Peer Community In
Infections

Usutu virus: Importance of a participatory research network to document the spatio-temporal circulation of USUV virus.

Florian Liégeois *based on peer reviews by* ***David Roiz*** *and 1 anonymous reviewer*

Malika Bouchez-Zacria, Clément Calenge, Alexandre Villers, Sylvie Lecollinet, Gaelle Gonzalez, Benoit Quintard, Antoine Leclerc, Florence Baurier, Marie-Claire Paty, Eva Faure, Cyril Eraud, Anouk Decors (2024) Relevance of the synergy of surveillance and populational networks in understanding the Usutu virus outbreak within common blackbirds (*Turdus merula*) in Metropolitan France, 2018. bioRxiv, ver. 2, peer-reviewed and recommended by Peer Community in Infections. `https://doi.org/10.1101/2024.07.22.604715`

Submitted: 25 July 2024, Recommended: 02 January 2025

Cite this recommendation as:
Liégeois, F. (2024) Usutu virus: Importance of a participatory research network to document the spatio-temporal circulation of USUV virus.. *Peer Community in Infections*, 100236. 10.24072/pci.infections.100236

Published: 02 January 2025

Usutu virus (USUV) is a neurotropic arbovirus of the family Flaviridae, genus *Orthoflavivirus* (`https://ictv.global/report/chapter/flaviviridae/flaviviridae/orthoflavivirus`). USUV is a member of the Japanese Encephalitis Virus serocomplex (JEV serocomplex) and frequently cocirculates with West Nile virus, with which it shares a similar natural life cycle involving mosquito species as primary vectors and avian species as amplifying hosts.

USUV was first discovered in 1959 in a *Culex neavi* mosquito species in South Africa and was subsequently detected in several African countries, including Madagascar. In 1996, USUV was detected in Italy (Weissenböck et al. 2013), and in France in 2015 (Lecollinet et al. 2016). Thus, USUV is currently endemic in Africa and Europe (Amy N. Nelson, Alexander Ploss, 2024).

Although USUV does not appear to be pathogenic in African bird populations, its introduction into Europe via migratory birds from Africa has had a devastating impact on local bird species, particularly in common blackbirds (Yannick Simonin, 2024). Besides, USUV can be transmitted to incidental hosts such as humans and thus represents an emerging threat for public health.

In a context of global change favoring the expansion of the habitats of the vectors involved in the transmission of USUV (and other emerging pathogens), it is essential to study the ecological and environmental factors facilitating its spread.

In this study presented by M. Bouchez-Zacria et al , the authors compiled data collected by various players in animal health (SAGIR and AFVPZ network) and avian wildlife conservation (REZOP network) in order to gain a better understanding of the spatial, temporal and population factors involved in the USUV epidemic event in France in 2018.

Although this study has a number of weaknesses, which are clearly identified by the authors, the originality of the methodological approach, which brings together different stakeholder networks, should be emphasised. It demonstrates the importance of a transdisciplinary approach in providing a better understanding of the factors involved in the spread of an emerging pathogen, and thus of the resources needed to combat this threat effectively.

References:

Weissenböck H, Bakonyi T, Rossi G, Mani P, Nowotny N. Usutu virus, Italy, 1996.Emerg Infect Dis. 2013 Feb;19(2):274-7. `https://doi.org/10.3201/eid1902.121191`.

Lecollinet S, Blanchard Y, Manson C, Lowenski S, Laloy E, Quenault H, Touzain F, Lucas P, Eraud C, Bahuon C, Zientara S, Beck C, Decors A. Dual Emergence of Usutu Virus in Common Blackbirds, Eastern France, 2015. Emerg Infect Dis. 2016 Dec;22(12):2225. `https://doi.org/10.3201/eid2212.161272`.

Amy N. Nelso, Alexander Ploss. Emerging mosquito-borne flaviviruses MBio December 2024 Volume 15 Issue 12 e02946-24. `https://doi.org/10.1128/mbio.02946-24`.

Simonin Y. Circulation of West Nile Virus and Usutu Virus in Europe: Overview and Challenges. Viruses. 2024 Apr 12;16(4):599. `https://doi.org/10.3390/v16040599`.

Bouchez-Zacria M., Calenge C., Villers S., Lecollinet S., Gonzalez G., Quintard B., Leclerc A., Baurier F., Paty MC, Faure E, Eraud C., Decors A. Relevance of the synergy of surveillance and populational networks in understanding the Usutu virus outbreak within common blackbirds (Turdus merula) in Metropolitan France, 2018. *bioRxiv* ver. 2, peer-reviewed and recommended by *PCI Infections*. `https://doi.org/10.1101/2024.07.22.604715`.

Reviews

Evaluation round #1

DOI or URL of the preprint: `https://doi.org/10.1101/2024.07.22.604715`
Version of the preprint: 1

Authors' reply, 18 December 2024

Download author's reply
Download tracked changes file

Decision by Florian Liégeois, posted 29 October 2024, validated 29 October 2024

Dear colleagues,

Your manuscript has been revieed by two referees. Your article has been positively evaluated, but it requires some revisions before it can be recommended.

I invite you to resubmit your manuscript, taking into account the reviewers' comments.

Yours sincerely

Reviewed by anonymous reviewer 1, 06 September 2024

Overall

The authors highlighted an important strategy on the potential use of data collected from different organization with different scope of work to describe an outbreak. I suggest that the utility of networks data synergies be added to the two objectives that are clearly indicated in lines (131-6). This clarifies that this aspect was part of the investigations as it is described throughout the manuscript, in the title and in the conclusion. The manuscript is sound, but it needs revision. My suggestions are provided below:Abstract

- A clear statement of the knowledge gap and the main objective of the study are currently missing in the abstract. This information could be summarized from the one presented in Lines 128-136
- Write (SAGIR) in full at first mention (Line 31)
- It is essential to specify the nature of the data collected regarding the 2018 USUV outbreak as part of the study details to provide context and support the research methodology (Lines 31-38).†
- Indicate the specific period of the USUV outbreak to give the reader an insight of what mid-July and August 2018 period meant in relation to the progression of the outbreak (Lines 31-38)
- Reporting the statistical parameters/ data of the main significant findings (Lines 38-40) would help the readers understand the quantitative aspects of the key findings †
- It would be beneficial to provide more specific details about the decline in findings by quoting relevant figures and statistical indicators (Lines 38-40).
- Mentioning the locations involved in the study and how they compare to one another would strengthen the abstract, which currently leans towards being primarily narrative.
- Conclusion currently absent

Introduction

- No need to repeat the abbreviation again since it has already been defined (Line 46)
- Almost 75 years now (Lines 68)
- There is a repetition of terms already defined eg ëevent basedÖ for SIGIR), Turdus merula for common blackbirds etc. This could be revised throughout the manuscript.

Materials and Methods

- While this section is thoroughly described to enable replication, it is rather too detailed, hence too long. I suggest the following revisions:
- Add study design section -eg. This study employed an observational ecological design, using data from existing surveillance networks to assess the spatial and temporal distribution of Usutu virus (USUV) infections among bird populations in France. Data were collected opportunistically from mortality events reported through the SAGIR and AFVPZ surveillance networks, encompassing wild and captive birds. The study design allowed for the examination of environmental and ecological factors influencing USUV distribution, such as proximity to wetlands and human population density, which serve as proxies for mosquito habitats and bird sampling pressures. We used spatial patterns and temporal trends at the population level, to understand the dynamics of USUV outbreaks and the identification of high-risk areas and informing future surveillance and management strategies.
- Summarize the section titled ”Epidemiological Surveillance Network and Provided Data” (L 170-249) focusing on the following key areas;

- Study Setting- Geographical area (Describe in 1 paragraph, the regions in France, covering the diverse habitats, urban and rural areas, wetland under study and where each of the network organizations operated). A map could help with the visualization of the study setting.
- Laboratory and surveillance infrastructure (A short summary of the scope of work of the accredited veterinary laboratories that conducted the various tests such as necropsy and virology etc.
- Data collection: Brief description of surveillance networks, SAGIR network, AFVPZ network and the type of data each collected
- Sampling and testing procedures (brief description of the necropsy and pathology testing - RT-PCR for USUV detection on tissue samples. This would not need to be detailed since this study used secondary data already gathered by the organizations. Provide details of the nature of data that was collected and used in this study and how it was reported and standardized

Results

- Use Figure or Table references in place of (see below) (L278; L309)
- Figure 1A needs to be interpreted further- It shows the comparison between the observed function and the simulated envelope under the complete spatial randomness (CSR) hypothesis (represented by the grey area) demonstrating significant spatial clustering of infected birds, indicating that cases are not randomly distributed but are concentrated in specific geographic areas.
- It is advisable to present the months in English since it is the language used in the manuscript. Alternatively provide key for English months (Figure 1C)
- Provide key to Figure 1B to identify the places described in text, eg. Paris, OrlÈans, Nantes (west of France; Fig. 1B). (L454-58). Alternatively provide a map showing the study area in the materials and methods under study setting so that readers can follow the write-up.
- Results could be tabulated for clearer view (L441-9). The table should also have a caption to describe the data presented in the table. This need to clear to show how these results are linked to the objectives of the study

DiscussionWell discussed.

————————————————————-

Title and abstract: Does the title clearly reflect the content of the article? [**X**] Yes, [ ] No (please explain), [ ] I don't know
Does the abstract present the main findings of the study? [**X**] Yes, [ ] No (please explain), [ ] I don't know
IntroductionAre the research questions/hypotheses/predictions clearly presented? **[X**] Yes, [ ] No (please explain), [ ] I don't know
Does the introduction build on relevant research in the field? [**X**] Yes, [ ] No (please explain), [ ] I don't know
Materials and methods Are the methods and analyses sufficiently detailed to allow replication by other researchers? [**X**] Yes, [ ] No (please explain), [ ] I don't know
Are the methods and statistical analyses appropriate and well described? [**X**] Yes, [ ] No (please explain), [ ] I don't know
ResultsIn the case of negative results, is there a statistical power analysis (or an adequate Bayesian analysis or equivalence testing)? [ ] Yes, [ ] No (please explain), [ ] I don't know **NA**
Are the results described and interpreted correctly? [**X**] Yes, [ ] No (please explain), [ ] I don't know
DiscussionHave the authors appropriately emphasized the strengths and limitations of their study/theory/methods/argument? [**X**] Yes, [ ] No (please explain), [ ] I don't know
Are the conclusions adequately supported by the results (without overstating the implications of the findings)? [**X**] Yes, [ ] No (please explain), [ ] I don't know

Reviewed by **David Roiz**, 28 October 2024

The authors presented a very interesting analysis based on the SAGIR, AFVPZ and REZOP networks to explain the epidemiological impact of Usutu on common blackbirds during 2018 in France. A very positive point is that the authors developed a package in R and that throughout the vignette of the supplementary materials it greatly helped to understand the analysis.

A negative point of the manuscript is the, not so clearly, explanations of the fact that the detected case locations were statistically associated with wetlands and high human log-density population areas. The authors stated that “the density of USUV cases varied as a function of wetlands and human density, two variables that are supposed to reflect mainly mosquito abundance“. (lines 652-654)

However, the underlying mechanism that explains the relation of wetlands with USUV cases is not well justified. The authors said that “the association between wetlands and USUV are consistent with the life cycle of USUV, with mosquitoes as vectors and wetlands known as suitable habitat for Cx. pipiens (Vogels et al., 2016)”. However, when reading this publication, the content it is not supporting this hypothesis. In the paper is stated that the “biotype Cx. pipiens pipiens (that is the ornitophilic biotype) is more abundant in peri-urban areas than in wetlands”, and that “Cx. pipiens populations that are dominated by biotype pipiens play an important role in the natural transmission cycle of WNV (and USUV) in birds…”.

Also, the underlying mechanism that explains the relation of high human population with USUV cases is not well justified. This might be mainly explained by the increasing reporting in these areas, and therefore, by a sampling bias. The solution is to weight by the possibility of reporting and make other analyses, if possible.

In fact, the authors said that “another part of the explanation could be Cx. pipiens, which have also been shown to be associated with urban (Haba and McBride 2022) or peri-urban (Vogels et al. 2016) environments, where breeding grounds favorable to mosquitoes could be found (e.g. rainwater collection containers or ponds in gardens) (Becker et al. 2010). This habitat preference might also explain the association we observed between cases of this vectorial disease and high human density”. (lines 676-681)

This explanation based on the Cx. pipiens abundance is contradictory to the one that said before that the vector is common in wetlands, so the explanation is that this is a synanthropic species related to human habitats. The sentence in lines 259-260 “Wetlands and human density were supposed to be a proxy for the density of Culex pipiens mosquitoes (Vogels et al., 2016)”

The discussion might be revised with more literature and particularly, adding more explanatory variables and covariables to explain accordingly the results of these interesting analyses.