Antimicrobico-resistenza: cure e ambiente #7

Nulla è costante, se non il cambiamento

CONVEGNO ECM - **Crediti: 7**

19 giugno 2024 ore 9.15-17.30

Auditorium di Sant'Apollonia via S. Gallo, 25/a - Firenze

Cambiamenti in atto nelle malattie da artropodi vettori

Michele Spinicci

Dipartimento di Medicina Sperimentale e Clinica, Università di Firenze
SOD Malattie Infettive e Tropicali, AOU Careggi, Firenze

- Vector-borne diseases involve parasites, bacteria or viruses that are transmitted to humans and other vertebrates by the bite of infected haematophagous arthropods, including mosquitoes, ticks, sandflies, midges, triatomine bugs and blackflies.

- Approximately 6.3 billion people live at risk of vector-borne diseases, which cause more than 300 million disease cases and more than 700,000 deaths annually

- Malaria and dengue fever cause the highest disease burdens
  - 219 million **malaria** cases and more than 500,000 deaths occur annually, disproportionally affecting children in Africa
  - 96 million **dengue** cases and 40,000 deaths annually

- Other prominent vector-borne human diseases include *yellow fever, chikungunya, Zika virus (ZIKV) diseases, West Nile virus (WNV) infections, Japanese encephalitis virus (JEV) infections, Rift Valley fever, leishmaniasis, plague, typhus, tick-borne encephalitis, Lyme disease, Chagas disease, lymphatic filariasis, onchocerciasis and human African trypanosomiasis, Toscana virus (TOSV) infection*

World Health Organization. Global vector control response 2017–2030; Nat Microbiol. 2019;4(9):15-1515;
Nat Rev Microbiol. 2024 Mar 14. doi: 10.1038/s41579-024-01026-0.

Effects of climate change on vector-borne diseases

- Transmission cycles can be limited to a small number of competent vectors and a single vertebrate host (e.g. *Plasmodium* spp., *Wuchereria bancrofti* (lymphatic filariasis) and DENV)

- Most vector-borne diseases are *zoonotic* and use various wild animals as *enzootic* hosts, with *spillover* infections to humans (e.g. WNV).

- Vectors are ectothermic (cold-blooded and unable to regulate their body temperature) and particularly affected by weather patterns (especially temperature but also humidity) and climate (long-term weather patterns)

- Weather and climate may have very different impacts on vector biology (rates of development, longevity and survival, fecundity, biting, and pathogen replication and development in the vector required for transmission)

Nat Rev Microbiol. 2024 Mar 14. doi: 10.1038/s41579-024-01026-0.

Impact of extreme weather on vectors and vector-borne diseases

High temperatures

Altered vector activity and bite rates
(for example, mosquitoes, ticks and midges)

Increased transmission risk
(for example, dengue, tularemia and leishmaniasis)

Altered extrinsic incubation period
(for example, mosquitoes and midges)

Increased survival of adult female vectors
(for example, mosquitoes)

Floods

Altered suitable aquatic environment for reproduction
(for example, mosquitoes, sandflies and midges)

Altered dipteran vector population
(for example, mosquitoes, sandflies and midges)

Increased exposure to vector bites
(for example, mosquitoes)

Decreased tick vector populations
(for example, hard ticks and soft ticks)

Droughts

Increased dipteran vector population
(for example, mosquitoes)

Increased transmission risk
(for example, West Nile and dengue viruses)

Increased exposure to vector bites
(for example, mosquitoes)

Decreased tick vector populations
(for example, hard ticks and soft ticks)

Effects of climate change on vector-borne diseases

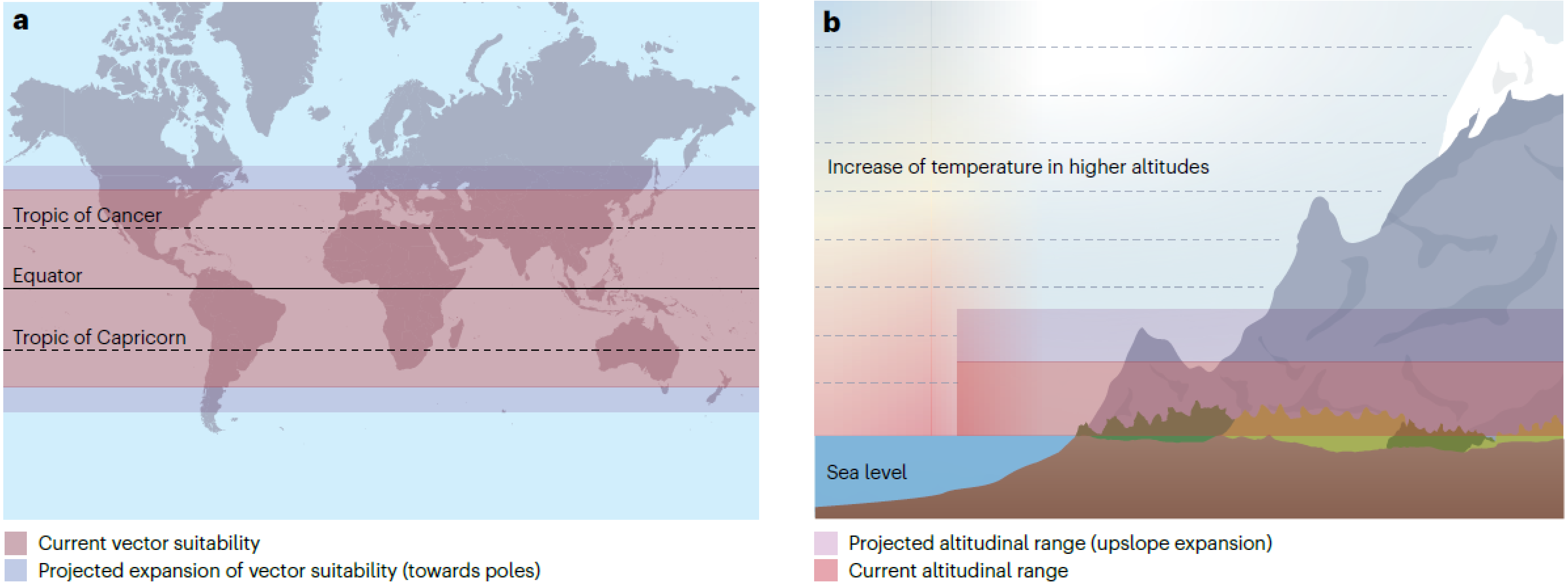
- **Impact on vector development and life cycles**
  - Weather and climate may have very different impacts on vectors with varying life spans (e.g. mosquitos *vs* ticks)
  - Intense precipitation may create more suitable aquatic environments for oviposition, larval development and survival of vectors *vs* very heavy rainfall associated may wash away immature aquatic mosquitoes, strong winds associated with flooding storms may kill many adult mosquitoes
  - Drought alters transmission by increasing the vector–host ratio (due to lower host reproduction), or if patterns of host–vector contact are altered

- **Impact on vector-borne pathogen transmission**
  - Climate and weather can directly or indirectly influence all four components of vectorial capacity: parasite's extrinsic incubation period (EIP; n days), the mosquito to human ratio (m), daily mosquito survival (p) and the human biting rate (a): $\mathbf{V = ma^2p^n/-\ln(p)}$

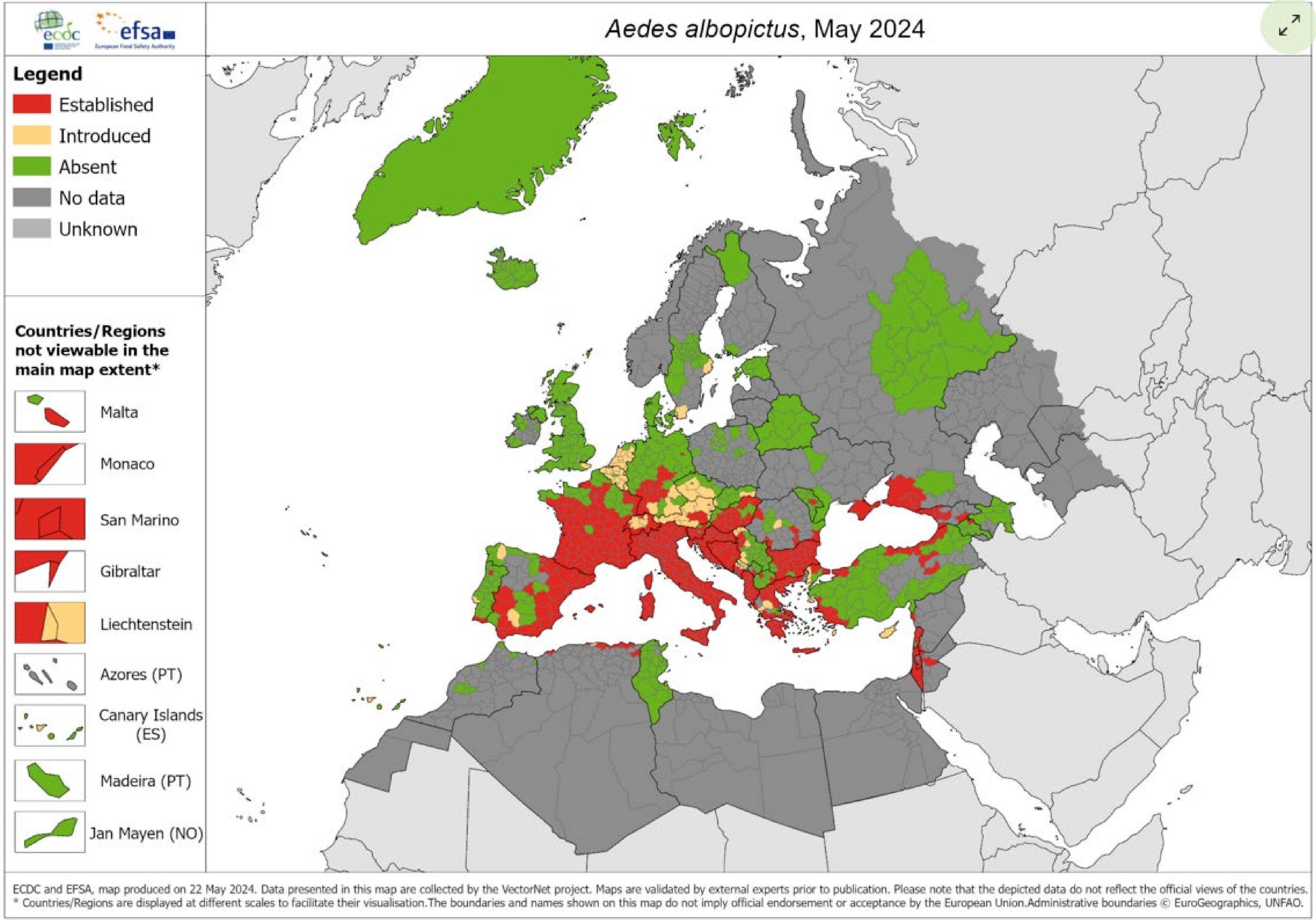
- **Impact on the distribution of vector-borne pathogens**
  - Climate change will promote a redistribution of vectors and vector-borne diseases
  - Climate change can promote a shift among vector-borne diseases within the same region, e.g. warming temperatures projected in many regions will likely transfer the malaria disease burden to *A. aegypti*-borne viruses (DENV, ZIKV, YFV and CHIKV) in sub-Saharan Africa

Nat Rev Microbiol. 2024 Mar 14. doi: 10.1038/s41579-024-01026-0.

Potential impact of climate change on geographical distribution of vectors



Some vectors (for example, *Aedes aegypti*, *Aedes albopictus*, *Culex quinquefasciatus* and *Dermacentor variabilis*) and vector-borne pathogens (for example, DENV, ZIKV and CHIKV) that are currently circulating predominantly in tropical and subtropical climate zones may expand latitudinally into previously temperate zones (towards poles). Also, the altitudinal gradient vector-borne pathogen range may extend to higher elevations due to warming temperatures in the current altitudinal range owing to climate change.


Aedes albopictus, May 2024
Legend
Established
Introduced
Absent
No data
Unknown
Countries/Regions not viewable in the main map extent*
Malta
Monaco
San Marino
Gibraltar
Liechtenstein
Azores (PT)
Canary Islands (ES)
Madeira (PT)
Jan Mayen (NO)
ECDC and EFSA, map produced on 22 May 2024. Data presented in this map are collected by the VectorNet project. Maps are validated by external experts prior to publication. Please note that the depicted data do not reflect the official views of the countries.
* Countries/Regions are displayed at different scales to facilitate their visualisation.The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union.Administrative boundaries © EuroGeographics, UNFAO.

Infection with chikungunya virus in Italy: an outbreak in a temperate region

G Rezza*, L Nicoletti*, R Angelini, R Romi, A C Finarelli, M Panning, P Cordioli, C Fortuna, S Boros, F Magurano, G Silvi, P Angelini, M Dottori, M G Ciufolini, G C Majori, A Cassone, for the CHIKV study group†

Lancet 2007; 370: 1840–46

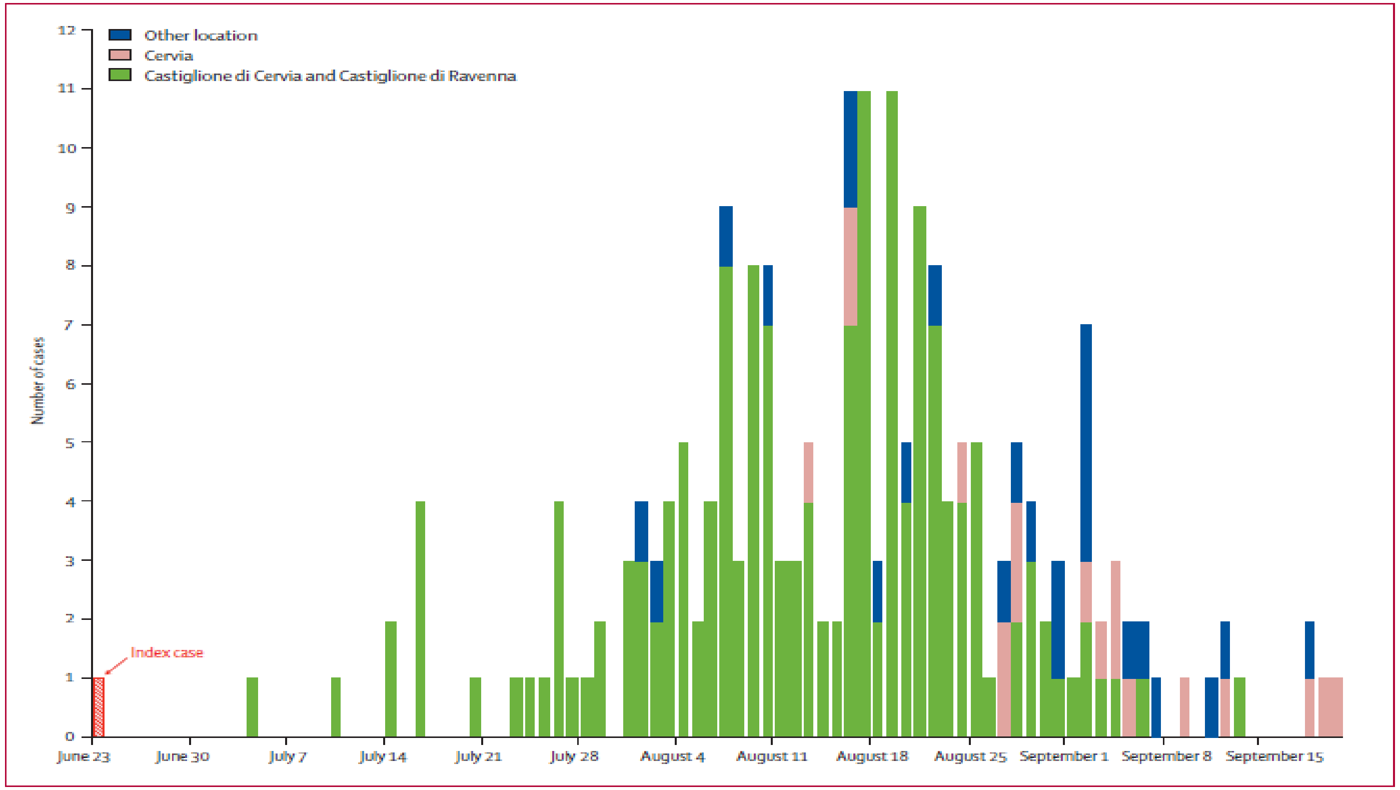


***Figure 1*: Epidemic curve**
Distribution of dates of onset of symptoms for CHIKV cases by presumed place of infection (ie, Castiglione di Cervia and Castiglione di Ravenna, Cervia, or other/unknown location).

	Number of cases (%)
Fever*	205 (100%)
Joint pain†	199 (97%)
Fatigue	190 (93%)
Skin rash	106 (52%)
Headache	105 (51%)
Muscle pain	94 (46%)
Diarrhoea	48 (23%)
Itching	42 (20%)
Vomiting	40 (19%)
Photophobia	31 (15%)
Conjunctivitis	7 (3%)

*Mandatory in the case definition. †Not mandatory if diagnosis is laboratory confirmed.

***Table 2*: Distribution of symptoms**

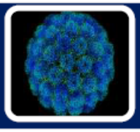
CHIKUNGUNYA – Outbreak in Italy

ITALY: AUTOCHTONOUS CASES OF CHIKUNGUNYA VIRUS
(updated 27 October 2017)

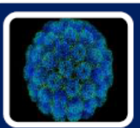
402 Total notified cases:
- **331** Lazio Region
- **63** Calabria Region
- **5** Emilia-Romagna Region
- **1** Marche Region
- **2** European Countries (France/Germany)

225 Total confirmed cases:
- **176** Lazio Region (Anzio, Roma and Latina)
- **45** Calabria Region (Guardavalle marina)
- **1** Emilia-Romagna Region with epidemiological link to Anzio
- **1** Marche Region with epidemiological link to Anzio
- **1** France with epidemiological link to Anzio
- **1** Germany with epidemiological link to Roma

177 Total probable cases:
- **155** Lazio Region (Anzio, Roma e Latina)
- **18** Calabria Region (Guardavalle marina)
- **3** Emilia-Romagna Region with epidemiological link to Guardavalle marina
- **1** Emilia-Romagna Region with epidemiological link to Roma



189 (46 %) MALES
213 (54 %) FEMALES
Median age: **55 years** (range: 0-93 ys)

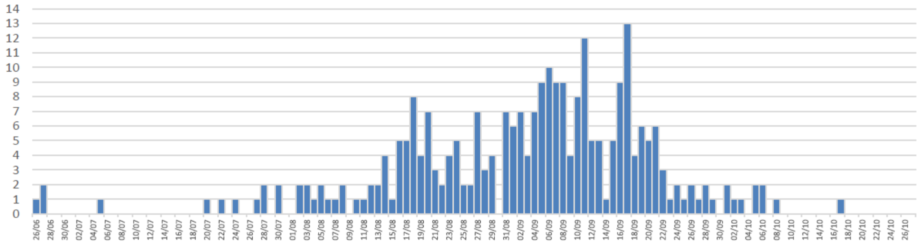


Severity of infection
Hospitalized **30** (7 %)
Mortality: **1** confirmed

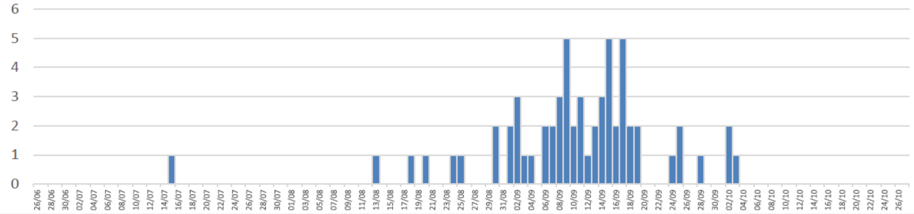
Ministero della Salute

ISTITUTO SUPERIORE DI SANITÀ

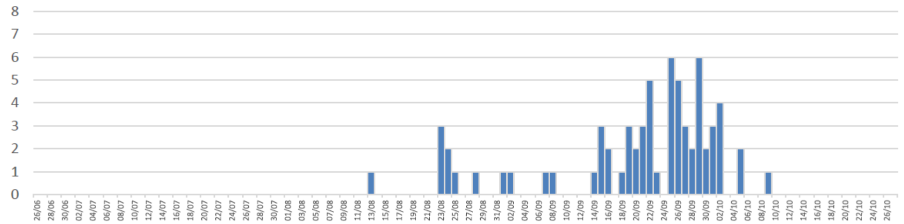
ANZIO: Curva Epidemica (abitanti ad Anzio o casi epidemiologicamente correlati), per data insorgenza
ANZIO: Epidemic curve (Anzio residents or cases or epidemiologically linked), date of onset



ROMA: Curva Epidemica (nessuna storia di viaggio) per data insorgenza sintomi
ROME: Epidemic Curve (no history of travel), date of onset

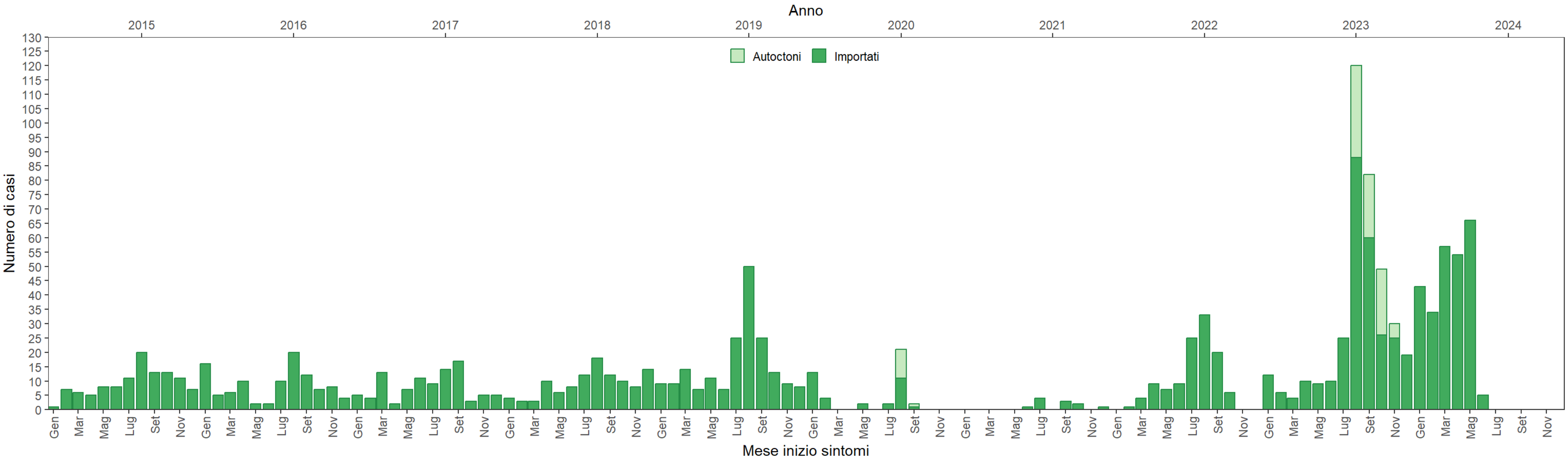


Regione Calabria (Guardavalle marina): Curva Epidemica, per data insorgenza sintomi
Calabria Region: Epidemic Curve, date of onset

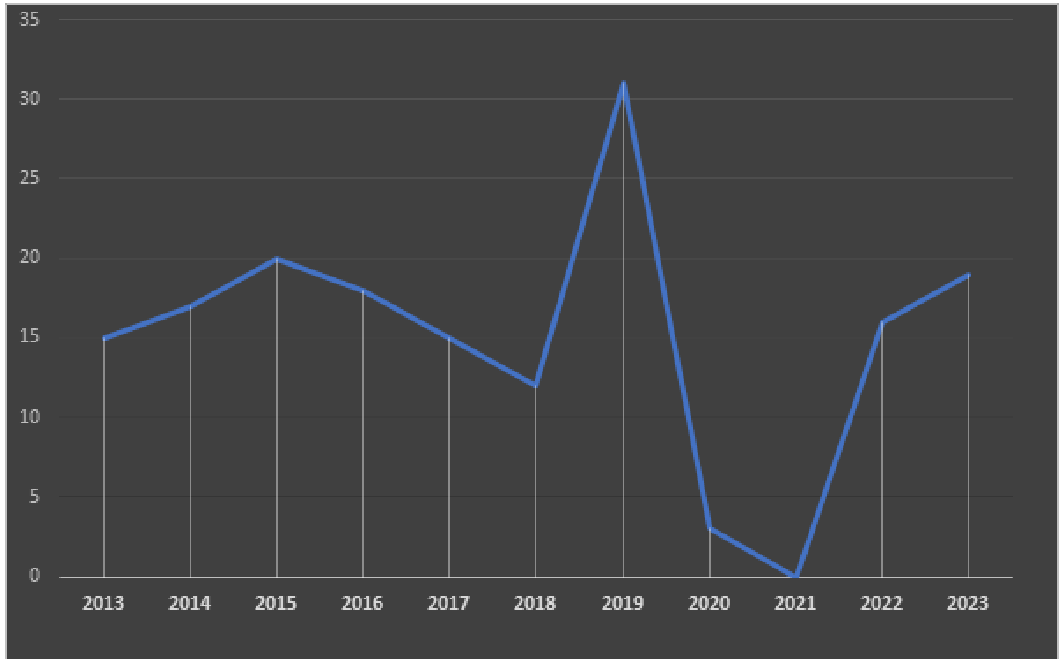


Fonte:

Casi confermati di Dengue dal 2015 al 2024*



Arbovirosi in Italia – 2024 **Data di ultimo aggiornamento**: 10 giugno 2024
https://www.epicentro.iss.it/arbovirosi/dashboard



Numero di casi di Dengue per anno. Toscana, anni 2013-2023. Fonte: ARS

https://www.ars.toscana.it/2-articoli/5123-aumentato-rischio-contrarre-virus-dengue-a-seguito-diffusione-zanzare-aedes.html

Rai News.it

CRONACA

Disposta una disinfestazione nelle aree interessate

Firenze: donna di 50 anni muore dopo aver contratto la febbre dengue

La donna, ritornata da un viaggio in Thailandia, già soffriva di altre patologie gravi. L'Asl spiega che dopo i primi sintomi il quadro clinico è notevolmente peggiorato

17/11/2023

JOURNAL ARTICLE ACCEPTED MANUSCRIPT

Emergence of dengue fever: sentinel travellers uncover outbreak in Sharm El-sheikh, Egypt, may 2024

Tommaso Manciulli, MD PhD, Lorenzo Zammarchi, MD ✉, Filippo Lagi, MD PhD, Costanza Fiorelli, MD, Jessica Mencarini, MD PhD, Marco Fognani, MD, Gian Maria Rossolini, MD, Simona Pollini, PhD, Alessandro Bartoloni, MD, Michele Spinicci, MD

Journal of Travel Medicine, taae080, https://doi.org/10.1093/jtm/taae080

Published: 10 June 2024 **Article history ▾**

Ministero della Salute

EX DIREZIONE GENERALE DELLA PREVENZIONE SANITARIA
IL DIRETTORE GENERALE

OGGETTO: Misure di vigilanza sanitaria nei confronti del virus della dengue. Chiarimenti alla circolare n. prot. 4753 del 14 febbraio 2024.

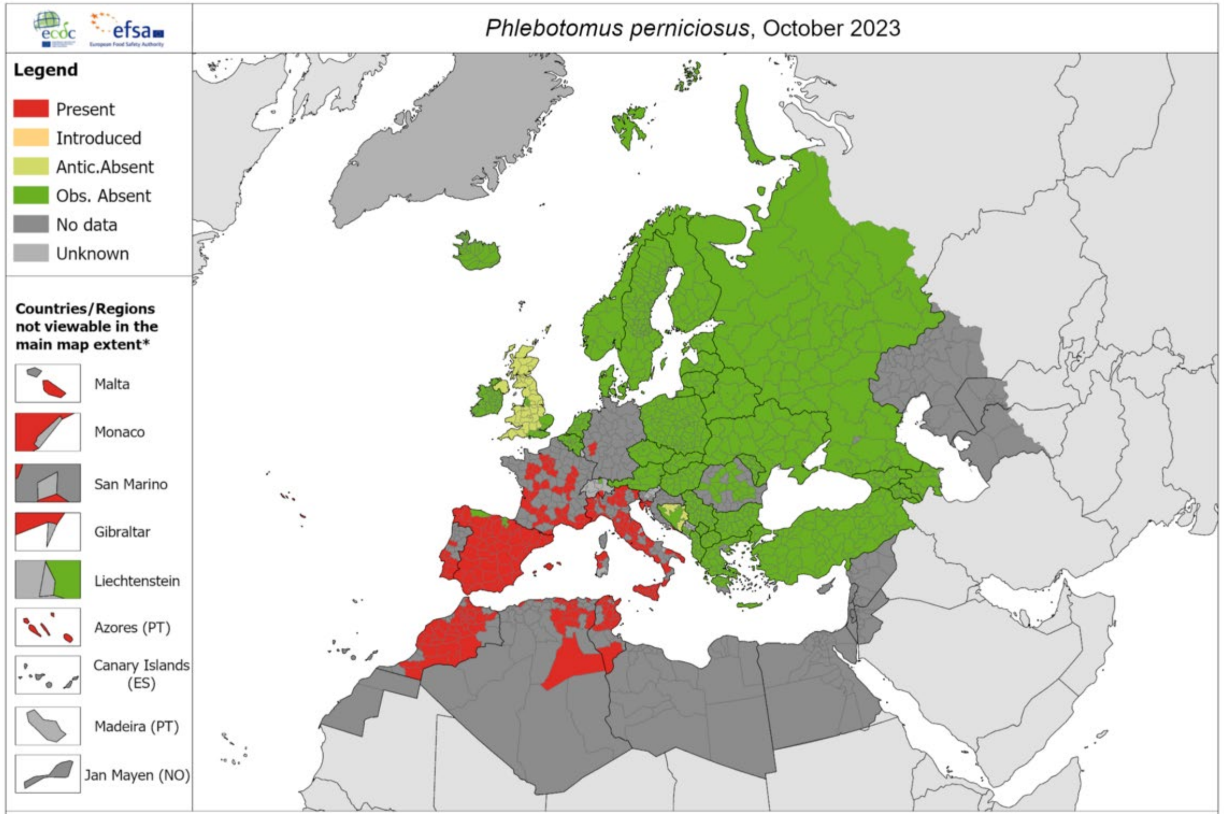
1. Introduzione

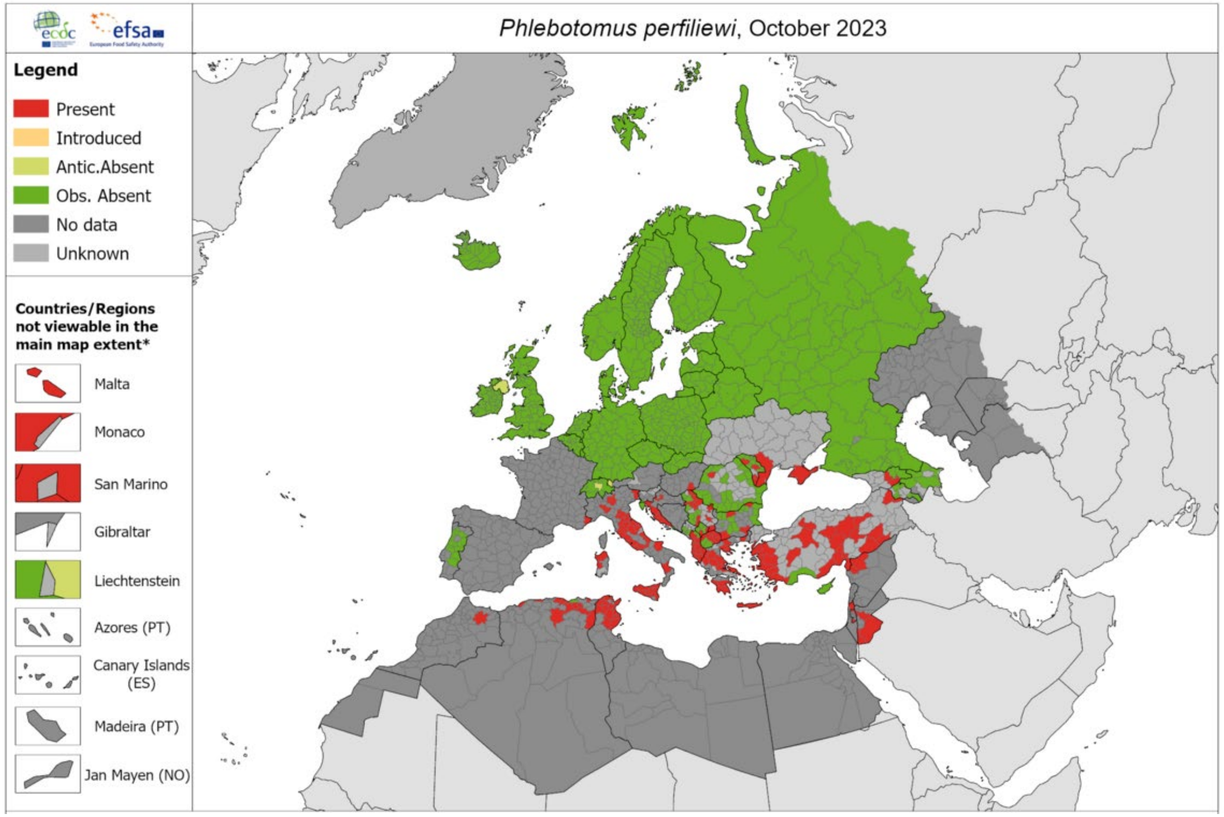
Si fa seguito alla circolare di cui all'oggetto, prot. 4753-14/02/2024-DGPRE-MDS-P, recante "*Innalzamento livello di allerta relativamente alla diffusione della dengue presso i Punti di ingresso italiani*", per fornire ulteriori precisazioni e chiarimenti.

Occorre anzitutto specificare che le misure di vigilanza sanitaria si applicano ai mezzi di trasporto ed alle merci che provengono dai Paesi in cui è presente l'*Aedes aegypti*, vettore maggiormente competente per la trasmissione della dengue, nonché dai Paesi dove il rischio di contrarre la patologia sia frequente e continuo, secondo quanto riportato dal Centre for Disease Control and Prevention (CDC) statunitense (https://www.cdc.gov/dengue/areaswithrisk/around-the-world.html), ed in ossequio a quanto previsto dal Piano Nazionale di prevenzione, sorveglianza e risposta alle Arbovirosi (PNA) 2020-2025. (Cfr. Circolare del 14 febbraio 2024 - **Allegato 1**).

Ciò in ragione del fatto che l'obiettivo primario è di impedire che il vettore venga introdotto in Italia.

Phlebotomine sandfly





Toscana Virus

- Due to its neuroinvasiveness, TOSV is currently the most public-health relevant phlebovirus transmitted by sandflies
- In France, Italy and Tunisia, Toscana virus ranks within the three most common causes of summer meningitis after enteroviruses and herpesviruses (HSV, VZV)
- To date, only *P. perniciosus* and *P. perfiliewi* have been formally identified as vectors
- The reservoir for maintenance of Toscana virus circulation is not yet been determined
- 862 published cases of infection with TOSV in residents of or travelers to Mediterranean countries
- Evidence that TOSV is present in North Africa (Algeria, Morocco, Tunisia), in the Balkan Peninsula (Greece, Croatia, Kosovo, Bosnia Herzegovina), and in the Mediterranean islands (Elba, Baleares, Malta, Corsica, Sardinia, Cyprus, Crete).

Clinical Microbiology and Infection 26 (2020) 1017e1023

TOSMANIA study

Epidemiological and clinical characteristics of human leishmaniasis in Tuscany region, Italy in the period 2018-2023

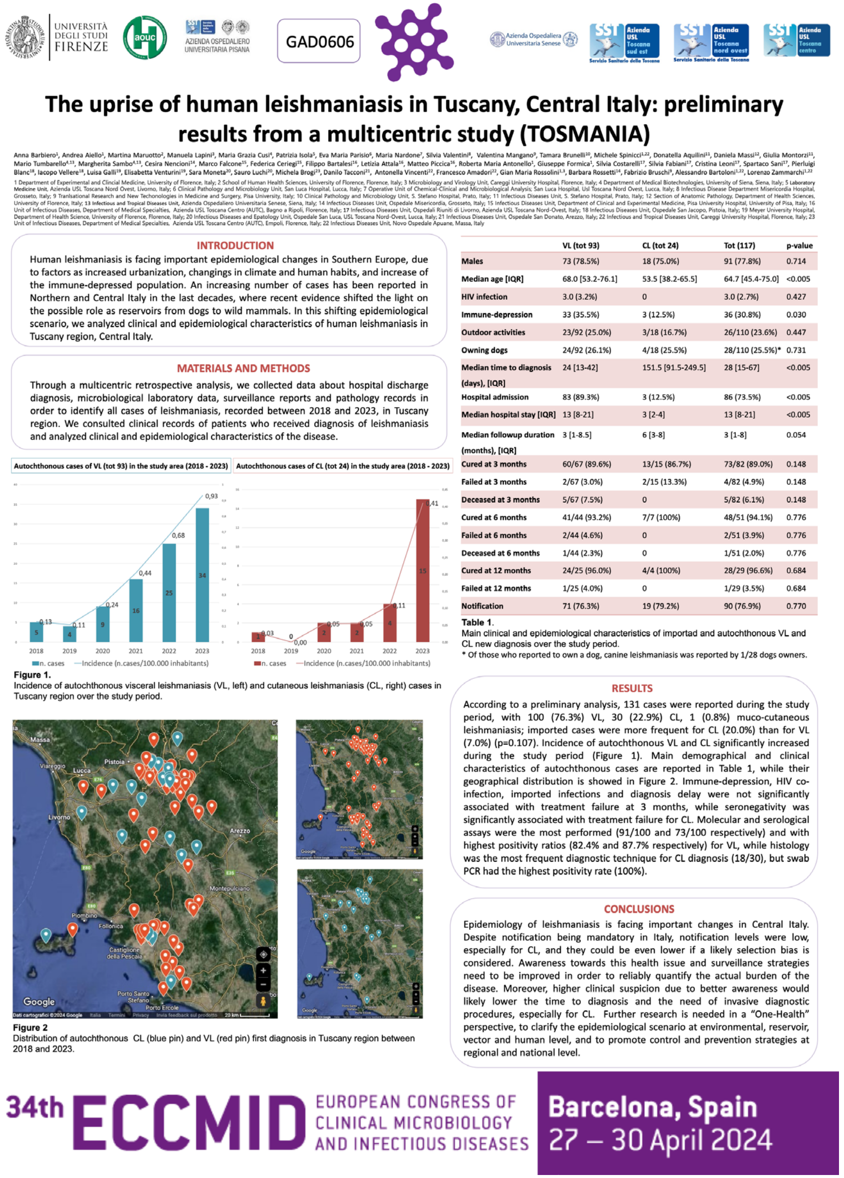
MATERIALI E METODI

- Coinvolgimento di tutti i centri di malattie infettive della Toscana: **12 centri in totale** (inclusa la popolazione pediatrica)
- Raccolta dati da: SDO, positività microbiologiche, diagnosi di anatomia patologica, notifiche

RISULTATI PRELIMINARI

- 156 casi totali:
- 119 (76.3%) VL + 36 (23.1%) CL + 1 (0.6%) MCL

- 136 casi AUTOCTONI: 107 VL + 29 CL



The uprise of human leishmaniasis in Tuscany, Central Italy: preliminary results from a multicentric study (TOSMANIA)

INTRODUCTION

Human leishmaniasis is facing important epidemiological changes in Southern Europe, due to factors as increased urbanization, changings in climate and human habits, and increase of the immune-depressed population. An increasing number of cases has been reported in Northern and Central Italy in the last decades, where recent evidence shifted the light on the possible role as reservoirs from dogs to wild mammals. In this shifting epidemiological scenario, we analyzed clinical and epidemiological characteristics of human leishmaniasis in Tuscany region, Central Italy.

MATERIALS AND METHODS

Through a multicentric retrospective analysis, we collected data about hospital discharge diagnosis, microbiological laboratory data, surveillance reports and pathology records in order to identify all cases of leishmaniasis, recorded between 2018 and 2023, in Tuscany region. We consulted clinical records of patients who received diagnosis of leishmaniasis and analyzed clinical and epidemiological characteristics of the disease.

Figure 1. Incidence of autochthonous visceral leishmaniasis (VL, left) and cutaneous leishmaniasis (CL, right) cases in Tuscany region over the study period.

Figure 2 Distribution of autochthonous CL (blue pin) and VL (red pin) first diagnosis in Tuscany region between 2018 and 2023.

	VL (tot 93)	CL (tot 24)	Tot (117)	p-value
Males	73 (78.5%)	18 (75.0%)	91 (77.8%)	0.714
Median age [IQR]	68.0 [53.2-76.1]	53.5 [38.2-65.5]	64.7 [45.4-75.0]	<0.005
HIV infection	3.0 (3.2%)	0	3.0 (2.7%)	0.427
Immune-depression	33 (35.5%)	3 (12.5%)	36 (30.8%)	0.030
Outdoor activities	23/92 (25.0%)	3/18 (16.7%)	26/110 (23.6%)	0.447
Owning dogs	24/92 (26.1%)	4/18 (25.5%)	28/110 (25.5%)*	0.731
Median time to diagnosis (days), [IQR]	24 [13-42]	151.5 [91.5-249.5]	28 [15-67]	<0.005
Hospital admission	83 (89.3%)	3 (12.5%)	86 (73.5%)	<0.005
Median hospital stay [IQR]	13 [8-21]	3 [2-4]	13 [8-21]	<0.005
Median followup duration (months), [IQR]	3 [1-8.5]	6 [3-8]	3 [1-8]	0.054
Cured at 3 months	60/67 (89.6%)	13/15 (86.7%)	73/82 (89.0%)	0.148
Failed at 3 months	2/67 (3.0%)	2/15 (13.3%)	4/82 (4.9%)	0.148
Deceased at 3 months	5/67 (7.5%)	0	5/82 (6.1%)	0.148
Cured at 6 months	41/44 (93.2%)	7/7 (100%)	48/51 (94.1%)	0.776
Failed at 6 months	2/44 (4.6%)	0	2/51 (3.9%)	0.776
Deceased at 6 months	1/44 (2.3%)	0	1/51 (2.0%)	0.776
Cured at 12 months	24/25 (96.0%)	4/4 (100%)	28/29 (96.6%)	0.684
Failed at 12 months	1/25 (4.0%)	0	1/29 (3.5%)	0.684
Notification	71 (76.3%)	19 (79.2%)	90 (76.9%)	0.770

Table 1. Main clinical and epidemiological characteristics of importad and autochthonous VL and CL new diagnosis over the study period.
* Of those who reported to own a dog, canine leishmaniasis was reported by 1/28 dogs owners.

RESULTS

According to a preliminary analysis, 131 cases were reported during the study period, with 100 (76.3%) VL, 30 (22.9%) CL, 1 (0.8%) muco-cutaneous leishmaniasis; imported cases were more frequent for CL (20.0%) than for VL (7.0%) (p=0.107). Incidence of autochthonous VL and CL significantly increased during the study period (Figure 1). Main demographical and clinical characteristics of autochthonous cases are reported in Table 1, while their geographical distribution is showed in Figure 2. Immune-depression, HIV co-infection, imported infections and diagnosis delay were not significantly associated with treatment failure at 3 months, while seronegativity was significantly associated with treatment failure for CL. Molecular and serological assays were the most performed (91/100 and 73/100 respectively) and with highest positivity ratios (82.4% and 87.7% respectively) for VL, while histology was the most frequent diagnostic technique for CL diagnosis (18/30), but swab PCR had the highest positivity rate (100%).

CONCLUSIONS

Epidemiology of leishmaniasis is facing important changes in Central Italy. Despite notification being mandatory in Italy, notification levels were low, especially for CL, and they could be even lower if a likely selection bias is considered. Awareness towards this health issue and surveillance strategies need to be improved in order to reliably quantify the actual burden of the disease. Moreover, higher clinical suspicion due to better awareness would likely lower the time to diagnosis and the need of invasive diagnostic procedures, especially for CL. Further research is needed in a "One-Health" perspective, to clarify the epidemiological scenario at environmental, reservoir, vector and human level, and to promote control and prevention strategies at regional and national level.

34th ECCMID EUROPEAN CONGRESS OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES
Barcelona, Spain 27 – 30 April 2024

TOSMANIA study

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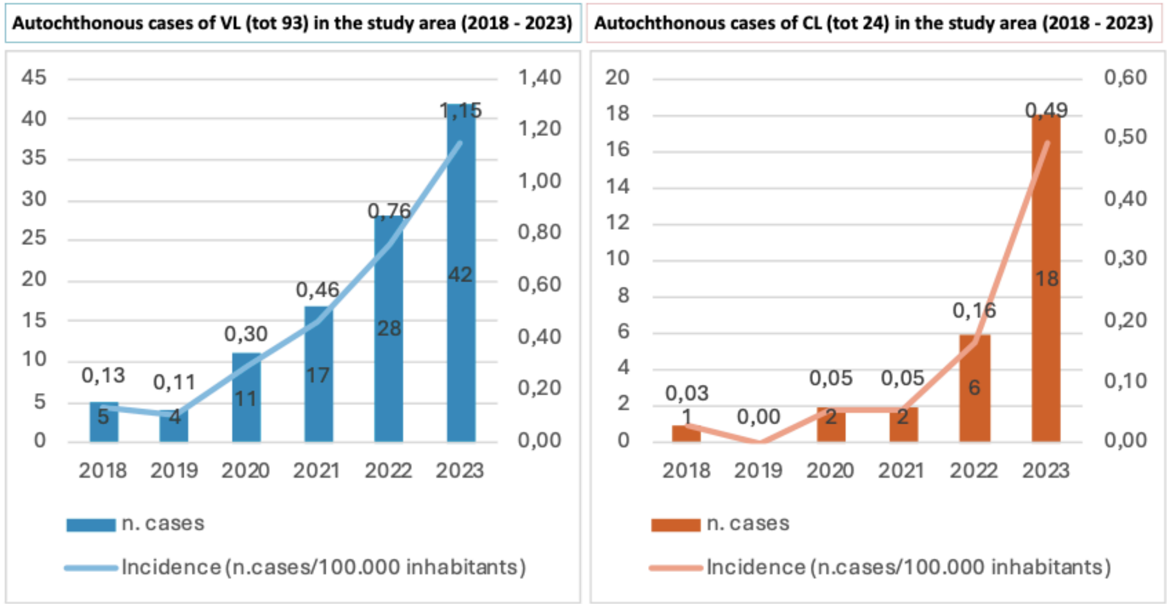


Figure1. Incidence of autochthonous visceral leishmaniasis (VL, left) and cutaneous leishmaniasis (CL, right) cases in Tuscany region over the study period.

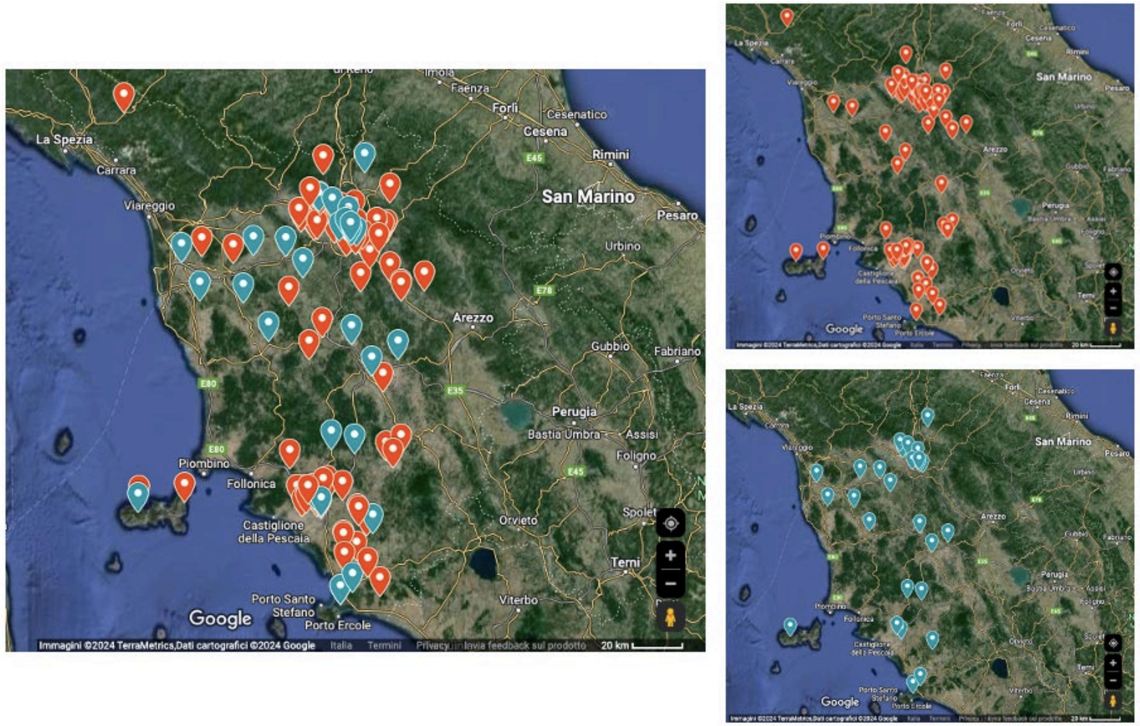


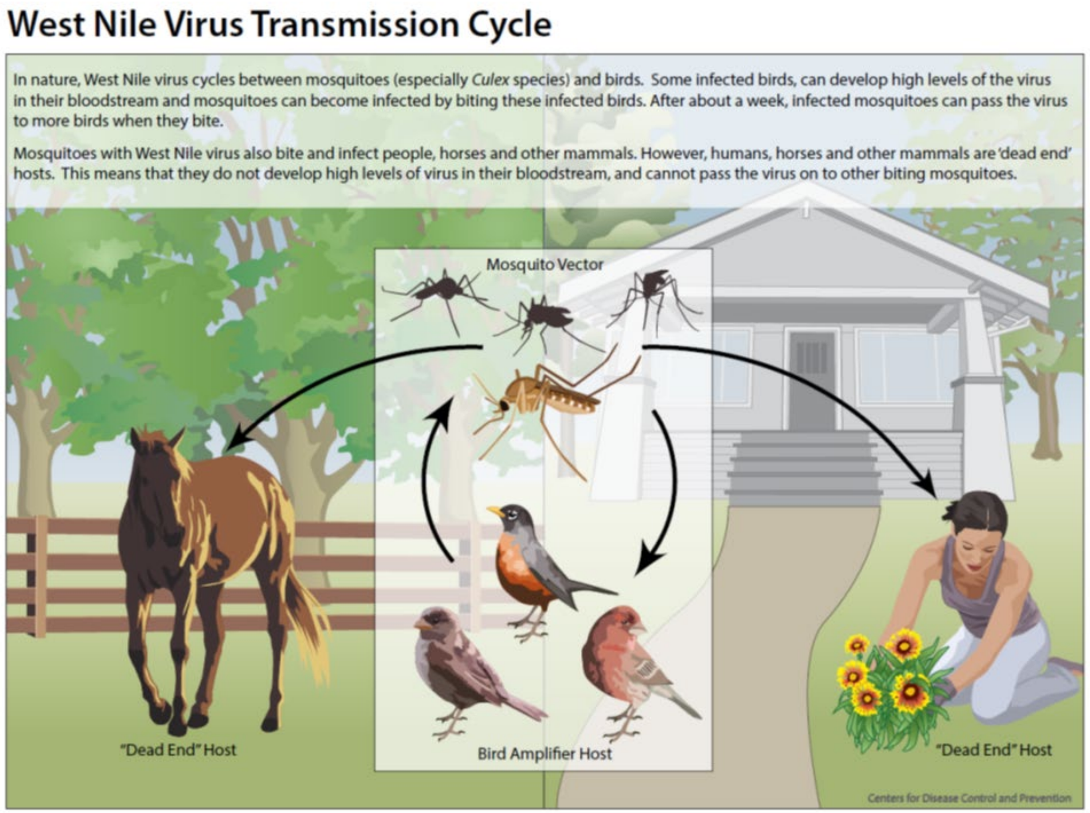
Figure2. Distribution of autochthonous CL (blue pins) and VL (red pin) first diagnosis in Tuscany region between 2018 and 2023

CONCLUSIONI

- L'epidemiologia della leishmaniosi si sta modificando in Toscana, così come in altre regioni italiane
- Importanza della sensibilizzazione sull'attuale quadro epidemiologico della leishmaniosi umana in Italia
- Formazione e aggiornamento del personale sanitario
- Necessaria una riduzione dei livelli di sotto-notifica
- Necessità di ulteriori studi in ottica *One-Health*

West Nile Virus

- Flavivirus, Vector-borne disease
- Reservoir: resident and migratory birds
- Vector: ornithophilic mosquitoes Culex spp.
- Other routes of transmission: transplants, transfusions, vertical transmission



- Incubation: 1-6 days

- **Asymptomatic** infection (80%),
- **Influenza-like syndrome** (20%): fever, headache, asthenia, malaise, myalgia and muscle weakness, gastrointestinal disorders and macular rash on the trunk and extremities
- **Rarely**: hepatitis, pancreatitis, orchitis, myocarditis, rhabdomyolysis, chorioretinitis, arrhythmias
- **Neuroinvasive infection** (<1%): meningitis/encephalitis, Guillain-Barré syndrome/radiculitis, flaccid paralysis

West Nile: in Italy (2023)

- **283 cases** in Italy in humans from the beginning of May 2023 to 28 September 2023
- **166 neuro-invasive** form (32 Piedmont, 53 Lombardy, 18 Veneto, 1 Liguria, 52 Emilia-Romagna, 4 Puglia, 1 Sicily, 3 Sardinia) 2 imported cases (1 Hungary, 1 France)
- 63 cases identified in **blood donors** (13 Piedmont, 31 Lombardy, 3 Veneto, 1 Friuli-Venezia Giulia, 14 Emilia-Romagna) 1 imported case (Germany)
- 54 cases of **fever** (5 Piedmont, 14 Lombardy, 29 Veneto, 5 Emilia-Romagna, 1 Puglia).
- **17 deaths**

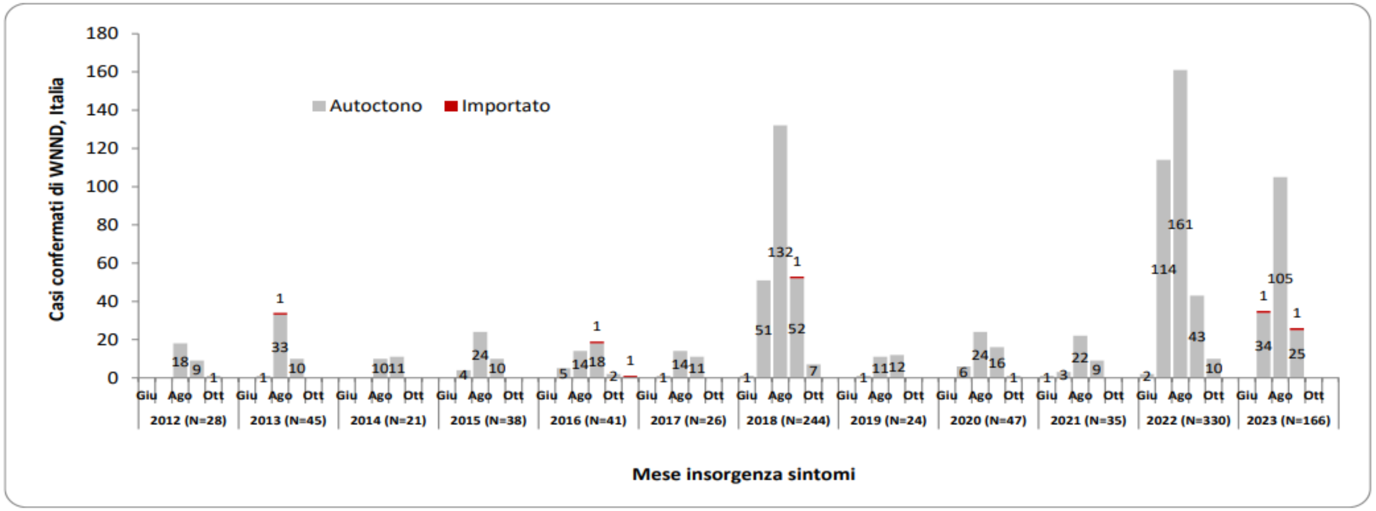
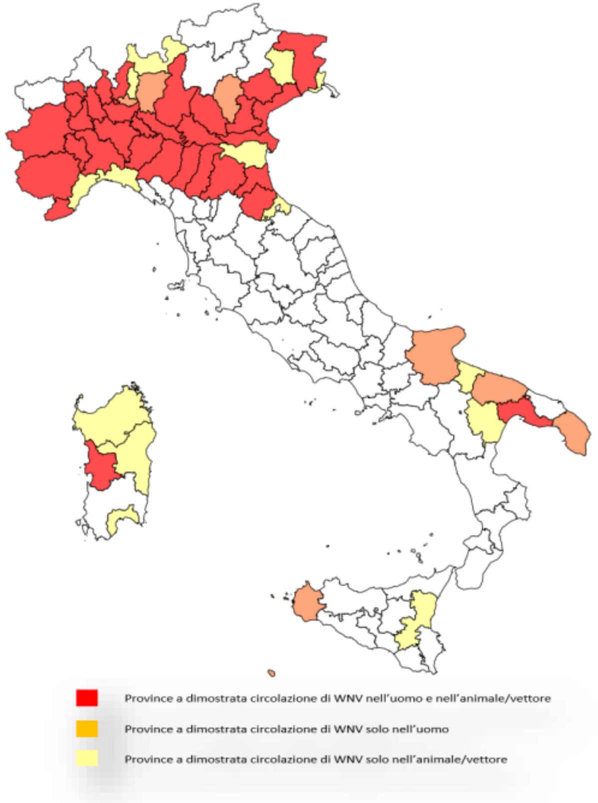


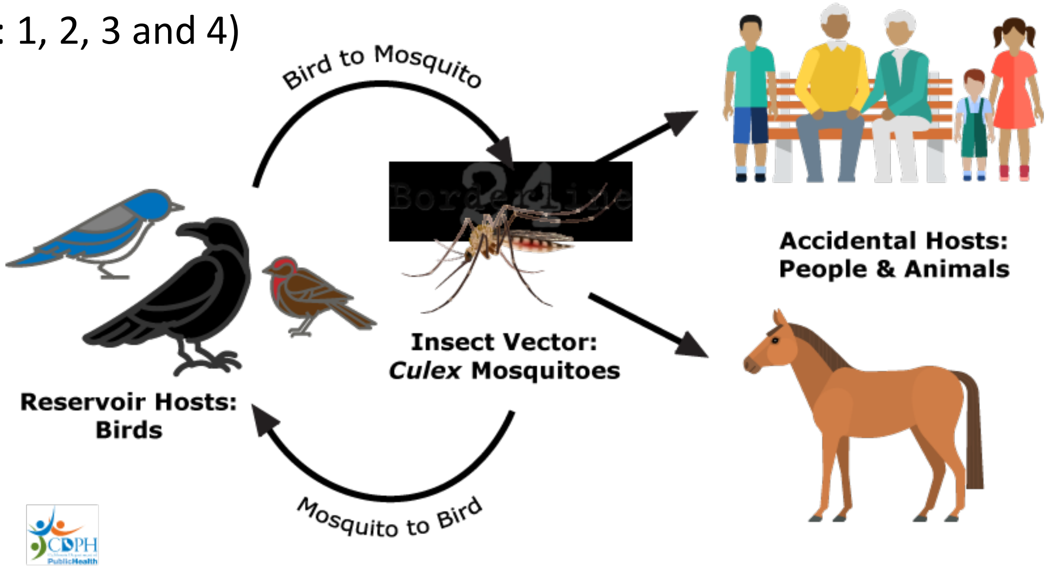
Figura 1. Andamento dei casi confermati di WNND per mese insorgenza sintomi. Italia: **2012 – 2023.**

Figura 1. *Province con dimostrata circolazione di WNV in vettori, animali e uomo (donatori asintomatici, febbri e casi neuroinvasivi confermati)*



Usutu Virus

- Isolated for the first time in South Africa in 1959
- First human case in Central African Republic in 1981
- Introduced in Tuscany in 1996 (archived tissue samples from birds)
- Main reservoir and amplifyng host: birds (highly viremic)
- Vector: infected mosquitos of *Culex* species, mainly *Culex pipiens*
- Dead-end-host: horses and humans
- Several lineages (prevalent in Europe: 1, 2, 3 and 4)



Usutu: in Italy (2023)

Sorveglianza integrata del WN e Usutu virus

7 **Sorveglianza USUTU virus**

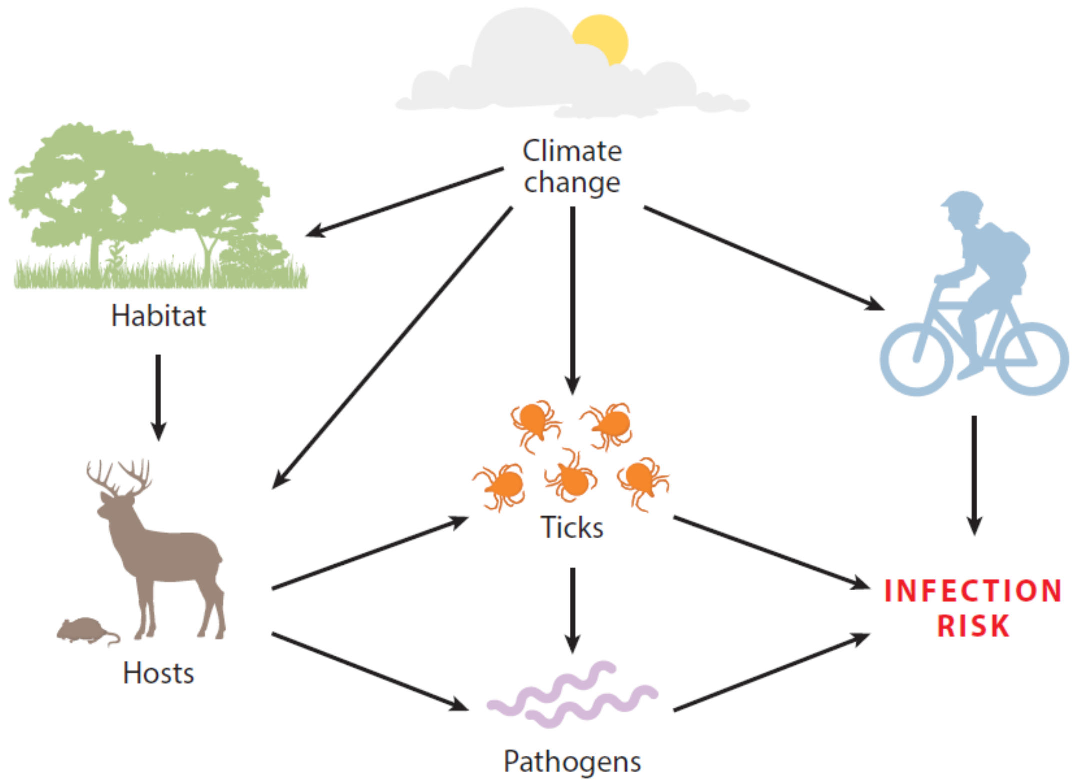
Il **virus Usutu** è stato identificato in **65 pool di zanzare e 81 uccelli in Abruzzo, Emilia Romagna, Toscana, Veneto, Lombardia, Marche, Sardegna e Piemonte.**

Figura 9 Distribuzione geografica dei pool di zanzare ed uccelli risultati positivi nei confronti dell'USUV - **2023**

- Between 2017 and 2021 detected in 5 regions (Emilia Romagna, Friuli Venezia Giulia, Latium, Lombardy, Veneto)
- 8 human cases in 2018, 1 in 2019 and 2020, 2 in 2021 and 2022
- Often misidentified with WNV (serological cross-reactions)
- Significant seroprevalence (blood donors and asymptomatic subjects)

The Impacts of Climate Change on Ticks and Tick-Borne Disease Risk

- For species like *I. ricinus* and *I. scapularis*, climate change is likely to have direct effects primarily at the far edges of its latitudinal and altitudinal range.
- It has been demonstrated for *I. ricinus* that warmer temperatures speed up oviposition rates, egg development rates, and interstadial development rates
- Climate change may also operate indirectly on tick distribution and abundance via changes in hosts
- *I. ricinus* populations and Lyme disease risk may increase with climate warming, at least in cool, temperate northwestern Europe and at higher altitudes
- It is crucial to be able to distinguish the effects of climate change from those of other drivers of tick-borne disease change (such as changes in populations of deer, rodents, and predators or in human behavior).



Annu. Rev. Entomol. 2021. 66:373–88

Tick borne encephalitis (TBE) Virus

- The tick-borne encephalitis virus (TBEV) is the arboviral etiological agent of tick-borne encephalitis (TBE), considered to be one of the most important tick-borne viral diseases in Europe and Asia.
- In recent years, an increase in the incidence of TBE as well as an increasing geographical range of the disease have been noted.
- The virus is transmitted between ticks, animals, and humans.
- Humans are incidental hosts, infected through the bite of an infected tick or by the alimentary route, through the consumption of unpasteurized milk or milk products from TBEV-infected animals.
- TBEV infections in humans may be asymptomatic, but the symptoms can range from mild flu-like to severe neurological.
- While there is currently no effective treatment for TBE, immunization and protection against tick bites are critical in preventing this disease.

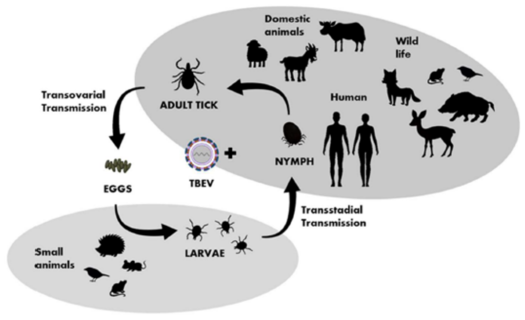


Figure 3. Transmission of TBEV in the life cycle of ixodid ticks, shaded fields indicate the host group characteristic for particular developmental stages of ticks.

J. Clin. Med. 2023, 12, 6603.

Tick borne encephalitis (TBE) Virus: in Italy

Istituto Superiore di Sanità
EpiCentro - L'epidemiologia per la sanità pubblica

Zecche

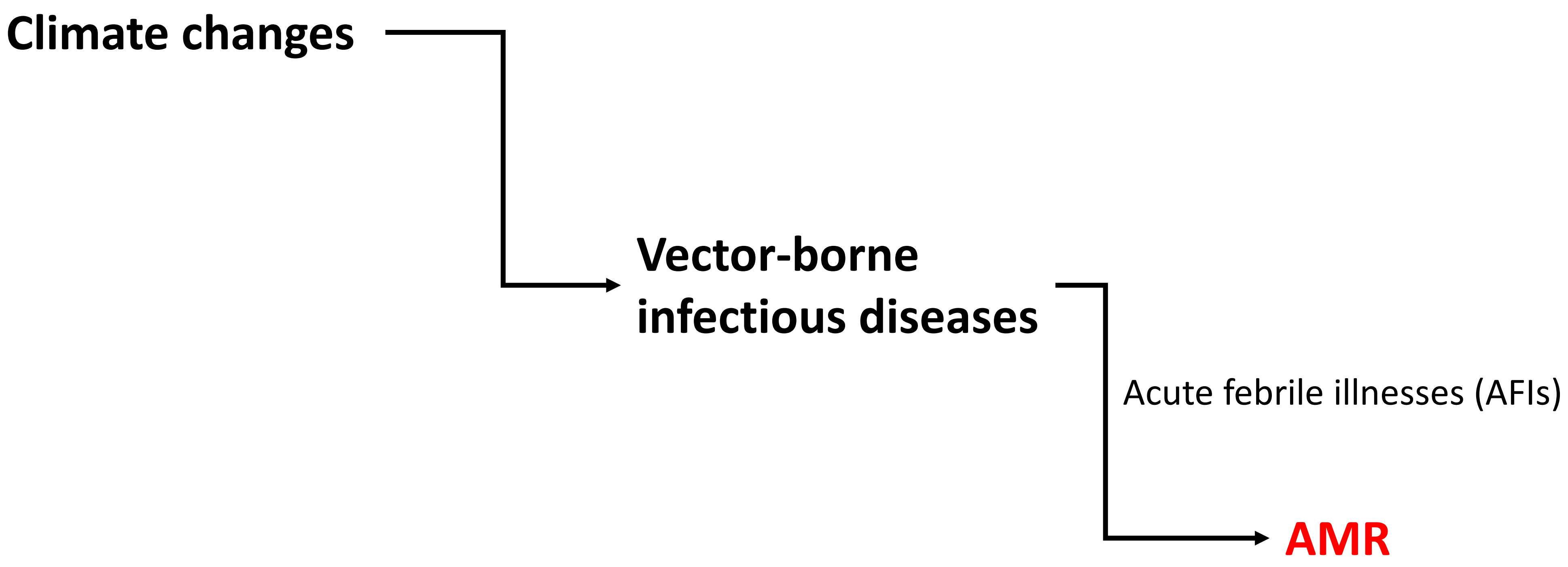
- 9 casi confermati di infezione neuro-invasiva-TBE, encefalite da zecca, (7 autoctoni, età mediana di 49,5 anni, 87,5% di sesso maschile e nessun decesso)

https://www.epicentro.iss.it/zecche/meningoencefalite

- A total of 103 Italian cases occurred between 2017 and 2020, 100 of them in the Triveneto, with a pooled incidence rate (IR) of 0.35 per 100,000 [95%CI 0.28-0.42]

- Annual estimates peaked in 2018 (0.54 per 100,000 [95%CI 0.39-0.74]), but overall figures remain quite low, in particular when compared to nearby countries likewise Austria (399 cases, mean IR 1.51 per 100,000) or Slovenia (366 cases, mean IR 4.61 per 100,000), and Switzerland (377 cases reported in 2018 alone; crude IR 4.41 per 100,000)

Acta Biomed. 2021 Nov 3;92(5):e2021229


Climate changes
Vector-borne infectious diseases
Acute febrile illnesses (AFIs)
AMR

- Acute febrile illnesses (AFIs) are a major public health problem and the reason for most outpatient clinic consultations at primary healthcare centers

- Malaria remains the most common AFI diagnosis in various tropical countries, particularly in Sub-Saharan Africa, but was only observed at 1% in Southeast Asia. In Southeast and South Asia, dengue fever was the most common, accounting for 11.8% of cases, followed by leptospirosis, typhoid, scrub typhus and influenza

- Distinguishing between bacterial and viral infectious causes of AFIs is challenging even in high-income countries, but is more magnified in low- and middle-income countries where access to accurate diagnostics is limited

- This diagnostic uncertainty is a driver of antibiotic prescriptions for AFIs -> Unnecessary ***just-in-case*** prescription of antibiotics contributes to a rise in AMR

- In malaria-endemic countries, the deployment of malaria rapid diagnostic tests (RDT), according to the WHO *test-and-treat* recommendation for febrile patients resulted in better targeted use of antimalarial drugs overall

- The ability to establish a correct diagnosis between viral and bacterial causes of fever is central to reduce unnecessary antibiotic prescriptions

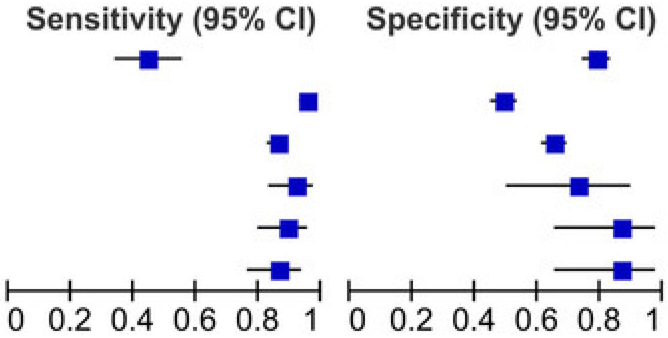
Trop Med Infect Dis **2022**;7:159; *CID* **2023**:77 (Suppl 2); *BMC Infect Dis* **2019**, *19*, 577; *Lancet Glob Health* **2017;**5:e157-67

Review Article Usefulness of C-Reactive Protein and Other Host BioMarker Point-of-Care Tests in the Assessment of Non-Malarial Acute Febrile Illnesses: A Systematic Review with Meta-Analysis

The SROC presented AUC = 0.77 (CI: 0.73–0.81), which indicates good accuracy to distinguish bacterial from nonbacterial infections. However, the optimal cutoff of CRP could not be assessed, and we found insufficient evidence about its impact on antibiotic prescription and clinical outcome. The role of CRP and other host biomarker POCTs for the assessment of acute non-malarial febrile illnesses in resource-constraint settings deserves further studies.

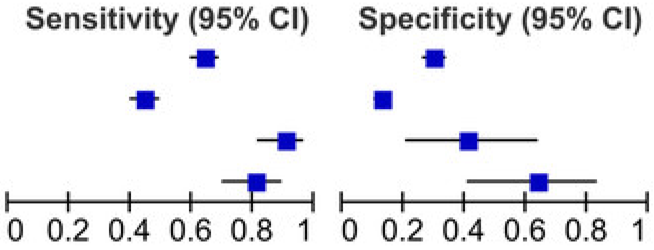
Forest plot for studies on the accuracy of C-reactive protein.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Hildenwall - cutoff 19	40	73	50	268	0.44 [0.34, 0.55]	0.79 [0.74, 0.83]
Lubell - cutoff 10	404	283	21	272	0.95 [0.93, 0.97]	0.49 [0.45, 0.53]
Lubell - cutoff 20	366	194	60	361	0.86 [0.82, 0.89]	0.65 [0.61, 0.69]
Wangrangsimakul - cutoff 20	66	6	6	16	0.92 [0.83, 0.97]	0.73 [0.50, 0.89]
Wangrangsimakul - cutoff 36	64	3	8	19	0.89 [0.79, 0.95]	0.86 [0.65, 0.97]
Wangrangsimakul - cutoff 40	62	3	10	19	0.86 [0.76, 0.93]	0.86 [0.65, 0.97]



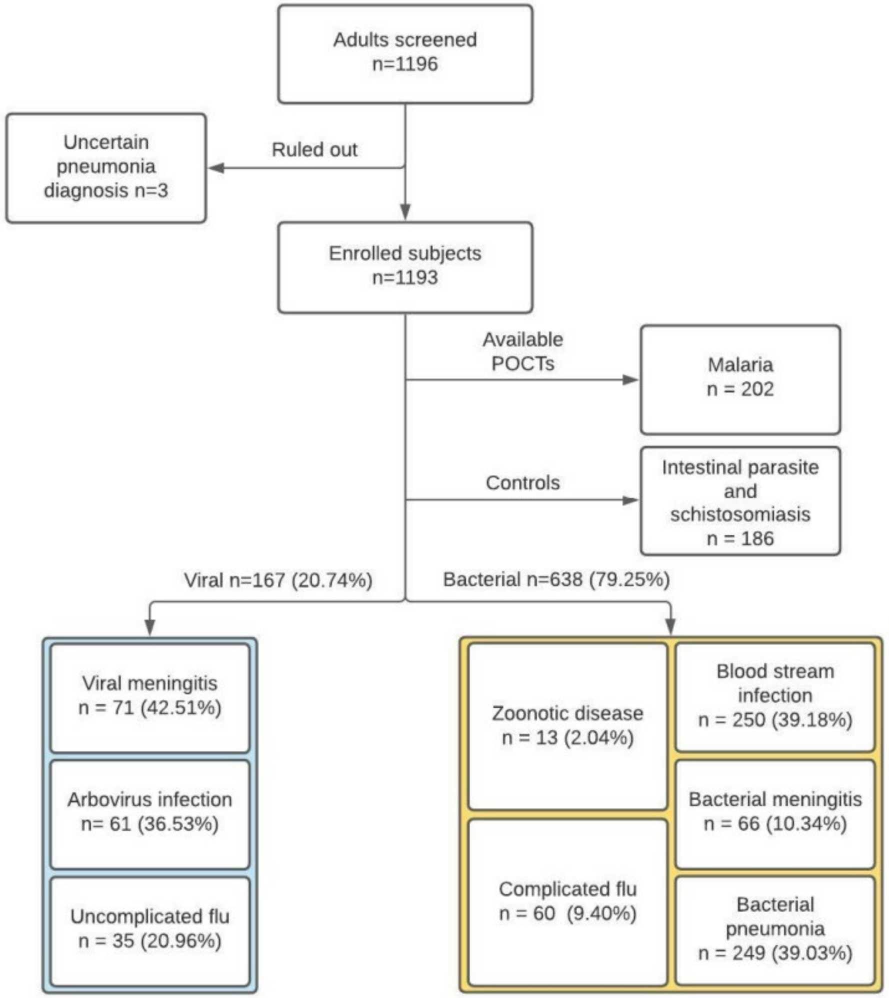
Forest plot for studies on the accuracy of procalcitonin

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Lubell - cutoff 0.1	272	389	153	166	0.64 [0.59, 0.69]	0.30 [0.26, 0.34]
Lubell - cutoff 0.5	189	482	236	73	0.44 [0.40, 0.49]	0.13 [0.10, 0.16]
Wangrangsimakul - cutoff 0.25	65	13	7	9	0.90 [0.81, 0.96]	0.41 [0.21, 0.64]
Wangrangsimakul - cutoff 0.5	58	8	14	14	0.81 [0.70, 0.89]	0.64 [0.41, 0.83]



Am. J. Trop. Med. Hyg., 103(5), 2020, pp. 1797–1802

C-Reactive Protein for the Early Assessment of Non-Malarial Febrile Patients: A Retrospective Diagnostic Study



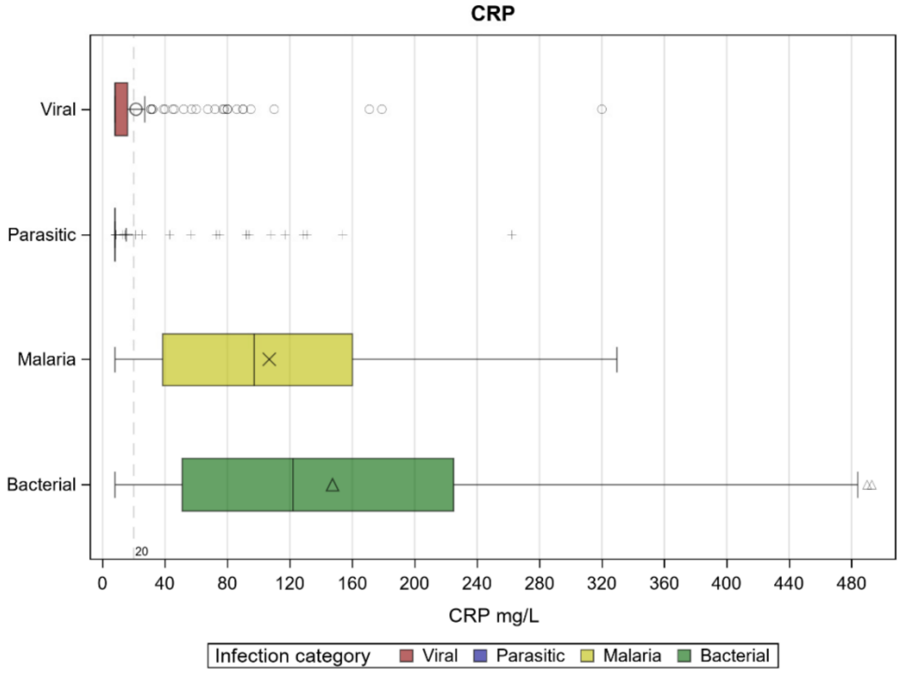


Table 5. Biomarkers' cut-offs with corresponding sensitivity and specificity. Cut-offs were obtained maximizing the percentage of correctly classified cases.

Biomarkers	Cut-Off	Sensitivity (95% CI)	Specificity (95% CI)
CRP	11.00	92.8 (90.8–94.8)	69.3 (62.3–76.3)
WBC	3.60	93.7 (91.8–95.6)	32.3 (25.2–39.4)
FIBRINOGEN	3.85	93.5 (91.4–95.5)	48.3 (40.1–56.4)
NEUTROPHILS	1.60	95.1 (93.3–96.8)	29.2 (22.2–36.2)

CRP: C-Reactive Protein, WBC: White Blood Cells, CI: Confidence Interval.

Diagnostics 2021, 11, 1728

Arbo-Score: A Rapid Score for Early Identification of Patients with Imported Arbovirosis Caused by Dengue, Chikungunya and Zika Virus

90 patients fulfilling inclusion criteria: 34 cases and 56 controls. Among the cases, 22 were diagnosed with DENV infection (20 confirmed and 2 probable cases), 8 with ZIKV infection (all confirmed), and 4 with CHIKV infection (all confirmed).

ARBO-SCORE

- myalgia +1 point
- rash +1 point
- respiratory symptoms −1 point

- leukopenia +2 points
- hypertransaminasemia +1 point

Cut-off Point	Sensibility (%)	Specificity (%)	Youden Index
≥−1	100.00	0.00	0
≥0	100.00	14.29	0.14
≥1	94.12	58.93	0.53
≥2	82.35	96.43	0.79
≥3	52.94	98.21	0.51
≥4	23.53	100.00	0.23
≥5	11.76	100.00	0.12
>5	0	100.00	0

Microorganisms 2020, 8, 1731