a Mathematical and Physical Character*, *115*(772), 700–721. <https://doi.org/10.1098/rspa.1927.0118>
- Khanyari, M., Suryawanshi, K. R., Milner-Gulland, E. J., Dickinson, E., Khara, A., Rana, R. S., Rose Vineer, H., & Morgan, E. R. (2021). Predicting Parasite Dynamics in Mixed-Use Trans-Himalayan Pastures to Underpin Management of Cross-Transmission Between Livestock and Bharal. *FRONTIERS IN VETERINARY SCIENCE*, *8*. <https://doi.org/10.3389/fvets.2021.714241>
- Khomenko, S., Beltrán-Alcrudo, D., Rozstalnyy, A., Pinto, J., Lubroth, J., Martin, V., Gogin, A., Kolbasov, D., & Animal Production and Health Division. (2013). *African swine fever in the Russian*

- Federation: Risk factors for Europe and beyond.* FAO.  
<https://www.fao.org/publications/card/es/c/456c5e1d-f450-524f-a664-/>
- Kim, Y.-J., Park, B., & Kang, H.-E. (2021). Control measures to African swine fever outbreak: Active response in South Korea, preparation for the future, and cooperation. *Journal of Veterinary Science*, 22(1), e13. <https://doi.org/10.4142/jvs.2021.22.e13>
- Kitching, R. P., Thrusfield, M. V., & Taylor, N. M. (2006). Use and abuse of mathematical models: An illustration from the 2001 foot and mouth disease epidemic in the United Kingdom. *Revue Scientifique Et Technique (International Office of Epizootics)*, 25(1), 293–311. <https://doi.org/10.20506/rst.25.1.1665>
- Klov Dahl, A. S. (1985). Social networks and the spread of infectious diseases: The AIDS example. *Social Science & Medicine (1982)*, 21(11), 1203–1216. [https://doi.org/10.1016/0277-9536\(85\)90269-2](https://doi.org/10.1016/0277-9536(85)90269-2)
- Knight-Jones, T. J. D., & Rushton, J. (2013). The economic impacts of foot and mouth disease—What are they, how big are they and where do they occur? *Preventive Veterinary Medicine*, 112(3–4), 161–173. <https://doi.org/10.1016/j.prevetmed.2013.07.013>
- Kretzschmar, M. (2020). Disease modeling for public health: Added value, challenges, and institutional constraints. *Journal of Public Health Policy*, 41(1), 39. <https://doi.org/10.1057/s41271-019-00206-0>
- Kretzschmar, M., van Duynhoven, Y. T., & Severijnen, A. J. (1996). Modeling prevention strategies for gonorrhoea and Chlamydia using stochastic network simulations. *American Journal of Epidemiology*, 144(3), 306–317. <https://doi.org/10.1093/oxfordjournals.aje.a008926>
- Kruschke, J., & Meredith, M. (2021). *BEST: Bayesian Estimation Supersedes the t-Test*. (0.5.4) [R]. <https://CRAN.R-project.org/package=BEST>
- Kukielka, E., Barasona, J. A., Cowie, C. E., Drewe, J. A., Gortazar, C., Cotarelo, I., & Vicente, J. (2013). Spatial and temporal interactions between livestock and wildlife in South Central Spain assessed by camera traps. *Preventive Veterinary Medicine*, 112(3), 213–221. <https://doi.org/10.1016/j.prevetmed.2013.08.008>
- Kumar, S., Stecher, G., Li, M., Knyaz, C., & Tamura, K. (2018). MEGA X: Molecular Evolutionary Genetics Analysis across Computing Platforms. *Molecular Biology and Evolution*, 35(6), 1547–1549. <https://doi.org/10.1093/molbev/msy096>
- Laddomada, A., Patta, C., Oggiano, A., Caccia, A., Ruiu, A., Cossu, P., & Firinu, A. (1994). Epidemiology of classical swine fever in Sardinia: A serological survey of wild boar and comparison with African swine fever. *The Veterinary Record*, 134(8), 183–187. <https://doi.org/10.1136/vr.134.8.183>

- Laffan, S. W., Wang, Z., & Ward, M. P. (2011). The effect of neighbourhood definitions on spatio-temporal models of disease outbreaks: Separation distance versus range overlap. *Preventive Veterinary Medicine*, 102(3), 218–229. <https://doi.org/10.1016/j.prevetmed.2011.07.009>
- Laguna, E., Barasona, J. A., Carpio, A. J., Vicente, J., & Acevedo, P. (2022). Permeability of artificial barriers (fences) for wild boar (*Sus scrofa*) in Mediterranean mixed landscapes. *Pest Management Science*, 78(6), 2277–2286. <https://doi.org/10.1002/ps.6853>
- Lamberga, K., Oļševskis, E., Seržants, M., Bērziņš, A., Viltrop, A., & Depner, K. (2020). African Swine Fever in Two Large Commercial Pig Farms in LATVIA—Estimation of the High Risk Period and Virus Spread within the Farm. *Veterinary Sciences*, 7(3), 105. <https://doi.org/10.3390/vetsci7030105>
- Landis, J. R., & Koch, G. G. (1977). The Measurement of Observer Agreement for Categorical Data. *Biometrics*, 33(1), 159–174. <https://doi.org/10.2307/2529310>
- Lange, M. (2015). Alternative control strategies against ASF in wild boar populations. *EFSA Supporting Publications*, 12(7), 843E. <https://doi.org/10.2903/sp.efsa.2015.EN-843>
- Lange, M., Guberti, V., & Thulke, H.-H. (2018). Understanding ASF spread and emergency control concepts in wild boar populations using individual-based modelling and spatio-temporal surveillance data. *EFSA Supporting Publications*, 15(11), 1521E. <https://doi.org/10.2903/sp.efsa.2018.EN-1521>
- Lange, M., & Thulke, H.-H. (2015). Mobile barriers as emergency measure to control outbreaks of African Swine Fever in wild boar. *Proceedings, SVEPM, Gent*, 122–132.
- Lange, M., & Thulke, H.-H. (2017). Elucidating transmission parameters of African swine fever through wild boar carcasses by combining spatio-temporal notification data and agent-based modelling. *Stochastic Environmental Research and Risk Assessment*, 31(2), 379–391. <https://doi.org/10.1007/s00477-016-1358-8>
- Le, V. P., Jeong, D. G., Yoon, S.-W., Kwon, H.-M., Trinh, T. B. N., Nguyen, T. L., Bui, T. T. N., Oh, J., Kim, J. B., Cheong, K. M., Van Tuyen, N., Bae, E., Vu, T. T. H., Yeom, M., Na, W., & Song, D. (2019). Outbreak of African Swine Fever, Vietnam, 2019. *Emerging Infectious Diseases*, 25(7), 1433–1435. <https://doi.org/10.3201/eid2507.190303>
- Leaper, R., Massei, G., Gorman, M. L., & Aspinall, R. (1999). The feasibility of reintroducing Wild Boar (*Sus scrofa*) to Scotland. *Mammal Review*, 29(4), 239–258. <https://doi.org/10.1046/j.1365-2907.1999.2940239.x>
- Lee, H. S., Thakur, K. K., Bui, V. N., Pham, T. L., Bui, A. N., Dao, T. D., Thanh, V. T., & Wieland, B. (2021). A stochastic simulation model of African swine fever transmission in domestic pig farms in the

- Red River Delta region in Vietnam. *Transboundary and Emerging Diseases*, 68(3), 1384–1391. <https://doi.org/10.1111/tbed.13802>
- Lenormand, M., Jabot, F., & Deffuant, G. (2012). *Adaptive approximate Bayesian computation for complex models*. <https://hal.archives-ouvertes.fr/hal-00638484>
- Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gøtzsche, P. C., Ioannidis, J. P. A., Clarke, M., Devereaux, P. J., Kleijnen, J., & Moher, D. (2009). The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration. *PLOS Medicine*, 6(7), e1000100. <https://doi.org/10.1371/journal.pmed.1000100>
- Lim, J.-S., Kim, E., Ryu, P.-D., & Pak, S.-I. (2021). Basic reproduction number of African swine fever in wild boars (*Sus scrofa*) and its spatiotemporal heterogeneity in South Korea. *Journal of Veterinary Science*, 22(5), e71. <https://doi.org/10.4142/jvs.2021.22.e71>
- Loi, F., Cappai, S., Coccollone, A., & Rolesu, S. (2019). Standardized Risk Analysis Approach Aimed to Evaluate the Last African Swine Fever Eradication Program Performance, in Sardinia. *Frontiers in Veterinary Science*, 6. <https://www.frontiersin.org/articles/10.3389/fvets.2019.00299>
- Loi, F., Cappai, S., Laddomada, A., Feliziani, F., Oggiano, A., Franzoni, G., Rolesu, S., & Guberti, V. (2020). Mathematical Approach to Estimating the Main Epidemiological Parameters of African Swine Fever in Wild Boar. *Vaccines*, 8(3), Article 3. <https://doi.org/10.3390/vaccines8030521>
- Lyra, T. M. P. (2006). The eradication of African swine fever in Brazil, 1978-1984. *Revue Scientifique Et Technique (International Office of Epizootics)*, 25(1), 93–103.
- Macdonald, G. (1957). The Epidemiology and Control of Malaria. *The Epidemiology and Control of Malaria*. <https://www.cabdirect.org/cabdirect/abstract/19581000237>
- Malogolovkin, A., Burmakina, G., Titov, I., Sereda, A., Gogin, A., Baryshnikova, E., & Kolbasov, D. (2015). Comparative Analysis of African Swine Fever Virus Genotypes and Serogroups. *Emerging Infectious Diseases*, 21(2), 312–315. <https://doi.org/10.3201/eid2102.140649>
- Manlove, K. R., Sampson, L. M., Borremans, B., Cassirer, E. F., Miller, R. S., Pepin, K. M., Besser, T. E., & Cross, P. C. (2019). Epidemic growth rates and host movement patterns shape management performance for pathogen spillover at the wildlife-livestock interface. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, 374(1782), 20180343. <https://doi.org/10.1098/rstb.2018.0343>
- Marion, G., Smith, L. A., Swain, D. L., Davidson, R. S., & Hutchings, M. R. (2008). Agent-based modelling of foraging behaviour: The impact of spatial heterogeneity on disease risks from faeces in grazing systems. *JOURNAL OF AGRICULTURAL SCIENCE*, 146(5), 507–520. <https://doi.org/10.1017/S0021859608008022>



- Maselli, V., Rippa, D., Russo, G., Ligrone, R., Soppelsa, O., D’Aniello, B., Raia, P., & Fulgione, D. (2014). Wild boars’ social structure in the Mediterranean habitat. *Italian Journal of Zoology*, *81*(4), 610–617. <https://doi.org/10.1080/11250003.2014.953220>
- Mason-D’Croz, D., Bogard, J. R., Herrero, M., Robinson, S., Sulser, T. B., Wiebe, K., Willenbockel, D., & Godfray, H. C. J. (2020). Modelling the global economic consequences of a major African swine fever outbreak in China. *Nature Food*, *1*(4), Article 4. <https://doi.org/10.1038/s43016-020-0057-2>
- Mateus-Anzola, J., Wiratsudakul, A., Rico-Chávez, O., & Ojeda-Flores, R. (2019). Simulation modeling of influenza transmission through backyard pig trade networks in a wildlife/livestock interface area. *Tropical Animal Health and Production*, *51*(7), 2019–2024. <https://doi.org/10.1007/s11250-019-01892-4>
- Mazur-Panasiuk, N., Żmudzki, J., & Woźniakowski, G. (2019). African swine fever virus – persistence in different environmental conditions and the possibility of its indirect transmission. *Journal of Veterinary Research*, *63*(3), 303–310. <https://doi.org/10.2478/jvetres-2019-0058>
- McCallum, H. (2016). Models for managing wildlife disease. *Parasitology*, *143*(7), 805–820. <https://doi.org/10.1017/S0031182015000980>
- McInerney, J. P., Howe, K. S., & Schepers, J. A. (1992). A framework for the economic analysis of disease in farm livestock. *Preventive Veterinary Medicine*, *13*(2), 137–154. [https://doi.org/10.1016/0167-5877\(92\)90098-Z](https://doi.org/10.1016/0167-5877(92)90098-Z)
- McKercher, P. D., Hess, W. R., & Hamdy, F. (1978). Residual viruses in pork products. *Applied and Environmental Microbiology*, *35*(1), 142–145.
- McKercher, P. D., Yedloutschnig, R. J., Callis, J. J., Murphy, R., Panina, G. F., Civardi, A., Bugnetti, M., Foni, E., Laddomada, A., Scarano, C., & Scatozza, F. (1987). Survival of Viruses in “Prosciutto di Parma” (Parma Ham). *Canadian Institute of Food Science and Technology Journal*, *20*(4), 267–272. [https://doi.org/10.1016/S0315-5463\(87\)71198-5](https://doi.org/10.1016/S0315-5463(87)71198-5)
- Mebus, C., Arias, M., Pineda, J. M., Tapiador, J., House, C., & Sánchez-Vizcaíno, J. M. (1997). Survival of several porcine viruses in different Spanish dry-cured meat products. *Food Chemistry*, *59*(4), 555–559. [https://doi.org/10.1016/S0308-8146\(97\)00006-X](https://doi.org/10.1016/S0308-8146(97)00006-X)
- Mebus, C., House, C., Gonzalvo, F. R., Pineda, J. M., Tapiador, J., Pire, J. J., Bergada, J., Yedloutschnig, R. J., Sahu, S., Becerra, V., & Sanchez-Vizcaino, J. M. (1993). Survival of foot-and-mouth disease, African swine fever, and hog cholera viruses in Spanish serrano cured hams and Iberian cured hams, shoulders and loins. *Food Microbiology*, *10*(2), 133–143. <https://doi.org/10.1006/fmic.1993.1014>

- Mellor, P. S., Kitching, R. P., & Wilkinson, P. J. (1987). Mechanical transmission of capripox virus and African swine fever virus by *Stomoxys calcitrans*. *Research in Veterinary Science*, *43*(1), 109–112. [https://doi.org/10.1016/S0034-5288\(18\)30753-7](https://doi.org/10.1016/S0034-5288(18)30753-7)
- Mighell, E., & Ward, M. P. (2021). African Swine Fever spread across Asia, 2018-2019. *Transboundary and Emerging Diseases*, *68*(5), 2722–2732. <https://doi.org/10.1111/tbed.14039>
- Miller, R. S., Farnsworth, M. L., & Malmberg, J. L. (2013). Diseases at the livestock–wildlife interface: Status, challenges, and opportunities in the United States. *Preventive Veterinary Medicine*, *110*(2), 119–132. <https://doi.org/10.1016/j.prevetmed.2012.11.021>
- Mollison, D. (1977). Spatial Contact Models for Ecological and Epidemic Spread. *Journal of the Royal Statistical Society. Series B (Methodological)*, *39*(3), 283–326.
- Moore, J. L., Rout, T. M., Hauser, C. E., Moro, D., Jones, M., Wilcox, C., & Possingham, H. P. (2010). Protecting islands from pest invasion: Optimal allocation of biosecurity resources between quarantine and surveillance. *Biological Conservation*, *143*(5), 1068–1078. <https://doi.org/10.1016/j.biocon.2010.01.019>
- Morelle, K., Bubnicki, J., Churski, M., Gryz, J., Podgórski, T., & Kuijper, D. P. J. (2020). Disease-Induced Mortality Outweighs Hunting in Causing Wild Boar Population Crash After African Swine Fever Outbreak. *Frontiers in Veterinary Science*, *7*, 378. <https://doi.org/10.3389/fvets.2020.00378>
- Moreno-Torres, K. I., Pomeroy, L. W., Moritz, M., Saville, W., Wolfe, B., & Garabed, R. (2017). Host species heterogeneity in the epidemiology of *Nesopora caninum*. *PLoS One*, *12*(8), e0183900. <https://doi.org/10.1371/journal.pone.0183900>
- Morgan, E. R., Medley, G. F., Torgerson, P. R., Shaikenov, B. S., & Milner-Gulland, E. J. (2007). Parasite transmission in a migratory multiple host system. *ECOLOGICAL MODELLING*, *200*(3–4), 511–520. <https://doi.org/10.1016/j.ecolmodel.2006.09.002>
- Morris, R. S., Wilesmith, J. W., Stern, M. W., Sanson, R. L., & Stevenson, M. A. (2001). Predictive spatial modelling of alternative control strategies for the foot-and-mouth disease epidemic in Great Britain, 2001. *The Veterinary Record*, *149*(5), 137–144. <https://doi.org/10.1136/vr.149.5.137>
- Mort, M., Convery, I., Baxter, J., & Bailey, C. (2005). Psychosocial effects of the 2001 UK foot and mouth disease epidemic in a rural population: Qualitative diary based study. *BMJ (Clinical Research Ed.)*, *331*(7527), 1234. <https://doi.org/10.1136/bmj.38603.375856.68>
- Mortasivu, C. (2021). *Personal communication* [Personal communication].
- Muñoz, F., Pleydell, D. R. J., & Jori, F. (2022). A combination of probabilistic and mechanistic approaches for predicting the spread of African swine fever on Merry Island. *Epidemics*, *40*, 100596. <https://doi.org/10.1016/j.epidem.2022.100596>

- Muñoz-Gómez, V., Solodiankin, O., Rudova, N., Gerilovych, A., Nychyk, S., Hudz, N., Ukhovska, T., Sytiuk, M., Polischuk, V., Mustra, D., De Nardi, M., Lechner, I., & Schuppers, M. (2021). Supporting control programs on African swine fever in Ukraine through a knowledge, attitudes, and practices survey targeting backyard farmers. *Veterinary Medicine and Science*, 7(5), 1786–1799. <https://doi.org/10.1002/vms3.578>
- Muñoz-Pérez, C., Jurado, C., & Sánchez-Vizcaíno, J. M. (2021). African swine fever vaccine: Turning a dream into reality. *Transboundary and Emerging Diseases*, 68(5), 2657–2668. <https://doi.org/10.1111/tbed.14191>
- Mur, L., Sánchez-Vizcaíno, J. M., Fernández-Carrión, E., Jurado, C., Rolesu, S., Feliziani, F., Laddomada, A., & Martínez-López, B. (2018). Understanding African Swine Fever infection dynamics in Sardinia using a spatially explicit transmission model in domestic pig farms. *Transboundary and Emerging Diseases*, 65(1), 123–134. <https://doi.org/10.1111/tbed.12636>
- Naqibzadeh, A., Sarhangzadeh, J., Sotoudeh, A., Mashkour, M., & Thomalsky, J. (2021). *Habitat Suitability Modeling for Wildlife Management Objectives by Using Maximum Entropy Method*.
- Nguyen-Thi, T., Pham-Thi-Ngoc, L., Nguyen-Ngoc, Q., Dang-Xuan, S., Lee, H. S., Nguyen-Viet, H., Padungtod, P., Nguyen-Thu, T., Nguyen-Thi, T., Tran-Cong, T., & Rich, K. M. (2021). An Assessment of the Economic Impacts of the 2019 African Swine Fever Outbreaks in Vietnam. *Frontiers in Veterinary Science*, 8. <https://www.frontiersin.org/articles/10.3389/fvets.2021.686038>
- Niederwerder, M. C., Stoian, A. M. M., Rowland, R. R. R., Dritz, S. S., Petrovan, V., Constance, L. A., Gebhardt, J. T., Olcha, M., Jones, C. K., Woodworth, J. C., Fang, Y., Liang, J., & Hefley, T. J. (2019). Infectious Dose of African Swine Fever Virus When Consumed Naturally in Liquid or Feed. *Emerging Infectious Diseases*, 25(5), 891–897. <https://doi.org/10.3201/eid2505.181495>
- Nielsen, J. P., Larsen, T. S., Halasa, T., & Christiansen, L. E. (2017). Estimation of the transmission dynamics of African swine fever virus within a swine house. *Epidemiology & Infection*, 145(13), 2787–2796. <https://doi.org/10.1017/S0950268817001613>
- Nigsch, A., Costard, S., Jones, B. A., Pfeiffer, D. U., & Wieland, B. (2013). Stochastic spatio-temporal modelling of African swine fever spread in the European Union during the high risk period. *Preventive Veterinary Medicine*, 108(4), 262–275. <https://doi.org/10.1016/j.prevetmed.2012.11.003>
- Njau, E. P., Domelevo Entfellner, J.-B., Machuka, E. M., Bochere, E. N., Cleaveland, S., Shirima, G. M., Kusiluka, L. J., Upton, C., Bishop, R. P., Pelle, R., & Okoth, E. A. (2021). The first genotype II African swine fever virus isolated in Africa provides insight into the current Eurasian pandemic. *Scientific Reports*, 11(1), Article 1. <https://doi.org/10.1038/s41598-021-92593-2>

- Nunes, B., Caetano, C., Antunes, L., & Dias, C. (2020). Statistics in times of pandemics: The role of statistical and epidemiological methods during the covid-19 emergency (invited paper with discussion). *Revstat Statistical Journal*, *18*, 553–564. <https://doi.org/10.57805/revstat.v18i5.317>
- Nurmoja, I., Mõtus, K., Kristian, M., Niine, T., Schulz, K., Depner, K., & Viltrop, A. (2020). Epidemiological analysis of the 2015-2017 African swine fever outbreaks in Estonia. *Preventive Veterinary Medicine*, *181*, 104556. <https://doi.org/10.1016/j.prevetmed.2018.10.001>
- Nyerere, N., Luboobi, L. S., Mpeshe, S. C., & Shirima, G. M. (2020). Modeling the Impact of Seasonal Weather Variations on the Infectiology of Brucellosis. *Computational and Mathematical Methods in Medicine*, *2020*, 8972063. <https://doi.org/10.1155/2020/8972063>
- Odeniran, P. O., Onifade, A. A., MacLeod, E. T., Ademola, I. O., Alderton, S., & Welburn, S. C. (2020). Mathematical modelling and control of African animal trypanosomosis with interacting populations in West Africa-Could biting flies be important in maintaining the disease endemicity? *PloS One*, *15*(11), e0242435. <https://doi.org/10.1371/journal.pone.0242435>
- O’Hare, A., Orton, R. J., Bessell, P. R., & Kao, R. R. (2014). Estimating epidemiological parameters for bovine tuberculosis in British cattle using a Bayesian partial-likelihood approach. *Proceedings. Biological Sciences*, *281*(1783), 20140248. <https://doi.org/10.1098/rspb.2014.0248>
- Olesen, A. S., Lohse, L., Boklund, A., Halasa, T., Gallardo, C., Pejsak, Z., Belsham, G. J., Rasmussen, T. B., & Bøtner, A. (2017). Transmission of African swine fever virus from infected pigs by direct contact and aerosol routes. *Veterinary Microbiology*, *211*, 92–102. <https://doi.org/10.1016/j.vetmic.2017.10.004>
- Oļševskis, E., Guberti, V., Seržants, M., Westergaard, J., Gallardo, C., Rodze, I., & Depner, K. (2016). African swine fever virus introduction into the EU in 2014: Experience of Latvia. *Research in Veterinary Science*, *105*, 28–30. <https://doi.org/10.1016/j.rvsc.2016.01.006>
- O’Neill, X., White, A., Ruiz-Fons, F., & Gortázar, C. (2020). Modelling the transmission and persistence of African swine fever in wild boar in contrasting European scenarios. *Scientific Reports*, *10*(1), Article 1. <https://doi.org/10.1038/s41598-020-62736-y>
- Orbann, C., Sattenspiel, L., Miller, E., & Dimka, J. (2017). Defining epidemics in computer simulation models: How do definitions influence conclusions? *Epidemics*, *19*, 24–32. <https://doi.org/10.1016/j.epidem.2016.12.001>
- Oura, C. A., Powell, P. P., Anderson, E., & Parkhouse, R. M. (1998). The pathogenesis of African swine fever in the resistant bushpig. *The Journal of General Virology*, *79* ( Pt 6), 1439–1443. <https://doi.org/10.1099/0022-1317-79-6-1439>

- Pan, I. C., & Hess, W. R. (1984). Virulence in African swine fever: Its measurement and implications. *American Journal of Veterinary Research*, *45*(2), 361–366.
- Pardi, F., & Gascuel, O. (2016). Distance-Based Phylogenetic Inference. In R. M. Kliman (Ed.), *Encyclopedia of Evolutionary Biology* (pp. 458–465). Academic Press. <https://doi.org/10.1016/B978-0-12-800049-6.00206-7>
- Pensaert, M. B. (1989). Virus infections of porcines. *Virus Infections of Vertebrates (Netherlands)*. [https://scholar.google.com/scholar\\_lookup?title=Virus+infections+of+porcines&author=Pen+saert%2C+M.B.+%28Laboratory+of+Virology%2C+Gent+%28Belgium%29%29&publication\\_year=1989](https://scholar.google.com/scholar_lookup?title=Virus+infections+of+porcines&author=Pen+saert%2C+M.B.+%28Laboratory+of+Virology%2C+Gent+%28Belgium%29%29&publication_year=1989)
- Pepin, K. M., Golnar, A. J., Abdo, Z., & Podgórski, T. (2020). Ecological drivers of African swine fever virus persistence in wild boar populations: Insight for control. *Ecology and Evolution*, *10*(6), 2846–2859. <https://doi.org/10.1002/ece3.6100>
- Pereira de Oliveira, R., Hutet, E., Paboeuf, F., Duhayon, M., Boinas, F., Perez de Leon, A., Filatov, S., Vial, L., & Le Potier, M.-F. (2019). Comparative vector competence of the Afrotropical soft tick *Ornithodoros moubata* and Palearctic species, *O. erraticus* and *O. verrucosus*, for African swine fever virus strains circulating in Eurasia. *PloS One*, *14*(11), e0225657. <https://doi.org/10.1371/journal.pone.0225657>
- Pérez, J., Fernández, A. I., Sierra, M. A., Herráez, P., Fernández, A., & Martín de las Mulas, J. (1998). Serological and immunohistochemical study of African swine fever in wild boar in Spain. *The Veterinary Record*, *143*(5), 136–139. <https://doi.org/10.1136/vr.143.5.136>
- Perez, L., & Dragicevic, S. (2009). An agent-based approach for modeling dynamics of contagious disease spread. *International Journal of Health Geographics*, *8*(1), 50. <https://doi.org/10.1186/1476-072X-8-50>
- Phengsavanh, P., Ogle, B., Stür, W., Frankow-Lindberg, B. E., & Lindberg, J. E. (2010). Feeding and performance of pigs in smallholder production systems in Northern Lao PDR. *Tropical Animal Health and Production*, *42*(8), 1627–1633. <https://doi.org/10.1007/s11250-010-9612-4>
- Phepa, P. B., Chirove, F., & Govinder, K. S. (2016). Modelling the role of multi-transmission routes in the epidemiology of bovine tuberculosis in cattle and buffalo populations. *Mathematical Biosciences*, *277*, 47–58. <https://doi.org/10.1016/j.mbs.2016.04.003>
- Picault, S., Vergne, T., Mancini, M., Bareille, S., & Ezanno, P. (2022). The African swine fever modelling challenge: Objectives, model description and synthetic data generation. *Epidemics*, *40*, 100616. <https://doi.org/10.1016/j.epidem.2022.100616>
- Pietschmann, J., Guinat, C., Beer, M., Pronin, V., Tauscher, K., Petrov, A., Keil, G., & Blome, S. (2015). Course and transmission characteristics of oral low-dose infection of domestic pigs and

- European wild boar with a Caucasian African swine fever virus isolate. *Archives of Virology*, 160(7), 1657–1667. <https://doi.org/10.1007/s00705-015-2430-2>
- Pig333. (2021, July 7). *China: Excess pork production has lowered prices*. [https://www.pig333.com/latest\\_swine\\_news/excess-pork-production-in-china-has-lowered-pork-prices-says-usda\\_17610/](https://www.pig333.com/latest_swine_news/excess-pork-production-in-china-has-lowered-pork-prices-says-usda_17610/)
- Pineda-Krch, M., O'Brien, J. M., Thunes, C., & Carpenter, T. E. (2010). Potential impact of introduction of foot-and-mouth disease from wild pigs into commercial livestock premises in California. *American Journal of Veterinary Research*, 71(1), 82–88. <https://doi.org/10.2460/ajvr.71.1.82>
- Plowright, W., Parker, J., & Pierce, M. A. (1969). The epizootiology of African swine fever in Africa. *The Veterinary Record*, 85(24), 668–674.
- Pol, F., Rossi, S., Mesplède, A., Kuntz-Simon, G., & Le Potier, M.-F. (2008). Two outbreaks of classical swine fever in wild boar in France. *The Veterinary Record*, 162(25), 811–816. <https://doi.org/10.1136/vr.162.25.811>
- Porter, R., Norman, R., & Gilbert, L. (2011). Controlling tick-borne diseases through domestic animal management: A theoretical approach. *THEORETICAL ECOLOGY*, 4(3), 321–339. <https://doi.org/10.1007/s12080-010-0080-2>
- Probst, C., Gethmann, J., Amler, S., Globig, A., Knoll, B., & Conraths, F. J. (2019). The potential role of scavengers in spreading African swine fever among wild boar. *Scientific Reports*, 9(1), Article 1. <https://doi.org/10.1038/s41598-019-47623-5>
- Probst, C., Globig, A., Knoll, B., Conraths, F. J., & Depner, K. (2017). Behaviour of free ranging wild boar towards their dead fellows: Potential implications for the transmission of African swine fever. *Royal Society Open Science*, 4(5), 170054. <https://doi.org/10.1098/rsos.170054>
- ProMED-mail. (2020, September 9). African swine fever—Europe (18): Germany (BB) wild boar. Conf, OIE. *ProMED-Mail*. <https://promedmail.org/promed-post/>
- R Core Team. (2022). *R: A language and environment for statistical computing*. R Foundation for Statistical Computing. <https://www.R-project.org/>
- Ramsey, D. S. L., O'Brien, D. J., Smith, R. W., Cosgrove, M. K., Schmitt, S. M., & Rudolph, B. A. (2016). Management of on-farm risk to livestock from bovine tuberculosis in Michigan, USA, white-tailed deer: Predictions from a spatially-explicit stochastic model. *Preventive Veterinary Medicine*, 134, 26–38. <https://doi.org/10.1016/j.prevetmed.2016.09.022>
- Ray, R.-R., Seibold, H., & Heurich, M. (2014). Invertebrates outcompete vertebrate facultative scavengers in simulated lynx kills in the Bavarian Forest National Park, Germany. *Animal Biodiversity and Conservation*, 37(1), Article 1. <https://doi.org/10.5167/uzh-130585>

- Revilla, Y., Pérez-Núñez, D., & Richt, J. A. (2018). African Swine Fever Virus Biology and Vaccine Approaches. *Advances in Virus Research*, 100, 41–74. <https://doi.org/10.1016/bs.aivir.2017.10.002>
- Roberts, M., Dobson, A., Restif, O., & Wells, K. (2021). Challenges in modelling the dynamics of infectious diseases at the wildlife–human interface. *Epidemics*, 37, 100523. <https://doi.org/10.1016/j.epidem.2021.100523>
- Rock, D. L. (2017). Challenges for African swine fever vaccine development—“... perhaps the end of the beginning.” *Veterinary Microbiology*, 206, 52–58. <https://doi.org/10.1016/j.vetmic.2016.10.003>
- Roger, F., Ratovonjato, J., Vola, P., & Uilenberg, G. (2001). Ornithodoros Porcinus Ticks, Bushpigs, and African Swine Fever in Madagascar. *Experimental & Applied Acarology*, 25(3), 263–269. <https://doi.org/10.1023/A:1010687502145>
- Romanian ministry of development, public works, and administration. (2021). *Agenția Națională de Cadastru și Publicitate Imobiliară (ANCP)*. <https://www.ancpi.ro/>
- Rong, X., Fan, M., Zhu, H., & Zheng, Y. (2021). Dynamic modeling and optimal control of cystic echinococcosis. *Infectious Diseases of Poverty*, 10(1), 38. <https://doi.org/10.1186/s40249-021-00807-6>
- Rose, N., & Boisseleau, D. (2018). *Rapport de la mission réalisée du 27 au 31 aout 2018 en Roumanie* (p. 28). ANSES.
- Rosell, C., Romero, S., Navás, F., & Dalmasas, I. de. (2004). Activity Patterns and Social Organization of wild boar (*Sus scrofa*, L.) in a Wetland Environment: Preliminary Data on the Effects of Shooting Individuals. *Galemys: Boletín Informativo de La Sociedad Española Para La Conservación y Estudio de Los Mamíferos*, 16(Extra 1), 157–166.
- Rousseau, G., Giorgini, B., Livi, R., & Chaté, H. (1997). Dynamical phases in a cellular automaton model for epidemic propagation. *Physica D: Nonlinear Phenomena*, 103(1), 554–563. [https://doi.org/10.1016/S0167-2789\(96\)00285-0](https://doi.org/10.1016/S0167-2789(96)00285-0)
- Rowden, A. A., Anderson, O. F., Georgian, S. E., Bowden, D. A., Clark, M. R., Pallentin, A., & Miller, A. (2017). High-Resolution Habitat Suitability Models for the Conservation and Management of Vulnerable Marine Ecosystems on the Louisville Seamount Chain, South Pacific Ocean. *Frontiers in Marine Science*, 4. <https://www.frontiersin.org/articles/10.3389/fmars.2017.00335>
- Rowlands, R. J., Michaud, V., Heath, L., Hutchings, G., Oura, C., Vosloo, W., Dwarka, R., Onashvili, T., Albina, E., & Dixon, L. K. (2008). African swine fever virus isolate, Georgia, 2007. *Emerging Infectious Diseases*, 14(12), 1870–1874. <https://doi.org/10.3201/eid1412.080591>

- Roy, S., McElwain, T. F., & Wan, Y. (2011). A network control theory approach to modeling and optimal control of zoonoses: Case study of brucellosis transmission in sub-Saharan Africa. *PLoS Neglected Tropical Diseases*, 5(10), e1259. <https://doi.org/10.1371/journal.pntd.0001259>
- Rushton, J. (2009). Part II: A review of the application of economics to animal diseases and health problems. In *The Economics of Animal Health and Production* (pp. 193–197). CAB International.
- Rushton, J., Thornton, P. K., & Otte, M. J. (1999). Methods of economic impact assessment. *Revue Scientifique Et Technique (International Office of Epizootics)*, 18(2), 315–342. <https://doi.org/10.20506/rst.18.2.1172>
- Russell, R. E., Katz, R. A., Richgels, K. L. D., Walsh, D. P., & Grant, E. H. C. (2017). A Framework for Modeling Emerging Diseases to Inform Management. *Emerging Infectious Diseases*, 23(1), 1–6. <https://doi.org/10.3201/eid2301.161452>
- Saitou, N., & Nei, M. (1987). The neighbor-joining method: A new method for reconstructing phylogenetic trees. *Molecular Biology and Evolution*, 4(4), 406–425. <https://doi.org/10.1093/oxfordjournals.molbev.a040454>
- Salazar, L. G., Rose, N., Hayes, B. H., Hammami, P., Baubet, E., Desvaux, S., & Andraud, M. (2022). Effects of Habitat Fragmentation and Hunting Activities on African Swine Fever Dynamics Among Wild Boar Populations. *Preventive Veterinary Medicine*, 208. <https://doi.org/10.1016/j.prevetmed.2022.105750>
- Sanchez Botija, C., & Badiola, C. (1966). [Presencia of the African swine pest virus in Haematopinus suis]. *Bulletin - Office International Des Epizooties*, 66(1), 699–705.
- Sánchez, E. G., Pérez-Núñez, D., & Revilla, Y. (2019). Development of vaccines against African swine fever virus. *Virus Research*, 265, 150–155. <https://doi.org/10.1016/j.virusres.2019.03.022>
- Sanchez-Botija, C. (1963). Reservorios del virus de la Peste Porcina Africana. Investigación del virus de la P. P. A. en las arthropodos mediante la prueba de la hemadsocion. *Bull. Off. Int. Epizootiol.*, 60, 895–899.
- Sanchez-Botija, C. (1982). Peste porcina africana. Nuevos desarrollos. *Revue Scientifique Et Technique (International Office of Epizootics)*, 1(4), 991–1094. <https://doi.org/10.20506/rst.1.4.91>
- Sánchez-Vizcaíno, J. M., Martínez-López, B., Martínez-Avilés, M., Martins, C., Boinas, F., Vialc, L., Michaud, V., Jori, F., Etter, E., Albina, E., & Roger, F. (2009). Scientific review on African Swine Fever. *EFSA Supporting Publications*, 6. <https://doi.org/10.2903/sp.efsa.2009.EN-5>
- Sánchez-Vizcaíno, J. M., Mur, L., Gomez-Villamandos, J. C., & Carrasco, L. (2015). An Update on the Epidemiology and Pathology of African Swine Fever. *Journal of Comparative Pathology*, 152(1), 9–21. <https://doi.org/10.1016/j.jcpa.2014.09.003>



- Santos, N., Richomme, C., Nunes, T., Vicente, J., Alves, P. C., de la Fuente, J., Correia-Neves, M., Boschioli, M.-L., Delahay, R., & Gortázar, C. (2020). Quantification of the Animal Tuberculosis Multi-Host Community Offers Insights for Control. *Pathogens (Basel, Switzerland)*, 9(6). <https://doi.org/10.3390/pathogens9060421>
- Sauter-Louis, C., Conraths, F. J., Probst, C., Blohm, U., Schulz, K., Sehl, J., Fischer, M., Forth, J. H., Zani, L., Depner, K., Mettenleiter, T. C., Beer, M., & Blome, S. (2021). African Swine Fever in Wild Boar in Europe—A Review. *Viruses*, 13(9), 1717. <https://doi.org/10.3390/v13091717>
- Sauter-Louis, C., Schulz, K., Richter, M., Staubach, C., Mettenleiter, T. C., & Conraths, F. J. (2021). African swine fever: Why the situation in Germany is not comparable to that in the Czech Republic or Belgium. *Transboundary and Emerging Diseases*. <https://doi.org/10.1111/tbed.14231>
- Schulz, K., Conraths, F. J., Blome, S., Staubach, C., & Sauter-Louis, C. (2019). African Swine Fever: Fast and Furious or Slow and Steady? *Viruses*, 11(9), 866. <https://doi.org/10.3390/v11090866>
- Schulz, K., Staubach, C., & Blome, S. (2017). African and classical swine fever: Similarities, differences and epidemiological consequences. *Veterinary Research*, 48, 84. <https://doi.org/10.1186/s13567-017-0490-x>
- Shi, R., Li, Y., & Wang, C. (2020). Stability analysis and optimal control of a fractional-order model for African swine fever. *Virus Research*, 288, 198111. <https://doi.org/10.1016/j.virusres.2020.198111>
- Shirley, M. D. F., & Rushton, S. P. (2005). The impacts of network topology on disease spread. *Ecological Complexity*, 2(3), 287–299. <https://doi.org/10.1016/j.ecocom.2005.04.005>
- Simeón-Negrín, R. E., & Frías-Lepoureau, M. T. (2002). Eradication of African Swine Fever in Cuba (1971 and 1980). In *Trends in Emerging Viral Infections of Swine* (pp. 125–131). John Wiley & Sons, Ltd. <https://doi.org/10.1002/9780470376812.ch4b>
- Sindryakova, I., Morgunov, Yu. P., Chichikin, A. Y., Gazaev, I., Kudryashov, D. A., & Tsybanov, S. Z. (2016). The influence of temperature on the Russian isolate of African swine fever virus in pork products and feed with extrapolation to natural conditions. *Sel'skokhozyaistvennaya Biologiya*, 51, 467–474. <https://doi.org/10.15389/agrobiol.2016.4.467eng>
- Śmietanka, K., Woźniakowski, G., Kozak, E., Niemczuk, K., Frączyk, M., Bocian, Ł., Kowalczyk, A., & Pejsak, Z. (2016). African Swine Fever Epidemic, Poland, 2014–2015. *Emerging Infectious Diseases*, 22(7), 1201–1207. <https://doi.org/10.3201/eid2207.151708>
- Smith, G. (2006). Persistence of disease in territorial animals: Insights from spatial models of Tb. *NEW ZEALAND JOURNAL OF ECOLOGY*, 30(1), 35–41.

- Smith, G., Cheeseman, C., Clifton-Hadley, R., & Wilkinson, D. (2001). A model of bovine tuberculosis in the badger *Meles meles*: An evaluation of control strategies. *JOURNAL OF APPLIED ECOLOGY*, 38(3), 509–519. <https://doi.org/10.1046/j.1365-2664.2001.00609.x>
- Smith, G., Cheeseman, C., Wilkinson, D., & Clifton-Hadley, R. (2001). A model of bovine tuberculosis in the badger *Meles meles*: The inclusion of cattle and the use of a live test. *JOURNAL OF APPLIED ECOLOGY*, 38(3), 520–535. <https://doi.org/10.1046/j.1365-2664.2001.00610.x>
- Smith, G., Delahay, R. J., McDonald, R. A., & Budgey, R. (2016). Model of Selective and Non-Selective Management of Badgers (*Meles meles*) to Control Bovine Tuberculosis in Badgers and Cattle. *PloS One*, 11(11), e0167206. <https://doi.org/10.1371/journal.pone.0167206>
- Song, W., Kim, E., Lee, D., Lee, M., & Jeon, S.-W. (2013). The sensitivity of species distribution modeling to scale differences. *Ecological Modelling*, 248, 113–118. <https://doi.org/10.1016/j.ecolmodel.2012.09.012>
- Spitz, F., & Janeau, G. (1990). Spatial strategies: An attempt to classify daily movements of wild boar. [Http://Katalog.Pan.Pl/Webpac-Bin/223bzbsPL/Wgbroker.Exe?New+Access+top+search+open+NR+ee95400552](http://Katalog.Pan.Pl/Webpac-Bin/223bzbsPL/Wgbroker.Exe?New+Access+top+search+open+NR+ee95400552). <https://doi.org/10.4098/AT.arch.90-14>
- Ståhl, K., Sternberg-Lewerin, S., Blome, S., Viltrop, A., Penrith, M.-L., & Chenais, E. (2019). Lack of evidence for long term carriers of African swine fever virus—A systematic review. *Virus Research*, 272, 197725. <https://doi.org/10.1016/j.virusres.2019.197725>
- Stevenson, M. A., Sanson, R. L., Stern, M. W., O’Leary, B. D., Sujau, M., Moles-Benfell, N., & Morris, R. S. (2013). InterSpread Plus: A spatial and stochastic simulation model of disease in animal populations. *Preventive Veterinary Medicine*, 109(1–2), 10–24. <https://doi.org/10.1016/j.prevetmed.2012.08.015>
- Stocks, T., Britton, T., & Höhle, M. (2017). *pomp-astic Inference for Epidemic Models: Simple vs. Complex* (p. 125880). bioRxiv. <https://doi.org/10.1101/125880>
- Stocks, T., Britton, T., & Höhle, M. (2018). Model selection and parameter estimation for dynamic epidemic models via iterated filtering: Application to rotavirus in Germany. *Biostatistics (Oxford, England)*, 21(3), 400–416. <https://doi.org/10.1093/biostatistics/kxy057>
- Sun, E., Huang, L., Zhang, X., Zhang, J., Shen, D., Zhang, Z., Wang, Z., Huo, H., Wang, W., Huangfu, H., Wang, W., Li, F., Liu, R., Sun, J., Tian, Z., Xia, W., Guan, Y., He, X., Zhu, Y., ... Bu, Z. (2021). Genotype I African swine fever viruses emerged in domestic pigs in China and caused chronic infection. *Emerging Microbes & Infections*, 10(1), 2183–2193. <https://doi.org/10.1080/22221751.2021.1999779>
- Susser, M., & Susser, E. (1996). Choosing a future for epidemiology: II. From black box to Chinese boxes and eco-epidemiology. *American Journal of Public Health*, 86(5), 674–677.

- Takamatsu, H.-H., Denyer, M. S., Lacasta, A., Stirling, C. M. A., Argilaguet, J. M., Netherton, C. L., Oura, C. A. L., Martins, C., & Rodríguez, F. (2013). Cellular immunity in ASFV responses. *Virus Research*, *173*(1), 110–121. <https://doi.org/10.1016/j.virusres.2012.11.009>
- Taylor, R. A., Podgórski, T., Simons, R. R. L., Ip, S., Gale, P., Kelly, L. A., & Snary, E. L. (2021). Predicting spread and effective control measures for African swine fever—Should we blame the boars? *Transboundary and Emerging Diseases*, *68*(2), 397–416. <https://doi.org/10.1111/tbed.13690>
- Thomson, G. R. (1985). The epidemiology of African swine fever: The role of free-living hosts in Africa. *The Onderstepoort Journal of Veterinary Research*, *52*(3), 201–209.
- Thomson, G. R., Gainaru, M. D., & Van Dellen, A. F. (1980). Experimental infection of warthos (*Phacochoerus aethiopicus*) with African swine fever virus. *The Onderstepoort Journal of Veterinary Research*, *47*(1), 19–22.
- Thulke, H.-H., & Lange, M. (2017). Simulation-based investigation of ASF spread and control in wildlife without consideration of human non-compliance to biosecurity. *EFSA Supporting Publications*, *14*(11), 1312E. <https://doi.org/10.2903/sp.efsa.2017.EN-1312>
- Tildesley, M. J., Deardon, R., Savill, N. J., Bessell, P. R., Brooks, S. P., Woolhouse, M. E. J., Grenfell, B. T., & Keeling, M. J. (2008). Accuracy of models for the 2001 foot-and-mouth epidemic. *Proceedings of the Royal Society B: Biological Sciences*, *275*(1641), 1459–1468. <https://doi.org/10.1098/rspb.2008.0006>
- Tildesley, M. J., & Keeling, M. J. (2008). Modelling foot-and-mouth disease: A comparison between the UK and Denmark. *Preventive Veterinary Medicine*, *85*(1–2), 107–124. <https://doi.org/10.1016/j.prevetmed.2008.01.008>
- Toni, T., Welch, D., Strelkowa, N., Ipsen, A., & Stumpf, M. P. H. (2009). Approximate Bayesian computation scheme for parameter inference and model selection in dynamical systems. *Journal of The Royal Society Interface*, *6*(31), 187–202. <https://doi.org/10.1098/rsif.2008.0172>
- Turlewicz-Podbielska, H., Kuriga, A., Niemyjski, R., Tarasiuk, G., & Pomorska-Mól, M. (2021). African Swine Fever Virus as a Difficult Opponent in the Fight for a Vaccine—Current Data. *Viruses*, *13*(7), Article 7. <https://doi.org/10.3390/v13071212>
- Ungur, A., Cazan, C. D., Panait, L. C., Taulescu, M., Balmoş, O. M., Mihaiu, M., Bărbuceanu, F., Mihalca, A. D., & Cătoi, C. (2021). Genotyping of African Swine Fever Virus (ASFV) Isolates in Romania with the First Report of Genotype II in Symptomatic Pigs. *Veterinary Sciences*, *8*(12), 290. <https://doi.org/10.3390/vetsci8120290>
- United States Geological Survey (USGS). (2002). What in the world is Epidemioecology? *Epidemiology News*, *1*(1).

- Urner, N., Seržants, M., Užule, M., Sauter-Louis, C., Staubach, C., Lamberg, K., Oļševskis, E., Conraths, F. J., & Schulz, K. (2021). Hunters' view on the control of African swine fever in wild boar. A participatory study in Latvia. *Preventive Veterinary Medicine*, 186, 105229. <https://doi.org/10.1016/j.prevetmed.2020.105229>
- USDA, APHIS. (2020). *African Swine Fever Response Plan: The Red Book*. USDA Animal and Plant Health Inspection Service, Veterinary Services. [https://www.aphis.usda.gov/animal\\_health/emergency\\_management/downloads/asf-responseplan.pdf](https://www.aphis.usda.gov/animal_health/emergency_management/downloads/asf-responseplan.pdf)
- USDA, APHIS. (2021). *USDA Statement on Confirmation of African Swine Fever in the Dominican Republic*. [https://www.aphis.usda.gov/aphis/newsroom/news/sa\\_by\\_date/sa-2021/asf-confirm](https://www.aphis.usda.gov/aphis/newsroom/news/sa_by_date/sa-2021/asf-confirm)
- van den Driessche, P. (2008). Spatial Structure: Patch Models. In F. Brauer, P. van den Driessche, & J. Wu (Eds.), *Mathematical Epidemiology* (pp. 179–189). Springer. [https://doi.org/10.1007/978-3-540-78911-6\\_7](https://doi.org/10.1007/978-3-540-78911-6_7)
- Van Goethem, B. (2021, September 1). *Update on African swine fever situation in the EU*. European Commission Directorate-General for Health and Food Safety, Crisis preparedness in food, animals and plants.
- Van Schepen, M. D., & Kunes, J. P. (1981). African Swine Fever: An Overview. *Undefined*. <https://www.semanticscholar.org/paper/African-Swine-Fever%3A-An-Overview-Schepen-Kunes/a34ec909c8c3c21c77df181185e0840e46aec0b2>
- Vergne, T., Andraud, M., Bonnet, S., De Regge, N., Desquesnes, M., Fite, J., Eto, F., Garigliany, M.-M., Jori, F., Lempereur, L., Le Potier, M.-F., Quillery, E., Saegerman, C., Vial, L., & Bouhsira, E. (2021). Mechanical transmission of African swine fever virus by *Stomoxys calcitrans*: Insights from a mechanistic model. *Transboundary and Emerging Diseases*, 68(3), 1541–1549. <https://doi.org/10.1111/tbed.13824>
- Vergne, T., Gogin, A., & Pfeiffer, D. U. (2017). Statistical Exploration of Local Transmission Routes for African Swine Fever in Pigs in the Russian Federation, 2007–2014. *Transboundary and Emerging Diseases*, 64(2), 504–512. <https://doi.org/10.1111/tbed.12391>
- Vergne, T., Guinat, C., & Pfeiffer, D. U. (2020). Undetected Circulation of African Swine Fever in Wild Boar, Asia. *Emerging Infectious Diseases*, 26(10), 2480–2482. <https://doi.org/10.3201/eid2610.200608>
- Vergne, T., Korennoy, F., Combelles, L., Gogin, A., & Pfeiffer, D. U. (2016). Modelling African swine fever presence and reported abundance in the Russian Federation using national surveillance

- data from 2007 to 2014. *Spatial and Spatio-Temporal Epidemiology*, 19, 70–77. <https://doi.org/10.1016/j.sste.2016.06.002>
- Viboud, C., Sun, K., Gaffey, R., Ajelli, M., Fumanelli, L., Merler, S., Zhang, Q., Chowell, G., Simonsen, L., & Vespignani, A. (2018). The RAPIDD ebola forecasting challenge: Synthesis and lessons learnt. *Epidemics*, 22, 13–21. <https://doi.org/10.1016/j.epidem.2017.08.002>
- Vynnycky, E., & White, R. (2010). *An Introduction to Infectious Disease Modelling*. Oxford University Press.
- Wade, A., Achenbach, J. E., Gallardo, C., Settypalli, T. B. K., Souley, A., Djonwe, G., Loitsch, A., Dauphin, G., Ngang, J. J. E., Boyomo, O., Cattoli, G., Diallo, A., & Lamien, C. E. (2019). Genetic characterization of African swine fever virus in Cameroon, 2010-2018. *Journal of Microbiology (Seoul, Korea)*, 57(4), 316–324. <https://doi.org/10.1007/s12275-019-8457-4>
- Walker, J. G., Evans, K. E., Rose Vineer, H., van Wyk, J. A., & Morgan, E. R. (2018). Prediction and attenuation of seasonal spillover of parasites between wild and domestic ungulates in an arid mixed-use system. *The Journal of Applied Ecology*, 55(4), 1976–1986. <https://doi.org/10.1111/1365-2664.13083>
- Walton, G. (1962). The *Ornithodoros moubata* superspecies problem in relation to human relapsing fever epidemiology. In D. Arthur (Ed.), *Aspects of Disease Transmission by Ticks* (6th ed., pp. 83–156). The Society.
- Ward, M., Garner, M., & Cowled, B. (2015). Modelling foot-and-mouth disease transmission in a wild pig–domestic cattle ecosystem. *Australian Veterinary Journal*, 93(1–2), 4–12. <https://doi.org/10.1111/avj.12278>
- Ward, M. P., Laffan, S. W., & Highfield, L. D. (2011). Disease spread models in wild and feral animal populations: Application of artificial life models. *Revue Scientifique et Technique (International Office of Epizootics)*, 30(2), 437–446. <https://doi.org/10.20506/rst.30.2.2042>
- Weaver, T. R. D., & Habib, N. (2020). *Evaluating Losses Associated with African Swine Fever in the People’s Republic of China and Neighboring Countries* (Cambodia, China, People’s Republic of, Lao People’s Democratic Republic, Myanmar, Viet Nam). Asian Development Bank. <https://www.adb.org/publications/losses-african-swine-fever-prc-neighboring-countries>
- White, S. H., del Rey, A. M., & Sánchez, G. R. (2007). Modeling epidemics using cellular automata. *Applied Mathematics and Computation*, 186(1), 193–202. <https://doi.org/10.1016/j.amc.2006.06.126>
- Widgren, S., Bauer, P., Eriksson, R., & Engblom, S. (2019). SimInf: An R Package for Data-Driven Stochastic Disease Spread Simulations. *Journal of Statistical Software*, 91, 1–42. <https://doi.org/10.18637/jss.v091.i12>

- Wilkinson, D., Smith, G., Delahay, R., & Cheeseman, C. (2004). A model of bovine tuberculosis in the badger *Meles meles*: An evaluation of different vaccination strategies. *JOURNAL OF APPLIED ECOLOGY*, 41(3), 492–501. <https://doi.org/10.1111/j.0021-8901.2004.00898.x>
- Wilkinson, P. (1989). African Swine Fever Virus. In M. Pensaert, *Virus Infections of Porcines*. Elsevier Science.
- Wilson, E. B., & Burke, M. H. (1942). The Epidemic Curve. *Proceedings of the National Academy of Sciences of the United States of America*, 28(9), 361–367.
- WOAH. (2019a). *Self-declaration of the recovery of freedom from African swine fever in all suids by the Czech Republic*. WOAH.
- WOAH. (2019b). *Bovine tuberculosis: Global distribution and implementation of prevention and control measures according to WAHIS data* (p. 3). OIE. <https://bulletin.woah.org/?panorama=3-01-tb-wahis-en>
- WOAH. (2019c). *Technical Disease Card. African swine fever*. WOAH. [https://www.woah.org/en/document/african\\_swine\\_fever/](https://www.woah.org/en/document/african_swine_fever/)
- WOAH. (2021). *Terrestrial Animal Health Code* (29th ed.). WOAH. <https://www.oie.int/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/>
- WOAH. (2022a). *Animal Disease Information System (ADIS)*. WOAH. <https://wahis.woah.org/>
- WOAH. (2022b). *African swine fever (ASF)—Situation Report 11* (Situation Report, p. 5). WOAH. <https://www.woah.org/app/uploads/2022/05/asf-report11.pdf>
- WOAH. (2022c, May 23). Implementing stronger biosecurity to avoid disease spread to new areas. *WOAH - World Organisation for Animal Health*. <https://www.woah.org/en/implementing-stronger-biosecurity-to-avoid-disease-spread-to-new-areas/>
- WOAH. (2022d). *African swine fever (ASF)—Situation report 17* (Situation Report, p. 6). OIE. <https://www.woah.org/app/uploads/2022/07/asf-report17-1.pdf>
- Wolfram, S. (1984). Universality and complexity in cellular automata. *Physica D: Nonlinear Phenomena*, 10(1), 1–35. [https://doi.org/10.1016/0167-2789\(84\)90245-8](https://doi.org/10.1016/0167-2789(84)90245-8)
- Wolfram, S. ., Author, & Gad-el-Hak, M. ., Reviewer. (2003). A New Kind of Science. *Applied Mechanics Reviews*, 56(2), B18–B19. <https://doi.org/10.1115/1.1553433>
- Yang, A., Schlichting, P., Wight, B., Anderson, W. M., Chinn, S. M., Wilber, M. Q., Miller, R. S., Beasley, J. C., Boughton, R. K., VerCauteren, K. C., Wittemyer, G., & Pepin, K. M. (2021). Effects of social structure and management on risk of disease establishment in wild pigs. *Journal of Animal Ecology*, 90(4), 820–833. <https://doi.org/10.1111/1365-2656.13412>
- Yoo, D. S., Kim, Y., Lee, E. S., Lim, J. S., Hong, S. K., Lee, I. S., Jung, C. S., Yoon, H. C., Wee, S. H., Pfeiffer, D. U., & Fournié, G. (2021). Transmission Dynamics of African Swine Fever Virus, South Korea,

2019. *Emerging Infectious Diseases*, 27(7), 1909–1918.  
<https://doi.org/10.3201/eid2707.204230>
- Yoon, H., Hong, S.-K., Lee, I., Choi, D.-S., Lee, J.-H., Lee, E., & Wee, S.-H. (2021). Arthropods as potential vectors of African swine fever virus outbreaks in pig farms in the Republic of Korea. *Veterinary Medicine and Science*, 7(5), 1841–1844. <https://doi.org/10.1002/vms3.545>
- You, S., Liu, T., Zhang, M., Zhao, X., Dong, Y., Wu, B., Wang, Y., Li, J., Wei, X., & Shi, B. (2021). African swine fever outbreaks in China led to gross domestic product and economic losses. *Nature Food*, 2(10), Article 10. <https://doi.org/10.1038/s43016-021-00362-1>
- Zani, L., Forth, J. H., Forth, L., Nurmoja, I., Leidenberger, S., Henke, J., Carlson, J., Breidenstein, C., Viltrop, A., Höper, D., Sauter-Louis, C., Beer, M., & Blome, S. (2018). Deletion at the 5'-end of Estonian ASFV strains associated with an attenuated phenotype. *Scientific Reports*, 8(1), Article 1. <https://doi.org/10.1038/s41598-018-24740-1>
- Zorzenon dos Santos, R. M., & Coutinho, S. (2001). Dynamics of HIV infection: A cellular automata approach. *Physical Review Letters*, 87(16), 168102.  
<https://doi.org/10.1103/PhysRevLett.87.168102>

**Titre :** Modélisation mathématique de la peste porcine africaine à l'interface entre élevages de cochons et sangliers : implications pour la lutte

**Mots clés :** peste porcine, modélisation, simulation, diffusion, transmission inter-spécifique, contrôle

**Résumé :** En 2007, le virus de la peste porcine africaine (PPA) a émergé sur le continent européen et a décimé les populations de porcs domestiques et de sangliers. Avec la propagation virale entre les compartiments sauvages et domestiques qui complique les efforts de contrôle, et l'absence de vaccins disponibles, la PPA est l'une des maladies infectieuses les plus difficiles à contrôler. Les modèles mathématiques ont fait leurs preuves en matière d'aide à la prise de décision, mais aucun modèle existant de la PPA ne tient compte de cette interface entre les porc domestiques et les sangliers. La Roumanie, l'état membre de l'Union européenne le plus gravement touché par la maladie, est riche en élevages porcins de basse-cour, suspectés d'être particulièrement exposés aux populations de sangliers. Pour mieux comprendre la dynamique de l'épizootie, nous avons construit un modèle

mécaniste spatial et stochastique de transmission de la PPA, intégrant à la fois les compartiments domestique et sauvage. Le modèle a été calibré en combinant une revue de la littérature scientifique et un ajustement à l'épizootie observée en Roumanie, permettant d'évaluer la contribution relative des compartiments domestique et sauvage à la propagation du virus. Des stratégies de contrôle alternatives ont été explorées, révélant que le dépeuplement de l'ensemble de la population porcine des villages infectés, plutôt que seulement des lots touchés, aurait pu réduire l'épidémie de manière conséquente. Ce modèle peut maintenant être adapté à d'autres pays, comme la Corée du Sud pour évaluer l'efficacité des barrières, ou comme la France pour tester des scénarii de gestion en cas d'apparition de foyers de PPA.

**Titre :** Mathematical modelling of African swine fever at the domestic-wildlife interface: Implications for control

**Keywords:** swine fever, modelling, simulation, multihost transmission, diffusion, control

**Abstract:** In 2007, African swine fever virus (ASFV) escaped again from sub-Saharan Africa and has been decimating domestic pig and wild boar populations around the world. With viral spillover between the wild and domestic compartments complicating control efforts, and the absence of an available vaccine, ASF is one of the most difficult infectious diseases to control. Mathematical models have a proven record of assisting policy makers in epizootic decision-making, but as shown through a systematic review of the modelling literature, no existing ASF models account for such spillover transmission. Romania, the most severely affected European Union Member State, is rich in backyard swine farming—and suspected to be particularly exposed to wild boar populations. To better understand the observed epizootic dynamics, we

built a spatial and stochastic mechanistic model of ASF transmission, integrating both domestic and wild compartments. The model was calibrated by combining a review of the scientific literature and a fit to the epizootic observed in Romania, allowing to evaluate the relative contribution of the domestic and wild compartments to the virus spread. Alternative control strategies were able to be explored, revealing that depopulation of the entire pig population in the infected villages, rather than just the affected batches, could have significantly reduced the epidemic. This model can now be adapted to other countries, such as South Korea to evaluate the effectiveness of barriers, or France to test management scenarios in the event of an ASF outbreak.