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KOÇ UNIVERSITY - İŞBANK
CENTER FOR INFECTIOUS DISEASES

Kırım Kongo Kanamalı Ateşi

Dr. Önder Ergönül

Koç Universitesi Tıp Fakültesi
İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji
6 Eylül 2026
KLİMİK

Content

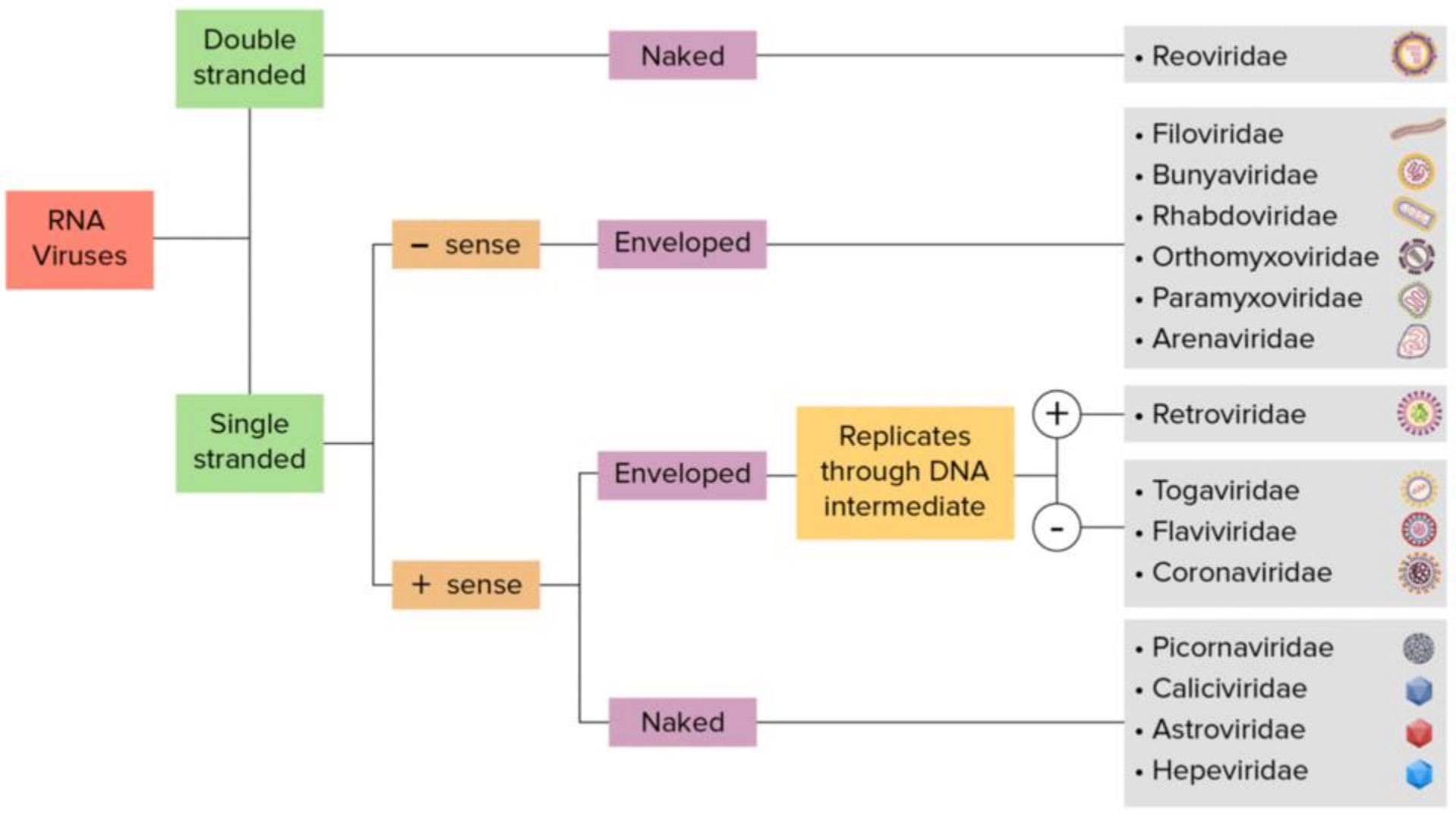
Epidemiology

Clinical Course

Treatment Options

>20 years experience of Türkiye

From the perspective of other VHFs and COVID-19 Perspectives


RNA Viruses
Double stranded
Single stranded
Naked
Enveloped
− sense
+ sense
Enveloped
Naked
Replicates through DNA intermediate
+
-
• Reoviridae
• Filoviridae
• Bunyaviridae
• Rhabdoviridae
• Orthomyxoviridae
• Paramyxoviridae
• Arenaviridae
• Retroviridae
• Togaviridae
• Flaviviridae
• Coronaviridae
• Picornaviridae
• Caliciviridae
• Astroviridae
• Hepeviridae

Bunyavirales

Crimean Congo Hemorrhagic Fever

Severe Thrombocytopenic Fever Syndrome

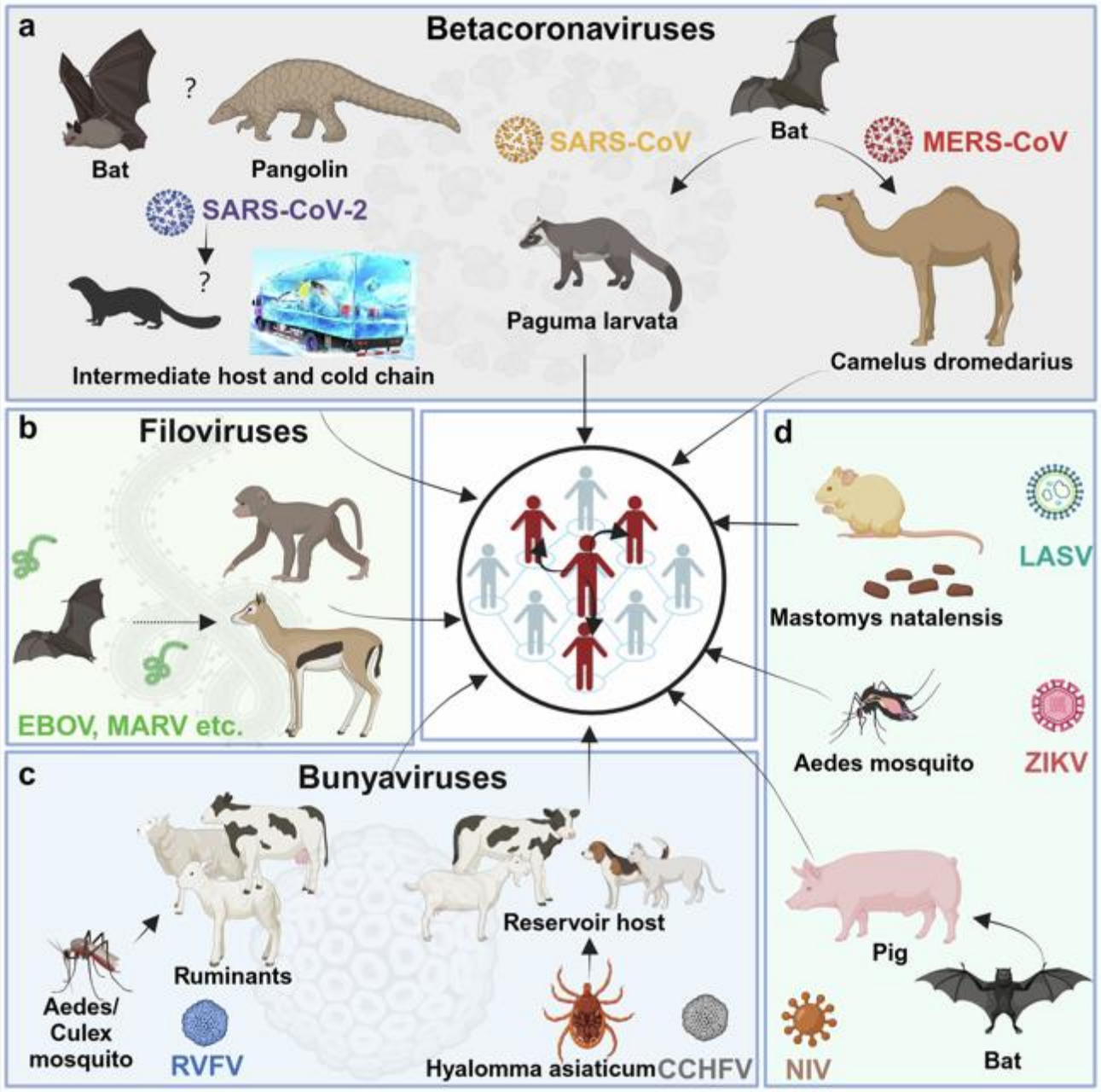
Rift Valley Fever

Hantavirus infection

- Lanka virus (Muthusinghe DS, 2025)

Sin Nombre virus

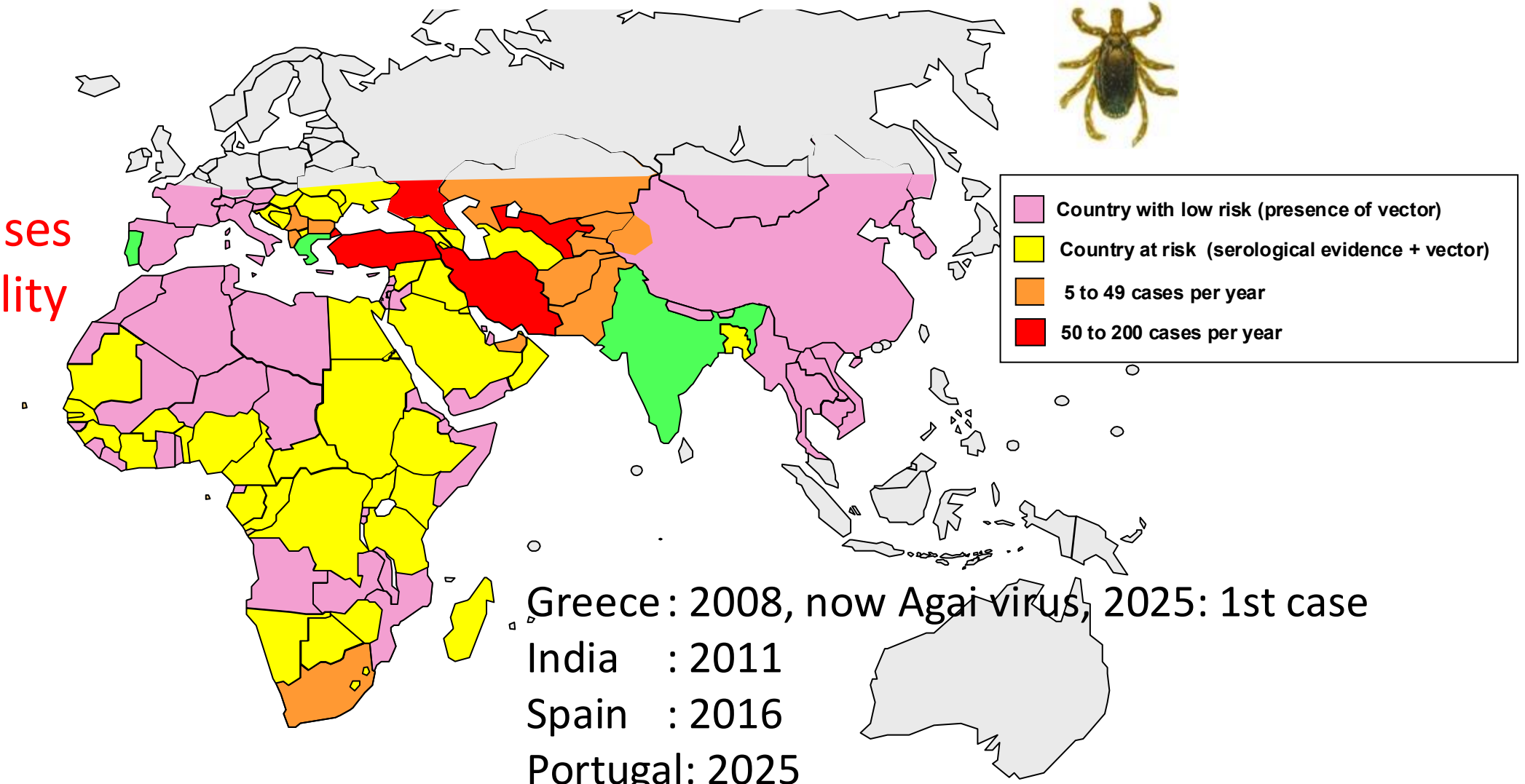
Sandly Fever


a
Betacoronaviruses
Bat
?
Pangolin
SARS-CoV-2
?
Intermediate host and cold chain
SARS-CoV
Bat
MERS-CoV
Paguma larvata
Camelus dromedarius
b
Filoviruses
EBOV, MARV etc.
d
LASV
Mastomys natalensis
Aedes mosquito
ZIKV
Pig
Bat
NIV
c
Bunyaviruses
Aedes/
Culex
mosquito
Ruminants
RVFV
Reservoir host
Hyalomma asiaticum
CCHFV

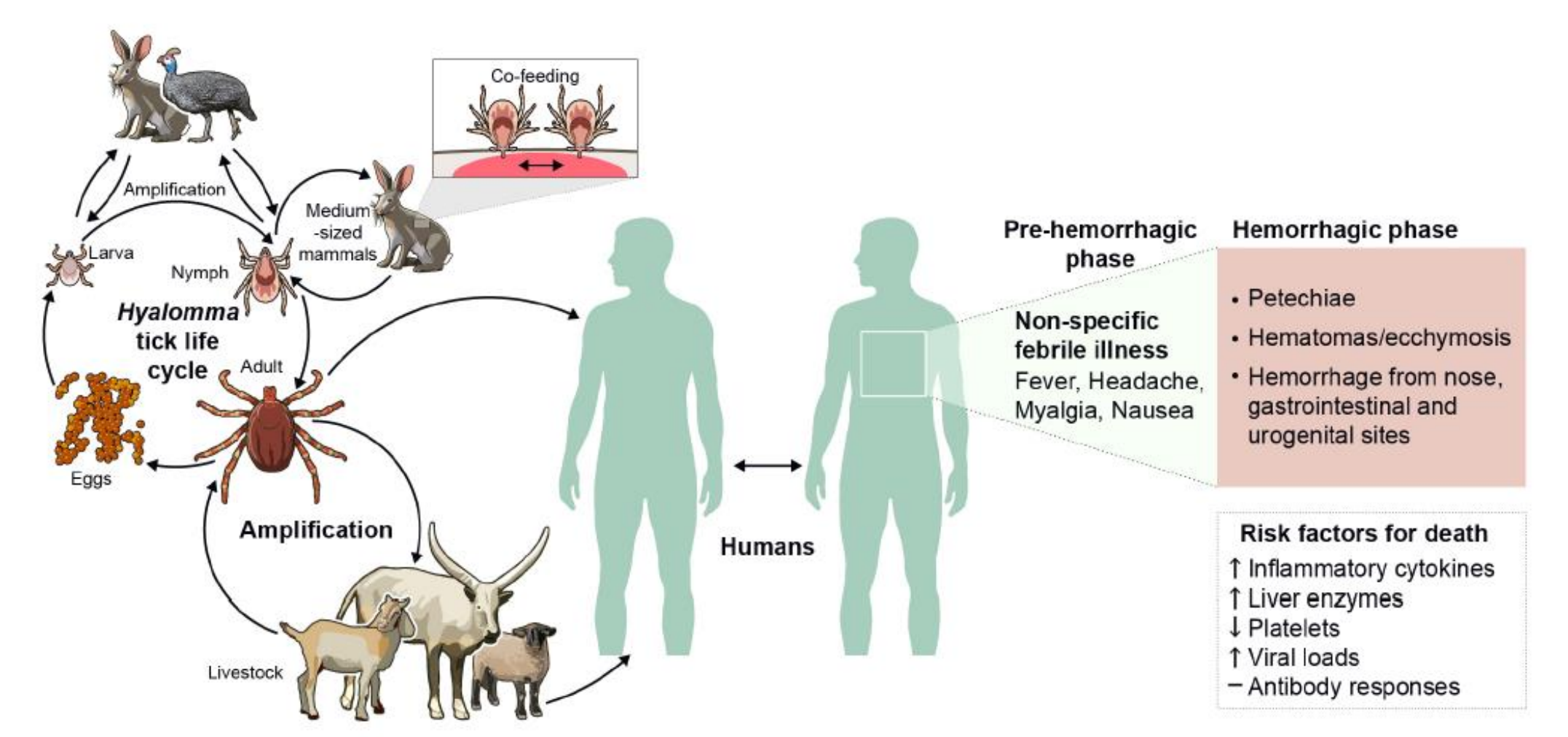
Crimean-Congo Haemorrhagic Fever Geographic Distribution

50° North limit for *Hyalomma* ticks

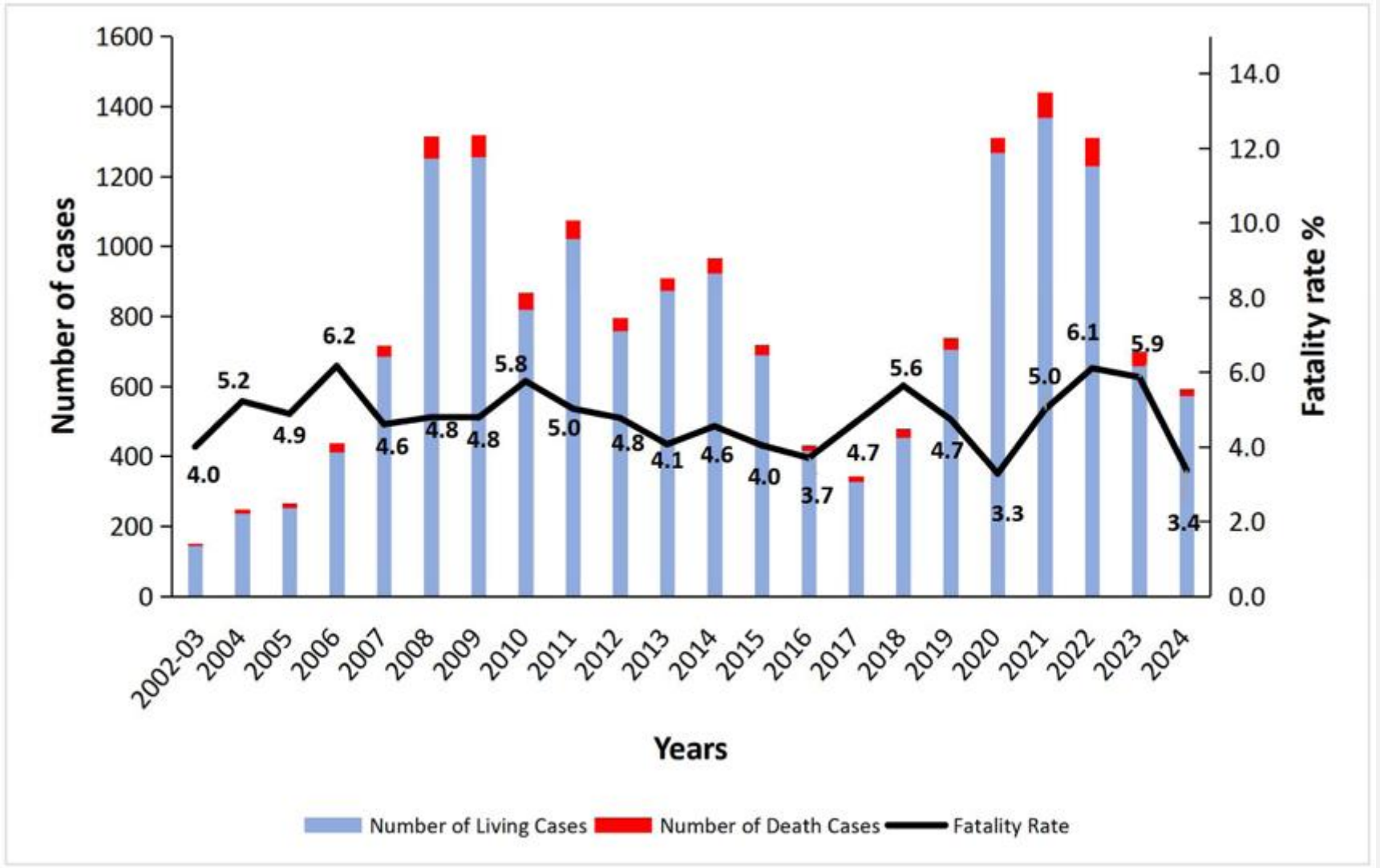
>30 000 cases
5-40% fatality



Greece : 2008, now Agai virus, 2025: 1st case
India : 2011
Spain : 2016
Portugal: 2025



Feldman, 2018



Şahan S, Topluoğlu S, Temel F, Coşgun Y, Öz E, Demirkol ME, Birinci Ş. Evaluation of epidemiological characteristics of Crimean-Congo haemorrhagic fever patients reported to the National Surveillance System in Türkiye, 2011-2024. Acta Trop. 2025

Distribution of Cases in Türkiye

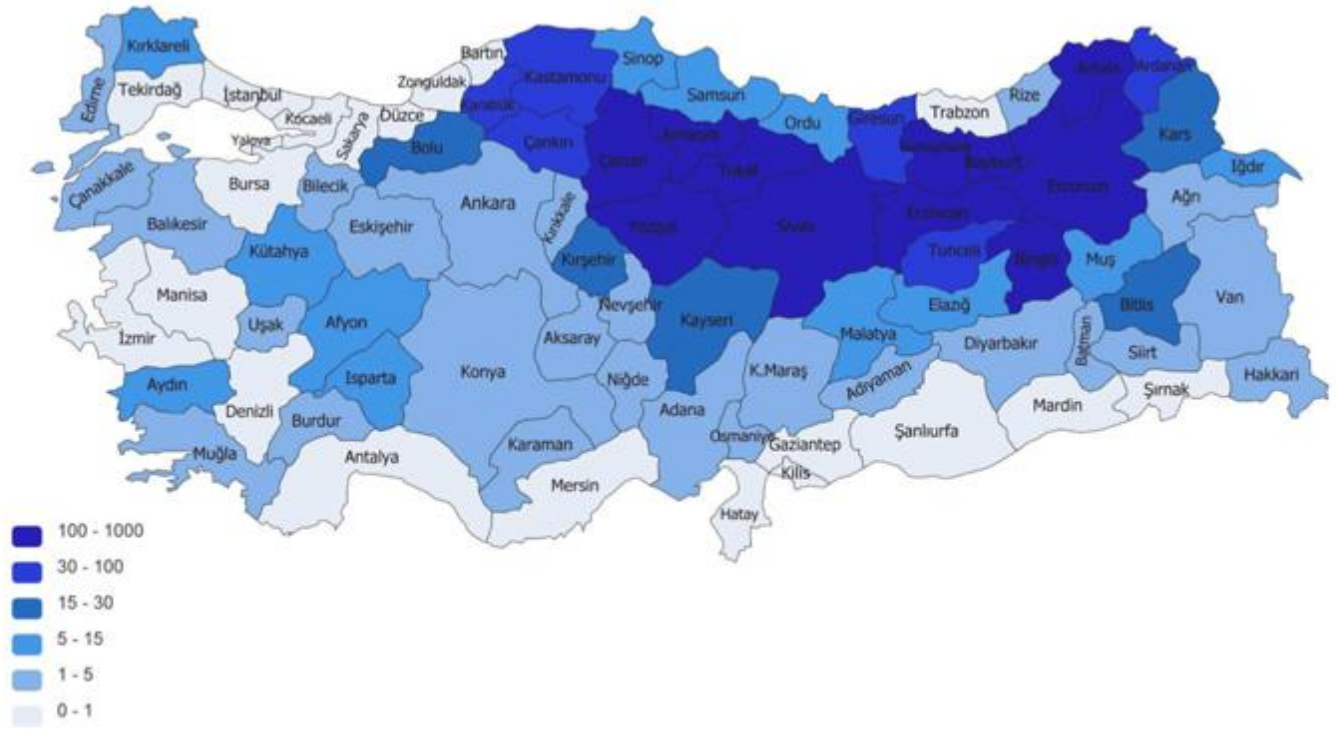
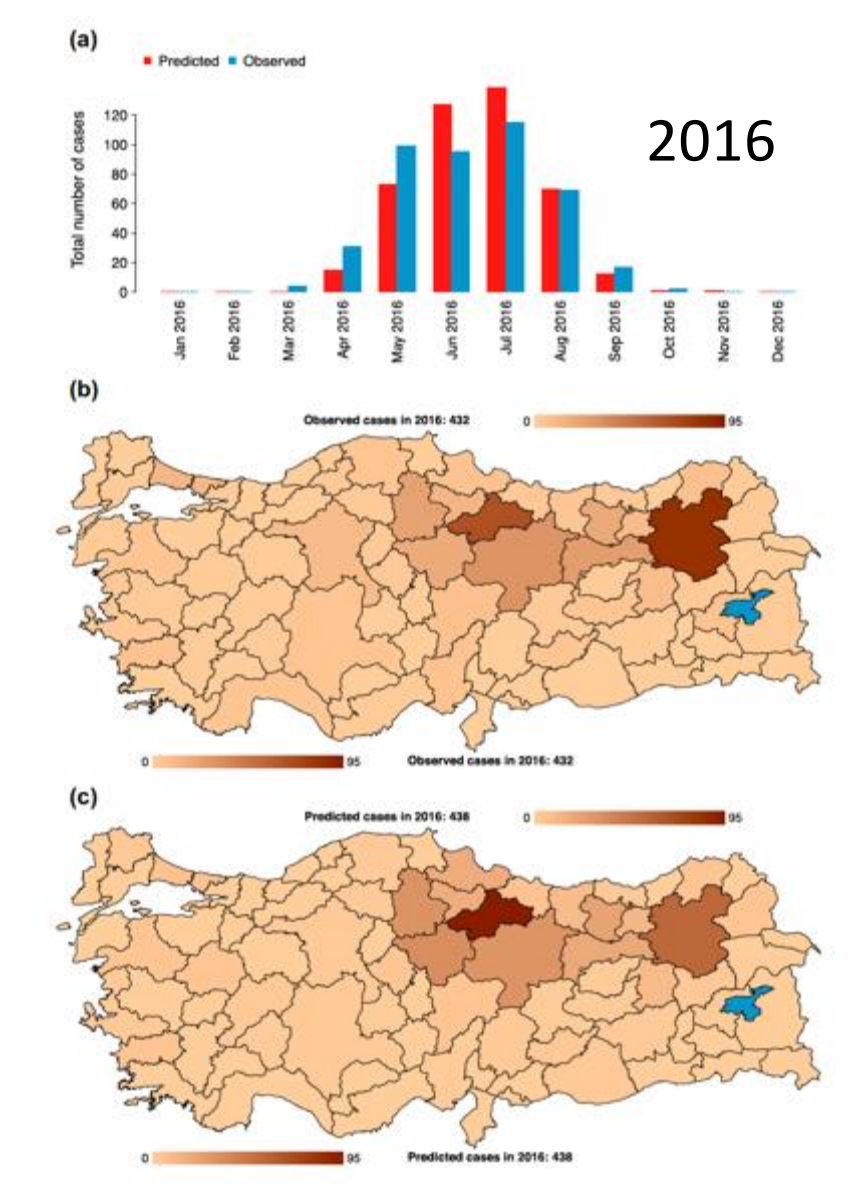
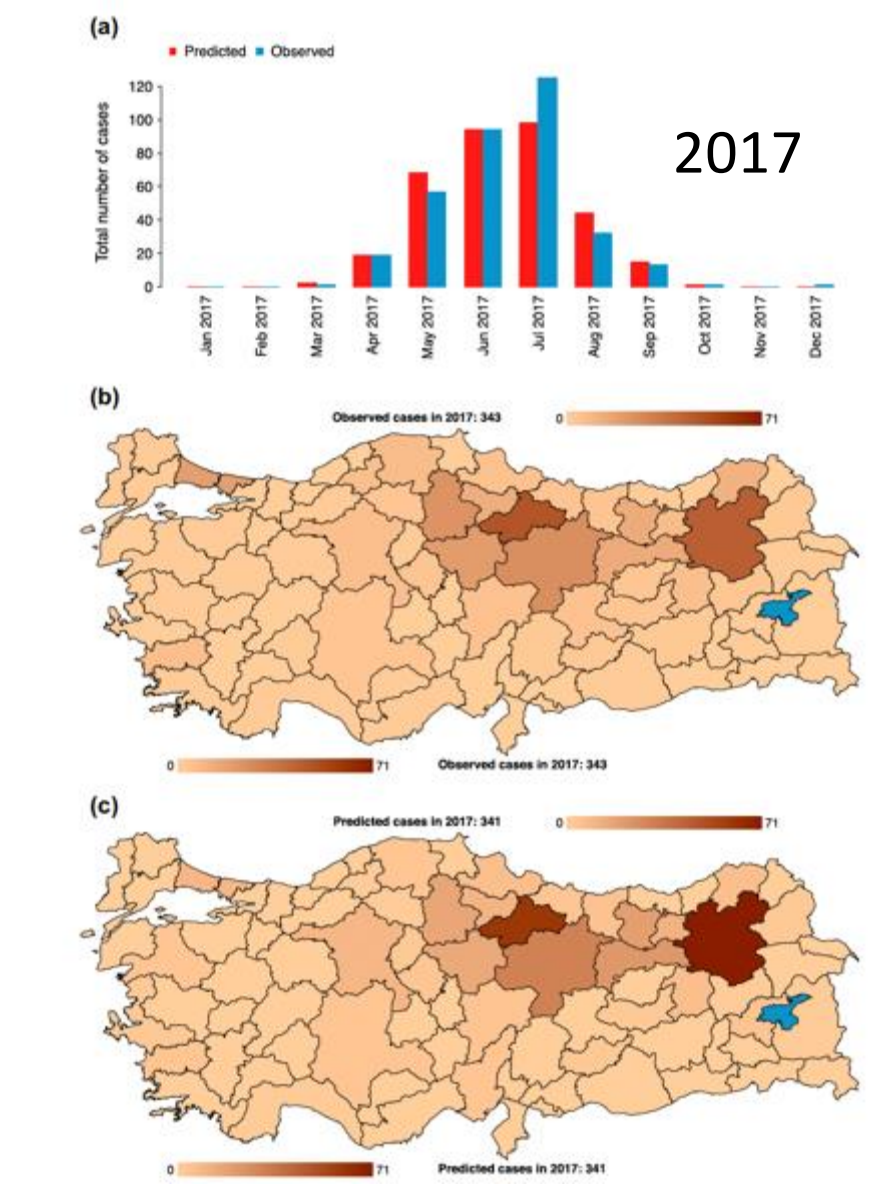


Fig. 3. Incidence rates (per 100,000) of CCHF by province, Türkiye, 2011–2024 A choropleth map showing cumulative case counts per province, with darker shading representing higher incidence. Data aggregated from the national CCHF Information System (2011–2024). Provincial boundaries obtained from the Turkish Statistical Institute.

Şahan S, Topluoğlu S, Temel F, Coşgun Y, Öz E, Demirkol ME, Birinci Ş. Evaluation of epidemiological characteristics of Crimean-Congo haemorrhagic fever patients reported to the National Surveillance System in Türkiye, 2011-2024. Acta Trop. 2025

Prospective Prediction Tool for Turkey

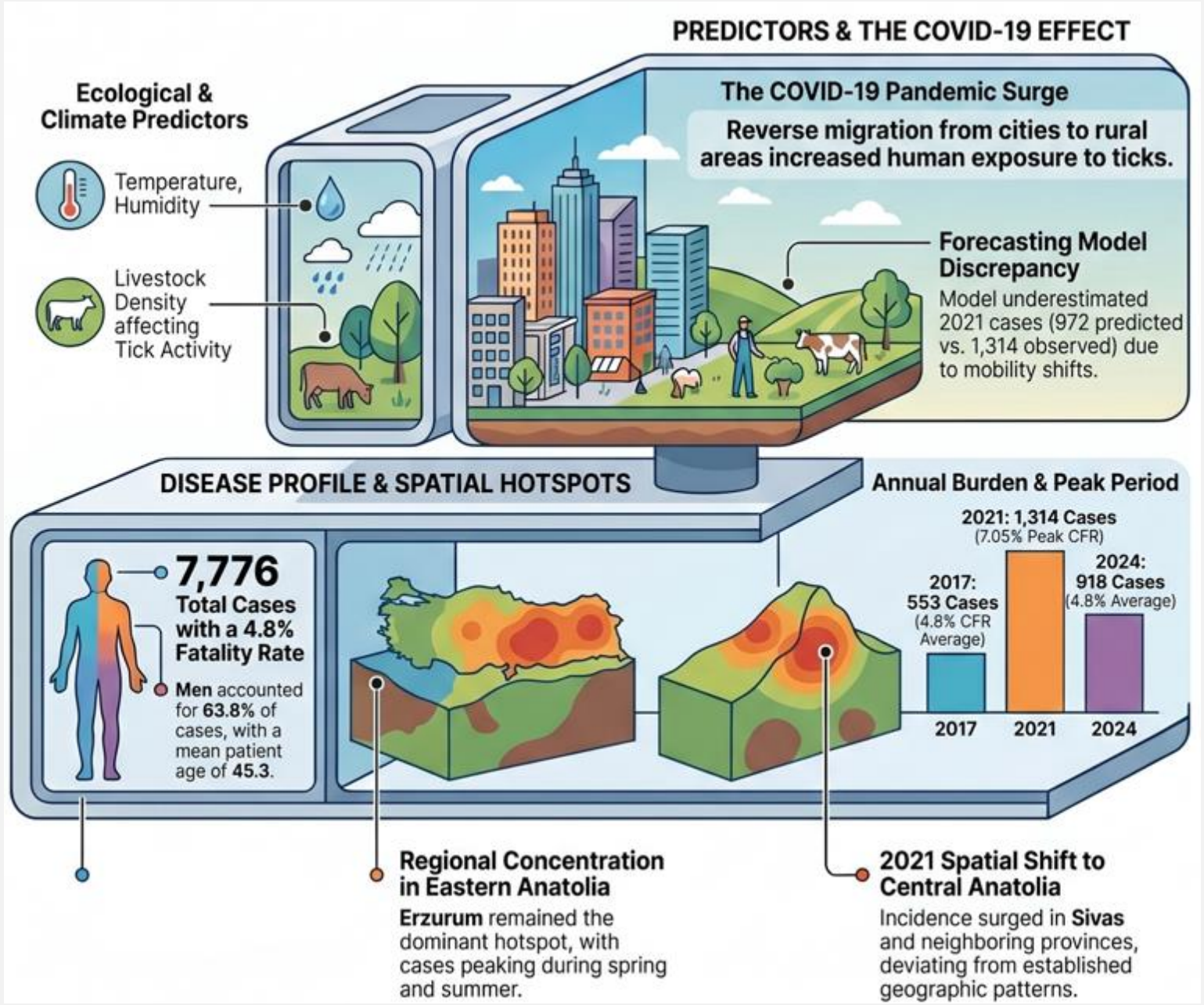




Ak, Ergönül, Gönen. *Clin Microbiol Infect* 2020

Crimean-Congo Hemorrhagic Fever Epidemiology

(2017-2024)



Karanfil Ö, et al. Int J Infect Dis 2026


ECOLOGICAL RESEARCH NETWORK


Ficedula parva 1y
ringed: 13 sept
recaptured: 24 sept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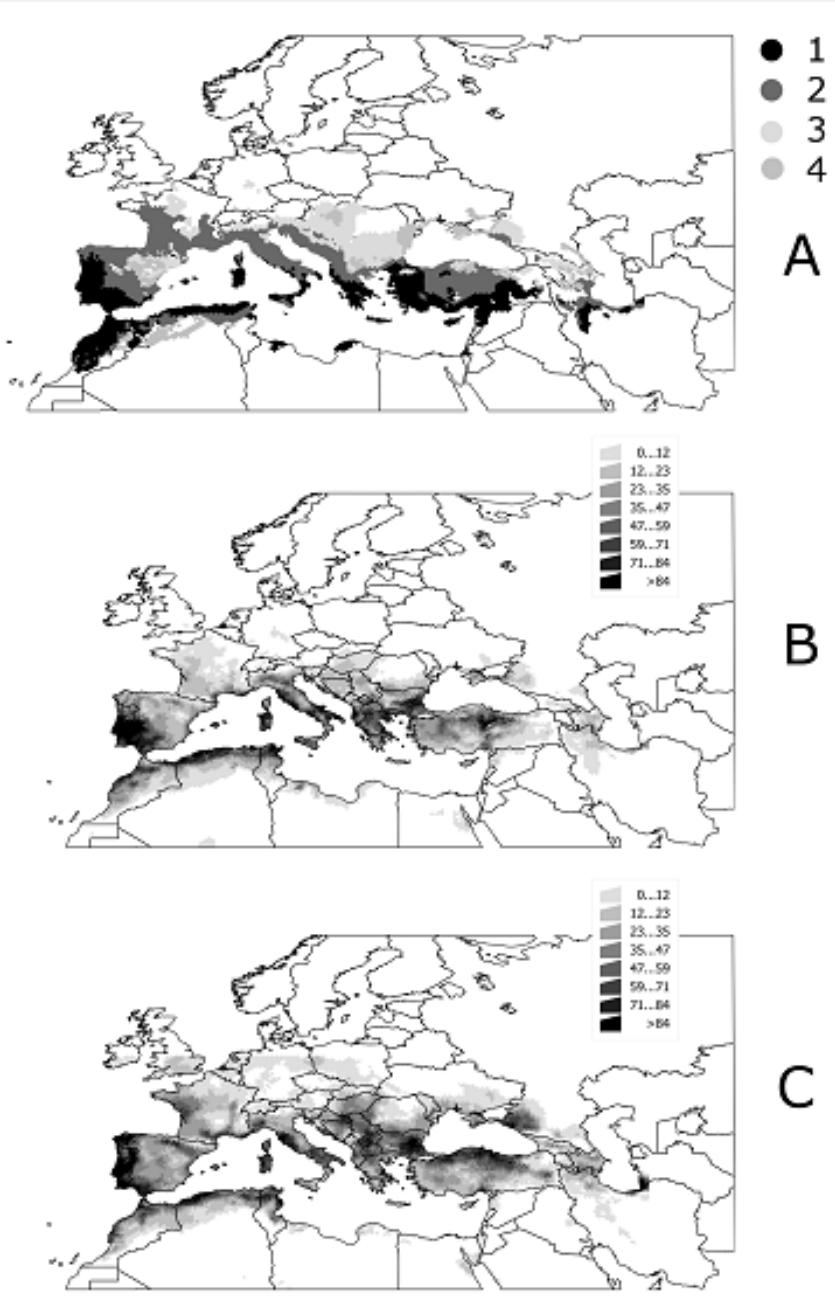
MARMARA


Viruses
Riboviria
Orthornavirae
Colorado tick fever orthornavirae
Colorado tick fever virus 20%
Gammaretrovirus
Avian retrovirus
Retroviridae
Gibbon ape leuk
Duplodnaviria
Caudoviricetes
unclassified Caudoviricetes
24% Sodalis phage phiSG1
Purevirus RCS47
5% Escherichia phage RCS47
Nucleocytoviricota
Megaviricetes
Mimiviridae
Betanudivirus
unclassified Avipoxvirus
Alphaherpesvirinae
Betaherpesvirinae herpesvirus
Faserviricetes
Fadolivirus
5% Fadolivirus algeromassiliense
5% Megamimivirus
Flamingopox virus FGPV/KC
Lymphocystivirus
Eyach orthornavirae
Eyach virus 20%



Known records of *Hyalomma marginatum*

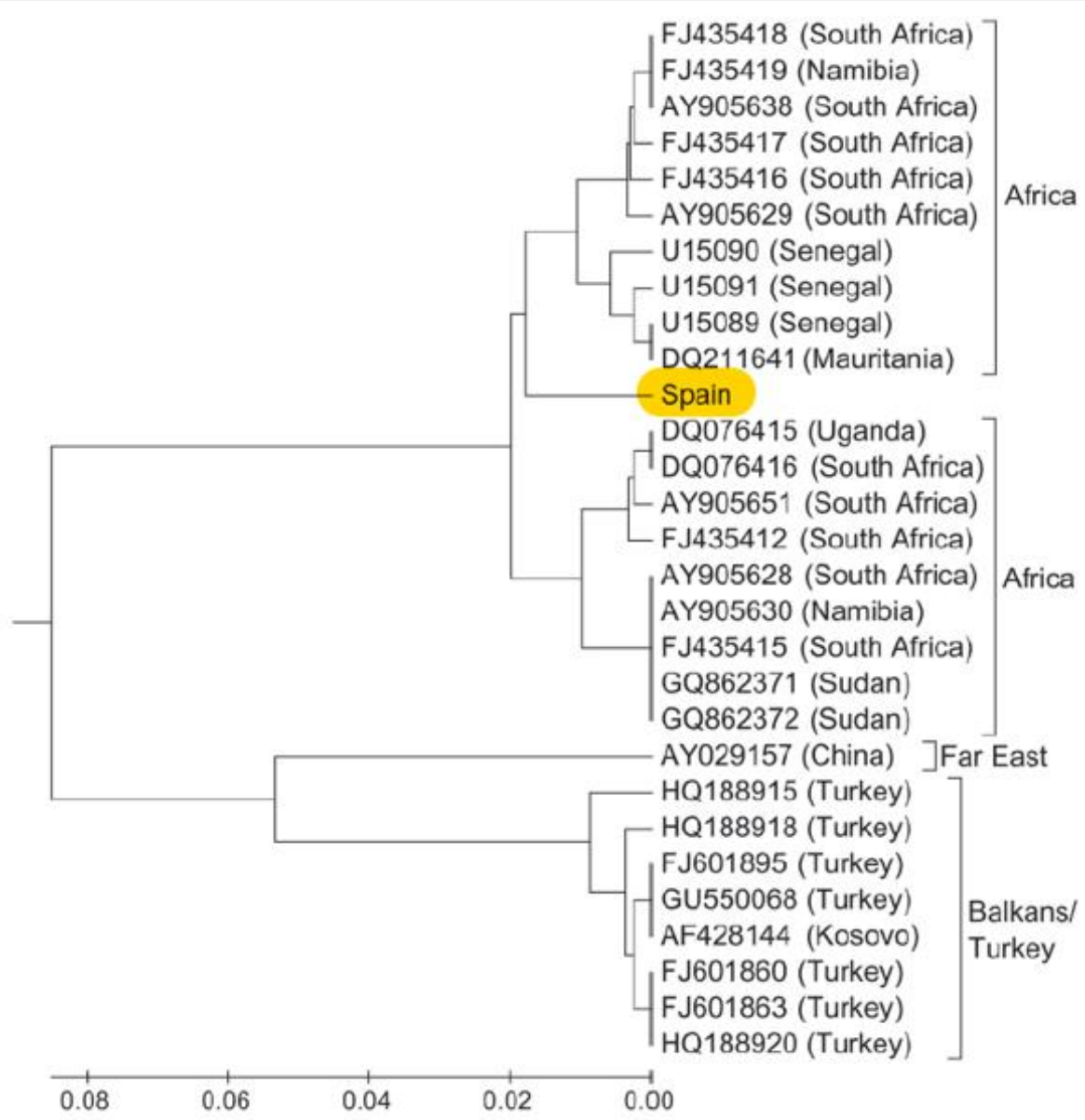
The predicted climate suitability for the tick *H. marginatum* in the area of analysis with current (1970-2000) climate conditions

The predicted climate suitability as projected for the year 2050

Estrada-Pena 2009

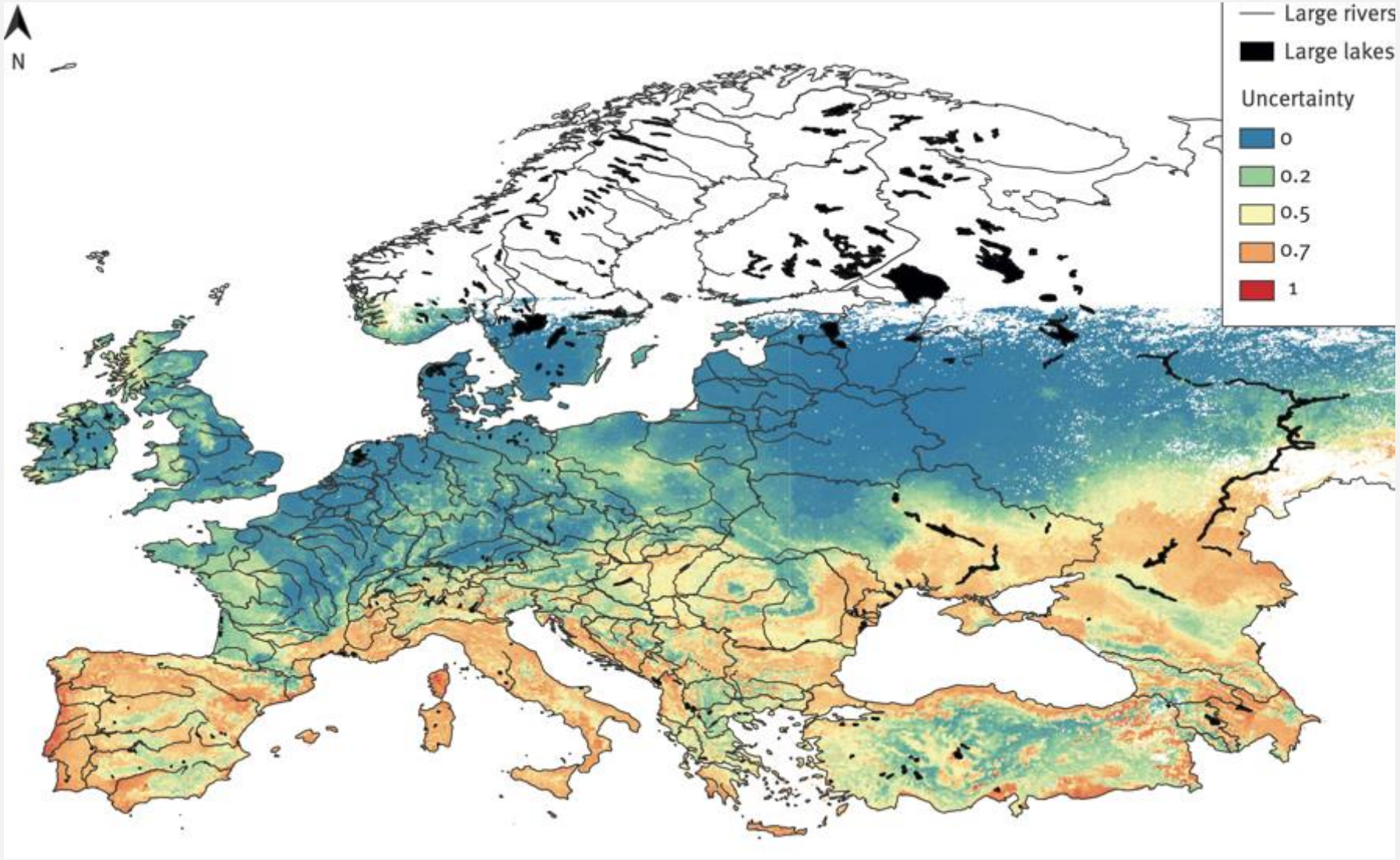
Crimean-Congo Hemorrhagic Fever Virus in Ticks, Southwestern Europe, 2010

This finding suggests the circulation of CCHFV in southwestern Europe. The close affinity of the strain from Spain with strains circulating in western Africa and the lack of similarity with isolates from eastern Europe suggest the introduction of this virus from nearby countries of northern Africa. Migratory movements of birds could explain the presence of the virus in southwestern Europe because birds are common hosts of immature *H. marginatum*, which was reportedly introduced into Europe through annual migratory flights along the western coast of Africa (*10*). Because



Estrada-Pena, *Emerg Infect Dis* 2010

Epidemic intelligence from Open Sources (EIOS) of CCHF in European Region, 2012 to 2022: a new opportunity for risk mapping of neglected diseases



Fanelli A, Schnitzler JC, De Nardi M, Donachie A, Capua I, Lanave G, Buonavoglia D, Caceres-Soto P, Tizzani P. Euro Surveill. 2023

CCHF virus in *Hyalomma marginatum* ticks in Southern France (2023)

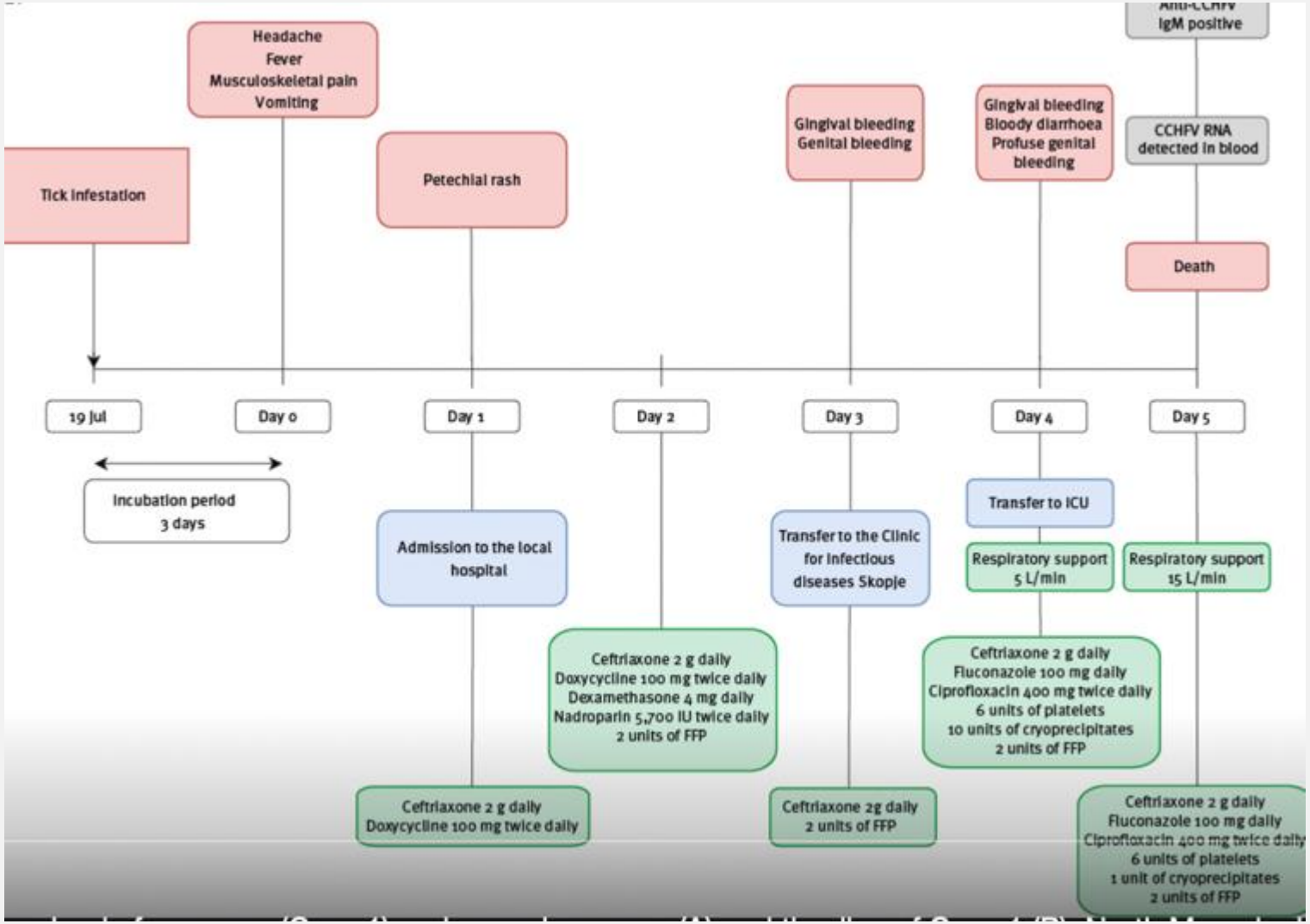
2022: 13/997 (1.3%) ticks
All from the same cattle farm in Pyrénées-Orientales

2023: 142/ 1,001 (14.2%)
H. marginatum ticks were positive for CCHFV.

in Pyrénées-Orientales, 15 cattle farms, 3 farms with cattle and horses 3 farms with horses.

Bernard C, et al.. Euro Surveill. 2024

Cases of Crimean-Congo haemorrhagic fever in North Macedonia, 2023



Case 1 in a rural area of the eastern part of North Macedonia, died.

Case 2: healthcare worker.

Contact monitoring 1/67 +

(PPE) including gloves, mask, apron and face shield were used. The exposure could have occurred during possible improper removal of the PPE.

Case 3: from another region of the country, with no epidemiological link to the confirmed cases or identified contacts from contact tracing, was admitted to our clinic.

Jakimovski D, et al. Euro Surveill. 2023

CCHF in Europe: Total cases since 2013

	Bulgaria	Spain	Portugal	Macedonia	Greece	Total
2013	2/8	1				2/9
2014	1/8 + 1 (UK)					1/9
2015	2/4					2/4
2016	4	1/2				1/6
2017	2					2
2018	1/6 + 1 (GR)	1/2				2/9
2019	2					2
2020	1	1/3				1/4
2021		2				2
2022	1/2	1/2				2/4
2023	3	1		1/3		1/7
2024	1	2/4	1/1			2/6
2025		3			1/2	1/5
Total	7/43	6/17	1/1	1/3	1/2	13/63 (23%)

ECDC: end of 2025

The Presentation of a Case

37 years old male came to the outpatient clinic.

He has myalgia, sometimes high fever.

The first step is CBC

Platelet count	78,000/ml
Leukocyte count	3800/ml
CRP	30
Procalcitonin	0.8

The History of tick bite, location

Differential Diagnosis

- COVID-19
- CCHF
- West Nile
- Chikungunya
- Zika
- Sandfly
- Hanta virus
- Influenza
- Dengue
- EBV

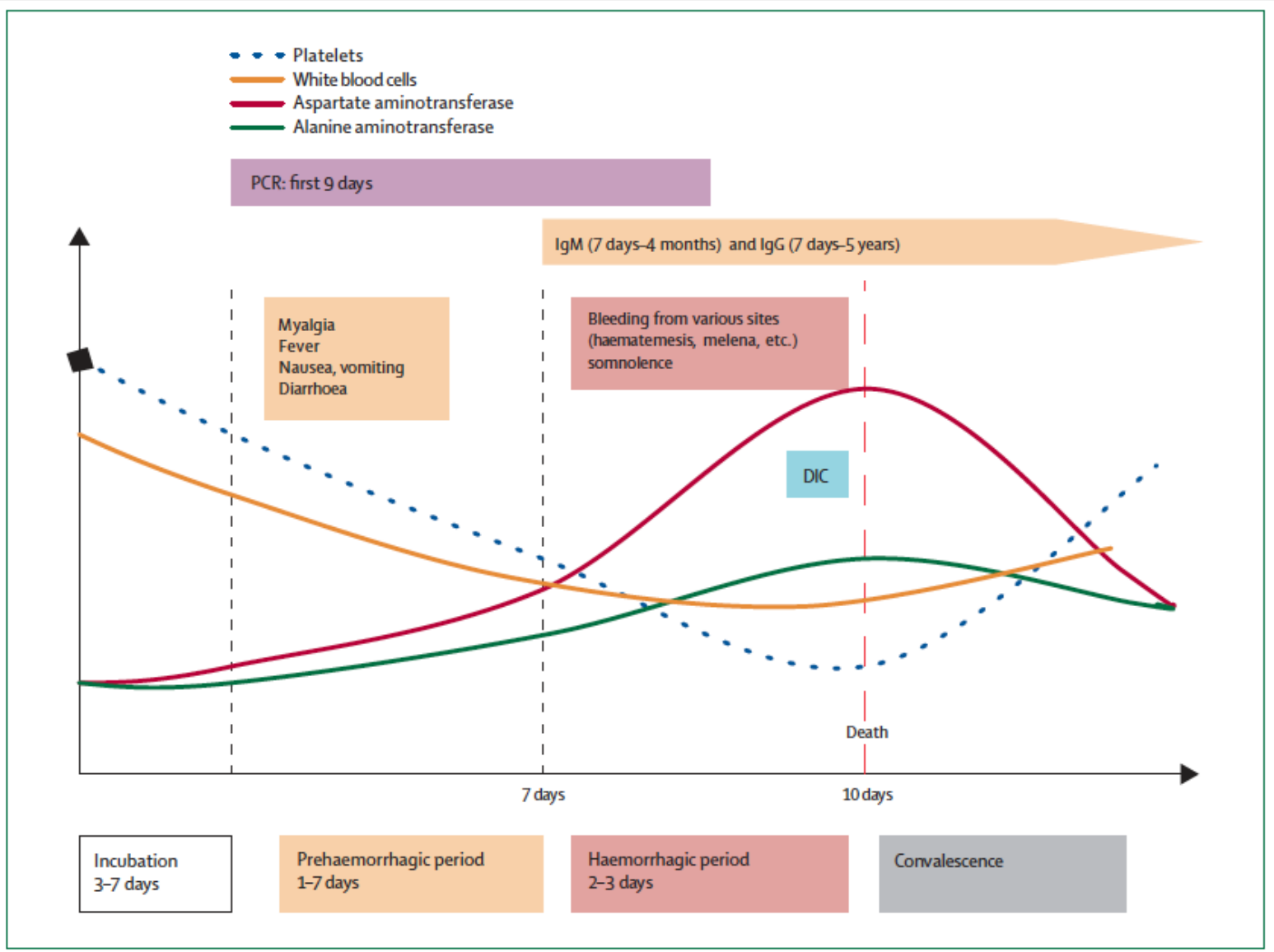
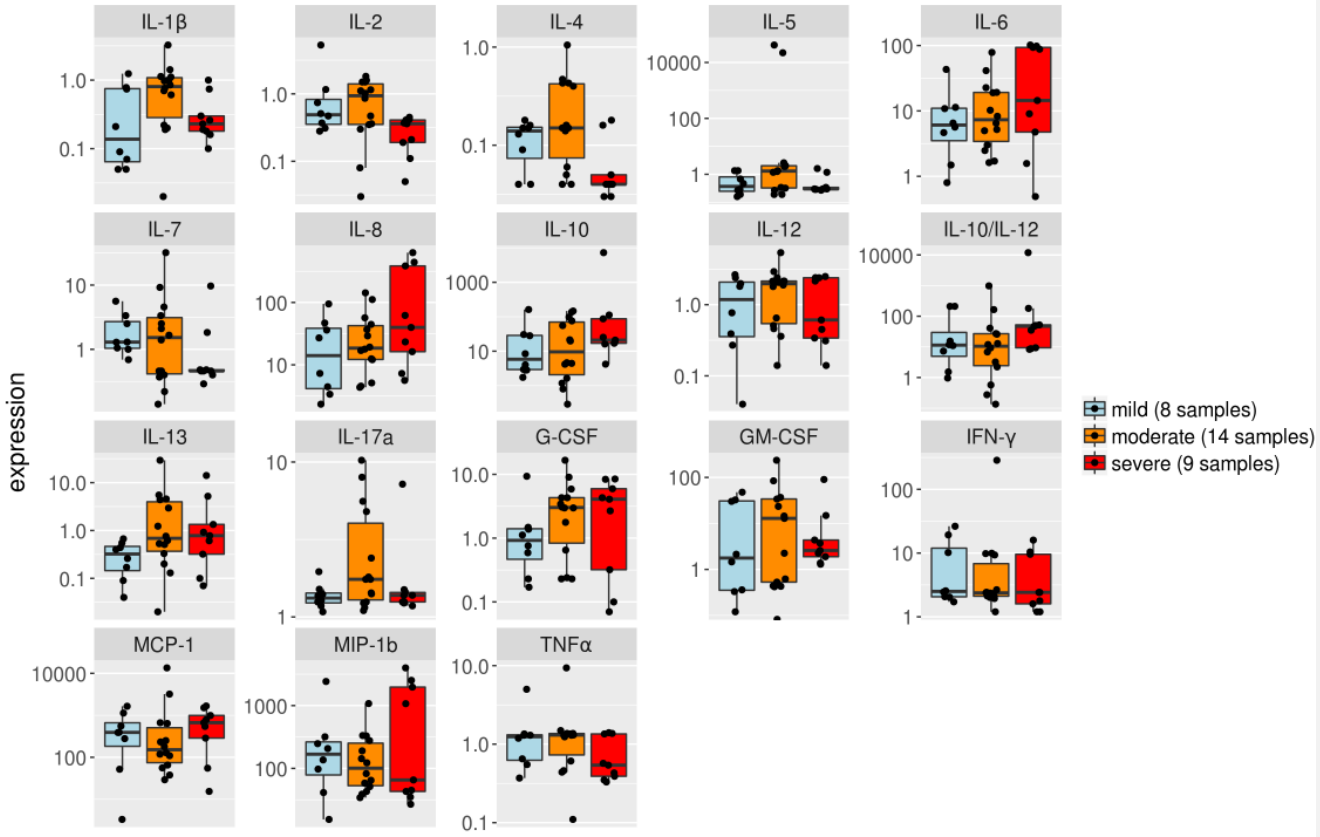


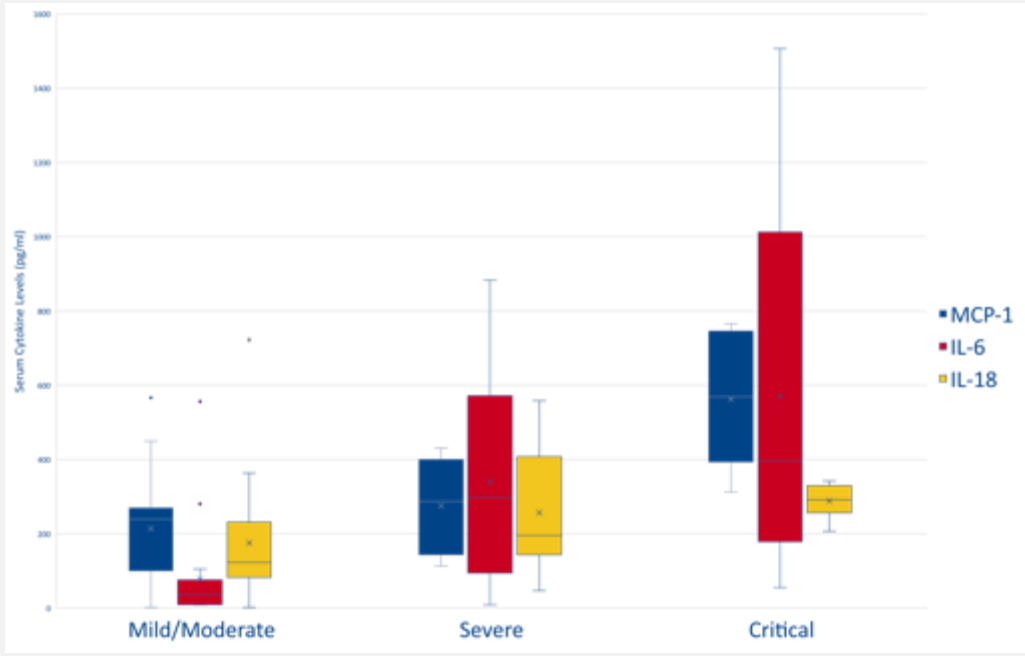
Figure 3: **Clinical and laboratory course of CCHF**
DIC=disseminated intravascular coagulation.

Ergonul O, Lancet ID, 2006

Cytokine Levels of Different Severity Groups for First Five Days

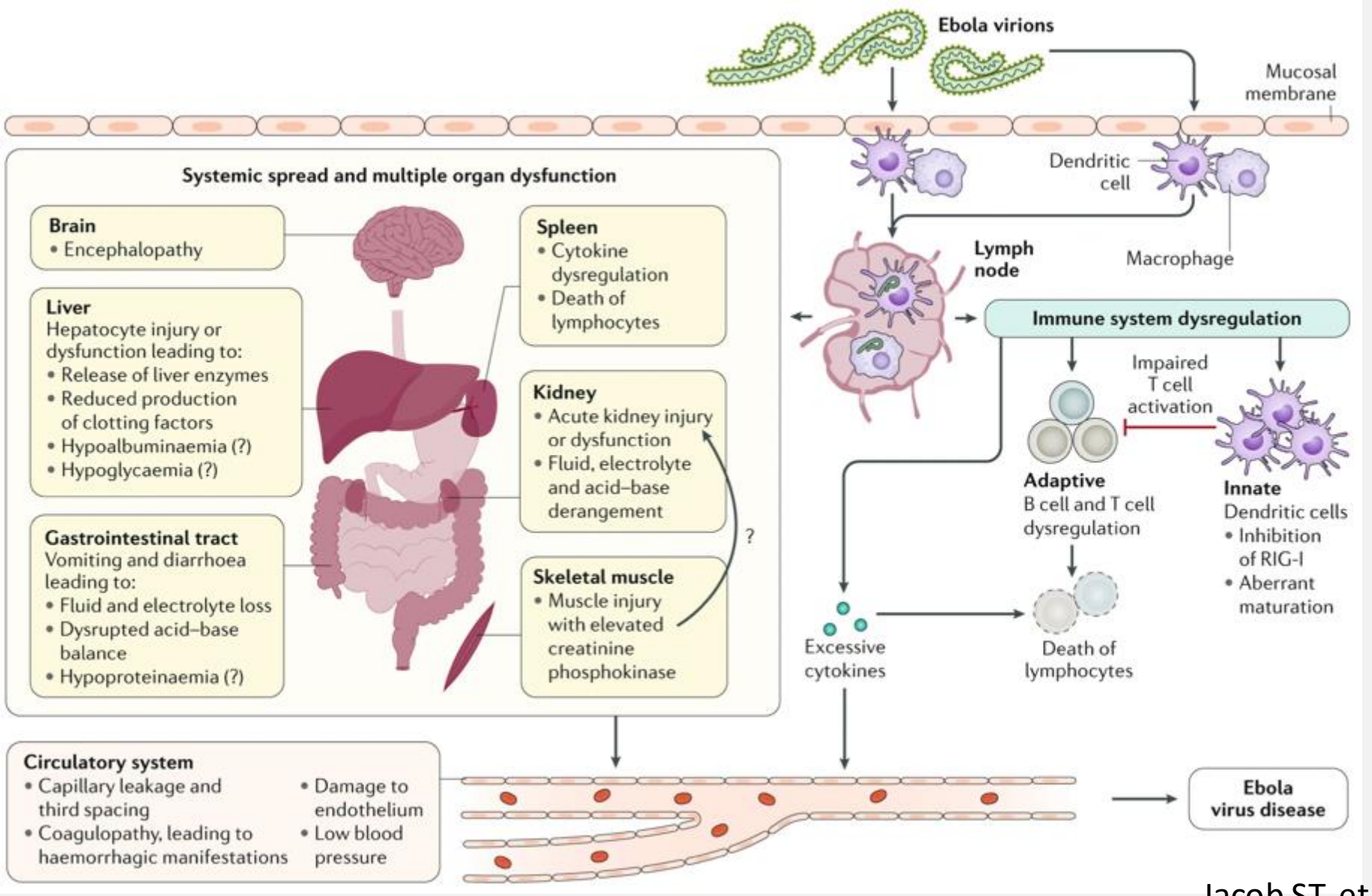


CCHF: J Med Virol 2017



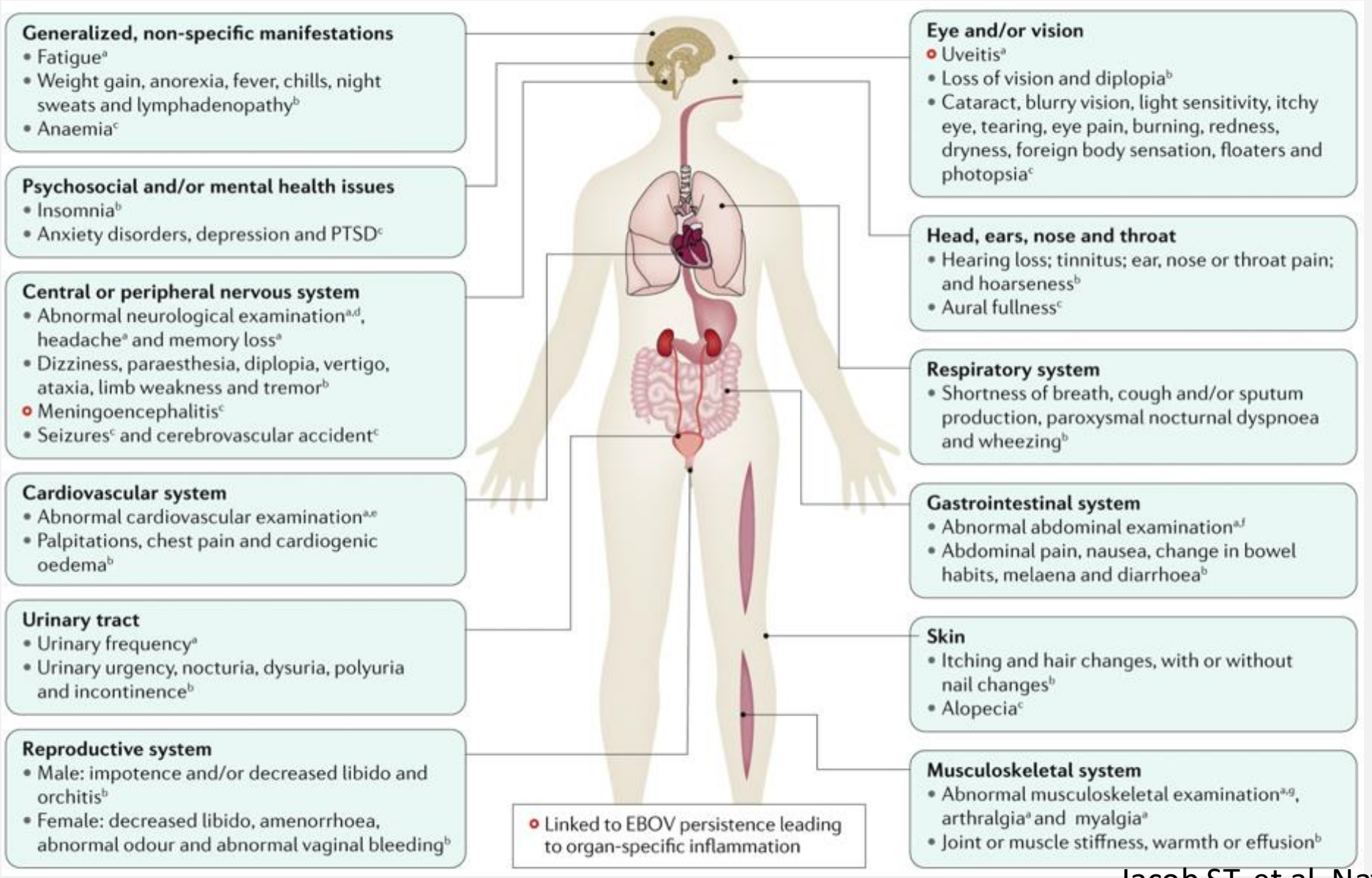
COVID-19: ECCMID 2022

Pathogenesis of Ebola



Jacob ST, et al. Nat Rev 2020

Clinical Sequela of **Ebola Virus Disease** Survivors



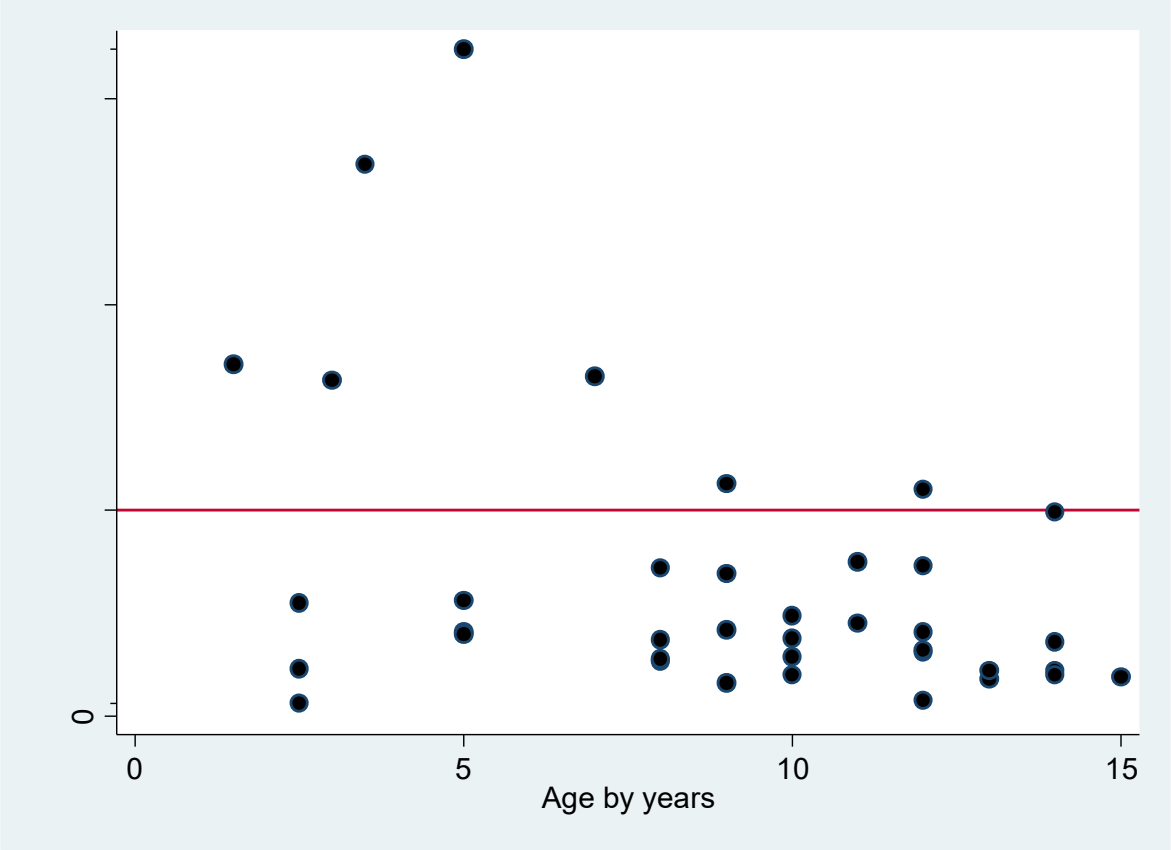
Jacob ST, et al. Nat Rev 2020

Fatality Among Hospitalized Children

33 children in İran: 24% (Sharifi-Mood, et al. Ped Infect Dis J 2008)

31 children in Turkey: 0% (Tezer H, et al. J Clin Virol 2010)

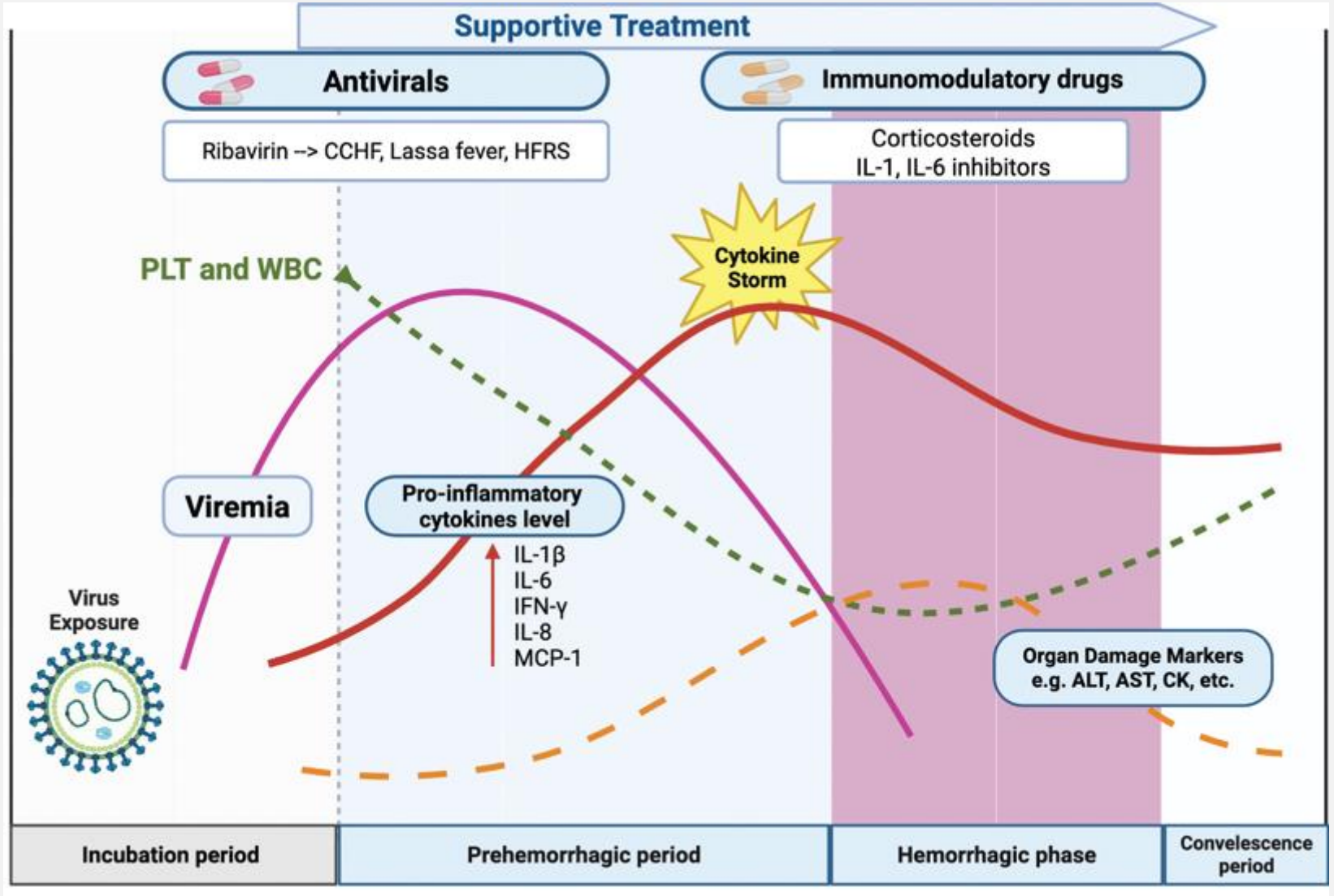
50 children in Turkey; 0% (Tuygun N, et al. Pediatr Int 2011)



Treatment Options

1. Blood products
2. Repurposed drugs
3. Ribavirin
4. Monoclonal antibodies
5. Immunomodulators

Conceptual overview of disease course and therapeutic windows in viral hemorrhagic fevers



Güllü D, Keske Ş, Ergönül Ö. Viral hemorrhagic fevers - therapeutic trial advances and challenges. Expert Rev Anti Infect Ther. 2025

Blood Products in Viral Hemorrhagic Fevers

Blood Products	Primary indications	Standard regimen/considerations	Expected outcomes	References
Packed Red Blood Cells (PRBCs)	Severe anemia (Hb ≤6 g/dL), acute hemorrhagic shock with tissue hypoxia, increase oxygen-carrying capacity.	Dosage adjusted based on clinical response and ongoing/anticipated blood loss. Restrictive transfusion thresholds (Hb 7–8 g/dL) often supported.	Prevent tissue hypoxia. Rarely the primary cause of death is direct blood loss in VHFs.	[8,12,13]
Fresh Frozen Plasma (FFP)	Documented coagulation factor deficiencies, abnormal coagulation tests (prolonged aPTT) with active bleeding, liver disease, DIC.	Typically, 10–20 mL/kg (raises factor levels by ≈20%).	Restores coagulation factors. Contraindicated for simple volume expansion, protein supplementation, or coagulopathy without active bleeding/ impending procedure.	[8,13,14]
Platelets	Significant thrombocytopenia (PLT ≤20,000/μL is predictor of fatal CCHF outcomes) to prevent spontaneous bleeding or stop active hemorrhage.	Guided by careful clinical assessment of bleeding, not solely platelet counts. It can increase the platelet count by approximately 30,000–60,000/μL per apheresis unit or a pool of 4–6 units	Improves platelet count and hemostatic function. Routine prophylactic platelet transfusion is generally NOT recommended (e.g. in Dengue) due to limited efficacy and side effects.	[8,13,15–17]
Cryoprecipitate	Fibrinogen replacement (hypofibrinogenemia or dysfibrinogenemia) in actively bleeding patients or high hemorrhage risk.	Fibrinogen ≤2 g/L in life-threatening bleeding; ≤ 1 g/L with microvascular bleeding. Typical dose: 1 unit per 10 kg (approx. 10 units for adult) to increase fibrinogen by ≈0.5 g/L.	Provides fibrinogen, Factor VIII, vWF, Factor XIII.	[13,18,19]
Balanced Transfusion Strategy (PRBCs, FFP, Platelets)	Massive hemorrhage (loss of > 15% total blood volume or hemorrhagic shock).	Ratios typically 1:1:1 to 2:1:1.	Control life-threatening bleeding.	[8]

Güllü D, Keske Ş, Ergönül Ö. Viral hemorrhagic fevers - therapeutic trial advances and challenges. Expert Rev Anti Infect Ther. 2025

Current Treatment of Viral Hemorrhagic Fevers

Viral hemorrhagic fever	Antivirals			Immunomodulator drugs		Monoclonal antibodies
	Ribavirin	Favipiravir	Other antivirals	Steroids	IL-Inhibitors	
Ebola virus disease	No study	Beneficial in a retrospective study; no effect on non-randomized clinical trials [37–39]	Remdesivir in clinical trial; some benefit [33]	No study	No study	mAb114, REGN-EB3 showed survival benefit in clinical trial [32]
Marburg virus disease	No study	No major clinical trial	None	No data	No data	Nothing approved, or on study
Crimean-Congo Hemorrhagic Fever	Observational studies and meta-analysis show benefit, especially when given early [81,82]	Compassionate use only, no RCTs	None	Potential benefit in severe cases [82]; no RCTs	No trials	Human mAbs under study; no clinical trials yet
Lassa fever	Observational studies show mortality benefit, especially when given early [65,66]	Small Phase-II study is conducted; results are pending [69]	None	No data	No data	Promising Arevirumab-3 cocktail, clinical data is needed [71]
Dengue fever	No study	No completed clinical trials; limited data	Celgosivir and balapiravir was tried in RCTs, no benefit [93]	Used in severe dengue; mixed evidence [97–99]	Not routinely used	No approved mAbs
Yellow Fever	No clear benefit	Not studied	None	No data	No data	Demonstrated good tolerance in phase I a/b clinical trial [118]
Rift Valley Fever	No clinical study	Not studied	None	No data	No data	No approved mAbs
Hantavirus	Effective in HFRS, especially when given early [132], not in HPS [134,135]	No data	None	Used in severe HPS; no controlled trials	No trials	No approved mAbs
Other Arenaviruses	No clinical study	No clinical study	None	No data	No data	No clinical mAbs

Güllü D, Keske Ş, Ergönül Ö. Viral hemorrhagic fevers - therapeutic trial advances and challenges. Expert Rev Anti Infect Ther. 2025

Re-purposed Drugs

Ebola

- Favipiravir
- Brinsidofovir
- Remdesivir

CCHF

- Favipiravir
- Remdesivir
- Molnupiravir
- Nirmetralvir
- Monoclonal antibodies

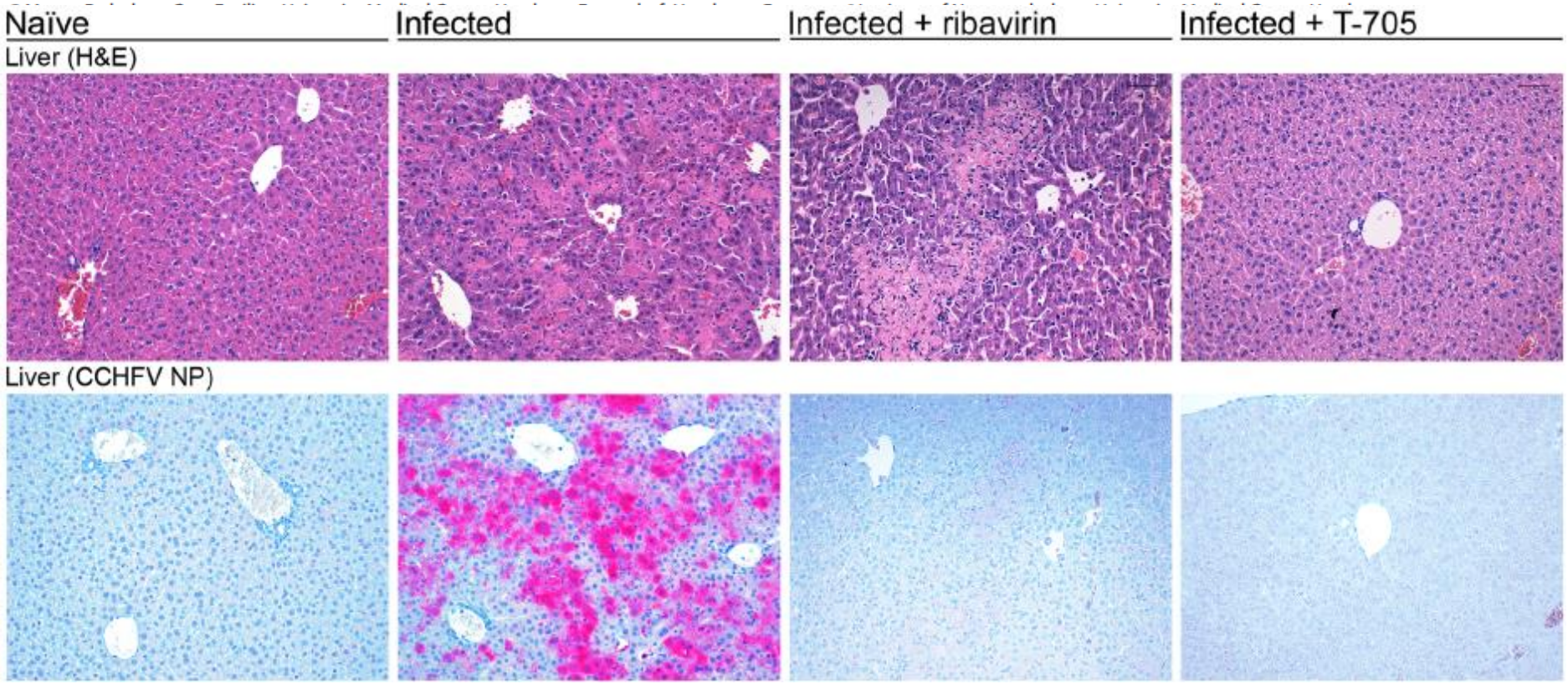
OPEN ACCESS Freely available online

PLOS | NEGLECTED TROPICAL DISEASES

Evaluation of Antiviral Efficacy of Ribavirin, Arbidol, and T-705 (Favipiravir) in a Mouse Model for Crimean-Congo Hemorrhagic Fever

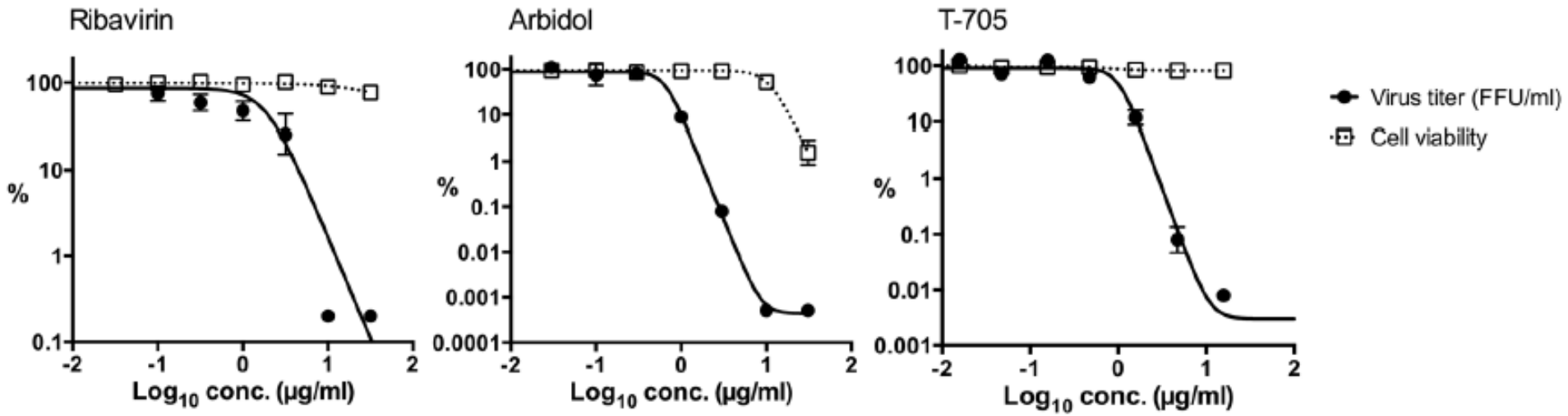
Lisa Oestereich[1,2☯], Toni Rieger[1,2☯], Melanie Neumann[3], Christian Bernreuther[4], Maria Lehmann[1,2], Susanne Krasemann[3], Stephanie Wurr[1,2], Petra Emmerich[1,2], Xavier de Lamballerie[5], Stephan Ölschläger[1¶¤], Stephan Günther[1,2¶*]

1 Department of Virology, Bernhard-Nocht-Institute for Tropical Medicine, Hamburg, Germany, **2** German Centre for Infection Research (DZIF), Hamburg, Germany,



Ostereich L, et al. Plos One, 2014

Favipiravir (T-705) is more effective in vitro and in vivo



	Ribavirin (n=2)	Arbidol (n=3)	T-705 (n=2)
IC_{50}	2.8 µg/ml (1.9–3.7)	0.6 µg/ml (0.08–1.2)	1.1 µg/ml (1.0–1.1)
IC_{90}	4.7 µg/ml (4.6–4.8)	1.2 µg/ml (0.2–2.4)	1.6 µg/ml (1.5–1.7)
IC_{99}	9.5 µg/ml (5.8–13.2)	2.0 µg/ml (0.5–3.8)	2.5 µg/ml (2.0–2.9)

Ostereich L, et al. Plos One, 2014

Research paper

Efficacy of favipiravir (T-705) against Crimean-Congo hemorrhagic fever virus infection in cynomolgus macaques

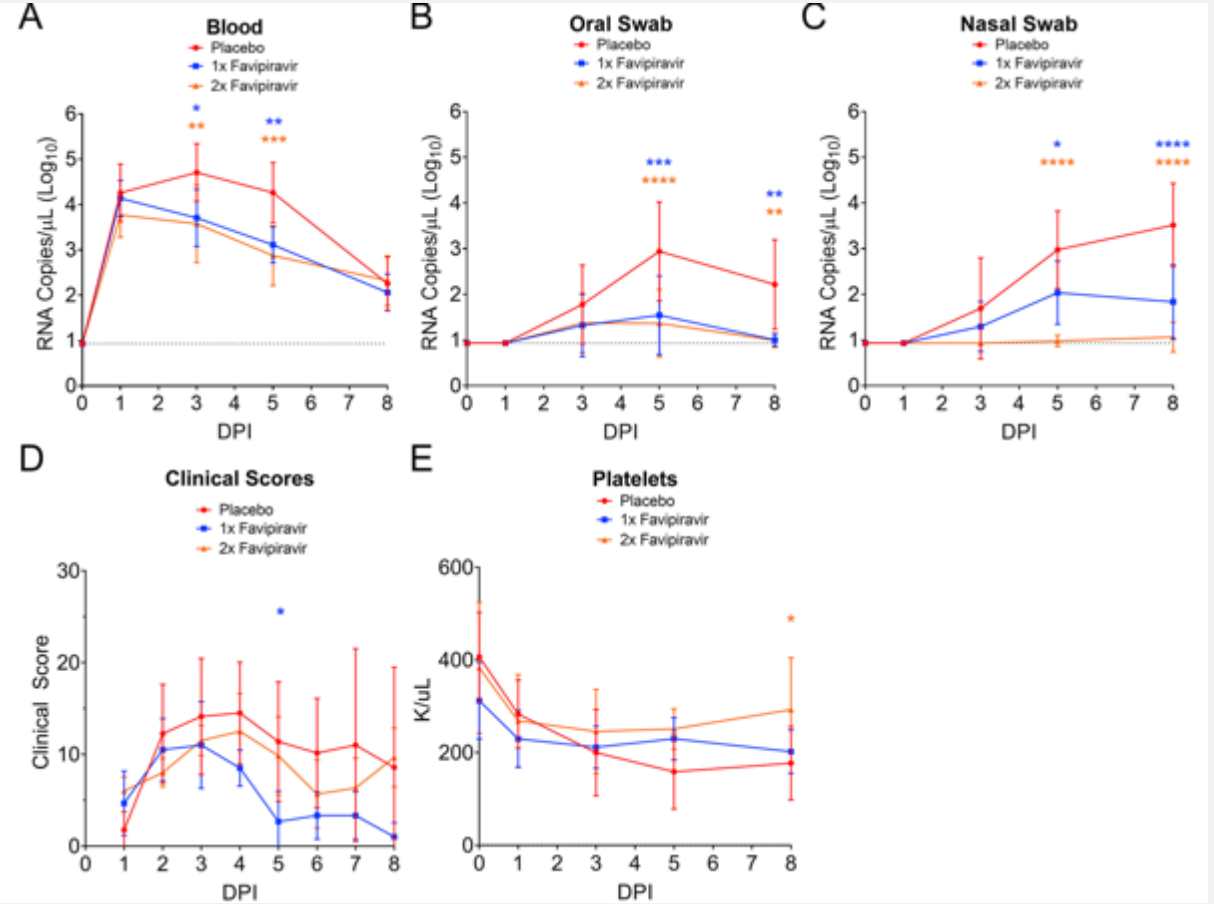
David W. Hawman [a], Elaine Haddock [a], Kimberly Meade-White [a], Glenn Nardone [b], Friederike Feldmann [a], Patrick W. Hanley [a], Jamie Lovaglio [a], Dana Scott [a], Takashi Komeno [c], Nozomi Nakajima [c], Yousuke Furuta [c], Brian B. Gowen [d], Heinz Feldmann [a]

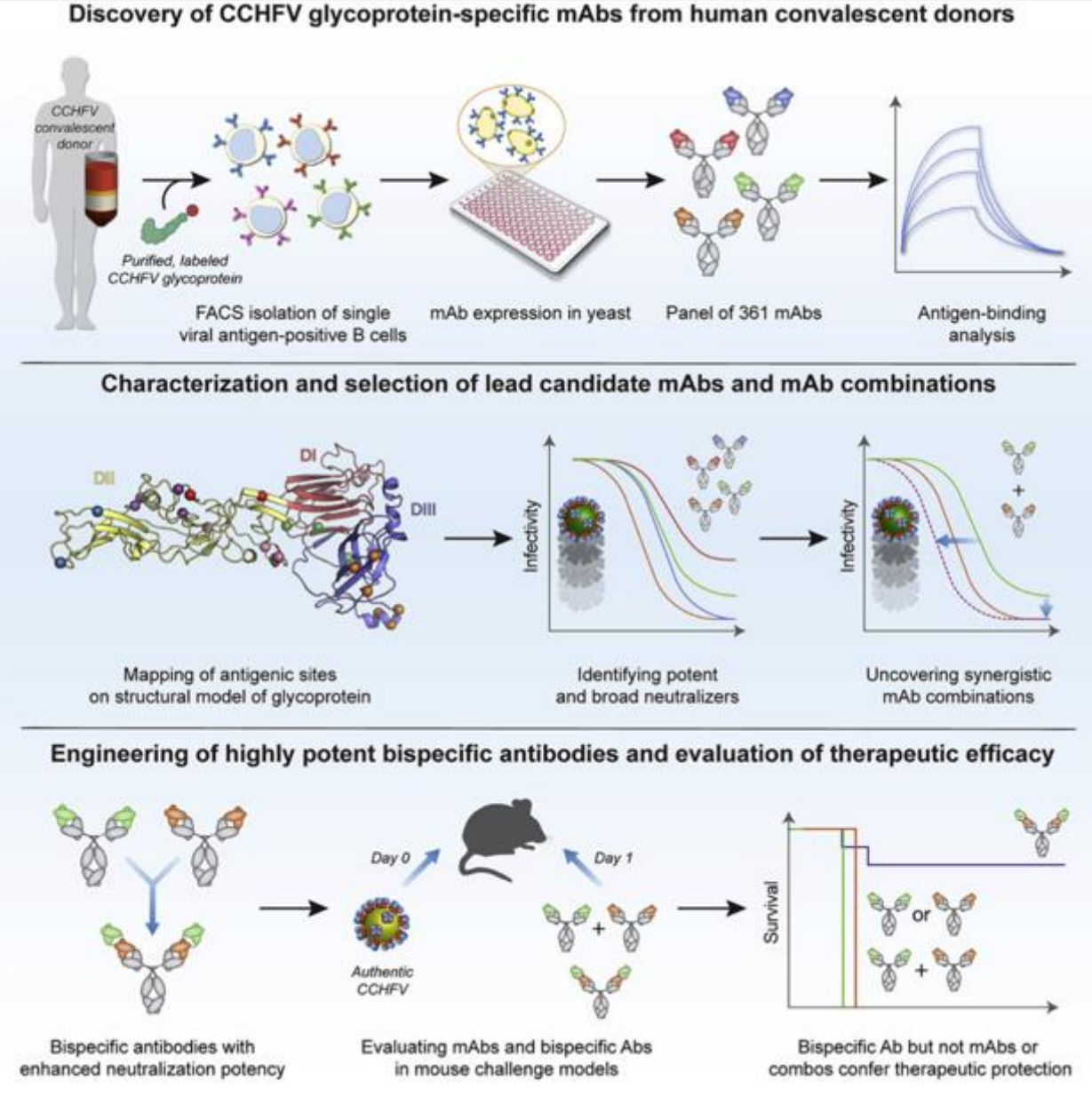
Once- or twice-daily favipiravir suppressed viremia and viral shedding in CCHFV infected macaques.

Viral loads within key tissues of favipiravir-treated animals trended lower than in placebo-treated animals.

Study highlights the importance of the macaque model of CCHF in evaluating antivirals for human CCHF cases.

Antivir Res 2020





Cell
Volume 184, Issue 13, 24 June 2021, Pages 3486-3501.e21
CellPress

Article

Protective neutralizing antibodies from human survivors of Crimean-Congo hemorrhagic fever

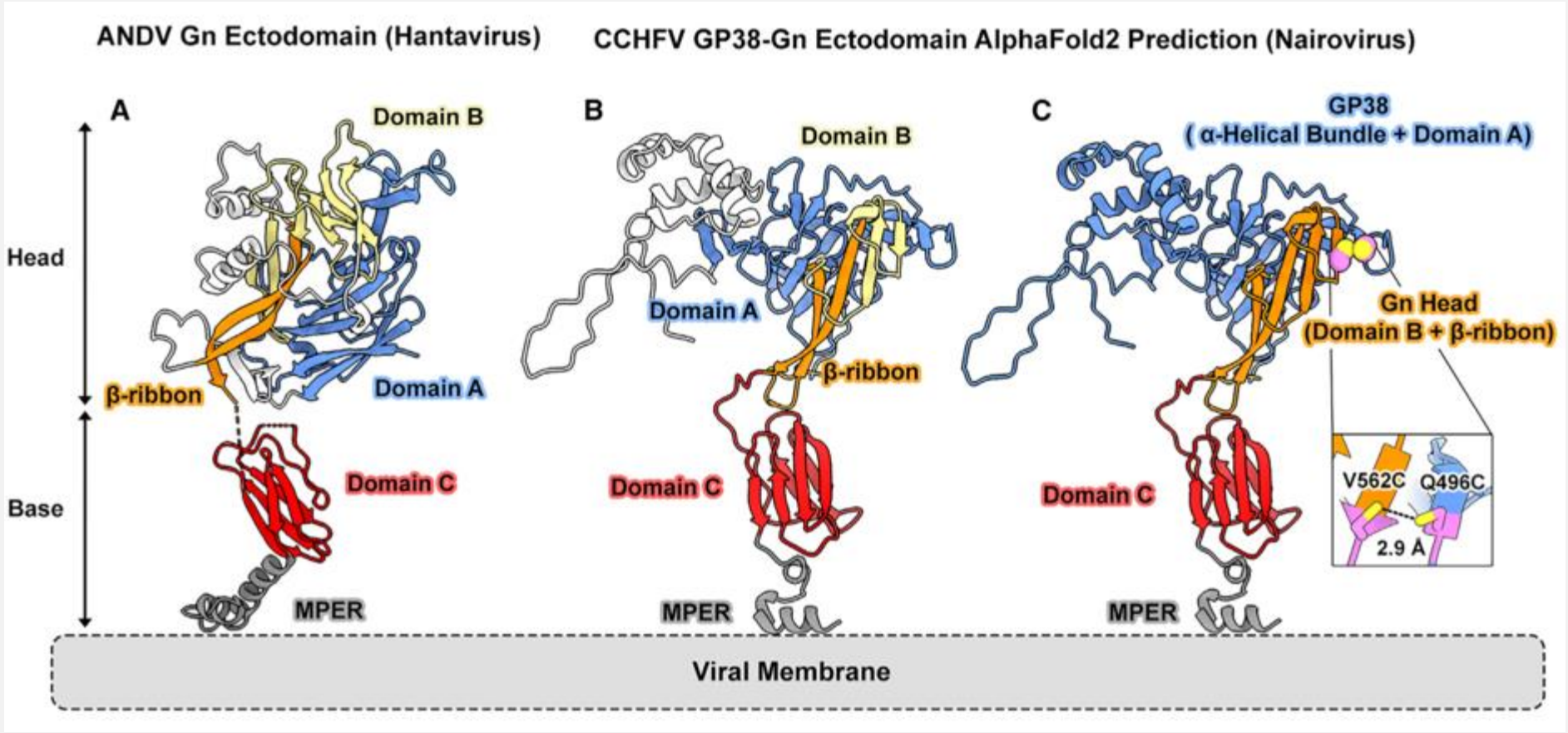
J. Maximilian Fels [1, 15], Daniel P. Maurer [2, 15], Andrew S. Herbert [3, 14, 15], Ariel S. Wirchnianski [1, 4], Olivia Vergnolle [4, 16], Robert W. Cross [5, 6], Dafna M. Abelson [7], Crystal L. Moyer [7], Akaash K. Mishra [8], Jennifer T. Aguilan [12], Ana I. Kuehne [3], Noel T. Pauli [2], Russell R. Bakken [3], Elisabeth K. Nyakatura [4, 16], Jan Hellert [9, 17], Gregory Quevedo [4], Leslie Lobel [10, 18], Stephen Balinandi [11] ... Kartik Chandran [1, 19, 20]

361 monoclonal antibodies against CCHFV glycoproteins isolated from human survivors

- Potent and broad neutralizers targeting six antigenic sites in Gc identified
- Specific combinations of noncompeting antibodies afford synergistic neutralization
- Bispecific antibody combining synergistic antibodies confers therapeutic protection

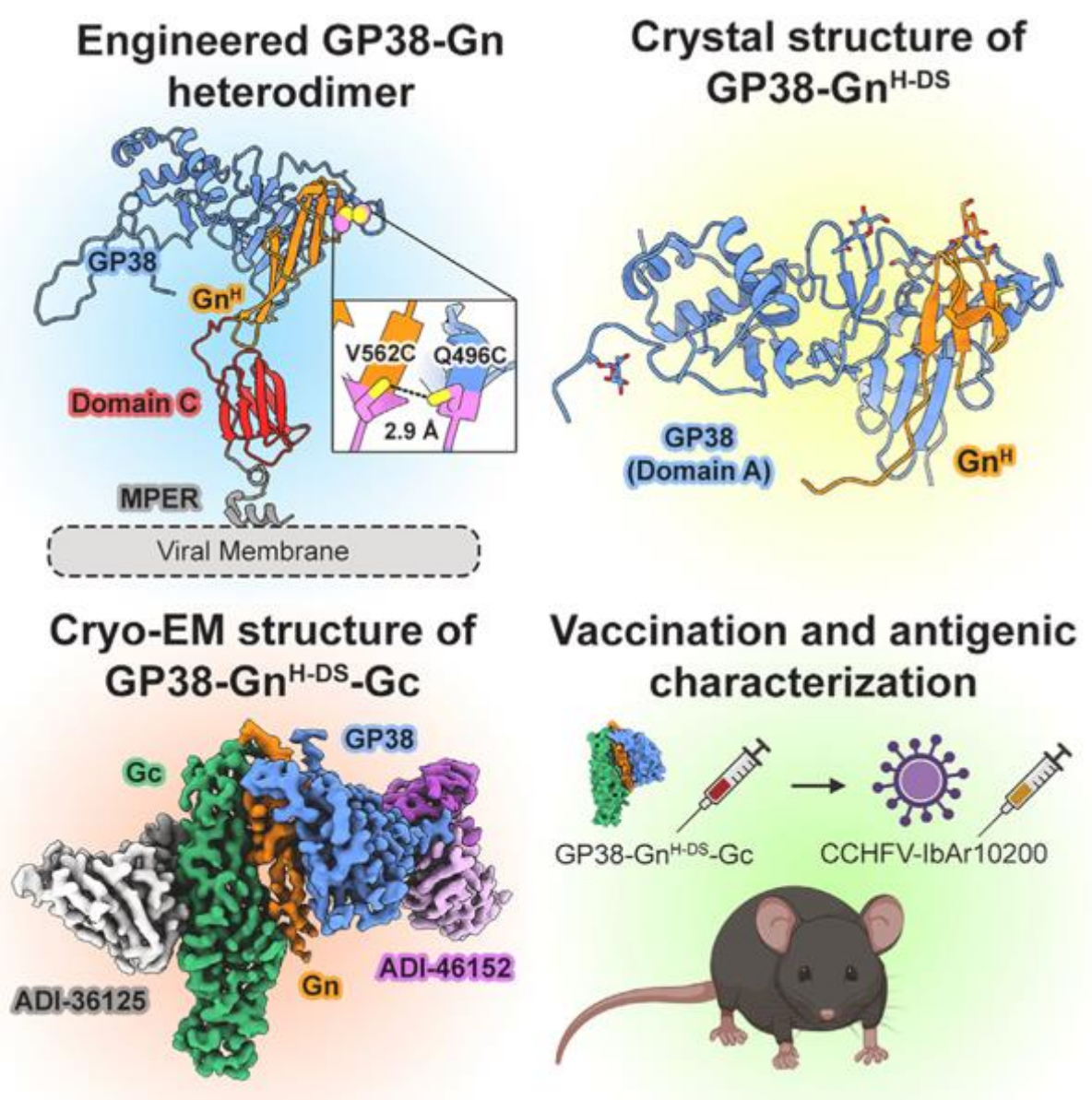
Cell 2021

Structure of CCHFV glycoprotein complex

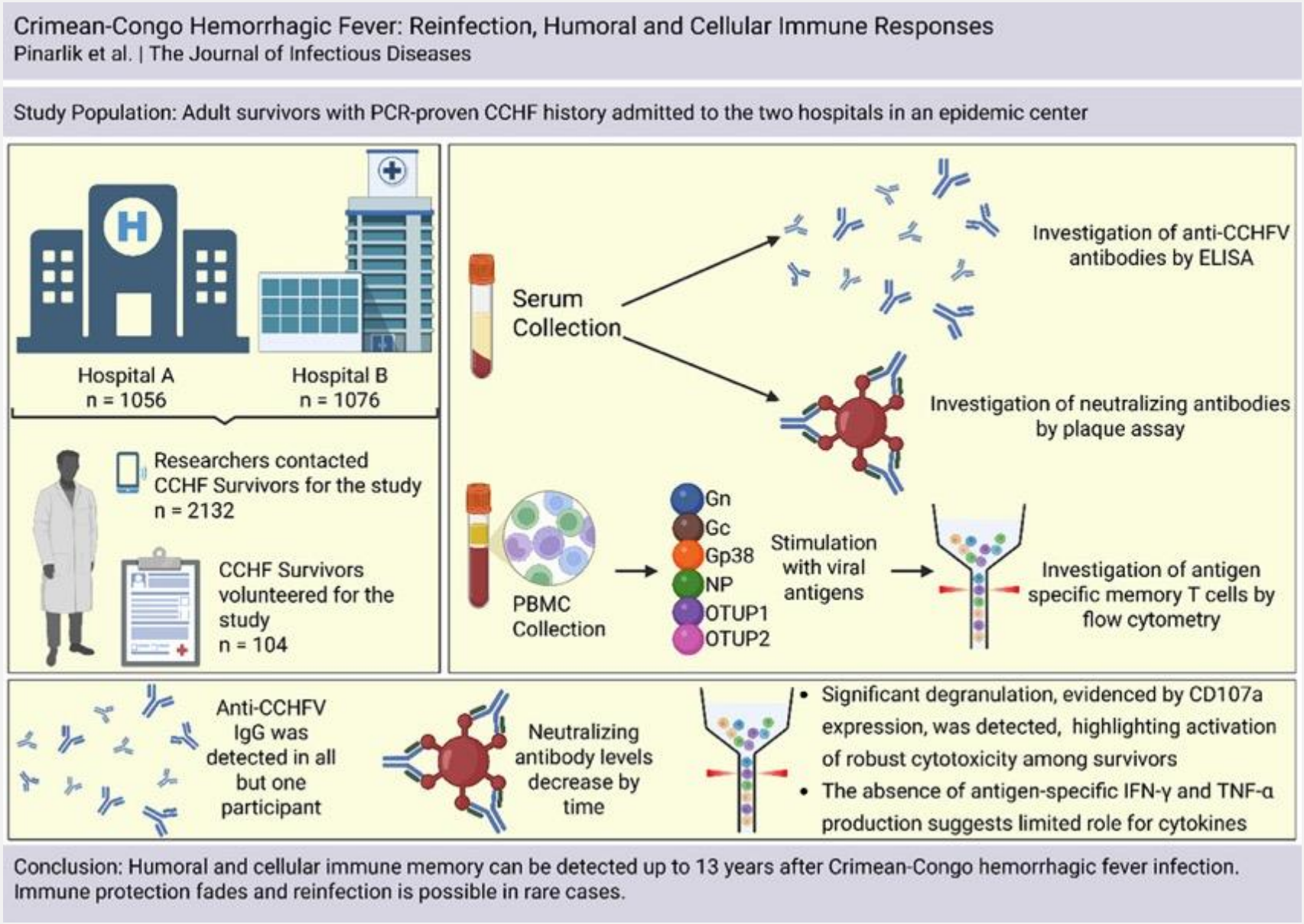


McFadden E, et al. Cell. 2025

Engineering and structures of CCHFV glycoprotein complexes



McFadden E, et al. Cell. 2025



Pınarlık F, et al. (submitted)

JCI The Journal of Clinical Investigation

Human antibody targeting Crimean-Congo hemorrhagic fever virus glycoprotein 38 protects mice against heterologous virus challenge

Gc-specific antibodies to diverse antigenic sites neutralized only weakly and did not protect against heterologous virus challenge.

GP38-specific antibodies bound to two dominant antigenic sites on the glycoprotein. Although GP38-specific antibodies did not neutralize the virus, one mediated protection against heterologous virus challenge in an experimental model of infection in mice primarily by complement-mediated activity.

These studies support the model of development of CCHFV countermeasures that induce protection against GP38 in vivo.

Chapman NS, Borisevich V, Kose N, Myers L, Priest S, Bergeron É, Trigo Esteban E, Sanchez-Seco MP, Melero J, Geisbert T, Cross RW, Crowe JE Jr.. J Clin Invest. 2026

Ribavirin

Arenaviridae
Lassa Fever
South America HF
Bunyavirales
Hanta
Rift Valley
CCHF

Problems in Study Design: What We Learned?

A. Study Design

1. Inclusion criteria
    1. Severity (Confounding by indication)
    2. Number of days from onset of symptoms
        1. Prehemorhagic
        2. Hemorhagic
2. Ineffective application:

    GIS symptoms in oral use (hematemesis)

3. Duration of treatment

B. Statistical Analysis

1. P value is not everything; sample size is important
2. Meta-analysis: oranges & apples; early vs late

Time zero is vital in infectious diseases

Exposure Point: This is the true beginning of the history. First moment of contact with a pathogen (e.g., tick bite, contact with an infected person, or consumption of contaminated water)

The incubation period of the disease can be calculated accordingly

Onset of Symptoms: In the patient's history, "time zero" is usually taken as the moment the first symptoms are felt. Epidemiological curves (epi-curves) are plotted relative to this point. If this point is misremembered (recall bias), calculations about the source of the outbreak can be completely skewed.

Clinical Threshold and Presentation: For the healthcare system, time zero is the moment the patient walks through the door.

İmmortal Bias

The Crimean-Congo Hemorrhagic Fever (CCHF) and Ribavirin Controversy (International Breakthrough)

Conclusion: Analyses using this method have clarified that ribavirin is actually effective not in every case, but especially when started early (within the first 4 days), and does not make a significant difference when started late.

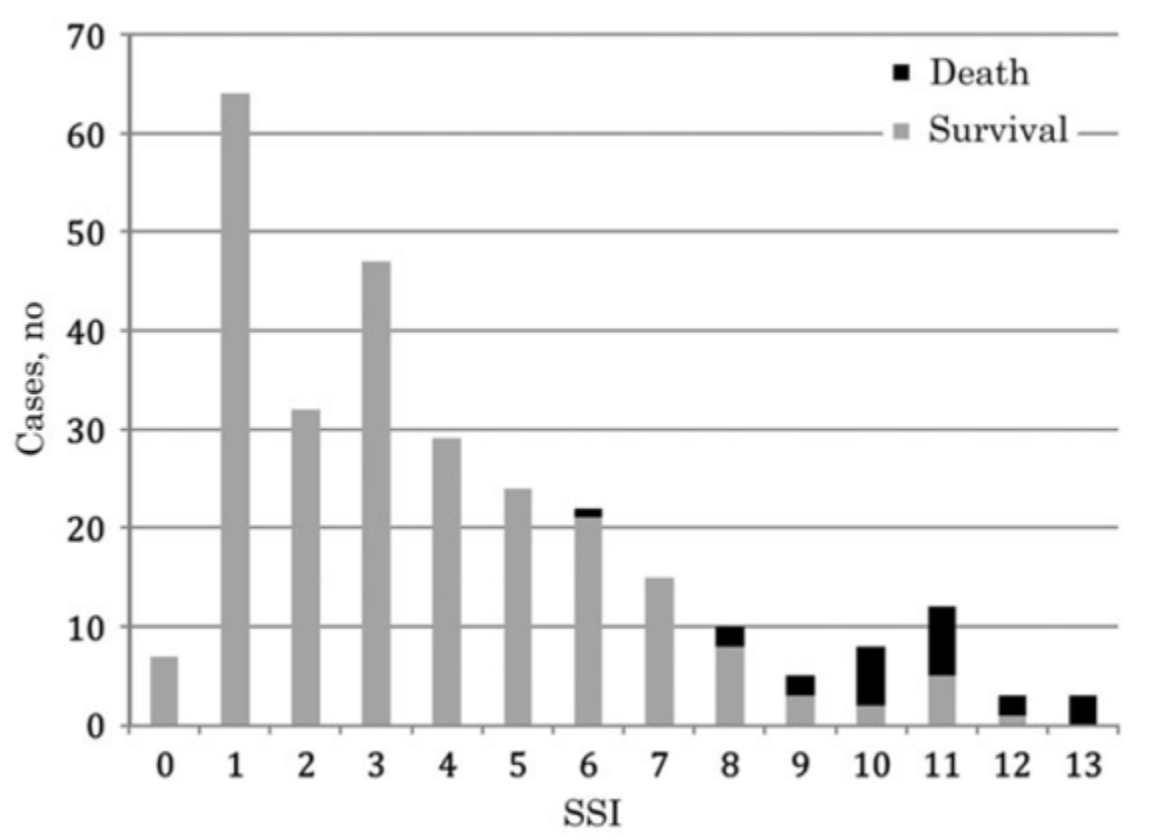
"Target Trial Emulation"
The best way to avoid immortal time bias when analyzing observational data is to fix the "time zero" as if you were conducting a Randomized Controlled Trial (RCT).

Rule: If a patient meets the inclusion criteria for the study on day 3, their data should only be processed from day 3 onwards.

Severity Scoring Index for Crimean-Congo Hemorrhagic Fever and the Impact of Ribavirin and Corticosteroids on Fatality

Başak Dokuzoguz,[1] Aysel Kocagül Celikbas,[1] Şebnem Eren Gök,[1] Nurcan Baykam,[1] Mustafa Necati Eroglu,[1] and Önder Ergönül[2]

[1]Clinical Microbiology and Infectious Diseases Clinic, Ankara Numune Education and Research Hospital, Ankara, and [2]Infectious Diseases and Clinical Microbiology, Koç University, School of Medicine, Istanbul, Turkey



Clin Infect Dis 2013

Table 1. Characteristics of SSI Parameters for Crimean-Congo Hemorrhagic Fever

SSI Parameter	Score
Platelet count, $\times 10^3$ platelets/mm^3	
>150	0
150–50	1
49–20	2
<20	3
aPTT, sec	
≤34	0
35–45	1
46–59	2
>60	3
Fibrinogen level, mg/dL	
≥180	0
179–160	1
159–120	2
<120	3
Bleeding	
No	0
Petechia	1
Ecchymosis	2
Bleeding	3
Somnolence	
No	0
Yes	1

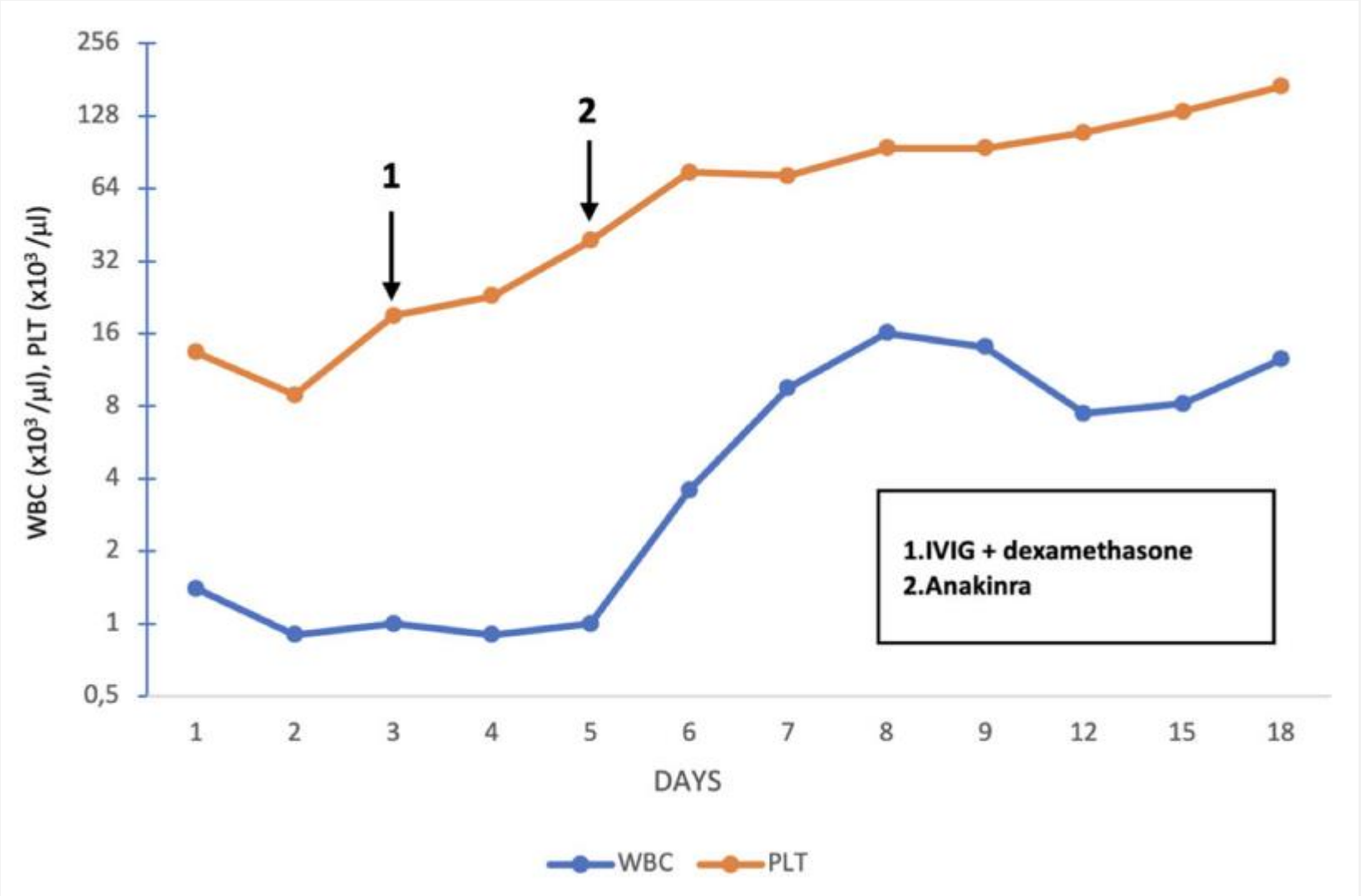
Table 3. Univariate and Adjusted Analysis for Prediction of Death

	Univariate Analysis		Adjusted Analysis	
Factor	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
SSI	2.49 (1.82–3.41)	<.001	3.27 (2.09–5.13)	<.001
Ribavirin use	0.68 (.23–1.93)	.470	0.04 (.004–.48)	.01
Corticosteroid use	5.65 (2.31–13.77)	<.001	0.22 (.039–1.27)	.092

Abbreviations: CI, confidence interval; OR, odds ratio; SSI, severity scoring index.

Dokuzoğuz B, et al. Clin Infect Dis 2013

Utility of anakinra in CCHF with haemophagocyctic lymphohistiocytosis

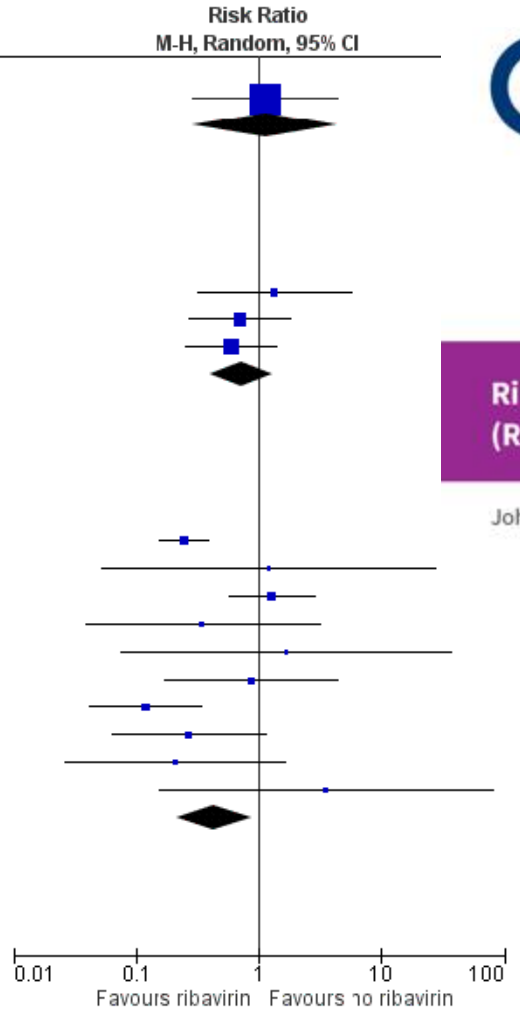


13years old,
14female

Çelik Ü, et al. Trans R Soc Trop Med Hyg. 2025

Figure 7. Forest plot of subsidiary descriptive analysis: ribavirin versus no ribavirin, outcome: mortali

Study or Subgroup	Ribavirin Events	Total	No Ribavirin Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
3.1.1 RCT						
Koksal 2010	4	64	4	72	100.0%	1.13 [0.29, 4.32]
Subtotal (95% CI)		**64**		**72**	**100.0%**	**1.13 [0.29, 4.32]**
Total events	4		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.17 (P = 0.86)						
3.1.2 Non-randomized studies (serious risk of bias)						
Bodur 2011	2	10	6	40	15.8%	1.33 [0.32, 5.64]
Dokuzoguz 2013	18	235	5	46	37.4%	0.70 [0.28, 1.80]
Elaldi 2009	9	126	11	92	46.8%	0.60 [0.26, 1.38]
Subtotal (95% CI)		**371**		**178**	**100.0%**	**0.72 [0.41, 1.28]**
Total events	29		22			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.90$, df = 2 (P = 0.64); $I^2 = 0\%$						
Test for overall effect: Z = 1.11 (P = 0.27)						
3.1.3 Non-randomized studies (critical risk of bias)						
Alavi-Nani 2006	37	236	12	19	20.6%	0.25 [0.16, 0.39]
Belet 2014	1	39	0	15	3.9%	1.20 [0.05, 27.94]
Cevik 2008 (1)	5	9	7	16	17.2%	1.27 [0.57, 2.84]
Ergonul 2006 (2)	1	22	3	23	6.9%	0.35 [0.04, 3.10]
Ertugrul 2009	1	17	0	9	4.0%	1.67 [0.07, 37.21]
Ozkurt 2006	2	22	4	38	10.1%	0.86 [0.17, 4.34]
Sannikova 2009	4	264	18	140	14.7%	0.12 [0.04, 0.34]
Tasdelen Fisgin 2009	3	41	3	11	11.2%	0.27 [0.06, 1.15]
Tulek 2012	1	91	8	152	7.5%	0.21 [0.03, 1.64]
Tuygun 2012	1	23	0	27	3.9%	3.50 [0.15, 81.99]
Subtotal (95% CI)		**764**		**450**	**100.0%**	**0.43 [0.22, 0.86]**
Total events	56		55			
Heterogeneity: $Tau^2 = 0.55$; $Chi^2 = 21.22$, df = 9 (P = 0.01); $I^2 = 58\%$						
Test for overall effect: Z = 2.37 (P = 0.02)						



Test for subgroup differences: $Chi^2 = 2.05$, df = 2 (P = 0.36), $I^2 = 2.3\%$

Footnotes

(1) Severe cases

(2) Severe cases

Cochrane Library

Cochrane Database of Systematic Reviews

Ribavirin for treating Crimean Congo haemorrhagic fever (Review)

Johnson S, Henschke N, Maayan N, Mills I, Buckley BS, Kakourou A, Marshall R

PAPER

A randomised controlled trial of ribavirin in Crimean Congo haemorrhagic fever: ethical considerations

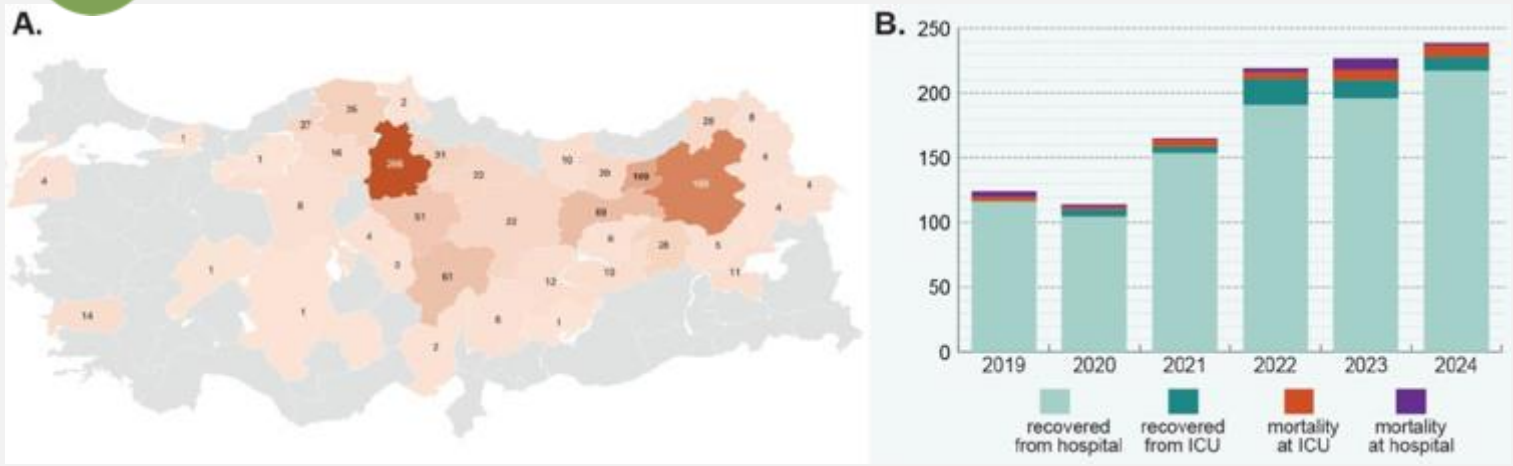
B Arda,[1] A Aciduman,[1] J C Johnston[2,3]

CONCLUSION

There is universal agreement that placebo-controlled trials should be prohibited in life-threatening conditions if an existing treatment is effective at prolonging or preserving life. The available literature provides convincing evidence that CCHF may be effectively treated with prompt administration of ribavirin. It is the standard of care in several nations, and ratified by the Centers for Disease Control and WHO. Therefore, it would be decidedly unethical to conduct an RCT of ribavirin in patients harbouring this life-threatening disease.

J Med Ethics 2011

Predictors of ICU Admission



- 18 centers, 1103 lab confirmed cases (2019-2024)
- ICU Admission 8%
- Case fatality rate 5.1%

Table 3
Time-dependent Cox regression model evaluating the effect of early ribavirin administration on in-hospital mortality truncated at 30 days

Variables	aHR	95% CI	p value
Being a female	0.611	0.323–1.153	0.128
Age (≥50 y)	2.565	1.241–5.301	**0.011**
Being a farmer	0.604	0.328–1.114	0.106
Diabetes mellitus	2.708	1.278–5.739	**0.009**
Chronic heart disease	1.242	0.481–3.208	0.654
Hypertension	0.951	0.404–2.239	0.909
Ribavirin initiation within ≤96 h	0.214	0.066–0.694	**0.010**

Güllü D, et al. Key predictors of mortality in Crimean-Congo haemorrhagic fever: a retrospective multicentre cohort study.

Clin Microbiol Infect. 2025

VHF	Human to human transmission
Ebola	High
Marburg	High
CCHF	High
Lassa	Moderate
Orthohantavirus	Low
Rift Valley Fever	No
Yellow fever	No
Dengue	No

Ebola Virus in Semen: West Africa: 2014 to 2016

267 male survivors, viral RNA in the semen of 30% of survivors, mean 19 months, max 40 months. (Longitidunal study in Liberia, NEJM 2019).

The concentration of viral RNA in semen during early recovery was 4 logs higher than in blood during peak infection (Barnes KG, et al. CID 2017)

Risk factors for persistence of EBOV in semen:

- Older age,
- decreased illness severity,
- elevated total serum IgG3 and HLA-C*03:04 allele expression

(Dyal J, et al. CID 2023).

CCHF: sexual transmission

Ergonul O, et al. Potential sexual transmission of CCHF infection. Jpn J Infect Dis 2014

Pshenichnaya NY, et al. Possible sexual transmission of CCHF. Int J Infect Dis 2016

Maternal and fetal outcomes of Crimean-Congo hemorrhagic fever in pregnancy:

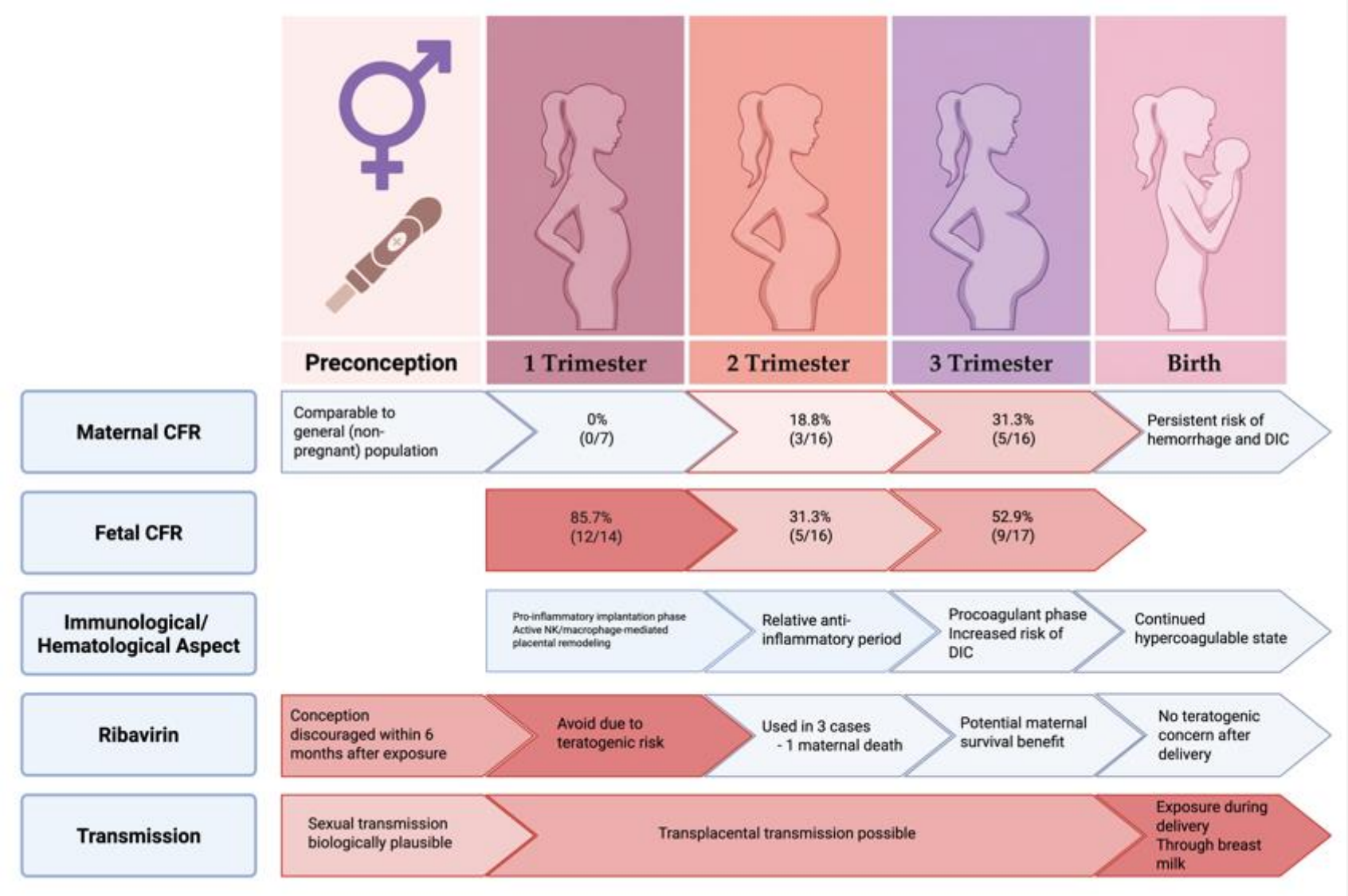
an individual patient data meta-analysis

Donk B, et al.

ESCMID Global 2026

Emerg Infect Dis 2026, October

Maternal and fetal outcomes of CCHF in pregnancy



Donk B, et al. Emerg Infect Dis 2026

Ribavirin Use in Pregnancy

Table 1. The association of ribavirin usage on maternal mortality in pregnant patients infected with CCHF

	N (%)	Maternal mortality, N (%)	OR	95% CI	p-value
Total cohort	52 (94.5)	15 (28.8)			
No ribavirin	29 (67.4)	9 (20.9)			
Ribavirin	14 (32.6)	1 (2.3)	0.171	0.019-1.513	0.112
First trimester	6 (11.5)	0 (0)			
No ribavirin	6 (100)	0 (0)			
Ribavirin	0 (0)				
Second trimester	16 (30.8)	3 (18.8)			
No ribavirin	13 (81.2)	2 (66.7)			
Ribavirin	3 (18.8)	1 (33.3)	2.750	0.162-46.8	0.489
Third trimester	14 (26.9)	5 (35.7)			
No ribavirin	8 (57.1)	5 (100)			
Ribavirin	6 (42.9)	0 (0)	0.333	0.132-0.840	**0.031**

Donk B, et al. Emerg Infect Dis 2026

Hand hygiene and use of PPE based on risk assessment

- Always before and after patient contact, and after contact with contaminated environmental surfaces or equipment
- If direct contact with patient's blood and body fluids, secretions, excretions, mucous membranes or non-intact skin
- If there is a risk of spills onto the health-care worker's face






Рекомендуемый порядок снятия СИЗ
How to put on PPE (when all PPE items are needed)
Step 1
Step 2
Step 3a
OR
Step 3b
Step 4
Step 1
Step 2
Step 3a
Step 3b
Step 4

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Perspective

Probable Crimean-Congo hemorrhagic fever virus transmission occurred after aerosol-generating medical procedures in Russia: nosocomial cluster

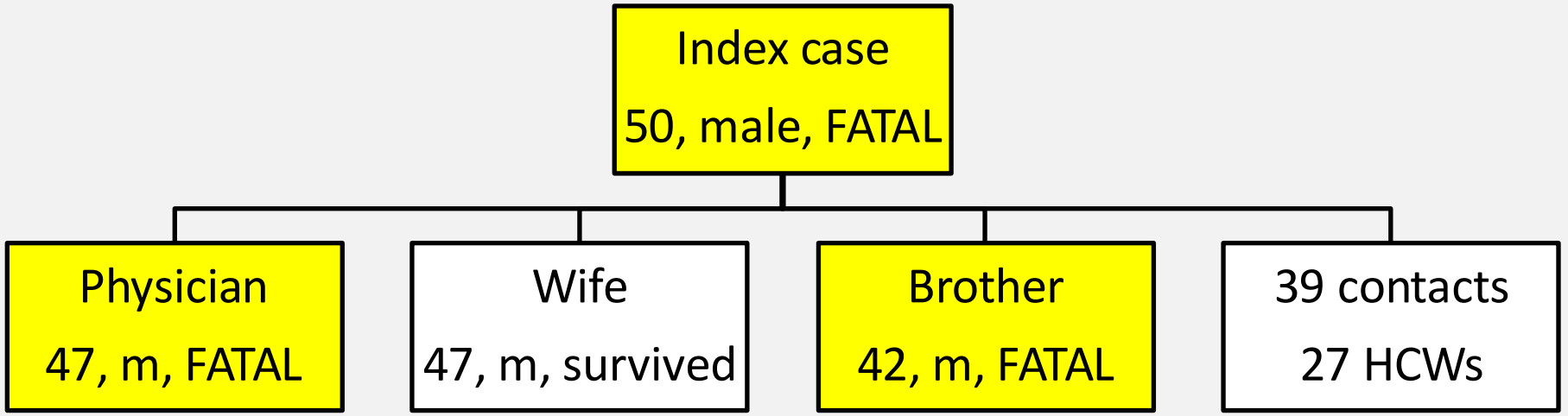
Natalia Yurievna Pshenichnaya *, Svetlana Alexeevna Nenadskaya

Rostov State Medical University, Rostov-on-Don, Russia

This case of airborne transmission of CCHF demonstrates that during performance of any AGMPs for any CCHF patient, airborne precautions should always be added to standard precautions (particulate respirator protective to N95 or equivalent standard, eye protection, single airborne precaution room or well-ventilated setting, etc.) according to WHO guidelines[16] for all HCWs who are in a patient's room. Access to any room where the aerosol-generating procedures are performed should be extremely limited.

IJID, 2015

Nosocomial Infection in Tajikistan, 2009



Ergonul O, et al. WHO report, Tajikistan 2009

Crimean-Congo Hemorrhagic Fever among Health Care Workers, Turkey

Aysel Kocagul Celikbas, Başak Dokuzoğuz, Nurcam Baykam, Sebnem Eren Gok, Mustafa Necati Eroğlu, Kenan Midilli, Herve Zeller, and Onder Ergonul

Table 1. Clinical and laboratory findings of HCWs in whom Crimean-Congo hemorrhagic fever developed after occupational exposure, Turkey, 2004–2011*†

HCW, outcome	Body temperature, °C	Bleeding	Leukocytes/ mm^3	Platelets/ mm^3	AST	ALT	APTT	Fibrinogen	SSI
1, survived	38.5	No	800	42,000	425	346	44	225	Moderate
2, survived	37.2	No	1100	53,000	145	81	43	270	Mild
3, died	40.5	Ecchymosis, hematemesis, melena, hematuria	11,100	40,000	251	277	90	171	Severe
4, survived	40.5	No	2,900	78,000	150	110	37.4	250	Mild
5, survived	39	Epistaxis	1,800	58,000	167	129	64	218	Moderate
6, survived	40.5	No	1,800	44,000	123	216	40.5	165	Moderate
7, survived	39.1	No	3,100	13,000	418	132	40.9	170	Moderate

*HCW, health care worker; AST, aspartate aminotransferase; ALT, alanine aminotransferase; APTT, activated partial thromboplastin time ; SSI, severity score index.
†Reference values: leukocytes, 4,000–11,000/mm^3; platelets, 150,000–450,000/mm^3; AST, <50 IU/L; ALT, <50 IU/L; APTT, 24–36 sec; fibrinogen, 200–400 mg/dL.

Emerg Infect Dis 2014

Table 2. Demographic features of HCWs with occupational exposure to Crimean-Conger hemorrhagic fever virus, Turkey, 2004–2011*

Episode, outcome†	HCW age, y/sex/profession	Procedure	Transmission route	Ribavirin for postexposure prophylaxis	Ribavirin for therapy (no. d after symptom onset)	Fatal
Episode 1; survived, her baby died	36/M/nurse	Wound care	Contact with surgical wound without protective equipment	No	Yes (0)	No
	31/F/nurse	Intubation, aspiration	Aerosol and droplet and contact without protective equipment	No	No	No
Episode 2; died	28/F/nurse	Phlebotomy	Needlestick	No	Yes (3)	Yes
Episode 3; died	41/M/physician	Resuscitation	Aerosol and droplet	–	Yes (0)	No
	26/M/physician	Nasal tamponade	Indirect contact	–	Yes (0)	No
	29/M/physician	Nasal tamponade	Indirect contact	–	Yes (0)	No
Episode 4; survived	30/M/nurse	Phlebotomy	Needlestick	No	Yes (1)	No
Episode 5; survived	30/F/nurse	Phlebotomy	Needlestick	Yes	–	No
Episode 6; survived	24/F/physician	Phlebotomy	Needlestick	Yes	–	No

*HCW, health care worker; –, ribavirin not necessary.
†Outcome for the index case-patient in each episode.

Emerg Infect Dis 2014

Eline iğne batan 18 yaşındaki Kübra KKKA'dan öldü

14/06/2009 02:00 A+ A-

Kırsal kesimde, 1200 köyde can alan KKKA bu kez genç sağlık teknikerini öldürdü. Hastayla ilgilenirken eline iğne batan Kübra Yazım kurtarılamadı

Haber: İSMAİL TEMİZ / Arşivi
MURAT SANDIKÇI / Arşivi

Kübra Yazım (solda), ilgilendiği hastanın öldüğü gün yüksek ateş, titreme ve halsizlik şikâyetleriyle yoğun bakıma kaldırılmıştı.

2009

İğneyi yanlışlıkla kendine batıran doktor öldü

Ondokuz Mayıs Üniversitesi (OMÜ) Sağlık Araştırma ve Uygulama Merkezi acil servisine başvuran Kırım Kongo Kanamalı Ateşi (KKKA) hastasında kullanılan iğneyi yanlışlıkla kendine batıran doktor Mustafa Bilgiç, tedavi gördüğü yoğun bakım servisinde müdahalelere rağmen kurtarılamadı.

AA | 22 EYLÜL 2012, 11:42

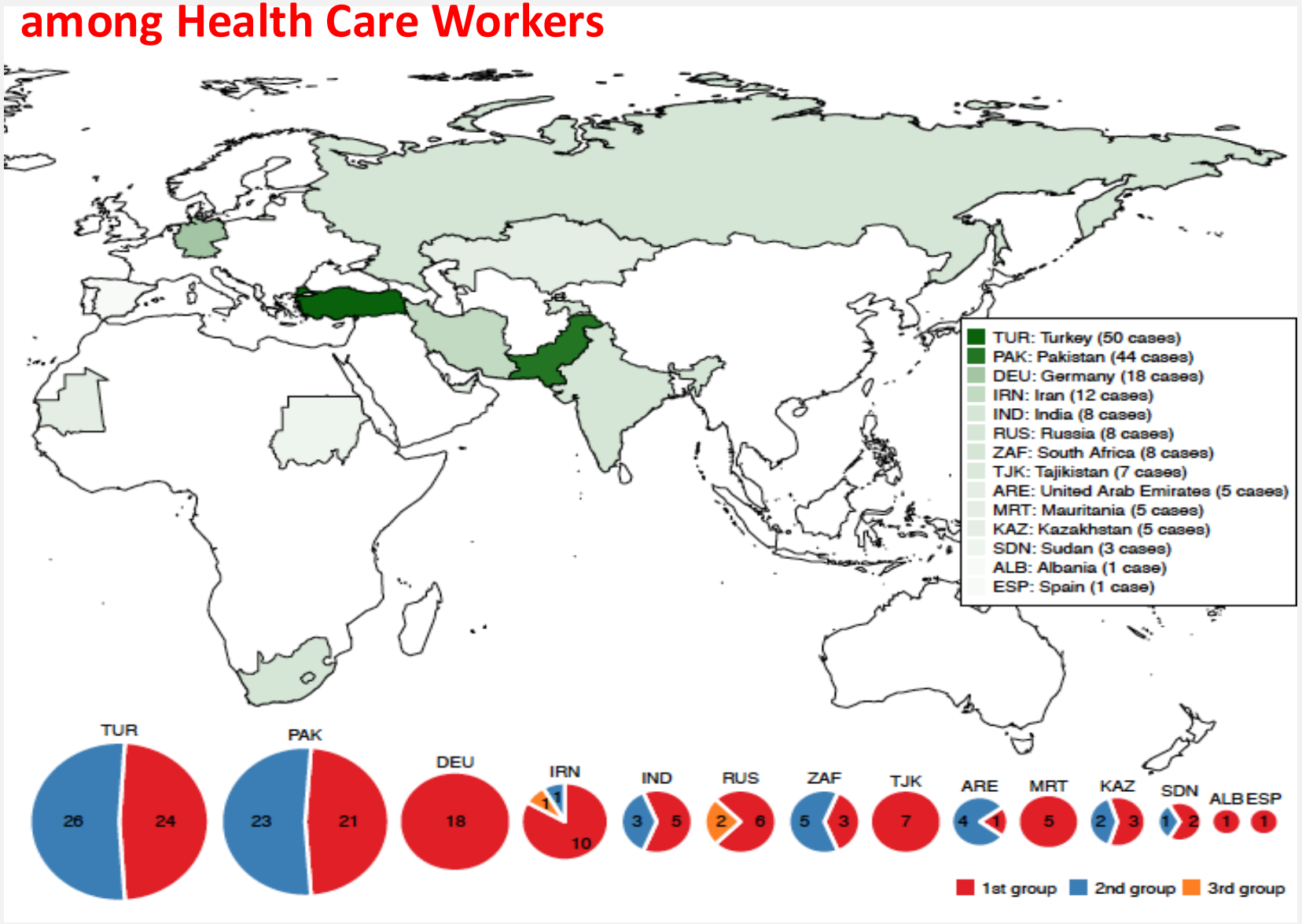
GÜNDEM

GÜNDEM

Sarayda Hanedan'ın muhteşem düğünü

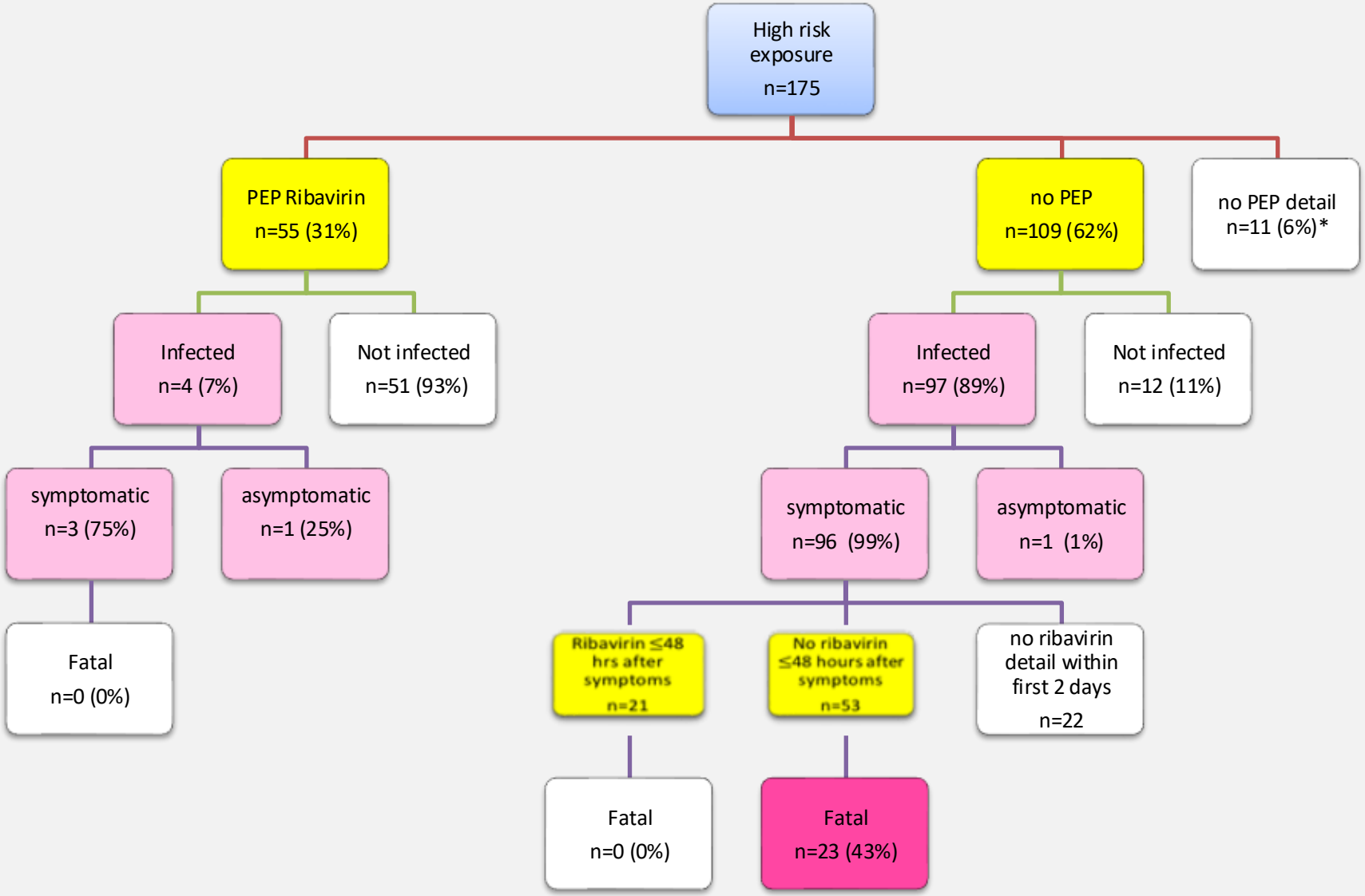
2012

Systematic Review of Crimean-Congo Hemorrhagic Fever among Health Care Workers



Ergönül et al Emerg Infect Dis 2018

Crimean-Congo Hemorrhagic Fever among Health Care Workers

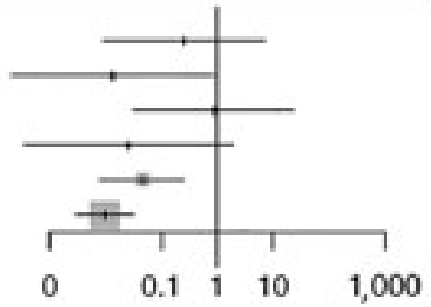


Ergönül et al Emerg Infect Dis 2018

Ribavirin use among Health Care Workers

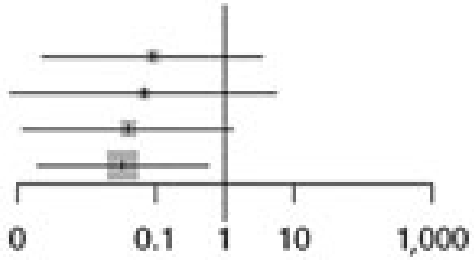
A

Study (reference)	PEP		No PEP		OR (95% CI)
	Infected	Not infected	Infected	Not infected	
Altaf et al. (*16*)	0	2	3	4	0.26 (0.01–7.27)
Celikbas et al. (*6*)	0	2	7	0	0.01 (0–0.87)
Conger et al. (*7*)	2	14	0	2	0.86 (0.03–23.84)
Guner et al. (*8*)	0	6	1	0	0.03 (0–1.90)
Nadari et al. (*34*)	0	24	11	6	0.05 (0.01–0.26)
Pooled estimate (4 studies)	2	51	98	12	0.01 (0–0.03)
Pooled estimate (all studies)	4				



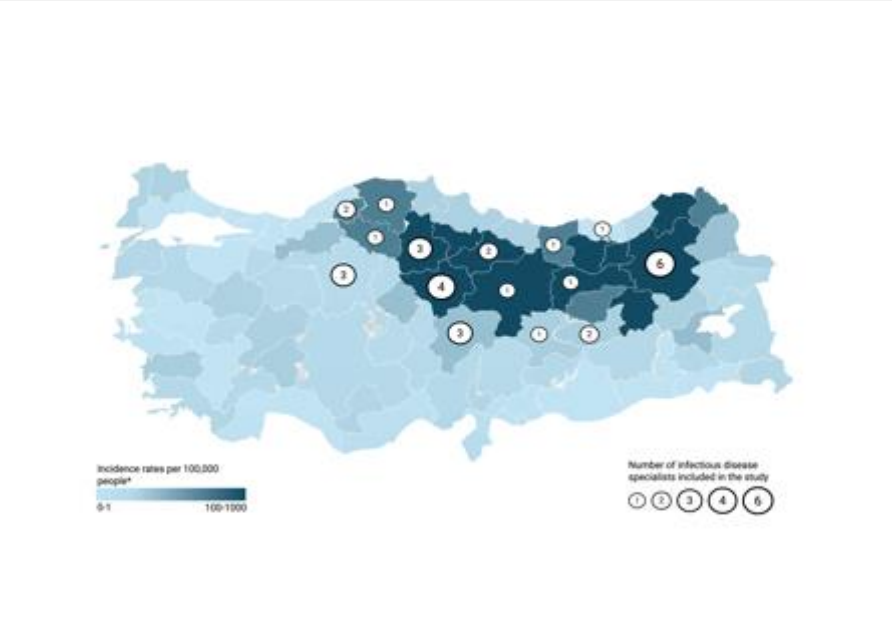
B

Study (reference)	Early ribavirin		No early ribavirin		OR (95% CI)
	Fatal	Survived	Fatal	Survived	
Celikbas et al. (*6*)	0	5	1	1	0.09 (0–3.59)
Nadari et al. (*34*)	0	2	1	0	0.07 (0–5.49)
Pooled estimate (2 studies)	0	7	2	1	0.04 (0–1.33)
Pooled estimate (all studies)	0	20	24	33	0.03 (0–0.58)



Ergönül et al Emerg Infect Dis 2018

Diagnosis, management, and prevention of CCHF: a Delphi-based consensus from two decades of experience in Türkiye



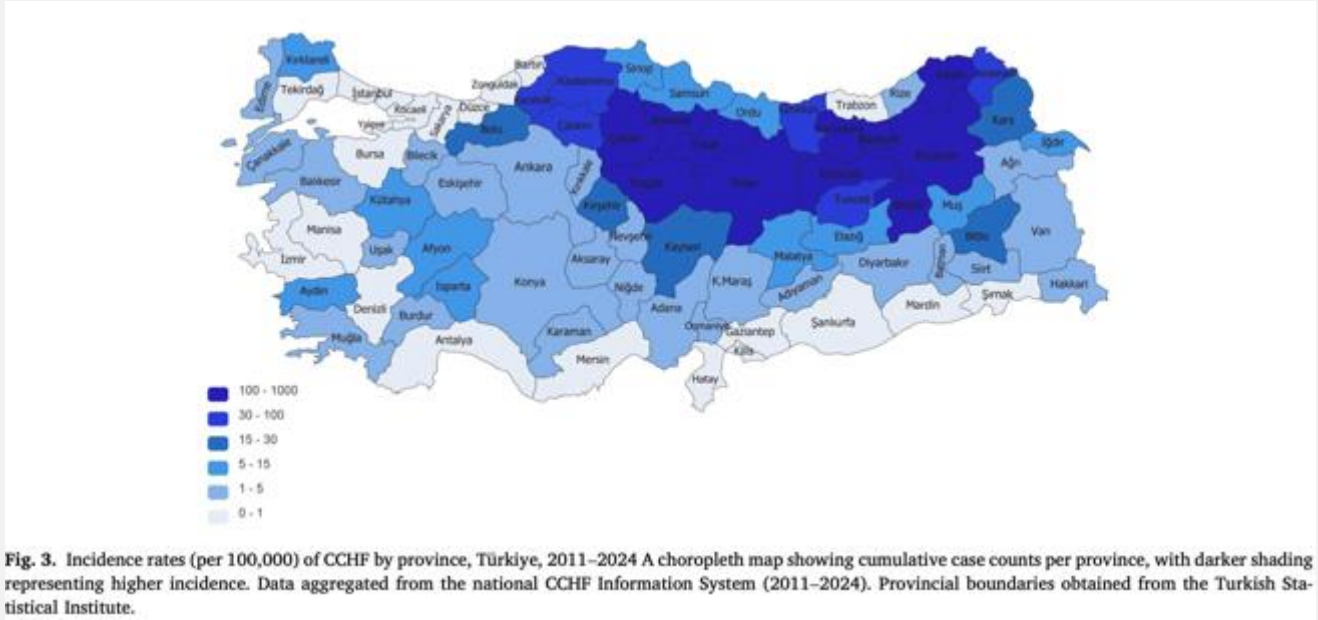
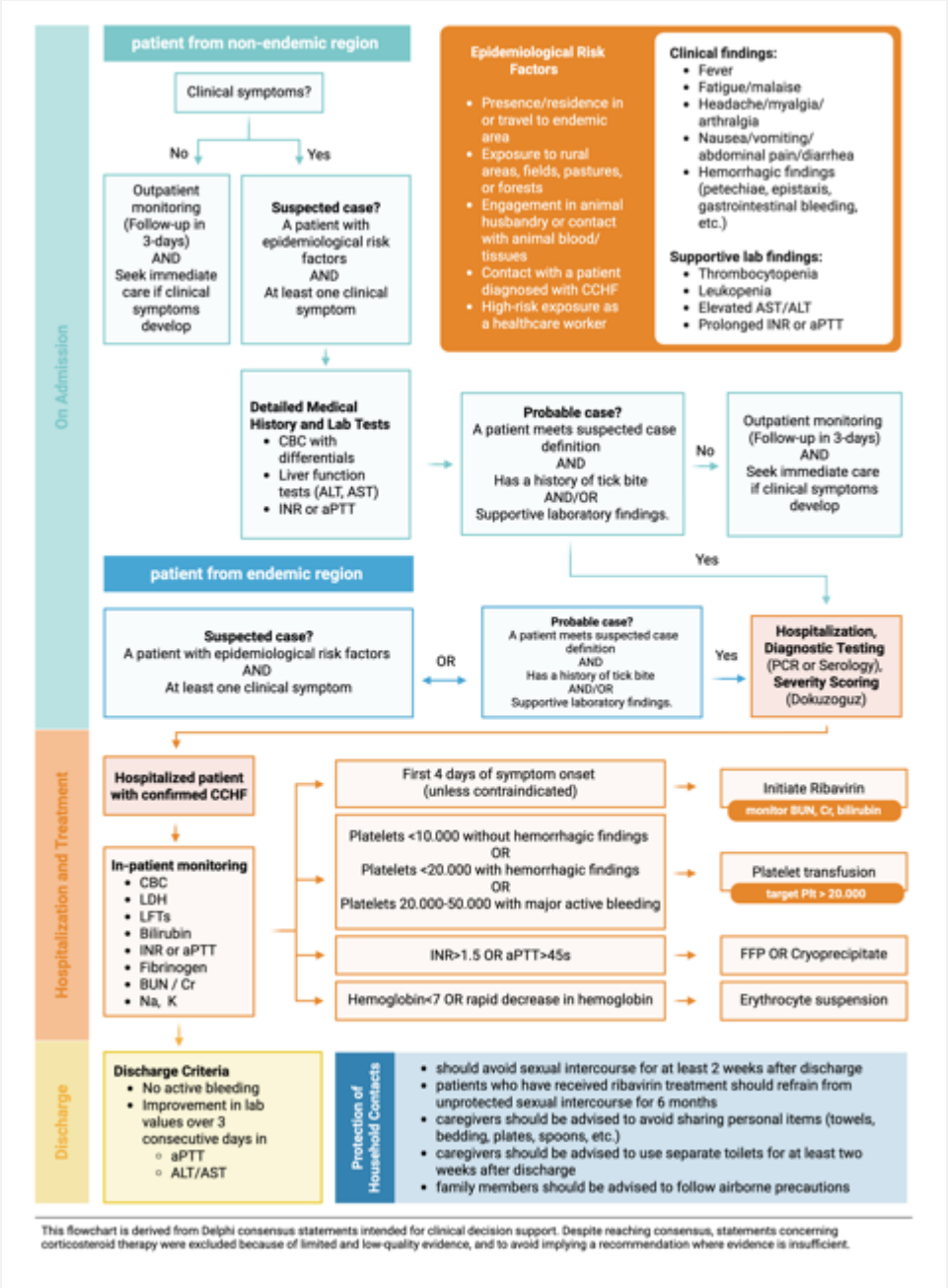


Fig. 3. Incidence rates (per 100,000) of CCHF by province, Türkiye, 2011–2024 A choropleth map showing cumulative case counts per province, with darker shading representing higher incidence. Data aggregated from the national CCHF Information System (2011–2024). Provincial boundaries obtained from the Turkish Statistical Institute.

Turkish Consortium

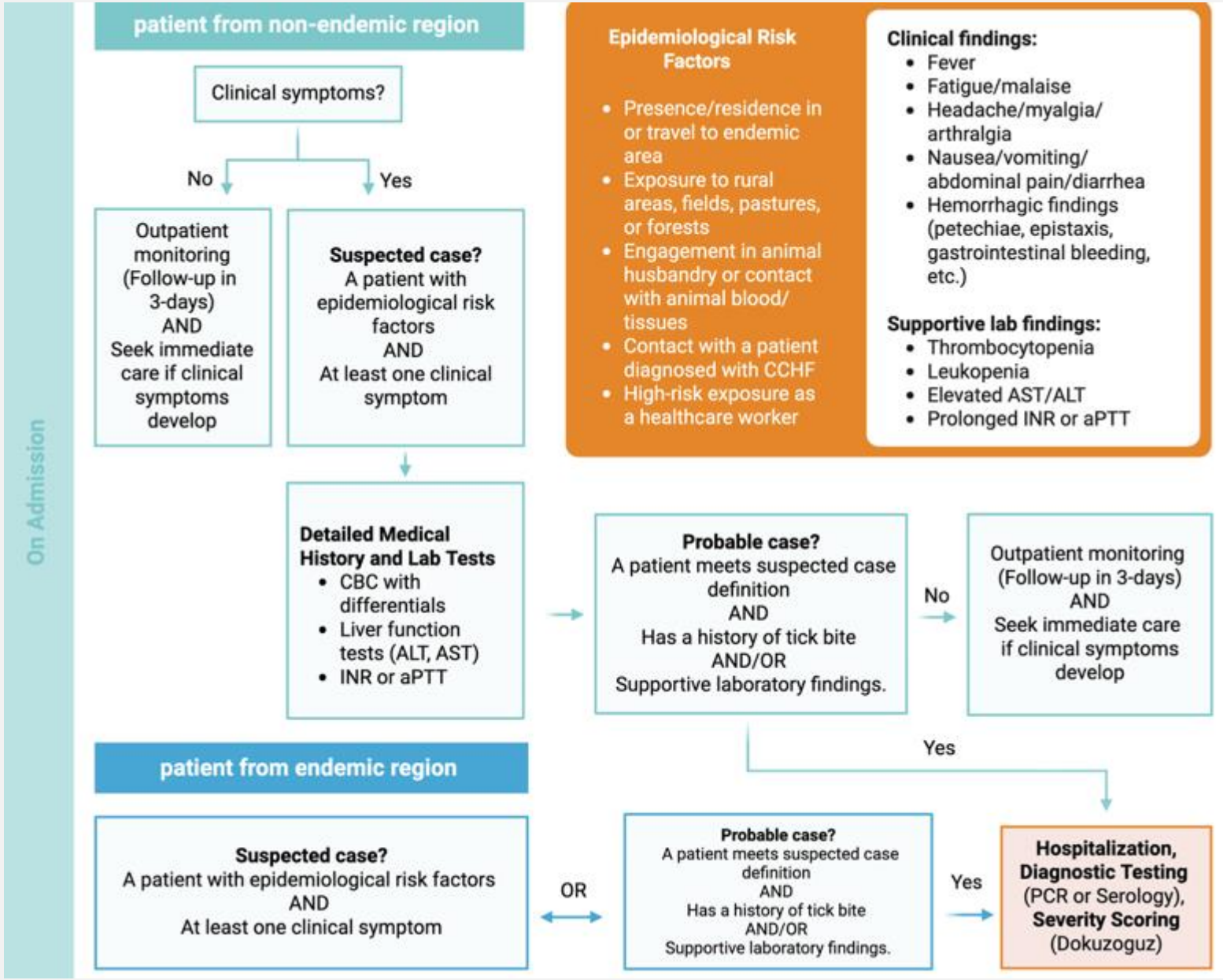
Şahan S, Topluoğlu S, Temel F, Coşgun Y, Öz E, Demirkol ME, Birinci Ş. Evaluation of epidemiological characteristics of Crimean-Congo haemorrhagic fever patients reported to the National Surveillance System in Türkiye, 2011-2024. Acta Trop. 2025



Diagnosis, management, and prevention of Crimean-Congo haemorrhagic fever: a Delphi-based consensus from two decades of experience in Türkiye

TR-Consortium

Ergönül Ö, et al. Eclinicalmedicine 2026



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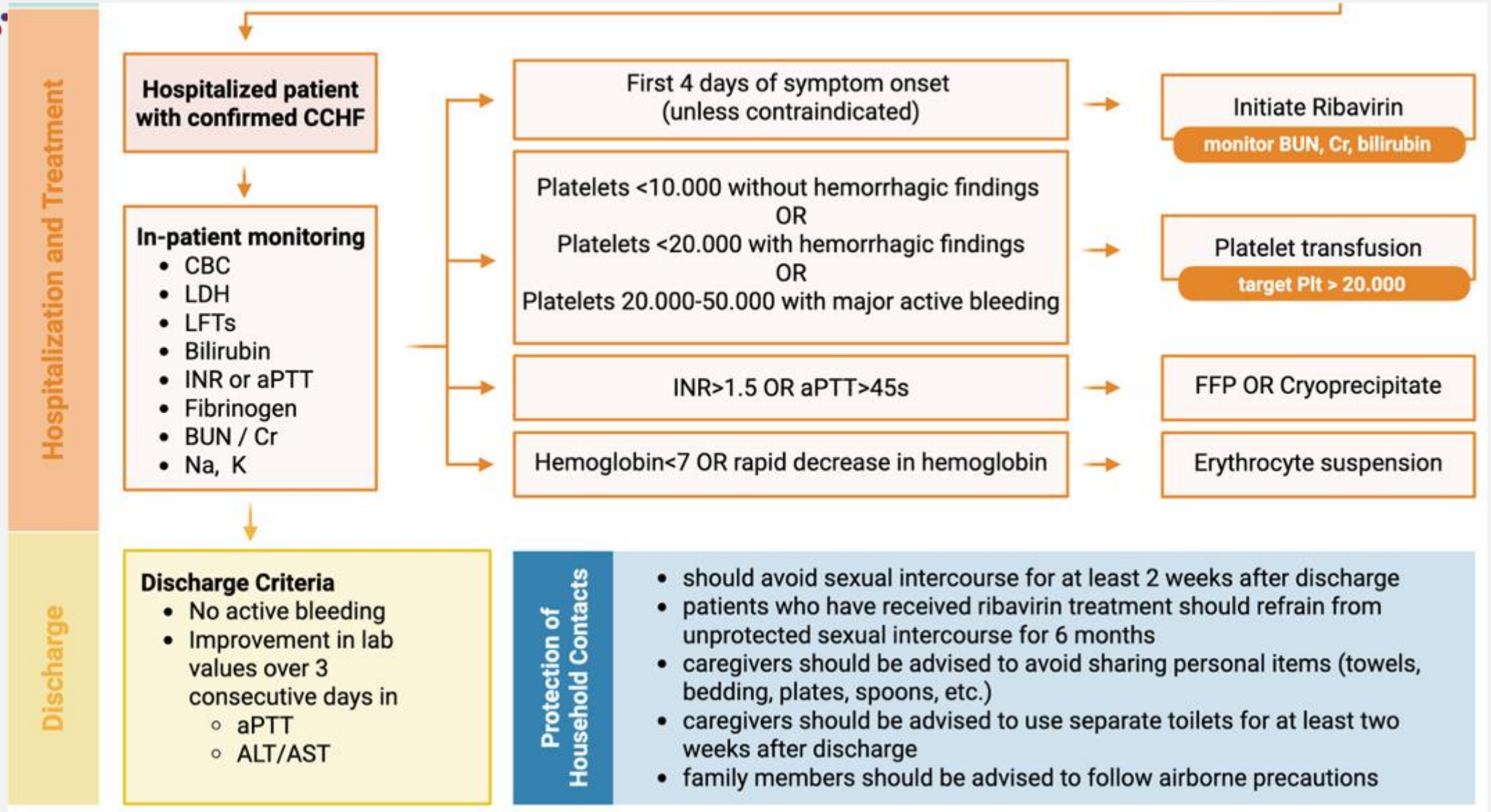

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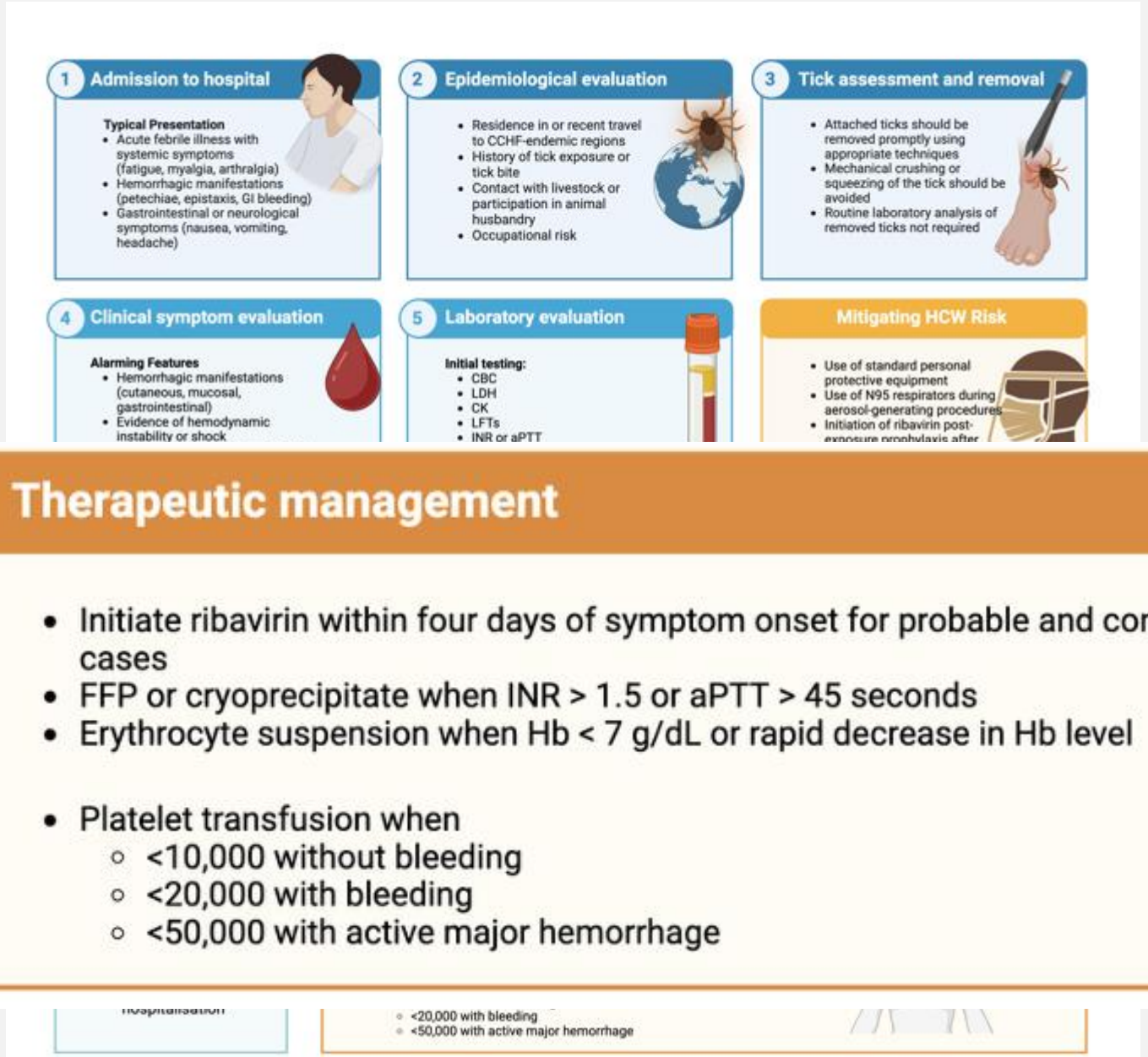

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Summary

Therapy is predominantly supportive.

In majority of the centers early ribavirin use and is part of standard of care.

- Corticosteoids and IL inhibitors are in use, but to be studied.
- Monoclonal antibodies
- New antivirals

Standart “applicable” infection control measures

Koç University, Hospital and KUISCID

Thank you

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