

DISSERTATION

SIMULATION MODELING AS A TOOL FOR THE CONTROL OF FOOT-AND-MOUTH DISEASE (FMD) IN  
ENDEMIC REGIONS

Submitted by

Muhammad Usman Zaheer

Department of Clinical Sciences

In partial fulfillment of the requirements

For the Degree of Doctor of Philosophy

Colorado State University

Fort Collins, Colorado

Fall 2019

Doctoral Committee:

Advisor: Sangeeta Rao

Co-Advisor: Mo D. Salman

Katie Steneroden

Steve Weber

Sheryl Magzamen

Copyright by Muhammad Usman Zaheer 2019

All Rights Reserved

## ABSTRACT

### SIMULATION MODELING AS A TOOL FOR THE CONTROL OF FOOT-AND-MOUTH DISEASE IN ENDEMIC REGIONS

Foot and mouth disease (FMD) is endemic in many parts of the world (Anjum et al., 2006; Farooq et al., 2018, 2017a, 2017b, 2017c, 2016; Gleeson, 2002; Jamal et al., 2010; Navid et al., 2018; Rweyemamu et al., 2008; Yano et al., 2018), and it is associated with substantial economic losses (Ferrari et al., 2014; Jemberu et al., 2014; Knight-Jones and Rushton, 2013), which amount to USD 6.5 and 21 billion, and > USD 1.5 billion in endemic and disease-free settings, respectively (Knight-Jones and Rushton, 2013). International organizations such as the Food and Agriculture Organization of the United Nations (FAO), the World Organization for Animal Health (OIE), the European Commission for the Control of Foot and Mouth Disease (EuFMD) have called for a more targeted control strategy in the ‘Progressive Control Pathway for FMD’ to reduce the disease burden and high economic costs associated with it (Abbas et al., 2014; Jamal and Belsham, 2013; Paton et al., 2009; Rweyemamu et al., 2008a; Sumption et al., 2012).

Simulation modeling has become common for investigating the spread of highly contagious diseases such as FMD, and for conducting risk assessments (Dorjee et al., 2016; Guitian and Pfeiffer, 2006; Kao, 2002; Keeling, 2005; Morris et al., 2002). Many models have been developed to mimic the spread of FMD in specific regions or countries (Bates et al., 2003d; Garner and Beckett, 2005; Harvey et al., 2007b; Stevenson et al., 2013; Wongsathapornchai et al., 2008). In disease-free countries, models are used to identify gaps in the preparedness such as estimating required resources (Garner et al., 2016; Roche et al., 2014), whereas, in endemic countries, models can be useful to compare mitigation strategies to guide future directions of FMD control program (Souley Kouato et al., 2018).

Most of the reported literature on FMD simulation models is, however, associated with disease-free countries with minimal application of these models in countries with an endemic status of FMD (Pomeroy et al., 2017). Use of simulation models to endemic settings, therefore, would be beneficial in advancing our knowledge and understanding of FMD dynamics, and to facilitate both local and global control of FMD (Pomeroy et al., 2017). The overall goal of this dissertation was to build and demonstrate the application of spatially-explicit stochastic simulation models as a tool to evaluate mitigation strategies for FMD control in endemic settings.

Most of the reported literature on FMD simulation models is, however, associated with disease-free countries with minimal application of these models in countries with an endemic status of FMD (Pomeroy et al., 2017). Chapter 1 of this dissertation followed the guidelines (Moher et al., 2009) established in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The aim was to review the existing published original research on spatially explicit stochastic simulation models (SESS) of FMD spread, with a specific focus on assessing these models for their application in FMD-endemic settings. The goal was to identify the specific components of endemic FMD needed to adapt the SESS models for application in FMD-endemic settings. It was revealed that existing SESS should be adapted by incorporating multiple co-circulating serotypes, livestock population dynamics, and routine prophylactic vaccination (RPV) to extend their potential use in FMD-endemic settings.

Application of SESS models require datasets on the location and population of individual livestock holdings, and these data are often not available for developing countries. To overcome this lack of data, Chapter 2 of this dissertation demonstrated the methodology to generate these data synthetically for livestock in Pakistan and Thailand. The approach consisted of three main steps, i.e., microsimulating aggregate census data, creating geospatial probability surface, and, finally, distributing the microsimulated dataset on the geospatial probability surface. The resulting simulated dataset is a crucial

input for the application of SESS models in endemic regions for modeling FMD spread and evaluating mitigation strategies for its control.

The use of SESS models in endemic regions requires adaptation of these models to incorporate necessary components of endemic FMD such as livestock population dynamics, multiple co-circulating serotypes, and routine prophylactic vaccination (RPV). Chapter 3 of this dissertation aimed to modify the underlying modeling framework of the North American Animal Disease Spread Model (NAADSM) to include RPV as an additional mitigation strategy for FMD control. The resulting framework is called “Simulation Model for Infectious Animal Diseases in Endemic Regions (SMIAD-ER).” The SMIAD-ER is a uniquely equipped model to simulate the spread and evaluate alternative mitigation strategies for infectious animal diseases such as FMD in endemic regions. A demonstration of the prototype version of SMIAD-ER to FMD in Punjab, Pakistan, revealed that there was no aberrant behavior of FMD spread, which gave confidence that modification in underlying code did not result in any unintended change to the framework. Besides, the implementation of RPV as a mitigation strategy contributed to building regional herd immunity for FMD control.

Model building is an iterative process which moves from being simple to add complexity to the framework gradually. The prototype version of SMIAD-ER did not have the flexibility to incorporate capacity and coverage for RPV. Since the capacity and coverage are critical components of vaccination programs, Chapter 4 of this dissertation aimed to enhance SMIAD-ER by modifying the underlying modeling framework to allow users with the flexibility to parameterize capacity and coverage for RPV to mimic the situation of a control program in endemic regions more realistically. As a demonstration for Sindh province, Pakistan, four scenarios, i.e., baseline, enhanced movement restrictions, improved disease detection, enhanced RPV, were parameterized to compare two performance indices, i.e. outbreak duration, vaccine immune holdings by the end of the outbreak, and the ratio of these two indices. Results indicated that improved FMD detection scenario resulted in the least number of

holdings vaccinated with a day increase in outbreak duration followed by baseline, enhanced movement restriction, and enhanced RPV scenario. The results should, however, be considered for decision-making in line with the limitations of the study and assumptions of SMIAD-ER.

Like any study, there are limitations to the approach taken by this dissertation. Chapter 5 of this dissertation aimed to present the limitations of the approach and to suggest recommendations for future work. The limitations, for instance, include reliance on the opinions of a very limited number of veterinarians to parameterize SMIAD-ER, the use of FMD outbreaks data as a proxy for prevalence. Future work should select a large number of stakeholders to glean model parameters, obtain reliable estimates on the FMD prevalence preferably by production-type and region, reach a consensus in expert opinions through the Delphi approach. Moreover, endemic countries need to strengthen their monitoring and surveillance systems, implement stricter movement restrictions through legislation and public awareness, and implement aggressive vaccination campaigns to reduce the burden FMD to ensure economic gains for future. Also, a graphical user interface should be added to SMIAD-ER to facilitate novice modelers from endemic settings to benefit from the model. Besides, SMIAD-ER should be enhanced to equip it with the capability to model multiple co-circulating serotypes and livestock population dynamics since these are unequivocally the necessary components of endemic FMD.

## ACKNOWLEDGMENTS

I want to thank my doctoral advisors, Drs. Sangeeta Rao and Mo Salman, my committee members, Dr. Katie Steneroden, Steve Weber and Sheryl Magzamen, ex officios, Shaun Case, and Dr. Chris Burdett for providing the support and guidance throughout the Ph.D. program.

I am also grateful to Sadie Skeels, Veterinary Teaching Hospital Library, Colorado State University, for her support with database search during the conduct of the systematic review. Besides, I would like to acknowledge the inputs and guidance from Drs. Melinda Laituri and Julia Sharp, James McAndrew, Emma Giles, Yashad Samant, Sophia Linn, Joshua Reyling, CSU's GeoSpatial Centroid staff, anonymous survey respondents from Pakistan and Thailand during the process of estimating the location and population of individual livestock holdings in developing countries.

Moreover, collaborations with UNFAO-Pakistan team members Dr. Muhammad Afzal, Dr. Manzoor Hussain, Dr. Muhmmad Javed Arshad, for the project "GCP/PAK/123/USA Development of Technical Framework for the Control of Foot and Mouth Disease in Pakistan", Dr. Syed Jamal from University of Malakand, KPK, Pakistan, anonymous field veterinarian from Livestock and Dairy Development Department, Punjab, Pakistan, and , and Drs. Sith Premashtira and Tosapol Dejyong from the Department of Livestock Development Thailand and UNFAO's Regional Office for Asia and Pacific, respectively, played a significant role in the completion of this dissertation.

I am also obliged to the US Department of State's Foreign Fulbright Program, implemented by the Institute of International Education and the United States Educational Foundation in Pakistan, and the United States Department of Agriculture (USDA), National Institute of Food and Agriculture, Animal Health and Disease project 2015-05040 "Adaptation and validation of a climate-based simulation model for Foot-and-Mouth Disease (FMD) spread in non-endemic and endemic countries/regions." for

providing the financial support for my doctoral studies. Acknowledgments are also due for the Colorado State University's Office of resources for Disabled Students for providing me with necessary accommodations to complement my efforts in the Ph.D. program.

In the end, I would like to thank my family and friends for their continued support during the doctoral program.

Muhammad Usman Zaheer  
DVM, MPhil, Diplomate ACVPM  
Fall 2019



## DEDICATION

I dedicate this dissertation to five incredible women in my life, i.e., my amazing mother, Samina Zaheer, my lovely wife Anza Usman, my angelical daughters Areeha Usman and Nurhan Usman, and my sweet sister Amnah Zaheer.

## TABLE OF CONTENTS

ABSTRACT.....	ii
ACKNOWLEDGMENTS.....	vi
DEDICATION.....	viii
REFERENCES.....	xiv
CHAPTER 1: CHALLENGES TO THE APPLICATION OF SPATIALLY EXPLICIT STOCHASTIC SIMULATION MODELS FOR FOOT-AND-MOUTH DISEASE CONTROL IN ENDEMIC SETTINGS: A SYSTEMATIC REVIEW.....	
1	1
Summary.....	1
Highlights.....	2
1 Introduction.....	3
2 Methods.....	5
2.1 Protocol.....	5
2.2 Definition of SESS.....	5
2.3 Eligibility criteria.....	5
2.4 Information sources and search strategy.....	6
2.4.1 Databases.....	6
2.4.2 Search strategy.....	6
2.5 Screening and inclusion/exclusion criteria.....	6
2.5.1 Screening criteria.....	6
2.5.2 Inclusion criteria.....	6
2.6 Assessment of final citations and data extraction.....	7
3 Results.....	7
3.1 Database searches and screening.....	7
3.2 Inclusion criteria.....	8
3.3 Unique SESS models.....	8
3.4 Top five SESS models.....	8
3.4.1 Warwick model.....	8
3.4.2 DADS model.....	9
3.4.3 AusSpread model.....	10
3.4.4 ISP model.....	10
3.4.5 NAADSM model.....	11

3.5	<i>Assessment of SESS models</i> .....	11
3.6	<i>Multiple SESS models</i> .....	12
4	Discussion.....	12
5	Conclusion.....	17
	Funding: .....	18
	Conflict of Interest: .....	18
	Figures.....	19
	Tables.....	20
	REFERENCES.....	21
CHAPTER 2: ESTIMATING THE LOCATION OF INDIVIDUAL LIVESTOCK HOLDINGS AND THEIR POPULATIONS IN TWO DEVELOPING COUNTRIES FOR USE IN SPATIAL DISEASE SPREAD MODELS .....		
1	Introduction .....	39
2	Methods.....	43
2.1	<i>Study area and animal types</i> .....	43
2.1.1	<i>Pakistan</i> .....	43
2.1.2	<i>Thailand</i> .....	44
2.2	<i>Datasets</i> .....	44
2.3	<i>Microsimulation of census data</i> .....	45
2.3.1	<i>Pakistan</i> .....	46
2.3.2	<i>Thailand</i> .....	46
2.4	<i>Creation of the geospatial probability surface</i> .....	47
2.4.1	<i>Acquisition and geoprocessing of data</i> .....	47
2.4.2	<i>Expert opinion and estimation of weights</i> .....	47
2.4.3	<i>Initial geospatial probability surface</i> .....	48
2.4.4	<i>Empirical holding locations and personal communications for additional probability buffers</i> 48	
2.4.5	<i>Final geospatial probability surface</i> .....	49
2.5	<i>Distribution of random holdings on the categorized geospatial probability surface</i> .....	49
2.5.1	<i>Holdings on categorized geospatial probability surface</i> .....	49
2.5.2	<i>Minimum distance between holdings</i> .....	49
2.5.3	<i>Creation of random holdings</i> .....	50
2.5.4	<i>Joining location and population data</i> .....	51
2.6	<i>Creation of density maps</i> .....	51
3	Results.....	51

3.1	<i>Microsimulation of census data</i> .....	51
3.2	<i>Geospatial probability surfaces</i> .....	51
3.3	<i>Individual holdings with associated location and population</i> .....	52
3.4	<i>Livestock holding density</i> .....	52
4	Discussion.....	53
5	Conclusion.....	56
	Funding .....	56
	Conflict of Interest .....	57
	Figures.....	58
	Tables.....	73
	REFERENCES.....	80
CHAPTER 3: ADAPTATION OF THE NORTH AMERICAN ANIMAL DISEASE SPREAD MODEL FOR FOOT-AND-MOUTH DISEASE IN ENDEMIC SETTINGS: A PILOT ASSESSMENT AND DEMONSTRATION .....		
1	Introduction .....	90
2	Methods.....	93
2.1	<i>Data sources</i> .....	93
2.2	<i>Assumptions of SMIAD-ER</i> .....	93
2.3	<i>Scenarios</i> .....	95
2.3.1	<i>Baseline scenario (sc1)</i> .....	95
2.3.2	<i>Enhanced scenario (sc2)</i> .....	95
2.4	<i>Scenario parameters</i> .....	95
2.4.1	<i>Production types and their status</i> .....	95
2.4.2	<i>Progression parameters</i> .....	96
2.4.3	<i>Spread parameters</i> .....	96
2.4.4	<i>FMD detection parameters</i> .....	96
2.4.5	<i>Disease tracing</i> .....	96
2.4.6	<i>Zones</i> .....	97
2.4.7	<i>Vaccination</i> .....	97
2.4.8	<i>Destruction parameters</i> .....	98
2.4.9	<i>Iterations and set-up</i> .....	98
2.5	<i>Statistical analysis</i> .....	98
3	Results and Discussion .....	98
	Funding: .....	102

Conflict of Interest: .....	102
Tables .....	103
REFERENCES .....	105
CHAPTER 4: SIMULATION MODEL FOR INFECTIOUS ANIMAL DISEASES IN ENDEMIC REGIONS (SMIAD-ER): APPLICATION FOR FOOT-AND-MOUTH DISEASE CONTROL STRATEGIES .....	114
1 Introduction .....	114
2 Methods .....	117
2.1 Assumptions of SMIAD-ER .....	118
2.2 Additional features to SMIAD-ER .....	119
2.3 Data sources .....	120
2.4 Model parameters .....	120
2.4.1 Production-types and their status .....	120
2.4.2 Progression parameters .....	121
2.4.3 Spread parameters .....	121
2.4.4 FMD detection parameters .....	122
2.4.5 Disease tracing .....	122
2.4.6 Examination of traced holdings .....	123
2.4.7 Diagnostic testing of traced holdings .....	123
2.4.8 Zones .....	123
2.4.9 Destruction .....	123
2.4.10 Vaccination .....	123
2.5 Scenarios .....	124
2.6 Performance indices .....	125
2.7 Statistical analysis .....	125
3 Results .....	126
3.1 Outbreak duration .....	126
3.2 Vaccine immune holdings by the end of the outbreak .....	126
3.3 VO ratio .....	127
4 Discussion .....	127
Funding: .....	131
Conflict of Interest: .....	131
Tables .....	132
Figures .....	137

REFERENCES .....	139
CHAPTER 5: CONTROL OF FOOT-AND-MOUTH DISEASE IN ENDEMIC REGIONS: CONCLUSIONS, LIMITATIONS AND RECOMMENDATIONS .....	148
APPENDICES .....	152
Chapter 1.....	152
<i>PRISMA checklist</i> .....	152
Chapter 2.....	154
<i>List of provinces by region, Thailand</i> .....	154
<i>Description of datasets used</i> .....	155
<i>Geoprocessing</i> .....	156
<i>Projections and coordinate system</i> .....	156
<i>Administrative Boundary:</i> .....	156
<i>Waterbodies:</i> .....	156
<i>Road networks:</i> .....	156
<i>Elevation:</i> .....	157
<i>Land cover:</i> .....	157
<i>Probability surfaces</i> .....	162
<i>Density maps</i> .....	170
<i>Questionnaire</i> .....	178
<i>Starting status of holdings</i> .....	191
<i>Estimation of holding-level clinical duration</i> .....	191
<i>Spread Parameters</i> .....	193
<i>Contact Spread</i> .....	193
<i>Airborne spread</i> .....	195
<i>Disease Detection</i> .....	197
<i>Emergency vaccination</i> .....	198
Chapter 4.....	199
<i>Holding-level clinical infectious period</i> .....	199
REFERENCES .....	201

## REFERENCES

- Anjum, R., Hussain, M., Zahoor, A.B., Irshad, H., Farooq, U., 2006. Epidemiological analyses of foot and mouth disease in Pakistan. *Int. J. Agric. Biol.* 8.
- Bates, T.W., Thurmond, M.C., Carpenter, T.E., 2003a. Description of an epidemic simulation model for use in evaluating strategies to control an outbreak of foot-and-mouth disease. *Am. J. Vet. Res.* 64, 195–204. <https://doi.org/10.2460/ajvr.2003.64.195>
- Bates, T.W., Thurmond, M.C., Carpenter, T.E., 2003b. Results of epidemic simulation modeling to evaluate strategies to control an outbreak of foot-and-mouth disease. *Am. J. Vet. Res.* 64, 205–210. <https://doi.org/10.2460/ajvr.2003.64.205>
- Dorjee, S., Revie, C.W., Poljak, Z., McNab, W.B., Sanchez, J., 2016. One-Health Simulation Modelling: A Case Study of Influenza Spread between Human and Swine Populations using *NAADSM*. *Transbound. Emerg. Dis.* 63, 36–55. <https://doi.org/10.1111/tbed.12215>
- Dürr, S., Fasel-Clemenz, C., Thür, B., Schwermer, H., Doherr, M.G., Dohna, H. zu, Carpenter, T.E., Perler, L., Hadorn, D.C., 2014. Evaluation of the benefit of emergency vaccination in a foot-and-mouth disease free country with low livestock density. *Prev. Vet. Med.* 113, 34–46. <https://doi.org/10.1016/J.PREVETMED.2013.10.015>
- Farooq, U., Ahmed, Z., Naeem, K., Bertram, M., Brito, B., Stenfeldt, C., Pauszek, S.J., LaRocco, M., Rodriguez, L., Arzt, J., 2018. Characterization of naturally occurring, new and persistent subclinical foot-and-mouth disease virus infection in vaccinated Asian buffalo in Islamabad Capital Territory, Pakistan. *Transbound. Emerg. Dis.* 65, 1836–1850. <https://doi.org/10.1111/tbed.12963>
- Farooq, U., Irshad, H., Ullah, A., Latif, A., Zahur, A.B., Naeem, K., Ahmed, Z., Rodriguez, L.L., 2017a. Sero-

- prevalence of foot-and-mouth disease in small ruminants of Pakistan. *J. Anim. Plant Sci.* 27, 1197–1201.
- Farooq, U., Naeem, K., Zahur, A.B., Khan, M.A., Sidique, U., 2017b. Foot-and-mouth disease outbreaks investigations at Sindh, Punjab and Islamabad, Pakistan during the year 2012-2013. *Int. J. Biosci.* 11, 346–356. <https://doi.org/10.12692/ijb/11.5.346-356>
- Farooq, U., Naeem, K., Zahur, A.B., Khan, M.A., Sidique, U., Qureshi, S., 2017c. Epidemiological analysis and economic impact assessment of foot-and-mouth disease at Landhi dairy colony Karachi. *Asian J. Agric. Biol.* 5, 7–14.
- Farooq, U., Ullah, A., Irshad, H., Latif, A., Naeem, K., Zahur, A. Bin, Ahmad, Z., Rodriguez, L.L., 2016. Seroprevalence of foot-and-mouth disease in large ruminants in periurban dairy farms near Islamabad, Pakistan. *Asian Biomed.* 10, 123–127. <https://doi.org/10.5372/1905-7415.1002.472>
- Ferguson, N.M., Donnelly, C.A., Anderson, R.M., 2001. Transmission intensity and impact of control policies on the foot and mouth epidemic in Great Britain. *Nature* 413, 542–548. <https://doi.org/10.1038/35097116>
- Ferrari, G., Tasciotti, L., Khan, E., Kiani, A., 2014. Foot-and-Mouth Disease and Its Effect on Milk Yield: An Economic Analysis on Livestock Holders in Pakistan. *Transbound. Emerg. Dis.* 61, e52–e59. <https://doi.org/10.1111/tbed.12072>
- Garner, M., Beckett, S., 2005. Modelling the spread of foot-and-mouth disease in Australia. *Aust. Vet. J.* 83, 758–766. <https://doi.org/10.1111/j.1751-0813.2005.tb11589.x>
- Garner, M.G., Bombardieri, N., Cozens, M., Conway, M.L., Wright, T., Paskin, R., East, I.J., 2016. Estimating Resource Requirements to Staff a Response to a Medium to Large Outbreak of Foot and Mouth Disease in Australia. *Transbound. Emerg. Dis.* 63, e109–e121.



<https://doi.org/10.1111/tbed.12239>

Gleeson, L.J., 2002. A review of the status of foot and mouth disease in South-East Asia and approaches to control and eradication. *Rev. Sci. Tech.* 21, 465–75.

Guitian, J., Pfeiffer, D., 2006. Should we use models to inform policy development? *Vet. J.* 172, 393–395.  
<https://doi.org/10.1016/j.tvjl.2006.03.001>

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. *Prev. Vet. Med.* 82, 176–197. <https://doi.org/10.1016/J.PREVETMED.2007.05.019>

Jamal, S.M., Ahmed, S., Hussain, M., Ali, Q., 2010. Status of foot-and-mouth disease in Pakistan. *Arch. Virol.* 155, 1487–1491. <https://doi.org/10.1007/s00705-010-0732-y>

Jemberu, W.T., Mourits, M.C.M., Woldehanna, T., Hogeveen, H., 2014. Economic impact of foot and mouth disease outbreaks on smallholder farmers in Ethiopia. *Prev. Vet. Med.* 116, 26–36.  
<https://doi.org/10.1016/J.PREVETMED.2014.06.004>

Kao, R.R., 2002. The role of mathematical modelling in the control of the 2001 FMD epidemic in the UK. *Trends Microbiol.* 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. Biol. Sci.* 272, 1195–202.  
<https://doi.org/10.1098/rspb.2004.3046>

Keeling, M.J., Woolhouse, M.E., 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 (80-. )*. 294, 813–817.  
<https://doi.org/10.1126/science.1065973>

- 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? *Prev. Vet. Med.* 112, 161–173.  
<https://doi.org/10.1016/J.PREVETMED.2013.07.013>
- McReynolds, S.W., Sanderson, M.W., Reeves, A., Hill, A.E., 2014. Modeling the impact of vaccination control strategies on a foot and mouth disease outbreak in the Central United States. *Prev. Vet. Med.* 117, 487–504. <https://doi.org/10.1016/J.PREVETMED.2014.10.005>
- Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G., Group, T.P., 2009. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med.* 6, e1000097.  
<https://doi.org/10.1371/journal.pmed.1000097>
- Morris, R.S., Sanson, R.L., Stern M.W., Stevenson M., Wilesmith J.W., 2002. Decision-support tools for foot and mouth disease control. *Rev. sci. tech. Off. int. Epiz.* 21, 557–567.  
<https://doi.org/10.20506/rst.21.3.1363>
- 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. *Vet. Rec.* 149, 137–44. <https://doi.org/10.1136/vr.149.5.137>
- Navid, M.T., Farooq, U., Latif, A., Awais, M.M., Anwar, M.I., Akhtar, M., Zahur, A.B., 2018. Prevalence of foot and mouth disease virus in apparently healthy buffaloes brought to Islamabad slaughterhouse in Pakistan. *Trop. Biomed.* 35, 161–167.
- Pomeroy, L.W., Bansal, S., Tildesley, M., Moreno-Torres, K.I., Moritz, M., Xiao, N., Carpenter, T.E., Garabed, R.B., 2017. Data-Driven Models of Foot-and-Mouth Disease Dynamics: A Review. *Transbound. Emerg. Dis.* 64, 716–728. <https://doi.org/10.1111/tbed.12437>
- Roche, S.E., Garner, M.G., Wicks, R.M., East, I.J., de Witte, K., 2014. How do resources influence control

- measures during a simulated outbreak of foot and mouth disease in Australia? *Prev. Vet. Med.* 113, 436–446. <https://doi.org/10.1016/J.PREVETMED.2013.12.003>
- Rweyemamu, M., Roeder, P., Mackay, D., Sumption, K., Brownlie, J., Leforban, Y., Valarcher, J.-F., Knowles, N.J., Saraiva, V., 2008. Epidemiological Patterns of Foot-and-Mouth Disease Worldwide. *Transbound. Emerg. Dis.* 55, 57–72. <https://doi.org/10.1111/j.1865-1682.2007.01013.x>
- Souley Kouato, B., De Clercq, K., Abatih, E., Dal Pozzo, F., King, D., Thys, E., Marichatou, H., Saegerman, C., 2018. Review of epidemiological risk models for foot-and-mouth disease: Implications for prevention strategies with a focus on Africa. *PLoS One* 13, e0208296. <https://doi.org/10.1371/journal.pone.0208296>
- 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. *Prev. Vet. Med.* 109, 10–24. <https://doi.org/10.1016/J.PREVETMED.2012.08.015>
- Tomassen, F.H.M., de Koeijer, A., Mourits, M.C.M., Dekker, A., Bouma, A., Huirne, R.B.M., 2002. A decision-tree to optimise control measures during the early stage of a foot-and-mouth disease epidemic. *Prev. Vet. Med.* 54, 301–324. [https://doi.org/10.1016/S0167-5877\(02\)00053-3](https://doi.org/10.1016/S0167-5877(02)00053-3)
- Wongsathapornchai, K., Salman, M.D., Edwards, J.R., Morley, P.S., Keefe, T.J., Campen, H. V., Weber, S.E., Premashthira, S., 2008. Use of epidemiologic risk modeling to evaluate control of foot-and-mouth disease in southern Thailand. *Am. J. Vet. Res.* 69, 240–251. <https://doi.org/10.2460/ajvr.69.2.240>
- Yano, T., Premashthira, S., Dehyong, T., Tangtrongsup, S., Salman, M.D., 2018. The Effectiveness of a Foot and Mouth Disease Outbreak Control Programme in Thailand 2008–2015: Case Studies and Lessons Learned. *Vet. Sci.* <https://doi.org/10.3390/vetsci5040101>

Yoon, H., Wee, S.-H., Stevenson, M.A., O'Leary, B.D., Morris, R.S., Hwang, I.-J., Park, C.-K., Stern, M.W.,  
2006. Simulation analyses to evaluate alternative control strategies for the 2002 foot-and-mouth  
disease outbreak in the Republic of Korea. *Prev. Vet. Med.* 74, 212–225.  
<https://doi.org/10.1016/J.PREVETMED.2005.12.002>

CHAPTER 1: CHALLENGES TO THE APPLICATION OF SPATIALLY EXPLICIT STOCHASTIC SIMULATION  
MODELS FOR FOOT-AND-MOUTH DISEASE CONTROL IN ENDEMIC SETTINGS: A SYSTEMATIC REVIEW<sup>1</sup>

Summary

Simulation modeling has become common for estimating the spread of highly contagious animal diseases. Many models have been developed to mimic the spread of foot and mouth disease (FMD) in specific regions or countries to conduct risk assessment, to analyze outbreaks using historical data or hypothetical scenarios, to assist in policy decisions during epidemics, and policy formulation in preparedness planning, and in evaluating economic impacts. Most of the available FMD simulation models were designed for and applied in disease-free countries, while there has been limited use of such models in FMD endemic countries.

The objective of this paper is to report the findings from a study conducted to review the existing published original research literature on spatially explicit stochastic simulation models (SESS) of FMD spread, with a specific focus to assess these models for their potential use in endemic settings. The goal

---

<sup>1</sup> This chapter of the dissertation is intended for publication in the Preventive Veterinary Medicine journal and is formatted in line with journal requirements. The manuscript has been submitted to the journal on July 23, 2019.

Muhammad Usman Zaheer<sup>a</sup>, Mo Salman<sup>a</sup>, Katie Steneroden<sup>a</sup>, Sheryl Magzamen<sup>b</sup>, Steve Weber<sup>a</sup>, Shaun Case<sup>c</sup>, Sangeeta Rao<sup>a\*</sup>

<sup>a</sup>Animal Population Health Institute, Department of Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins CO 80523, USA, <sup>b</sup>Department of Environmental and Radiological Health Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins CO 80523, USA, <sup>c</sup>Department of Civil and Environmental Engineering, Walter Scott, Jr. College of Engineering, Colorado State University, Fort Collins CO 80523, USA

\*Corresponding Author: Sangeeta.Rao@ColoState.Edu

is to identify the specific components of endemic FMD needed to adapt the SESS models for their potential application in FMD endemic settings.

This systematic review follows the PRISMA guidelines, and three databases were searched, which resulted in 1176 citations. Eighty citations finally met the inclusion criteria and were included in the qualitative synthesis, which identified nine unique SESS models. These SESS models were assessed for their potential application in endemic settings. All of the assessed SESS models can be adapted for use in FMD endemic countries by modifying the underlying code to include multiple co-circulating serotypes, routine prophylactic vaccination (RPV), and livestock population dynamics to more realistically mimic the endemic characteristics of FMD.

The application of SESS models in endemic settings will help evaluate strategies for FMD control, which will improve livestock health, provide economic gains for producers, help alleviate poverty and hunger, and will complement efforts to attain Sustainable Development Goals and the 2030 Agenda.

#### Highlights

- Endemic countries are underrepresented in the literature on SESS models for FMD
- SESS models can mimic FMD spread in disease-free settings, but not in endemic settings
- SESS models should be adapted to extend their application in endemic settings
- Their use in endemic settings will guide future directions for FMD control programs
- FMD control will be beneficial for animal health, food security, and economic gains

#### Keywords

Foot and Mouth Disease, FMD, Systematic review, Modeling, Spatially explicit, Endemic, Simulation, Stochastic

## 1 Introduction

Foot and mouth disease is endemic in many parts of the world (Anjum et al., 2006; Farooq et al., 2018, 2017a, 2017b, 2017c, 2016; Gleeson, 2002; Jamal et al., 2010; Navid et al., 2018; Rweyemamu et al., 2008b; Yano et al., 2018), and is associated with substantial economic losses (Ferrari et al., 2014; Jemberu et al., 2014; Knight-Jones and Rushton, 2013). The costs associated with production decline and vaccination in endemic regions amount to between USD 6.5 and 21 billion, and the annual outbreak-associated losses in FMD-free countries and zones exceed USD 1.5 billion (Knight-Jones and Rushton, 2013). International organizations such as the Food and Agriculture Organization of the United Nations (FAO), the World Organization for Animal Health (OIE), the European Commission for the Control of Foot and Mouth Disease (EuFMD) have called for a more targeted control strategy in the ‘Progressive Control Pathway for FMD’ to reduce the disease burden and high economic costs associated with it (Abbas et al., 2014; Jamal and Belsham, 2013; Paton et al., 2009; Rweyemamu et al., 2008a; Sumption et al., 2012).

Simulation modeling has become common for investigating the spread of highly contagious diseases and for conducting risk assessments (Dorjee et al., 2016; Guitian and Pfeiffer, 2006; Kao, 2002; Keeling, 2005; Morris et al., 2002). These models can be categorized as deterministic or stochastic based on the way randomness incorporated, and non-spatial or spatially-explicit based on how spatial relationships are considered (Carpenter, 2011). Spatial models require “locational data” for herds of animals and incorporate spatial proximity and spatial relationships in estimating disease risk (Carpenter, 2011). The spatially explicit stochastic simulation models incorporate uncertainty in the inputs and outputs parameters, heterogeneity in disease processes, and integrate geographic locations and spatial proximity of herds that affect their relative exposure and transmission risk (Carpenter, 2011; Patyk et al., 2011).

Many models have been developed to mimic the spread of FMD in specific regions or countries (Bates et al., 2003b; Garner and Beckett, 2005; Harvey et al., 2007; Stevenson et al., 2013;

Wongsathapornchai et al., 2008). These models have been used for risk assessment, to analyze outbreaks using historical data or hypothetical scenarios, to assist in policy decisions during outbreaks, and policy formulation in preparedness planning, and in evaluating economic impacts (Bates et al., 2003a; Dürr et al., 2014; Ferguson et al., 2001a; Keeling et al., 2001; McReynolds et al., 2014; Morris et al., 2001; Tomassen et al., 2002; Yoon et al., 2006a). In disease-free countries, models are used to identify gaps in the preparedness such as estimating required resources (Garner et al., 2016a; Roche et al., 2014), whereas, in endemic countries, models can be useful to compare mitigation strategies to guide future directions of FMD control program (Souley Kouato et al., 2018).

Most of the reported literature on FMD simulation models is, however, associated with disease-free countries with minimal application of these models in countries with an endemic status of FMD (Pomeroy et al., 2017). The development of simulation models of infectious livestock diseases such as FMD in endemic settings is enormously challenging for the reasons such as the lack of interest and understanding of perceived needs, political or economic constraints, insufficient data to support model parameters, and complexity of FMD epidemiology in endemic settings (Brooks-Pollock et al., 2015; Knight-Jones et al., 2016b). For instance, routine prophylactic vaccination (RPV) is practiced in endemic settings to control FMD, but factors such as duration of natural immunity, the rate of vaccine-induced antibody waning and the rate of disease reintroduction influence FMD control and are critical determinants of the success of vaccination programs (Ringa and Bauch, 2014). Also, the circulation of multiple serotypes of FMD virus is a common characteristic in endemic settings (Ahmed et al., 2018; Ullah et al., 2017). The transmission patterns and duration of immunity are variable for different serotypes (Pomeroy et al., 2015). Application of simulation models to endemic settings, therefore, would be beneficial in advancing our knowledge and understanding of FMD dynamics, and to facilitate both local and global control of FMD (Pomeroy et al., 2017).



The objective of this paper was to report the findings from a study conducted to review the existing published original research literature on spatially explicit stochastic simulation models (SESS) of FMD spread, with a specific focus on assessing these models for their potential use in endemic settings. The goal was to identify the specific components of endemic FMD needed to adapt the SESS models for their potential application in FMD endemic settings. The use of SESS models in endemic settings will help evaluate strategies for FMD control which will improve livestock health, provide economic gains for producers, help alleviate poverty and hunger, which and will complement efforts to attain Sustainable Development Goals and the 2030 Agenda.

## 2 Methods

### 2.1 *Protocol*

This systematic review follows the guidelines established in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher et al., 2009).

### 2.2 *Definition of SESS*

For this systematic review, the definition of a SESS model was developed to facilitate the process of identifying the search items that could be included in the qualitative synthesis (adapted from Carpenter, 2011; Patyk et al., 2011). A SESS model was defined as “one that takes input parameters in the form of statistical distributions, consequently generating a distribution of values for results and incorporates geographic locations and spatial proximity of animals or herds that affect their relative exposure and transmission risk.”

### 2.3 *Eligibility criteria*

Any original research in the English language published during any timespan that described or used a SESS model for simulating FMD spread or evaluating mitigation in any part of the world would be included.

## 2.4 *Information sources and search strategy*

### 2.4.1 *Databases*

Three databases, i.e., Google Scholar (GS), PubMed, and Web of Science (WoS), were chosen to identify the relevant literature.

### 2.4.2 *Search strategy*

All three databases were searched by the primary author on the same day, i.e., October 7, 2018, to identify the literature. The keywords used were *((foot and mouth disease OR FMD OR FMDV) AND (stochastic AND simulation))*. These keywords were consistent across all databases searched. These keywords were chosen to be sensitive in capturing all possible publications, including these keywords. The resulting citations were managed in Microsoft Excel (2016).

## 2.5 *Screening and inclusion/exclusion criteria*

The citations identified through the database search were first screened (Step 1-3) and then assessed to identify SESS models for FMD (step 4-5). Eventually, a flowchart (Figure 1.1) was created as per PRISMA guidelines (Moher et al., 2009).

### 2.5.1 *Screening criteria*

The search results were screened in three steps. In step 1, citations were checked for duplicates across databases and within the database. All duplicates were removed from the pool of citations at this stage. In the second step, citations were screened for their publication language. Citations not in the English language were removed. In step 3, citations were checked for their document type. Only the publications that were original research were retained, and all other document types were excluded because their validity was challenging to evaluate.

### 2.5.2 *Inclusion criteria*

In step 4, the title and abstract of remaining citations were evaluated to determine if they contained the word(s) foot and mouth disease, FMD or FMDV, and those citations that did not include these words

were excluded. The rationale for this strict criterion was to move from being sensitive as indicated above to be specific to the disease of interest, i.e., FMD.

In step 5, remaining citations were evaluated to determine if they describe or use a SESS model to understand FMD spread, and to evaluate mitigation strategies. Citations that did not meet this criterion were excluded, and the remaining citations were selected for qualitative synthesis.

The remaining citations were grouped based on the unique SESS model they described or used. An additional group was created for citations that compared different models to evaluate alternative mitigation strategies and aid in decision making.

## *2.6 Assessment of final citations and data extraction*

Each unique SESS was then evaluated for its assumptions, epidemiologic design with specific emphasis on its application in endemic settings. Specifically, each SESS model was assessed for its ability to model multiple serotypes of FMD virus in parallel, the range of mitigation strategies (emergency vaccination, RPV, stamping-out), and livestock population dynamics. These factors were chosen because of their epidemiologic significance in endemic FMD.

After evaluation of each SESS, the data on various features were extracted for comparison of different SESS. Each SESS was then summarized, and limitations in each SESS were highlighted. Finally, suggestions were made for adaptation of the SESS models for their potential use in endemic settings.

## **3 Results**

Figure 1.1 shows the flow chart that summarizes the process of identifying citations from different databases, screening of citations, and assessment against inclusion criteria.

### *3.1 Database searches and screening*

The database search resulted in 1176 accessible citations: 1011, 39, and 126 from GS, PubMed, and WoS, respectively. In step 1, all of the 39 citations from PubMed and 97 citations from WoS were

identified as duplicate with GS citations. Out of 1011 GS citations, four were duplicated within GS. All 140 duplicate citations were removed.

In step 2, the remaining 1036 citations were screened for the language of their publication, and 22 were removed because they were not in the English language. In step 3, the remaining 1014 citations were checked for document type, and 287 were excluded because they were not published original research.

### *3.2 Inclusion criteria*

After screening, of the remaining 727 citations, 647 were excluded because the citations either did not contain the word(s) foot and mouth disease, FMD, FMDV in their title or abstract, or did not describe or use a SESS for FMD, and hence failed to meet the inclusion criteria. The remaining 80 citations were included in the qualitative synthesis.

### *3.3 Unique SESS models*

Nine unique SESS models were identified, and relevant citations were grouped in Table 1.1. Each unique SESS model was assessed for its assumptions, epidemiologic design with specific emphasis on its application in endemic settings.

### *3.4 Top five SESS models*

Below is a short description of the top five SESS models (based on the number of citations identified in the study) with emphasis on their suitability for the general aim of this study. For a more detailed description of these SESS models, readers are referred to the original citations specified in Table 1.1.

#### *3.4.1 Warwick model*

In response to an outbreak of FMD that hit the UK in 2001, a stochastic, spatial model was developed to simulate between farm spread of FMD (Keeling et al., 2001). The model was designed to act as a decision support tool during the 2001 epidemic. Since then, this SESS model has undergone various adaptations (Keeling et al., 2003; Tildesley et al., 2006) and is now termed the Warwick model.

The Warwick model has been used for FMD to: understand predictors of transmission risk (Savill et al., 2006), identify high risk areas (Le Menach et al., 2005), understand spatio-temporal process (Diggle, 2006), evaluate mitigation strategies (Tildesley et al., 2012, 2009), determine optimal control strategies (Tildesley and Keeling, 2008; Tildesley and Ryan, 2012), guide policy makers (Porphyre et al., 2013), assist in real-time policy making (Probert et al., 2018), understand effect of vaccine availability constraints on epidemiologic and economic outcomes (Porphyre et al., 2018), estimate prevalence of asymptomatic carriers (Arnold et al., 2008), understand effect of livestock density vs. farm density (Meadows et al., 2018), assess agreement between model outputs and epidemic data (Tildesley et al., 2008), understand impact of resolution of spatial data to inform control policies (Tildesley et al., 2010), determine the predictor of final epidemic size (Tildesley and Keeling, 2009), and computation advancement (Sellman et al., 2018).

#### 3.4.2 *DADS model*

The Davis Animal Disease Simulation (DADS) model is a stochastic, spatial simulation model to simulate the spread and evaluate the alternative mitigation strategies for FMD control in a designated geographical area (Bates et al., 2003a, 2003b). It has been used to: estimate FMD spread (Carpenter et al., 2007; Zingg et al., 2015), examine epidemic and economic impacts (Carpenter et al., 2011), evaluate mitigation strategies (Dickey et al., 2008; Dürr et al., 2014; Pineda-Krch et al., 2010), evaluate the effect of animal movement tracing (Mardones et al., 2013), and to examine the importance to stochasticity and modifying the assumption of homogeneous mixing (Carpenter, 2011).

An optimal control model was formulated based on the DADS structure to evaluate the control strategies for FMD in the USA (Kobayashi et al., 2007a, 2007b). The DADS has been recently modified at the Technical University of Denmark and is now termed as DTU-DADS. This modified DTU-DADS is being used in FMD free countries to understand the spread of FMD as a result of a hypothetical incursion,

evaluation of mitigation strategies and helping with contingency planning (Boklund et al., 2017, 2013; Dórea et al., 2017; Halasa et al., 2015, 2014).

#### 3.4.3 *AusSpread model*

AusSpread is a stochastic, spatial simulation model that operates in a GIS environment to simulate between herds the spread of FMD (Beckett and Garner, 2007; Garner and Beckett, 2005). AusSpread is the outcome of more than ten years of extensive work of the Australian Government's Department of Agriculture, Fisheries, and Forestry (Garner and Lack, 1995a, 1995b). The intention behind this extensive effort was to have a model that could be used as a decision-support tool for infectious diseases like FMD that pose the most significant economic threat to Australia (Productivity Commission, 2002).

Since the development of AusSpread model, it has continuously been used in FMD-free regions to: evaluate alternative mitigation strategies (East et al., 2014; Elbakidze et al., 2009; Ward et al., 2009), assist in preparedness planning (East et al., 2016), estimate resources (Garner et al., 2016a; Roche et al., 2014), evaluate benefits of effective traceability system (Hagerman et al., 2013) and early detection (Garner et al., 2016b).

#### 3.4.4 *ISP model*

InterSpread Plus (ISP) is a stochastic, spatial simulation model of between farm spread of infectious diseases such as FMD (Stevenson et al., 2013). The ISP was developed to mimic the spread of FMD in New Zealand, a country free of FMD, to aid in preparedness planning and decision making (Owen et al., 2011; Stevenson et al., 2013). The ISP is a revised version of the InterSpread (IS) model that has been used to model alternative mitigation strategies during the 2001 FMD epidemic in the UK (Morris et al., 2001).

The ISP has been used for FMD to: evaluate alternative mitigation strategies (Sanson et al., 2017; Velthuis and Mourits, 2007; Wada et al., 2017; Yoon et al., 2006), assist in design of contingency

plan (Martínez-López et al., 2010), and evaluate benefits of effective traceability system (Sanson et al., 2014).

#### 3.4.5 *NAADSM model*

The North American Animal Disease Spread Model (NAADSM) is a stochastic, spatial model developed in the US with the capability of modeling between farms spread of infectious animal diseases such as FMD, CSF (Harvey et al., 2007; Schoenbaum and Disney, 2003).

The NAADSM is the only open-source SESS model with a friendly user interface, and it has been used for FMD to: understand FMD spread and evaluate alternative mitigation strategies (Gale et al., 2015), identify optimal vaccination strategy (McReynolds et al., 2014), evaluate economic impacts (Pendell et al., 2015; Schroeder et al., 2015), and understand the effect of model complexity on model prediction (Zagmutt et al., 2016).

#### 3.5 *Assessment of SESS models*

The SESS models assessed in this systematic review are equipped to simulate the impact of emergency vaccination because of their design and underlying assumption of application in epidemic settings, which are otherwise disease-free. ‘Routine Prophylactic Vaccination (RPV)’ is practiced cyclically in endemic settings to control FMD, hence application of these SESS models in such settings would require modification of SESS models to equip them with a capability to evaluate the impact of RPV on FMD dynamics.

All of the assessed SESS models were designed and applied in for FMD-free countries to mimic the spread of FMD and evaluate alternative mitigation strategies in the face of the incursion. In such an application, modelers assume that there is be only one circulating serotype and use the progression parameters for that serotype. In endemic settings, however, co-circulation of multiple serotypes is a crucial component of FMD epidemiology, which needs to be added as an additional option for the modeler to include progression parameters for multiple serotypes in parallel.

Additionally, the assessed SESS models do not take into consideration population dynamics, i.e., births and deaths that might be occurring during the simulation, except in the case of stamping-out. Any application of these models in endemic settings would require the addition of population dynamic parameters.

### 3.6 *Multiple SESS models*

As indicated in Table 1.1, ten citations reported using more than one SESS model. These studies ranged from model comparisons and country comparisons (Boklund et al., 2013; Dubé et al., 2007; Garner et al., 2016c; Hagersman et al., 2012; Halasa et al., 2014; Rawdon et al., 2018; Roche et al., 2015; Sanson et al., 2011) to ensemble modeling and structured decision-making (Probert et al., 2016; Webb et al., 2017). The model comparison highlights the consistency in outcomes from commonly used SESS models. These findings are essential for increasing end-user confidence in model outcomes and their use in informed decision making.

## 4 Discussion

Published original research describing or using SESS model(s) were assessed in this study with the goal to identify the specific components of endemic FMD needed to adapt the SESS models for their potential application in FMD endemic settings. It should be emphasized that this current study did not review all models, but only spatially explicit, stochastic simulation (SESS) models used for FMD as identified through the database search. Although all of the assumptions of these SESS models were reviewed, only the elements necessary for endemicity were considered. A potential bias could have arisen from restricting this review to the English language, published original research articles, and the specific category of models included, i.e., SESS. Many different types of models could have been selected, ranging from deterministic to automata models, to non-spatial models. It should be emphasized, that only spatially explicit models were included because of their ability to account for uncertainty in the inputs and outputs, the importance of geography, demography and heterogeneity in



disease processes, and their role in the choice of disease control options. We, however, acknowledge the work of all models on FMD, and our decision to include one type of model does not imply that other models were not useful. Other models may be more suitable for the specific objectives for which they were constructed, and for their intended use.

It was surprising to identify nine SESS models which leads to think why there was a need for such a large number of models. One potential reasoning for this lies in the fact that different kinds of data may be available in different circumstances to simulate FMD spread. For example, the Warwick model (Keeling et al., 2001) uses a transmission kernel method to model FMD spread which encompasses all possible routes of spread. On the other hand, models such as NAADSM (Harvey et al., 2007), incorporate different modes of diseases spread such as contact spread and airborne. Second potential reason for a large number of SESS models is the level of complexity models incorporate based on local animal husbandry, and perceived disease epidemiology in case of incursion. For example, AusSpread model (Beckett and Garner, 2007; Garner and Beckett, 2005) allows to incorporate animal assembly areas and wildlife in the disease spread, while NAADSM (Harvey et al., 2007) do not incorporate congregation points and ignores effect of wildlife. Despite differences in the way SESS models incorporate disease spread, animal husbandry and perceived epidemiology, studies conducted on model comparisons and country comparisons (Boklund et al., 2013; Dubé et al., 2007; Garner et al., 2016c; Hagersman et al., 2012; Halasa et al., 2014; Rawdon et al., 2018; Roche et al., 2015; Sanson et al., 2011) highlight the consistency in outcomes from commonly used SESS models. These findings are essential to increase end-user confidence in model outcomes and their usefulness in informing decision making.

Foot and mouth disease is endemic in several parts of the world (Anjum et al., 2006; Gleeson, 2002; Jamal et al., 2010; Rweyemamu et al., 2008b), and it is associated with substantial economic losses (Ferrari et al., 2014; Jemberu et al., 2014; Knight-Jones and Rushton, 2013). Livestock population dynamics, multiple co-circulating serotypes, and routine prophylactic vaccination are key characteristics

of endemic FMD (Ahmed et al., 2018; Hunter, 1998; Knight-Jones et al., 2016a; Ullah et al., 2017).

Published original research describing or using SESS model(s) for understanding the dynamics of FMD and evaluating mitigation strategies for its control were qualitatively assessed for their ability to mimic endemic FMD and potential application in endemic settings. None of the SESS models mentioned in Table 1.1 and described above are applicable in endemic settings in their current form, taking into consideration the characteristics of endemic FMD. The sole reason for this is that these SESS models were developed with an aim to mimic the characteristics of FMD in disease-free settings, and the assumptions of these models vary from the features of FMD in endemic settings. For instance, stamping-out is often employed as a mitigation strategy in disease-free countries. However, it may not be applied as an appropriate mitigation strategy in endemic settings because of limited resources and the inability to pay compensation to livestock owners (Hunter, 1998).

All of the SESS models described in this review can model emergency vaccination as a mitigation strategy, but none of them can model RPV which is often cyclically practiced in endemic settings and is relied upon as one of the key measures for control and eradication (Cai et al., 2014; Doel, 2003; Hunter, 1998; Knight-Jones et al., 2016a). The reason behind this drawback is very straightforward - models are a simplification of a complex system. Since these SESS models are designed to simplify the system of FMD in disease-free countries, they do not include RPV as a mitigation strategy. For adapting a SESS model such as NAADSM for endemic settings, it must have the option to model the effect of RPV as part of FMD control strategies. The adapted SESS models should have flexible user-defined options for specifying the frequency of vaccination. The option to alter the effectiveness of vaccines should be available. The use of the same vaccine in emergency situations could show more effectiveness when compared to RPV in endemic settings (Enekave et al., 2013). Vaccine factors such as maintenance of cold chain, type of serotype, quality control of vaccine and duration of immunity greatly influence its effectiveness (Jamal et al., 2014, 2008; Ringa and Bauch, 2014). Although the SESS models include

emergency vaccination, the modified SESS must have the option to alter the parameters associated with RPV, such as the inclusion of duration of vaccine immunity, coverage, efficacy, and capacity, in order to more realistically mimic endemic FMD.

The FMD-free countries usually employ SESS models for preparedness planning and as a decision support tool. To inform these decisions, modelers and epidemiologists do not include multiple co-circulating serotypes; hence, parameters for only one serotype are used to model the spread. Although all the SESS models realistically mimic the underlying system of FMD-free countries, they have a limited ability to be applied to the conditions when the disease is endemic. Multiple co-circulating serotypes, for instance, are common in endemic countries (Ahmed et al., 2018; Ullah et al., 2017; Vosloo et al., 2002) which complicates disease spread and ultimately its control and eradication. The existing SESS model(s) such as NAADSM need to be adapted by changing the underlying code to include options for modeling multiple co-circulating serotypes. Simplifying assumptions should be made to find the balance between model realism vs. complexity while modeling multiple co-circulating serotypes. The adaptation should be coupled with sensitivity analysis and adapted SESS models must undergo rigorous model verification and validation (Reeves et al., 2011).

In FMD-free countries, when these SESS models are used for preparedness planning, culling is usually employed with or without emergency vaccination. These strict actions in conjunction with disease tracing, surveillance, and availability of resources have led to prompt disease control and subsequent eradication, which results in simulations ending in a very short time and population dynamics having little impact. Therefore, modelers have not considered population dynamics during simulation runs because of it being close to the reality of disease-free settings. Furthermore, when SESS models would be used in endemic settings, FMD outbreaks would continue for a longer duration, and it would take longer to control the disease; therefore, eradication cannot be considered a short-term goal. Population turnover is associated with FMD dynamics, such as herd-immunity. As newborns are added

to the herd, it increases the proportion of unvaccinated naive hosts, thus decreasing herd immunity (Knight-Jones et al., 2016a). Thus, population demographics are also associated with herd susceptibility and infectivity, which are of key significance in disease modeling. Application of SESS models in endemic settings should afford the flexibility to parameterize population dynamics (birth, death processes) to realistically mimic the natural spread of FMD and assess the impact of a changing susceptible population. For example, the underlying code of any of these SESS model should allow modifications to add the option of increasing the number of animals in the herd when disease simulation runs exceed 365 days and continue this after every 365 days. Some simplifying assumptions should be made, such as applying a country-level growth rate. Subsequently, complexity can be added, such as using a production type-specific growth rate or applying a regional growth rate to account for birth and death process in a specific production type or a geographic region, respectively.

In endemic settings, FMD is associated with substantial economic losses (Ferrari et al., 2014; Jemberu et al., 2014; Knight-Jones and Rushton, 2013). International organizations such as the Food and Agriculture Organization of the United Nations (FAO), the World Organization for Animal Health (OIE), the European Commission for the Control of Foot and Mouth Disease (EuFMD) have called for a more targeted control strategy in the 'Progressive Control Pathway for FMD' to reduce the disease burden and high economic costs associated with it (Jamal and Belsham, 2013; Paton et al., 2009; Rweyemamu et al., 2008a; Sumption et al., 2012). Endemic countries can benefit from the virtual lab of simulation modeling and evaluate alternative mitigation strategies for FMD control and ultimate eradication. The SESS models, however, should have flexible stop conditions. For instance, a stop condition can be added to NAADSM to "end simulation when prevalence reaches a certain threshold." Such flexible stop conditions can help countries evaluate their progress and identify the key actions that can be taken to achieve project-specific goals and milestones.

Model building is a resource-intensive process requiring financial resources as well as technical expertise. Since the process is intensive, it would be wise to adopt a model built for one country to mimic the situation in another country. The model adaptation can be a small change of parameters used in one country to parameters for another country, or it may require changing the underlying code and logic. Before embarking on model adaptation, the researcher should understand the intended purpose of the existing model as well as the adapted model. Model adaptation provides several advantages for both the modeler and the end user. It provides modelers access to datasets that can be used for model validation. The adaptation process also provides a platform to exchange model outcomes among researchers and provides opportunities for end users such as disease modelers, epidemiologists, and experts from endemic countries (Dubé et al., 2011). Such interactions are essential for modelers to get acquainted with animal production systems to inform the models in a better way (Salman, 2004). For end-users, it is cheaper to adapt a model than building one from scratch and gives them technical expertise in epidemiology and disease modeling (Dubé et al., 2011). The modified model should, however, undergo rigorous verification and validation (Reeves et al., 2011). The extended use of adapted models will lead to an improvement in FMD control and reduce the global burden of the disease. Finally, model adaptation would be a win-win situation for modelers, epidemiologists, and end-users in endemic settings.

## 5 Conclusion

Simulation modeling is a useful tool to understand the spread and to evaluate the mitigation strategies for FMD. Several varieties of models have been developed to understand FMD dynamics. The available literature on simulation modeling for FMD is often restricted to FMD-free countries, and existing spatially explicit stochastic simulation models for FMD require modifications before their application in endemic settings. More specifically, these models should be adapted by incorporating components of FMD epidemiology in endemic settings to mimic endemicity. The adapted models should

undergo sensitivity analysis, verification, validation, and agreement analysis for transparency and to build credibility. The application of such models in endemic countries can complement FMD control which will improve livestock health, provide economic gains for producers, help alleviate poverty and hunger, which and will complement efforts to attain Sustainable Development Goals and the 2030 Agenda.

**Funding:**

This work did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Conflict of Interest:**

The authors declare no conflict of interest.

Figures

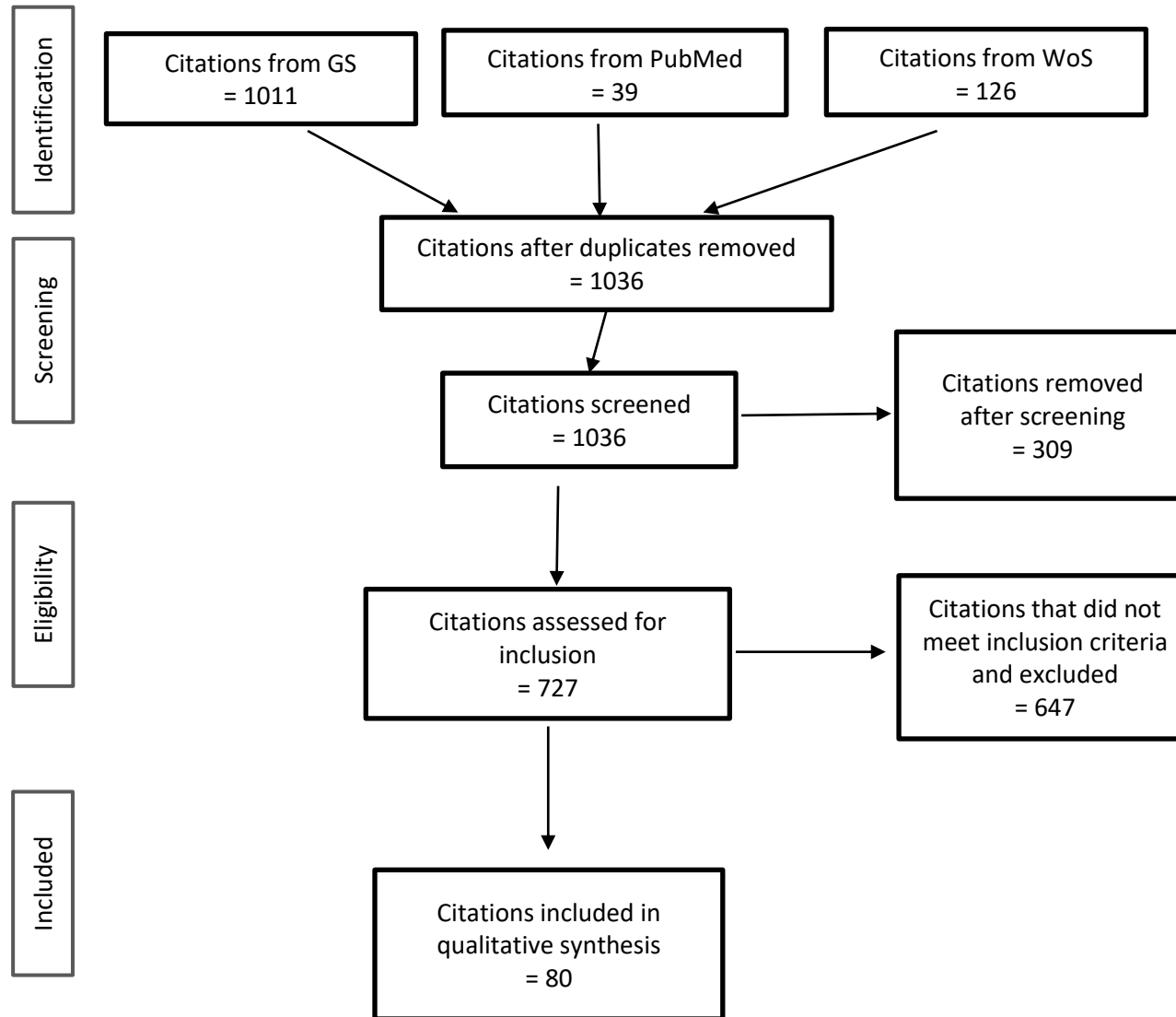


Figure 1.1: Flow diagram of the literature search, screening and inclusion/exclusion criteria (adapted from Moher et al., 2009)

## Tables

Table 1.1: SESS models with corresponding citations

SESS Model (number of citations)	Reference of search results
Warwick model (19)	(Arnold et al., 2008; Diggle, 2006; Keeling et al., 2003, 2001; Le Menach et al., 2005; Meadows et al., 2018; Porphyre et al., 2018, 2013; Probert et al., 2018; Savill et al., 2006; Sellman et al., 2018; Tildesley et al., 2012, 2010, 2009, 2008, 2006; Tildesley and Keeling, 2009, 2008; Tildesley and Ryan, 2012)
Davis Animal Disease Simulation model (16)	(Bates et al., 2003a, 2003b; Boklund et al., 2017; Carpenter, 2011; Carpenter et al., 2011, 2007; Dickey et al., 2008; Dórea et al., 2017; Dürr et al., 2014; Halasa et al., 2014, 2015; Kobayashi et al., 2007a, 2007b; Mardones et al., 2013; Pineda-Krch et al., 2010; Zingg et al., 2015)
AusSpread model (10)	(Beckett and Garner, 2007; East et al., 2016, 2014; Elbakidze et al., 2009; Garner and Beckett, 2005; Garner et al., 2016a, 2016b; Hagerman et al., 2013; Roche et al., 2014; Ward et al., 2009)
InterSpread Plus model (9)	(Martínez-López et al., 2010; Morris et al., 2001; Owen et al., 2011; Sanson et al., 2017, 2014; Stevenson et al., 2013; Velthuis and Mourits, 2007; Wada et al., 2017; Yoon et al., 2006a)
North American Animal Disease Spread Model (7)	(Gale et al., 2015; Harvey et al., 2007; McReynolds et al., 2014; Pendell et al., 2015; Schoenbaum and Disney, 2003; Schroeder et al., 2015; Zagmutt et al., 2016)
Australian Animal Disease Spread model (3)	(Bradhurst et al., 2016, 2015; Van Andel et al., 2018)
Central Veterinary Institute model (2)	(Backer et al., 2012; Bergevoet and Van Asseldonk, 2014)
Traulsen model (2)	(Traulsen et al., 2011, 2010)
Hayama model (2)	(Hayama et al., 2016, 2013)
Multiple models (10)	(Boklund et al., 2013; Dubé et al., 2007; Garner et al., 2016c; Hagerman et al., 2012; Halasa et al., 2014; Probert et al., 2016; Rawdon et al., 2018; Roche et al., 2015; Sanson et al., 2011; Webb et al., 2017)



## REFERENCES

- Abbas, T., Younus, M., Muhmmad, S.A., Ijaz, M., Shakoor, A., 2014. Some Challenges to Progressive Control of Foot and Mouth Disease in Pakistan - Findings of a Pilot Survey. *Transbound. Emerg. Dis.* 61, 81–85. <https://doi.org/10.1111/tbed.12008>
- Ahmed, Z., Pauszek, S.J., Ludi, A., LaRocco, M., Khan, E. -u.-H., Afzal, M., Arshed, M.J., Farooq, U., Arzt, J., Bertram, M., Brito, B., Naeem, K., Abubakar, M., Rodriguez, L.L., 2018. Genetic diversity and comparison of diagnostic tests for characterization of foot-and-mouth disease virus strains from Pakistan 2008-2012. *Transbound. Emerg. Dis.* 65, 534–546. <https://doi.org/10.1111/tbed.12737>
- Anjum, R., Hussain, M., Zahoor, A.B., Irshad, H., Farooq, U., 2006. Epidemiological analyses of foot and mouth disease in Pakistan. *Int. J. Agric. Biol.* 8.
- Arnold, M.E., Paton, D.J., Ryan, E., Cox, S.J., Wilesmith, J.W., 2008. Modelling studies to estimate the prevalence of foot-and-mouth disease carriers after reactive vaccination. *Proc. R. Soc. B. Biol. Sci.* 275, 107–115. <https://doi.org/10.1098/rspb.2007.1154>
- Backer, J.A., Hagenaars, T.J., Nodelijk, G., van Roermund, H.J.W., 2012. Vaccination against foot-and-mouth disease I: Epidemiological consequences. *Prev. Vet. Med.* 107, 27–40. <https://doi.org/10.1016/j.pvetmed.2012.05.012>
- Bates, T.W., Thurmond, M.C., Carpenter, T.E., 2003a. Description of an epidemic simulation model for use in evaluating strategies to control an outbreak of foot-and-mouth disease. *Am. J. Vet. Res.* 64, 195–204. <https://doi.org/10.2460/ajvr.2003.64.195>
- Bates, T.W., Thurmond, M.C., Carpenter, T.E., 2003b. Results of epidemic simulation modeling to

- evaluate strategies to control an outbreak of foot-and-mouth disease. *Am. J. Vet. Res.* 64, 205–210.  
<https://doi.org/10.2460/ajvr.2003.64.205>
- Beckett, S., Garner, M.G., 2007. Simulating disease spread within a geographic information system environment. *Vet. Ital.* 43, 595-604.
- Bergevoet, R., Van Asseldonk, M., 2014. Economics of eradicating Foot-and-Mouth disease epidemics with alternative control strategies # Análisis económico de la erradicación de brotes de fiebre aftosa usando estrategias alternativas de control. *Arch Med Vet* 46, 381–388.
- Boklund, A., Halasa, T., Christiansen, L.E., Enøe, C., 2013. Comparing control strategies against foot-and-mouth disease: Will vaccination be cost-effective in Denmark? *Prev. Vet. Med.* 111, 206–219.  
<https://doi.org/10.1016/J.PREVETMED.2013.05.008>
- Boklund, A., Mortensen, S., Johansen, M.H., Halasa, T., 2017. Resource Estimations in Contingency Planning for Foot-and-Mouth Disease. *Front. Vet. Sci.* 4, 64.  
<https://doi.org/10.3389/fvets.2017.00064>
- Bradhurst, R.A., Roche, S.E., East, I.J., Kwan, P., Garner, M.G., 2016. Improving the computational efficiency of an agent-based spatiotemporal model of livestock disease spread and control. *Environ. Model. Softw.* 77, 1–12. <https://doi.org/10.1016/J.ENVSOF.2015.11.015>
- Bradhurst, R.A., Roche, S.E., East, I.J., Kwan, P., Garner, M.G., 2015. A hybrid modeling approach to simulating foot-and-mouth disease outbreaks in Australian livestock. *Front. Environ. Sci.* 3, 17.  
<https://doi.org/10.3389/fenvs.2015.00017>
- Brooks-Pollock, E., de Jong, M.C.M., Keeling, M.J., Klinkenberg, D., Wood, J.L.N., 2015. Eight challenges in modelling infectious livestock diseases. *Epidemics* 10, 1–5.  
<https://doi.org/10.1016/J.EPIDEM.2014.08.005>

- Cai, C., Li, H., Edwards, J., Hawkins, C., Robertson, I.D., 2014. Meta-analysis on the efficacy of routine vaccination against foot and mouth disease (FMD) in China. *Prev. Vet. Med.* 115, 94–100.  
<https://doi.org/10.1016/J.PREVETMED.2014.03.020>
- Carpenter, T.E., 2011. Stochastic, spatially-explicit epidemic models. *Rev. sci. tech. Off. int. Epiz* 30, 417–424.
- Carpenter, T.E., Christiansen, L.E., Dickey, B.F., Thunes, C., Hullinger, P.J., 2007. Potential impact of an introduction of foot-and-mouth disease into the California State Fair. *J. Am. Vet. Med. Assoc.* 231, 1231–1235. <https://doi.org/10.2460/javma.231.8.1231>
- Carpenter, T.E., O'Brien, J.M., Hagerman, A.D., McCarl, B.A., 2011. Epidemic and Economic Impacts of Delayed Detection of Foot-And-Mouth Disease: A Case Study of a Simulated Outbreak in California. *J. Vet. Diagnostic Investig.* 23, 26–33. <https://doi.org/10.1177/104063871102300104>
- Dickey, B.F., Carpenter, T.E., Bartell, S.M., 2008. Use of heterogeneous operation-specific contact parameters changes predictions for foot-and-mouth disease outbreaks in complex simulation models. *Prev. Vet. Med.* 87, 272–287. <https://doi.org/10.1016/J.PREVETMED.2008.04.006>
- Diggle, P.J., 2006. Spatio-temporal point processes, partial likelihood, foot and mouth disease. *Stat. Methods Med. Res.* 15, 325–336. <https://doi.org/10.1191/0962280206sm454oa>
- Doel, T., 2003. FMD vaccines. *Virus Res.* 91, 81–99. [https://doi.org/10.1016/S0168-1702\(02\)00261-7](https://doi.org/10.1016/S0168-1702(02)00261-7)
- Dórea, F.C., Nöremark, M., Widgren, S., Frössling, J., Boklund, A., Halasa, T., Ståhl, K., 2017. Evaluation of Strategies to Control a Potential Outbreak of Foot-and-Mouth Disease in Sweden. *Front. Vet. Sci.* 4, 118. <https://doi.org/10.3389/fvets.2017.00118>
- Dorjee, S., Revie, C.W., Poljak, Z., McNab, W.B., Sanchez, J., 2016. One-Health Simulation Modelling: A Case Study of Influenza Spread between Human and Swine Populations using *NAADSM*.

Transbound. Emerg. Dis. 63, 36–55. <https://doi.org/10.1111/tbed.12215>

Dubé, C., Stevenson, M., Garner, M., Sanson, R., Corso, B., Harvey, N., Griffin, J., Wilesmith, J., Estrada, C., Griffi, J., 2007. A comparison of predictions made by three simulation models of foot-and-mouth disease A comparison of predictions made by three simulation models of foot-and-mouth disease. *New Zeal. Vet. J.* 55, 280–288. <https://doi.org/10.1080/00480169.2007.36782>

Dubé, Caroline, Sánchez, J., Dubé, C, Sanchez, J., Reeves, A., 2011. Adapting existing models of highly contagious diseases to countries other than their country of origin. *Rev. sci. tech. Off. int. Epiz* 30, 581–589. <https://doi.org/10.20506/rst.30.2.2061>

Dürr, S., Fasel-Clemenz, C., Thür, B., Schwermer, H., Doherr, M.G., Dohna, H. zu, Carpenter, T.E., Perler, L., Hadorn, D.C., 2014. Evaluation of the benefit of emergency vaccination in a foot-and-mouth disease free country with low livestock density. *Prev. Vet. Med.* 113, 34–46. <https://doi.org/10.1016/J.PREVETMED.2013.10.015>

East, I.J., Martin, P.A.J., Langstaff, I., Iglesias, R.M., Sergeant, E.S.G., Garner, M.G., 2016. Assessing the delay to detection and the size of the outbreak at the time of detection of incursions of foot and mouth disease in Australia. *Prev. Vet. Med.* 123, 1–11. <https://doi.org/10.1016/J.PREVETMED.2015.12.005>

East, I.J., Roche, S.E., Wicks, R.M., de Witte, K., Garner, M.G., 2014. Options for managing animal welfare on intensive pig farms confined by movement restrictions during an outbreak of foot and mouth disease. *Prev. Vet. Med.* 117, 533–541. <https://doi.org/10.1016/J.PREVETMED.2014.10.002>

Elbakidze, L., Highfield, L., Ward, M., McCarl, B.A., Norby, B., 2009. Economics Analysis of Mitigation Strategies for FMD Introduction in Highly Concentrated Animal Feeding Regions. *Rev. Agric. Econ.* 31, 931–950. <https://doi.org/10.1111/j.1467-9353.2009.01477.x>

- Elnekave, E., Li, Y., Zamir, L., Even-Tov, B., Hamblin, P., Gelman, B., Hammond, J., Klement, E., 2013. The field effectiveness of routine and emergency vaccination with an inactivated vaccine against foot and mouth disease. *Vaccine* 31, 879–885. <https://doi.org/10.1016/J.VACCINE.2012.12.011>
- Farooq, U., Ahmed, Z., Naeem, K., Bertram, M., Brito, B., Stenfeldt, C., Pauszek, S.J., LaRocco, M., Rodriguez, L., Arzt, J., 2018. Characterization of naturally occurring, new and persistent subclinical foot-and-mouth disease virus infection in vaccinated Asian buffalo in Islamabad Capital Territory, Pakistan. *Transbound. Emerg. Dis.* 65, 1836–1850. <https://doi.org/10.1111/tbed.12963>
- Farooq, U., Irshad, H., Ullah, A., Latif, A., Zahur, A.B., Naeem, K., Ahmed, Z., Rodriguez, L.L., 2017a. Seroprevalence of foot-and-mouth disease in small ruminants of Pakistan. *J. Anim. Plant Sci.* 27, 1197–1201.
- Farooq, U., Naeem, K., Zahur, A.B., Khan, M.A., Sidique, U., 2017b. Foot-and-mouth disease outbreaks investigations at Sindh, Punjab and Islamabad, Pakistan during the year 2012-2013. *Int. J. Biosci.* 11, 346–356. <https://doi.org/10.12692/ijb/11.5.346-356>
- Farooq, U., Naeem, K., Zahur, A.B., Khan, M.A., Sidique, U., Qureshi, S., 2017c. Epidemiological analysis and economic impact assessment of foot-and-mouth disease at Landhi dairy colony Karachi. *Asian J. Agric. Biol.* 5, 7–14.
- Farooq, U., Ullah, A., Irshad, H., Latif, A., Naeem, K., Zahur, A. Bin, Ahmad, Z., Rodriguez, L.L., 2016. Seroprevalence of foot-and-mouth disease in large ruminants in periurban dairy farms near Islamabad, Pakistan. *Asian Biomed.* 10, 123–127. <https://doi.org/10.5372/1905-7415.1002.472>
- Ferguson, N.M., Donnelly, C.A., Anderson, R.M., 2001. Transmission intensity and impact of control policies on the foot and mouth epidemic in Great Britain. *Nature* 413, 542–548. <https://doi.org/10.1038/35097116>

- Ferrari, G., Tasciotti, L., Khan, E., Kiani, A., 2014. Foot-and-Mouth Disease and Its Effect on Milk Yield: An Economic Analysis on Livestock Holders in Pakistan. *Transbound. Emerg. Dis.* 61, e52–e59.  
<https://doi.org/10.1111/tbed.12072>
- Gale, S.B., Miller, G.Y., Eshelman, C.E., Wells, S.J., Ave, G., 2015. Epidemic simulation of a foot and mouth disease outbreak in Minnesota. *Rev. Sci. Tech. Off. Int. Epiz* 34.
- Garner, M., Beckett, S., 2005. Modelling the spread of foot-and-mouth disease in Australia. *Aust. Vet. J.* 83, 758–766. <https://doi.org/10.1111/j.1751-0813.2005.tb11589.x>
- Garner, M.G., Bombardieri, N., Cozens, M., Conway, M.L., Wright, T., Paskin, R., East, I.J., 2016a. Estimating Resource Requirements to Staff a Response to a Medium to Large Outbreak of Foot and Mouth Disease in Australia. *Transbound. Emerg. Dis.* 63, e109–e121.  
<https://doi.org/10.1111/tbed.12239>
- Garner, M.G., East, I.J., Kompas, T., Ha, P.V., Roche, S.E., Nguyen, H.T.M., 2016b. Comparison of alternatives to passive surveillance to detect foot and mouth disease incursions in Victoria, Australia. *Prev. Vet. Med.* 128, 78–86. <https://doi.org/10.1016/J.PREVETMED.2016.04.009>
- Garner, M.G., East, I.J., Stevenson, M.A., Sanson, R.L., Rawdon, T.G., Bradhurst, R.A., Roche, S.E., Van Ha, P., Kompas, T., 2016c. Early Decision Indicators for Foot-and-Mouth Disease Outbreaks in Non-Endemic Countries. *Front. Vet. Sci.* 3, 109. <https://doi.org/10.3389/fvets.2016.00109>
- Garner, M.G., Lack, M.B., 1995a. An evaluation of alternate control strategies for foot-and-mouth disease in Australia: a regional approach. *Prev. Vet. Med.* 23, 9–32. [https://doi.org/10.1016/0167-5877\(94\)00433-J](https://doi.org/10.1016/0167-5877(94)00433-J)
- Garner, M.G., Lack, M.B., 1995b. Modelling the potential impact of exotic diseases on regional Australia. *Aust. Vet. J.* 72, 81–87. <https://doi.org/10.1111/j.1751-0813.1995.tb15013.x>

- Gleeson, L.J., 2002. A review of the status of foot and mouth disease in South-East Asia and approaches to control and eradication. *Rev. Sci. Tech.* 21, 465–75.
- Guitian, J., Pfeiffer, D., 2006. Should we use models to inform policy development? *Vet. J.* 172, 393–395.  
<https://doi.org/10.1016/j.tvjl.2006.03.001>
- Hagerman, A.D., McCarl, B.A., Carpenter, T.E., Ward, M.P., O'Brien, J., 2012. Emergency Vaccination to Control Foot-and-mouth Disease: Implications of its Inclusion as a U.S. Policy Option. *Appl. Econ. Perspect. Policy* 34, 119–146. <https://doi.org/10.1093/aep/34.3.119>
- Hagerman, A.D., Ward, M.P., Anderson, D.P., Looney, J.C., McCarl, B.A., 2013. Rapid effective trace-back capability value: A case study of foot-and-mouth in the Texas High Plains. *Prev. Vet. Med.* 110, 323–328. <https://doi.org/10.1016/j.pvetmed.2012.12.011>
- Halasa, T., Boklund, A., Stockmarr, A., Enøe, C., Christiansen, L.E., 2014. A Comparison between Two Simulation Models for Spread of Foot-and-Mouth Disease. *PLoS One* 9, e92521.  
<https://doi.org/10.1371/journal.pone.0092521>
- Halasa, T., Toft, N., Boklund, A., 2015. Improving the Effect and Efficiency of FMD Control by Enlarging Protection or Surveillance Zones. *Front. Vet. Sci.* 2, 70. <https://doi.org/10.3389/fvets.2015.00070>
- 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. *Prev. Vet. Med.* 82, 176–197. <https://doi.org/10.1016/j.pvetmed.2007.05.019>
- Hayama, Y., Yamamoto, T., Kobayashi, S., Muroga, N., Tsutsui, T., 2016. Potential impact of species and livestock density on the epidemic size and effectiveness of control measures for foot-and-mouth disease in Japan. *J. Vet. Med. Sci* 78, 13–22. <https://doi.org/10.1292/jvms.15-0224>

- Hayama, Y., Yamamoto, T., Kobayashi, S., Muroga, N., Tsutsui, T., 2013. Mathematical model of the 2010 foot-and-mouth disease epidemic in Japan and evaluation of control measures. *Prev. Vet. Med.* 112, 183–193. <https://doi.org/10.1016/J.PREVETMED.2013.08.010>
- Hunter, P., 1998. Vaccination as a means of control of foot-and-mouth disease in sub-saharan Africa. *Vaccine* 16, 261–264. [https://doi.org/10.1016/S0264-410X\(97\)00170-9](https://doi.org/10.1016/S0264-410X(97)00170-9)
- Jamal, S.M., Ahmed, S., Hussain, M., Ali, Q., 2010. Status of foot-and-mouth disease in Pakistan. *Arch. Virol.* 155, 1487–1491. <https://doi.org/10.1007/s00705-010-0732-y>
- Jamal, S.M., Belsham, G.J., 2013. Foot-and-mouth disease: past, present and future. *Vet. Res.* 44, 116. <https://doi.org/10.1186/1297-9716-44-116>
- Jamal, S.M., Bouma, A., van den Broek, J., Stegeman, A., Chénard, G., Dekker, A., 2008. Foot-and-mouth disease vaccine potency testing: The influence of serotype, type of adjuvant, valency, fractionation method, and virus culture on the dose–response curve in cattle. *Vaccine* 26, 6317–6321. <https://doi.org/10.1016/J.VACCINE.2008.09.021>
- Jamal, S.M., Shah, S.I., Ali, Q., Mehmood, A., Afzal, M., Afzal, M., Dekker, A., 2014. Proper Quality Control of Formulated Foot-and-Mouth Disease Vaccines in Countries with Prophylactic Vaccination is Necessary. *Transbound. Emerg. Dis.* 61, 483–489. <https://doi.org/10.1111/tbed.12051>
- Jemberu, W.T., Mourits, M.C.M., Woldehanna, T., Hogeveen, H., 2014. Economic impact of foot and mouth disease outbreaks on smallholder farmers in Ethiopia. *Prev. Vet. Med.* 116, 26–36. <https://doi.org/10.1016/J.PREVETMED.2014.06.004>
- Kao, R.R., 2002. The role of mathematical modelling in the control of the 2001 FMD epidemic in the UK. *Trends Microbiol.* 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. Biol. Sci.* 272, 1195–202.  
<https://doi.org/10.1098/rspb.2004.3046>
- Keeling, M.J., Woolhouse, M.E., 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 (80-. )*. 294, 813–817.  
<https://doi.org/10.1126/science.1065973>
- Keeling, M.J., Woolhouse, M.E.J., May, R.M., Davies, G., Grenfell, B.T., 2003. Modelling vaccination strategies against foot-and-mouth disease. *Nature* 421, 136–142.  
<https://doi.org/10.1038/nature01343>
- Knight-Jones, T.J.D., Gubbins, S., Bulut, A.N., Stärk, K.D.C., Pfeiffer, D.U., Sumption, K.J., Paton, D.J., 2016a. Mass vaccination, immunity and coverage: modelling population protection against foot-and-mouth disease in Turkish cattle. *Sci. Rep.* 6, 22121. <https://doi.org/10.1038/srep22121>
- Knight-Jones, T.J.D., Robinson, L., Charleston, B., Rodriguez, L.L., Gay, C.G., Sumption, K.J., Vosloo, W., 2016b. Global Foot-and-Mouth Disease Research Update and Gap Analysis: 2 - Epidemiology, Wildlife and Economics. *Transbound. Emerg. Dis.* 63, 14–29. <https://doi.org/10.1111/tbed.12522>
- 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? *Prev. Vet. Med.* 112, 161–173.  
<https://doi.org/10.1016/J.PREVETMED.2013.07.013>
- Kobayashi, M., Carpenter, T.E., Dickey, B.F., Howitt, R.E., 2007a. A dynamic, optimal disease control model for foot-and-mouth-disease:: II. Model results and policy implications. *Prev. Vet. Med.* 79, 274–286. <https://doi.org/10.1016/J.PREVETMED.2007.01.001>
- Kobayashi, M., Carpenter, T.E., Dickey, B.F., Howitt, R.E., 2007b. A dynamic, optimal disease control

model for foot-and-mouth disease:: I. Model description. *Prev. Vet. Med.* 79, 257–273.

<https://doi.org/10.1016/J.PREVETMED.2007.01.002>

Le Menach, A., Legrand, J., Grais, R.F., Viboud, C., Valleron, A.J., Flahault, A., 2005. Modeling spatial and temporal transmission of foot-and-mouth disease in France: Identification of high-risk areas. *Vet. Res.* 36, 699–712. <https://doi.org/10.1051/vetres:2005025>

Mardones, F.O., zu Donha, H., Thunes, C., Velez, V., Carpenter, T.E., 2013. The value of animal movement tracing: A case study simulating the spread and control of foot-and-mouth disease in California. *Prev. Vet. Med.* 110, 133–138. <https://doi.org/10.1016/J.PREVETMED.2012.11.024>

Martínez-López, B., Perez, A.M., Sánchez-Vizcaíno, J.M., 2010. A simulation model for the potential spread of foot-and-mouth disease in the Castile and Leon region of Spain. *Prev. Vet. Med.* 96, 19–29. <https://doi.org/10.1016/J.PREVETMED.2010.05.015>

McReynolds, S.W., Sanderson, M.W., Reeves, A., Hill, A.E., 2014. Modeling the impact of vaccination control strategies on a foot and mouth disease outbreak in the Central United States. *Prev. Vet. Med.* 117, 487–504. <https://doi.org/10.1016/J.PREVETMED.2014.10.005>

Meadows, A.J., Mundt, C.C., Keeling, M.J., Tildesley, M.J., 2018. Disentangling the influence of livestock vs. farm density on livestock disease epidemics. *Ecosphere* 9, e02294.

<https://doi.org/10.1002/ecs2.2294>

Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G., Group, T.P., 2009. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med.* 6, e1000097.

<https://doi.org/10.1371/journal.pmed.1000097>

Morris, R.S., Sanson, R.L., Stern M.W., Stevenson M., Wilesmith J.W., 2002. Decision-support tools for foot and mouth disease control. *Rev. sci. tech. Off. int. Epiz.* 21, 557–567.

<https://doi.org/10.20506/rst.21.3.1363>

- 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. *Vet. Rec.* 149, 137–44. <https://doi.org/10.1136/vr.149.5.137>
- Navid, M.T., Farooq, U., Latif, A., Awais, M.M., Anwar, M.I., Akhtar, M., Zahur, A.B., 2018. Prevalence of foot and mouth disease virus in apparently healthy buffaloes brought to Islamabad slaughterhouse in Pakistan. *Trop. Biomed.* 35, 161–167.
- Owen, K., Stevenson, M.A., Sanson, R.L., 2011. A sensitivity analysis of the New Zealand standard model of foot and mouth disease. *Rev. sci. tech. Off. int. Epiz* 30, 513–526.
- Paton, D.J., Sumption, K.J., Charleston, B., 2009. Options for control of foot-and-mouth disease: knowledge, capability and policy. *Philos. Trans. R. Soc. Lond. B. Biol. Sci.* 364, 2657–67. <https://doi.org/10.1098/rstb.2009.0100>
- Patyk, K., Caraguel, C., Kristensen, C., Forde-Folle, K., 2011. Lexicon of disease spread modelling terms. *Rev. sci. tech. Off. int. Epiz* 30, 547–554.
- Pendell, D.L., Marsh, T.L., Coble, K.H., Lusk, J.L., Szmania, S.C., 2015. Economic Assessment of FMDv Releases from the National Bio and Agro Defense Facility. *PLoS One* 10, e0129134. <https://doi.org/10.1371/journal.pone.0129134>
- 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. *Am. J. Vet. Res.* 71, 82–88. <https://doi.org/10.2460/ajvr.71.1.82>
- Pomeroy, L.W., Bansal, S., Tildesley, M., Moreno-Torres, K.I., Moritz, M., Xiao, N., Carpenter, T.E., Garabed, R.B., 2017. Data-Driven Models of Foot-and-Mouth Disease Dynamics: A Review.

- Transbound. Emerg. Dis. 64, 716–728. <https://doi.org/10.1111/tbed.12437>
- Pomeroy, L.W., Bjørnstad, O.N., Kim, H., Jumbo, S.D., Abdoukadi, S., Garabed, R., 2015. Serotype-Specific Transmission and Waning Immunity of Endemic Foot-and-Mouth Disease Virus in Cameroon. *PLoS One* 10, e0136642. <https://doi.org/10.1371/journal.pone.0136642>
- Porphyre, T., Auty, H.K., Tildesley, M.J., Gunn, G.J., Woolhouse, M.E.J., 2013. Vaccination against Foot-And-Mouth Disease: Do Initial Conditions Affect Its Benefit? *PLoS One* 8, e77616. <https://doi.org/10.1371/journal.pone.0077616>
- Porphyre, T., Rich, K.M., Auty, H.K., 2018. Assessing the Economic Impact of Vaccine Availability When Controlling Foot and Mouth Disease Outbreaks. *Front. Vet. Sci.* 5, 47. <https://doi.org/10.3389/fvets.2018.00047>
- Probert, W.J.M., Jewell, C.P., Werkman, M., Fonnesebeck, C.J., Goto, Y., Runge, M.C., Sekiguchi, S., Shea, K., Keeling, M.J., Ferrari, M.J., Tildesley, M.J., 2018. Real-time decision-making during emergency disease outbreaks. *PLOS Comput. Biol.* 14, e1006202. <https://doi.org/10.1371/journal.pcbi.1006202>
- Probert, W.J.M., Shea, K., Fonnesebeck, C.J., Runge, M.C., Carpenter, T.E., Dürr, S., Garner, M.G., Harvey, N., Stevenson, M.A., Webb, C.T., Werkman, M., Tildesley, M.J., Ferrari, M.J., 2016. Decision-making for foot-and-mouth disease control: Objectives matter. *Epidemics* 15, 10–19. <https://doi.org/10.1016/J.EPIDEM.2015.11.002>
- Productivity Commission, 2002. Impact of a Foot and Mouth Disease Outbreak on Australia 1–207.
- Rawdon, T.G., Garner, M.G., Sanson, R.L., Stevenson, M.A., Cook, C., Birch, C., Roche, S.E., Patyk, K.A., Forde-Folle, K.N., Dubé, C., Smylie, T., Yu, Z.D., 2018. Evaluating vaccination strategies to control foot-and-mouth disease: a country comparison study. *Epidemiol. Infect.* 146, 1138–1150.

<https://doi.org/10.1017/S0950268818001243>

Reeves, A., Salman, M.A., Hill, A.E., 2011. Approaches for evaluating veterinary epidemiological models: verification, validation and limitations. *Rev. Sci. Tech.* 30, 499–512.

Ringa, N., Bauch, C.T., 2014. Dynamics and control of foot-and-mouth disease in endemic countries: A pair approximation model. *J. Theor. Biol.* 357, 150–159. <https://doi.org/10.1016/J.JTBI.2014.05.010>

Roche, S.E., Garner, M.G., Sanson, R.L., Cook, C., Birch, C., Backer, J.A., Dube, C., Patyk, K.A., Stevenson, M.A., Yu, Z.D., Rawdon, T.G., Gauntlett, F., 2015. Evaluating vaccination strategies to control foot-and-mouth disease: a model comparison study. *Epidemiol. Infect.* 143, 1256–1275.

<https://doi.org/10.1017/S0950268814001927>

Roche, S.E., Garner, M.G., Wicks, R.M., East, I.J., de Witte, K., 2014. How do resources influence control measures during a simulated outbreak of foot and mouth disease in Australia? *Prev. Vet. Med.* 113, 436–446. <https://doi.org/10.1016/J.PREVETMED.2013.12.003>

Rweyemamu, M., Roeder, P., MacKay, D., Sumption, K., Brownlie, J., Leforban, Y., 2008a. Planning for the Progressive Control of Foot-and-Mouth Disease Worldwide. *Transbound. Emerg. Dis.* 55, 73–87. <https://doi.org/10.1111/j.1865-1682.2007.01016.x>

Rweyemamu, M., Roeder, P., Mackay, D., Sumption, K., Brownlie, J., Leforban, Y., Valarcher, J.-F., Knowles, N.J., Saraiva, V., 2008b. Epidemiological Patterns of Foot-and-Mouth Disease Worldwide. *Transbound. Emerg. Dis.* 55, 57–72. <https://doi.org/10.1111/j.1865-1682.2007.01013.x>

Salman, M.D., 2004. Controlling emerging diseases in the 21st century. *Prev. Vet. Med.* 62, 177–184. <https://doi.org/10.1016/J.PREVETMED.2003.11.003>

Sanson, R.L., Dubé, C., Cork, S.C., Frederickson, R., Morley, C., 2014. Simulation modelling of a hypothetical introduction of foot-and-mouth disease into Alberta. *Prev. Vet. Med.* 114, 151–163.

<https://doi.org/10.1016/J.PREVETMED.2014.03.005>

Sanson, R.L., Garner, M.G., Davies, T.M., Hazelton, M.L., 2011. Foot and mouth disease model verification and 'relative validation' through a formal model comparison. *Rev. sci. tech. Off. int. Epiz.* 30, 527–540. <https://doi.org/10.20506/rst.30.2.2051>

Sanson, R.L., Rawdon, T., Owen, K., Hickey, K., Van Andel, M., Yu, Z.D., 2017. Evaluating the benefits of vaccination when used in combination with stamping-out measures against hypothetical introductions of foot-and-mouth disease into New Zealand: a simulation study Evaluating the benefits of vaccination when used in combination with stamping-out measures against hypothetical introductions of foot-and-mouth disease into New Zealand: a simulation study. *N. Z. Vet. J.* 65, 124–133. <https://doi.org/10.1080/00480169.2016.1263165>

Savill, N., Shaw, D., Deardon, R., Tildesley, M., Keeling, M., Woolhouse, M., Brooks, S., Grenfell, B., 2006. Topographic determinants of foot and mouth disease transmission in the UK 2001 epidemic. *BMC Vet. Res.* 2, 3. <https://doi.org/10.1186/1746-6148-2-3>

Schoenbaum, M.A., Disney, W.T., 2003. Modeling alternative mitigation strategies for a hypothetical outbreak of foot-and-mouth disease in the United States. *Prev. Vet. Med.* 58, 25–52. [https://doi.org/10.1016/S0167-5877\(03\)00004-7](https://doi.org/10.1016/S0167-5877(03)00004-7)

Schroeder, T.C., Pendell, D.L., Sandersen, M.W., McReynolds, S., 2015. Economic impact of alternative FMD emergency vaccination strategies in the midwestern United States. *J. Agric. Appl. Econ.* 47, 47–76. <https://doi.org/10.1017/aae.2014.5>

Sellman, S., Tsao, K., Tildesley, M.J., Brommesson, P., Webb, C.T., Wennergren, U., Keeling, M.J., Lindström, T., 2018. Need for speed: An optimized gridding approach for spatially explicit disease simulations. *PLOS Comput. Biol.* 14, e1006086. <https://doi.org/10.1371/journal.pcbi.1006086>

- Souley Kouato, B., De Clercq, K., Abatih, E., Dal Pozzo, F., King, D., Thys, E., Marichatou, H., Saegerman, C., 2018. Review of epidemiological risk models for foot-and-mouth disease: Implications for prevention strategies with a focus on Africa. *PLoS One* 13, e0208296.  
<https://doi.org/10.1371/journal.pone.0208296>
- 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. *Prev. Vet. Med.* 109, 10–24. <https://doi.org/10.1016/J.PREVETMED.2012.08.015>
- Sumption, K., Domenech, J., Ferrari, G., 2012. Progressive control of FMD on a global scale. *Vet. Rec.* 170, 637–9. <https://doi.org/10.1136/vr.e4180>
- Tildesley, M.J., Bessell, P.R., Keeling, M.J., Woolhouse, M.E.J., 2009. The role of pre-emptive culling in the control of foot-and-mouth disease. *Proc. R. Soc. B. Biol. Sci.* 276, 3239–48.  
<https://doi.org/10.1098/rspb.2009.0427>
- 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. *Proc. R. Soc. B. Biol. Sci.* 275, 1459–68. <https://doi.org/10.1098/rspb.2008.0006>
- Tildesley, M.J., House, T.A., Bruhn, M.C., Curry, R.J., O'Neil, M., Allpress, J.L.E., Smith, G., Keeling, M.J., 2010. Impact of spatial clustering on disease transmission and optimal control. *Proc. Natl. Acad. Sci. U. S. A.* 107, 1041–6. <https://doi.org/10.1073/pnas.0909047107>
- Tildesley, M.J., Keeling, M.J., 2009. Is  $R_0$  a good predictor of final epidemic size: Foot-and-mouth disease in the UK. *J. Theor. Biol.* 258, 623–629. <https://doi.org/10.1016/J.JTBI.2009.02.019>
- Tildesley, M.J., Keeling, M.J., 2008. Modelling foot-and-mouth disease: A comparison between the UK and Denmark. *Prev. Vet. Med.* 85, 107–124. <https://doi.org/10.1016/J.PREVETMED.2008.01.008>

- Tildesley, M.J., Ryan, S.J., 2012. Disease Prevention versus Data Privacy: Using Landcover Maps to Inform Spatial Epidemic Models. *PLoS Comput. Biol.* 8, e1002723.  
<https://doi.org/10.1371/journal.pcbi.1002723>
- Tildesley, M.J., Savill, N.J., Shaw, D.J., Deardon, R., Brooks, S.P., Woolhouse, M.E.J., Grenfell, B.T., Keeling, M.J., 2006. Optimal reactive vaccination strategies for a foot-and-mouth outbreak in the UK. *Nature* 440, 83–86. <https://doi.org/10.1038/nature04324>
- Tildesley, M.J., Smith, G., Keeling, M.J., 2012. Modeling the spread and control of foot-and-mouth disease in Pennsylvania following its discovery and options for control. *Prev. Vet. Med.* 104, 224–239. <https://doi.org/10.1016/J.PREVETMED.2011.11.007>
- Tomassen, F.H.M., de Koeijer, A., Mourits, M.C.M., Dekker, A., Bouma, A., Huirne, R.B.M., 2002. A decision-tree to optimise control measures during the early stage of a foot-and-mouth disease epidemic. *Prev. Vet. Med.* 54, 301–324. [https://doi.org/10.1016/S0167-5877\(02\)00053-3](https://doi.org/10.1016/S0167-5877(02)00053-3)
- Traulsen, I., Rave, G., Krieter, J., 2010. Sensitivity analysis of a stochastic simulation model for foot and mouth disease. *Arch. Anim. Breed.* 53, 529–544. <https://doi.org/10.5194/aab-53-529-2010>
- Traulsen, I., Rave, G., Teuffert, J., Krieter, J., 2011. Consideration of different outbreak conditions in the evaluation of preventive culling and emergency vaccination to control foot and mouth disease epidemics. *Res. Vet. Sci.* 91, 219–224. <https://doi.org/10.1016/J.RVSC.2010.12.016>
- Ullah, A., Jamal, S.M., Romey, A., Gorna, K., Kakar, M.A., Abbas, F., Ahmad, J., Zientara, S., Bakkali Kassimi, L., 2017. Genetic Characterization of Serotypes A and Asia-1 Foot-and-mouth Disease Viruses in Balochistan, Pakistan, in 2011. *Transbound. Emerg. Dis.* 64, 1569–1578.  
<https://doi.org/10.1111/tbed.12548>
- Van Andel, M., Hollings, T., Bradhurst, R., Robinson, A., Burgman, M., Gates, M.C., Bingham, P.,



- Carpenter, T., 2018. Does Size Matter to Models? Exploring the Effect of Herd Size on Outputs of a Herd-Level Disease Spread Simulator. *Front. Vet. Sci.* 5, 78.  
<https://doi.org/10.3389/fvets.2018.00078>
- Velthuis, A.G.J., Mourits, M.C.M., 2007. Effectiveness of movement-prevention regulations to reduce the spread of foot-and-mouth disease in The Netherlands. *Prev. Vet. Med.* 82, 262–281.  
<https://doi.org/10.1016/J.PREVETMED.2007.05.023>
- Vosloo, W., Bastos, A.D.S., Sangare, O., Hargreaves, S.K., Thomson, G.R., 2002. Review of the status and control of foot and mouth disease in sub-Saharan Africa. *Rev. sci. tech. Off. int. Epiz.* 21, 437–449.
- Wada, M., Stevenson, M., Cogger, N., Carpenter, T., 2017. Evaluation of the Control Strategy for the 2010 Foot-and-Mouth Disease Outbreak in Japan Using Disease Simulation. *Transbound. Emerg. Dis.* 64, 978–989. <https://doi.org/10.1111/tbed.12467>
- Ward, M.P., Highfield, L.D., Vongseng, P., Graeme Garner, M., 2009. Simulation of foot-and-mouth disease spread within an integrated livestock system in Texas, USA. *Prev. Vet. Med.* 88, 286–297.  
<https://doi.org/10.1016/J.PREVETMED.2008.12.006>
- Webb, C.T., Ferrari, M., Lindström, T., Carpenter, T., Dürr, S., Garner, G., Jewell, C., Stevenson, M., Ward, M.P., Werkman, M., Backer, J., Tildesley, M., 2017. Ensemble modelling and structured decision-making to support Emergency Disease Management. *Prev. Vet. Med.* 138, 124–133.  
<https://doi.org/10.1016/J.PREVETMED.2017.01.003>
- Wongsathapornchai, K., Salman, M.D., Edwards, J.R., Morley, P.S., Keefe, T.J., Campen, H. V., Weber, S.E., Premashthira, S., 2008. Use of epidemiologic risk modeling to evaluate control of foot-and-mouth disease in southern Thailand. *Am. J. Vet. Res.* 69, 240–251.  
<https://doi.org/10.2460/ajvr.69.2.240>

- Yano, T., Premashthira, S., Dejong, T., Tangtrongsup, S., Salman, M.D., 2018. The Effectiveness of a Foot and Mouth Disease Outbreak Control Programme in Thailand 2008–2015: Case Studies and Lessons Learned. *Vet. Sci.* <https://doi.org/10.3390/vetsci5040101>
- Yoon, H., Wee, S.-H., Stevenson, M.A., O’Leary, B.D., Morris, R.S., Hwang, I.-J., Park, C.-K., Stern, M.W., 2006. Simulation analyses to evaluate alternative control strategies for the 2002 foot-and-mouth disease outbreak in the Republic of Korea. *Prev. Vet. Med.* 74, 212–225.  
<https://doi.org/10.1016/J.PREVETMED.2005.12.002>
- Zagmutt, F.J., Schoenbaum, M.A., Hill, A.E., 2016. The Impact of Population, Contact, and Spatial Heterogeneity on Epidemic Model Predictions. *Risk Anal.* 36, 939–953.  
<https://doi.org/10.1111/risa.12482>
- Zingg, D., Häslar, S., Schuepbach-Regula, G., Schwermer, H., Dürr, S., 2015. Evidence for Emergency Vaccination Having Played a Crucial Role to Control the 1965/66 Foot-and-Mouth Disease Outbreak in Switzerland. *Front. Vet. Sci.* 2, 72. <https://doi.org/10.3389/fvets.2015.00072>

CHAPTER 2: ESTIMATING THE LOCATION OF INDIVIDUAL LIVESTOCK HOLDINGS AND THEIR  
POPULATIONS IN TWO DEVELOPING COUNTRIES FOR USE IN SPATIAL DISEASE SPREAD MODELS<sup>2</sup>

1 Introduction

Globally, the livelihoods of one billion people are linked directly to livestock (FAO, 2011, 2009). Healthy livestock are a critical element to ensure food security and achieve Sustainable Development Goals (FAO, 2018). However, infectious diseases of livestock such as Foot-and-Mouth Disease (FMD), Classical Swine fever (CSF), and African Swine Fever (ASF) pose severe detrimental impacts on the trade of animals, animal products, and subsequently endanger global food security.

Foot and mouth disease is endemic in many parts of the world (Anjum et al., 2006; Farooq et al., 2018, 2017a, 2017b, 2017c, 2016; Gleeson, 2002; Jamal et al., 2010; Navid et al., 2018; Rweyemamu et al., 2008b; Yano et al., 2018), and is associated with substantial economic losses (Ferrari et al., 2014; Jemberu et al., 2014; Knight-Jones and Rushton, 2013). For instance, annual losses associated with production decline and vaccination in FMD-endemic regions range from USD 6.5 and 21 billion, and in FMD-free countries and zones, annual outbreaks associated losses exceed USD 1.5 billion (Knight-Jones and

---

<sup>2</sup> This chapter of the dissertation is intended for publication in the Agriculture, Ecosystems & Environment journal and is formatted to meet journal requirements.

Muhammad Usman Zaheer<sup>a</sup>, Christopher Burdett<sup>b</sup>, Katie Steneroden<sup>a</sup>, Shaun Case<sup>c</sup>, Steve Weber<sup>a</sup>, Mo Salman<sup>a</sup>, Sangeeta Rao<sup>a</sup>, Sheryl Magzamen<sup>d</sup>

<sup>a</sup>Animal Population Health Institute, Department of Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins CO 80523, USA, <sup>d</sup>Department of Biology, College of Natural Sciences, Colorado State University, Fort Collins CO 80523, USA, <sup>c</sup>Department of Civil and Environmental Engineering, Walter Scott, Jr. College of Engineering, Colorado State University, Fort Collins CO 80523, USA, <sup>d</sup>Department of Environmental and Radiological Health Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins CO 80523, USA

Rushton, 2013). These economic losses call for efforts to conduct a risk assessment, preparedness planning and to evaluate the effectiveness of mitigation strategies which will fit within the sociopolitical and socioeconomic constraints of different countries (Marsot et al., 2014).

Simulation modeling has become a common tool for estimating the spread and impact of highly contagious diseases and for conducting risk assessments (Dorjee et al., 2016; Guitian and Pfeiffer, 2006; Kao, 2002; Keeling, 2005; Morris et al., 2002). Several models have been developed to simulate the spread of FMD in specific regions or countries (Bates et al., 2003a, 2003b; Garner and Beckett, 2005; Harvey et al., 2007; Stevenson et al., 2013; Wongsathapornchai et al., 2008). These models have been used for risk assessment, analysis of outbreaks using historical data or hypothetical scenarios, assistance with policy decisions during outbreaks, policy formulation in preparedness planning, and in evaluation of economic impacts (Bates et al., 2003a; Dürr et al., 2014; Ferguson et al., 2001a; Keeling et al., 2001; McReynolds et al., 2014; Morris et al., 2001; Tomassen et al., 2002; Yoon et al., 2006a).

Simulation models can be categorized as deterministic or stochastic based on the way uncertainty is considered, and non-spatial or spatially-explicit based on how spatial relationships are treated (Carpenter, 2011). Spatial models require locational data for herds of animals, which are essential for risk assessment, modeling contact spread, assessing animal movements, and implementation of control strategies (Robinson et al., 2007). The spatially explicit stochastic simulation models incorporate uncertainty in the inputs and outputs parameters, heterogeneity in disease processes, and integrate geographic locations and spatial proximity of holdings that affect their relative exposure and transmission risk.

Although many of the existing spatially-explicit stochastic simulation models (SESS) for FMD were designed for and applied in FMD-free settings (Zaheer et al. 2019, submitted), ongoing efforts have resulted in the development of the Simulation Model for Infectious Animal Diseases in FMD Endemic Regions (SMIAD-ER), an adapted SESS model (Zaheer et al., in preparation). The application of SMIAD-ER

in FMD endemic countries requires data on the location and population of individual livestock holdings. The SMIAD-ER incorporates demography and geography of holdings, and infection rate to be a function of demographics, distances between holdings and interaction among them. Therefore, if reliable and accurate data on the demography and geography of holdings are not available, the outputs of and recommendations from the model will be inaccurate and unrealistic.

As such, data on the size and distribution of at-risk livestock populations and relative proximity to the source of infection are essential to adequately prepare for and respond to disease events (Woolhouse, 2003). Quantification and mapping of disease risk locations are essential for the implementation of successful control and eradication programs. A better understanding of the geography of livestock holdings is essential for assessing the risk of livestock diseases such as FMD. Likewise, the demographic data on livestock holdings are fundamental to our understanding of how an infectious disease would spread (Buhnerkempe et al., 2014; Porphyre et al., 2013b), and for identifying the holdings at risk of becoming infected. This information, in turn, facilitates decision making for effective control (Bessell et al. 2010; Tomassen et al. 2002; Hugh-Jones 1976).

Several efforts have been made to predict the location and population of livestock holdings or population density at different spatial resolutions. The US Department of Agriculture and Colorado State University utilized aerial photography, environmental, topographic and meteorological covariates to develop a spatial microsimulation tool called the Farm Location and Agricultural Production Simulator (FLAPS) which simulates the distribution and population of individual livestock holdings in the coterminous USA (Burdett et al., 2015). The Food and Agriculture Organization of the United Nations (FAO) developed Gridded Livestock of the World (GLW) (Wint and Robinson, 2007), a global dataset of livestock population at 1 km<sup>2</sup> resolution utilizing predictors such as climatologic, topographic, demographic and land-cover data (Robinson et al., 2014). Moreover, agro-ecological factors have been

used to map the 1 Km<sup>2</sup> distribution of chickens, ducks, and geese across the extent of China (Prosser et al., 2011) and domestic ducks in Monsoon Asia (Van Boeckel et al., 2011). Moreover, in New Zealand, environmental and socioeconomic data have been used to predict the number of cattle and livestock units on farms (van Andel et al., 2017). However, the prediction of the location and population of individual livestock holdings in developing countries has several challenges.

For example, the GLW dataset is considered coarse and only provides population density at 1 Km<sup>2</sup> and not the spatial coordinates and the number of livestock at an individual holding level, which is required for SESS models (Harvey et al., 2007, Zaheer et al., in preparation). The data at 1 Km<sup>2</sup> do not allow the differentiation between holdings of different production type within an area which is required to model the disease spread among different combinations of production types. The progression and spread of disease vary from production type to production type because of biological differences and animal husbandry. Therefore, the data should be available for the location and population of individual livestock holdings.

The FLAPS model, for example, utilizes aerial imagery and remote sensing techniques to differentiate between farm and non-farm structures; the lack of structured farming system in many developing countries precludes this approach for location identification by aerial imagery. For instance, according to the most recent national census of livestock on Pakistan, 67.5% cattle, and 71.4% buffalo were in holdings with one to ten animals that are generally housed in backyards (Pakistan Bureau of Statistics, 2006). Moreover, methods that utilize agro-ecological, environmental, and socioeconomic data are not applicable in developing countries due to the lack of reliable predictor datasets.

Due to these limitations, there is a need to adapt the practical and reliable existing methods to generate a simulated dataset of location and population of individual livestock holdings, in developing countries for use in SESS models. Our objective is to generate a spatially-resolved simulated dataset on

the location and population density of individual livestock holdings in developing countries by microsimulating census data, creating geospatial probability surfaces and, finally, distributing the microsimulated dataset on the geospatial probability surface. The simulated dataset will be a key input for application of SMIAD-ER in developing countries for modeling FMD spread and evaluating mitigation strategies for its control.

## 2 Methods

The process of generating the simulated data on the location and population density (Figure 3.1) of individual livestock holdings comprised of three key steps, i.e., microsimulation of census data, creation of a geospatial probability surface, and distribution of holdings on a probability surface.

### 2.1 *Study area and animal types*

Two developing countries, Pakistan (Figure 3.2) and Thailand (Figure 3.3), were selected to demonstrate this approach. Both of these countries are endemic for FMD and lack data on the location and population of individual livestock holdings. Generated datasets from this approach will be used as a key input for SMIAD-ER.

#### 2.1.1 *Pakistan*

Pakistan has a human population of about 207 million (Central Intelligence Agency, 2019) and is comprised of five provinces, Baluchistan, Khyber Pakhtunkhwa (KPK), Gilgit-Baltistan (GB), Punjab and Sindh, and three territories, Islamabad Capital Territory (ICT), Federally Administered Tribal Areas (FATA) and Azad Kashmir. These provinces and territories represent the first administrative level (Figure 3.2). For this study, two provinces, Punjab and Sindh, and one territory, ICT, were selected because of their role in the livestock sector. Punjab and ICT were treated as one unit, as done elsewhere (Pakistan Bureau of Statistics, 2006), and are hereafter referred to as Punjab. The selected provinces have a variety of livestock, such as cattle, buffalo, sheep, and goats. There are; however, no domesticated pigs

in Pakistan owing to cultural and religious barriers (Deka et al., 2014). For this demonstration, only cattle and buffalo population were used and termed as “bovines.”

### 2.1.2 *Thailand*

Thailand has a human population of 68.15 million and is comprised of 77 provinces, which represent the first administrative level (Central Intelligence Agency, 2019). Thailand can also be divided into four distinct regions, i.e., central, northeastern, northern and southern (Figure 3.3), as demonstrated in the most recent agricultural census conducted in 2013 (National Statistical Office, 2013). For this study, three regions, central (26 provinces), northeastern (20 provinces), and northern (17 provinces), were selected because of their role in the livestock sector. A list of provinces included in three selected regions is available in the appendix. Thailand has a variety of livestock such as beef cattle, buffalo, dairy, sheep, goat, swine. However, only beef cattle, buffalo, dairy cattle, and swine were included in the study.

For simplicity and consistency, in the rest of the manuscript, the term “region” refers to provinces in Pakistan and regions in Thailand, unless otherwise noted. Likewise, the term “livestock” refers to the livestock of interest to this study unless indicated otherwise.

## 2.2 *Datasets*

Datasets used in our analyses included livestock census (National Statistical Office, 2013; Pakistan Bureau of Statistics, 2006), geographical features and land cover (Broxton et al., 2014; ESRI, 1992; GADM, 2015; Jarvis et al., 2008; OpenStreetMap Contributors, 2018), empirical holding locations from Pakistan and Thailand (spatial coordinates for a set of holding with associated livestock population), surveys of expert veterinarians from Pakistan and Thailand, and expert opinions. A description of each dataset is provided in the appendix.



### 2.3 *Microsimulation of census data*

Microsimulation (Harland, 2013; Harland et al., 2012; Lovelace and Dumont, 2016) was used to generate a simulated dataset of the livestock population in individual holdings by downscaling the census data based on statistical distributions (Burdett et al., 2015), using R Studio 3.4.1 (R Core Team, 2017) and Python 2.7 (Van Rossum and Drake Jr, 1995). We downscaled the census data to individual holdings based on uniform and lognormal distribution.

For each livestock, the census data (Table 3.1) is formatted in different herd-class. For each herd-class, the lower and upper class bound is provided except in the case of the largest herd-classes which upper bound is not available. In that case, the upper bound is based on expert-opinion of field-based personnel (Anonymous, Personal Communication). The census data provide the number of livestock holdings for each herd-class and the corresponding number of livestock in that herd-class.

When a uniform distribution was used, it was assumed that within a bin (class-interval) there is an approximately an equal number of holdings for each bin (class) element. For example, if the bin size is 1 - 5, then there are — roughly an equal number of holdings with 1, 2, 3, 4, and five animals. First, the algorithm makes an array of numbers between lower and upper boundary of the bin and divides the total number of holdings into parts that equal the number of bin elements. Second, it multiplies each element of the bin with the respective number of holdings and sums all numbers ( $s_1$ ) and compares  $s_1$  with the expected number of holdings for that bin ( $s_2$ ). If  $s_1 > s_2$ , it decreases one holding from the highest element of the bin and adds it to the lowest element of the bin and compares  $s_1$  and  $s_2$  again. If  $s_1 < s_2$ , it decreases one holding from the lower element of the bin and adds it to the highest element. The loop continues, and at each iteration, it compares  $s_1$  with  $s_2$ . The loop concludes when  $s_1$  equals  $s_2$ . Finally, Microsoft Excel 2016 files were written that lists all the holdings for each herd-class and the corresponding number of animals in individual holdings.

When a lognormal distribution was used, the algorithm generates a list of holdings with the corresponding number of animals ( $s_1$ ) and compares it with the expected number of animals ( $s_2$ ). If  $s_1 > s_2$ , it calculates the number exceeding  $s_2$ , then it randomly selects the equivalent number of holdings and reduces the corresponding number of animals in the selected holdings by 1. If  $s_1 < s_2$ , it calculates the number lagging  $s_2$ , then it randomly selects an equivalent number of holdings and increments the corresponding number of animals in the selected holdings by 1. Finally, an MS Excel file is written that has a list of all the holdings for herd-class 5 with the corresponding number of animals.

### *2.3.1 Pakistan*

The most recent national-level livestock census was conducted in 2006 (Pakistan Bureau of Statistics, 2006). The census provides data on the number of holdings and the number of livestock by species and herd-class, all aggregated to the district (equivalent to a county in the US), or second administrative level in the census. For this study, aggregate data at the provincial level were used since there have been changes to the number of districts and their boundaries after 2006. The census data for bovines are represented in nine herd classes (based on the number of animals), but we consolidated them to five herd classes (Table 3.2), as detail on small herd sizes was not needed from the perspective of local animal husbandry, and FMD spread in Pakistan. Uniform and lognormal distributions were assumed to downscale aggregate census data to individual livestock holdings for herd-class 1 through 4 and herd-class 5, respectively.

### *2.3.2 Thailand*

The most recent national-level livestock census was conducted in 2013 (National Statistical Office, 2013). The census provides data on the number of holdings and the number of animals by species and herd-class, all aggregated to the provincial level (equivalent to a state in the US), or second administrative level in the census. For this study, aggregate data at the regional level were used based

on the expert opinion of field personnel (Anonymous, personal communication). The census data for beef cattle, dairy cattle, and swine are reported in nine herd-classes (based on the number of animals). For buffalo, the data are represented by seven herd-classes (based on the number of animals). Similar to our approach in Pakistan, the census herd-classes were consolidated to five herd classes (Table 3.3), which was appropriate from the perspective of animal husbandry and FMD spread in Thailand. Lognormal distributions were assumed to downscale aggregate census data to individual livestock holdings for all herd-classes.

#### *2.4 Creation of the geospatial probability surface*

The creation of geospatial probability surface was a multistep process that involved, acquisition and geoprocessing of data, a survey of expert veterinarians' opinions to estimate weights for different geographic features, empirical holding locations to make additional probability buffers around different geographic features, and creation of the final geospatial probability surface.

##### *2.4.1 Acquisition and geoprocessing of data*

The geographic datasets (Table 3.4) on administrative boundaries (GADM, 2015), water bodies (ESRI, 1992), road networks (OpenStreetMap Contributors, 2018), elevation (Jarvis et al., 2008), and land cover (Broxton et al., 2014) were clipped to match the boundary of the regions of interest and were projected and resampled to a cell size of 100 m. The details on geoprocessing are available in the appendix.

##### *2.4.2 Expert opinion and estimation of weights*

A critical step in the creation of probability was to estimate the weights for different land cover types and geographic features. An anonymous questionnaire was developed, and pilot tested to seek expert opinions from veterinarians in Pakistan and Thailand. The questionnaire was approved by the Research Integrity and Compliance Review Office (RICRO) at the Colorado State University.

A convenience sample of veterinarians was selected, and consent was sought for participation in the survey. The questionnaire requested data on duration of experience with animal health, the domain of experience, and the region they represent. The questionnaire contained detailed questions seeking the participant's opinion on the importance of different land cover and geographic features such as croplands, open lands, urban areas, and slope on animal agriculture. The questions were included for all livestock types and their herd-classes. A copy of the questionnaire is available in the appendix.

The survey responses from different regions were combined for each country to overcome the small sample size. Then, median weights were estimated for all livestock types and regions.

#### *2.4.3 Initial geospatial probability surface*

For the creation of initial geospatial probability surface, the land cover and slope were multiplied with their respective weights estimated from survey responses, using the raster calculator in Spatial Analyst Tools in ArcGIS 10.5 (ESRI, 2012). Permanent water bodies were masked out as they could not realistically be locations for livestock holdings.

#### *2.4.4 Empirical holding locations and personal communications for additional probability buffers*

Each survey participant was requested to share a list of empirical holding locations with associated animal population and species. Empirical holding locations were also obtained through open-source such as Google Maps for large bovine holdings in Pakistan. These data helped to a determined distance of these holdings from the main, primary, and smaller highway since livestock holdings are more likely to be closer to highways because of the importance of road networks in the transport of feed, other equipment, live animals, and their products.

Based on the percentage of empirical holdings that fell within 1,000 m, 500 m, and 100 m from main, primary, and smaller highways respectively, additional weights were assigned to buffers around these highways.

Moreover, based on personal communications with veterinarians, additional probability values were assigned to a 5 km radius around urban areas. The rationale for these weights was to ensure that areas in the vicinity of urban build-up were assigned a higher probability and more likely to contain livestock holdings due to supply-demand needs.

#### *2.4.5 Final geospatial probability surface*

In the final step of creating the geospatial probability surface, additional weights for buffers around highways and urban areas were added to the raster calculator in combination with weights for different land cover types and slope. This resulted in the creation of a final probability raster for all herd-classes of each livestock type in the regions of interest. The final probability rasters were normalized (0 – 100) using the raster calculator in Spatial Analyst tools in ArcGIS 10.5 (ESRI, 2012).

The final normalized probability surface was classified into three equal intervals, i.e., low, medium, and high. For the next section of methods, the probability surface will be termed as the categorized probability surface.

### *2.5 Distribution of random holdings on the categorized geospatial probability surface*

#### *2.5.1 Holdings on categorized geospatial probability surface*

The empirical holding locations were used to estimate the percentage of holdings which fall on low, medium, and high probability zones of the probability raster (see appendix). Based on the resulting percentage, an equivalent number of holdings of different livestock type and herd-class were identified to be randomly distributed on the categorized probability raster.

#### *2.5.2 Minimum distance between holdings*

Based on personal communication with veterinarians and empirical information, the minimum distance, a minimum distance between holdings was assigned to ensure holdings are placed within a

specified distance from each other (see appendix). The minimum distances were unique to small holdings (herd-class 1), medium holdings (herd-class 2 & 3), large holdings (herd-class 4 & 5).

### 2.5.3 *Creation of random holdings*

The “random point generator” was used to create random holdings within the low, medium, and high probability zones in predefined polygons representing regions in Pakistan and Thailand. At the level of region, the algorithm created a collection of random points within the predefined polygons (low, medium, and high). Each generated point was tested to make sure that it was not within its minimum distance from any other point. The placement of points with a larger minimum distance was prioritized so that the larger distance points have fewer chances of a conflict. Once the predefined number of non-conflicting points was created in each region, the point layers were merged, and a MultiPoint output layer was created.

In this process, the largest herd-class (i.e., 5) is given priority followed by holdings with the largest distance between holdings. The largest herd-class was given priority so that they had the best chance of being placed in the appropriate probability zone. This was necessary to ensure that the largest holdings were placed in the high probability zone, which would be closest to the main highways, around urban areas and other suitable land cover features. If more than one livestock type had similar value for minimum distance between holdings, then, dairy was preferred over beef and beef was preferred over swine.

The geographical boundaries of the data were projected to “Web Mercator” because of computational ease and conservation of distances (ESRI, 2010). During the creation of random holdings, each polygon (low, medium and high) was split into many smaller pieces, and a proportional number of holdings were assigned to each small piece of the polygon. Then, a spatial index was used to determine if any holdings were within the minimum distance from each new holding. If a holding was within the

minimum distance, a new holding was assigned. Once all holdings were assigned, holdings were merged into one large multipoint geometry. The final multipoint geometry was exported as an ESRI Shapefile and was projected to WGS84 (EPSG:4326) from Web Mercator (ESPG:3857).

#### 2.5.4 *Joining location and population data*

In this step, the datasets on the locations of individual holdings (output from section 2.5) and microsimulated livestock population in individual holdings, were joined. The resulting file contained the data on the locations and populations of individual livestock holdings in Pakistan and Thailand for each livestock-type.

#### 2.6 *Creation of density maps*

The combined dataset on the location and population of individual livestock holdings was processed to create a separate file for each herd-class of livestock by region and country. These files were used to generate per square Kilometer kernel density of holdings using the Kernel Density function in the Spatial Analyst tools of ArcGIS 10.2 (ESRI, 2012). The population field was set to “none,” and the cell size was set to 1,000 m.

### 3 Results

#### 3.1 *Microsimulation of census data*

The census data for livestock were downscaled to individual livestock holdings to estimate the number of livestock using microsimulation assuming uniform (Table 3.5) and lognormal distribution. The datasets provide a list of individual livestock holdings with the corresponding number of animals in each holding. Other microsimulated datasets can be obtained from authors, upon request.

#### 3.2 *Geospatial probability surfaces*

A total of nine and seven veterinarians from Pakistan and Thailand, respectively, responded to the questionnaire. The weights used to create intermediate and final geospatial probability surface are

presented (Table 3.6). The resulting final probability surfaces (Figure 3.4-3.9) for each herd-class of livestock in Pakistan and Thailand are categorized into three intervals - low, medium, high which represent 0-33, 33-67 and 67-100 percent probability areas, respectively. The geospatial probability surfaces for the central and northern region of Thailand are available in the appendix.

### *3.3 Individual holdings with associated location and population*

The resulting joined dataset on the location of randomly distributed holdings on geospatial probability surface and downscaled data on livestock population in individual holdings is available from the primary author upon request

### *3.4 Livestock holding density*

For a demonstration of Kernel Density maps of bovines in Pakistan (Figure 2.10-2.11), herd-class 2 & 3, and 4 & 5 were merged and termed 'medium holdings,' and 'large holdings,' respectively. The herd-class one was termed as 'small holdings.' For beef, dairy, and swine in Thailand (Figure 3.12-3.15), herd-class 2 through 5 were merged and are termed 'large holdings.' The herd-class one is termed 'small holdings.' For buffalo in Thailand, herd-class 1 through 3 and 4 & 5 were merged and are termed 'small holdings' and 'large holdings,' respectively. The Kernel Density maps for livestock central and northern region of Thailand are available in the appendix.

Density maps provide quite interesting information on the areas with varying density of livestock holdings. For instance, Figure 2.11(a) shows density of small bovine holdings (herd-class 1) for Sindh, Pakistan with a range of up to 141.45 holdings/Km<sup>2</sup>. A simple analysis of this density map reveals that approximately 98.7% area of Sindh region has 1-50 holdings of small bovines/Km<sup>2</sup>, 0.6% area has >50-100 holdings/Km<sup>2</sup>, while another 0.3% has >100-144.45 holdings/Km<sup>2</sup>. Figure 2.11(b) shows density of medium bovine holdings (herd-class 2 and 3) for Sindh, Pakistan with a range of up to 6.97 holdings/Km<sup>2</sup>. A simple analysis of this density map reveals that approximately 85% area of Sindh region



has up to 3 holdings of medium bovines/Km<sup>2</sup>, and 14.4% area has >3-6.97 holdings/Km<sup>2</sup>. Figure 2.11(c) shows density of large bovine holdings (herd-class 4 and 5) for Sindh, Pakistan with a range of up to 1.078 holdings/Km<sup>2</sup>. A simple analysis of this density map reveals that approximately 97.7% area of Sindh region has up to 1 holdings of large bovines/Km<sup>2</sup>, and 0.6% area has >1-1.078 holdings/Km<sup>2</sup>.

#### 4 Discussion

To our knowledge, this is the first ever attempt to downscale census data to individual holdings and to use the geographic information system to generate a microsimulated synthetic dataset on the location and population of individual livestock holdings. We successfully produced a synthetic dataset on the location and population of individual livestock holdings in two developing countries, Pakistan and Thailand. As such, these data are essential to adequately prepare for and respond to disease events (Woolhouse, 2003).

Firstly, the agricultural census dataset used for Pakistan is more than a decade old and may not reflect the actual number of livestock holdings and associated populations. Although newer census data for Punjab province was made available in 2018 (L & DD, 2018), this dataset does not provide the number of holdings for each herd class and the associated animal population. Albeit the newer census was not used, it would not have affected the results of this study significantly because there was not a significant change in the number of animals from 2006 to 2018 (L & DD, 2018). The authors believe that the applied method can be replicated when a newer census when the required information is available.

Secondly, a very small convenience sample, comprised solely of veterinarians, was chosen for the questionnaire ignoring other relevant professionals. This might have affected the validity of responses which were less variable among different herd-classes as evident from geospatial probability surfaces Figure 3.5–3.10. Despite these shortcomings, our method provides a starting point as veterinarians are the critical stakeholders for animal health in any given country (Bellemain, 2013). In the future, if

resources are available to expand on this study, increasing the sample size, selecting respondents systematically, and including other relevant professionals such as agricultural and natural resource scientists who may have had different opinions and experiences would yield more reliable estimates to create geospatial probability surface. Also, more work is needed on algorithm optimization to fit all holdings within the boundary of regions which can be achieved by adjusting weights for different features and the minimum distance between holdings through more stakeholder consultations on the role of different factors on animal agriculture in Pakistan and Thailand.

Thirdly, we only had a very small number of empirical holding locations which were used to estimate additional probability values. For example, there were only 220 empirical holdings data available from Pakistan, which were very small compared to the total number of holdings to be distributed. Therefore, the use of this small number of holdings to determine additional probability and determining the percentage of holdings onto different probability zones might have been an oversimplification of a rather complex mechanism. Out of those 220 empirical holding locations, 55% were large holdings followed by 33% medium holdings, and 1% small holdings. Likewise, only 430 empirical holding locations were available from Thailand. This small number was further divided into four animal types, with the highest number of holdings available from dairy, followed by swine, beef, and buffalo. Future work should focus on obtaining more data on empirical holding locations to have more confidence in additional probability buffers and distributing random holdings on the surface.

Despite these limitations, this is first ever attempt to estimate the locations and populations of individual livestock holdings in developing countries. Developing countries often lack detailed datasets, though some developed countries do not make this data public owing to privacy issues. The generation of these synthetic, simulated datasets can have several uses in endemic countries. These data can help authorities in determining resources needed in regions with varying livestock density in peace-time and

during times of infectious disease outbreaks and natural disasters such as floods, earthquakes. It can, also, guide the authorities in developing sentinel sites close to highly dense areas or areas around critically important livestock, to act as an early warning system.

The geospatial probability surface, for instance, provide a very useful visualization of a regions landscape in terms of its suitability for animal agriculture. Figure 2.5(a) shows a geospatial probability surface for bovines of herd-class 1 in Sindh, Pakistan. It is evident that most of the region's landscape is covered by medium and high probability areas for animal agriculture oif herd-class-1 with minimal area with low probability. This is quite intuitive from the perspective of backyard or subsistence animal agriculture system which is found almost everywhere in that region. On the other hand, figure 2.5(b-e), show that for bovine herd-class 2 through 5, there are distinct areas of low medium and high probability for animal agriculture. Most of the high probability areas are around urban-buildups with medium probability areas in areas dense with croplands. This information is quite useful for departments of agriculture and livestock to know where livestock holdings are more likely to be and hence invest resources in that area for management of animal diseases. For example, areas that are highly favorable for animal agriculture around urban areas with intensive road connectivity may play a significant role in the favoring the spread of infectious animal diseases such as Foot-and-Mouth Disease, African swine Fever etc. The same visual information can also be useful to know which areas should be focused for sentinel surveillance for such diseases and implementation of control actions such as quarantine, movement restriction, risk based vaccination programs and stamping out.

Additionally, the data on the location and population of individual livestock holdings can be used in spatial modeling for infectious animal diseases, such as FMD, ASF, and CSF. For example, one application could be to use these datasets in SMIAD-ER to understand the spread of FMD and evaluating alternative mitigation strategies for its control in developing countries such as Pakistan and Thailand (Zaheer et al.,

in preparation). In the spatial models, these data are essential to assess the risk, model contact spread, and movements, and implement control strategies (Robinson et al., 2007) which makes the distribution and population of livestock holdings a critical component in estimation of an effective reproductive number (Porphyre et al., 2013). The effective reproduction number is a key indicator of whether an outbreak is under control and hence guides planning and policy formulation to promote safe, sustainable and equitable livestock sector development (Paine et al., 2010, Robinson et al., 2014).

## 5 Conclusion

The data depicting the size and distribution of at-risk livestock populations and their proximity to the source of infection is essential to prepare for and respond to disease events adequately. These data are, however, not available in the desired form or at the required spatial resolution for use by animal health officials. The importance of spatial demographic datasets of livestock, therefore, calls for its free availability through a central open-access data repository. This study generates a simulated dataset on the locations and populations of individual livestock holdings in two developing countries, Pakistan and Thailand. This synthetic dataset will have applications in animal health, preparedness planning, and policymaking. Particularly, these data could be used in spatially-explicit stochastic simulation models such as the Simulation Model for Infectious Animal Diseases in Endemic Regions (SMIAD-ER) to understand the spread of FMD and evaluate mitigation strategies for its control. The control of such high consequence animal disease would improve livestock health, improve economic gains for producers, and help alleviate poverty and hunger, which and will complement efforts to attain the Sustainable Development Goals and the 2030 Agenda.

## Funding

No specific funding was received for this project. The doctoral program of the primary author is, however, funded by the US Department of State through the Pakistan Fulbright Scholarship Program.

## Conflict of Interest

The authors declared no conflict of interest.

Figures

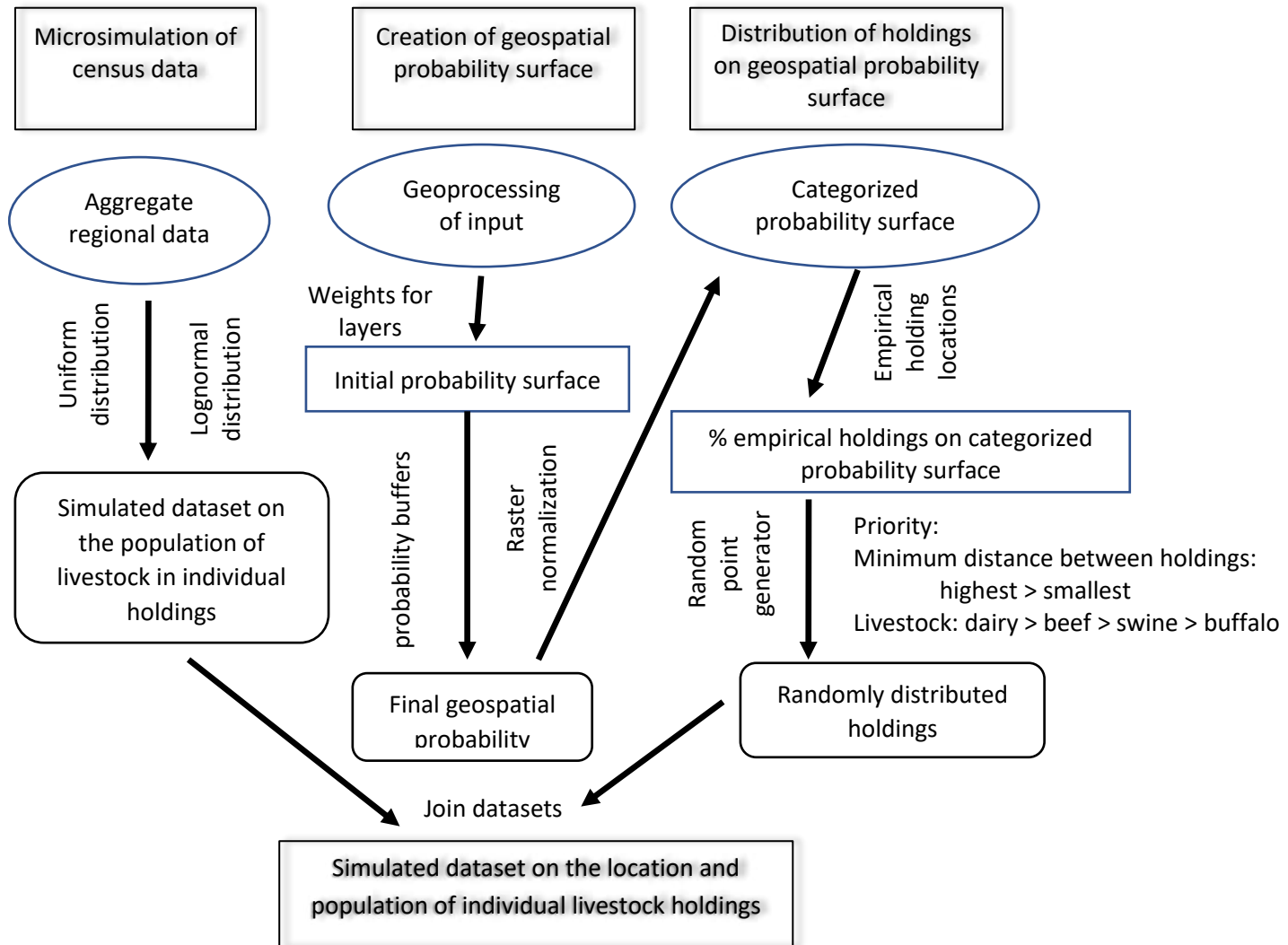


Figure 2.1: Flow diagram of generating simulated dataset on location and population of individual livestock holdings

**Provinces and Territories**

-  Azad Kashmir
-  Baluchistan
-  Federally Administered Tribal Areas
-  Islamabad Capital Territory
-  Khyber Pakhton Khwa
-  Gilgit-Baltistan
-  Punjab
-  Sindh

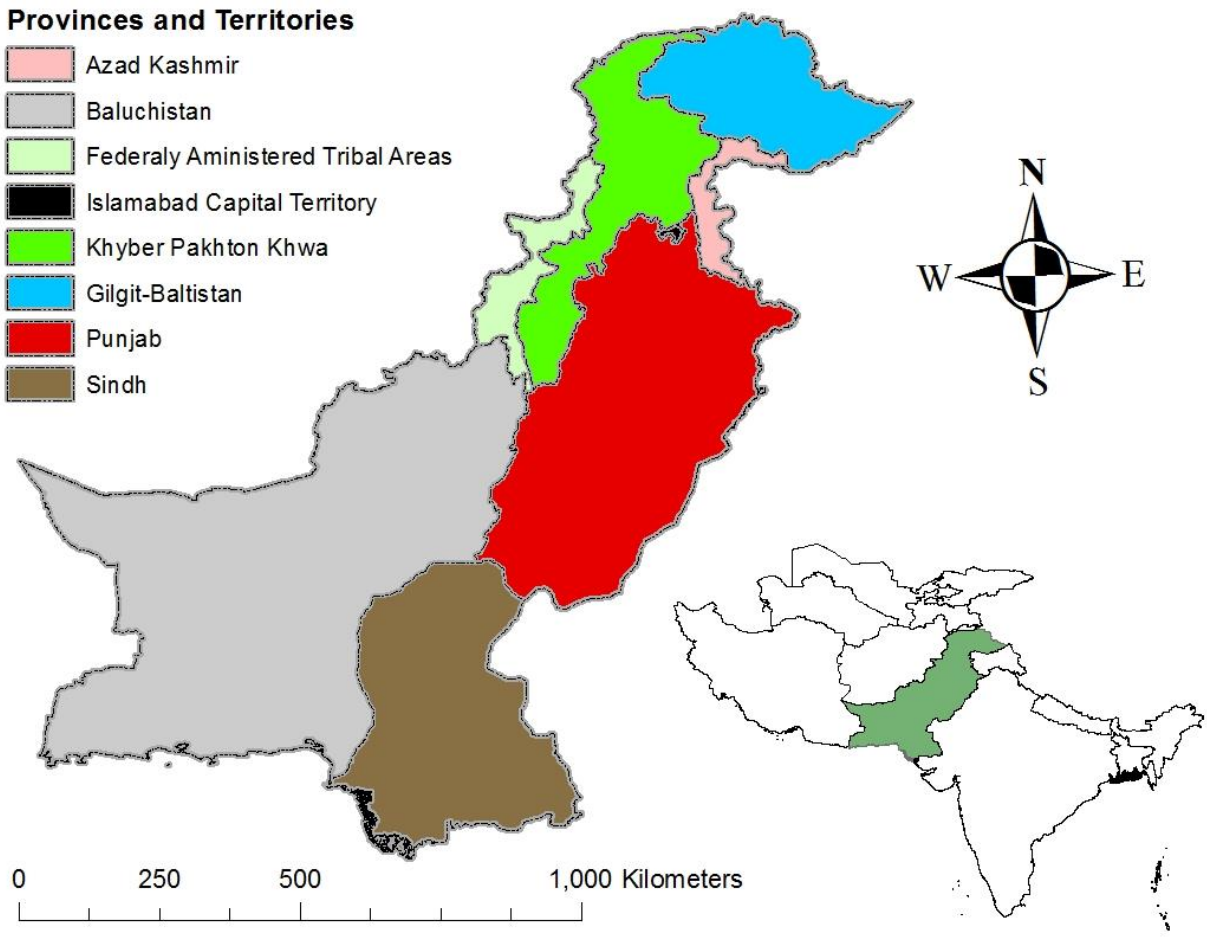


Figure 2.2: Map of Pakistan showing its provinces and territories

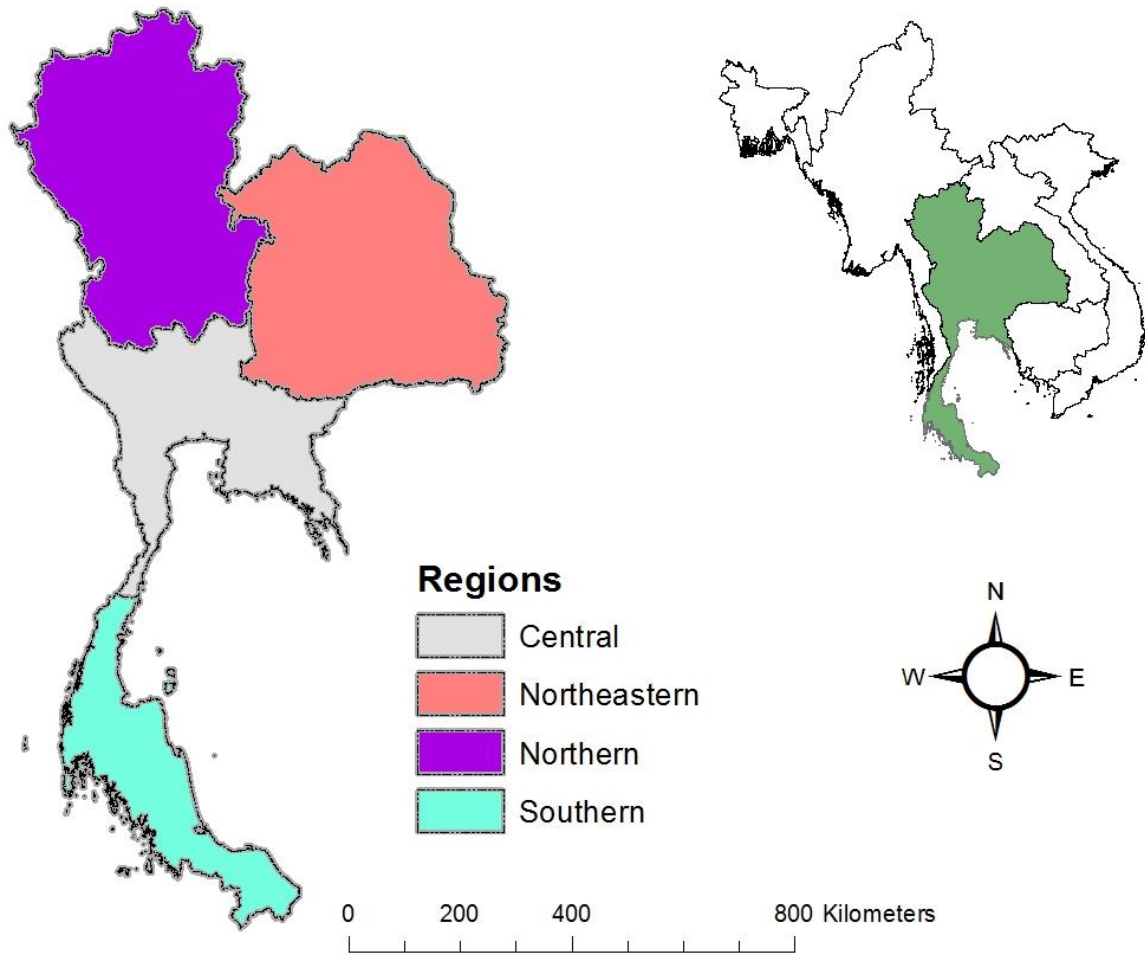


Figure 2.3: Map of Thailand showing its regions



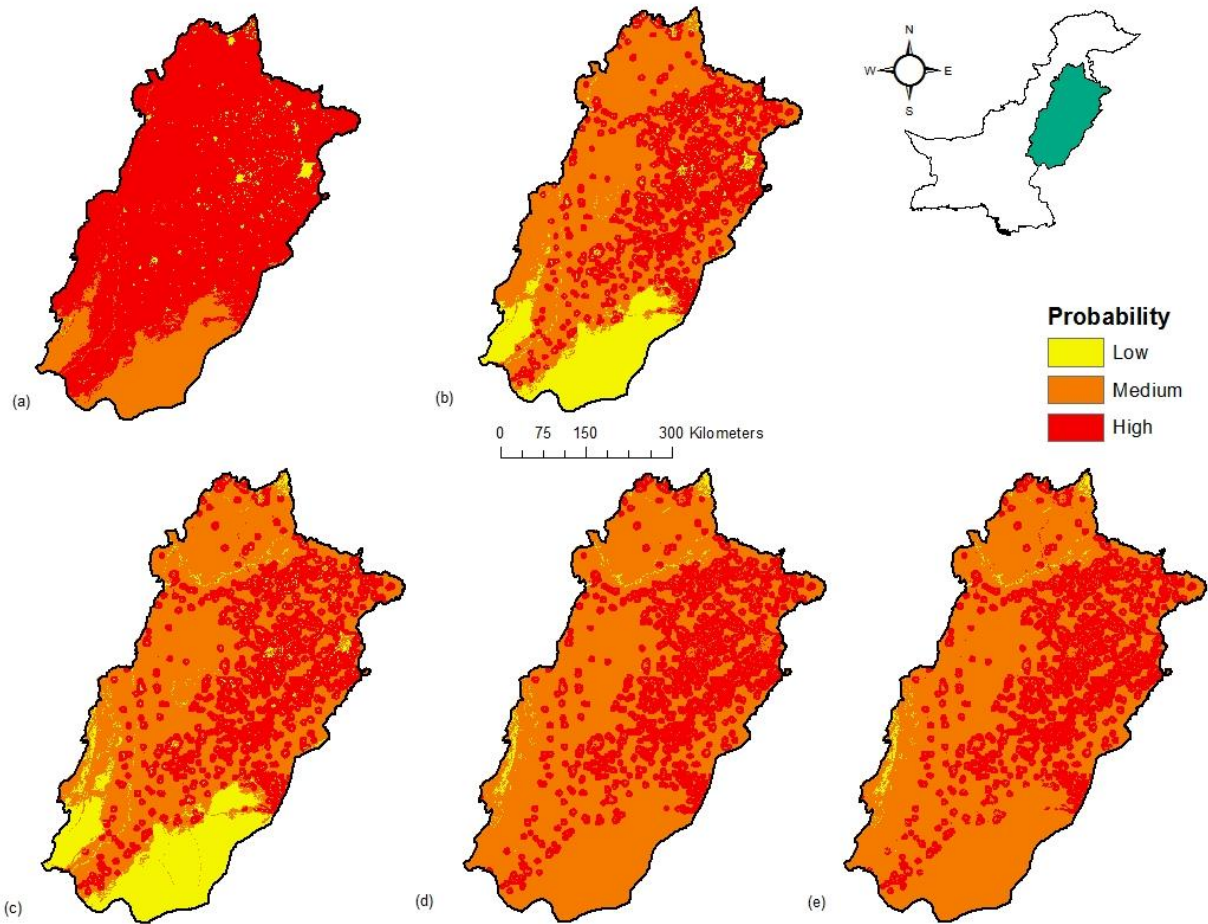


Figure 2.4: Geospatial probability surface for bovines in Punjab, Pakistan where (a) to (e) represent herd-class 1 through 5, respectively

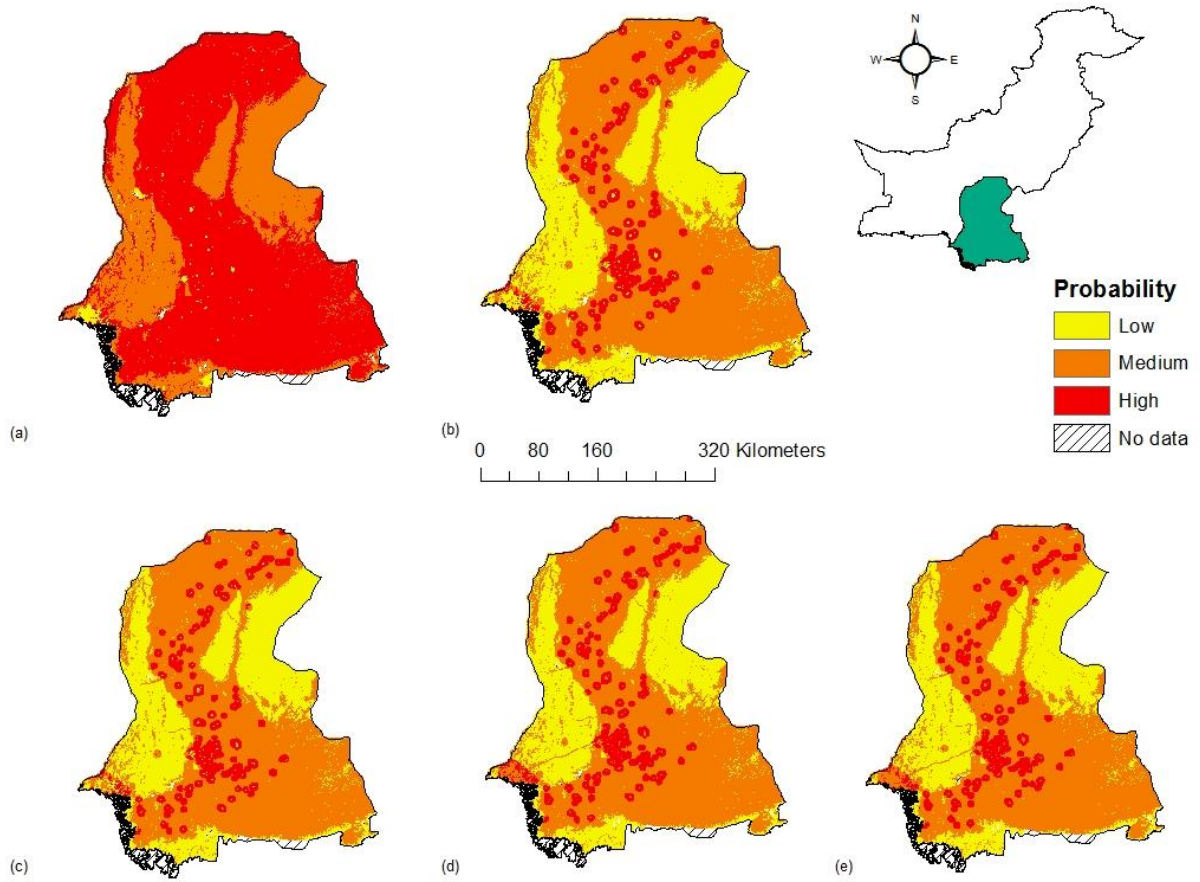


Figure 2.5: Geospatial probability surface for bovines in Sindh, Pakistan where (a) to (e) represent herd-class 1 through 5, respectively

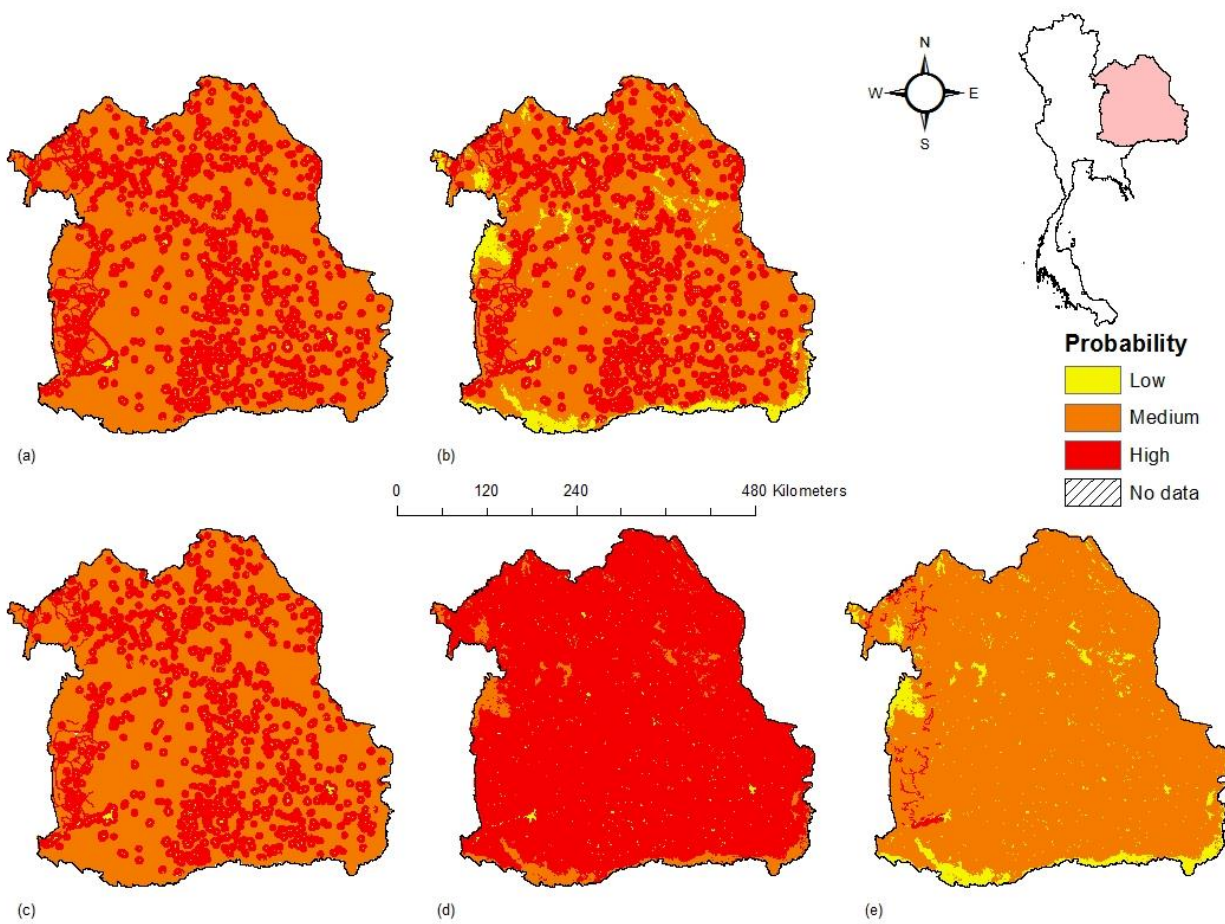


Figure 2.6: Geospatial probability surface for dairy cattle in Northeastern, Thailand where (a) to (e) represent herd-class 1 through 5, respectively

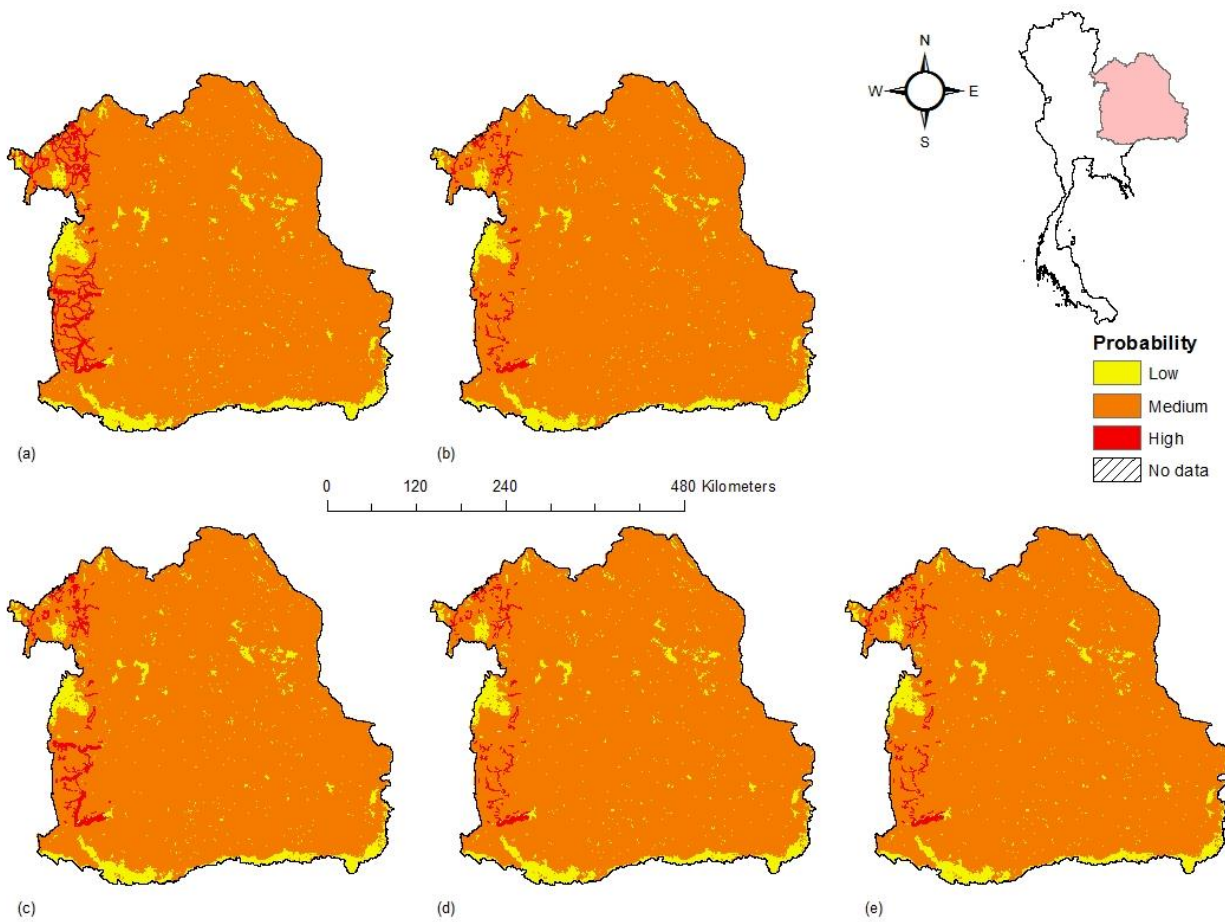


Figure 2.7: Geospatial probability surface for beef cattle in Northeastern, Thailand where (a) to (e) represent herd-class 1 through 5, respectively

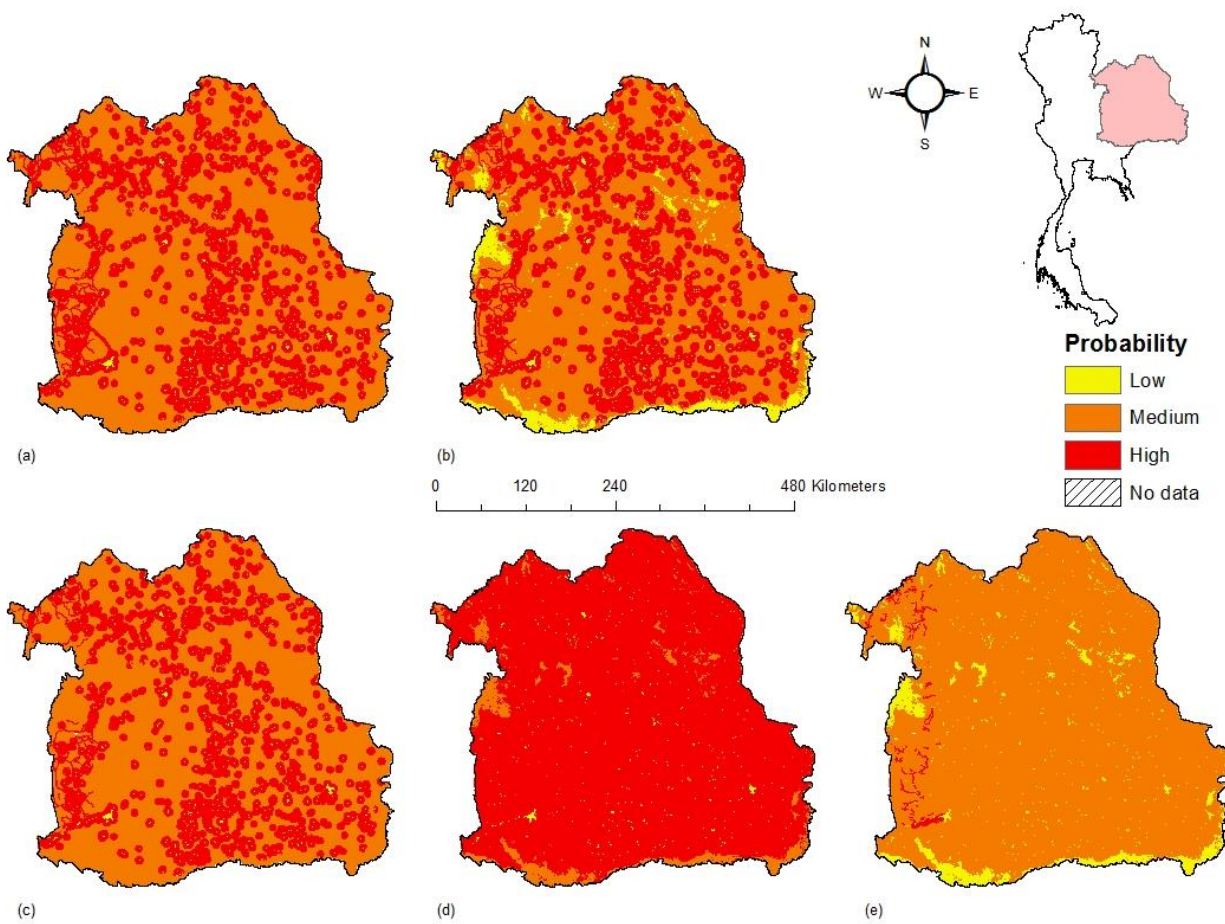


Figure 2.8: Geospatial probability surface for swine in Northeastern, Thailand where (a) to (e) represent herd-class 1 through 5, respectively

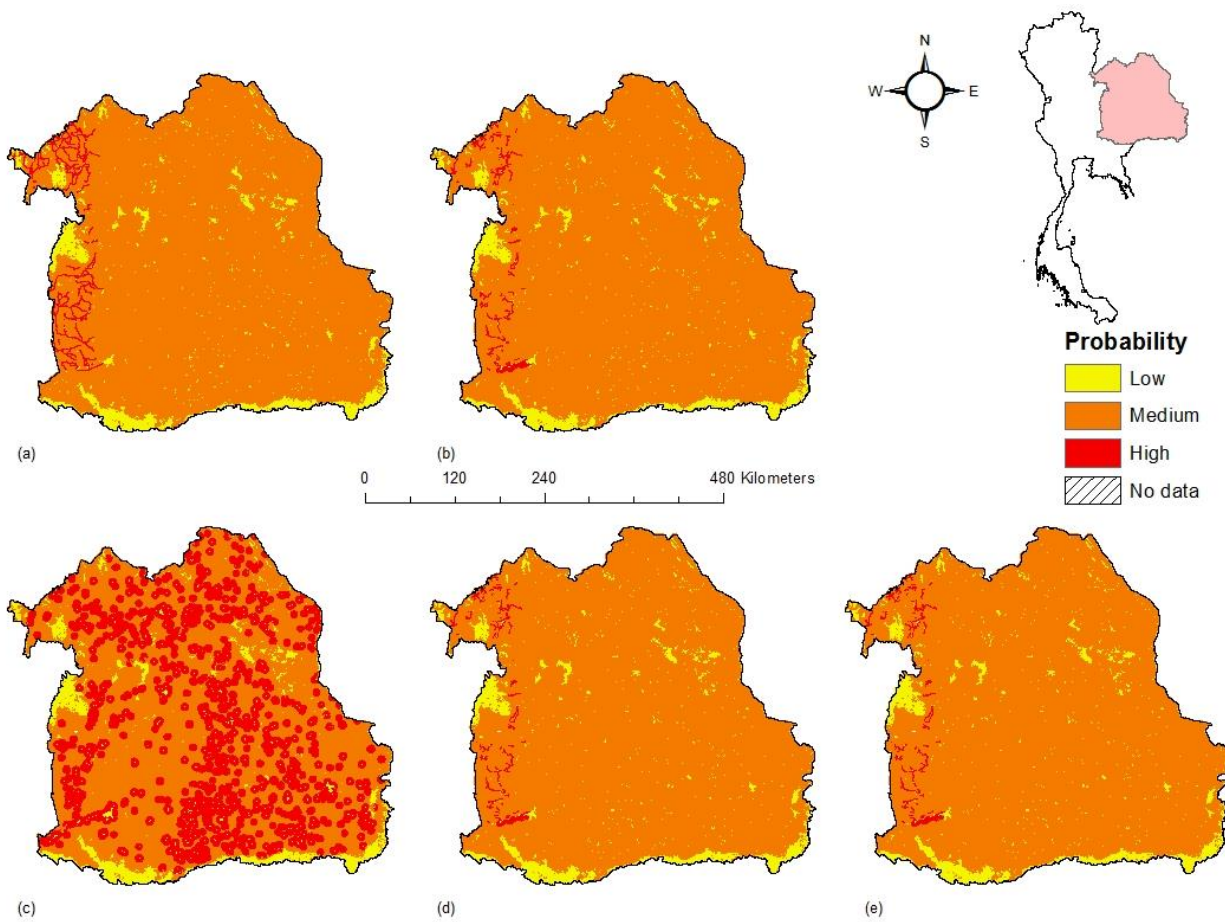


Figure 2.9: Geospatial probability surface for buffalo in Northeastern, Thailand where (a) to (e) represent herd-class 1 through 5, respectively

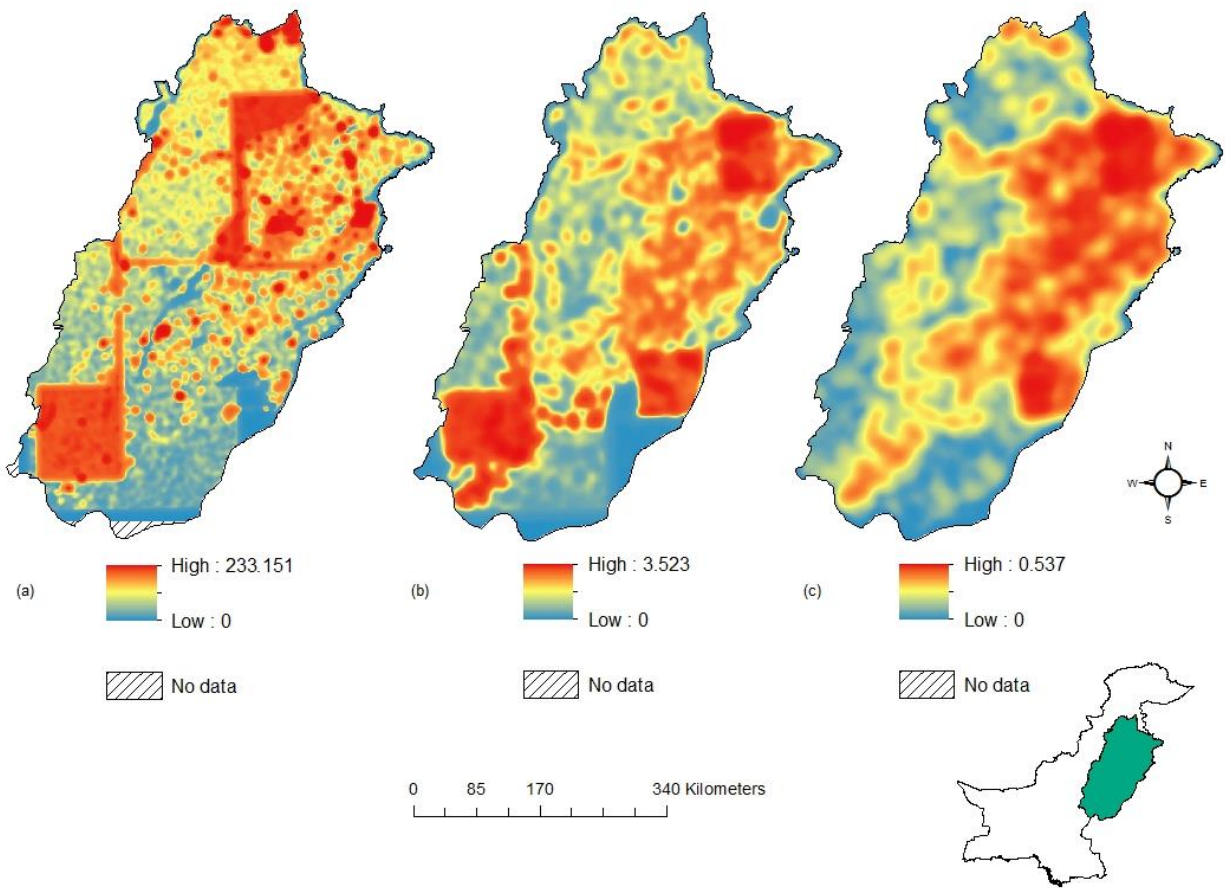


Figure 2.10: Holding density (/Km<sup>2</sup>) for bovines in Punjab, Pakistan where (a) to (c) represent small, medium and high density

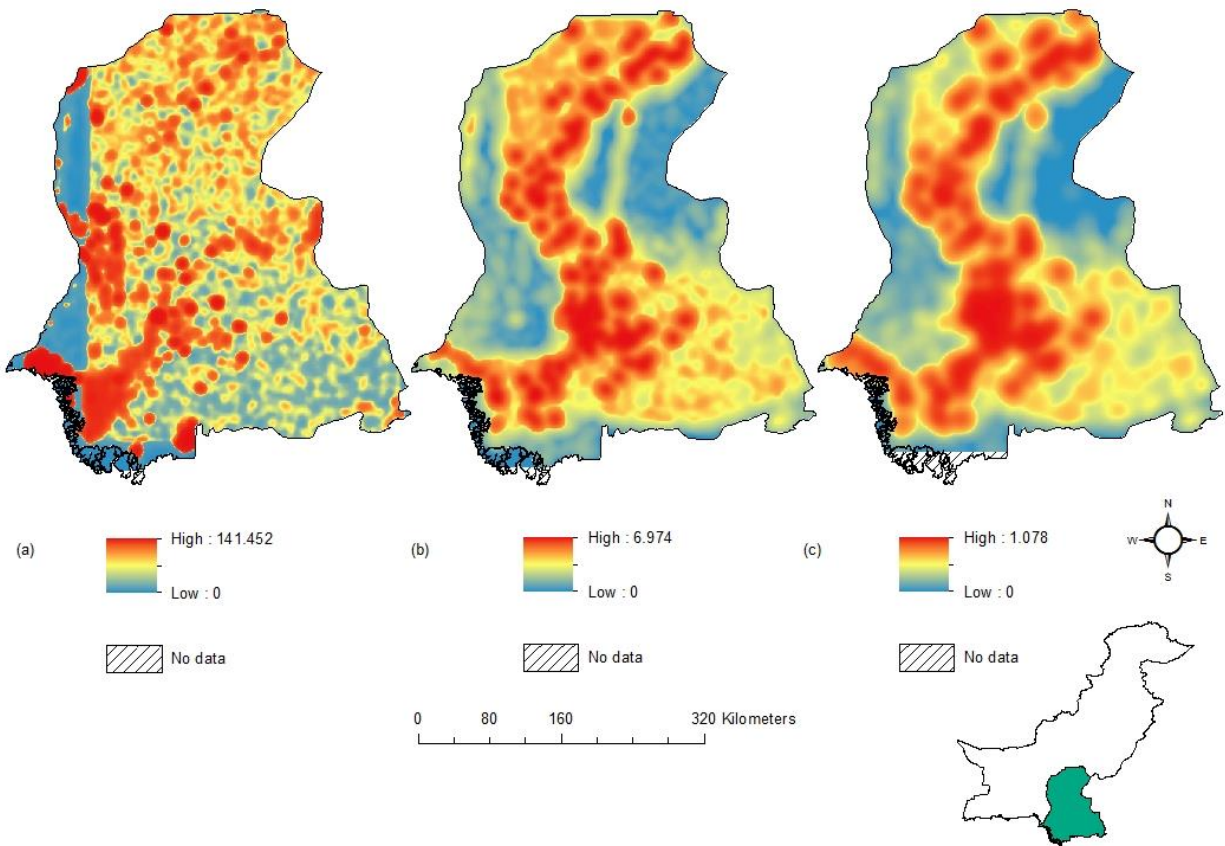


Figure 2.11: Holding density (/Km<sup>2</sup>) for bovines in Sindh, Pakistan where (a) to (c) represent small, medium and high density



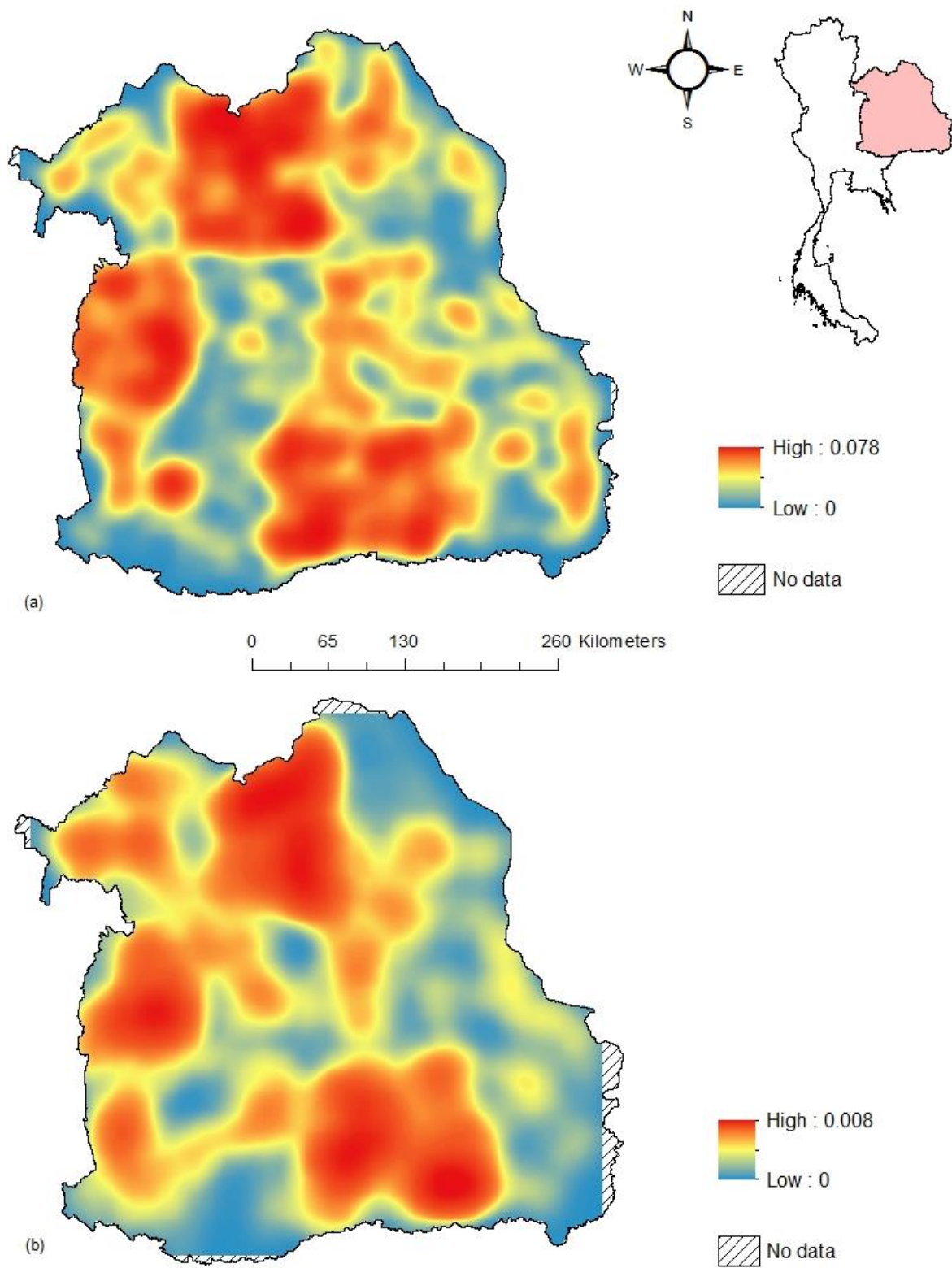


Figure 2.12: Holding density (/Km<sup>2</sup>) for dairy cattle in Northeastern, Thailand were (a) and (b) represent small, and large holdings

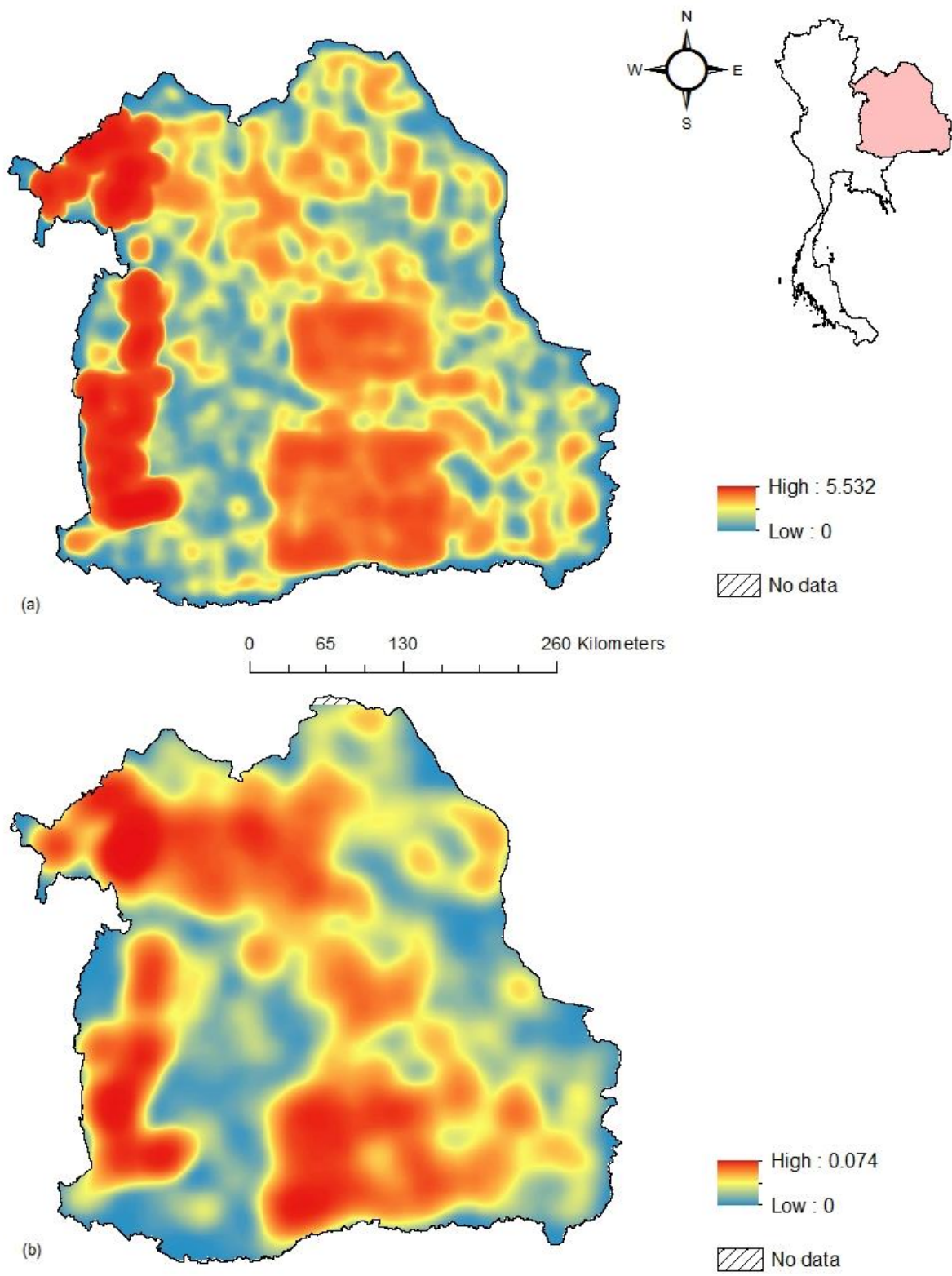


Figure 2.13: Holding density (/Km<sup>2</sup>) for beef cattle in Northeastern, Thailand were (a) and (b) represent small, and large holdings

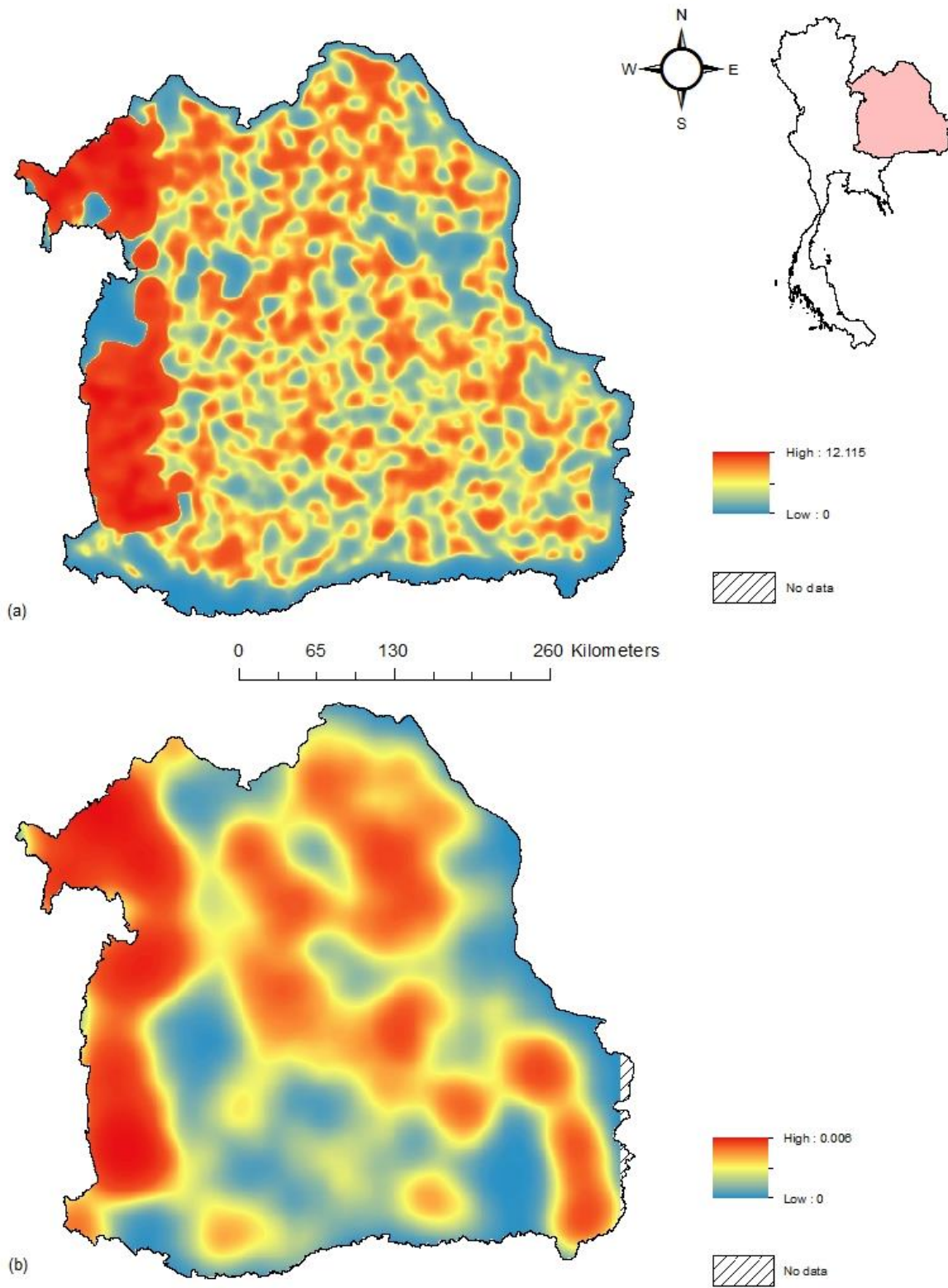


Figure 2.14: Holding density (/Km<sup>2</sup>) for swine in Northeastern, Thailand were (a) and (b) represent small, and large holdings

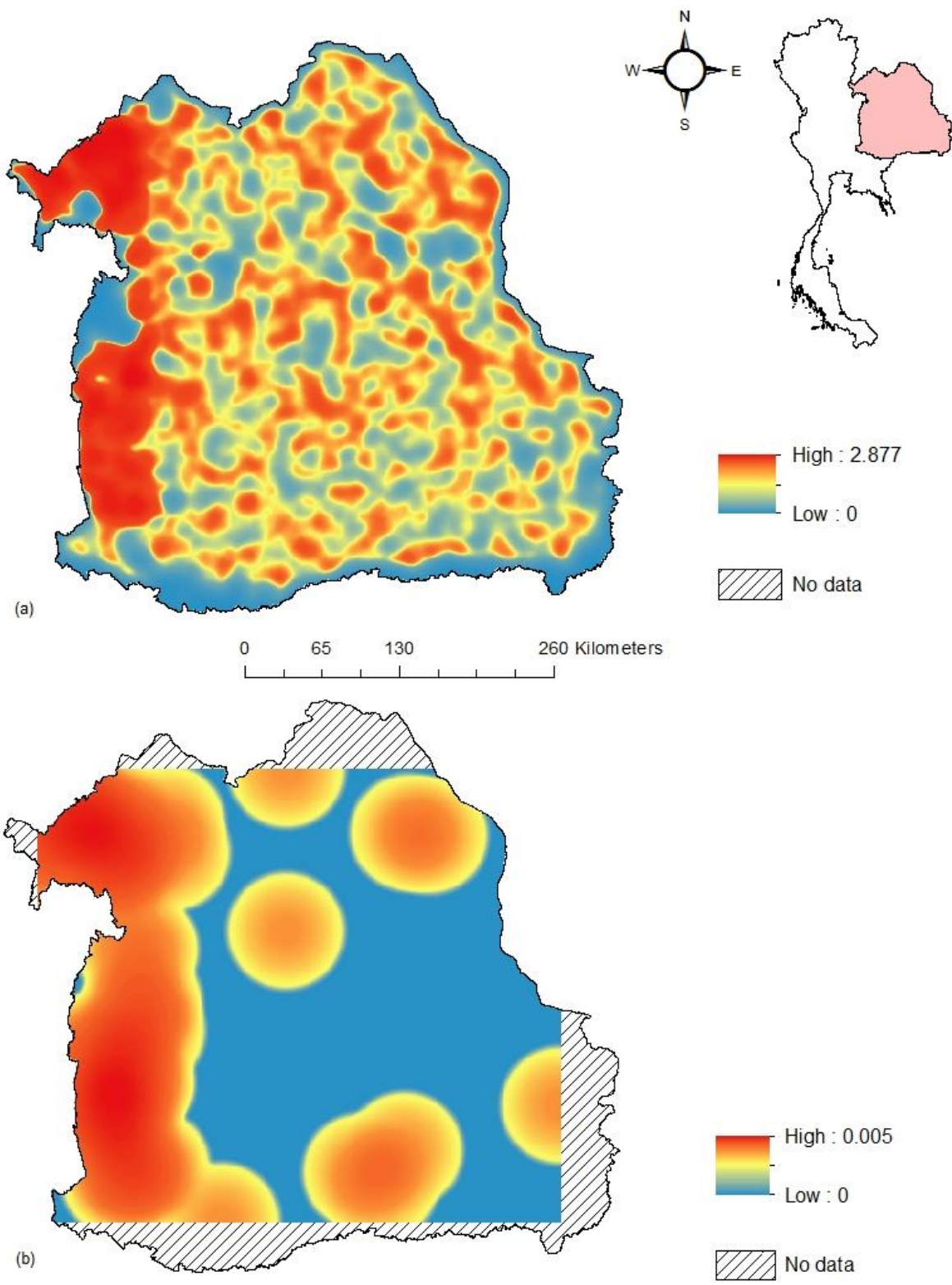


Figure 2.15: Holding density (/Km<sup>2</sup>) for Buffalo in Northeastern, Thailand, where (a) and (b) represent small, and large holdings

Tables

Table 2.1: Aggregate census data for Pakistan and Thailand by region, attribute, and herd-class

Country	Region	Livestock	Attribute	Herd class					Total	
				1	2	3	4	5		
Pakistan	Punjab	Bovines	Holdings	7,265,425	271,459	41,574	19,220	13,986	7,611,664	
			Animals	23,930,959	3,723,894	1,016,475	724,486	2,763,831	32,159,645	
	Sindh	Bovines	Holdings	2,162,006	195,776	29,917	12,444	9,150	2,409,293	
			Animals	8,663,463	2,738,237	724,828	476,474	1,662,188	14,265,190	
Thailand	Central	Dairy	Holdings	9,058	1,155	128	3	1	10,345	
			Animals	172,756	70,211	16,191	1,070	734	260,962	
		Beef	Holdings	45,351	1,412	441	32	16	47,252	
			Animals	405,157	85,837	55,672	10,955	15,470	573,091	
		Swine	Holdings	11,393	725	692	340	967	14,117	
			Animals	116,678	44,044	106,003	124,033	2,775,481	3,166,239	
		Buffalo	Holdings	2,141	693	459	63	11	3,367	
			Animals	8,850	8,856	12,356	3,747	1,749	35,558	
		Northeastern	Dairy	Holdings	5,001	454	51	1	0	5,507
				Animals	64,524	27,790	6,669	350	0	99,333
	Beef		Holdings	385,406	378	87	9	11	385,891	
			Animals	1,576,184	23,122	11,273	3,287	14,960	1,628,826	
	Swine		Holdings	68,991	1,437	627	201	522	71,778	
			Animals	588,055	87,928	89,415	77,116	632,278	1,474,792	
	Buffalo		Holdings	149,881	4,757	822	55	18	155,533	
			Animals	468,220	57,239	20,634	3,248	10,841	560,182	
	Northern		Dairy	Holdings	1,633	273	29	1	2	1,938
				Animals	30,399	16,347	3,584	300	6,150	56,780
		Beef	Holdings	47,807	911	128	12	48	48,906	

	Animals	422,502	54,483	16,030	4,000	154,970	651,985
Swine	Holdings	49,294	1,325	619	127	492	51,857
	Animals	383,048	80,277	90,793	45,057	579,900	1,179,075
Buffalo	Holdings	10,139	1,999	781	94	10	13,023
	Animals	41,810	25,250	20,751	5,569	1,247	94,627

Table 2.2: Census and new herd-classes for livestock in Pakistan

Census herd-class	New herd-class
1 – 2	1
3 – 4	1
5 – 6	1
7 – 10	1
11 – 15	2
16 – 20	2
21 – 30	3
31 – 50	4
>50	5

Table 2.3: Census and new herd-classes for livestock in Thailand

Livestock-Type	Census herd-class	New herd-class
Beef, dairy, swine	1 – 2	1
	3 – 4	1
	5 – 9	1
	10 – 19	1
	20 – 49	1
	50 – 99	2
	100 – 299	3
	300 – 499	4
	≥500	5
Buffalo	1 – 2	1
	3 – 4	1
	5 – 9	1
	10 – 19	2
	20 – 49	3
	50 – 99	4
	≥99	5



Table 2.4: Datasets used to create the geospatial probability surface

Dataset	Description	Usage
Administrative boundary	Boundaries for different administrative levels in Pakistan and Thailand	Used as the base map, for processing extent and other geoprocessing
Waterbodies	Waterbodies in Pakistan and Thailand	Used to mask out the water bodies from probability surface
Road network	Road network for different road types in Pakistan and Thailand	Used to make probability buffers around different highway types
Elevation	This dataset provides the elevation for Pakistan and Thailand	This dataset was used to calculate slope to be included in the probability surface
Landcover	Different land cover types in Pakistan and Thailand	Creation of geospatial probability surface
Expert-based opinions	With anonymous veterinarians in Pakistan and Thailand	To aid in determining arbitrary upper bound for herd-class 5 To discuss probability buffers around different geographic features
Survey questionnaire	Anonymous veterinarians from Pakistan and Thailand responding to	To seek weights for different geographic features for animal agriculture in Pakistan and Thailand
Empirical holding locations	The physical location of holdings with associated animal population	To aid in the creation of probability buffers around different highway types To help in the placement of random holdings on probability surface

Table 2.5: Disaggregated number of holdings for each bin element (Sindh province, bovines, herd-class 3)

Animals	Holdings
21	2227
22	2181
23	2155
24	2133
25	2120
26	722
27	709
28	687
29	661
30	611

Table 2.6: Weights for different geographical features estimated using expert opinion and empirical holding locations

Country	Animal Type	Herd Class	Croplands	Urban areas	Open-lands	Slope (>10%)	Around urban areas	Main highways	Primary highways	Smaller highways
Pakistan	Bovines	1	100	-40	20	-20	0	24	4	12
		2	80	20	20	-40	70	8	21	7
		3	80	20	20	-60	70	8	21	7
		4	40	60	20	-60	70	25	11	19
		5	80	60	20	-80	70	25	11	19
Thailand	Dairy	1	80	-100	20	-40	30	11.4	8.9	44
		2	80	-100	0	-40	50	11.1	11.1	50
		3	60	-100	0	-40	50	22.3	5.6	50
		4	70	-100	-10	-60	70	0	0	0
		5	80	-100	-10	-60	70	66.7	0	66.7
	Beef	1	100	-80	60	-20	30	7.4	22.2	51.8
		2	80	-80	40	-20	50	57.1	20	80
		3	100	-100	60	-20	50	57.1	50	50
		4	90	-100	40	-50	70	66.7	33.5	100
		5	90	-100	40	-50	70	66.7	33.5	100
	Swine	1	0	-60	20	-20	30	50	0	66.7
		2	0	-100	40	-40	50	0	0	0
		3	0	-100	60	-60	50	0	0	0
		4	0	-100	60	-60	70	25	50	50
		5	0	-100	60	-60	70	60	26	48
Buffalo	1	80	-70	60	-30	30	12.5	12.5	50	
	2	80	-80	60	-30	50	50	0	50	
	3	80	-80	60	-40	50	0	0	0	
	4	90	-100	60	-40	70	80	20	80	
	5	90	-90	50	-50	70	80	20	80	

## REFERENCES

- Anjum, R., Hussain, M., Zahoor, A.B., Irshad, H., Farooq, U., 2006. Epidemiological analyses of foot and mouth disease in Pakistan. *Int. J. Agric. Biol.* 8.
- Bates, T.W., Thurmond, M.C., Carpenter, T.E., 2003a. Results of epidemic simulation modeling to evaluate strategies to control an outbreak of foot-and-mouth disease. *Am. J. Vet. Res.* 64, 205–210. <https://doi.org/10.2460/ajvr.2003.64.205>
- Bates, T.W., Thurmond, M.C., Carpenter, T.E., 2003b. Description of an epidemic simulation model for use in evaluating strategies to control an outbreak of foot-and-mouth disease. *Am. J. Vet. Res.* 64, 195–204. <https://doi.org/10.2460/ajvr.2003.64.195>
- Bates, T.W., Thurmond, M.C., Carpenter, T.E., 2003c. Results of epidemic simulation modeling to evaluate strategies to control an outbreak of foot-and-mouth disease. *Am. J. Vet. Res.* 64, 205–210. <https://doi.org/10.2460/ajvr.2003.64.205>
- Bellemain, V., 2013. The role of veterinary services in animal health and food safety surveillance, and coordination with other services. *Rev. Sci. Tech.* 32, 371–81.
- Bessell, P.R., Shaw, D.J., Savill, N.J., Woolhouse, M.E.J., 2010. Statistical modeling of holding level susceptibility to infection during the 2001 foot and mouth disease epidemic in Great Britain. *Int. J. Infect. Dis.* 14. <https://doi.org/10.1016/j.ijid.2009.05.003>
- Broxton, P.D., Zeng, X., Sulla-Menashe, D., Troch, P.A., 2014. A Global Land Cover Climatology Using MODIS Data. *J. Appl. Meteorol. Climatol.* 53, 1593–1605. <https://doi.org/10.1175/JAMC-D-13-0270.1>

- Buhnerkempe, M.G., Tildesley, M.J., Lindström, T., Grear, D.A., Portacci, K., Miller, R.S., Lombard, J.E., Werkman, M., Keeling, M.J., Wennergren, U., Webb, C.T., 2014. The impact of movements and animal density on continental scale cattle disease outbreaks in the United States. *PLoS One* 9. <https://doi.org/10.1371/journal.pone.0091724>
- Burdett, C.L., Kraus, B.R., Garza, S.J., Miller, R.S., Bjork, K.E., 2015. Simulating the Distribution of Individual Livestock Farms and Their Populations in the United States: An Example Using Domestic Swine (*Sus scrofa domesticus*) Farms. *PLoS One* 10, e0140338. <https://doi.org/10.1371/journal.pone.0140338>
- Carpenter, T.E., 2011. Stochastic, spatially-explicit epidemic models. *Rev. sci. tech. Off. int. Epiz* 30, 417–424.
- Central Intelligence Agency, 2019. The World Factbook [WWW Document]. World Factb. URL <https://www.cia.gov/library/publications/the-world-factbook/geos/pk.html> (accessed 6.30.19).
- Deka, R., Grace, D., Lapar, M., Lindahl, J., 2014. Sharing Lessons of Smallholders' Pig System in South Asia and Southeast Asia: a Review, in: National Conference on Opportunities and Strategies for Sustainable Pig Production. ILRI, Nairobi, Kenya, Guwahati, India. <https://doi.org/https://hdl.handle.net/10568/53928>
- Dorjee, S., Revie, C.W., Poljak, Z., McNab, W.B., Sanchez, J., 2016. One-Health Simulation Modelling: A Case Study of Influenza Spread between Human and Swine Populations using *NAADSM*. *Transbound. Emerg. Dis.* 63, 36–55. <https://doi.org/10.1111/tbed.12215>
- Dürr, S., Fasel-Clemenz, C., Thür, B., Schwermer, H., Doherr, M.G., Dohna, H. zu, Carpenter, T.E., Perler, L., Hadorn, D.C., 2014. Evaluation of the benefit of emergency vaccination in a foot-and-mouth disease free country with low livestock density. *Prev. Vet. Med.* 113, 34–46.

<https://doi.org/10.1016/J.PREVETMED.2013.10.015>

ESRI, 2012. ArcGIS.

ESRI, 1992. The Digital Chart of the World (DCW) database. Redlands, CA.

FAO, 2018. Transforming the livestock sector through the Sustainable Development Goals. Rome, Italy.

FAO, 2011. World Livestock 2011: Livestock in food security. Rome.

FAO, 2009. Livestock in the balance: The State of Food and Agriculture. Rome.

Farooq, U., Ahmed, Z., Naeem, K., Bertram, M., Brito, B., Stenfeldt, C., Pauszek, S.J., LaRocco, M., Rodriguez, L., Arzt, J., 2018. Characterization of naturally occurring, new and persistent subclinical foot-and-mouth disease virus infection in vaccinated Asian buffalo in Islamabad Capital Territory, Pakistan. *Transbound. Emerg. Dis.* 65, 1836–1850. <https://doi.org/10.1111/tbed.12963>

Farooq, U., Irshad, H., Ullah, A., Latif, A., Zahur, A.B., Naeem, K., Ahmed, Z., Rodriguez, L.L., 2017a. Seroprevalence of foot-and-mouth disease in small ruminants of Pakistan. *J. Anim. Plant Sci.* 27, 1197–1201.

Farooq, U., Naeem, K., Zahur, A.B., Khan, M.A., Sidique, U., 2017b. Foot-and-mouth disease outbreaks investigations at Sindh, Punjab and Islamabad, Pakistan during the year 2012-2013. *Int. J. Biosci.* 11, 346–356. <https://doi.org/10.12692/ijb/11.5.346-356>

Farooq, U., Naeem, K., Zahur, A.B., Khan, M.A., Sidique, U., Qureshi, S., 2017c. Epidemiological analysis and economic impact assessment of foot-and-mouth disease at Landhi dairy colony Karachi. *Asian J. Agric. Biol.* 5, 7–14.

Farooq, U., Ullah, A., Irshad, H., Latif, A., Naeem, K., Zahur, A. Bin, Ahmad, Z., Rodriguez, L.L., 2016. Seroprevalence of foot-and-mouth disease in large ruminants in periurban dairy farms near

- Islamabad, Pakistan. *Asian Biomed.* 10, 123–127. <https://doi.org/10.5372/1905-7415.1002.472>
- Ferguson, N.M., Donnelly, C.A., Anderson, R.M., 2001. Transmission intensity and impact of control policies on the foot and mouth epidemic in Great Britain. *Nature* 413, 542–548.  
<https://doi.org/10.1038/35097116>
- Ferrari, G., Tasciotti, L., Khan, E., Kiani, A., 2014. Foot-and-Mouth Disease and Its Effect on Milk Yield: An Economic Analysis on Livestock Holders in Pakistan. *Transbound. Emerg. Dis.* 61, e52–e59.  
<https://doi.org/10.1111/tbed.12072>
- GADM, 2015. GADM database of Global Administrative Areas [WWW Document]. URL <https://www.diva-gis.org/gdata> (accessed 4.23.19).
- Garner, M.G., Beckett, S.D., 2005. Modelling the spread of foot-and-mouth disease in Australia. *Aust. Vet. J.* 83, 758–766. <https://doi.org/10.1111/j.1751-0813.2005.tb11589.x>
- Gleeson, L.J., 2002. A review of the status of foot and mouth disease in South-East Asia and approaches to control and eradication. *Rev. Sci. Tech.* 21, 465–75.
- Guitian, J., Pfeiffer, D., 2006. Should we use models to inform policy development? *Vet. J.* 172, 393–395.  
<https://doi.org/10.1016/j.tvjl.2006.03.001>
- Harland, K., 2013. Microsimulation model user guide: flexible modelling framework (No. Version 1.0), NCRM Working Papers. Leeds.
- Harland, K., Heppenstall, A., Smith, D., Birkin, M., 2012. Creating realistic synthetic populations at varying spatial scales: A comparative critique of population synthesis techniques. *J. Artif. Soc. Soc. Simul.* 15, 1. <https://doi.org/10.18564/jasss.1909>
- 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., 2007a. The North American Animal Disease Spread Model: A simulation model to assist decision making in evaluating animal disease incursions. *Prev. Vet. Med.* 82, 176–197. <https://doi.org/10.1016/j.prevetmed.2007.05.019>
- 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., 2007b. The North American Animal Disease Spread Model: A simulation model to assist decision making in evaluating animal disease incursions. *Prev. Vet. Med.* 82, 176–197. <https://doi.org/10.1016/J.PREVETMED.2007.05.019>
- 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., 2007c. The North American Animal Disease Spread Model: A simulation model to assist decision making in evaluating animal disease incursions. *Prev. Vet. Med.* 82, 176–197. <https://doi.org/10.1016/J.PREVETMED.2007.05.019>
- Hughjones, M.E., 1976. Epidemiological-Studies on 1967-1968 Foot-and-Mouth-Disease Epidemic - Reporting of Suspected Disease. *J. Hyg. (Lond)*. 77, 299–306.
- International Society For Animal Hygiene, 2004. Animal production in Europe : The way forward in a changing world. *Anim. Prod. Eur. W. Forw. a Chang. world* 1, 533.
- Jamal, S.M., Ahmed, S., Hussain, M., Ali, Q., 2010. Status of foot-and-mouth disease in Pakistan. *Arch. Virol.* 155, 1487–1491. <https://doi.org/10.1007/s00705-010-0732-y>
- Jarvis, A., H.I. Reuter, A. Nelson, E. Guevara., 2008. Hole-filled SRTM for the globe Version 4, [WWW Document]. CGIAR-CSI SRTM 90m Database. URL <http://srtm.csi.cgiar.org>. (accessed 2.1.18).
- Jemberu, W.T., Mourits, M.C.M., Woldehanna, T., Hogeveen, H., 2014. Economic impact of foot and mouth disease outbreaks on smallholder farmers in Ethiopia. *Prev. Vet. Med.* 116, 26–36. <https://doi.org/10.1016/J.PREVETMED.2014.06.004>



- Kao, R.R., 2002. The role of mathematical modelling in the control of the 2001 FMD epidemic in the UK. *Trends Microbiol.* 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. Biol. Sci.* 272, 1195–202. <https://doi.org/10.1098/rspb.2004.3046>
- Keeling, M.J., Woolhouse, M.E., 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 (80-. )*. 294, 813–817. <https://doi.org/10.1126/science.1065973>
- 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? *Prev. Vet. Med.* 112, 161–173. <https://doi.org/10.1016/J.PREVETMED.2013.07.013>
- 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? *Prev. Vet. Med.* 112, 162–173. <https://doi.org/10.1016/j.prevetmed.2013.07.013>
- L & DD, 2018. Livestock Census Punjab 2018. Livestock and Dairy Development Department. Lahore, Punjab, Pakistan.
- Lovelace, R., Dumont, M., 2016. *Spatial Microsimulation with R*. CRC Press.
- Marsot, M., Rautureau, S., Dufour, B., Durand, B., 2014. Impact of Stakeholders Influence, Geographic Level and Risk Perception on Strategic Decisions in Simulated Foot and Mouth Disease Epizootics in France. *PLoS One* 9, e86323. <https://doi.org/10.1371/journal.pone.0086323>
- McReynolds, S.W., Sanderson, M.W., Reeves, A., Hill, A.E., 2014. Modeling the impact of vaccination control strategies on a foot and mouth disease outbreak in the Central United States. *Prev. Vet.*

Med. 117, 487–504. <https://doi.org/10.1016/J.PREVETMED.2014.10.005>

Morris, R.S., Sanson, R.L., Stern M.W., Stevenson M., Wilesmith J.W., 2002. Decision-support tools for foot and mouth disease control. *Rev. sci. tech. Off. int. Epiz.* 21, 557–567.

<https://doi.org/10.20506/rst.21.3.1363>

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. *Vet. Rec.* 149, 137–44. <https://doi.org/10.1136/vr.149.5.137>

National Statistical Office, 2013. 2013 Agricultural Census. Ministry of Information and Communication Technology. Bangkok, Thailand.

Navid, M.T., Farooq, U., Latif, A., Awais, M.M., Anwar, M.I., Akhtar, M., Zahur, A.B., 2018. Prevalence of foot and mouth disease virus in apparently healthy buffaloes brought to Islamabad slaughterhouse in Pakistan. *Trop. Biomed.* 35, 161–167.

OpenStreetMap contributors, 2018. The Humanitarian Data Exchange [WWW Document]. URL

<https://www.openstreetmap.org> (accessed 4.23.19).

Paine, S., Mercer, G.N., Kelly, P.M., Bandaranayake, D., Baker, M.G., Huang, Q.S., Mackereth, G., Bissielo, A., Glass, K., Hope, V., 2010. Transmissibility of 2009 pandemic influenza A(H1N1) in New Zealand: Effective reproduction number and influence of age, ethnicity and importations. *Eurosurveillance* 15, 1–9. <https://doi.org/19591> [pii]

Pakistan Bureau of Statistics, 2006. Pakistan Livestock Census. Islamabad, Islamabad.

Porphyre, T., Auty, H.K., Tildesley, M.J., Gunn, G.J., Woolhouse, M.E.J., 2013a. Vaccination against Foot-And-Mouth Disease: Do Initial Conditions Affect Its Benefit? *PLoS One* 8, 1–14.

<https://doi.org/10.1371/journal.pone.0077616>

Porphyre, T., Mckenzie, J., Byrom, A.E., Nugent, G., Shepherd, J., Yockney, I., 2013b. Spatial prediction of brushtail possum ( *Trichosurus vulpecula* ) distribution using a combination of remotely sensed and field-observed environmental data 40, 578–587.

Prosser, D.J., Wu, J., Ellis, E.C., Gale, F., Van Boeckel, T.P., Wint, W., Robinson, T., Xiao, X., Gilbert, M., 2011. Modelling the distribution of chickens, ducks, and geese in China. *Agric. Ecosyst. Environ.* 141, 381–389. <https://doi.org/10.1016/j.agee.2011.04.002>

R Core Team, 2017. R: A language and environment for statistical computing.

Robinson, T.P., Franceschini, G., Wint, W., 2007. The Food and Agriculture Organization’s Gridded Livestock of the World. *Vet. Ital.* 43, 745–751.

Robinson, T.P., William Wint, G.R., Conchedda, G., Van Boeckel, T.P., Ercoli, V., Palamara, E., Cinardi, G., D’Aielli, L., Hay, S.I., Gilbert, M., 2014. Mapping the global distribution of livestock. *PLoS One* 9. <https://doi.org/10.1371/journal.pone.0096084>

Rweyemamu, M., Roeder, P., Mackay, D., Sumption, K., Brownlie, J., Leforban, Y., Valarcher, J.-F., Knowles, N.J., Saraiva, V., 2008. Epidemiological Patterns of Foot-and-Mouth Disease Worldwide. *Transbound. Emerg. Dis.* 55, 57–72. <https://doi.org/10.1111/j.1865-1682.2007.01013.x>

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. *Prev. Vet. Med.* 109, 10–24. <https://doi.org/10.1016/J.PREVETMED.2012.08.015>

Tomassen, F. H M, De Koeijer, a., Mourits, M.C.M., Dekker, a., Bouma, a., Huirne, R.B.M., 2002. A decision-tree to optimise control measures during the early stage of a foot-and-mouth disease epidemic. *Prev. Vet. Med.* 54, 301–324. [https://doi.org/10.1016/S0167-5877\(02\)00053-3](https://doi.org/10.1016/S0167-5877(02)00053-3)

Tomassen, F.H.M., de Koeijer, A., Mourits, M.C.M., Dekker, A., Bouma, A., Huirne, R.B.M., 2002. A

- decision-tree to optimise control measures during the early stage of a foot-and-mouth disease epidemic. *Prev. Vet. Med.* 54, 301–324. [https://doi.org/10.1016/S0167-5877\(02\)00053-3](https://doi.org/10.1016/S0167-5877(02)00053-3)
- van Andel, M., Jewell, C., McKenzie, J., Hollings, T., Robinson, A., Burgman, M., Bingham, P., Carpenter, T., 2017. Predicting farm-level animal populations using environmental and socioeconomic variables. *Prev. Vet. Med.* 145, 121–132. <https://doi.org/10.1016/j.prevetmed.2017.07.005>
- Van Boeckel, T.P., Prosser, D., Franceschini, G., Biradar, C., Wint, W., Robinson, T., Gilbert, M., 2011. Modelling the distribution of domestic ducks in Monsoon Asia. *Agric. Ecosyst. Environ.* 141, 373–380. <https://doi.org/10.1016/j.agee.2011.04.013>
- Van Rossum, G., Drake Jr, F., 1995. Python tutorial, Technical Report CS-R9526. Amsterdam, The Netherlands.
- Wint, W., Robinson, R., 2007. Gridded Livestock of the World, Organization. <https://doi.org/10.1017/CBO9781107415324.004>
- Wongsathapornchai, K., Salman, M.D., Edwards, J.R., Morley, P.S., Keefe, T.J., Campen, H. V., Weber, S., Premashthira, S., 2008. Use of epidemiologic risk modeling to evaluate control of foot-and-mouth disease in southern Thailand. *Am. J. Vet. Res.* 69, 240–251. <https://doi.org/10.2460/ajvr.69.2.240>
- Woolhouse, M.E.J., 2003. Foot-and-mouth disease in the UK: What should we do next time? *J. Appl. Microbiol.* 94, 126–130. <https://doi.org/10.1046/j.1365-2672.94.s1.15.x>
- Woolhouse, M E J, 2003. Foot-and-mouth disease in the UK: what should we do next time? *J. Appl. Microbiol.* 94 Suppl, 126S--130S. <https://doi.org/10.1046/j.1365-2672.94.s1.15.x>
- Yano, T., Premashthira, S., Dehyong, T., Tangtrongsup, S., Salman, M.D., 2018. The Effectiveness of a Foot and Mouth Disease Outbreak Control Programme in Thailand 2008–2015: Case Studies and Lessons Learned. *Vet. Sci.* <https://doi.org/10.3390/vetsci5040101>

Yoon, H., Wee, S.-H., Stevenson, M.A., O'Leary, B.D., Morris, R.S., Hwang, I.-J., Park, C.-K., Stern, M.W.,  
2006. Simulation analyses to evaluate alternative control strategies for the 2002 foot-and-mouth  
disease outbreak in the Republic of Korea. *Prev. Vet. Med.* 74, 212–225.  
<https://doi.org/10.1016/J.PREVETMED.2005.12.002>

CHAPTER 3: ADAPTATION OF THE NORTH AMERICAN ANIMAL DISEASE SPREAD MODEL FOR FOOT-AND-  
MOUTH DISEASE IN ENDEMIC SETTINGS: A PILOT ASSESSMENT AND DEMONSTRATION<sup>3</sup>

1 Introduction

Foot and mouth disease (FMD) is endemic in many parts of the world (Anjum et al., 2006; Farooq et al., 2018, 2017a, 2017b, 2017c, 2016; Gleeson, 2002; Jamal et al., 2010; Navid et al., 2018; Rweyemamu et al., 2008b; Yano et al., 2018), and is associated with substantial economic losses (Ferrari et al., 2014; Jemberu et al., 2014; Knight-Jones and Rushton, 2013). International organizations such as the Food and Agriculture Organization of the United Nations (FAO), the World Organization for Animal Health (OIE), the European Commission for the Control of Foot and Mouth Disease (EuFMD) have called for a more targeted control strategy in the 'Progressive Control Pathway for FMD' to reduce the disease burden and high economic costs associated with it (Abbas et al., 2014; Jamal and Belsham, 2013; Paton et al., 2009; Rweyemamu et al., 2008a; Sumption et al., 2012).

Simulation modeling has become a useful tool to investigate the spread and evaluate the effectiveness of alternative mitigation strategies for infectious diseases including FMD (Dorjee et al., 2016; Guitian and Pfeiffer, 2006; Kao, 2002; Keeling, 2005; Morris et al., 2002). Many models have been

---

<sup>3</sup> This chapter of the dissertation is intended for publication in the Preventive Veterinary Medicine journal and is formatted in line with journal requirements.

Muhammad Usman Zaheer<sup>a</sup>, Mo Salman<sup>a</sup>, Shaun Case<sup>b</sup>, Katie Steneroden<sup>a</sup>, Sheryl Magzamen<sup>c</sup>, Steve Weber<sup>a</sup>, Sangeeta Rao<sup>a</sup>

<sup>a</sup>Animal Population Health Institute, Department of Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins CO 80523, USA, <sup>b</sup>Department of Civil and Environmental Engineering, Walter Scott, Jr. College of Engineering, Colorado State University, Fort Collins CO 80523, USA, <sup>c</sup>Department of Environmental and Radiological Health Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins CO 80523, USA

developed to mimic the spread of FMD in specific regions or countries (Bates et al., 2003d; Garner and Beckett, 2005; Harvey et al., 2007b; Stevenson et al., 2013; Wongsathapornchai et al., 2008). These models have been used for various purposes such as for risk assessment, to analyze outbreaks using historical data or hypothetical scenarios, to assist in policy decisions during outbreaks, and policy formulation in preparedness planning, and in evaluating economic impacts (Bates et al., 2003c; Dürr et al., 2014; Ferguson et al., 2001a; Keeling et al., 2001; McReynolds et al., 2014; Morris et al., 2001; Tomassen et al., 2002; Yoon et al., 2006a). Overall, however, the purpose of the application of simulation models differs among countries depending on the interest as well as the status of the disease in the applied geographical areas. In disease-free countries, models are used to identify gaps in the preparedness such as estimating required resources (M. G. Garner et al., 2016; Roche et al., 2014), whereas, in endemic countries, models can be useful to compare mitigation strategies to guide future directions of FMD control program (Souley Kouato et al., 2018).

Most of the reported literature on FMD simulation models is, however, associated with disease-free countries with minimal application of these models in countries with an endemic status of FMD (Pomeroy et al., 2017). The development of simulation models of infectious livestock diseases such as FMD in endemic settings is enormously challenging for reasons such as the lack of interest and understanding of perceived needs, political or economic constraints, insufficient data to support model parameters, and the complexity of FMD epidemiology in endemic settings (Brooks-Pollock et al., 2015; Knight-Jones et al., 2016b).

Recently, a systematic review of the existing spatially-explicit simulation models (SESS) revealed a set of possible additions to these models to extend their applicability to FMD-endemic regions to understand FMD spread and to evaluate the effectiveness of alternative mitigation strategies for its control (Zaheer et al., 2019, submitted). The key findings were to include components such as: a module to simulate co-circulating FMD serotypes, ability to alter the livestock population dynamics during the

simulation runs (growth rate), flexibility to implement “routine prophylactic vaccination’ (RPV), and alteration of existing simulation stop conditions to make them flexible for endemic settings (Zaheer et al., 2019, submitted). The identified additional components are known to be key characteristics of FMD epidemiology in the endemic region (Ahmed et al., 2018; FAO and OIE, 2016; Hunter, 1998; Knight-Jones et al., 2015, 2016a; Ullah et al., 2017).

One SESS included in the systematic review was the North American Animal Disease Simulation Model (NAADSM) (Harvey et al., 2007b; Schoenbaum and Disney, 2003). The NAADSM is a spatially explicit, stochastic, state-transition model (Harvey et al., 2007b; Schoenbaum and Disney, 2003), in which disease spread occurs between animal holdings at precisely specified locations and is affected by the relative locations and distances between holdings. If disease occurs within a certain holding, it follows a natural, predictable cycle over time, moving from one disease state to the next. This cycle may be interrupted by disease control measures – destruction, vaccination, movement control, etc. (Harvey et al., 2007b). The existing model and simulation engine component of NAADSM was developed exclusively for the North American continent under a collaboration among the United States Department of Agriculture, the Canadian Food Inspection Agency, the University of Guelph, and the Animal Population Health Institute of Colorado State University. The model and simulation framework continue to concentrate only on the United States and Canadian policy and animal husbandry techniques unique to North America, which limits the use of NAADSM elsewhere. A more detailed description of NAADSM is available elsewhere (Harvey et al., 2007b).

The intent to use NAADSM in endemic countries would require its adaption to include required endemicity components (Zaheer et al., 2019 submitted). This paper aims to adapt NAADSM to have a modeling framework equipped with components needed to simulate the spread of and evaluate the effective mitigation strategies for infectious animal diseases such as FMD for use in endemic settings. The first objective of this study was to ascertain the behavior of the adapted model when parameterized



with estimates from endemic settings. The second objective was to demonstrate the application of the model to assess the use of ‘routine prophylactic vaccination’ (RPV) as a mitigation strategy. The resulting framework will be called “Simulation Model for Infectious Animal Diseases in Endemic Regions (SMIAD-ER),” which will be a spatially explicit, stochastic, state-transition simulation model.

## 2 Methods

To build the prototype version of SMIAD-ER, the underlying source code of NAADSM 3.2.19 was modified to equip the model with ‘routine prophylactic vaccination (RPV),’ as an additional disease control strategy. This addition will provide users with the flexibility to enable/disable implementation of RPV during the simulation. Once RPV is enabled, the frequency of vaccination can be input as a point estimate such as 1, 2, or 3, which refers to every 365, 180, and 120 days, respectively. In addition, a probability distribution function is specified to model the ‘duration of immunity’ for RPV.

### 2.1 Data sources

The data sources used in this demonstration included: FMD outbreaks data (FAO Pakistan, unpublished data), a simulated dataset on the location and population of individual bovine holdings (Zaheer et al., in preparation), expert opinions and personal communications with anonymous veterinarians in Pakistan.

### 2.2 Assumptions of SMIAD-ER

Demonstration of the functionality of the prototype version of SMIAD-ER in this paper was based on the following assumptions:

- The input livestock holdings included in this demonstration represented the total number of bovine holdings in Punjab, Pakistan, for 2006.

- There were only two production-types in Punjab, Pakistan, i.e., cattle and buffalo. And the holdings only have >50 animals. All holdings of cattle and buffalo with <51 animals were ignored.
- No effect of small ruminants (sheep, goat) and wild animals (wild boar) on FMD spread was included.
- Occurrence of FMD and its spread beyond the provincial boundary of Punjab, Pakistan was ignored.
- The impact of seasonality and meteorological factors on FMD spread was not included.
- The bovine population is closed, and the population size was constant. Individual holdings did not enter or leave the study area except via stamping-out as a control measure.
- All holdings in the same production-type had the same disease progression parameters.
- Individual animals within a holding were equally likely to come into contact with any other individual from other holdings.
- There were homogenous contact rates between specific pairs of production types, such as cattle to cattle, buffalo to cattle, etc.
- The disease spread parameters and other parameters used in this demonstration represented the field situation of FMD in Punjab, Pakistan.
- Mortality from FMD or other causes during the simulation duration was not included.
- There was only one circulating serotype of FMD, i.e., O.
- There was no carrier status among recovered holdings.
- The coverage and efficacy of emergency vaccination and RPV were 100%.
- The infection status at the start of the simulation represented the prevalence of FMD in Punjab, Pakistan.

- Holdings of both production-types were assumed to have been attempted to be vaccinated based on the user-defined period before the start of the simulation and it was termed 'last vaccination day'.

## 2.3 Scenarios

For the demonstration of a prototype version of SMIAD-ER, two scenarios were developed to ascertain the behavior of the model when parameterized with estimates from endemic settings and application of 'routine prophylactic vaccination' (RPV) as a mitigation strategy.

### 2.3.1 Baseline scenario (sc1)

In the baseline scenario (sc1), the model was parameterized to mimic the field situation of FMD in Punjab, Pakistan, in 2012-2014. In this scenario, only emergency vaccination, i.e. only in the face of detection, was implemented as a mitigation strategy. This scenario was parameterized to show the functionality of the model when parameterized with baseline parameters (field conditions as expressed by anonymous veterinarians).

### 2.3.2 Enhanced scenario (sc2)

In the enhanced scenario (sc2), in addition to the parameters used in the baseline scenario, the model was parameterized to enable RPV, with default coverage and efficacy of 100%, as an additional mitigation strategy. This scenario was parameterized to show the functionality of the model when parameterized with a combination of baseline parameters and application of RPV, as a common mitigation strategy in FMD endemic countries.

## 2.4 Scenario parameters

The prototype of SMIAD-ER was parameterized to mimic the situation of FMD in Punjab, Pakistan.

### 2.4.1 Production types and their status

Two production types, i.e., cattle and buffalo, were included in this demonstration. Data on the population and location of 13,986 individual holdings of cattle and buffalo with >50 animals were

obtained from a study that utilized a microsimulation approach and geographic information system to generate a simulated dataset on the location and population of individual livestock holdings in developing countries (Zaheer et al., in preparation). Based on FMD outbreaks data from 2012-14 (unpublished data, FAO Pakistan) and personal communication with expert veterinarians, holdings were randomly assigned one of the six possible status, i.e., 100 clinical infectious, 200 subclinical infectious, 600 latent infected, 900 naturally immune, 210 vaccine immune, and 11,976 susceptible.

#### *2.4.2 Progression parameters*

FMD progression parameters were based on the assumption that only one serotype of FMD was circulating, i.e. O, and similar progression parameters were used for both production types. The parameters (as shown in Table 2.1) were obtained from published literature and estimated using Within-Herd model 0.9.7 (see appendix).

#### *2.4.3 Spread parameters*

For each production type combination, the parameters for contact and airborne spread were obtained from an anonymous veterinarian with more than nine years of experience working with FMD outbreaks in Punjab, Pakistan (see appendix).

#### *2.4.4 FMD detection parameters*

For both production types, the estimated probability of observing clinical signs of FMD, given the number of days the holding had been clinically infectious, and the estimated probability of reporting an observed clinical holding, given the number of days since FMD was first detected in any holding was obtained from an anonymous veterinarian from Punjab, Pakistan with extensive experience with FMD outbreaks (see appendix).

#### *2.4.5 Disease tracing*

The SMIAD-ER has an assumption that when tracing is enabled if a holding is identified as having contact with another infected holding, the holding is quarantined and can no longer take part in disease

spread through contacts (both direct and indirect). Based on personal communications with FMD experts in Pakistan, it was revealed that no such tracing mechanism exists in the country and also, there is no existing mechanism to quarantine holdings if identified as being a source of or having exposure from other holdings. Therefore, tracing was disabled for this demonstration.

#### 2.4.6 *Zones*

Based on the opinion of a veterinarian from Pakistan, a zone with a 3-km radius was created around detected infected holdings of each production-type. Inside the zone, the probability of FMD detection was multiplied with 1.5.

#### 2.4.7 *Vaccination*

The parameters for emergency vaccination and RPV were based on a combination of personal communications, expert opinion, and published literature.

##### 2.4.7.1 *Emergency vaccination*

The threshold for implementing emergency vaccination was set to the detection of FMD in four holdings of any production-type. The emergency vaccination capacity was set to increase to 35 holdings/day at day 15 post detection and was constant after that (see appendix). For both production types, the delay in mounting an immune response was set to four days and minimum day between two emergency vaccinations was set to 21 days. The model was set to implement emergency vaccination to infected holdings which were detected, and a vaccination ring of a 10-km radius was established. The duration of immunity for emergency vaccination was modeled using a triangular distribution (30, 180, 210). Buffalo holdings were given a priority when implementing emergency vaccination.

##### 2.4.7.2 *Routine prophylactic vaccination (RPV)*

For sc2, RPV was enabled as a control strategy. For both production types, the frequency of RPV was set to twice every year, i.e., once every 180 days. The duration of immunity linked to RPV was modeled using triangular distribution (180, 270, 365 days). The livestock holdings were assigned a random value

between 1 to 20 for 'last vaccinated day' which refers to 'days in state.' Based on this value and the probability distribution function (PDF) for 'vaccine immunity,' 'days left in-state' were estimated. Once a holding became eligible to receive the first dose of RPV, the vaccine was administered, and it mounted immune response based on the point estimate for 'time needed to mount an immune response.' The parameters for capacity, coverage, and biological efficacy of RPV were not included in the demonstration of a prototype version of SMIAD-ER.

#### *2.4.8 Destruction parameters*

Based on personal communications with animal health experts in Pakistan, destruction of holdings, as a control strategy, in response to detection of FMD was not modeled.

#### *2.4.9 Iterations and set-up*

Both scenarios were run for 1000 iterations and simulations were set up to stop at day 370 of the iteration.

### *2.5 Statistical analysis*

The output from both the scenarios was used to produce descriptive statistics such as minimum, maximum, mean, standard deviation, and quartiles for the duration of the outbreak, the number of vaccine immune holdings by the end of outbreak and day 370 of the iteration using R (R Core Team, 2017).

## **3 Results and Discussion**

The prototype version of SMIAD-ER was run until day 370 for 1,000 iterations to ascertain the behavior of the model when parameterized with estimates from endemic settings and to determine if the model can be used to evaluate the effectiveness of RPV as a mitigation strategy. The outputs from both scenarios were extracted for three performance indices, i.e. 'outbreak duration,' 'vaccine immune holdings by the end of the outbreak,' and 'vaccine immune holdings by day 370 of iteration'. Due to

computer hard-drive issues, outputs were not extracted for eight iterations of 'baseline scenario' (partially available for one of the eight iterations). The outputs were available for all 1,000 iterations of 'enhanced scenario.'

The summary statistics (Table 2.2) and hypotheses testing reveals that there was no statistically significant difference between scenarios for 'outbreak duration' (p-value=0.18). Although, the summary statistics in Table 2.2 show that there were more (1.47%) 'vaccine immune holdings by the end of the outbreak' in sc1 compared to sc2, yet this difference was not statistically significant (p-value=0.08), and this difference can be attributed to the stochastic nature of the simulations. There was, however, a difference between scenarios for 'vaccine immune holdings by day 370 of simulation' (p-value=<0.001) with more vaccine immune holdings in sc2 compared to sc1 (Table 2.2).

To the best of our knowledge, SMIAD-ER is the first-ever spatially-explicit, stochastic, state-transition simulation model built for endemic regions to model the spread and evaluate the effectiveness of alternative mitigation strategies for infectious animal diseases such as FMD.

The similarity in the 'duration of outbreak' and 'vaccine immune holdings by the end of outbreak' between 'baseline' and 'enhanced' scenarios give us confidence that SMIAD-ER behaved in the same way and no aberrant outputs were obtained. Ideally, the outbreak duration for 'enhanced scenario' should be smaller than the outbreak duration in the 'baseline scenario' where RPV was not implemented. The reason for this outcome is that we had assigned a 'last vaccination day' to all the holdings in the range of 1-20 days before the start of simulations. Due to this, the first round of RPV did not start until 161-180 day of simulation. At that time in the simulation, the outbreak had already ended, and there were no available infected holdings to keep the infection going. Therefore, although RPV had initiated, it did not have any effect on reducing the duration of the outbreak. Likewise, since RPV did not begin until at least day 161 of simulation, which is after the end of the outbreak, there was no difference in the number of vaccine immune holdings by the end of the outbreak in both scenarios.

As expected, there was a difference in the vaccine immune holdings between the two scenarios with more holdings being vaccine immune by day 370 in 'enhanced scenario' compared to the 'baseline scenario' (Table 2;2). Although the application of RPV in 'enhanced scenario' did not reduce the outbreak duration, it gives confidence that RPV strategy was implemented without any aberrant behavior of the model, and holdings became immune adding to the regional herd-immunity. This also gives hope that, if the random values for the 'last vaccination day' of RPV were not limited to between 1-20 and rather kept in the range of 1-180 days prior to the start of the simulation, the RPV will start early in the simulation and lead to considerable differences between the two scenarios in terms of 'duration of outbreak' and 'vaccine immune holdings by the end of outbreak'. We also believe that the high number of vaccine immune holding by day 370 for 'enhanced scenario' is an overestimation since our prototype version of SMIAD-ER did not account for the coverage, capacity, and efficacy of RPV. These factors are highly related to assessing the effect of RPV as a mitigation strategy in endemic settings where limited resources, lack of infrastructure and paucity of good quality vaccine has a significant role to play in the overall effectiveness of RPV in FMD control programs (Jamal et al., 2014, 2008; Ringa and Bauch, 2014).

Surprisingly, the outbreak duration was quite short in both scenarios, which behaved similarly because of the factors described above. One reason for this quick suppression of disease spread is the fact that the initial status of holdings was based on data of FMD outbreaks which do not reflect the whole province of Punjab, Pakistan. Also, the reporting of FMD cases is very limited in the province with most reporting from areas where FAO is implementing a Progressive Control Pathway for FMD control. In addition, the literature on the prevalence of FMD is non-existent for Pakistan because of the complexity in estimating prevalence in a setting where the disease is endemic and about 83% of the reported outbreaks test positive for FMD (unpublished FAO Pakistan data). Future research should focus on using other ways to estimate infection status at the start of simulations to better mimic the field



situation. A potential solution could be to add a function such as 'new infection due to unaccounted for reasons' and model it as a probability distribution function based on personal communication with expert veterinarians. It would allow the model to add a certain number of infections randomly after a specified time period to account for the underestimation of initial infection status and new infections which model could not account for.

Another reason for the early end of an outbreak was that emergency vaccination continued at its full capacity, i.e., 35 holdings/day after day 15 until day 370. For endemic countries, it is unrealistic to implement emergency vaccination for a long time because of limited resources and the inability to keep track of infected holdings. Future research should focus on limiting the time period during which emergency vaccination is implemented to mimic the realistic situation of resources. Doing so would allow the model to keep the infection going as would happen in a field condition in an endemic setting.

Another limitation of this demonstration is that parameters for disease spread, detection, and vaccination could be biased because they were based on the expert opinion of one field veterinarian. Future demonstrations of the model should increase the number of expert veterinarians for parameter estimation using a Delphi approach (Hus and Sandford, Brian, 2007; Okoli and Pawlowski, 2004).

Future versions of SMIAD-ER should equip the model with the capability to model multiple co-circulating FMD serotypes in parallel, the ability to include livestock population dynamics to account for population susceptibility and herd-immunity. Also, the model should have the flexibility for users to specify the biological efficacy of emergency vaccination in addition to the coverage, capacity, and biological efficacy for RPV.

With the addition of more complex endemicity parameters to the modeling framework, changes would be needed to enhance its engine efficiency to deal with added complexity in the calculations and algorithms such as the use of vector mathematics, use of raster maps, Voronoi tessellations and

different coding frameworks. These changes in engine efficiency, coupled with the incorporation of endemicity, would make SMIAD-ER more useful in endemic settings.

Moreover, a graphical user interface should be added which will allow novice modelers from endemic regions to use the model for their current conditions and utilize modeling as a tool to evaluate alternative mitigation strategies for control of FMD in endemic regions. The control of FMD in endemic areas is critical and will help improve livestock health, provide economic gains for producers, help alleviate poverty and hunger, and will complement efforts to attain Sustainable Development Goals and the 2030 Agenda.

**Funding:**

This work was funded in part by the United States Department of Agriculture (USDA), National Institute of Food and Agriculture, Animal Health and Disease project 2015-05040. The doctoral program of the primary author is funded by the United States Department of State through the Pakistan Fulbright Scholarship Program.

**Conflict of Interest:**

The authors declare no conflict of interest.

## Tables

Table 3.6: FMD progression parameters for serotype-O

Parameter	Probability distribution function	Reference
Latent period	Weibull (1.78, 3.97)	Mardones et al., 2010
Subclinical infectious period	Gamma (1.22, 1.67)	Mardones et al., 2010
Clinical period	Gamma (23.20, 1.74)	NAADSM Development Team, 2012
Natural immunity	Gaussian (1095, 180)	Cunliffe, 1964; Moonen et al., 2004; USDA, 2013

Table 3.7: Performance indices from baseline and enhanced scenario

Statistic	Outbreak duration (days)		Vaccine immune holdings by the end of the outbreak		Vaccine immune holdings by the day 370	
	Baseline*	Enhanced**	Baseline*	Enhanced**	Baseline***	Enhanced**
Minimum	69.0	69.0	1708.0	1698.0	3123.0	1386.0
1st quartile	76.0	76.0	1854.0	1847.0	3228.0	12386.0
Mean	79.3	79.6	1919.0	1912.0	3255.7	12386.0
SD	4.6	4.6	88.8	88.9	41.6	0.2
3rd quartile	82.0	82.0	1971.0	1970.0	3285.0	12386.0
Maximum	102.0	102.0	2298.0	2264.0	3381.0	12387.0

\*Based on 993 iterations

\*\*Based on 1000 iterations

\*\*\*Based on 992 iterations

## REFERENCES

- Abbas, T., Younus, M., Muhammad, S.A., Ijaz, M., Shakoor, A., 2014. Some Challenges to Progressive Control of Foot and Mouth Disease in Pakistan - Findings of a Pilot Survey. *Transbound. Emerg. Dis.* 61, 81–85. <https://doi.org/10.1111/tbed.12008>
- Ahmed, Z., Pauszek, S.J., Ludi, A., LaRocco, M., Khan, E. -u.-H., Afzal, M., Arshed, M.J., Farooq, U., Arzt, J., Bertram, M., Brito, B., Naeem, K., Abubakar, M., Rodriguez, L.L., 2018. Genetic diversity and comparison of diagnostic tests for characterization of foot-and-mouth disease virus strains from Pakistan 2008-2012. *Transbound. Emerg. Dis.* 65, 534–546. <https://doi.org/10.1111/tbed.12737>
- Anjum, R., Hussain, M., Zahoor, A.B., Irshad, H., Farooq, U., 2006. Epidemiological analyses of foot and mouth disease in Pakistan. *Int. J. Agric. Biol.* 8.
- Bates, T.W., Thurmond, M.C., Carpenter, T.E., 2003a. Description of an epidemic simulation model for use in evaluating strategies to control an outbreak of foot-and-mouth disease. *Am. J. Vet. Res.* 64, 195–204. <https://doi.org/10.2460/ajvr.2003.64.195>
- Bates, T.W., Thurmond, M.C., Carpenter, T.E., 2003b. Results of epidemic simulation modeling to evaluate strategies to control an outbreak of foot-and-mouth disease. *Am. J. Vet. Res.* 64, 205–210. <https://doi.org/10.2460/ajvr.2003.64.205>
- Brooks-Pollock, E., de Jong, M.C.M., Keeling, M.J., Klinkenberg, D., Wood, J.L.N., 2015. Eight challenges in modelling infectious livestock diseases. *Epidemics* 10, 1–5. <https://doi.org/10.1016/J.EPIDEM.2014.08.005>

- Cunliffe, H., 1964. Observations on the duration of immunity in cattle after experimental infection with Foot-and-Mouth Disease virus. *Cornell Vet.* 54, 501–10.
- Dorjee, S., Revie, C.W., Poljak, Z., McNab, W.B., Sanchez, J., 2016. One-Health Simulation Modelling: A Case Study of Influenza Spread between Human and Swine Populations using *NAADSM*. *Transbound. Emerg. Dis.* 63, 36–55. <https://doi.org/10.1111/tbed.12215>
- Dürr, S., Fasel-Clemenz, C., Thür, B., Schwermer, H., Doherr, M.G., Dohna, H. zu, Carpenter, T.E., Perler, L., Hadorn, D.C., 2014. Evaluation of the benefit of emergency vaccination in a foot-and-mouth disease free country with low livestock density. *Prev. Vet. Med.* 113, 34–46. <https://doi.org/10.1016/J.PREVETMED.2013.10.015>
- FAO, OIE, 2016. Foot and mouth disease vaccination and post-vaccination monitoring: Guidelines. Food and Agriculture Organization of the United Nations, Rome, Italy, and World Organization for Animal Health, Paris, France.
- Farooq, U., Ahmed, Z., Naeem, K., Bertram, M., Brito, B., Stenfeldt, C., Pauszek, S.J., LaRocco, M., Rodriguez, L., Arzt, J., 2018. Characterization of naturally occurring, new and persistent subclinical foot-and-mouth disease virus infection in vaccinated Asian buffalo in Islamabad Capital Territory, Pakistan. *Transbound. Emerg. Dis.* 65, 1836–1850. <https://doi.org/10.1111/tbed.12963>
- Farooq, U., Irshad, H., Ullah, A., Latif, A., Zahur, A.B., Naeem, K., Ahmed, Z., Rodriguez, L.L., 2017a. Sero-prevalence of foot-and-mouth disease in small ruminants of Pakistan. *J. Anim. Plant Sci.* 27, 1197–1201.
- Farooq, U., Naeem, K., Zahur, A.B., Khan, M.A., Sidique, U., 2017b. Foot-and-mouth disease outbreaks investigations at Sindh, Punjab and Islamabad, Pakistan during the year 2012-2013. *Int. J. Biosci.* 11, 346–356. <https://doi.org/10.12692/ijb/11.5.346-356>

- Farooq, U., Naeem, K., Zahur, A.B., Khan, M.A., Sidique, U., Qureshi, S., 2017c. Epidemiological analysis and economic impact assessment of foot-and-mouth disease at Landhi dairy colony Karachi. *Asian J. Agric. Biol.* 5, 7–14.
- Farooq, U., Ullah, A., Irshad, H., Latif, A., Naeem, K., Zahur, A. Bin, Ahmad, Z., Rodriguez, L.L., 2016. Seroprevalence of foot-and-mouth disease in large ruminants in periurban dairy farms near Islamabad, Pakistan. *Asian Biomed.* 10, 123–127. <https://doi.org/10.5372/1905-7415.1002.472>
- Ferguson, N.M., Donnelly, C.A., Anderson, R.M., 2001. Transmission intensity and impact of control policies on the foot and mouth epidemic in Great Britain. *Nature* 413, 542–548. <https://doi.org/10.1038/35097116>
- Ferrari, G., Tasciotti, L., Khan, E., Kiani, A., 2014. Foot-and-Mouth Disease and Its Effect on Milk Yield: An Economic Analysis on Livestock Holders in Pakistan. *Transbound. Emerg. Dis.* 61, e52–e59. <https://doi.org/10.1111/tbed.12072>
- Garner, M., Beckett, S., 2005. Modelling the spread of foot-and-mouth disease in Australia. *Aust. Vet. J.* 83, 758–766. <https://doi.org/10.1111/j.1751-0813.2005.tb11589.x>
- Garner, M.G., Bombardieri, N., Cozens, M., Conway, M.L., Wright, T., Paskin, R., East, I.J., 2016. Estimating Resource Requirements to Staff a Response to a Medium to Large Outbreak of Foot and Mouth Disease in Australia. *Transbound. Emerg. Dis.* 63, e109–e121. <https://doi.org/10.1111/tbed.12239>
- Gleeson, L.J., 2002. A review of the status of foot and mouth disease in South-East Asia and approaches to control and eradication. *Rev. Sci. Tech.* 21, 465–75.
- Guitian, J., Pfeiffer, D., 2006. Should we use models to inform policy development? *Vet. J.* 172, 393–395. <https://doi.org/10.1016/j.tvjl.2006.03.001>

- 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. *Prev. Vet. Med.* 82, 176–197. <https://doi.org/10.1016/J.PREVETMED.2007.05.019>
- Hunter, P., 1998. Vaccination as a means of control of foot-and-mouth disease in sub-saharan Africa. *Vaccine* 16, 261–264. [https://doi.org/10.1016/S0264-410X\(97\)00170-9](https://doi.org/10.1016/S0264-410X(97)00170-9)
- Hus, C.-C., Sandford, Brian, A., 2007. The Delphi Technique: Making Sense of Consensus. *Pract. Assessment, Res. Eval.* 12.
- Jamal, S.M., Ahmed, S., Hussain, M., Ali, Q., 2010. Status of foot-and-mouth disease in Pakistan. *Arch. Virol.* 155, 1487–1491. <https://doi.org/10.1007/s00705-010-0732-y>
- Jamal, S.M., Belsham, G.J., 2013. Foot-and-mouth disease: past, present and future. *Vet. Res.* 44, 116. <https://doi.org/10.1186/1297-9716-44-116>
- Jamal, S.M., Bouma, A., van den Broek, J., Stegeman, A., Chénard, G., Dekker, A., 2008. Foot-and-mouth disease vaccine potency testing: The influence of serotype, type of adjuvant, valency, fractionation method, and virus culture on the dose–response curve in cattle. *Vaccine* 26, 6317–6321. <https://doi.org/10.1016/J.VACCINE.2008.09.021>
- Jamal, S.M., Shah, S.I., Ali, Q., Mehmood, A., Afzal, M., Afzal, M., Dekker, A., 2014. Proper Quality Control of Formulated Foot-and-Mouth Disease Vaccines in Countries with Prophylactic Vaccination is Necessary. *Transbound. Emerg. Dis.* 61, 483–489. <https://doi.org/10.1111/tbed.12051>
- Jemberu, W.T., Mourits, M.C.M., Woldehanna, T., Hogeveen, H., 2014. Economic impact of foot and mouth disease outbreaks on smallholder farmers in Ethiopia. *Prev. Vet. Med.* 116, 26–36.



<https://doi.org/10.1016/J.PREVETMED.2014.06.004>

Kao, R.R., 2002. The role of mathematical modelling in the control of the 2001 FMD epidemic in the UK.

*Trends Microbiol.* 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. Biol. Sci.* 272, 1195–202.

<https://doi.org/10.1098/rspb.2004.3046>

Keeling, M.J., Woolhouse, M.E., 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 (80-. )*. 294, 813–817.

<https://doi.org/10.1126/science.1065973>

Knight-Jones, T.J., Bulut, A., Gubbins, S., Stärk, K.D., Pfeiffer, D., Sumption, K., Paton, D., 2015.

Randomised field trial to evaluate serological response after foot-and-mouth disease vaccination in Turkey. *Vaccine* 33, 805–11. <https://doi.org/10.1016/j.vaccine.2014.12.010>

Knight-Jones, T.J.D., Gubbins, S., Bulut, A.N., Stärk, K.D.C., Pfeiffer, D.U., Sumption, K.J., Paton, D.J.,

2016a. Mass vaccination, immunity and coverage: modelling population protection against foot-and-mouth disease in Turkish cattle. *Sci. Rep.* 6, 22121. <https://doi.org/10.1038/srep22121>

Knight-Jones, T.J.D., Robinson, L., Charleston, B., Rodriguez, L.L., Gay, C.G., Sumption, K.J., Vosloo, W.,

2016b. Global Foot-and-Mouth Disease Research Update and Gap Analysis: 2 - Epidemiology, Wildlife and Economics. *Transbound. Emerg. Dis.* 63, 14–29. <https://doi.org/10.1111/tbed.12522>

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? *Prev. Vet. Med.* 112, 161–173.

<https://doi.org/10.1016/J.PREVETMED.2013.07.013>

Mardones, F., Perez, A., Sanchez, J., Alkhamis, M., Carpenter, T., 2010. Parameterization of the duration

of infection stages of serotype O foot-and-mouth disease virus: an analytical review and meta-analysis with application to simulation models. *Vet. Res.* 41, 45.

<https://doi.org/10.1051/vetres/2010017>

McReynolds, S.W., Sanderson, M.W., Reeves, A., Hill, A.E., 2014. Modeling the impact of vaccination control strategies on a foot and mouth disease outbreak in the Central United States. *Prev. Vet. Med.* 117, 487–504. <https://doi.org/10.1016/J.PREVETMED.2014.10.005>

Moonen, P., Jacobs, L., Crienen, A., Dekker, A., 2004. Detection of carriers of foot-and-mouth disease virus among vaccinated cattle. *Vet. Microbiol.* 103, 151–160.

<https://doi.org/10.1016/j.vetmic.2004.07.005>

Morris, R.S., Sanson, R.L., Stern M.W., Stevenson M., Wilesmith J.W., 2002. Decision-support tools for foot and mouth disease control. *Rev. sci. tech. Off. int. Epiz.* 21, 557–567.

<https://doi.org/10.20506/rst.21.3.1363>

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. *Vet. Rec.* 149, 137–44. <https://doi.org/10.1136/vr.149.5.137>

NAADSM Development Team, 2012. WH 0.9.7: A Simulation Model for With-in Unit Disease Dynamics. Animal Population Health Institute, Department of Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State university, Fort Collins, Colorado USA.

Navid, M.T., Farooq, U., Latif, A., Awais, M.M., Anwar, M.I., Akhtar, M., Zahur, A.B., 2018. Prevalence of foot and mouth disease virus in apparently healthy buffaloes brought to Islamabad slaughterhouse in Pakistan. *Trop. Biomed.* 35, 161–167.

Okoli, C., Pawlowski, S.D., 2004. The Delphi method as a research tool: an example, design

- considerations and applications. *Inf. Manag.* 42, 15–29. <https://doi.org/10.1016/j.im.2003.11.002>
- Paton, D.J., Sumption, K.J., Charleston, B., 2009. Options for control of foot-and-mouth disease: knowledge, capability and policy. *Philos. Trans. R. Soc. Lond. B. Biol. Sci.* 364, 2657–67. <https://doi.org/10.1098/rstb.2009.0100>
- Pomeroy, L.W., Bansal, S., Tildesley, M., Moreno-Torres, K.I., Moritz, M., Xiao, N., Carpenter, T.E., Garabed, R.B., 2017. Data-Driven Models of Foot-and-Mouth Disease Dynamics: A Review. *Transbound. Emerg. Dis.* 64, 716–728. <https://doi.org/10.1111/tbed.12437>
- R Core Team, 2017. R: A language and environment for statistical computing.
- Ringa, N., Bauch, C.T., 2014. Dynamics and control of foot-and-mouth disease in endemic countries: A pair approximation model. *J. Theor. Biol.* 357, 150–159. <https://doi.org/10.1016/J.JTBI.2014.05.010>
- Roche, S.E., Garner, M.G., Wicks, R.M., East, I.J., de Witte, K., 2014. How do resources influence control measures during a simulated outbreak of foot and mouth disease in Australia? *Prev. Vet. Med.* 113, 436–446. <https://doi.org/10.1016/J.PREVETMED.2013.12.003>
- Rweyemamu, M., Roeder, P., MacKay, D., Sumption, K., Brownlie, J., Leforban, Y., 2008a. Planning for the Progressive Control of Foot-and-Mouth Disease Worldwide. *Transbound. Emerg. Dis.* 55, 73–87. <https://doi.org/10.1111/j.1865-1682.2007.01016.x>
- Rweyemamu, M., Roeder, P., Mackay, D., Sumption, K., Brownlie, J., Leforban, Y., Valarcher, J.-F., Knowles, N.J., Saraiva, V., 2008b. Epidemiological Patterns of Foot-and-Mouth Disease Worldwide. *Transbound. Emerg. Dis.* 55, 57–72. <https://doi.org/10.1111/j.1865-1682.2007.01013.x>
- Schoenbaum, M.A., Disney, W.T., 2003. Modeling alternative mitigation strategies for a hypothetical outbreak of foot-and-mouth disease in the United States. *Prev. Vet. Med.* 58, 25–52. [https://doi.org/10.1016/S0167-5877\(03\)00004-7](https://doi.org/10.1016/S0167-5877(03)00004-7)

Souley Kouato, B., De Clercq, K., Abatih, E., Dal Pozzo, F., King, D., Thys, E., Marichatou, H., Saegerman, C., 2018. Review of epidemiological risk models for foot-and-mouth disease: Implications for prevention strategies with a focus on Africa. *PLoS One* 13, e0208296.

<https://doi.org/10.1371/journal.pone.0208296>

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. *Prev. Vet. Med.* 109, 10–24. <https://doi.org/10.1016/J.PREVETMED.2012.08.015>

Sumption, K., Domenech, J., Ferrari, G., 2012. Progressive control of FMD on a global scale. *Vet. Rec.* 170, 637–9. <https://doi.org/10.1136/vr.e4180>

Tomassen, F.H.M., de Koeijer, A., Mourits, M.C.M., Dekker, A., Bouma, A., Huirne, R.B.M., 2002. A decision-tree to optimise control measures during the early stage of a foot-and-mouth disease epidemic. *Prev. Vet. Med.* 54, 301–324. [https://doi.org/10.1016/S0167-5877\(02\)00053-3](https://doi.org/10.1016/S0167-5877(02)00053-3)

Ullah, A., Jamal, S.M., Romey, A., Gorna, K., Kakar, M.A., Abbas, F., Ahmad, J., Zientara, S., Bakkali Kassimi, L., 2017. Genetic Characterization of Serotypes A and Asia-1 Foot-and-mouth Disease Viruses in Balochistan, Pakistan, in 2011. *Transbound. Emerg. Dis.* 64, 1569–1578. <https://doi.org/10.1111/tbed.12548>

USDA, 2013. Parameters Used to Simulate the Spread of FMD in Texas Using the North American Animal Disease Spread Model (NAADSM) for use in FMD Response Workforce Requirement Estimates. Fort Collins, CO USA.

Wongsathapornchai, K., Salman, M.D., Edwards, J.R., Morley, P.S., Keefe, T.J., Campen, H. V., Weber, S.E., Premashthira, S., 2008. Use of epidemiologic risk modeling to evaluate control of foot-and-mouth disease in southern Thailand. *Am. J. Vet. Res.* 69, 240–251.

<https://doi.org/10.2460/ajvr.69.2.240>

Yano, T., Premashthira, S., Dejong, T., Tangtrongsup, S., Salman, M.D., 2018. The Effectiveness of a Foot and Mouth Disease Outbreak Control Programme in Thailand 2008–2015: Case Studies and Lessons Learned. *Vet. Sci.* <https://doi.org/10.3390/vetsci5040101>

Yoon, H., Wee, S.-H., Stevenson, M.A., O’Leary, B.D., Morris, R.S., Hwang, I.-J., Park, C.-K., Stern, M.W., 2006. Simulation analyses to evaluate alternative control strategies for the 2002 foot-and-mouth disease outbreak in the Republic of Korea. *Prev. Vet. Med.* 74, 212–225.

<https://doi.org/10.1016/J.PREVETMED.2005.12.002>

CHAPTER 4: SIMULATION MODEL FOR INFECTIOUS ANIMAL DISEASES IN ENDEMIC REGIONS (SMIAD-ER):  
APPLICATION FOR FOOT-AND-MOUTH DISEASE CONTROL STRATEGIES<sup>4</sup>

1 Introduction

Foot and mouth disease (FMD) is endemic in many parts of the world (Anjum et al., 2006; Farooq et al., 2018, 2017a, 2017b, 2017c, 2016; Gleeson, 2002; Jamal et al., 2010; Navid et al., 2018; Rweyemamu et al., 2008b; Yano et al., 2018), and is associated with substantial economic losses (Ferrari et al., 2014; Jemberu et al., 2014; Knight-Jones and Rushton, 2013). International organizations such as the Food and Agriculture Organization of the United Nations (FAO), the World Organization for Animal Health (OIE), the European Commission for the Control of Foot and Mouth Disease (EuFMD) have called for a more targeted control strategy in the 'Progressive Control Pathway for FMD' to reduce the disease burden and high economic costs associated with it (Abbas et al., 2014; Jamal and Belsham, 2013; Paton et al., 2009; Rweyemamu et al., 2008a; Sumption et al., 2012).

Simulation modeling has become a useful tool to investigate the spread and evaluate the effectiveness of alternative mitigation strategies for infectious diseases including FMD (Dorjee et al., 2016; Guitian and Pfeiffer, 2006; Kao, 2002; Keeling, 2005; Morris et al., 2002). Several models have

---

<sup>4</sup> This chapter of the dissertation is intended for publication in the Preventive Veterinary Medicine journal and is formatted accordingly.

Muhammad Usman Zaheer<sup>a</sup>, Mo Salman<sup>a</sup>, Shaun Case<sup>b</sup>, Katie Steneroden<sup>a</sup>, Steve Weber<sup>a</sup>, Sheryl Magzamen<sup>c</sup>, Sangeeta Rao<sup>a</sup>

<sup>a</sup>Animal Population Health Institute, Department of Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins CO 80523, USA, <sup>b</sup>Department of Civil and Environmental Engineering, Walter Scott, Jr. College of Engineering, Colorado State University, Fort Collins CO 80523, USA, <sup>c</sup>Department of Environmental and Radiological Health Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins CO 80523, USA

been developed to mimic the spread of FMD in specific regions or countries (Bates et al., 2003d; Garner and Beckett, 2005; Harvey et al., 2007b; Stevenson et al., 2013; Wongsathapornchai et al., 2008). These models have been used for various purposes such as for risk assessment, to analyze outbreaks using historical data or hypothetical scenarios, to assist in policy decisions during outbreaks, and policy formulation in preparedness planning, and in evaluating economic impacts (Bates et al., 2003c; Dürr et al., 2014; Ferguson et al., 2001a; Keeling et al., 2001; McReynolds et al., 2014; Morris et al., 2001; Tomassen et al., 2002; Yoon et al., 2006a). In disease-free countries, models are used to identify gaps in the preparedness such as estimating required resources (Garner et al., 2016; Roche et al., 2014), whereas, in endemic countries, models can also be useful for comparing mitigation strategies to guide future directions of FMD control program (Souley Kouato et al., 2018).

Most of the reported literature on FMD simulation models is, however, associated with disease-free countries with minimal application of these models in countries with an endemic status of FMD (Pomeroy et al., 2017). The development of simulation models of infectious livestock diseases such as FMD in endemic settings is enormously challenging for reasons such as the lack of interest and understanding of perceived benefits, political or economic constraints, insufficient data to support model parameters, and the complexity of FMD epidemiology in endemic settings (Brooks-Pollock et al., 2015; Knight-Jones et al., 2016b).

A systematic review of the existing spatially-explicit simulation models (SESS) revealed a set of possible additions to these models to extend their applicability to FMD-endemic regions to understand FMD spread and to evaluate the effectiveness of alternative mitigation strategies for its control (Zaheer et al., 2019, submitted). The key findings were to include components such as: a module to simulate co-circulating FMD serotypes, ability to alter the livestock population dynamics during the simulation runs (growth rate), flexibility to implement “routine prophylactic vaccination’ (RPV), and alteration of existing simulation stop conditions to make them flexible for endemic settings (Zaheer et al., 2019, submitted).

The identified additional components are known to be key characteristics of FMD epidemiology in endemic regions (Ahmed et al., 2018; FAO and OIE, 2016; Hunter, 1998; Knight-Jones et al., 2015, 2016a; Ullah et al., 2017).

One such SESS model is the North American Animal Disease Spread Model (NAADSM) (Harvey et al., 2007; Schoenbaum and Disney, 2003) which is being used in FMD-free settings to understand the dynamics of a hypothetical outbreak of FMD, evaluating alternative mitigation strategies, and aid in preparedness planning and decision-making (Gale et al., 2015; McReynolds et al., 2014; Pendell et al., 2015; Schroeder et al., 2015; Zagmutt et al., 2016).

Recently, researchers at the Colorado State University adapted the NAADSM for use in FMD-endemic countries by including RPV as an additional mitigation strategy (Zaheer et al., in preparation). The modified modeling framework is labeled the Simulation Model for Infectious Animal Diseases in Endemic Regions (SMIAD-ER), which is a state-transition, spatially-explicit, stochastic, simulation model of the between-herd spread of infectious animal diseases such as FMD. The prototype version of SMIAD-ER was used to demonstrate its application in Pakistan, an FMD endemic country. The model was parameterized with estimates derived from data obtained from Punjab, Pakistan, and model outputs revealed no aberrant behavior in simulation outputs from two scenarios, i.e., baseline scenario (no RPV) and RPV scenario (implementation of RPV) (Zaheer et al., in preparation).

The demonstration of SMIAD-ER (Zaheer et al., in preparation), resulted in a small 'outbreak duration' in both scenarios because of the small number of infected holdings at the start of the simulations. The infected livestock holdings were based on FMD outbreaks data and expert opinion. Another reason for the early end of an outbreak was that emergency vaccination continued at its full capacity, i.e., 35 holdings/day after day 15 until day 370. For endemic countries, it is unrealistic to implement emergency vaccination (e.g., ring vaccination) for a long period of time because of limited



resources and the inability to keep track of infected holdings. Therefore, future versions of SMIAD-ER should have the flexibility to restrict emergency vaccination at a user-specified time point to reflect the availability of resources.

Moreover, differences were found between 'baseline' and the 'RPV' scenario for 'vaccine immune holdings by day 370' of the simulation scenario, with more vaccine immune holdings in the latter scenario (Zaheer et al., in preparation). There were, however, no differences in the scenarios for 'vaccine immune holdings by the end of the outbreak' which suggests that implementation of RPV did not contribute to building herd-immunity during the outbreak. A possible reason for this similarity was the way holdings were assigned 'last vaccination day' which was set between 1-20 days before the start of the simulation (Personal Communication, anonymous veterinarian). Therefore, RPV did not start until day 161 of simulations. Hence, implementation of RPV did not have any impact on reducing outbreak duration since the outbreak had already ended. Also, the demonstration of the prototype version of SMIAD-ER did not incorporate the coverage, capacity, and efficacy of RPV. The future versions of SMIAD-ER should include these features to more realistically mimic the impact of RPV in reducing FMD burden during simulations.

This paper aimed to report the enhanced features of SMIAD-ER by modifying its underlying framework to better mimic FMD in endemic settings. The objective was to demonstrate the usefulness of SMIAD-ER in assessing the effectiveness of various mitigation strategies for FMD control by parameterizing the model with estimates from FMD-endemic settings.

## 2 Methods

This demonstration of SMIAD-ER was based on cattle and buffalo holdings in Sindh province of Pakistan (Figure 4.1), a country endemic for FMD (Anjum et al., 2006; Farooq et al., 2018, 2017a, 2017b, 2017c, 2016; Jamal et al., 2010; Navid et al., 2018).

## 2.1 Assumptions of SMIAD-ER

The demonstration of SMIAD-ER in this paper was based on the following assumptions:

- The input holdings represented the total holdings of the livestock of interest in Sindh, Pakistan for 2006.
- There were four production-types in Sindh, i.e., medium buffalo (11-30 animals), medium cattle (11-30 animals), large buffalo (>30 animals), large cattle (>30 animals).
- The population was closed, and the population size was constant. Individual holdings do not enter or leave the study area except via stamping-out as a control measure.
- The effect of bovine holdings with 1-10 animals, small ruminants (sheep, goat) and wild animals (deer, wild boar) on FMD spread was ignored (i.e., negligible risk).
- The occurrence of FMD and its spread beyond the provincial/regional boundary was ignored.
- The impact of seasonality and meteorological factors on FMD spread was not included.
- All holdings in the same production-type had the same disease progression parameters.
- Individual animals within a holding were equally likely to come into contact with any other individual animals from other holdings of any production-type.
- There were homogenous contact rates between specific pairs of production types, such as medium cattle to large buffalo, large buffalo to medium buffalo, etc.
- The disease spread parameters and other parameters used in this demonstration represented the field situation of FMD in Pakistan.
- The change in the population due to the potential mortality from FMD or other causes during the simulation duration was not considered.

- There was only one circulating serotype of FMD, i.e., Serotype O.
- There was no carrier status among recovered holdings.
- The infection status at the start of the simulation represented the prevalence of FMD in Sindh, Pakistan.
- Emergency vaccination was not performed beyond the user-defined time period due to limited resources.
- Routine prophylactic vaccination was not implemented beyond a user-defined time period.
- Holdings of all production-types were assumed to have been vaccinated based on the user-defined period before the start of the simulation, and it was termed 'last vaccination day.'

## 2.2 *Additional features to SMIAD-ER*

To mimic endemic FMD, the implementation of RPV in the prototype version of SMIAD-ER was modified in four ways.

- Firstly, we added an option for users to specify the coverage for RPV. At the start of the simulations, all units were assigned a value for 'last vaccination day' by production type. If a production-type was set to be vaccinated once a year, holdings for that production-type were assigned a value between 1-365 days for 'last vaccination day.' Based on the coverage, when a holding was due for a vaccination, its status was changed to 'susceptible.' The model then selected a random holding from the pool and attempted to vaccinate it.
- Secondly, we added a capacity function for RPV as point value to ensure that no more than a user-specified number of holdings could be vaccinated on each day when they come due. This is likely not to affect the model outputs because holdings will be vaccinated based on 'last vaccination day' and based on 'coverage,' not enough holdings will be selected randomly to

surpass the capacity. Nonetheless, if it happens, holdings exceeding capacity will not be vaccinated and remain 'susceptible'.

- Thirdly, we added a user-defined function for 'vaccine efficacy' as a probability distribution function (PDF). Based on a random number from the specified distribution, the holding which was vaccinated can either become immune and be labeled as 'vaccine immune' or cannot mount an immune response and remain 'susceptible'.
- Lastly, we added a condition to stop RPV at a user-defined day of simulation. Based on this stop condition for RPV, holdings that come due post that day were not subject to be vaccination.

### 2.3 *Data sources*

The datasets used in this demonstration included: unpublished FMD outbreaks data from FAO Pakistan<sup>5</sup>; simulated dataset from the location and population of individual livestock holdings in Pakistan (Zaheer et al., in preparation), expert opinions and personal communications with anonymous veterinarians in Pakistan.

### 2.4 *Model parameters*

In this section, the baseline parameters used in SMIAD-ER are described.

#### 2.4.1 *Production-types and their status*

The data on the population and location of individual livestock holdings were obtained from a study that utilized the microsimulation approach and geographic information system to generate a simulated dataset on the location and population of individual livestock holdings in Pakistan (Zaheer et al., in preparation).

---

<sup>5</sup> Progressive Control Pathway Project for FMD control in Pakistan, Food and Agriculture Organization of the United Nations, ASI premises, National Agricultural Research Center, Islamabad 44000, Pakistan.

We included four production-types of livestock (Table 4.1) from Sindh, i.e., medium buffalo (11-30 animals), medium cattle (11-30 animals), large buffalo (>30 animals), large cattle (>30 animals).

Based on FMD outbreaks data (unpublished data, FAO Pakistan) and personal communication with expert veterinarians, holdings were randomly assigned one of the six possible statuses, i.e., clinical infectious, subclinical infectious, latent infected, naturally immune, vaccine immune, and susceptible (Table 4.1).

#### *2.4.2 Progression parameters*

FMD progression parameters (Table 4.2) were based on the assumption that only one serotype of FMD is circulating, i.e., Serotype O. The parameters for the subclinical, latent and natural immune period were similar for all production-types (medium – buffalo and cattle, large – buffalo and cattle). The parameters for the clinical period were estimated using Within-Herd (WH) model 0.9.7 (NAADSM Development Team, 2012), and the parameters used in the WH model are available in appendix.

#### *2.4.3 Spread parameters*

For all 16 possible production-type combinations, the parameters for direct and indirect contact spread and airborne spread were obtained from a veterinarian (anonymous) with extensive experience working with FMD outbreaks in Pakistan.

For all production-type combinations, latent and subclinical holdings were assumed to be able to spread disease by direct contact. For indirect contact, only subclinical holdings were assumed to be infectious. The delay in shipment, for both direct and indirect contact, was set to zero days. The effect of movement restrictions on the baseline direct and indirect contact rate was set to zero as gleaned from expert opinion.

The probability of infection transfer from source to recipient holdings amid direct and indirect contact was set between 0-1 as suggested by an expert veterinarian from Pakistan. Likewise, the

distance distribution of recipient holdings for direct and indirect contact spread was specified by BetaPERT distribution. The probability of infection transfer and distance distribution parameters are not included here due to the sheer volume of the inputs, and these parameters can be obtained from the primary author upon request.

For airborne spread, the maximum distance for local area spread was set to 3-Km for all production type combinations. The rate of FMD spread was set to decline linearly from source holdings, and the direction of airborne spread was set to happen equally in 0-360° from the source holding. The probability of infection transfer was set between 0-1, and it is not included here due to the sheer volume of the inputs, and these parameters can be obtained from the primary author upon request.

#### *2.4.4 FMD detection parameters*

For all production-types in Pakistan (Table 4.3), the estimated probability of observing clinical signs of FMD, given the number of days the holding had been clinically infectious, and the estimated probability of reporting an observed clinical holding, given the number of days since FMD was first detected in any holding were gleaned from anonymous veterinarian from Pakistan with extensive experience with FMD outbreaks.

#### *2.4.5 Disease tracing*

The SMIAD-ER had an assumption that when tracing is enabled and a holding is identified as having had contact with another infected holding, the holding is quarantined and can no longer take part in disease spread through contacts (both direct and indirect). Based on personal communications with FMD experts in Pakistan, it was revealed that no such tracing mechanism exists in the country and also, no mechanism exists to quarantine holdings if identified as being a source of or having exposure from other holdings. Therefore, tracing was disabled for this demonstration.

#### *2.4.6 Examination of traced holdings*

In SMIAD-ER, examination of holdings identified by tracing is nested within the tracing. Since tracing was not enabled, the examination of holdings for clinical signs was not enabled.

#### *2.4.7 Diagnostic testing of traced holdings*

Diagnostic testing of holdings identified by tracing is nested within the tracing and examination of clinical signs. Since tracing was not enabled, diagnostic testing of holdings was not activated.

#### *2.4.8 Zones*

Based on the opinion of veterinarians from Pakistan, zones were not enabled.

#### *2.4.9 Destruction*

As gleaned from personal communications with FMD experts in Pakistan, the destruction of holdings was not enabled. Pakistan is currently at stage 2 of the Progressive Control Pathway for FMD. At this stage, countries focus on reducing disease burden and do not employ destruction as a control option (FAO and OIE, 2016).

#### *2.4.10 Vaccination*

The parameters for emergency vaccination and RPV were based on a combination of personal communications, expert opinion, and published literature (Doel, 1996).

##### *2.4.10.1 Emergency vaccination*

The threshold for implementing emergency vaccination was set to the detection of FMD in five holdings of any production-type. The emergency vaccination capacity was kept constant at five holdings/day of any production-type from when it first started. The emergency vaccination was set to end after 30 days from when it first started.

For all production-types, the delay in mounting an immune response was set to 14 days. The model was set to implement emergency vaccination to infected holdings which were detected, and a vaccination ring of 100 m radius was established for all production-types. The duration of immunity for emergency vaccination (days) was modeled using a triangular distribution (30, 180, 210). For the implementation of emergency vaccination, production-types were prioritized as large cattle > large buffalo > medium buffalo > medium cattle.

#### *2.4.10.2 Routine prophylactic vaccination (RPV)*

For large cattle and buffalo production-types, the frequency of RPV was set to twice a year. The duration of immunity (days) linked to RPV was modeled using triangular distribution (30, 120, 180 days). The biological efficacy (%) of RPV was modeled using triangular distribution (60, 75, 95). The RPV coverage for each of these two production-types was 0.35%, and the capacity was set to 250 holdings/day.

For medium cattle and buffalo production-types, the frequency of RPV was set to once a year. The duration of immunity (days) linked to RPV was modeled using triangular distribution (30, 120, 180 days). The biological efficacy (%) of RPV was modeled using triangular distribution (60, 75, 95). The RPV coverage for each of these two production-types was 0.125%, and the capacity was set to 250 holdings/day.

### *2.5 Scenarios*

As a demonstration, four scenarios (Table 4.4) were developed, i.e., baseline, enhanced movement restrictions, improved disease detection, enhanced RPV. All scenarios were run until day 200 of simulation for 15 iterations due to time constraints and available resources.



## 2.6 Performance indices

To ascertain if there were differences among scenarios, two important indices were extracted: 1) 'Outbreak duration' which provides the number of the days until the end of the outbreak in a simulated scenario 2) 'Vaccine immune holdings by the end of the outbreak' which is the number of holdings of different production-types that were immune because of vaccination by the end of the outbreak.

The ratio of 'vaccine immune holdings by the end of the outbreak' and 'outbreak duration' was calculated to compare the scenarios. For brevity, this index will be referred as 'VO ratio' in the rest of this manuscript. The 'VO ratio' is a unitless quantity depicting the change in the number of vaccine immune holdings by the end of the outbreak with each day increase in the outbreak duration.

## 2.7 Statistical analysis

The outputs from the four scenarios were used to produce descriptive statistics such as minimum, maximum, mean with confidence interval, quartiles and standard deviation for two performance indices, i.e. 'outbreak duration, and 'vaccine immune holdings by the end of outbreak' and the 'ratio of vaccine immune holdings by the end of outbreak and outbreak duration'. One Way Analysis of Variance (ANOVA) was used to test the significant difference among scenarios for two performance indices and the 'VO ratio'. To ensure that the assumptions of ANOVA were met, we performed a Shapiro-Wilk test for normality, and Levene's test for homogeneity of variances using package 'lawstat' (Hui et al., 2008). If either of these two assumptions was violated, we performed the Kruskal-Wallis test for ANOVA. If ANOVA results were significantly different, we performed posthoc multiple comparisons which were an extension of the Wilcoxon Rank Sum test, to further explore which pairs of scenarios were different from each other. We adjusted p-values using Bonferroni method to minimize the familywise error rate. All the analysis was performed using R (R Core Team, 2017). A p-value of <0.05 was considered statistically significant.

### 3 Results

Outputs from four scenarios which ranged from baseline (sc1), implemented movement restriction (sc2), improved disease detection (sc3) and enhanced RPV (sc4) were extracted for the two performance indices and 'VO ratio'. Due to computer hard-drive issues, outputs were not extracted for four iterations of sc1, four iterations of sc3 and one iteration of sc4.

#### 3.1 *Outbreak duration*

A comparison of 'outbreak duration' (Table 4.5) revealed that sc1 and sc4 have similar minimum, maximum, mean with 95% CI, standard deviation. Likewise, sc2 and sc3 had the similar minimum, 1<sup>st</sup> quartile, and maximum for 'outbreak duration'. The mean 'outbreak duration' and its confidence interval for sc1 were different than the mean and confidence interval of sc2 and sc3. The median 'outbreak duration' for sc1 and sc3 were similar; however, these are different from sc2 and sc4, which had a median of 99 and 98.5 days, respectively. The variability of the estimates using the standard deviation for sc1 (4.6 days) and sc4 (4.8 days) was different than sc2 (3.3 days) and sc3 (2.1 days). The figure, 4.2 provides a histogram of 'outbreak duration' among the four scenarios.

The data on the 'outbreak duration' were normally distributed with W-statistics of 0.93 for sc1, 0.91 for sc2, 0.90 for sc3, and 0.89 for sc4. Test for the homogeneity of variances suggested that variances were not equal among scenarios, and non-parametric ANOVA indicated that there were no differences in 'outbreak duration' among four scenarios.

#### 3.2 *Vaccine immune holdings by the end of the outbreak*

Test for normality of data on 'vaccine immune holdings by the end of the outbreak' suggested that observed data were normally distributed with W-statistics of 0.92 for sc1, 0.93 for sc2, 0.93 for sc3, and 0.90 for sc4. Test for the homogeneity of variances suggested that variances were not equal among scenarios, and One Way non-parametric ANOVA suggested that at least the median of one scenario was

not equal to the median of another scenario. Posthoc multiple comparisons (six comparisons) suggested no difference in the medians between sc1 and sc2. All other five comparisons suggested that medians were different, i.e.  $sc1 > sc3$ ,  $sc1 < sc4$ ,  $sc2 > sc3$ ,  $sc2 < sc4$ , and  $sc3 < sc4$ .

### 3.3 VO ratio

Normality testing revealed that data on the 'VO ratio' were normally distributed for all scenarios with W-statistics of 0.95 for sc1, 0.94 for sc2, 0.94 for sc3, and 0.89 for sc4. Test for the homogeneity of variances suggested that variances were not equal among scenarios, One Way non-parametric ANOVA suggested that the median of at least one was not equal to the median of another scenario. Posthoc multiple comparisons (six comparisons) suggested no difference in median 'VO ratio' between sc1 and sc2, and sc1 and sc3. All other four comparisons suggested that medians were different, i.e.  $sc1 < sc4$ ,  $sc2 > sc3$ ,  $sc2 < sc4$ , and  $sc3 < sc4$ .

## 4 Discussion

To the best of our knowledge, this is the first demonstration of SMIAD-ER as a tool to evaluate alternative mitigation strategies for FMD. SMIAD-ER is the first-ever spatially-explicit, stochastic, state-transition simulation model built for endemic regions.

Hypothesis testing for 'outbreak duration' revealed that there were no statistically significant differences among scenarios using outputs from our simulations. It might give the impression that in reality, there is no difference in the outbreak duration in the field among situations when movement restrictions are implemented, disease detection is improved and RPV is enhanced. We should, however, be cautious in making such a definite conclusion because our findings are only valid for the parameters we used in SMIAD-ER. For instance, we only implemented five and ten percent effect of movement restrictions on baseline direct and indirect contact rate on day four and seven post detection. It is possible that we would observe a difference in outbreak duration between the baseline scenario and

movement restriction scenario if a different level of movement restrictions are implemented. Likewise, we did not see a difference in outbreak duration between baseline and the improved FMD detection scenario which could also be explained for the fact that findings are only valid for the parameters we used, and higher levels of FMD detection probabilities may result in differences in outbreak duration when compared with the baseline scenario.

In terms of 'vaccine immune holdings by the end of the outbreak', we found statistically significant differences among the five pairs of scenarios. The statistically significant differences observed in the baseline scenario vs. improved disease detection scenario is borderline. Although we considered it as statistically significant, yet we believe this difference can be explained because of the stochastic nature of processes in SMIAD-ER. The statistically significant difference observed in the movement restriction scenario vs. improved FMD detection scenario can be attributed to disease spread processes happening during simulation in two scenarios. These processes could have resulted in different FMD spread patterns and consequently differences in vaccine immune holdings. On average, an improved FMD detection scenario has fewer vaccine immune holdings by the end of outbreak compared to a movement restriction scenario. This points to the fact that fewer vaccine immune holdings means saving limited resources spent on vaccination while vaccinating more holdings in the movement restriction scenario did not result in reducing outbreak duration compared to the improved FMD detection scenario. The differences observed in the baseline scenario vs the enhanced RPV scenario, the movement restriction scenario vs. the improved FMD detection scenario, the improved FMD detection scenario vs the enhanced RPV scenario are rather obvious because in the enhanced RPV scenario, coverage of RPV was increased 20 times compared to baseline, the movement restriction and improved FMD detection scenario which resulted in more vaccine immune holdings by the end of outbreak in enhanced RPV scenario compared to all other scenarios.

Looking alone at outbreak duration or vaccine immune holdings by the end of the outbreak does not provide insight into how both of these could be playing a role. 'VO ratio' is a unitless quantity that gives insight into how one day increase in outbreak duration translates to vaccine immune holdings by the end of the outbreak. For example, in the case of the baseline scenario, mean 'VO ratio' was 0.49 which means that on average, a one day increase in the outbreak duration in the baseline scenario resulted in about 0.49 less holding vaccinated. Likewise, a one day increase in outbreak duration resulted in, on average, 0.54 and 0.46 fewer holdings vaccinated in the movement restriction scenario and in the improved FMD detection scenario, respectively. In the enhanced RPV scenario, however, a one day increase in the outbreak duration resulted in, on average, nine more holdings becoming vaccine immune. This means that an increase in outbreak duration resulted in fewer vaccine immune holdings in the improved FMD detection scenario compared to the movement restriction scenario (median: 0.45 vs 0.52) and the enhanced RPV scenario (median: 0.45 vs 8.84). Similarly, the movement restriction scenario resulted in fewer vaccine immune holdings as the outbreak duration increased compared to the enhanced RPV scenario (median: 0.52 vs 8.84), and baseline resulted in fewer vaccine immune holdings with each day increase in the outbreak duration compared to the enhanced RPV scenario (median: 0.50 vs 8.84).

The 'VO ratio' has potential applications in policy-making, e.g., to choose a mitigation strategy which results in fewer vaccine immune holdings to limit the use of scarce resources on vaccinating more holdings without added benefit in terms of reducing outbreak duration. For example, in our demonstration, improved FMD detection had the smallest increase in mean (0.44) and median (0.45) number holdings vaccinated with each day increase in outbreak duration compared to the baseline, the movement restriction, and the enhanced RPV scenarios.

Our demonstration of SMIAD-ER in Sindh Pakistan to evaluate alternative mitigation strategies for FMD has four main limitations. Firstly, the inclusion of specific production-types, movement restrictions,

disease detection, and vaccination parameters were based on the opinion of a single veterinarian from Pakistan. Although the veterinarian had extensive experience in dealing with FMD in the field and laboratory and with the implementation of the control program, one veterinarian's professional opinion cannot account for all possibilities. Future work should focus on selecting a larger sample of veterinarians and the use of techniques such as the Delphi approach to reach a consensus on estimates to include in the model.

The second limitation is the use of outbreak data to inform starting disease states for holdings of different production types. Outbreak data are likely to under-represent true burden of the disease because these data lack a suitable denominator. Future work should also focus on obtaining reliable estimates on the spatiotemporal prevalence of FMD by production type. This will allow users to assign disease states closer to reality and not just randomly, as done in this demonstration.

Thirdly, we only simulated each scenario for 15 iterations which is quite a small number. The reason for this small number of iterations was the slow nature of SMIAD-ER's simulation engine. Future work should focus on enhancing the efficiency of the simulation engine to speed-up calculations and algorithms by using techniques such as vector mathematics, raster maps, Voronoi tessellations and different coding frameworks to incorporate more complicated process as they happen in endemic settings, and include more production-types with the increased number of holdings. These changes in engine efficiency would make SMIAD-ER more useful in endemic settings.

Lastly, one issue endemic settings often face is under-reporting of FMD cases. In the future, a potential solution could be to add a 'new infections module', and these new infections can be modeled as a probability distribution function based on expert veterinarians. It would allow the model to add a certain number of infections randomly after a specified time period to account for the underestimation of the initial infection status and new infections which the model could not account for.

Future versions of SMIAD-ER should also equip the model with the capability to model multiple co-circulating FMD serotypes in parallel, the ability to include livestock population dynamics to account for population susceptibility and herd-immunity. Also, the future model should have the flexibility for users to specify the biological efficacy of emergency vaccination in addition to the coverage, capacity, and biological efficacy of RPV.

Moreover, a graphical user interface should be added which will allow novice modelers from endemic regions to use the model for their current conditions and utilize modeling as a tool to evaluate alternative mitigation strategies for control of FMD in endemic areas. Control of FMD in endemic areas is critical and will help improve livestock health, provide economic gains for producers, help alleviate poverty and hunger, and will complement efforts to attain Sustainable Development Goals and the 2030 Agenda.

**Funding:**

This work was funded in part by the United States Department of Agriculture (USDA), National Institute of Food and Agriculture, Animal Health and Disease project 2015-05040. The doctoral program of the primary author is funded by the United States Department of State through the Pakistan Fulbright Scholarship Program.

**Conflict of Interest:**

The authors declare no conflict of interest.

Tables

Table 4.1: Status of holdings of each production-type in Sindh, Pakistan\*

Production type	Clinical	Subclinical	Latent	Naturally immune	Vaccine immune	Susceptible	Total
Medium buffalo	148	443	2,953	591	142	109,307	113,584
Medium cattle	143	574	3,586	717	138	105,190	110,348
Large buffalo	390	1,171	3,122	1,561	41	5,399	11,684
Large cattle	331	1,325	3,311	1,655	35	3,257	9,914
Total	1,012	3,513	12,972	4,524	356	233,153	245,530

\*Estimated from outbreaks data and expert opinion



Table 4.2: FMD progression parameters for different production-types in Sindh, Pakistan

Production-type	Latent*	Subclinical*	Clinical**	Natural immunity***
Medium holdings	Weibull (1.78, 3.97)	Gamma (1.22, 1.67)	Pearson 5 (21.55, 513.16)	Gaussian (1095, 180)
Large holdings	Weibull (1.78, 3.97)	Gamma (1.22, 1.67)	Beta (25.19, 174.6, 1.95, 387.4)	Gaussian (1095, 180)

\*Mardones et al., 2010

\*\*NAADSM Development Team, 2012

\*\*\*Cunliffe, 1964; Moonen et al., 2004; USDA, 2013

Table 4.3: FMD detection parameters for all production-types in Sindh, Pakistan

Probability	Day	Medium Buffalo	Large Buffalo	Medium Cattle	Large Cattle
Observing clinical signs, given the number of days the holding is clinically infectious	1	0.20	0.20	0.25	0.25
	4	0.50	0.50	0.50	0.50
	7	0.70	0.70	0.75	0.75
Reporting an observed clinical holding, given the number of days since the disease was first detected in any holding	1	0.10	0.10	0.10	0.10
	3	0.20	0.40	0.20	0.40
	5	0.50	0.70	0.50	0.70

Table 4.4: Scenarios for the demonstration of SMIAD-ER in Sindh, Pakistan

Scenario	Description
Baseline (sc1)	To show the baseline level of FMD spread and control as detailed in section 2.4
Implemented movement restrictions (sc2)	Assuming that the implementation of movement restriction will affect FMD spread Baseline effect of movement restrictions on the contact spread was enhanced to 5 and 10 percent reduction in mean baseline contact rate on day four and seven post-detection, respectively for all production-type combinations
Improved disease detection (sc3)	Assuming that improved disease detection will lead to early implementation of control strategies and hence reducing FMD burden
Enhanced RPV (sc4)	The baseline level of disease detection multiplied with 1.25 for all production-types Assuming that enhancing the frequency and coverage of RPV will help build herd-immunity, which will in turn help reduce disease burden  The baseline coverage of RPV was increased 20 times for all production-types

Table 4.5: Summary statistics of performance indices from four scenarios for the demonstration of SMIAD-ER in Sindh, Pakistan

Statistic	Outbreak duration				Vaccine immune holdings by the end of the outbreak				Ratio of vaccine immune holdings by the end of outbreak and outbreak duration			
	sc1	sc2	sc3	sc4	sc1	sc2	sc3	sc4	sc1	sc2	sc3	sc4
Minimum	92.0	92.0	93.0	93.0	41.0	48.0	39.0	721.0	0.38	0.47	0.39	6.68
1 <sup>st</sup> quartile	95.5	96.5	96.5	94.0	46.0	50.0	43.0	829.5	0.46	0.50	0.44	8.23
Mean	98.4	98.1	97.2	98.4	48.1	52.5	44.2	879.8	0.49	0.54	0.46	9.00
(95% CI)	(95.2, 101.5)	(96.3, 99.9)	(95.8, 98.6)	(95.6, 101.1)	(45.8, 50.4)	(50.7, 54.2)	(42.6, 45.8)	(831.8, 927.9)	(0.45, 0.53)	(0.51, 0.56)	(0.43, 0.48)	(8.28, 9.73)
Median	97.0	99.0	97.0	98.5	49.0	51.0	44.0	870.5	0.50	0.52	0.45	8.84
St. Dev.	4.6	3.3	2.1	4.8	3.4	3.2	2.4	83.2	0.05	0.05	0.03	1.26
3 <sup>rd</sup> quartile	101.0	100.0	97.5	100.8	50.5	55.0	45.0	958.5	0.53	0.57	0.47	10.20
Maximum	107.0	102.0	101.0	108.0	52.0	59.0	48.0	977.0	0.56	0.64	0.50	10.50

Figures

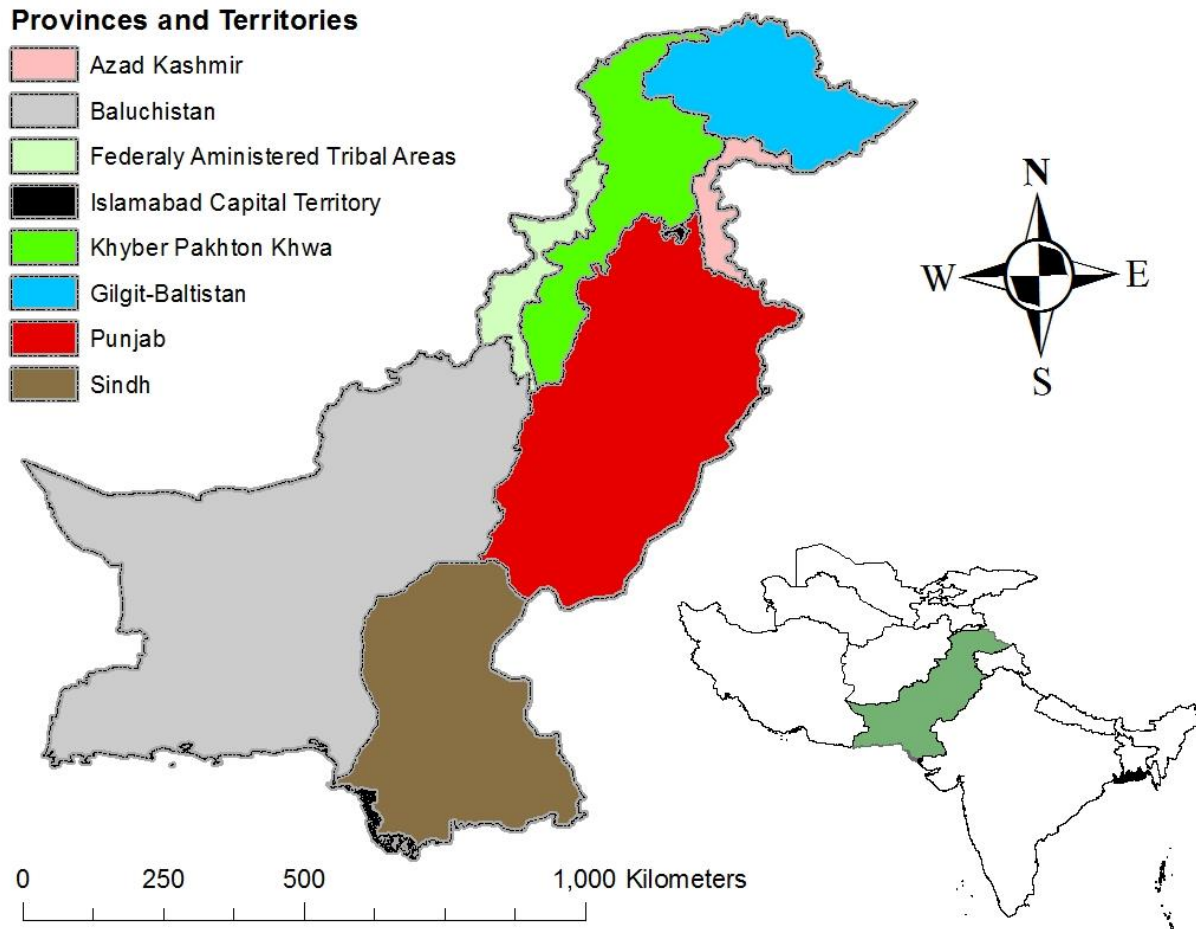


Figure 4.1: Map of Pakistan showing its provinces and territories (extracted from Zaheer et al., in preparation)

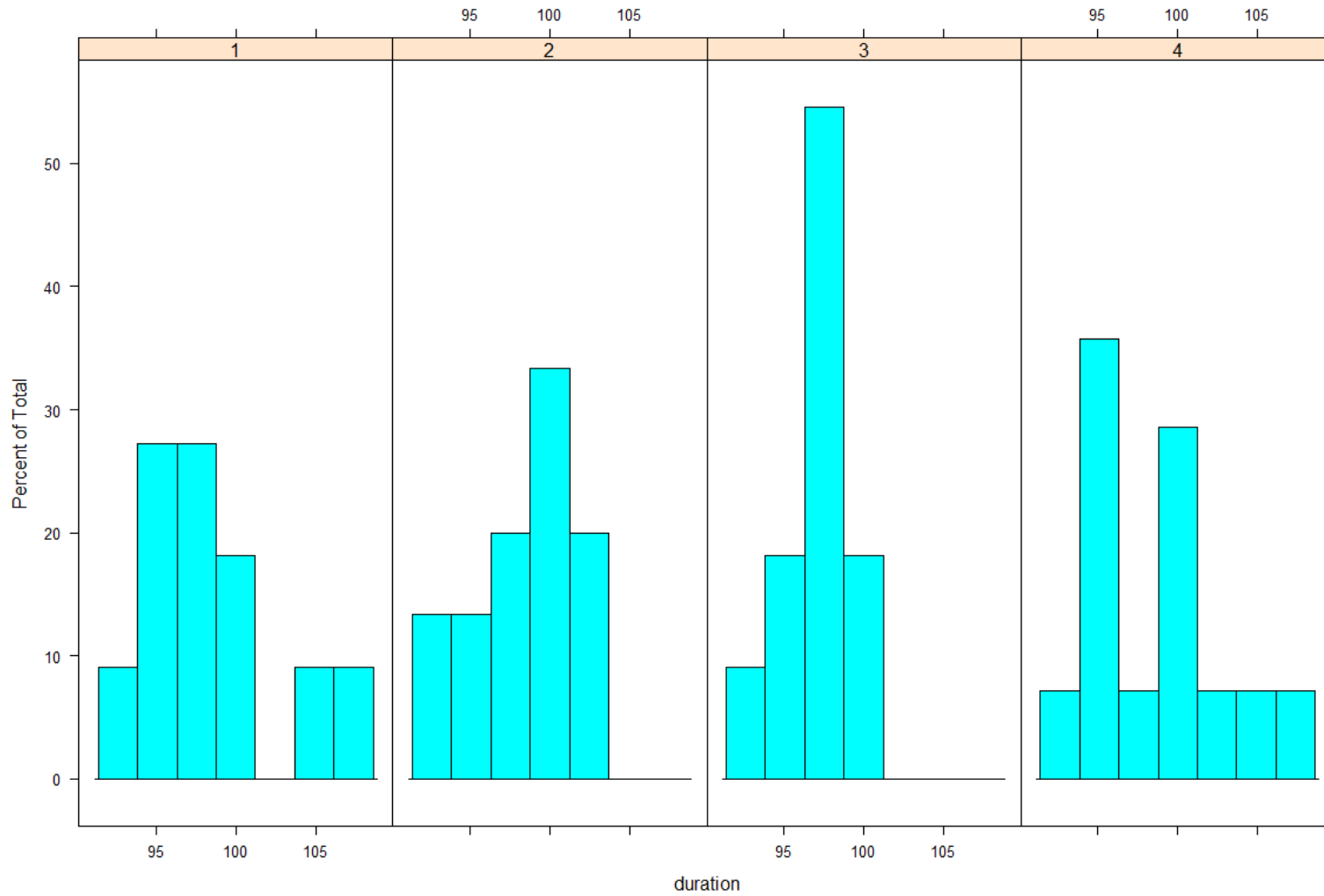


Figure 4.2: Histogram of outbreak duration (days) among four scenarios (1, 2, 3 and 4 represent sc1, sc2, sc3, and sc4, respectively)

## REFERENCES

- Abbas, T., Younus, M., Muhammad, S.A., Ijaz, M., Shakoor, A., 2014. Some Challenges to Progressive Control of Foot and Mouth Disease in Pakistan - Findings of a Pilot Survey. *Transbound. Emerg. Dis.* 61, 81–85. <https://doi.org/10.1111/tbed.12008>
- Ahmed, Z., Pauszek, S.J., Ludi, A., LaRocco, M., Khan, E. -u.-H., Afzal, M., Arshed, M.J., Farooq, U., Arzt, J., Bertram, M., Brito, B., Naeem, K., Abubakar, M., Rodriguez, L.L., 2018. Genetic diversity and comparison of diagnostic tests for characterization of foot-and-mouth disease virus strains from Pakistan 2008-2012. *Transbound. Emerg. Dis.* 65, 534–546. <https://doi.org/10.1111/tbed.12737>
- Anjum, R., Hussain, M., Zahoor, A.B., Irshad, H., Farooq, U., 2006. Epidemiological analyses of foot and mouth disease in Pakistan. *Int. J. Agric. Biol.* 8.
- Bates, T.W., Thurmond, M.C., Carpenter, T.E., 2003a. Description of an epidemic simulation model for use in evaluating strategies to control an outbreak of foot-and-mouth disease. *Am. J. Vet. Res.* 64, 195–204. <https://doi.org/10.2460/ajvr.2003.64.195>
- Bates, T.W., Thurmond, M.C., Carpenter, T.E., 2003b. Results of epidemic simulation modeling to evaluate strategies to control an outbreak of foot-and-mouth disease. *Am. J. Vet. Res.* 64, 205–210. <https://doi.org/10.2460/ajvr.2003.64.205>
- Brooks-Pollock, E., de Jong, M.C.M., Keeling, M.J., Klinkenberg, D., Wood, J.L.N., 2015. Eight challenges in modelling infectious livestock diseases. *Epidemics* 10, 1–5. <https://doi.org/10.1016/J.EPIDEM.2014.08.005>
- Cunliffe, H., 1964. Observations on the duration of immunity in cattle after experimental infection with

- Foot-and-Mouth Disease virus. *Cornell Vet.* 54, 501–10.
- Doel, T., 1996. Natural and vaccine-induced immunity to foot and mouth disease: the prospects for improved vaccines. *Rev. sci. tech. Off. int. Epiz* 15, 883–911.
- Dorjee, S., Revie, C.W., Poljak, Z., McNab, W.B., Sanchez, J., 2016. One-Health Simulation Modelling: A Case Study of Influenza Spread between Human and Swine Populations using *NAADSM*. *Transbound. Emerg. Dis.* 63, 36–55. <https://doi.org/10.1111/tbed.12215>
- Dürr, S., Fasel-Clemenz, C., Thür, B., Schwermer, H., Doherr, M.G., Dohna, H. zu, Carpenter, T.E., Perler, L., Hadorn, D.C., 2014. Evaluation of the benefit of emergency vaccination in a foot-and-mouth disease free country with low livestock density. *Prev. Vet. Med.* 113, 34–46. <https://doi.org/10.1016/J.PREVETMED.2013.10.015>
- FAO, OIE, 2016. Foot and mouth disease vaccination and post-vaccination monitoring: Guidelines. Food and Agriculture Organization of the United Nations, Rome, Italy, and World Organization for Animal Health, Paris, France.
- Farooq, U., Ahmed, Z., Naeem, K., Bertram, M., Brito, B., Stenfeldt, C., Pauszek, S.J., LaRocco, M., Rodriguez, L., Arzt, J., 2018. Characterization of naturally occurring, new and persistent subclinical foot-and-mouth disease virus infection in vaccinated Asian buffalo in Islamabad Capital Territory, Pakistan. *Transbound. Emerg. Dis.* 65, 1836–1850. <https://doi.org/10.1111/tbed.12963>
- Farooq, U., Irshad, H., Ullah, A., Latif, A., Zahur, A.B., Naeem, K., Ahmed, Z., Rodriguez, L.L., 2017a. Sero-prevalence of foot-and-mouth disease in small ruminants of Pakistan. *J. Anim. Plant Sci.* 27, 1197–1201.
- Farooq, U., Naeem, K., Zahur, A.B., Khan, M.A., Sidique, U., 2017b. Foot-and-mouth disease outbreaks investigations at Sindh, Punjab and Islamabad, Pakistan during the year 2012-2013. *Int. J. Biosci.*



11, 346–356. <https://doi.org/10.12692/ijb/11.5.346-356>

Farooq, U., Naeem, K., Zahur, A.B., Khan, M.A., Sidique, U., Qureshi, S., 2017c. Epidemiological analysis and economic impact assessment of foot-and-mouth disease at Landhi dairy colony Karachi. *Asian J. Agric. Biol.* 5, 7–14.

Farooq, U., Ullah, A., Irshad, H., Latif, A., Naeem, K., Zahur, A. Bin, Ahmad, Z., Rodriguez, L.L., 2016. Seroprevalence of foot-and-mouth disease in large ruminants in periurban dairy farms near Islamabad, Pakistan. *Asian Biomed.* 10, 123–127. <https://doi.org/10.5372/1905-7415.1002.472>

Ferguson, N.M., Donnelly, C.A., Anderson, R.M., 2001. Transmission intensity and impact of control policies on the foot and mouth epidemic in Great Britain. *Nature* 413, 542–548.  
<https://doi.org/10.1038/35097116>

Ferrari, G., Tasciotti, L., Khan, E., Kiani, A., 2014. Foot-and-Mouth Disease and Its Effect on Milk Yield: An Economic Analysis on Livestock Holders in Pakistan. *Transbound. Emerg. Dis.* 61, e52–e59.  
<https://doi.org/10.1111/tbed.12072>

Gale, S.B., Miller, G.Y., Eshelman, C.E., Wells, S.J., Ave, G., 2015. Epidemic simulation of a foot and mouth disease outbreak in Minnesota. *Rev. Sci. Tech. Off. Int. Epiz* 34.

Garner, M., Beckett, S., 2005. Modelling the spread of foot-and-mouth disease in Australia. *Aust. Vet. J.* 83, 758–766. <https://doi.org/10.1111/j.1751-0813.2005.tb11589.x>

Garner, M.G., Bombardieri, N., Cozens, M., Conway, M.L., Wright, T., Paskin, R., East, I.J., 2016. Estimating Resource Requirements to Staff a Response to a Medium to Large Outbreak of Foot and Mouth Disease in Australia. *Transbound. Emerg. Dis.* 63, e109–e121.  
<https://doi.org/10.1111/tbed.12239>

Gleeson, L.J., 2002. A review of the status of foot and mouth disease in South-East Asia and approaches

- to control and eradication. *Rev. Sci. Tech.* 21, 465–75.
- Guitian, J., Pfeiffer, D., 2006. Should we use models to inform policy development? *Vet. J.* 172, 393–395.  
<https://doi.org/10.1016/j.tvjl.2006.03.001>
- 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. *Prev. Vet. Med.* 82, 176–197. <https://doi.org/10.1016/J.PREVETMED.2007.05.019>
- Hui, W., Gel, Y.R., Gastwirth, J.L., 2008. Lawstat: An R package for law, public policy and biostatistics. *J. Stat. Softw.* 28. <https://doi.org/10.18637/jss.v028.i03>
- Hunter, P., 1998. Vaccination as a means of control of foot-and-mouth disease in sub-saharan Africa. *Vaccine* 16, 261–264. [https://doi.org/10.1016/S0264-410X\(97\)00170-9](https://doi.org/10.1016/S0264-410X(97)00170-9)
- Jamal, S.M., Ahmed, S., Hussain, M., Ali, Q., 2010. Status of foot-and-mouth disease in Pakistan. *Arch. Virol.* 155, 1487–1491. <https://doi.org/10.1007/s00705-010-0732-y>
- Jamal, S.M., Belsham, G.J., 2013. Foot-and-mouth disease: past, present and future. *Vet. Res.* 44, 116.  
<https://doi.org/10.1186/1297-9716-44-116>
- Jemberu, W.T., Mourits, M.C.M., Woldehanna, T., Hogeveen, H., 2014. Economic impact of foot and mouth disease outbreaks on smallholder farmers in Ethiopia. *Prev. Vet. Med.* 116, 26–36.  
<https://doi.org/10.1016/J.PREVETMED.2014.06.004>
- Kao, R.R., 2002. The role of mathematical modelling in the control of the 2001 FMD epidemic in the UK. *Trends Microbiol.* 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. Biol. Sci.* 272, 1195–202.

<https://doi.org/10.1098/rspb.2004.3046>

Keeling, M.J., Woolhouse, M.E., 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* (80-. ). 294, 813–817.  
<https://doi.org/10.1126/science.1065973>

Knight-Jones, T.J., Bulut, A., Gubbins, S., Stärk, K.D., Pfeiffer, D., Sumption, K., Paton, D., 2015. Randomised field trial to evaluate serological response after foot-and-mouth disease vaccination in Turkey. *Vaccine* 33, 805–11. <https://doi.org/10.1016/j.vaccine.2014.12.010>

Knight-Jones, T.J.D., Gubbins, S., Bulut, A.N., Stärk, K.D.C., Pfeiffer, D.U., Sumption, K.J., Paton, D.J., 2016a. Mass vaccination, immunity and coverage: modelling population protection against foot-and-mouth disease in Turkish cattle. *Sci. Rep.* 6, 22121. <https://doi.org/10.1038/srep22121>

Knight-Jones, T.J.D., Robinson, L., Charleston, B., Rodriguez, L.L., Gay, C.G., Sumption, K.J., Vosloo, W., 2016b. Global Foot-and-Mouth Disease Research Update and Gap Analysis: 2 - Epidemiology, Wildlife and Economics. *Transbound. Emerg. Dis.* 63, 14–29. <https://doi.org/10.1111/tbed.12522>

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? *Prev. Vet. Med.* 112, 161–173.  
<https://doi.org/10.1016/J.PREVETMED.2013.07.013>

Mardones, F., Perez, A., Sanchez, J., Alkhamis, M., Carpenter, T., 2010a. Parameterization of the duration of infection stages of serotype O foot-and-mouth disease virus: an analytical review and meta-analysis with application to simulation models. *Vet. Res.* 41, 45.  
<https://doi.org/10.1051/vetres/2010017>

Mardones, F., Perez, A., Sanchez, J., Alkhamis, M., Carpenter, T., 2010b. Parameterization of the

duration of infection stages of serotype O foot-and-mouth disease virus: an analytical review and meta-analysis with application to simulation models. *Vet. Res.* 41, 45.

<https://doi.org/10.1051/vetres/2010017>

McReynolds, S.W., Sanderson, M.W., Reeves, A., Hill, A.E., 2014. Modeling the impact of vaccination control strategies on a foot and mouth disease outbreak in the Central United States. *Prev. Vet. Med.* 117, 487–504. <https://doi.org/10.1016/J.PREVETMED.2014.10.005>

Moonen, P., Jacobs, L., Crienen, A., Dekker, A., 2004. Detection of carriers of foot-and-mouth disease virus among vaccinated cattle. *Vet. Microbiol.* 103, 151–160.

<https://doi.org/10.1016/j.vetmic.2004.07.005>

Morris, R.S., Sanson, R.L., Stern M.W., Stevenson M., Wilesmith J.W., 2002. Decision-support tools for foot and mouth disease control. *Rev. sci. tech. Off. int. Epiz.* 21, 557–567.

<https://doi.org/10.20506/rst.21.3.1363>

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. *Vet. Rec.* 149, 137–44. <https://doi.org/10.1136/vr.149.5.137>

NAADSM Development Team, 2012. WH 0.9.7: A Simulation Model for With-in Unit Disease Dynamics.

Animal Population Health Institute, Department of Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State university, Fort Collins, Colorado USA.

Navid, M.T., Farooq, U., Latif, A., Awais, M.M., Anwar, M.I., Akhtar, M., Zahur, A.B., 2018. Prevalence of foot and mouth disease virus in apparently healthy buffaloes brought to Islamabad slaughterhouse in Pakistan. *Trop. Biomed.* 35, 161–167.

Paton, D.J., Sumption, K.J., Charleston, B., 2009. Options for control of foot-and-mouth disease:

knowledge, capability and policy. *Philos. Trans. R. Soc. Lond. B. Biol. Sci.* 364, 2657–67.

<https://doi.org/10.1098/rstb.2009.0100>

Pendell, D.L., Marsh, T.L., Coble, K.H., Lusk, J.L., Szmania, S.C., 2015. Economic Assessment of FMDv Releases from the National Bio and Agro Defense Facility. *PLoS One* 10, e0129134.

<https://doi.org/10.1371/journal.pone.0129134>

Pomeroy, L.W., Bansal, S., Tildesley, M., Moreno-Torres, K.I., Moritz, M., Xiao, N., Carpenter, T.E., Garabed, R.B., 2017. Data-Driven Models of Foot-and-Mouth Disease Dynamics: A Review.

*Transbound. Emerg. Dis.* 64, 716–728. <https://doi.org/10.1111/tbed.12437>

R Core Team, 2017. R: A language and environment for statistical computing.

Roche, S.E., Garner, M.G., Wicks, R.M., East, I.J., de Witte, K., 2014. How do resources influence control measures during a simulated outbreak of foot and mouth disease in Australia? *Prev. Vet. Med.* 113, 436–446. <https://doi.org/10.1016/J.PREVETMED.2013.12.003>

Rweyemamu, M., Roeder, P., MacKay, D., Sumption, K., Brownlie, J., Leforban, Y., 2008a. Planning for the Progressive Control of Foot-and-Mouth Disease Worldwide. *Transbound. Emerg. Dis.* 55, 73–87. <https://doi.org/10.1111/j.1865-1682.2007.01016.x>

Rweyemamu, M., Roeder, P., Mackay, D., Sumption, K., Brownlie, J., Leforban, Y., Valarcher, J.-F., Knowles, N.J., Saraiva, V., 2008b. Epidemiological Patterns of Foot-and-Mouth Disease Worldwide. *Transbound. Emerg. Dis.* 55, 57–72. <https://doi.org/10.1111/j.1865-1682.2007.01013.x>

Schittkowski, K., 2002. EASY-FIT: a software system for data fitting in dynamical systems. *Struct. Multidiscip. Optim.* 23, 153–169. <https://doi.org/10.1007/s00158-002-0174-6>

Schoenbaum, M.A., Disney, W.T., 2003. Modeling alternative mitigation strategies for a hypothetical outbreak of foot-and-mouth disease in the United States. *Prev. Vet. Med.* 58, 25–52.

[https://doi.org/10.1016/S0167-5877\(03\)00004-7](https://doi.org/10.1016/S0167-5877(03)00004-7)

Schroeder, T.C., Pendell, D.L., Sandersen, M.W., McReynolds, S., 2015. Economic impact of alternative FMD emergency vaccination strategies in the midwestern United States. *J. Agric. Appl. Econ.* 47, 47–76. <https://doi.org/10.1017/aae.2014.5>

Souley Kouato, B., De Clercq, K., Abatih, E., Dal Pozzo, F., King, D., Thys, E., Marichatou, H., Saegerman, C., 2018. Review of epidemiological risk models for foot-and-mouth disease: Implications for prevention strategies with a focus on Africa. *PLoS One* 13, e0208296. <https://doi.org/10.1371/journal.pone.0208296>

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. *Prev. Vet. Med.* 109, 10–24. <https://doi.org/10.1016/J.PREVETMED.2012.08.015>

Sumption, K., Domenech, J., Ferrari, G., 2012. Progressive control of FMD on a global scale. *Vet. Rec.* 170, 637–9. <https://doi.org/10.1136/vr.e4180>

Tomassen, F.H.M., de Koeijer, A., Mourits, M.C.M., Dekker, A., Bouma, A., Huirne, R.B.M., 2002. A decision-tree to optimise control measures during the early stage of a foot-and-mouth disease epidemic. *Prev. Vet. Med.* 54, 301–324. [https://doi.org/10.1016/S0167-5877\(02\)00053-3](https://doi.org/10.1016/S0167-5877(02)00053-3)

Ullah, A., Jamal, S.M., Romey, A., Gorna, K., Kakar, M.A., Abbas, F., Ahmad, J., Zientara, S., Bakkali Kassimi, L., 2017. Genetic Characterization of Serotypes A and Asia-1 Foot-and-mouth Disease Viruses in Balochistan, Pakistan, in 2011. *Transbound. Emerg. Dis.* 64, 1569–1578. <https://doi.org/10.1111/tbed.12548>

USDA, 2013. Parameters Used to Simulate the Spread of FMD in Texas Using the North American Animal Disease Spread Model (NAADSM) for use in FMD Response Workforce Requirement Estimates. Fort

Collins, CO USA.

Wongsathapornchai, K., Salman, M.D., Edwards, J.R., Morley, P.S., Keefe, T.J., Campen, H. V., Weber, S.E., Premashthira, S., 2008. Use of epidemiologic risk modeling to evaluate control of foot-and-mouth disease in southern Thailand. *Am. J. Vet. Res.* 69, 240–251.

<https://doi.org/10.2460/ajvr.69.2.240>

Yano, T., Premashthira, S., Dejyong, T., Tangtrongsup, S., Salman, M.D., 2018. The Effectiveness of a Foot and Mouth Disease Outbreak Control Programme in Thailand 2008–2015: Case Studies and Lessons Learned. *Vet. Sci.* <https://doi.org/10.3390/vetsci5040101>

Yoon, H., Wee, S.-H., Stevenson, M.A., O’Leary, B.D., Morris, R.S., Hwang, I.-J., Park, C.-K., Stern, M.W., 2006. Simulation analyses to evaluate alternative control strategies for the 2002 foot-and-mouth disease outbreak in the Republic of Korea. *Prev. Vet. Med.* 74, 212–225.

<https://doi.org/10.1016/J.PREVETMED.2005.12.002>

Zagmutt, F.J., Schoenbaum, M.A., Hill, A.E., 2016. The Impact of Population, Contact, and Spatial Heterogeneity on Epidemic Model Predictions. *Risk Anal.* 36, 939–953.

<https://doi.org/10.1111/risa.12482>

## CHAPTER 5: CONTROL OF FOOT-AND-MOUTH DISEASE IN ENDEMIC REGIONS: CONCLUSIONS, LIMITATIONS AND RECOMMENDATIONS

This chapter aims to summarize our observations on the application of simulation models as a tool for the control of foot-and-mouth disease (FMD) in endemic settings with a specific emphasis on the limitations of our work and recommendations for future directions.

Several tools such as simulation modeling, risk analysis, and epidemiologic studies are available to assist in decision making processes for infectious animal disease control. Simulation modeling is a relatively cheaper and quicker tool to evaluate effectiveness of alternate mitigation strategies of infectious animal disease control. Although other simulation modeling approaches can be considered, our focus through this dissertation, has been on spatially-explicit stochastic simulation models (SESS). The advantage of using SESS models is that they can incorporate stochasticity and spatial relationships when mimicking the epidemiologic cycle of infectious animal diseases.

We have used foot-and-mouth (FMD) as an example of an infectious animal disease to demonstrate the application of SESS models in disease endemic settings. We have, however, recognized that several models exist to simulate incursion of FMD in disease-free countries but not for FMD-endemic countries. The SESS models require accurate data on the location and population of individual livestock holdings. Therefore, reliable field data are essential in our attempt to build and evaluate our SESS model. Through this dissertation, we were able to generate a first-ever dataset on the location and population of livestock holdings in certain areas of Pakistan and Thailand. Moreover, we have built a SESS modeling framework for infectious animal diseases in endemic regions. Our modeling framework is called the “Simulation Model for Infectious Animal Diseases in Endemic regions”.



Although we attempted to select FMD-endemic countries with available reliable outbreaks data, specific data on the location and population of individual livestock holdings were not available from Pakistan and Thailand. In absence of such data, approaches that integrate geographic information system can be used to synthesize these data based on a set of assumptions and assigning weights to geographic layers. A major hurdle faced in synthesizing data on the location and population of livestock holdings was the selection of surrogate variables such as croplands, open lands, urban areas, slope, which influence the presence or absence of livestock holdings. We sought the opinion of conveniently selected veterinarians from Pakistan and Thailand to estimate weights for different geographic features and land cover types to determine suitable locations for livestock holdings. We, however, acknowledge that veterinarians are only one of the several professionals such as natural resource scientists, agricultural experts, who could have contributed to approach with an expert opinion on animal agriculture. The simulated dataset on the location and population should be validated, which is impossible in the absence of actual field data. We had access to a very small dataset on the location and population of individual livestock holdings from Pakistan and Thailand, which could not be used for validation. These data were, however, used to inform the creation of geospatial probability surface to identify suitable locations for livestock holdings. The future work should attempt to have a large dataset on the location and population of true holdings to facilitate validation.

Data on the spatial prevalence of FMD are critical to the application of SESS models in endemic countries, and these data can be gleaned from sources such as cross-sectional studies, outbreak reports, national database, and reported outbreaks to OIE. These data are used to assign an initial disease state to holdings at the start of the simulation. In endemic settings, prevalence data is often lacking due to more focus on outbreaks. In the absence of prevalence data, we used outbreaks data as numerator and population data as a denominator to estimate the prevalence. We acknowledge that outbreaks reported

do not represent the true number of infected holdings in a specific area during a specified time period as there are concerns of under-reporting

Future work should focus on strengthening monitoring and surveillance system to obtain production-type specific and regional data on FMD prevalence for use in SESS models and beyond. Efforts should also be made to estimate contact networks from expert opinions using the Delphi approach. Data on contact networks, distance distributions and any associated delays is required in SESS models to simulate direct and indirect spread. Data on the estimates of the effectiveness of movements restrictions on contact spread should be gleaned from expert opinion through a Delphi approach. The future work should focus on the selection of a large number of experts with expertise in FMD epidemiology and vaccination to glean estimates for the incorporation of vaccination parameters in SESS models. Additionally, a user interface should be added to SMIAD-ER to allow epidemiologists and models from endemic settings to use SMIAD-ER as tool for FMD control. The simulation engine of SMIAD-ER should also be made efficient to allow models to incorporate more complexity and ease in computations.

Assumptions of the models should be well-documented, and these assumptions should be considered when interpreting the findings of the SESS models. The outputs and recommendations from this dissertation should be interpreted and taken for policy consideration in line with the assumptions. In our opinion, since our demonstration was based on the opinion of a single expert veterinarian from Pakistan, caution should be made when considering our findings for policy decisions. This demonstration will help in increasing the confidence of veterinarians in endemic countries on the usefulness of models in FMD control which will in turn facilitate gathering more data for model parameterization.

Finally, the control of FMD in endemic settings will help improve livestock health, provide economic gains for producers, help alleviate poverty and hunger, which can and will complement efforts to attain Sustainable Development Goals and the 2030 Agenda.

APPENDICES

Chapter 1

*PRISMA checklist*

Table 1.2: PRISMA Checklist

Title	
Title	The title of the paper identifies it as a systematic review
Abstract	
Abstract	Included
Introduction	
Rationale	Described
Objectives	Explicitly stated
Methods	
Protocol and registration	No approved and registered protocol exists However, it follows PRISMA protocol (PVM publishes systematic review and meta-analysis without approved and registered protocol)
Eligibility Criteria	I did specify study characteristics (language, document type, disease, simulation modeling, spatially explicit, stochastic)
Information sources	Rationale List databases, timespan and date searched
Search	Described the search strategy
Study selection	Screening criteria
Data collection process	Use of MS Excel and tabulation
Data items	List of variables for which data was sought Assessment of SESS models and data extraction
Risk of bias in individual studies	N/A, not a meta-analysis
Summary measures	N/A, not a meta-analysis
Synthesis of results	Qualitative synthesis based on assessment of SESS models
Risk of bias across studies	N/A, not a meta-analysis
Additional analyses	N/A, not a meta-analysis
Results	
Study selection	# identified, # duplicates, # screened, # assessed for eligibility, # excluded (reasons), # included in qualitative synthesis. Flow diagram Table 1.1
Study characteristics	SESS characteristics, Table 2
Risk of bias within studies	N/A
Results of individual studies	Table 2
Synthesis of results	N/A, not a meta-analysis
Risk of bias across studies	N/A, not a meta-analysis
Additional analysis	N/A, not a meta-analysis

Discussion	
Summary of evidence	Identified three key components of missing in the assessed models because of underlying assumptions and reasons behind the design (application in free-settings) Provided a framework for model adaptation
Limitations	Described that only assessed SESS models used for FMD Could be more models (not SESS, not published original research, not used for FMD)
Conclusions	Described
Funding	
Funding	No specific funding

## Chapter 2

This appendix contains the supporting material for the draft manuscript titled “estimating the location and population of livestock holdings in developing countries for spatial disease spread models.”

### *List of provinces by region, Thailand*

<b>Central</b>	<b>Northeastern</b>	<b>Northern</b>
Ang Thong	Amnat Charoen	Chiang Mai
Bangkok	Bueng Kan	Chiang Rai
Chachoengsao	Buri Ram	Kamphaeng Phet
Chai Nat	Chaiyaphum	Lampang
Chanthaburi	Kalasin	Lamphun
Chon Buri	Khon Kaen	Mae Hong Son
Kanchanaburi	Loei	Nakhon Sawan
Lop Buri	Maha Sarakham	Nan
Nakhon Nayok	Mukdahan	Phayao
Nakhon Pathom	Nakhon Phanom	Phetchabun
Nonthaburi	Nakhon Ratchasima	Phichit
Pathum Thani	Nong Bua Lam Phu	Phitsanulok
Phetchaburi	Nong Khai	Phrae
Phra Nakhon Si Ayutthaya	Roi Et	Sukhothai
Prachin Buri	Sakon Nakhon	Tak
Prachuap Khiri Khan	Si Sa Ket	Uthai Thani
Ratchaburi	Surin	Uttaradit
Rayong	Ubon Ratchathani	
Sa Kaeo	Udon Thani	
Samut Prakan	Yasothon	
Samut Sakhon		
Samut Songkhram		
Saraburi		
Sing Buri		
Suphan Buri		
Trat		

Figure 2.16: List of provinces by region, Thailand

## *Description of datasets used*

### 2.7: Description of datasets used

Dataset	Description	Usage
Administrative boundary	Boundaries for different administrative levels in Pakistan and Thailand	Used as the base map, for processing extent and other geoprocessing
Waterbodies	Waterbodies in Pakistan and Thailand	Used to mask out the water bodies from probability surface
Road network	Road network for different road types in Pakistan and Thailand	Used to make probability buffers around different highway types
Elevation	This dataset provides the elevation for Pakistan and Thailand	This dataset was used to calculate slope to be included in the probability surface
Landcover	Different land cover types in Pakistan and Thailand	Creation of geospatial probability surface
Expert-based opinions	With anonymous veterinarians in Pakistan and Thailand	To aid in determining arbitrary upper bound for herd-class 5 To discuss probability buffers around different geographic features
Survey questionnaire	Anonymous veterinarians from Pakistan and Thailand responding to	To seek weights for different geographic features for animal agriculture in Pakistan and Thailand
Empirical holding locations	Physical location of holdings with associated animal population	To aid in the creation of probability buffers around different highway types To help in the placement of random holdings on probability surface

## *Geoprocessing*

### *Projections and coordinate system*

For the creation of geospatial probability surfaces, the following projections and coordinate system were used:

- Punjab, Pakistan: Kalianpur 1962/India Zone I (EPSG: 24376)
- Sindh, Pakistan: Kalianpur 1962/India Zone IIa (EPSG: 24377)
- All regions, Thailand: Indian 1954/UTM Zone 47N (EPSG: 23947)

### *Administrative Boundary:*

Pakistan: The administrative boundary for provinces was used and “select by attribute” tool was used to create boundary files for Punjab (Punjab and ICT) and Sindh.

Thailand: Using the list of provinces in each of four regions of Thailand (available from 2013 agricultural census), the “select by attribute tool” was used to create boundary file for each region. Each regional file was dissolved to have single feature polygon.

These layers were projected accordingly.

### *Waterbodies:*

The country-level dataset on permanent waterbodies was clipped to the province/region and was projected accordingly.

### *Road networks:*

The country-level dataset on the road network was first clipped to the province/region of interest. Secondly, the roads were reclassified as below:

```
{"main": ["motorway", "motorway_link", "trunk", "trunk_link"],
```



"primary": ["primary", "primary\_link"],

"smaller": ["secondary", "secondary\_link", "tertiary", "tertiary\_link"]}

Finally, those roads projected accordingly.

#### *Elevation:*

The country-level elevation data was clipped to the province/region of interest. Then, the Slope tool from the Spatial Analyst tools in ArcGIS 10.x was used to calculate the percent slope. It was used to calculate slope %. The slope was reclassified as 0 (>10%) and 1 ( $\leq$ 10%). The slope raster was, then, projected accordingly.

#### *Land cover:*

The global land cover data was geoprocesed to the province/region of interest. Then, it was reclassified as:

- Open lands = open/barren lands/sparse vegetative
- Croplands = croplands/grasslands/woody savannas, natural vegetation/open-closed shrublands/savanna
- Urban = urban and built-ups
- Other = all other land cover types (of no interest)

The reclassified, landcover rasters were then, projected accordingly. Note: All datasets were resampled to the cell size of 100 m.

Table 2.8: Final holdings (%) on probability surface

Country	Livestock	Herd- class	Probability Zone		
			Low	Medium	high
Pakistan	Bovines	1	12.0	0.0	88.0
		2	0.0	64.0	36.0
		3	3.5	24.0	72.5
		4	0.0	20.0	80.0
		5	0.0	40.0	60.0
Thailand	Dairy	1	3.36	27.52	69.13
		2	2.78	34.72	62.50
		3	0	38.89	61.11
		4	0	0	100.00
		5	9.09	63.64	27.27
	Beef	1	0	80.77	19.23
		2	0	100.00	0
		3	0	0	100.00
		4	0	0	100.00
		5	12.50	62.50	25.00
	Swine	1	33.33	33.33	33.33
		2	0.00	0	100.00
		3	0.00	0	0.00
		4	0.00	25.00	75.00
		5	10.00	60.00	30.00
Buffalo	1	0	90.48	9.52	
	2	0.00	100.00	0	
	3	33.00	33.00	34.00	
	4	0	0.00	100.00	
	5	12.50	62.50	25.00	

Table 2.9: Processing order and the minimum distance between holdings

Country	Region	Herd Class	Livestock	Minimum distance (m)
	All		5	750
			4	750
Pakistan			3 Bovines	100
			2	100
			1	15
			5 Dairy	500
			5 Beef	500
			5 Swine	500
			5 Buffalo	200
			4 Dairy	250
			4 Beef	250
			4 Swine	250
			4 Buffalo	100
			3 Dairy	200
			3 Beef	200
Thailand	All		3 Swine	200
			3 Buffalo	50
			2 Dairy	100
			2 Beef	100
			2 Swine	100
			2 Buffalo	10
			1 Dairy	50
			1 Beef	50
			1 Swine	50
			1 Buffalo	5

Table 2.10: Holdings successfully placed on geospatial probability surface

Country	Region	Species	Herd class	Original holdings	Success
Pakistan	Punjab	Bovines	1	7,265,425	93.89%
			2	271,459	95.55%
			3	41,574	97.19%
			4	19,220	97.77%
			5	13,986	95.35%
	Sindh	Bovines	1	2,162,006	76.05%
			2	195,776	99.93%
			3	29,917	92.99%
			4	12,444	99.94%
			5	9,150	99.97%
		Dairy	1	9,058	94.16%
			2	1,155	91.95%
			3	128	86.72%
			4	3	100.00%
			5	1	0.00%
Thailand	Central	Beef	1	45,351	90.21%
			2	1,412	96.03%
			3	441	80.27%
			4	32	100.00%
			5	16	100.00%
	Northeastern	Swine	1	11,394	97.24%
			2	725	88.28%
			3	691	75.69%
			4	340	99.71%
			5	967	91.42%
		Buffalo	1	2,141	81.64%
			2	693	98.12%
			3	458	83.62%
			4	63	100.00%
			5	11	100.00%
Northeastern	Dairy	1	5,001	81.88%	
		2	454	97.14%	
		3	51	98.04%	
		4	1	0.00%	
		5	N/A	N/A	
	Beef	1	385,406	99.34%	
		2	378	82.54%	
		3	87	93.10%	
		4	9	100.00%	
		5	11	100.00%	
Swine	1	68,991	99.93%		

		2	1,437	99.86%
		3	627	100.00%
		4	201	100.00%
		5	522	99.81%
		1	149,880	99.05%
		2	4,757	81.94%
	Buffalo	3	822	99.88%
		4	55	100.00%
		5	18	100.00%
	Dairy	1	1,632	93.20%
		2	274	93.43%
		3	29	96.55%
		4	1	0.00%
		5	2	100.00%
		1	47,807	96.13%
		2	991	89.00%
	Beef	3	128	95.31%
		4	12	91.67%
		5	48	97.92%
Northern		1	49,294	97.31%
		2	1,325	97.89%
	Swine	3	618	99.19%
		4	127	97.64%
		5	492	94.92%
		1	10,138	93.08%
		2	1,999	98.70%
	Buffalo	3	782	94.50%
		4	94	96.81%
		5	10	100.00%

Probability surfaces

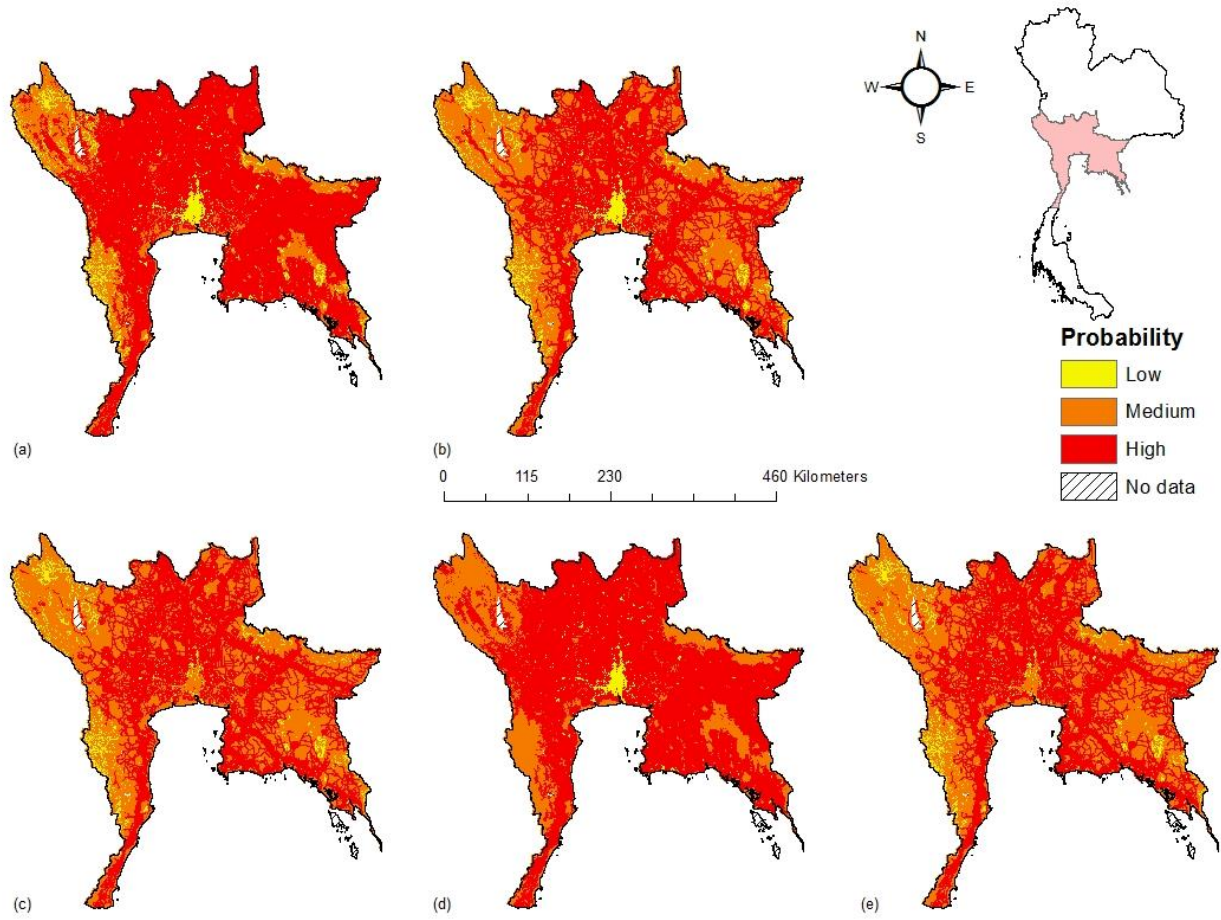


Figure 2.17: Geospatial probability surface for dairy cattle in Central, Thailand where (a) to (e) represent herd-class 1 through 5, respectively

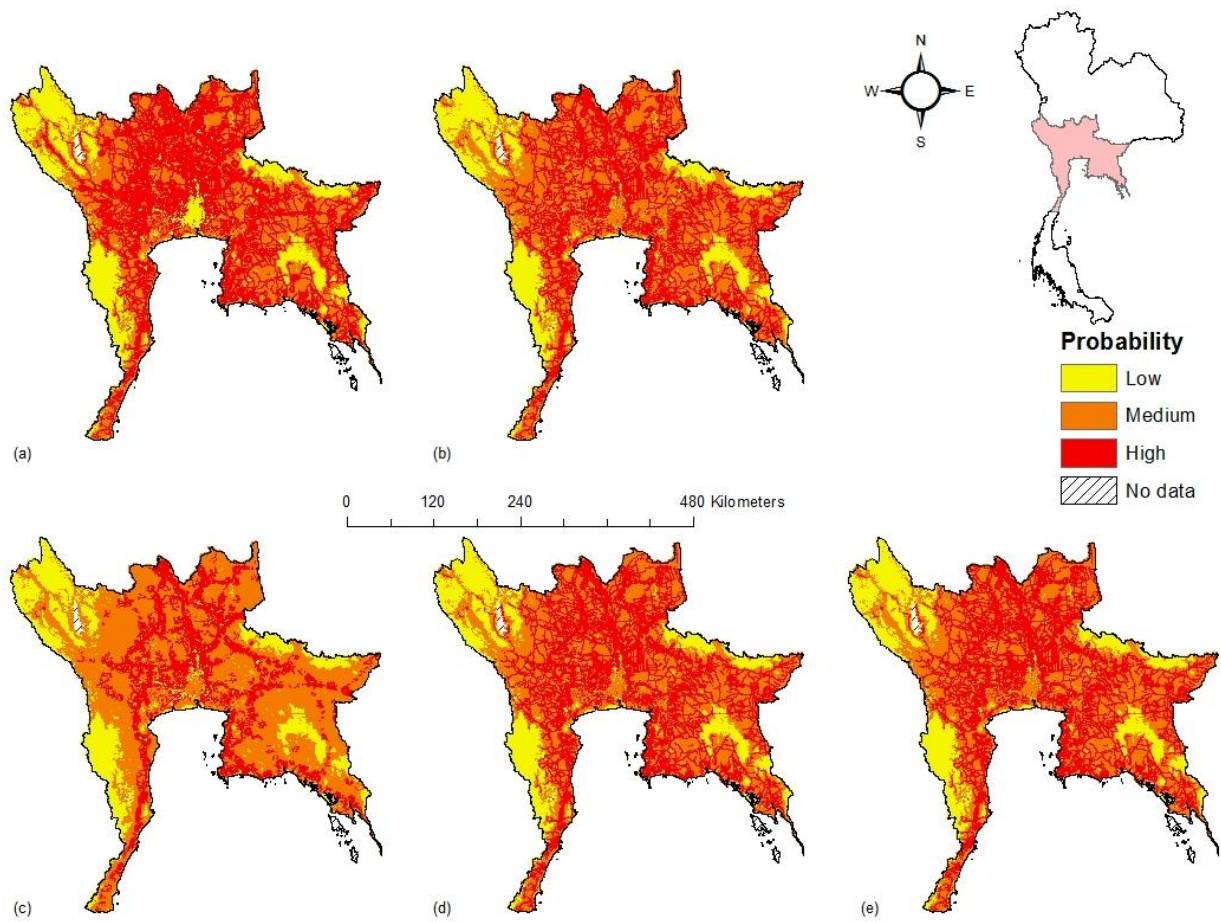


Figure 2.18: Geospatial probability surface for beef cattle in Central, Thailand where (a) to (e) represent herd-class 1 through 5, respectively

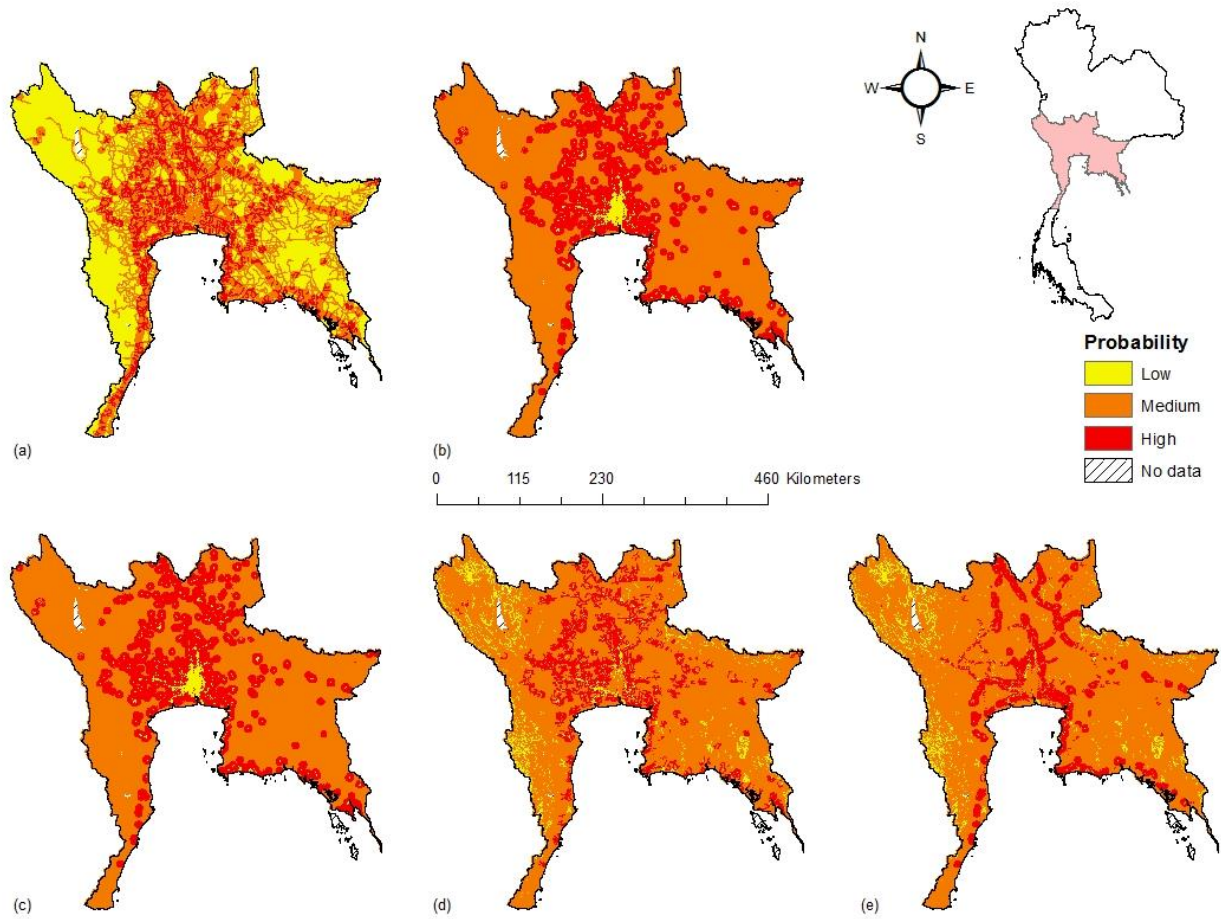


Figure 2.19: Geospatial probability surface for swine in Central, Thailand where (a) to (e) represent herd-class 1 through 5, respectively



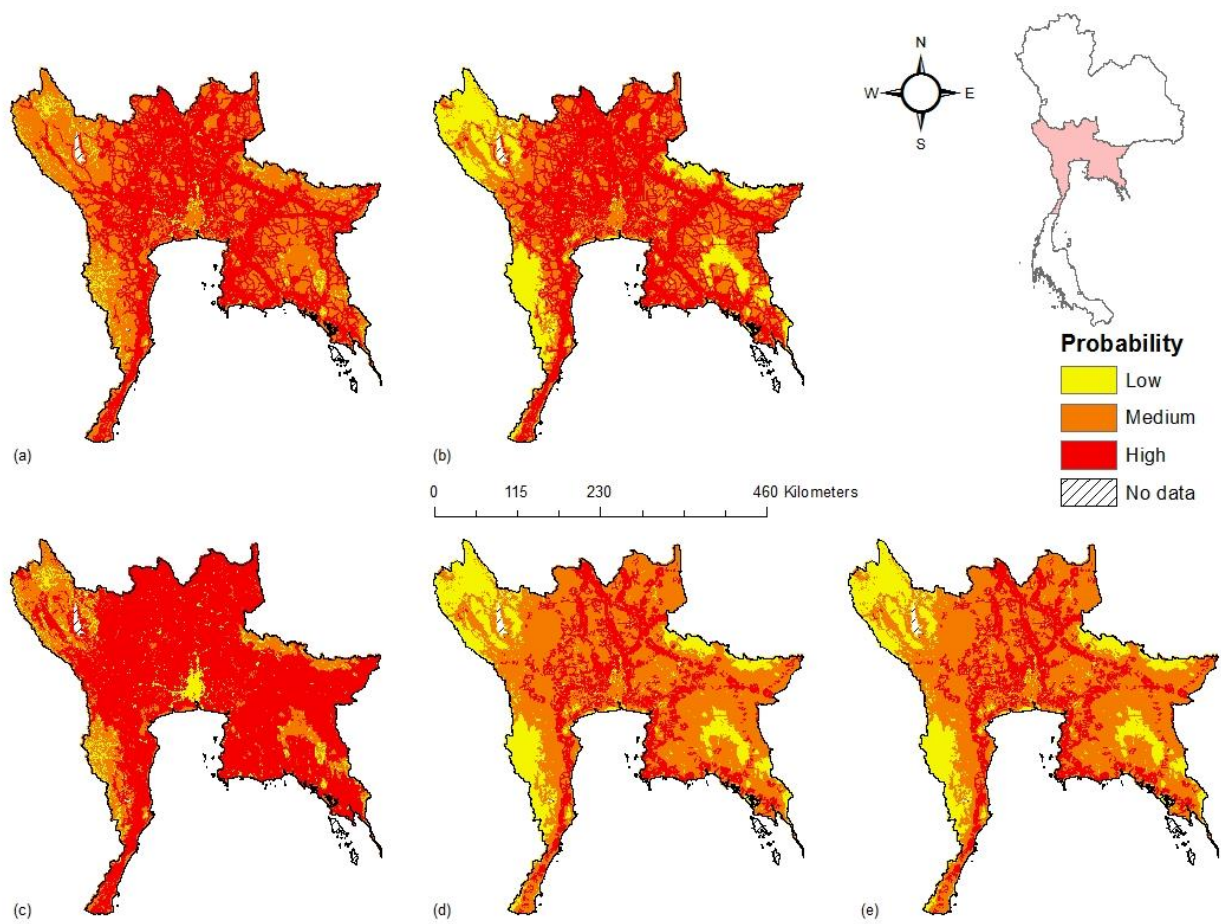


Figure 2.20: Geospatial probability surface for buffalo in Central, Thailand where (a) to (e) represent herd-class 1 through 5, respectively

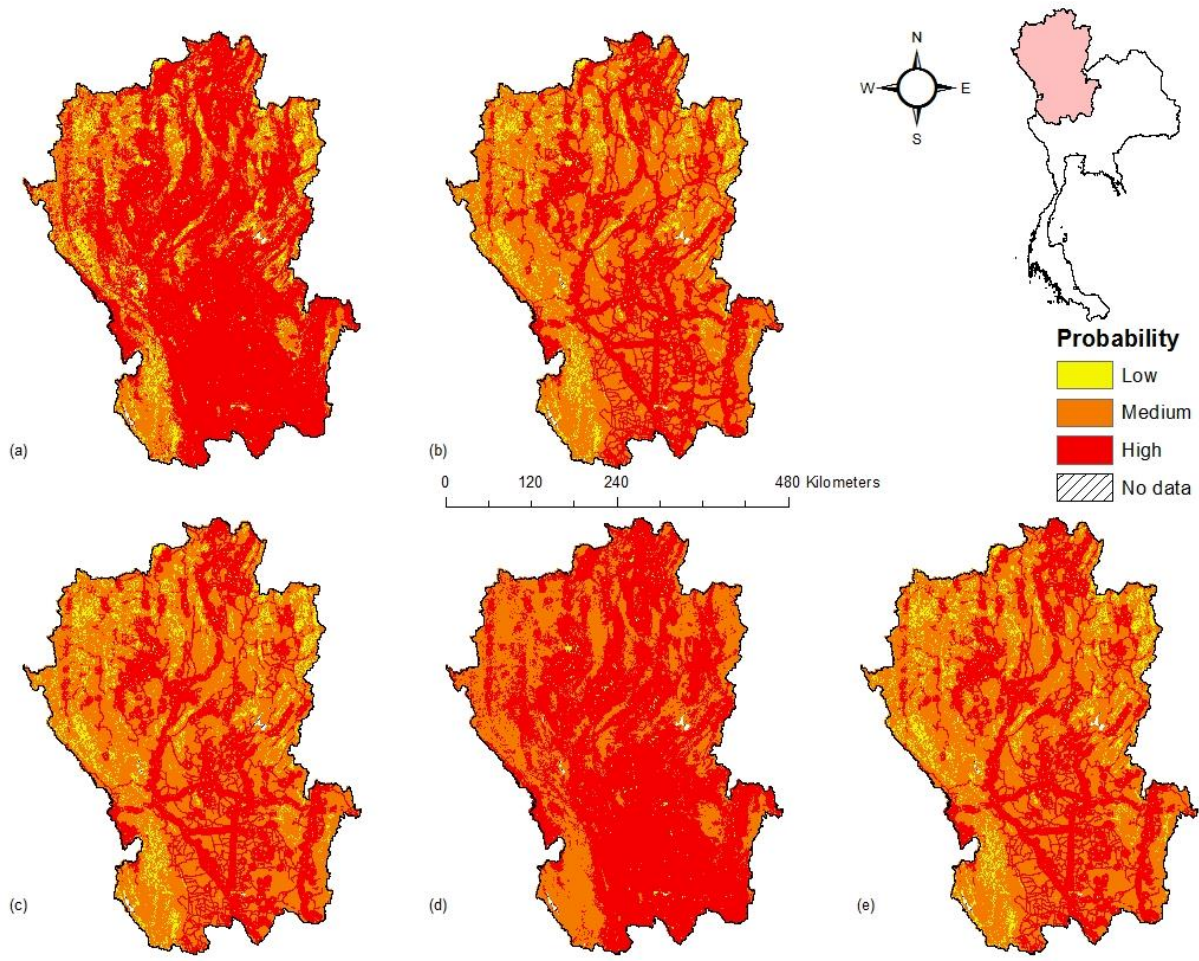


Figure 2.21: Geospatial probability surface for dairy cattle in Northern, Thailand where (a) to (e) represent herd-class 1 through 5, respectively

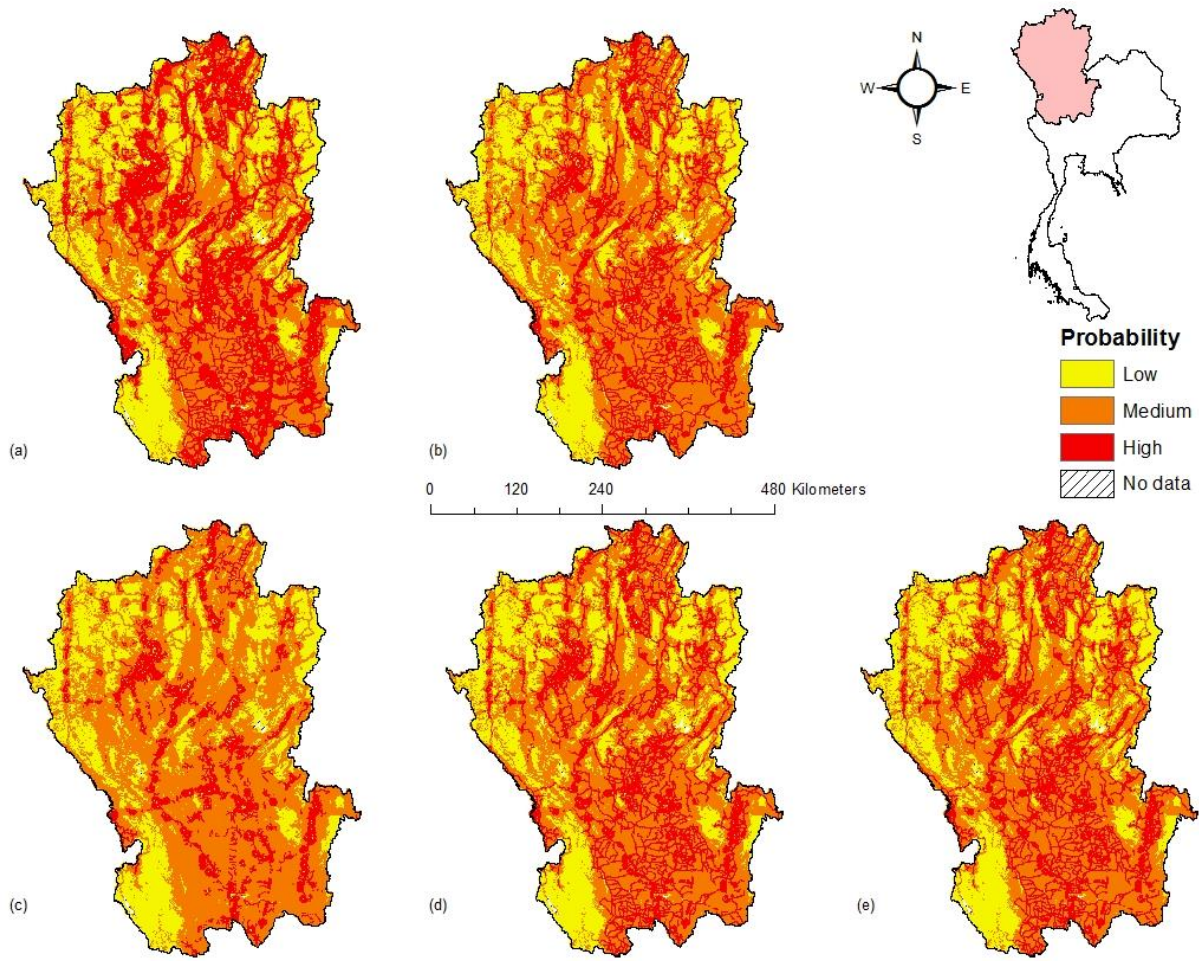


Figure 2.22: Geospatial probability surface for beef cattle in Northern, Thailand where (a) to (e) represent herd-class 1 through 5, respectively

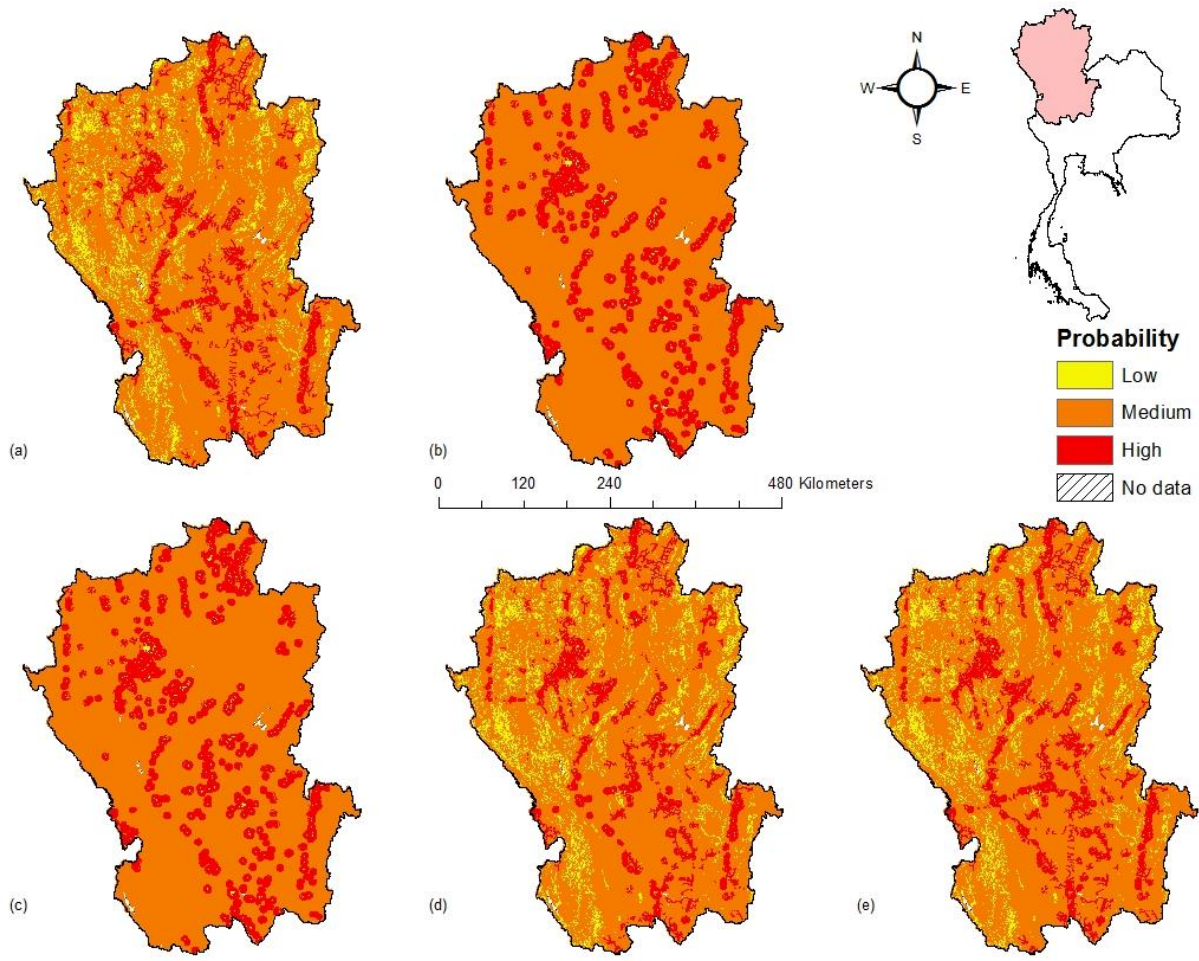


Figure 2.23: Geospatial probability surface for swine in Northern, Thailand where (a) to (e) represent herd-class 1 through 5, respectively

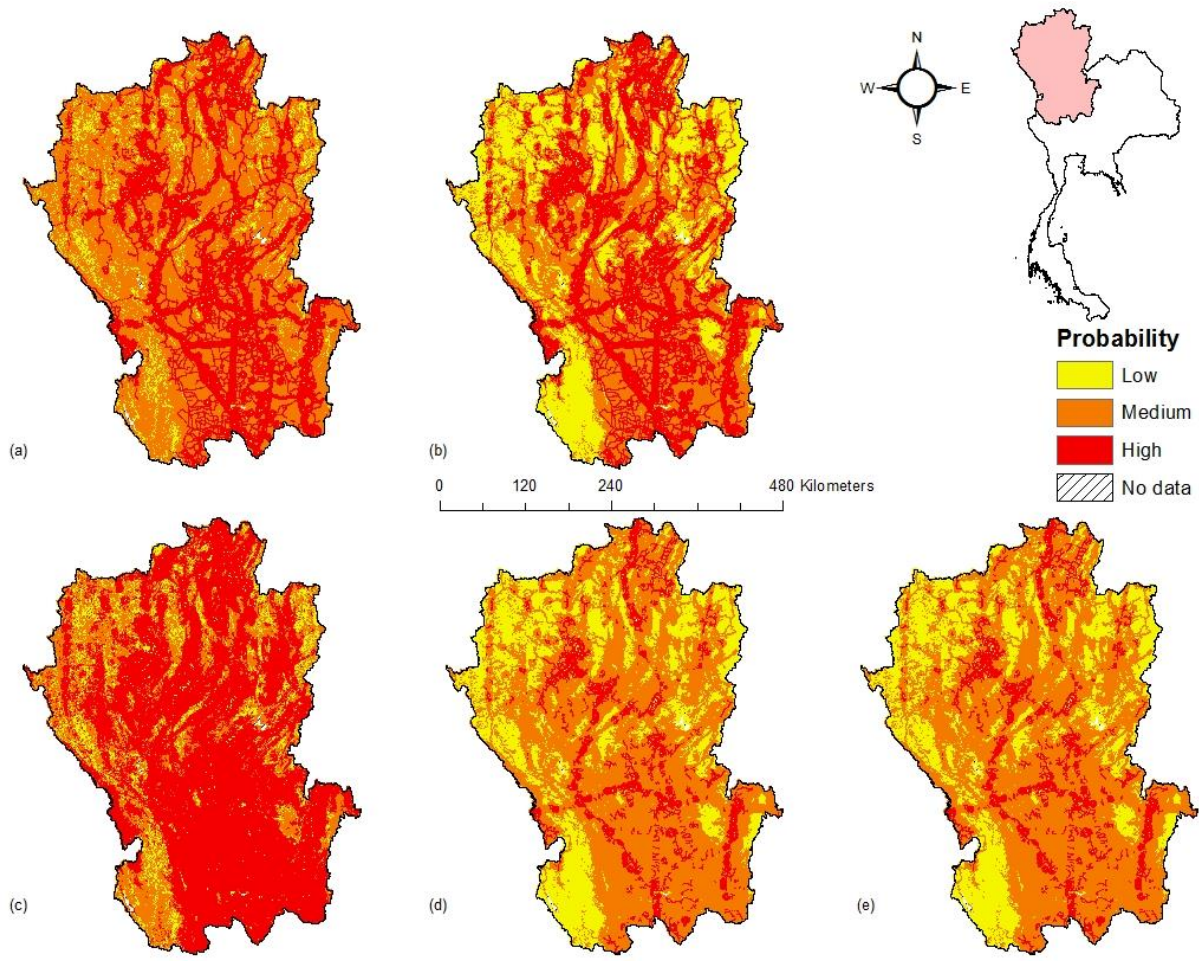


Figure 2.24: Geospatial probability surface for buffalo in Northern, Thailand where (a) to (e) represent herd-class 1 through 5, respectively

Density maps

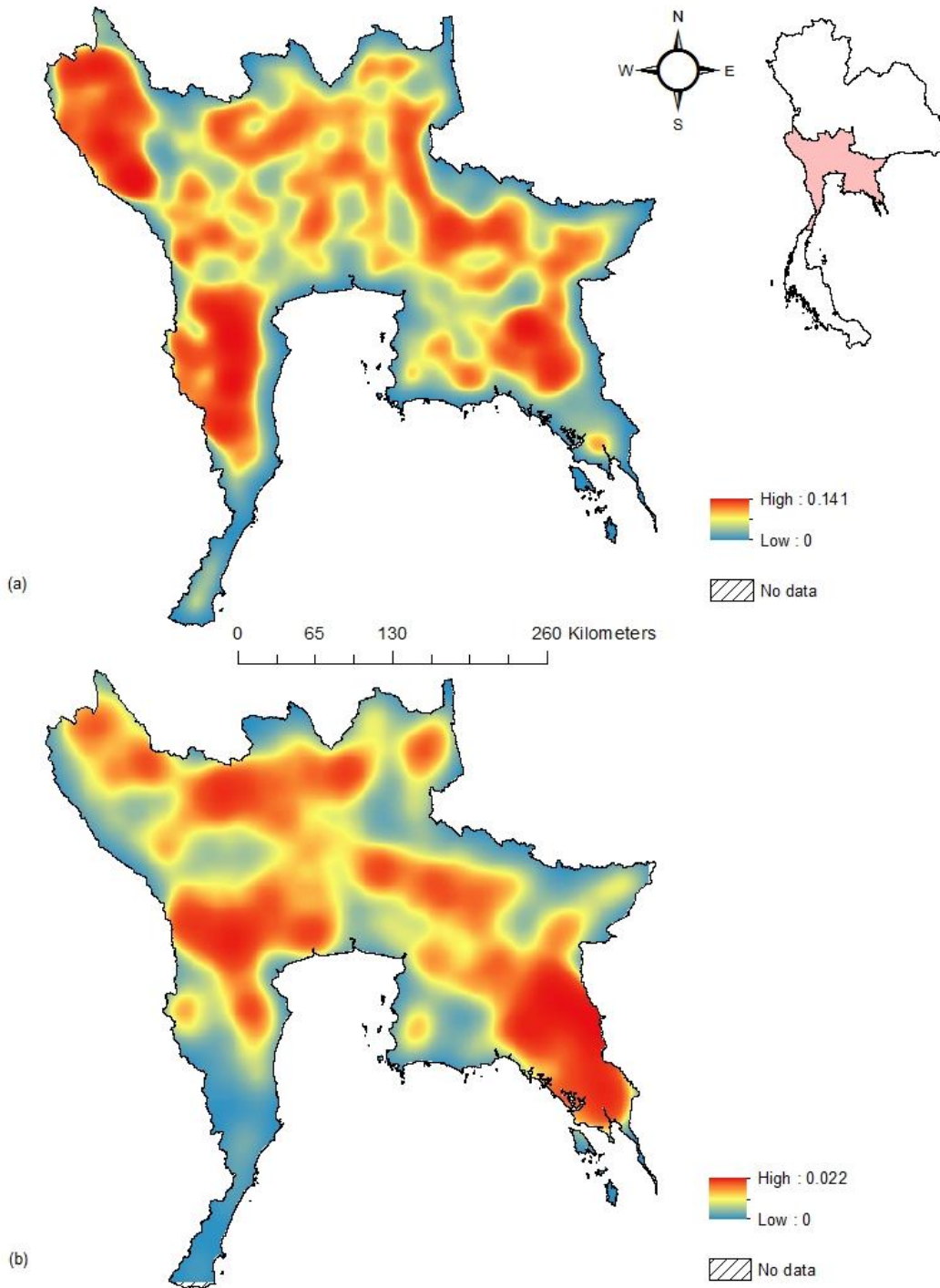


Figure 2.25: Holding density (/Km<sup>2</sup>) for dairy cattle in Central, Thailand, where (a) and (b) represent small, and large holdings

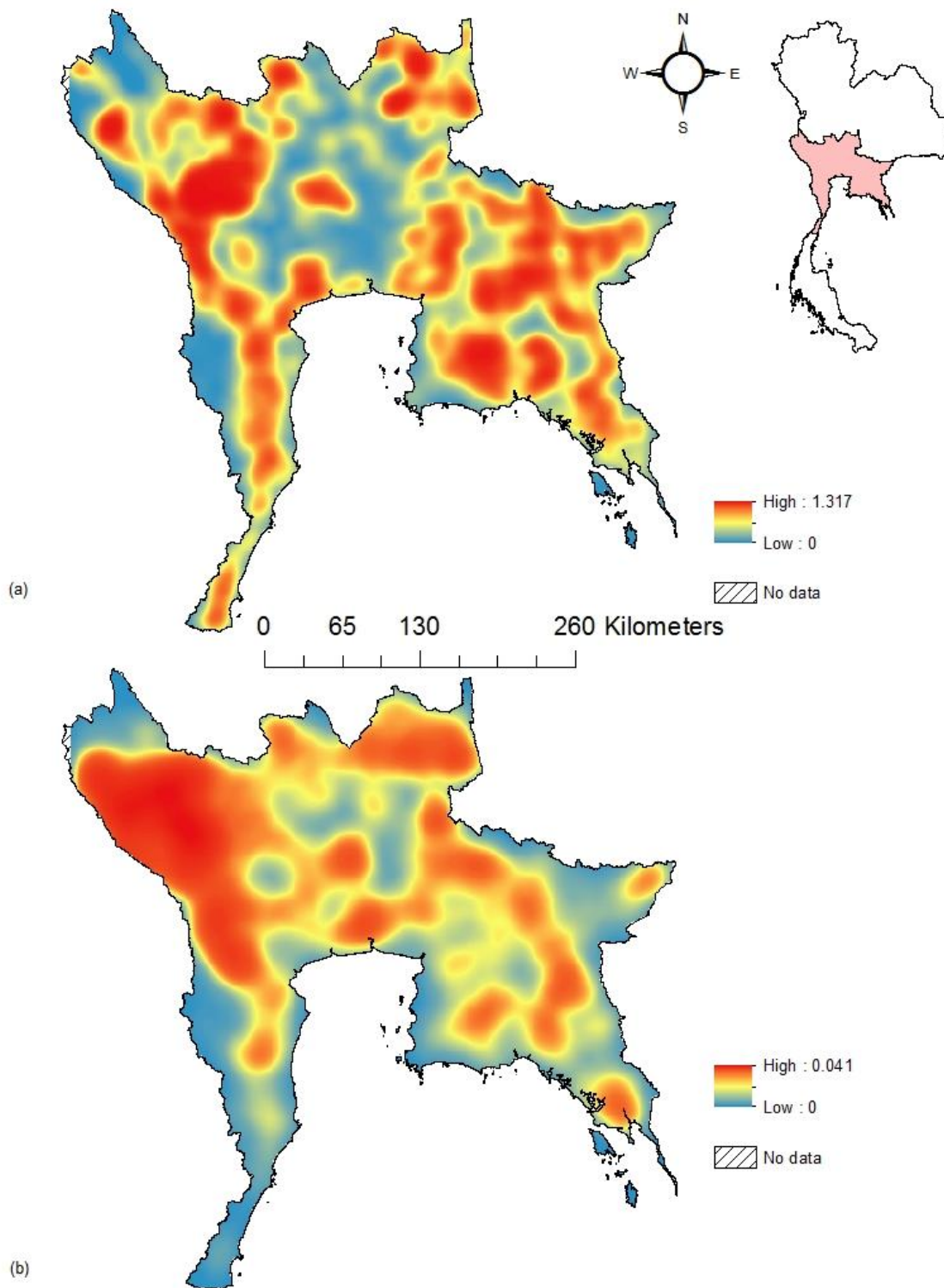


Figure 2.26: Holding density (/Km<sup>2</sup>) for beef cattle in Central, Thailand, where (a) and (b) represent small, and large holdings

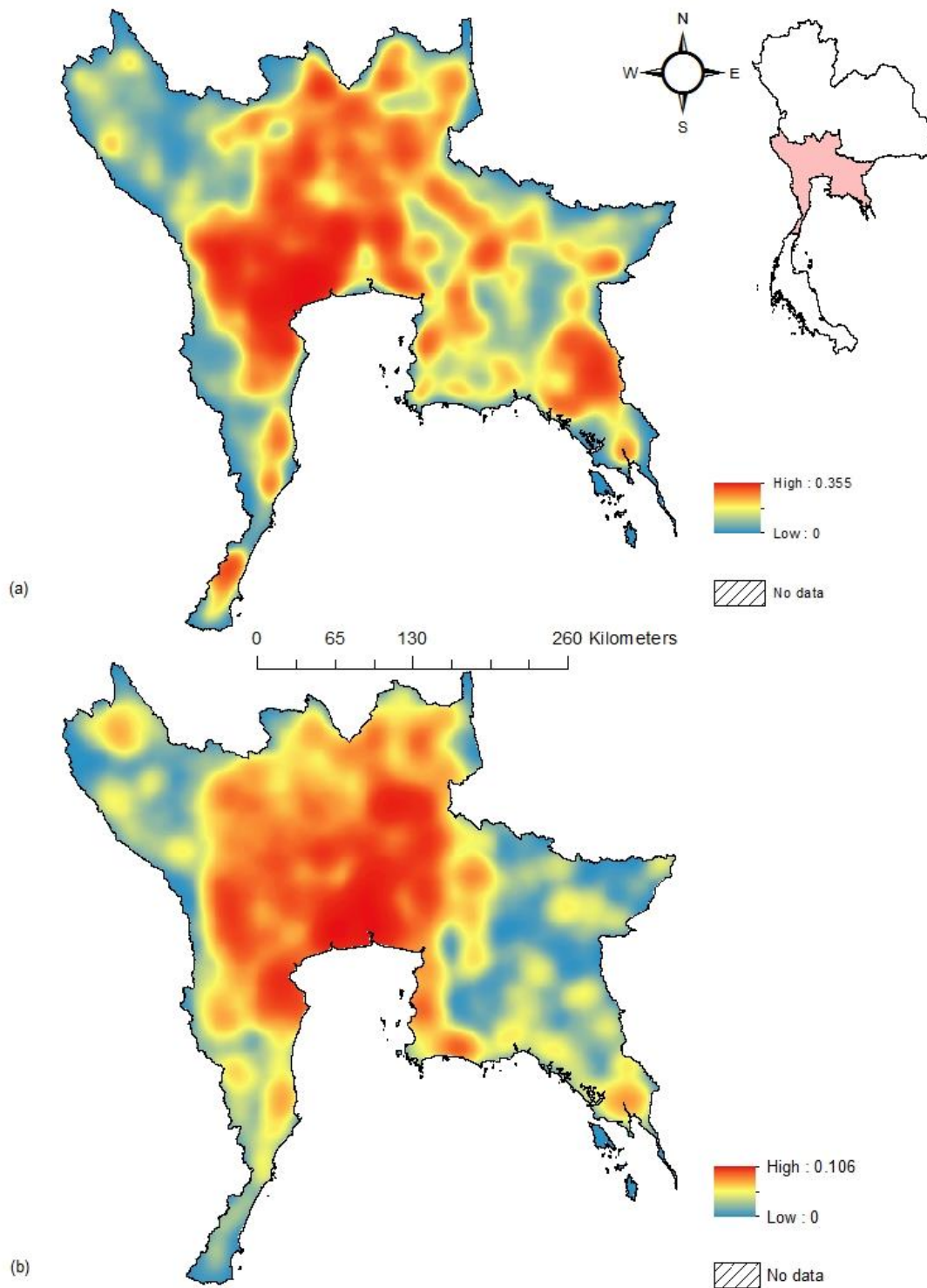


Figure 2.27: Holding density (/Km<sup>2</sup>) for swine in Central, Thailand, where (a) and (b) represent small, and large holdings



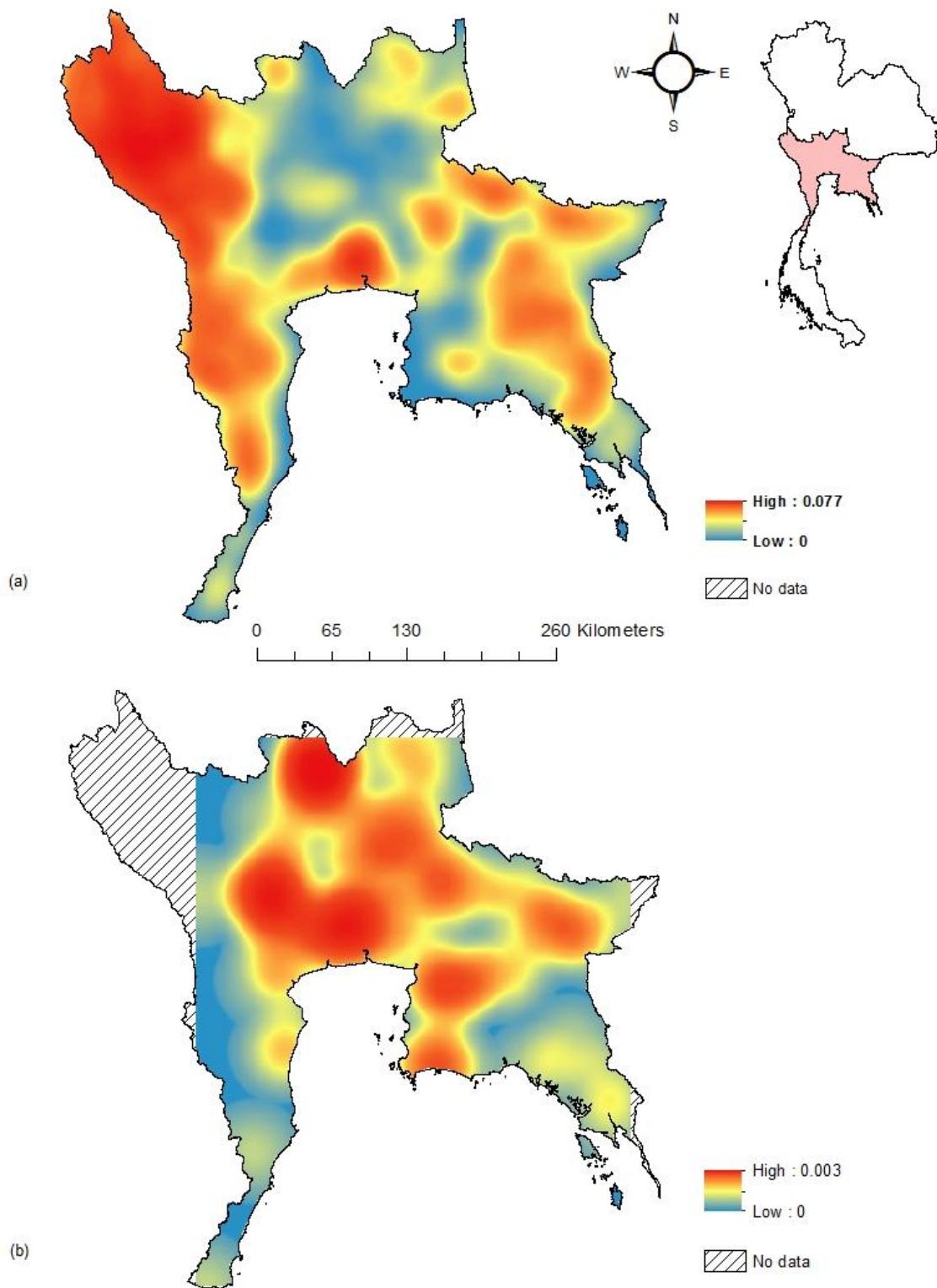


Figure 2.28: Holding density (/Km<sup>2</sup>) for buffalo in Central, Thailand, where (a) and (b) represent small, and large holdings

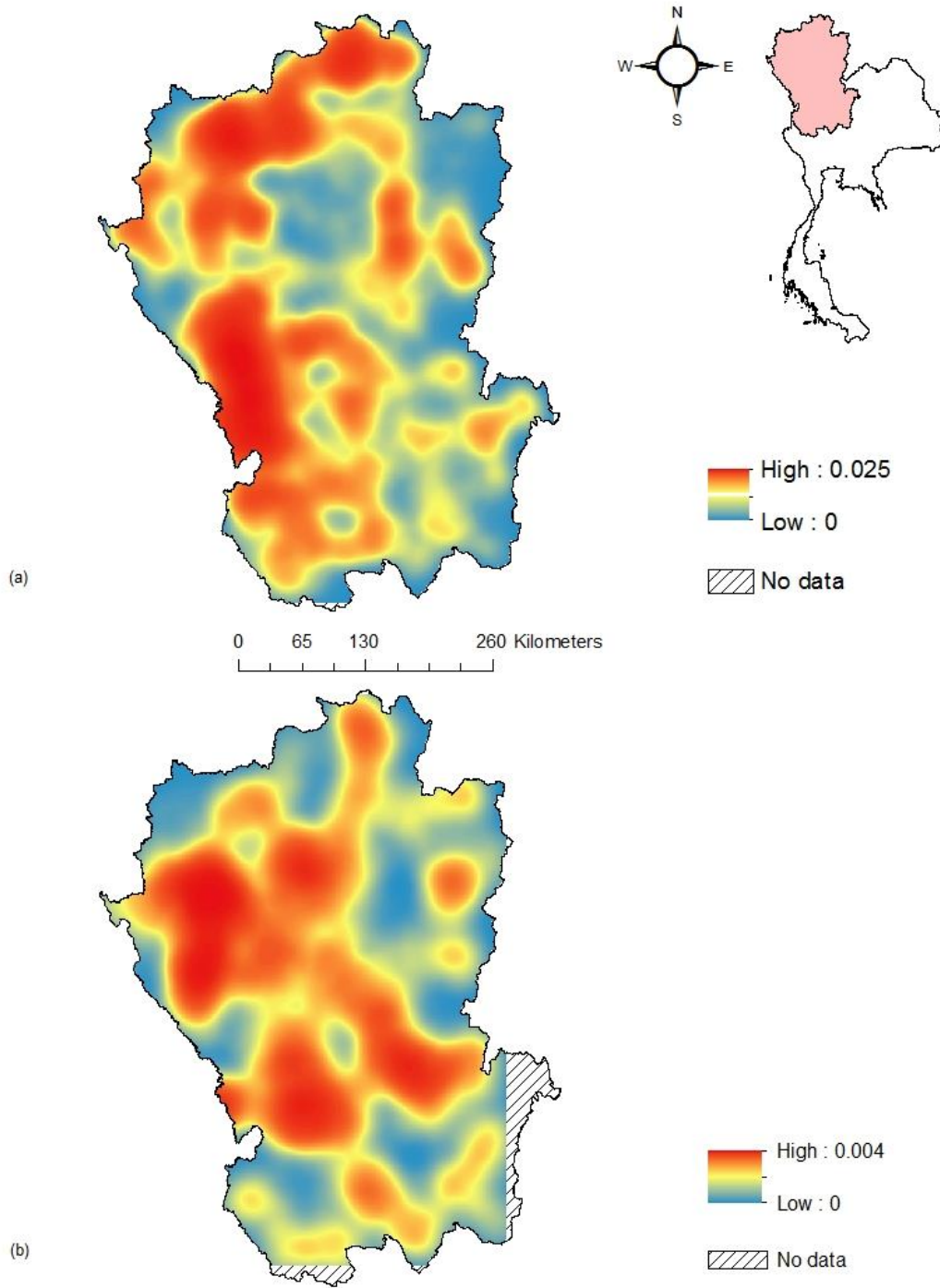


Figure 2.29: Holding density (/Km<sup>2</sup>) for dairy cattle in Northern, Thailand, where (a) and (b) represent small, and large holdings

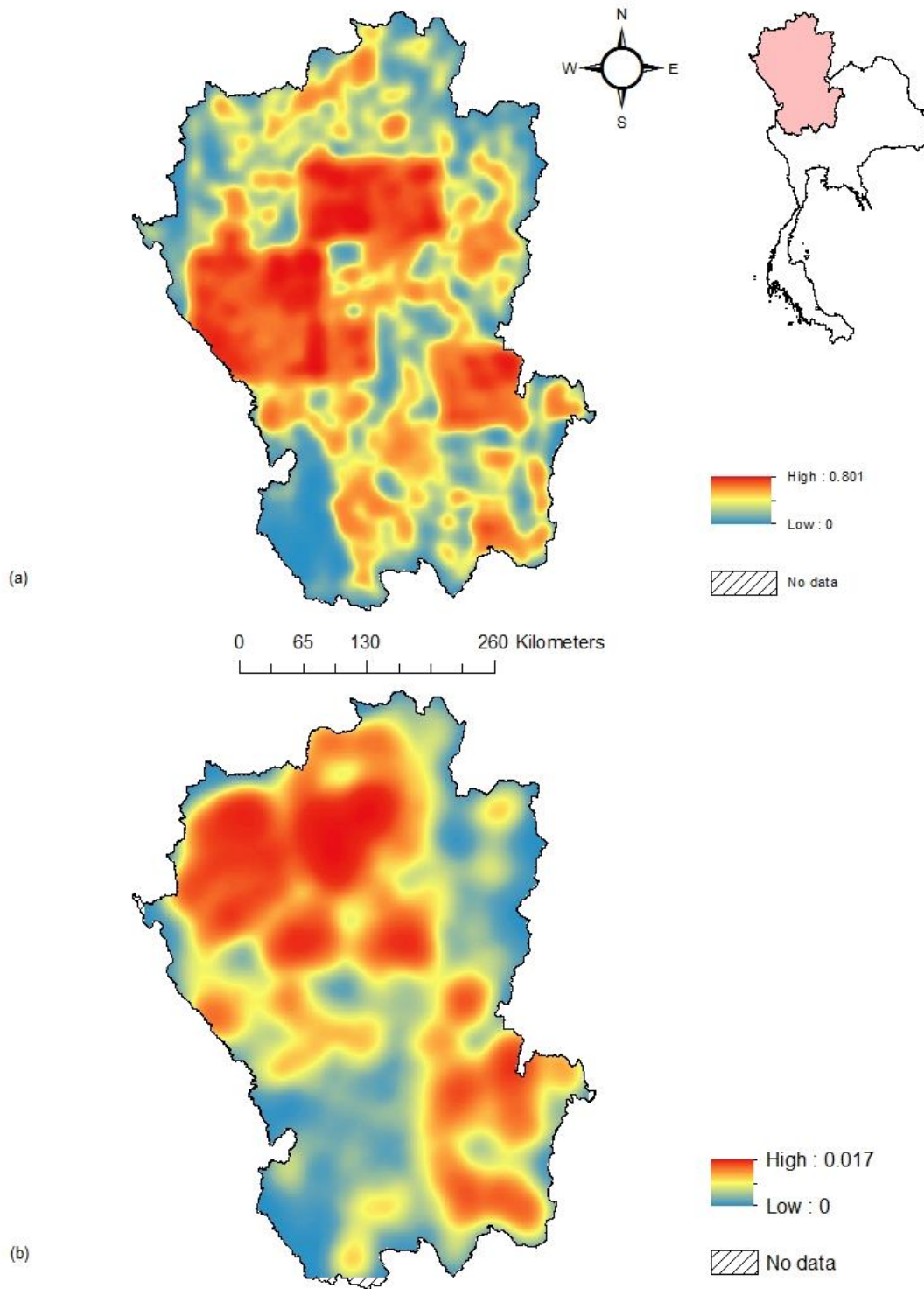


Figure 2.30: Holding density (/Km<sup>2</sup>) for beef cattle in Northern, Thailand, where (a) and (b) represent small, and large holdings

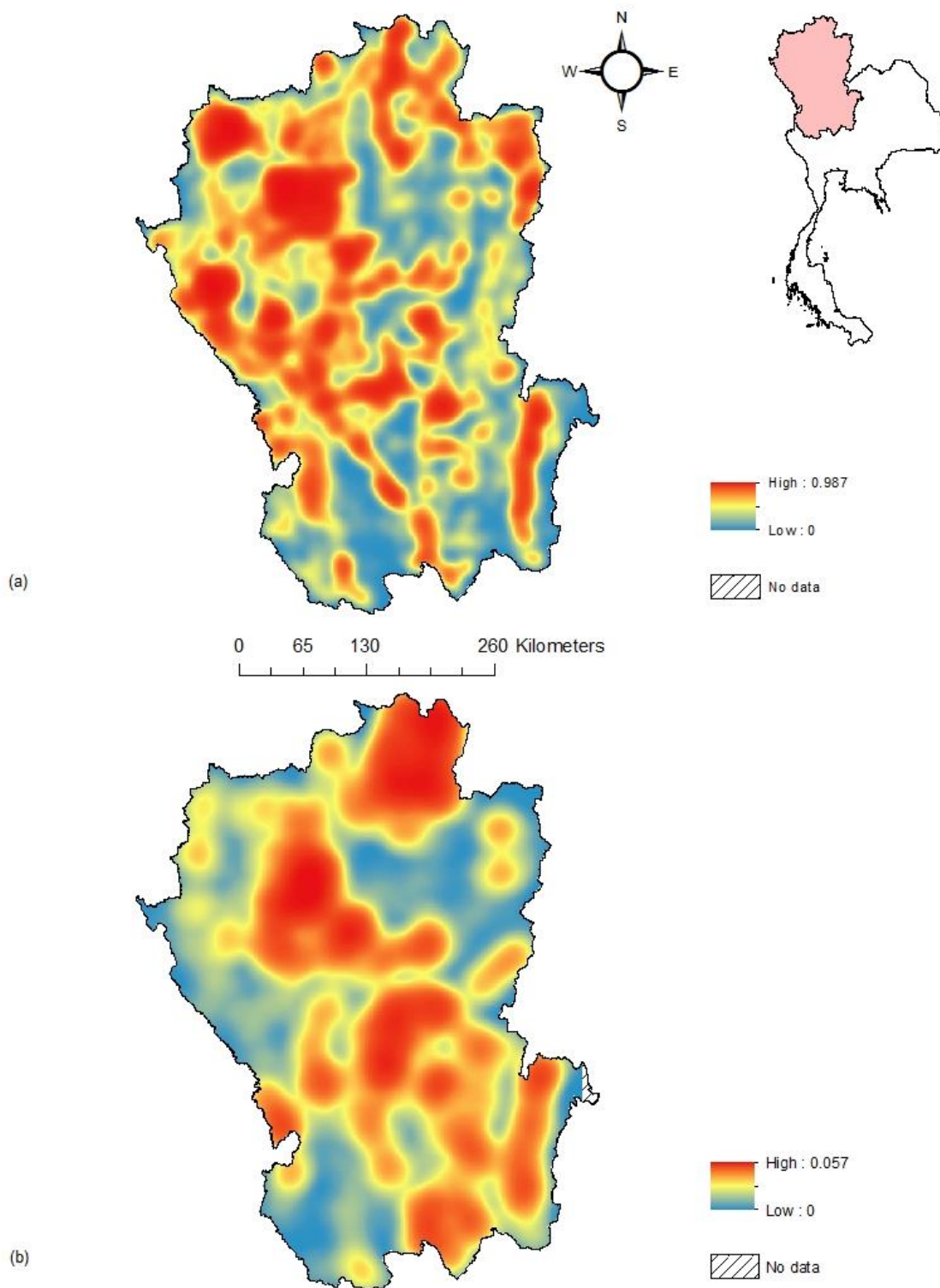


Figure 2.31: Holding density (/Km<sup>2</sup>) for swine in Northern, Thailand, where (a) and (b) represent small, and large holdings

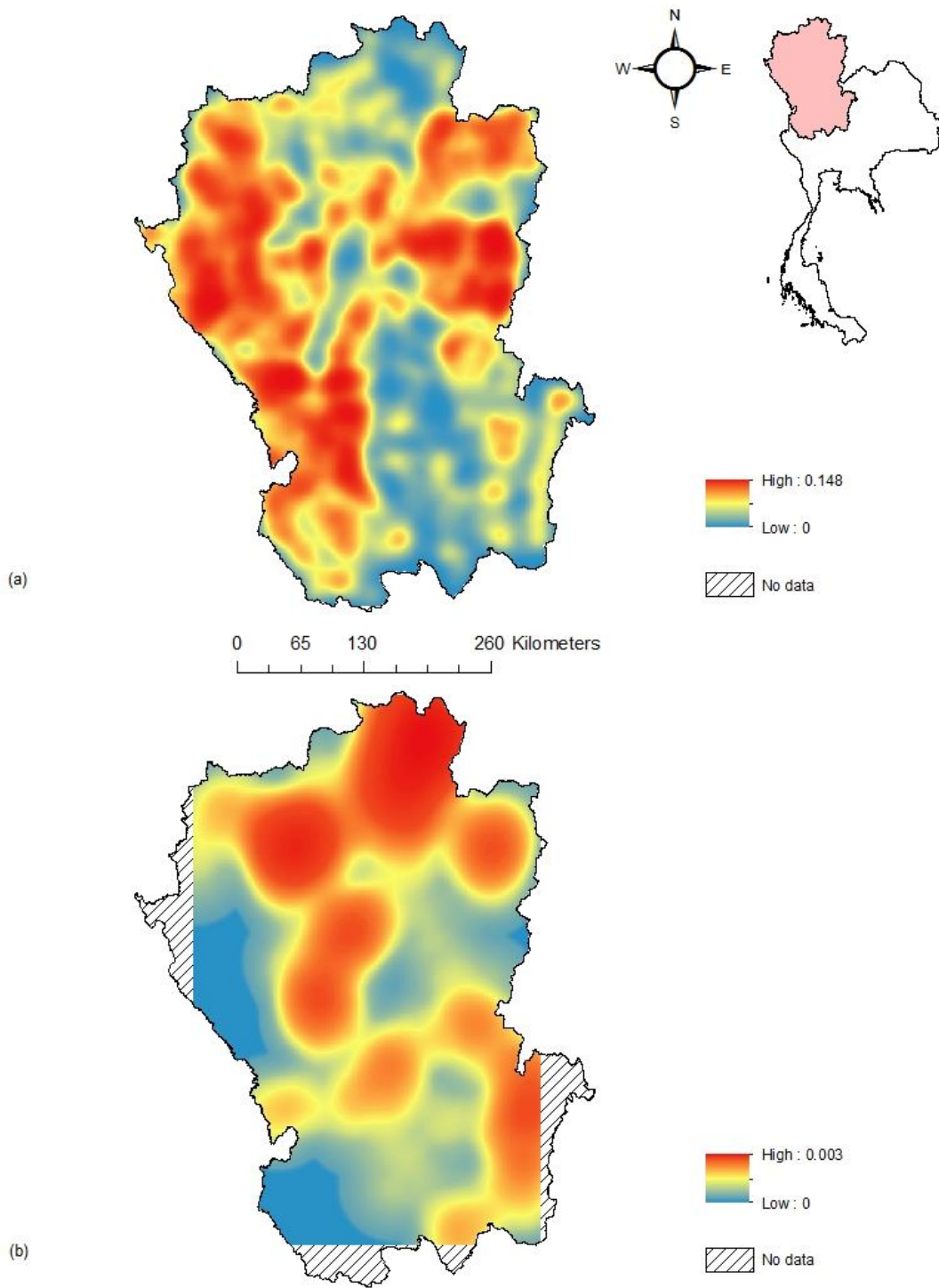


Figure 2.32: Holding density (/Km<sup>2</sup>) for buffalo in Northern, Thailand, where (a) and (b) represent small, and large holdings

## Questionnaire

VERBAL RECRUITMENT/CONSENT TEMPLATE: No Identifiers Collected

Hello, my name is Muhammad Usman Zaheer, and I am a Ph.D. candidate from Colorado State University in the Department of Clinical Sciences. We are conducting a research study on estimating the geolocation of livestock premises and their population. The title of our project is “Geolocation of livestock premises and their population in Pakistan and Thailand: A simulation process model.” The Principal Investigator is Dr. Sangeeta Rao, Department of Clinical Sciences, and I am the Co-Principal Investigator. Other investigators are Dr. Katie Steneroden, Dr. Mo. Salman, Dr. Stephen Weber, Dr. Sheryl Magzamen, Dr. Chris Burdett, and Mr. Shaun Case.

We would like you to use the attached anonymous questionnaire entitled “*Professional opinion of veterinarians about the role of different factors in estimating suitable geolocation for livestock premises and their population in Pakistan*” to provide your professional opinion about animal agriculture in your country based on your experience. A complete response to this questionnaire will take approximately 20-30 minute. Your participation in this research is voluntary. If you decide to participate in the study, you may withdraw your consent and stop participation at any time without penalty.

A minimum of five years of professional livestock experience is required to respond to this questionnaire.

Would you like to participate?

If yes: Proceed.

If no: Thank you for your time.

We will not collect your name or personal identifiers. When we report and share the data with others, we will combine the data from all participants. There are no known risks or direct benefits to

you, but we hope to be able to estimate geolocation of livestock premises and their population, subsequently use this set of data for evaluating risk, and a better understanding of animal disease spread such as Foot-and-Mouth Disease (FMD).

Please read the attached “Background and introduction of the project” and “List of the glossary.”

If you have any questions regarding understanding and answering the questionnaire, please do not hesitate to contact me at:

Dr. Muhammad Usman Zaheer

Ph.D. Candidate Epidemiology

Department of Clinical Sciences

CVMBS, CSU, CO 80523 USA

Phone: +1-509-919-8351

Email: [Usman.Zaheer@ColoState.Edu](mailto:Usman.Zaheer@ColoState.Edu)

If you have questions about your rights as a volunteer in this research, contact the CSU IRB at [RICRO\\_IRB@mail.colostate.edu](mailto:RICRO_IRB@mail.colostate.edu); +1-970-491-1553.

## *Geolocation of livestock premises and their population in Pakistan: A simulation process model*

### *Executive Summary:*

Availability of exact geolocation [longitude (x) and latitude (y) numerical coordinates] of livestock premises can be very useful in evaluating risk and understanding disease spread. The data on the geolocation of livestock premises, however, are usually not available at the herd/farm level due to privacy issues. Different factors such as land cover, roads, human population settlements/density, etc. play an important role in estimating suitable location for livestock premises. We aim to develop a simulation model to estimate the geolocation of the livestock premises and their population in Pakistan. The Farm Location and Agricultural Production Simulator (FLAPS) is a model that can simulate estimated geolocation of individual livestock premises and their population in the USA. The FLAPS model was developed using a Geographic Information System (GIS), and other statistical and simulation modeling techniques. There are, however, constraints when adapting FLAPS for use in developing countries such as Pakistan. One of these constraints is the lack of organized exclusive structured farming system and a relatively higher number of backyard/household farming. This constraint, however, can be addressed by obtaining the experienced opinion of veterinarians working in Pakistan using a questionnaire. The output from this questionnaire will be used to develop a probability surface to simulate geolocation of livestock premises and their population in Pakistan. Finally, the simulated geolocation of livestock premises and their population will be an important component for the development of an animal disease spread model such as Foot-and-Mouth Disease (FMD) model for Pakistan.



*Background and introduction of the project:*

Availability of exact geolocation [longitude (x) and latitude (y) numerical coordinates] of livestock premises can be very useful in evaluating risk and understanding disease spread. The data on the geolocation of livestock premises, however, are usually not available at the herd/farm level due to privacy issues. Different factors such as land cover (pastures, croplands, open areas, developed areas, water bodies, etc.), roads, slope, human population settlements/density, etc. play an important role in estimating suitable location for livestock premises. This estimation can be challenging in the absence of good quality data. We aim to develop a simulation model to estimate the geolocation of the livestock premises and their population in Pakistan.

The Farm Location and Agricultural Production Simulator (FLAPS) is a simulation model that is used in the USA to estimate the geolocation of individual livestock premises and their population because this information is withheld due to privacy and confidentiality concerns. The FLAPS model was developed using a Geographic Information System (GIS), and other statistical and simulation modeling techniques. In the development of the FLAPS, researchers randomly sampled for the presence or absence of livestock farms throughout the conterminous USA. Farms were recognized due to the presence of infrastructure indicating a livestock production system for various species (e.g., cattle, poultry, and swine). If a farm was found, they measured the distance between the farm and different geographical features such as open areas, grassland, urban areas, pastures, and roads. This process was then repeated for the remaining random sites where a farm was not found. These data were then used as input to statistical models whose results allowed them to create geospatial probability surface depicting the probability of livestock presence for the various species of interest. Herd size was then simulated from aggregated agricultural census data by disaggregating the state and county-level data to the level of individual premises. Finally, the location of farms was also simulated using the probability surface to guide placement.

There are, however, constraints when adapting this methodology in developing countries such as Pakistan. One of these constraints is the lack of an organized structured farming system and a relatively higher number of backyard/household farming in which there are 1-10 animals in a household. These households are non-differentiable from households without animals using satellite imagery. This constraint, however, can be addressed using the professional opinion of veterinarians working in Pakistan. A questionnaire is attached, which can be used to obtain the required data. The questions focus on the role of different geographic factors play in animal agriculture and geolocation of some livestock premises in Pakistan. The output from this questionnaire will be used to develop a probability surface to simulate geolocation of livestock premises and their population in Pakistan. The geolocation data of livestock premises will be used for model validation only, and it will not be shared as the final product of the model. Finally, the simulated geolocation of livestock premises and their population will be an important component for the development of an animal disease spread model such as Foot-and-Mouth Disease (FMD), for Pakistan.

## List of Glossary

- Livestock: refers only to Buffalo and cattle
- Livestock Premises: refers to a farm, ranch, household or any other establishment used for keeping/housing buffalo and cattle
- Land Cover: refers to the observed physical cover including the vegetation (natural or planted) and human constructions which cover the earth's surface.
- Geospatial Probability Surface: refers to a surface depicting the probability of the presence of livestock of one or more species
- Modeling: refers to an act of making a model and a model is an abstract representation of a complex system. In epidemiology, a model can be a representation of generalized characteristics of the system (such as, livestock population) divided into components that are of interest to a researcher (for simplicity and understanding) and removal of unnecessary information.
- Simulation: refers to a reality/environment on which the model lives. It helps to understand the behavior of a system (such as livestock population) in real life over time.
- Simulation Modelling: refer to a process in which a model lives a reality in a simulation environment and help us understand changes to output with changes in inputs.
- Herd-size Category: refers to the different categories for herd size (number of animals) derived directly from livestock/agricultural census or by combining two or more categories from the census for simplicity and computational ease
- The direction of Influence: refers to whether a factor influence/affect a certain herd-size category positively or negatively
- Level Influence: refers to the importance of a factor for a certain herd-size category. It ranges from 0 to 5
  - 0: If there is no influence of factor on herd size category

- 1: if the influence of factor on herd size category is more than 0% and less than equal to 20%
- 2: if the influence of factor on herd size category is more than 20% and less than equal to 40%
- 3: if the influence of factor on herd size category is more than 40% and less than equal to 60%
- 4: if the influence of factor on herd size category is more than 60% and less than equal to 80%
- 5: if the influence of factor on herd size category is more than 80% and less than equal to 100%

*Professional opinion of veterinarians about the role of different factors in estimating suitable geolocation for livestock premises and their population*

1. Name of Province/Region: \_\_\_\_\_
2. Number of years of professional livestock experience : \_\_\_\_\_
3. Which of the following describe your experience with animal agriculture (encircle all that apply):
  - a. Field veterinarian
  - b. Farm management
  - c. Laboratory researcher
  - d. Disease surveillance
  - e. Project management
  - f. Senior executive
  - g. Other (please explain) \_\_\_\_\_
4. Please provide your opinion on the following items in the table below:
  - a. "Direction of influence" (positive/negative) of 'each factor' on a 'herd size category.'
  - b. "Level of influence" (0-5) of 'each factor' on a 'herd size category.'
    - 0: If there is no influence of factor on herd size category
    - 1: if the influence of factor on herd size category is more than 0% and less than or equal to 20%
    - 2: if the influence of factor on herd size category is more than 20% and less than or equal to 40%
    - 3: if the influence of factor on herd size category is more than 40% and less than or equal to 60%
    - 4: if the influence of factor on herd size category is more than 60% and less than or equal to 80%

- 5: if the influence of factor on herd size category is more than 80% and less than or equal to 100%

Example:

- If in your opinion, “cropland/grassland/pasture” positively influence the herd-class 1 and the ‘level of influence’ is more than 60% and less than or equal to 80%, then you will put 4 in the respective cell.
- In contrast, if, in your opinion, “urban/developed area” negatively influence the herd-2 and the “level of influence’ is more than 80% and less than or equal to 100%, then you will put 5 in the respective cell.
  - This ‘direction of influence’ and ‘level of influence’ can be the same or different for other herd size categories.

Please see the sample in the table below:

Herd-class	Question	Factor			
		Cropland/ grassland / pasture	Open/barren land	Urban/developed area	Slope (≤10%)
1	Direction of influence (Positive/Negative)	Positive			
	Level of influence (0 to 5)	4			
2	Direction of influence (Positive/Negative)			Negative	
	Level of influence (0 to 5)			5	

Please provide your opinion in the table below, taking the above table as an example only.

Livestock: Bovines/beef cattle/buffalo/dairy cattle/swine

Herd-class	Question	Cropland/ grassland / pasture	Open/barren land	Urban/developed area	Slope ( $\leq 10\%$ )
1	Direction of influence (Positive/Negative)				
	Level of influence (0 to 5)				
2	Direction of influence (Positive/Negative)				
	Level of influence (0 to 5)				
3	Direction of influence (Positive/Negative)				
	Level of influence (0 to 5)				
4	Direction of influence (Positive/Negative)				
	Level of influence (0 to 5)				
5	Direction of influence (Positive/Negative)				
	Level of influence (0 to 5)				

Any additional comments:

---

---



Empirical locations of livestock holdings are necessary to create additional probability buffers around different highway types, and percent holdings to be placed on different probability zones. Please provide physical locations of livestock holdings (ranging from herd-class 1 to 5). Please provide as much address details as possible.

Note: Please extend the table to accommodate more livestock premises

Locational details of livestock premises			Livestock-type	Herd-class [Check (√) that apply]				
Province/Region	Longitude (x)	Latitude (y)		1	2	3	4	5

## Chapter 3

### *Starting status of holdings*

Under the UN-FAO project “GCP/PAK/123/USA Development of Technical Framework for the Control of Foot and Mouth Disease in Pakistan”, outbreaks data was collected in Pakistan. During 2012-2014, a total of 121 suspected outbreaks were reported from bovine holdings with > 50 animals, and 100 (82.6%) of them were positive by ELISA for latest one serotype of FMD. The period prevalence was calculated, i.e., 71.05 holding/10,000 holdings. It was assumed that each outbreak represents a unique holding and positive holdings were divided by a total number of holdings, i.e., 13,986 to calculate % of positive holdings. It was assumed that these positive holdings are clinical infectious.

In addition, the anonymous veterinarian was asked to provide his opinion on ‘for each clinical infectious holding, how many other holdings are present, which are subclinical infectious holdings.’ Also, the veterinarian was asked, ‘for each infectious holding (clinical and subclinical) holding, how many other holdings are exposed but not infectious yet.’ The response to these two questions was 2. Based on this information, 200 holdings were given a ‘subclinical’ status, and 600 holdings were given ‘latent’ status.

To ascertain the number of naturally immune holdings, it was assumed that all infected holdings (latent, subclinical and clinical) holdings would mount natural immunity upon recovery. Thus, 1600 holdings were assigned a ‘natural immune’ status. To account for the ‘vaccine immune’ holdings at the start of the simulation, based on the personal communication with expert veterinarians, 210 holdings were given ‘vaccine immune’ status, i.e. 0.14%. All other holdings were set to ‘susceptible’ status.

### *Estimation of holding-level clinical duration*

The estimates for holding level duration of clinical infection, WH 0.9.7 was used based on parameter estimates from personal communication with an anonymous veterinarian.

A total of 100 iterations were run, and the numbers of days for which the herd remained clinical was extracted from each iteration. That data was fitted to different distributions, and the best fitting distribution (Gamma) will be used in SMIAD-ER model.

Table 3.3: Parameters for WHO.9.7

Parameter	PDF/estimate	Reference
Population	Lognormal (197.61, 172.45)	Zaheer et al 2019 in preparation
Initially latent animals	Fixed value (1)	Personal Communication
Initially sub-clinical infectious animals	Fixed value (1)	Personal Communication
Initially clinical infectious animals	Fixed value (1)	Personal Communication
Adequate exposure/day	Uniform (1, 5)	Personal Communication
Latent Period	Weibull (1.78, 3.97)	Mardones et al., 2010
Sub-clinical infectious period	Gamma (1.22, 1.67)	Mardones et al., 2010
Clinical period	Exponential (4.75, 0.74)	USDA, 2013
Natural immunity	Gaussian (1095, 180)	Cunliffe, 1964; Moonen et al., 2004

The resulting data on the duration of clinical infection for 100 iterations were fit in R using *fitdistrplus* package, and Anderson-darling test was applied (Delignette-Muller and Dutang, 2015; R Core Team, 2017). The parameters for shape and scale were estimated using the Maximum Likelihood Estimation method. The Gamma distribution (23.20, 1.74) was used to model clinical infectious period of FMD progression for both production-types using SMIAD-ER.

#### *Spread Parameters*

#### *Contact Spread*

Table 3.4: Contact spread parameters for different production type combinations

Production Type Combination	Direct Contact		Indirect Contact	
<b>Cattle to Cattle</b>				
Can latent holdings spread FMD	Yes		No	
Can sub-clinical holdings spread FMD	Yes		Yes	
Mean baseline contact rate/day (point value)	0.2		3	
Distance distribution of recipient units	(0.1, 1, 30)		(0.05, 4, 50)	
BetaPERT	0.85		0.50	
Probability of infection transfer if source holding is infected (point value)	0.85		0.50	
Delay in shipments? (Number of days that on average it takes from shipment of animals reach from source to recipient unit)	0		0	
Effect of movement restrictions on mean baseline contact rate, after detection in any production type	Day	Prob.	Day	Prob.
	1	95	1	100
	4	80	4	90
	7	60	7	70
<b>Cattle to Buffalo</b>				
Can latent holdings spread FMD	Yes		No	
Can sub-clinical holdings spread FMD	Yes		Yes	
Mean baseline contact rate/day (point value)	0.033		3	
Distance distribution of recipient units	(1, 15, 50)		(0.05, 4, 50)	
BetaPERT	0.70		0.40	
Probability of infection transfer if source holding is infected (point value)	0.70		0.40	
Delay in shipments? (number of days that on average it takes from shipment of animals reach from source to recipient unit)	0		0	
Effect of movement restrictions on mean baseline contact rate, after detection in any production type	Day	Prob.	Day	Prob.
	1	95	1	100
	4	80	4	90
	7	60	7	70
<b>Buffalo to Buffalo</b>				
Can latent holdings spread FMD	Yes		No	
Can sub-clinical holdings spread FMD	Yes		Yes	
Mean baseline contact rate/day (point value)	3		3	
Distance distribution of recipient units (Km)	(0.02, 0.2, 10)		(0.05, 4, 50)	
BetaPERT	0.50		.30	
Probability of infection transfer if source holding is infected (point value)	0.50		.30	
Delay in shipments? (number of days that on average it takes from shipment of animals reach from source to recipient unit)	0		0	

Effect of movement restrictions on mean baseline contact rate, after detection in any production type	Day	Prob.	Day	Prob.
	1	95	1	100
	4	80	4	90
	7	60	7	70
<b>Buffalo to Cattle</b>				
Can latent holdings spread FMD	Yes		No	
Can sub-clinical holdings spread FMD	Yes		Yes	
Mean baseline contact rate/day (point value)	0.017		3	
Distance distribution of recipient units	(1, 7.5, 60)		(0.05, 4, 50)	
BetaPERT				
Probability of infection transfer if source holding is infected (point value)	1		0.60	
Delay in shipments? (number of days that on average it takes from shipment of animals reach from source to recipient unit)	0		0	
Effect of movement restrictions on mean baseline contact rate, after detection in any production type	Day	Prob.	Day	Prob.
	1	95	1	100
	4	80	4	90
	7	60	7	70

### *Airborne spread*

The parameters for local area spread were sought from anonymous veterinarian working on FMD outbreaks in Pakistan. It was assumed that maximum distance for local area spread is 3-Km for all production type combinations. It was assumed that the rate of FMD spread decreases linearly from the source.

Table 3.5: Parameters for local area spread of FMD (through aerosol, rodents, birds, stray animals)

Parameter	Cattle to Cattle	Cattle to Buffalo	Buffalo to Buffalo	Buffalo to Cattle
Probability of FMD spread/contagious day at 1 km distance, from average sized unit	0.90	0.65	0.60	0.80
Area at risk (0-360 degree)	360	360	360	360
Airborne transport delay (days)	0	0	0	0



*Disease Detection*

Based on the opinion of a field veterinarian

Table 3.6: Probability of observing and reporting clinical infectious holdings

Parameter	Cattle		Buffalo	
	Day	Prob.	Day	Prob.
Probability of observing clinical signs, given the number of days the unit is clinically infectious (relational function)	1	2	0	1
	3	45	3	40
	5	90	6	90
Probability of reporting an observed clinical unit, given the number of days since the disease was first detected in any unit (relational function)	Day	Prob.	Day	Prob.
	1	50	1	50
	2	90	2	90

*Emergency vaccination*

Table 3.7: Emergency vaccination capacity

Days	Holdings vaccinated
1	2
2	5
5	15
10	35

## Chapter 4

### *Holding-level clinical infectious period*

The With-in Herd (WH) model 0.9,7 was parameterized with estimates presented in table 4.6-4.7. The model was run for 1,000 iterations until the end of the outbreak. The clinical infectious period from all iterations was fit to different statistical distributions using Easy-Fit software (Schittkowski, 2002). The distribution with the highest rank for the Anderson-Darling test was selected for use in SMIAD-ER to model holding level clinical infectious period. If the highest ranked distribution was not available in SMIAD-ER, the next distribution was chosen.

Table 4.6: Input parameters for use in WH0.9.7 for medium holdings (cattle and buffalo)

Item	Parameters	Reference
Population	Uniform (11, 30)	Zaheer et al., in preparation
Initially latent animals	Fixed value (1)	N/A
Initially sub-clinical infectious animals	Fixed value (1)	N/A
Initially clinical infectious animals	Fixed value (1)	N/A
Adequate exposure/day	Uniform (1, 5)	N/A
Latent Period	Weibull (1.78, 3.97)	Mardones et al., 2010
Sub-clinical infectious period	Gamma (1.22, 1.67)	Mardones et al., 2010
Clinical period	Exponential (4.75, 0.74)	USDA, 2013
Natural immunity	Gaussian (1095, 180)	Cunliffe, 1964; Moonen et al., 2004

Table 4.7: Input parameters for use in WH0.9.7 for large holdings (cattle and buffalo)

Item	Parameters	Reference
Population	Uniform (31, 1707)	Zaheer et al., in preparation
Initially latent animals	Fixed value (1)	N/A
Initially sub-clinical infectious animals	Fixed value (1)	N/A
Initially clinical infectious animals	Fixed value (1)	N/A
Adequate exposure/day	Uniform (1, 5)	N/A
Latent Period	Weibull (1.78, 3.97)	Mardones et al., 2010
Sub-clinical infectious period	Gamma (1.22, 1.67)	Mardones et al., 2010
Clinical period	Exponential (4.75, 0.74)	USDA, 2013
Natural immunity	Gaussian (1095, 180)	Cunliffe, 1964; Moonen et al., 2004

## REFERENCES

- Cunliffe, H., 1964. Observations on the duration of immunity in cattle after experimental infection with Foot-and-Mouth Disease virus. *Cornell Vet.* 54, 501–10.
- Delignette-Muller, M.L., Dutang, C., 2015. **fitdistrplus** : An R Package for Fitting Distributions. *J. Stat. Softw.* 64, 1–34. <https://doi.org/10.18637/jss.v064.i04>
- Mardones, F., Perez, A., Sanchez, J., Alkhamis, M., Carpenter, T., 2010. Parameterization of the duration of infection stages of serotype O foot-and-mouth disease virus: an analytical review and meta-analysis with application to simulation models. *Vet. Res.* 41, 45.  
<https://doi.org/10.1051/vetres/2010017>
- Moonen, P., Jacobs, L., Crienen, A., Dekker, A., 2004. Detection of carriers of foot-and-mouth disease virus among vaccinated cattle. *Vet. Microbiol.* 103, 151–160.  
<https://doi.org/10.1016/j.vetmic.2004.07.005>
- R Core Team, 2017. R: A language and environment for statistical computing.
- USDA, 2013. Parameters Used to Simulate the Spread of FMD in Texas Using the North American Animal Disease Spread Model (NAADSM) for use in FMD Response Workforce Requirement Estimates. Fort Collins, CO USA.