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Illusion of epidemiological simplicity of H5N1 spread in cats in Poland - epidemiological remarks --Manuscript Draft--

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Corresponding Author:	Andrzej Jarynowski Interdisciplinary Research Institute Wroclaw, dolnośląskie POLAND
Corresponding Author's Institution:	Interdisciplinary Research Institute
First Author:	Andrzej Jarynowski
Order of Authors:	Andrzej Jarynowski
Suggested Reviewers:	Krzysztof Pyrc Jagiellonian University: Uniwersytet Jagiellonski w Krakowie k.a.pyrc@gmail.com Katarzyna Domańska PIWET: Panstwowy Instytut Weterynaryjny - Panstwowy Instytut Badawczy kasia.domanska@piwet.pulawy.pl Jakub Kubacki Veterinary Inspection jakub.kubacki@wetgiw.gov.pl
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Please copy/paste your covering letter here.	Remarks to: 1. Rabalski L, Milewska A, Pohlmann A, Gackowska K, Lepionka T, Szczepaniak K, et al. Emergence and potential transmission route of avian influenza A (H5N1) virus in domestic cats in Poland, June 2023. Eurosurveillance [Internet]. 2023 Aug 3 [cited 2023 Aug 6];28(31). Available from: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2023.28.31.2300390 2. Domańska-Blicharz K, Świętoń E, Świątalska A, Monne I, Fusaro A, Tarasiuk K, et

	al. Outbreak of highly pathogenic avian influenza A(H5N1) clade 2.3.4.4b virus in cats, Poland, June to July 2023. Eurosurveillance [Internet]. 2023 Aug 3 [cited 2023 Aug 6];28(31). Available from: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2023.28.31.2300366
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Have these findings already been published or is publication of these findings planned in a different format (e.g.: national or European report)?	
Do you have any conflicts of interest regarding your manuscript? If yes, please specify. If no, enter 'None'.	None
Have the nucleic acid sequence data been deposited in sustainable, public, and open access, databases?	No

Manuscript Classifications:	Poland; viral infections; influenza virus; geographic information system - GIS; outbreaks; surveillance
Author Comments:	One Health topics such as transmission of zoonotic agents of domestic/wild birds and environmental residue problems, food and feed safety become increasingly important to modern society in the post pandemic times. 2 articles were published about the H5N1 outbreak investigation and both suggest feed for cats as a possible source. I argue that the hypothesis of poultry meat (being feed for cats) contamination, seems to be unlikely (i.e. our study for veterinary inspection indicated that positive cases situated far from bird migratory paths were wrongly geocoded).

CONFIDENTIAL

Illusion of epidemiological simplicity of H5N1 spread in cats in Poland - epidemiological remarks

Recently published articles [1,2] on A/H5N1 spillover into mammals (cats) in Poland allow us to look at the emerging threat from different angles.

Rabalski et al. [1] involved a participatory approach with animal owners self-report and included in phylogenetic analysis isolates obtained from not-referenced labs collected without sanitary/veterinary supervision (which without understanding how the concept of infodemics could lead to wrong conclusions about distribution and cause of the infections). On the other hand, Domańska et al. [2] used the reference laboratory positive cases as the material (which without spatio-temporal context and non-including negative results could lead to missing important clustering and path forming patterns). Both approaches are complementary, but a kind of integrative approach is missing to incorporate strong and weak sides of each dataset. The authors adopted a number of simplifications, which should be justified, as papers may reach a wide audience and may be cited by one health community or journalists. Articles also require a deeper interpretation of data and methods quality for a professional reader [3].

Both articles have multiple errors i.e. in maps Figure 1.b Rabalski et al. [1] Figure 1 Domańska et al. [2] suggest that there were cases in Lubuskie and Łódzkie voivodeships, which was not the case at least in the time period marked by authors. However, this is acceptable as authors did not have time for proper data curation in rapid communication schema.

Therefore, the analyses (from an epidemiological point of view) require commentary because they may be misinterpreted by people who are not educated in the field of epidemiology [4]. As there is a range of possible limitations i.e. related to data collection (selective usage of sources) and analysis type (non-analytical), I have only picked up these, which authors could have control on.

1) Rabalski et al. [1] claimed that due to i) nationwide distribution of cat cases suspected of being related to the outbreak; ii) that both indoor and outdoor cats have contracted the infection, iii) monophyletic origin of the virus all together suggest a common exposure (feed for cats), even such kind of implication is doubtful. However, Domańska et al. [2], already proved that there were at least two separate A/H5N1 introductions into the feline population in east and west of Poland (different spring bird migration corridors [5]). Moreover, Rabalski et al. [1] did not attempt to differentiate signal from noise from citizens' databases [5,6]. Participatory cases can be analysed only together with a media driven background [6], which is known state of the art in infoveillance [4]. Thus, some other cats' diseases with neurological symptoms may be included in the citizen database and we see some clusters of FIV/FeLV and Toxoplasmosis among negative results from WOA reference lab [7].

2) Both Rabalski et al. [1] and Domańska et al. [2] did not perform any spatio-temporal analysis of the collected material. However, the clear difference between positive results and both negative cases [5,7] and community samples [5,6] appear. Positive cases from WOA reference lab [7] form two geographical chains with characteristic shorter nearest neighbours'

1 distance and smaller k-means betweenness from the comparator [5,7] Moreover, these chains
2 lay exactly on known bird migration corridors.

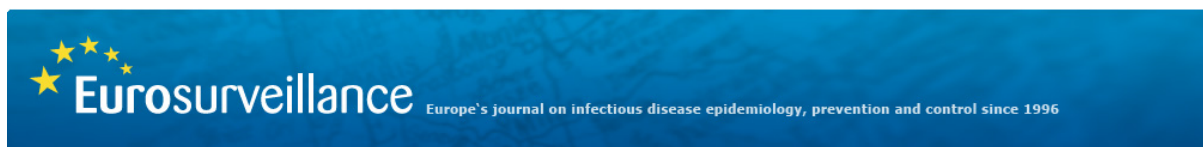
3 3) Both Rabalski et al. [1] and Domańska et al. [2] did not find spatial clusters on phylogenetic
4 trees. Spatio-temporal-genetic inference analysis indicates two clear clusters from Western
5 Poland and additional clusters being a mix of Pomerania and Lublin region cases i.e. using
6 DBscan mapping [5]. The only exception of meaningful clustering are inter-community links
7 between Gdańsk and Lublin with exchange of pathogens that may be, but not must be driven
8 by feed. Alternative explanation could be human mobility as Gdańsk metropolitan area is a
9 well-known touristic resort.

10 3) Domańska et al. [2] claim that simultaneous detection of multiple non-homogeneous
11 clusters of viruses (>10 SNP between clusters) points in the direction of an unidentified
12 intermediate food source (poultry meat contaminated with the virus). However, epidemic curve
13 shape [7] suggests that data obtained from a reference lab are coming from a late phase of
14 the outbreak. Thus, the early phase of the epizootic may be only inferred from other
15 repositories i.e. infoveillance [6]. Then, a clear gradient in time from south east to north [5–7]
16 can be observed (exactly on bird migration corridors).

17
18 In conclusion, the published articles may suggest to a reader that the source of the infection
19 is poultry meat in feed, but the outbreak investigation is not yet finished and other hypotheses
20 environmental with migrating birds or some hybrid forms are still valid. My comments are not
21 accusations but only remarks indicating the limitation and consequences of selective choice
22 of data sources and methods and only a triangulation of data and methods may lead to
23 explanation of such a phenomenon [3]. However, the authors proved, that in case of not-
24 known disease or spillover of known disease to a new host the European Surveillance System
25 (i.e. acting in Poland) is inefficient and needs reorganisation for future threats.

26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65

1. Rabalski L, Milewska A, Pohlmann A, Gackowska K, Lepionka T, Szczepaniak K, et al. Emergence and potential transmission route of avian influenza A (H5N1) virus in domestic cats in Poland, June 2023. *Eurosurveillance*. 2023; 28(31). Available from: <https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2023.28.31.2300390>
2. Domańska-Blicharz K, Świętoń E, Świątalska A, Monne I, Fusaro A, Tarasiuk K, et al. Outbreak of highly pathogenic avian influenza A(H5N1) clade 2.3.4.4b virus in cats, Poland, June to July 2023. *Eurosurveillance*. 2023; 28(31). Available from: <https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2023.28.31.2300366>
3. Jarynowski A. Reflection on contextual factors associated with burden of infectious diseases in multi-country modelling approach on the example of Eastern Europe. *E-Methodol*. 2021;8(8):99–105.
4. Jarynowski A, Wójta-Kempa M. Exploring the link between risk perception in internet media and the prevalence of COVID-19 in Europe. *Int J Infect Dis*. 2021;103:450–1.
5. Jarynowski A. Spatio-temporal analysis of H5N1 in cats in Poland (comparison of sources) [Internet]. 2023 Jul. Available from: <https://rpubs.com/gulakov/1069216> (updated 05.08 by including molecular dynamics)
6. Jarynowski A. Spatio-temporal analysis of H5N1 in cats in Poland (citizens data) [Internet]. 2023 Jul. Available from: <http://rpubs.com/gulakov/1069159>
7. Jarynowski A. Spatio-temporal analysis of H5N1 in cats in Poland based on data from WOA reference lab [Internet]. 2023 Jul. Available from: <https://rpubs.com/gulakov/1069204> (updated 05.08 i.e. correcting errors in official database)



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