In the name of God

CCHF epidemiology

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- A 62-year-old man who had a history of hypertension and obstructive sleep apnea and had been living in Madrid presented to the Infanta Leonor University Hospital with a 2-day history of high fever, abdominal pain, malaise, nausea, and diarrhea. During the ensuing hours, purpuric lesions and hematomas developed at venipuncture sites.

- The next day, the patient was transferred to the intensive care unit (ICU) because of severe coagulopathy, with macroscopic hematuria, purpuric skin lesions and hematomas, a low platelet count, and prolonged prothrombin and partial-thromboplastin times.
- The patient’s family reported that four days before admission, while visiting relatives, the patient had walked through the fields in a small village located in Ávila, a province of central-western Spain. When he returned to his relatives’ home, he noticed a tick on his left knee.

- After learning that the patient may have had a tick bite, clinicians initiated treatment with doxycycline.
- On the seventh day of illness, the patient’s clinical condition deteriorated rapidly. He had macroscopic hematuria, worsening of purpuric skin lesions and hematomas, fulminant hepatic failure, severe respiratory insufficiency, encephalopathy, hypoglycemia, and severe metabolic acidosis.
- Later that day, he was transferred to the ICU at Gregorio Marañón University General Hospital to be evaluated for liver transplantation.

- During the next 24 hours, the patient had distributive shock, oliguric renal failure, very high liver-enzyme levels, and persistent metabolic acidosis. All tests for routine infections were negative. The patient died on the ninth day of illness.
- The CCHF virus was isolated by means of in vitro cell cultures of the first plasma sample obtained. No antibodies against the virus were detected on the sixth day of illness.

- A 50-year-old female nurse was the second patient. she had assisted with the endotracheal intubation of the index patient and with the insertion of femoral venous and arterial catheters. Profuse bleeding complicated placement of the catheters, and the nurse’s hands were in direct contact with the patient’s blood, although the skin was not punctured.
- On the first day of her illness, August 27, fever, asthenia, and arthromyalgias developed.

- On the second day, the patient was admitted to the ICU owing to the presence of petechiae, thrombocytopenia, and a mild increase in aminotransferase levels. On the third day of illness, vaginal bleeding started, coinciding with expected time of her normal menstruation period.
- On the fourth day of illness, CCHF was suspected. Empiric treatment with ribavirin was started, with an oral dose of 1000 mg administered every 6 hours and continued for the next 24 hours. On the sixth day of illness, the dose of ribavirin was reduced to 500 mg every 8 hours, in keeping

- Levels of CCHF virus in the blood were highest in a stored sample obtained on the 2nd day of illness, at 3.6×10^{7} copies per milliliter.
- vaginal fluid was positive on the 4th day of illness, saliva on the 8th day, and conjunctival, nasal, and rectal swabs were sporadically positive, with very low viral titers.
- On the 9^{th} day of illness, vaginal bleeding stopped. Levels of aminotransferase and lactate dehydrogenase began to decrease on the 9th day of illness, and platelet levels began to increase on the 11th day.

- After the 14th day of illness, RT-PCR assays of all body fluids were negative. On the 22nd day of illness, the measures taken in the high-level isolation unit were discontinued when two consecutive RT-PCR assays of the blood were negative.

CCHF

- Crimean-Congo hemorrhagic fever (CCHF) is a zoonotic disease transmitted by ticks and characterized by fever and hemorrhage
- It was first described in Soviet soldiers in the Crimea in 1944 and was named Crimean fever. In 1956, the virus was isolated from a child with similar symptoms and was named Congo virus. The causative agent of both illnesses was shown to be the same virus, which was subsequently termed CCHF virus.
- CCHF infects a range of animals; humans are the only known host that develops disease.

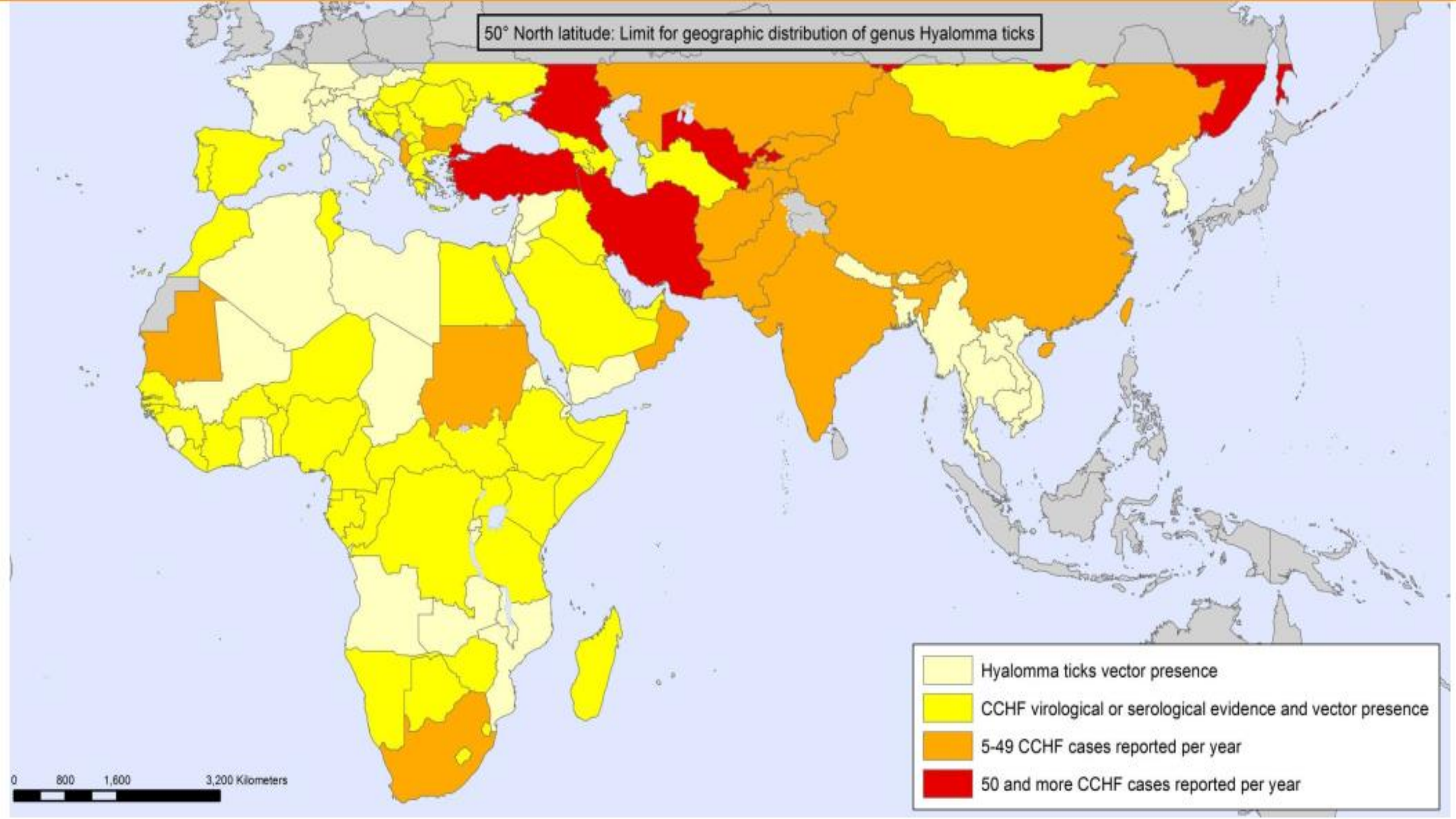
- CCHF is a tick-borne disease caused by CCHFV belonging to the genus *Orthonairovirus* of the family *Nairoviridae* within the order *Bunyavirales*
- CCHFV is maintained in nature through transmission by ticks of the family *Ixodidae*, and members of the genus *Hyalomma* are considered as the main vectors that spread the virus to humans and a variety of wild and domestic animals

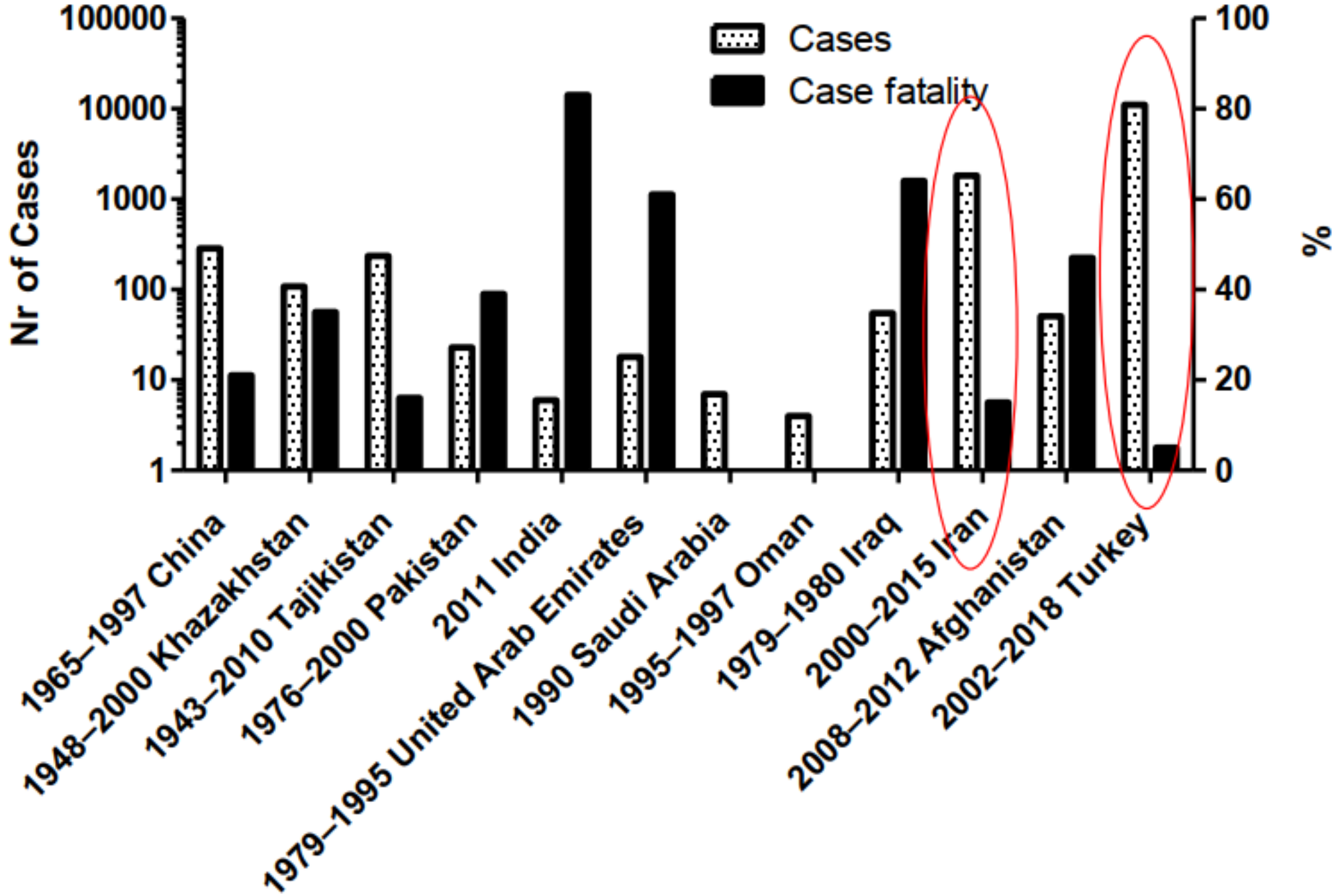
- Animals may serve as asymptomatic reservoirs of CCHFV and their distribution to human cases appears to be closely related to vector distribution.
- Humans are infected by tick bite, crushing it on an open wound, contact with blood, body fluids or tissues of a viremic animal or human, and possibly through sexual transmission

- Each year, more than 1000 human cases are reported from southeastern Europe and western Asia
- The presence of the ticks, CCHFV, CCHF, and death due to CCHFV are increasing in endemic areas and also in new areas. This is due various factors such as climate change, the increase in the tick number, the increasing exposure of animals and humans and the improvement of viral detection assays.

EPIDEMIOLOGY

- CCHF is endemic in parts of Africa, the Middle East, Asia, and southeastern Europe
- CCHF virus (CCHFV) has been observed in over 30 countries, including in Africa (Democratic Republic of Congo, South Africa, Nigeria, Senegal, Uganda, Tanzania, Mauritania, Kenya), Asia (Pakistan, Afghanistan, Tajikistan, Uzbekistan, Kazakhstan, China), the Middle East (Iran, Iraq, United Arab Emirates, Saudi Arabia, Oman), and southeastern Europe (the Russian Federation, Bulgaria, Albania, Kosovo, Turkey, Greece, and Spain)


50° North latitude: Limit for geographic distribution of genus Hyalomma ticks
Hyalomma ticks vector presence
CCHF virological or serological evidence and vector presence
5-49 CCHF cases reported per year
50 and more CCHF cases reported per year
0
800
1,600
3,200 Kilometers


Cases
Case fatality
Nr of Cases
%
100000
10000
1000
100
10
1
100
80
60
40
20
0
1965–1997 China
1948–2000 Khazakhstan
1943–2010 Tajikistan
1976–2000 Pakistan
2011 India
1979–1995 United Arab Emirates
1990 Saudi Arabia
1995–1997 Oman
1979–1980 Iraq
2000–2015 Iran
2008–2012 Afghanistan
2002–2018 Turkey

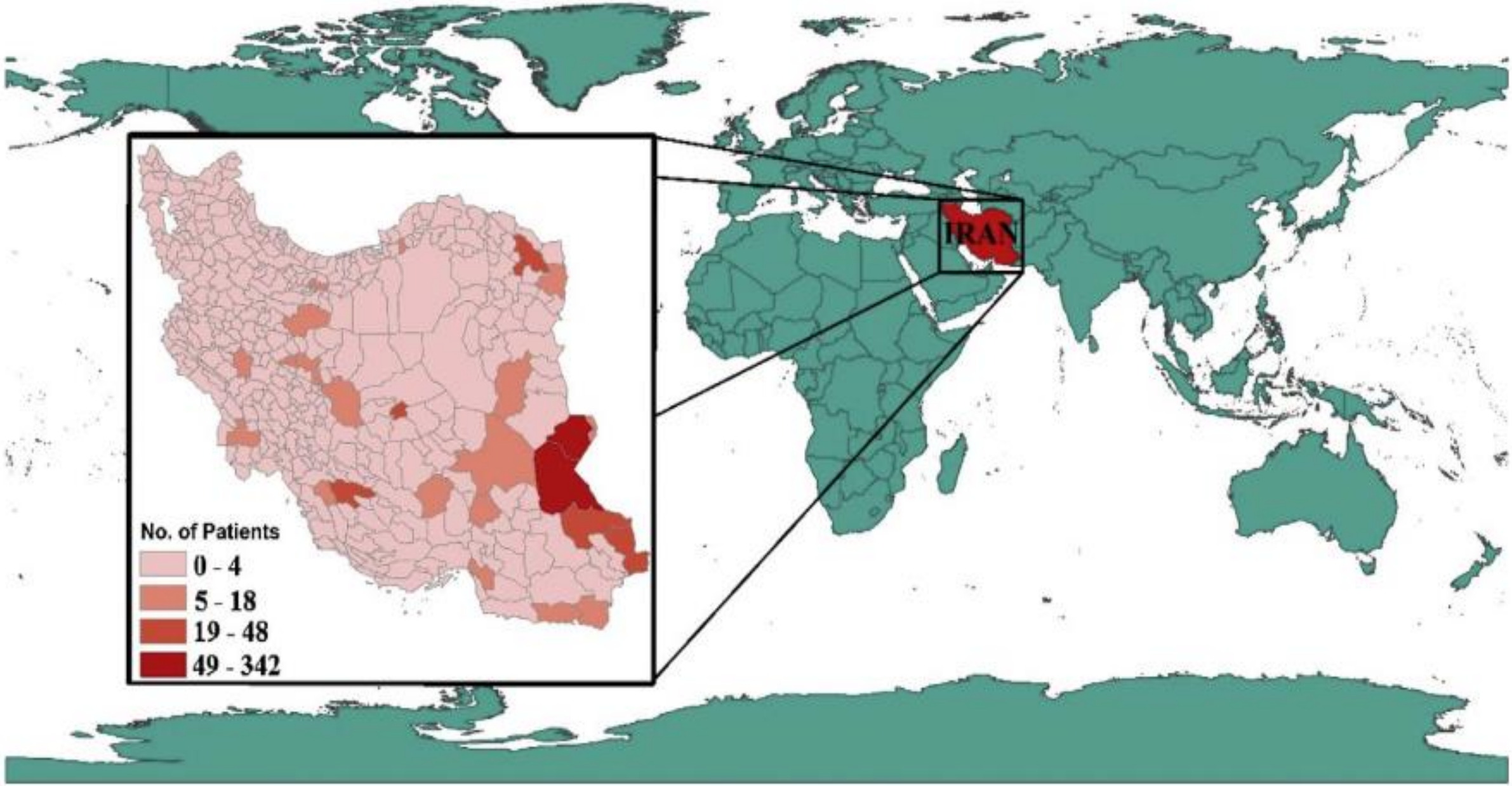
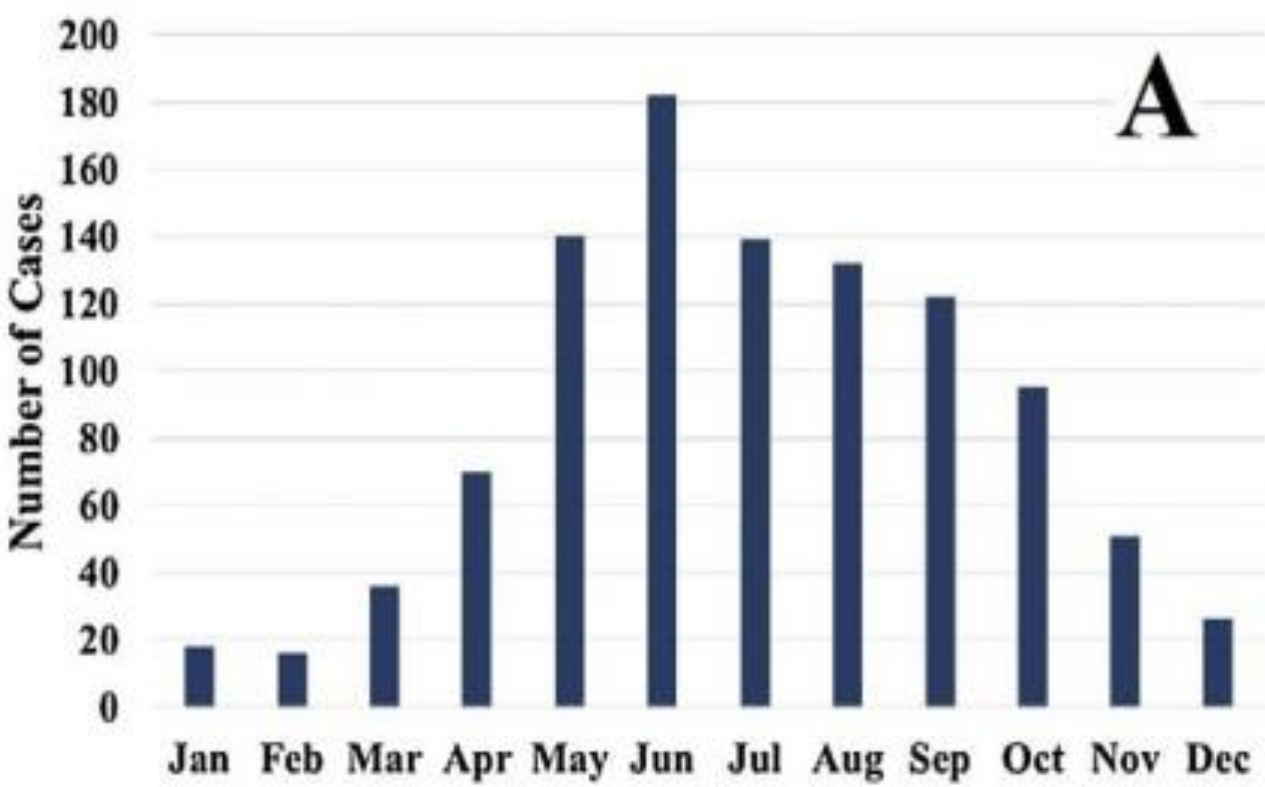
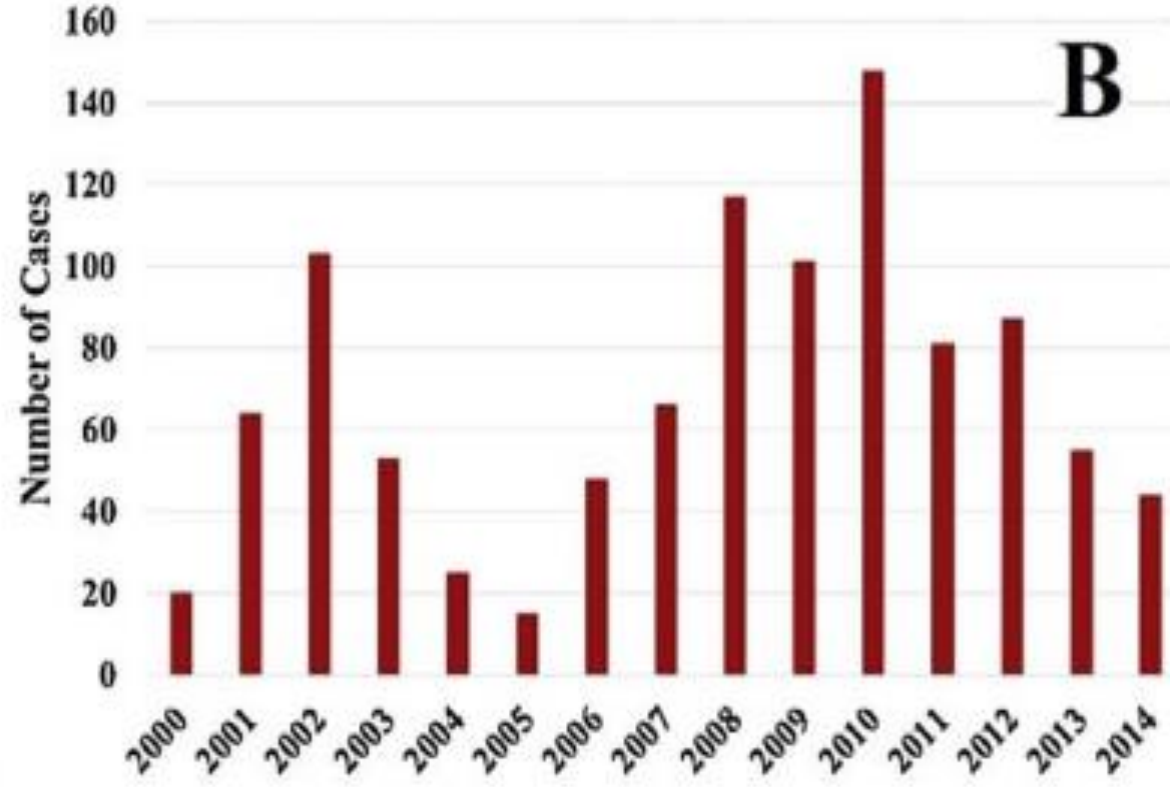


Fig. 1. The endemic country of Iran and CCHF cumulative incidence distribution during 2000–2014.


A
Number of Cases
0
20
40
60
80
100
120
140
160
180
200
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec


B
Number of Cases
0
20
40
60
80
100
120
140
160
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014

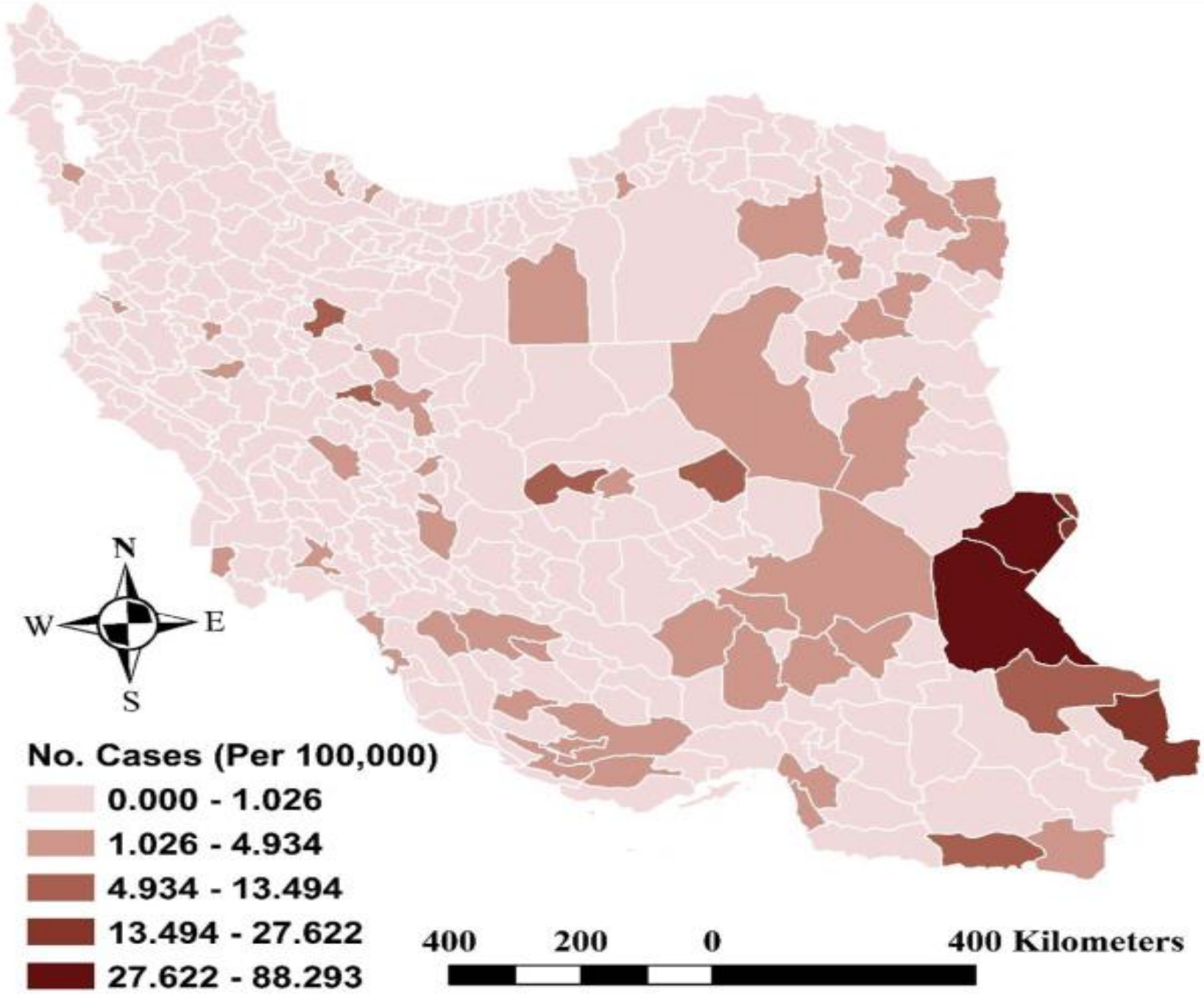
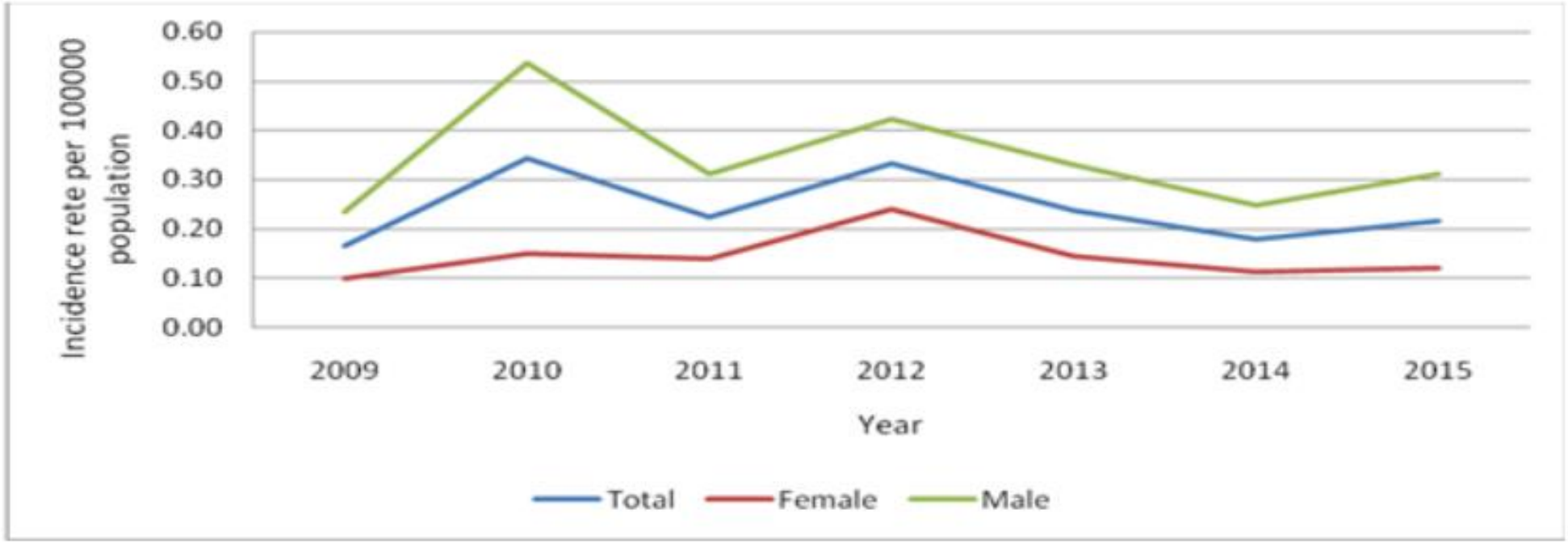
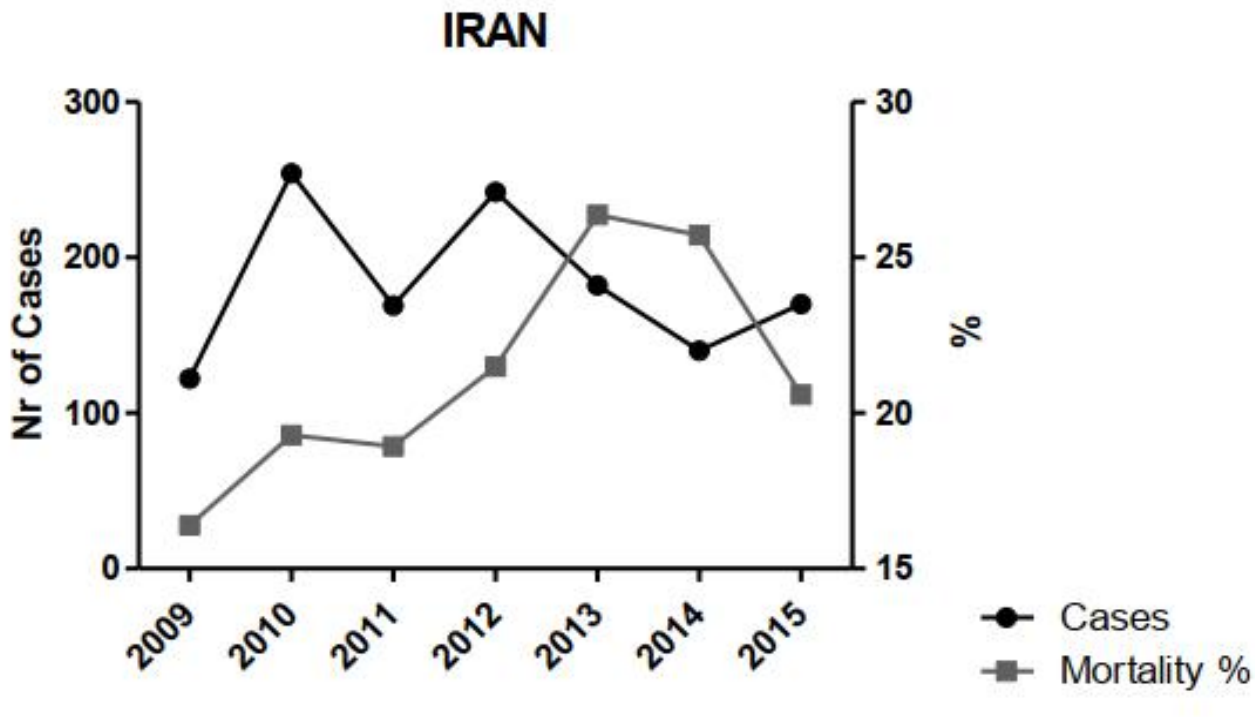


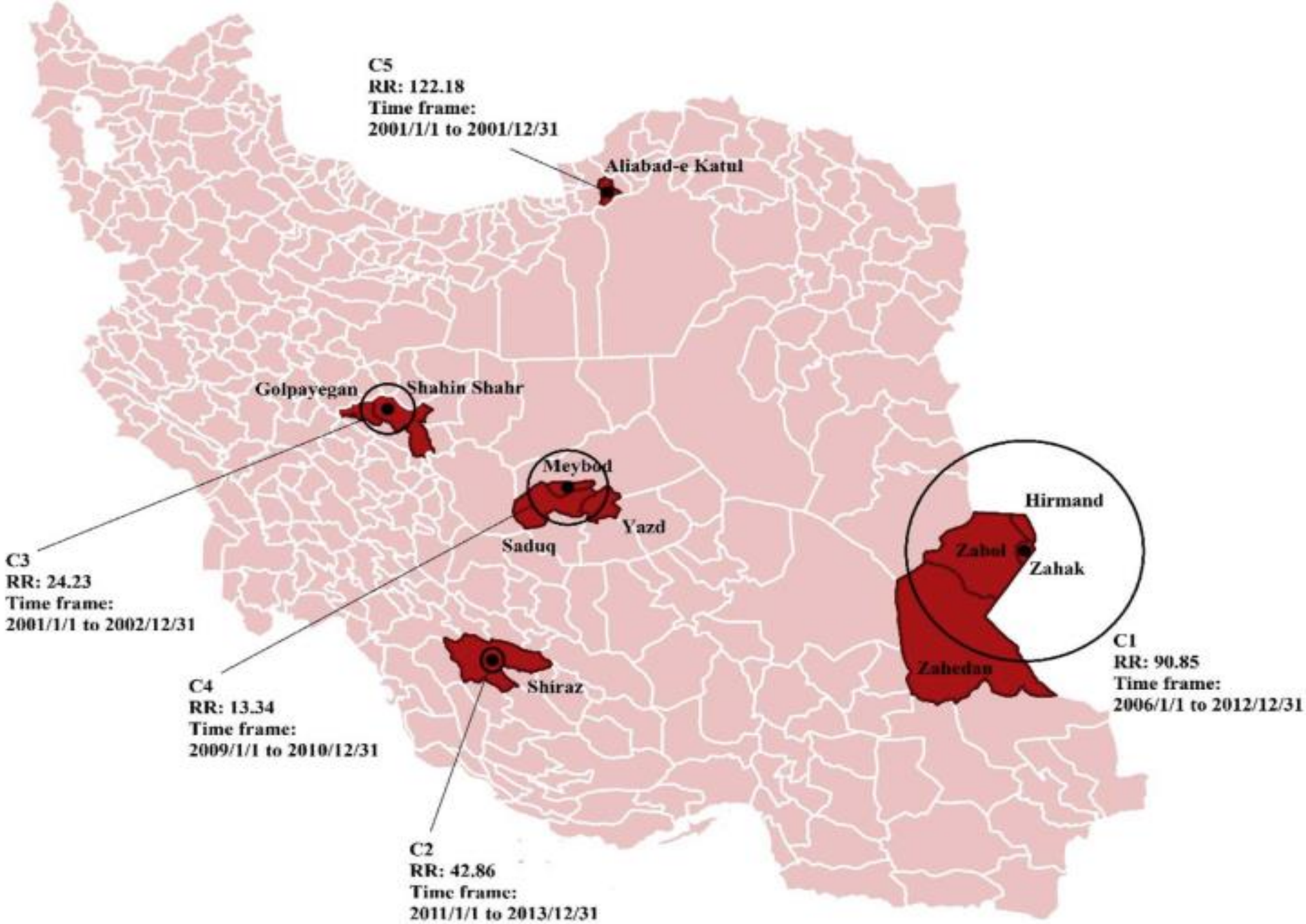
Fig. 4. Cumulative incidence (number of CCHF cases per 100,000) from 2000 to 2014, Iran.

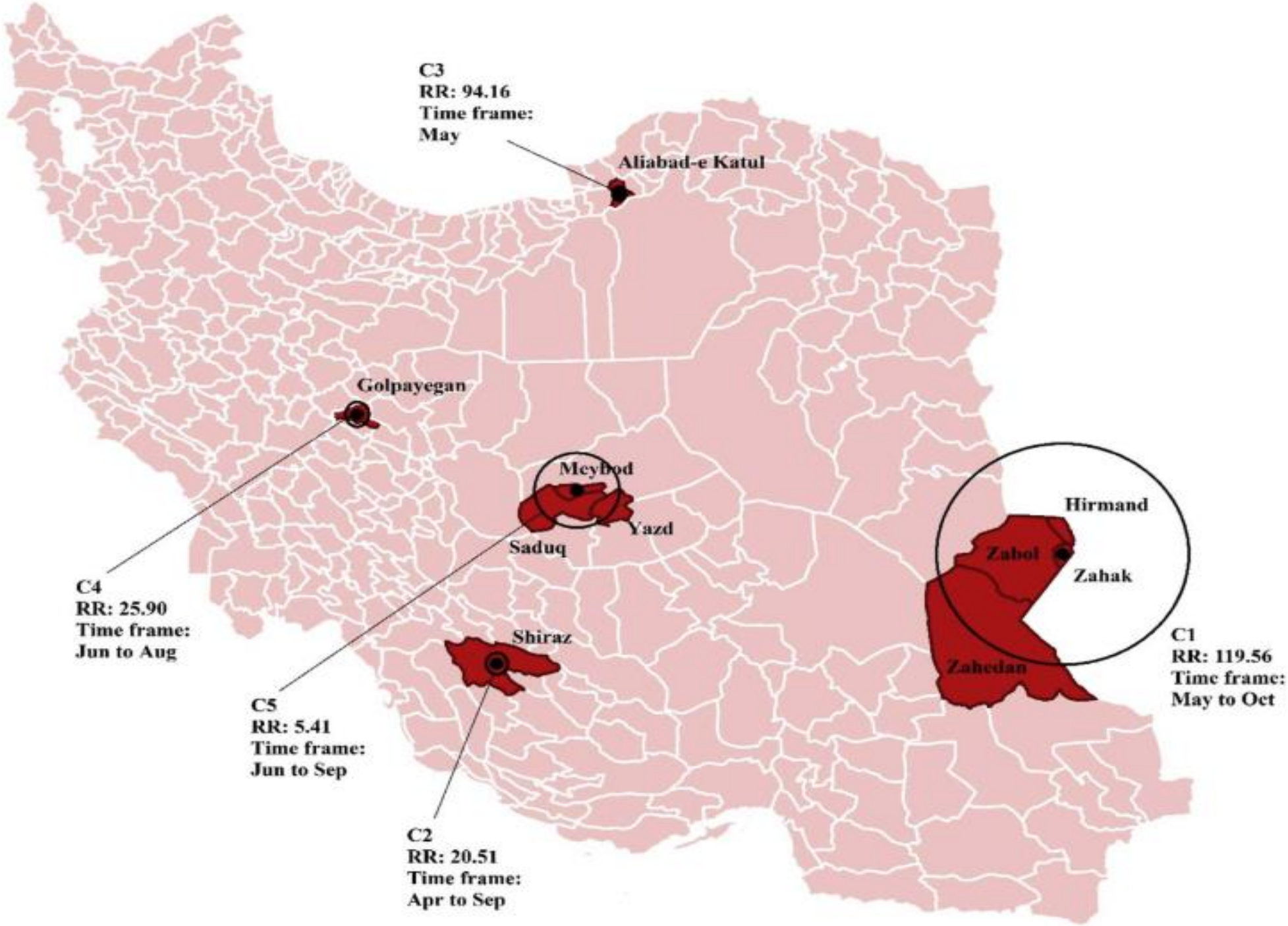

Incidence rete per 100000 population
0.60
0.50
0.40
0.30
0.20
0.10
0.00
2009
2010
2011
2012
2013
2014
2015
Year
Total
Female
Male


IRAN
Nr of Cases
300
200
100
0
30
25
20
15
%
2009
2010
2011
2012
2013
2014
2015
Cases
Mortality %

- Regarding the cluster detection, purely spatial scan statistics showed that there were three clusters in the eastern (Cluster 1), southern (Cluster 2) and western (Cluster 3) parts of the country. Cluster 1 includes Zahak, Hirmand, Zabol, and Zahedan; the second cluster contains Shiraz; and finally, Golpayegan is situated in the third cluster
- the first cluster occurred between the years 2006 and 2012 in the eastern counties of Iran, including Zahak, Hirmand, Zabol, and Zahedan. In the second cluster, Shiraz was obtained as a hotspot from 2011 to 2013.

- Cluster 3 contains Shahin Shahr and Golpayegan in Esfahan province, which records higher than expected rates of the disease between 2001 and 2002. Yazd, Saduq, and Meybod counties were included in cluster 4 in the period from 2009 to 2010, and finally, Aliabad-e Katul in the province of Golestan was identified as cluster 5 in the year 2001
- The summer months have been predominantly susceptible to facing higher rates of the disease since each cluster includes at least one summer month.


C5
RR: 122.18
Time frame:
2001/1/1 to 2001/12/31
Aliabad-e Katul
Golpayegan
Shahin Shahr
Meybod
Yazd
Saduq
Hirmand
Zabol
Zahak
Zahedan
Shiraz
C3
RR: 24.23
Time frame:
2001/1/1 to 2002/12/31
C4
RR: 13.34
Time frame:
2009/1/1 to 2010/12/31
C2
RR: 42.86
Time frame:
2011/1/1 to 2013/12/31
C1
RR: 90.85
Time frame:
2006/1/1 to 2012/12/31


C3
RR: 94.16
Time frame:
May
Aliabad-e Katul
Golpayegan
Meybod
Yazd
Saduq
Hirmand
Zabol
Zahak
Zahedan
Shiraz
C4
RR: 25.90
Time frame:
Jun to Aug
C5
RR: 5.41
Time frame:
Jun to Sep
C2
RR: 20.51
Time frame:
Apr to Sep
C1
RR: 119.56
Time frame:
May to Oct

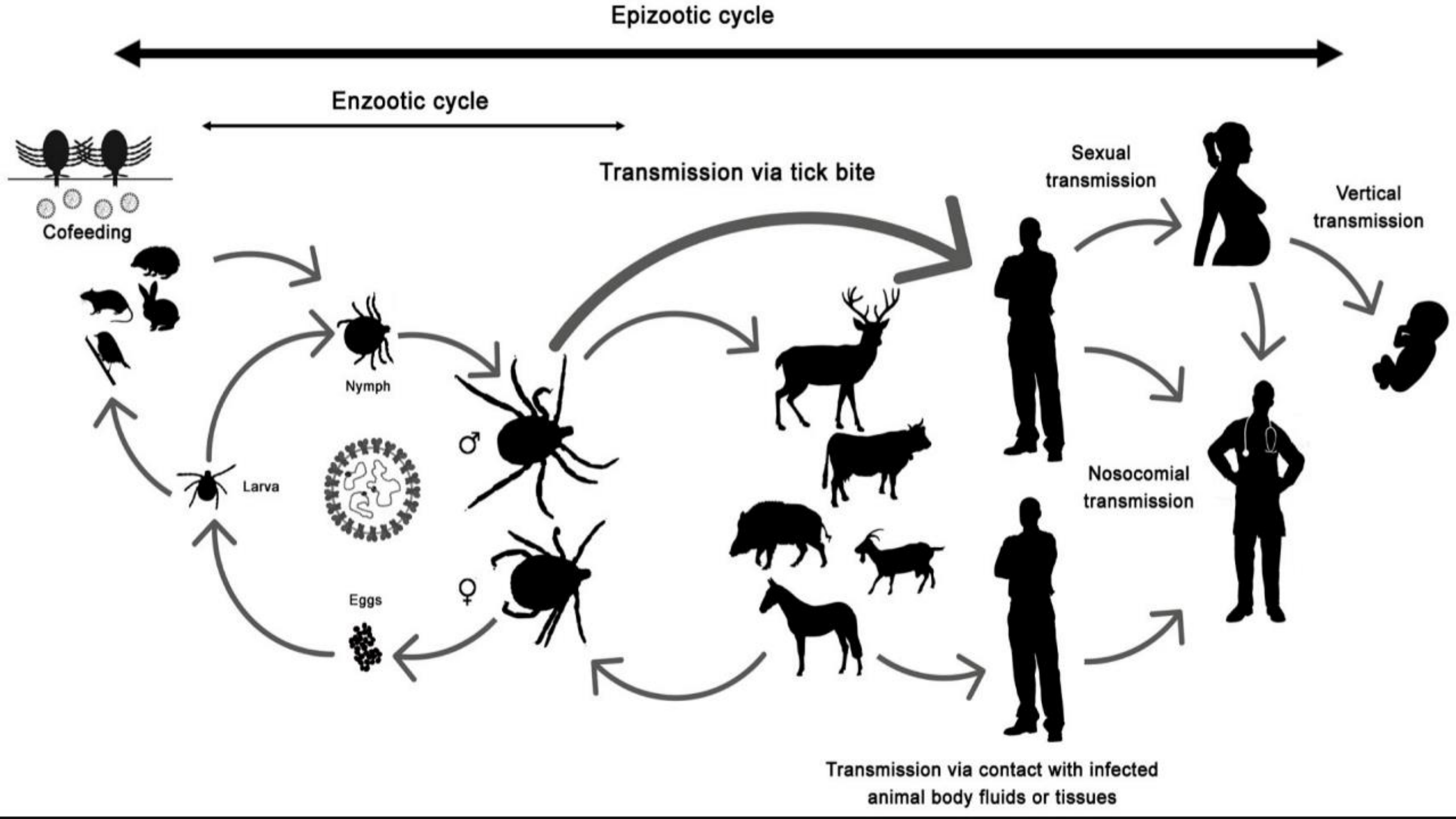
- Between 1998 and 2013, CCHF occurred most frequently in Turkey, Russia, Iran, Pakistan, and Afghanistan
- **Ticks**
- CCHFV is primarily transmitted via hard-bodied *Hyalomma* ticks of the family Ixodes*,* particularly *Hyalomma marginatum*
- The geography of CCHF infection reflects the distribution of *Hyalomma* ticks, which have a northern geographic limit of 48° north latitude

- The most common viral reservoirs are domestic livestock (sheep, goat, cattle, and pig), which are infected by adult ticks. Larvae and nymphs tend to feed on rodents, hares, hedgehogs, and ground-dwelling birds, which serve as amplifying hosts for the virus
- Ticks can remain attached for 2 to 13 days; after completion of feeding, the ticks detach from the host and begin to search for new hosts. The virus begins to multiply within 36 hours of attachment, it does not have the ability to survive outside the host but may persist in infected body fluids such as blood, stool, or vomit.

- Ticks survive most readily in relatively warm, dry habitats. Tick density increases markedly following a preceding mild winter and in the setting of diminished rainfall; these conditions are associated with increased numbers of human CCHF cases
- Changing tick habitats and elimination of usual host animals may lead to an increase in the spread of tick-borne disease. Environmental factors associated with CCHF infection include livestock grazing at the edge of forests and presence of scrub and herbaceous vegetation

- The incidence of CCHF appears to be increasing. Possible causes of CCHF outbreaks include changing agricultural practices, climate change, movement of domestic animals, migrating birds, increasing numbers of susceptible animals, and increasing tick populations
- **Transmission**
- CCHF is transmitted via ticks, direct contact with blood or other bodily fluids of infected animals, nosocomial transmission, and vertical transmission.

- CCHF is most commonly transmitted via tick bites or crushing ticks with bare fingers.
- Transmission can also occur via direct contact with blood or other bodily fluids of livestock; abattoir workers and farmers are at increased risk for infection
- The risk of community-based transmission to close contacts and relatives of patients with CCHF is low.


Epizootic cycle
Enzootic cycle
Cofeeding
Transmission via tick bite
Sexual transmission
Vertical transmission
Nymph
Larva
Eggs
♂
♀
Nosocomial transmission
Transmission via contact with infected animal body fluids or tissues

- Relatives and caregivers should avoid direct contact with infected patients and their blood/bodily fluids, wear gloves and protective clothes, and wash hands regularly. Personal items such as razors or toothbrushes should not be shared.
- Nosocomial transmission of CCHFV has been described. The risk is highest during later stages of disease, which are associated with higher viral loads as well as diarrhea, vomiting, and hemorrhage

- Direct contact with blood and body fluids, needle-stick injuries, and splash exposures are common causes of nosocomial transmission
- Health care personnel are also at risk of infection during aerosol-generating procedures. Transmission between patients sharing the same hospital room has occurred, likely due to contact with infected blood or body fluids

- Vertical (mother-to-child) transmission of CCHFV has been described; in such cases, fetal prognosis may be guarded
- Thus far, breastfeeding has **not** been associated with CCHFV transmission. The role of sexual transmission is uncertain; CCHF with epididymo-orchitis has been described as has detection of CCHFV in urine
- The risk of laboratory exposure to CCHFV while processing blood samples is low if routine laboratory procedures are followed

- **Risk groups**
- Individuals at risk for CCHFV infection include agricultural workers, individuals in rural areas engaged in animal husbandry, abattoir workers, veterinarians, leather factory workers in areas with high tick density, campers and hikers, hunters, soldiers, health care workers, and travelers to endemic areas (particularly in the setting of exposure to farming and slaughtering)

- In high-risk populations, the seroprevalence of CCHFV infection is 10 to 14 percent. Independent risk factors for seropositivity include history of tick bite, manually removing ticks from animals, animal husbandry or farming, age >60 years, and residence in a rural area.
- Data are insufficient regarding the risk of CCHFV infection in immunocompromised hosts.

Thanks for your attention