Institution: Imperial College London

Unit of Assessment: 5 – Biological Sciences

Title of case study: A5-7 Mitigation of emerging pathogens causing global amphibian declines through changes in international surveillance, biosecurity regulation and treatment of infection

Period when the underpinning research was undertaken: 2003 – December 2020

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
Matthew C. Fisher	Professor	2004 – present

Period when the claimed impact occurred: September 2013 – December 2020

Is this case study continued from a case study submitted in 2014? N

1. Summary of the impact (indicative maximum 100 words)

Pandemics of chytrid fungi, which cause the disease amphibian chytridiomycosis, have resulted in the greatest recorded loss of biodiversity attributable to an infection. Research at Imperial has played a critical role in identifying these pathogens and understanding their epidemiology. Our research led to the discovery of the origins, timing of emergence, and worldwide pathways of spread of these pathogens. This research resulted in the strengthening of international biosecurity legislation and new regulations restricting trade in disease vectors. We have trained scientists worldwide in how to study this disease and have developed widely-adopted best-practice to mitigate the onwards spread of infection. By identifying the amphibian species most at risk of chytridiomycosis and by developing treatment protocols, we have pioneered interventions that have been used to eradicate the pathogen in trial settings in nature.

2. Underpinning research (indicative maximum 500 words)

Researchers at the MRC Centre for Global Infectious Disease Analysis at Imperial College London are at the forefront of research aimed at understanding globally emerging fungal threats to animal, plant and ecosystem health **[1]**. Chytridiomycosis is a uniquely aggressive disease caused by the batrachochytrids B. dendrobatidis and B. salamandrivorans and is responsible for the greatest loss of biodiversity due to an infectious disease. Since 2004, our research on chytridiomycosis and global amphibian declines has led to breakthrough understanding of these pathogens epidemiology. This research has led to new policies being developed that strengthen international biosecurity, has steered conservation practice and has developed strategies to mitigate the impact of these pathogens in nature:

1) We have trained a global network of scientists to undertake research on chytrid pathogens through standardising protocols for isolation, monitoring and surveillance. This work has been used to map the disease worldwide and has contributed to a global, quantitative assessment of the amphibian chytridiomycosis pandemic, identifying chytrids as the causative agent in the declines of 500 amphibian species over the past half-century, including 90 presumed extinctions **[2]**. The evidence generated has been used to identify species most at risk of infection, to locate yet-uninfected regions of the planet, and to forecast future associations between global warming and the severity of infection in montane regions.

2) We have developed a non-lethal method for isolating amphibian-parasitising chytrids and have used this approach to build a culture collection of the organism from 5 continents, 23 countries and 62 amphibian species **[3]**. We used genomic analysis of this biological repository to identify the origins of B. dendrobatidis to East Asia, and to date this pathogens emergence to the early

20th Century **[4]**. This dataset has been key evidence identifying Asia as a hotspot for batrachochytrids, resulting in increased biosecurity for amphibians that are exported from this region.

3) Our work has been central in solving the enigmatic mass mortalities and declines of fire salamanders in the Netherlands, resulting in the discovery of a new species of pathogenic chytrid, B. salamandrivorans, which we identified as also having an Asian origin **[5]**. This discovery has led to bans in the trade of salamander species in a growing number of countries / regions alongside the listing of B. salamandrivorans by the OIE (World Organisation for Animal Health). To date, these listings and bans have prevented the establishment of this batrachochytrid in the Americas.

4) Our disease mitigation research is on-going, but has included investigating safe treatments to cure the disease in captive animals; whether field treatments can be used to reduce the impact of the disease on wild populations of amphibians; whether the impact of the pathogen can be reduced through pre-exposure of animals to a hypovirulent lineage of the fungus; and whether bacterial communities are protective against disease. Ongoing work on Mallorca has led to the local elimination of infections in the IUCN Red List Critically Endangered Alytes muletensis, and ongoing efforts are predicted to lead to complete clearance from the island.

3. References to the research (indicative maximum of six references)

[1] Fisher M. C. Henk D. A Briggs C. Brownstein J. S. Madoff L. McCraw S. L. Gurr S. (2012) Emerging fungal threats to animal, plant and ecosystem health. *Nature* 484: 186-194 https://doi:10.1038/nature10947

[2] Scheele, B., F. Pasmans, L. F. Skerratt, L. Berger, A. Martel, W. Beukema, A. A. Acevedo, P. A. Burrowes, T. Carvalho, A. Catenazzi, I. De la Riva, M. C. Fisher, S. V. Flechas, C. N. Foster, P. Frias-Alvarez, T. W. J. Garner, B. Gratwicke, J. M. Guayasamin, M. Hirschfeld, J. E. Kolby, T. A. Kosch, E. La Marca, D. B. Lindenmayer, K. R. Lips, A. V. Longo, R. Maneyro, C. A. McDonald, J. Mendelson, P. Palacios-Rodriguez, G. Parra-Olea, C. L. Richards-Zawacki, M. O. Rodel, S. M. Rovito, C. Soto-Azat, L. F. Toledo, J. Voyles, C. Weldon, S. M. Whitfield, M. Wilkinson, K. R. Zamudio, and S. Canessa. 2019. 'Amphibian fungal panzootic causes catastrophic and ongoing loss of biodiversity', *Science*, 363 https://doi.org/10.1126/science.aar1965

[3] Fisher, M. C.,…[54 co-authors]…, T. W. J. Garner. 2018. 'Development and worldwide use of non-lethal, and minimal population-level impact, protocols for the isolation of amphibian chytrid fungi', *Scientific Reports* ***8*****,** 7772 (2018) https://www.nature.com/articles/s41598-018-24472-2

[4] O'Hanlon, S. J.,…[56 co-authors]…, M. C. Fisher. 2018. 'Recent Asian origin of chytrid fungi causing global amphibian declines', *Science*, 360: 621 https://doi.org/10.1126/science.aar1965

[5] Martel, A., M. Blooi, C. Adriaensen, P. Van Rooij, W. Beukema, M. C. Fisher, R. A. Farrer, B. R. Schmidt, U. Tobler, K. Goka, K. R. Lips, C. Muletz, K. R. Zamudio, J. Bosch, S. Lotters, E. Wombwell, T. W. J. Garner, A. A. Cunningham, A. Spitzen-van der Sluijs, S. Salvidio, R. Ducatelle, K. Nishikawa, T. T. Nguyen, J. E. Kolby, I. Van Bocxlaer, F. Bossuyt, and F. Pasmans. 2014. 'Recent introduction of a chytrid fungus endangers Western Palearctic salamanders', *Science*, 346: 630-31 https://doi.org/10.1126/science.1258268

4. Details of the impact (indicative maximum 750 words)

Worldwide amphibian declines caused by pathogenic chytrid fungi are emblematic of emerging infectious diseases driven by globalisation. Amphibians are one of the most vulnerable animal lineages on the planet with over 40% of species threatened with extinction. Our research has described how the batrachochytrids *B. dendrobatidis* and *B. salamandrivorans* have emerged as

the leading infectious disease threat to biodiversity worldwide. We have shown how, to date, chytridiomycosis has decimated at least 501 amphibian species, representing the greatest loss of biodiversity due to a pathogen ever recorded. These losses have resulted in knock on effects for other biodiversity including snakes and ecosystem function more widely. Our research has led to widespread impact towards monitoring and controlling this panzootic in the following areas:

Chytrid surveillance

We have developed protocols and best practice guidelines for the non-lethal isolation of amphibian parasitising chytrids (**[3]**; **[A]**). These protocols have been used to train, guide and implement chytrid surveillance across 5 continents (Africa, Asia, Australia, Europe and South America) and 23 countries resulting in national risk assessments (e.g. Malagasy Sahonagasy Action Plan 2016 – 2020 **[B]**; Norwegian Risk Assessment **[C]**). Following our team's identification of *Bsal* in the Netherlands, worldwide screening of amphibian samples identified East Asia as the most likely origin of this infectious disease **[4, 5]**. This discovery has led to widespread changes in international biosecurity aimed at preventing further spread of this pathogen through controlling trade in disease vectors that we identified (see below).

International policy

Our implementation of genomic epidemiology across international scales has resulted in the identification of commercially gobally-traded disease vectors and has discovered the origins of both *Bd* and *Bsal* (research references 3-5). Our discoveries resulted in the listing of *Bsal* by the OIE (World Organisation for Animal Health) in 2018 **[D]**. Owing to the extreme risk posed to the salamander biodiversity that is native to the Americas and comprises the dominant vertebrate biomass in temperate broadleaf biomes, both the USA and Canada have imposed trade restrictions on salamanders (caudatans) as likely vectors of chytrid infections following our discovery of *Bsal* **[E, F]**. These trade restrictions were subsequently adopted by the EU **[G]**. Following a stakeholder engagement meeting in Brussels as part of our *RACE* (Risk Assessment of Chytridiomycosis to European amphians) project (principal investigator Fisher), we released an EU Policy Brief describing the risks to biodiversity due to emerging infections **[H]**. Consequentially the Bern convention has undertaken the 'Think outside the box' campaign to alert the wider public of the disease risks that that we revealed are posed by animal imports **[I]**. Thus far efforts to prevent the spread of *B. salamandrivorans* to the Americas have been successful with extensive surveillance showing no evidence of infection in wild or captive amphibians.

Mitigating the effects of chytridiomycosis

Our finding that *Bd* had been introduced into Mallorca **[J]**, infecting the IUCN RedList 'Critically Endangered' *Alytes muletensis*, led to widespread efforts to conserve this species including captive husbandry and an exhibition at ZSL London Zoo. Visitors to ZSL (annually ~1 million) can see our research outputs via the newly refurbished Amphibian Conservation Centre. Two dedicated video screens report results of the amphibian disease research program and daily live presentations made by keepers, researchers and trained presenters provide a proactive platform for informing the public regarding amphibian diseases, amphibian conservation, and our groups efforts to understand and mitigate the problem. In collaboration with the ZSL's Institute of Zoology the first tool for mapping cases of *Bd* infection globally was established **[K]**.

Our research at Imperial and with our collaborators into chemical disinfectants and antifungal compounds to treat amphibians with chytridiomycosis led to the first field-scale trial of antifungals leading to the eradication of chytridiomycosis in *A. muletensis* from infected drainage basins in the island of Mallorca in 2014 and the predicted elimination of this disease from the entire island **[L]**. This approach is now being trialled more widely by Spanish scientists across infected sites in Andalucia in the disease-threatened species *Alytes dickhelleni* (IUCN RedList category 'Vulnerable').

5. Sources to corroborate the impact (indicative maximum of 10 references)

[A] Global *Bd* surveillance and isolation: https://five.epicollect.net/project/bd-global-isolation-protocol (Archived here)

[B] Malagasy Sahonagasy Action plan (research cited on pages 28, 30, 32) https://www.researchgate.net/publication/304792717_New_Sahonagasy_Action_Plan_2016-2020 (Archived here)

[C] Norwegian Assessment of the risk to Norwegian biodiversity from the pathogenic fungi Batrachochytrium dendrobatidis (*Bd*) and Batrachochytrium salamandrivorans (*Bsal*) (May 2019: Reviewed by MC Fisher) Research cited on page 37, 38, 45, 51 https://vkm.no/english/riskassessments/allpublications/thepathogenicfungibatrachochytriumdendrobatidisandbatrachochytriumsalamandrivoransandriskofnegativeimpactonbiodiversity.4.2247e3031686ea532e099f6f.html (Archived here)

[D] OIE listing of *Bsal*: http://www.oie.int/fileadmin/Home/eng/Internationa_Standard_Setting/docs/pdf/A_BSAL_Disease_card.pdf (Archived here)

[E] USA Listing Salamanders as Injurious Due to Risk of Salamander Chytrid Fungus (January 12, 2016): https://www.fws.gov/injuriouswildlife/salamanders.html (Archived here) and research is cited in the rules document here https://www.federalregister.gov/documents/2016/01/13/2016-00452/injurious-wildlife-species-listing-salamanders-due-to-risk-of-salamander-chytrid-fungus (Archived here)

[F] Canadian listing of *Bsal*: https://www.canada.ca/en/environment-climate-change/services/convention-international-trade-endangered-species/import-species-harmful-ecosystems/restriction-salamanders.html (Archived here) and research cited here http://www.cwhc-rcsf.ca/salamander_chytridiomycosis.php (Archived here)

[G] EU listing of *Bsal*: COMMISSION IMPLEMENTING DECISION (EU) 2018/320 https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32018D0320&from=EN (Archived here)

[H] BiodivERsA Policy Brief (Sept. 2013): 'Wildlife diseases on the increase: A serious threat for Europe's biodiversity' http://www.biodiversa.org/552 (Archived here)

[I] Bern Convention 'Think outside the box' campaign http://unboxingdiseases.eu/exotic-species.html (2018) (Archived here)

[J] Walker SF, Bosch B, James TY, Litvintseva AP, Oliver Valls JA, Piña S, García G, Abadie Rosa G, Cunningham AA, Hole S, Griffiths R, Fisher MC. 2008. Invasive pathogens threaten species recovery programs. *Current Biology* doi.org/10.1016/j.cub.2008.07.033 (Archived here)

[K] Amphibian chytridiomycosis key achievement, ZSL, Institude of Zoology, https://www.zsl.org/amphibian-chytridiomycosis-key-achievements (Archived here)

[L] Bosch J, Sanchez-Tomé E, Fernández-Loras A, Oliver JA, Fisher MC, Garner TWJ. (2015) Successful elimination of a lethal wildlife infectious disease in nature. *Biology Letters.* https://doi.org/10.1098/rsbl.2015.0874 (Archived here)