Disclosure conflicts of interests speaker

Potential conflict of interest	None
Potentially relevant relationships with companies	Company names
• Sponsorship or grant for research • Other relationship, ……..	• Bavarian-Nordic (Rabipur™)

Leiden University Medical Center

‘Chikungunya vaccine, who is going to get it?’

Science 2023;382:503

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Chikungunya, a crippling *Aedes* mosquito-borne alpha virus infection

It's like someone has thrown a hand grenade into a very health body and walked away to leave me to deal with it. It's bone shattering. You **feel like every bone in your body is broken** and it's just … you can't take anything. I mean, every four hours I was on **paracetamol and ibuprofen** and **it didn't even touch the surface of the pain**'

Barbara Rogers

www.abc.net.au/radionational/programs

CHIKV - a crippling virus infection

1. **Expanding geographic distribution** of four genotypes with unpredictable and tremendous fastly spreading outbreaks

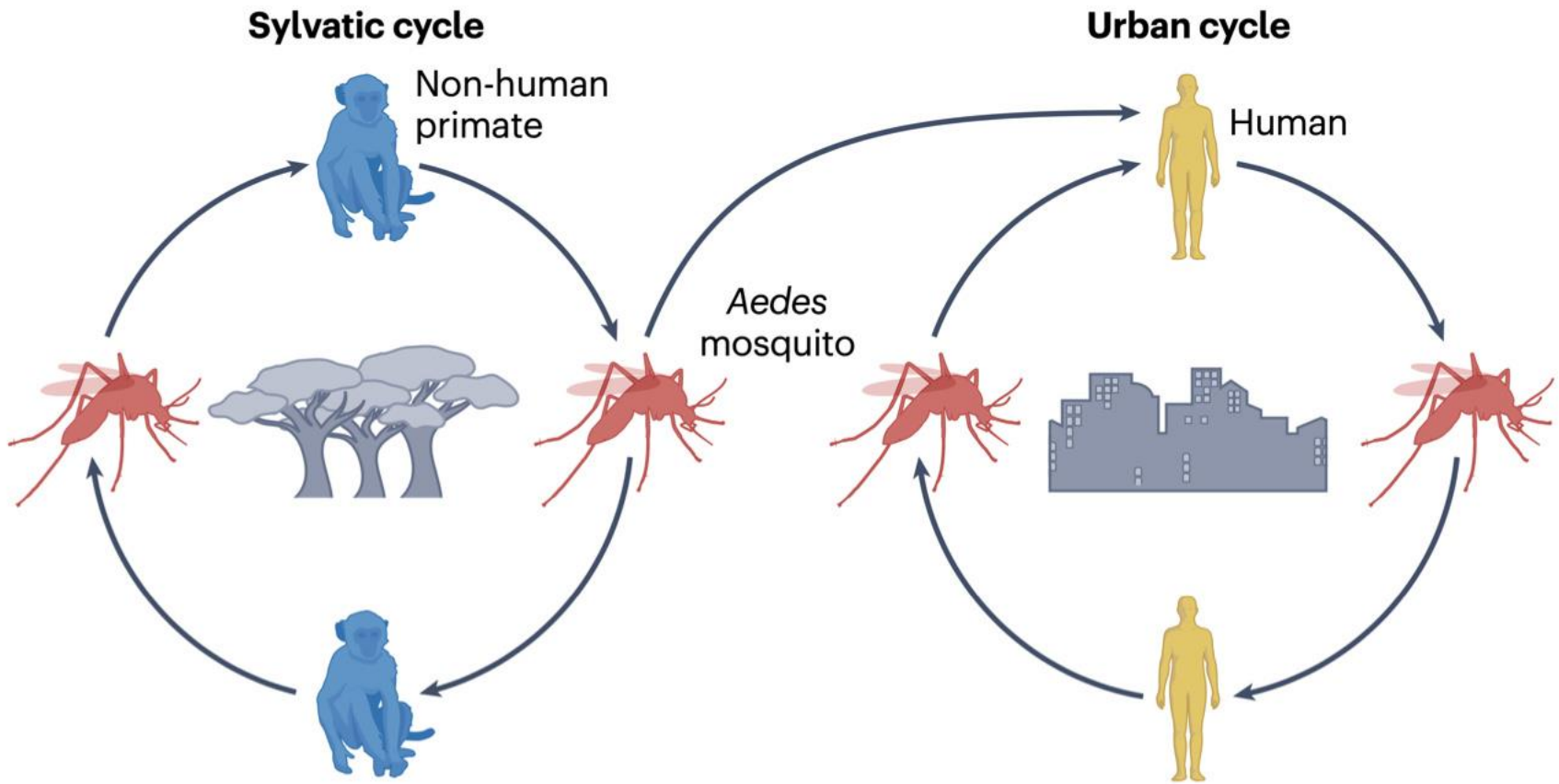
2. *Aedes* mosquito borne alpha virus infection with **short incubation period, high attack rate** and **rapid onset acute febrile illness with debilitating polyarthralgia** occurring in cycles of 10-18 years

3. **Severe disease in neonates** and **older people** with comorbidities, possibly driven by insufficient type 1 interferon response

4. **Chronic arthropathy** more likely in women, older age, and severe disease

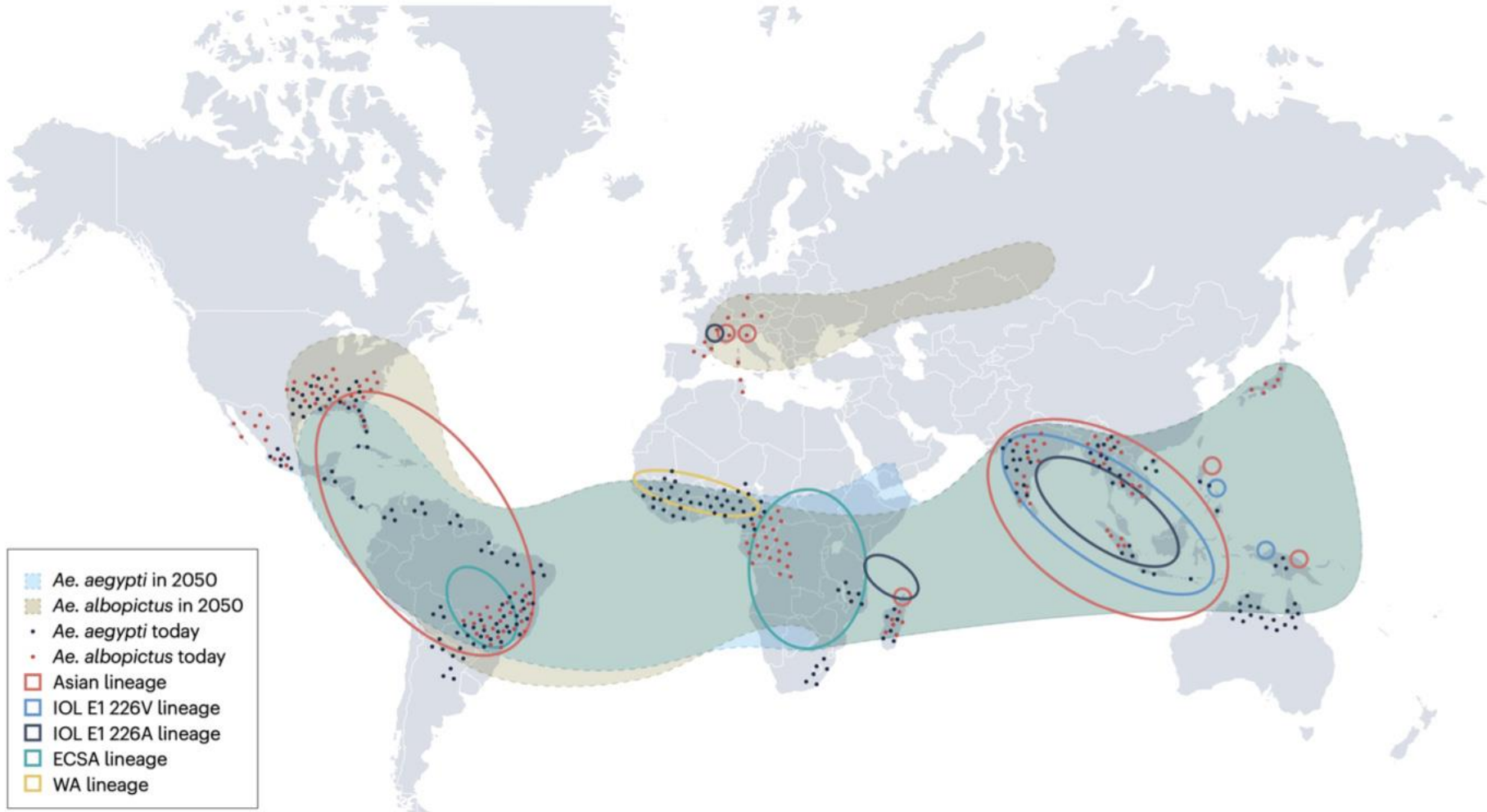
5. Chikungunya **vaccines for whom**?

Sylvatic cycles still exist in Africa and Asia, but urban transmission between humans and *Aedes aegypti* and *albopictus* mosquitoes is increasingly more important



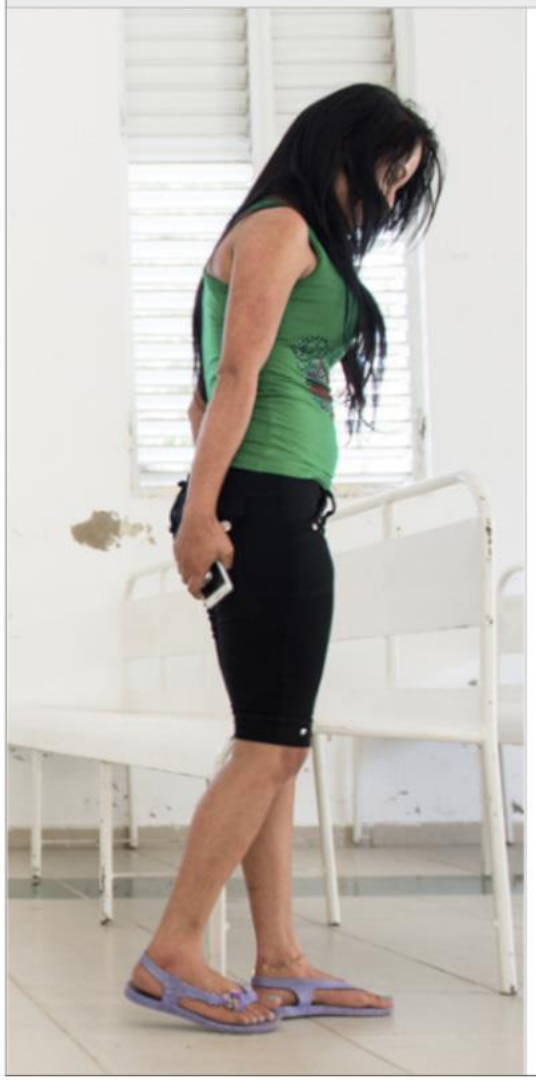
Bartholomeeuwsen K et al. Nature Reviews Disease Primers 2023;9:1

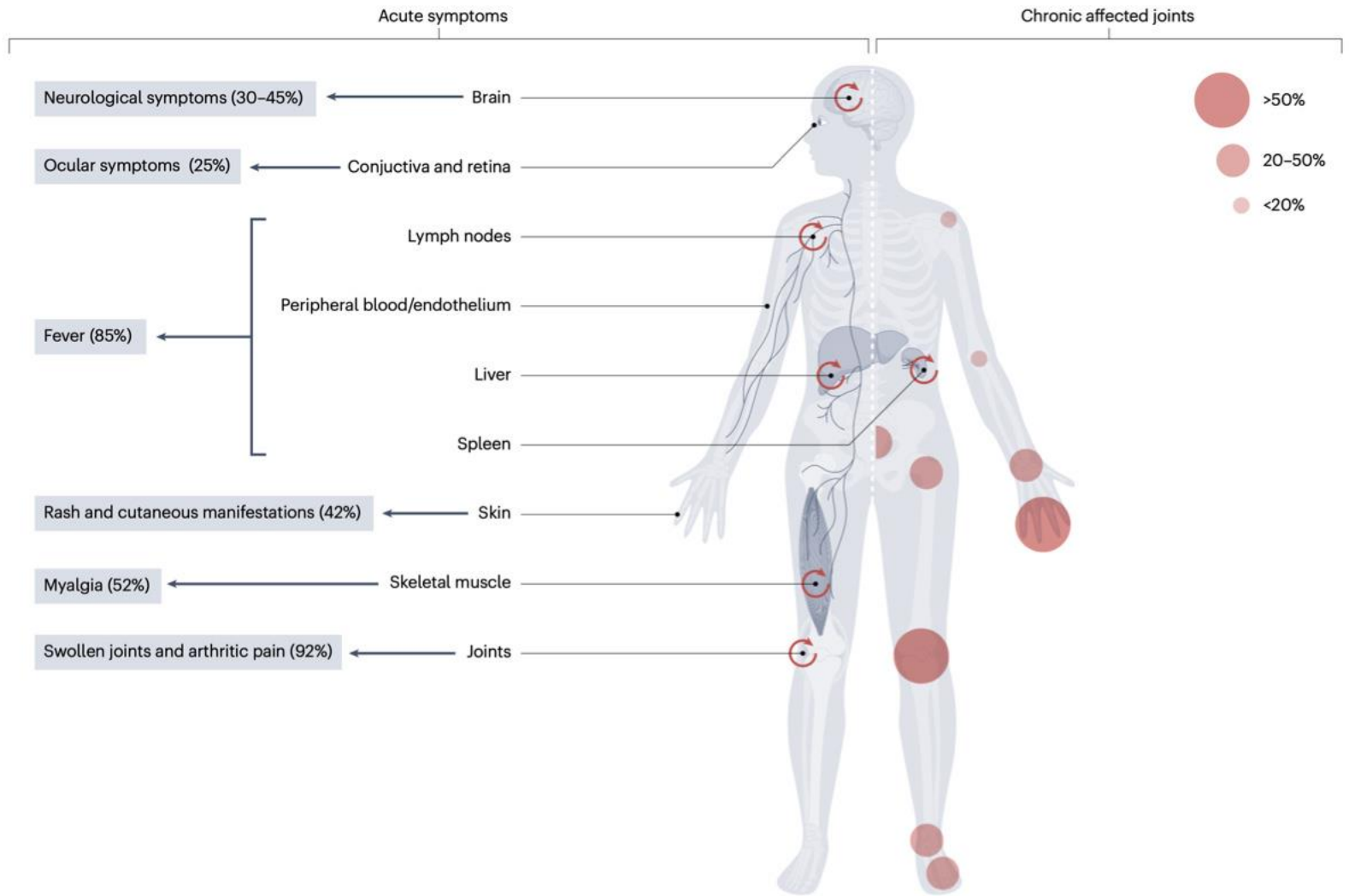
Expected expansion of CHIKV and *Aedes* mosquitoes due to human-driven environmental changes in next 15 years



Bartholomeeuwsen K et al. Nature Reviews Disease Primers 2023;9:1

High fever and debilitating joint pain are prominent symptoms during acute infection
Upto 50% of patients can progress to chronic joint pain (>3 months pi)

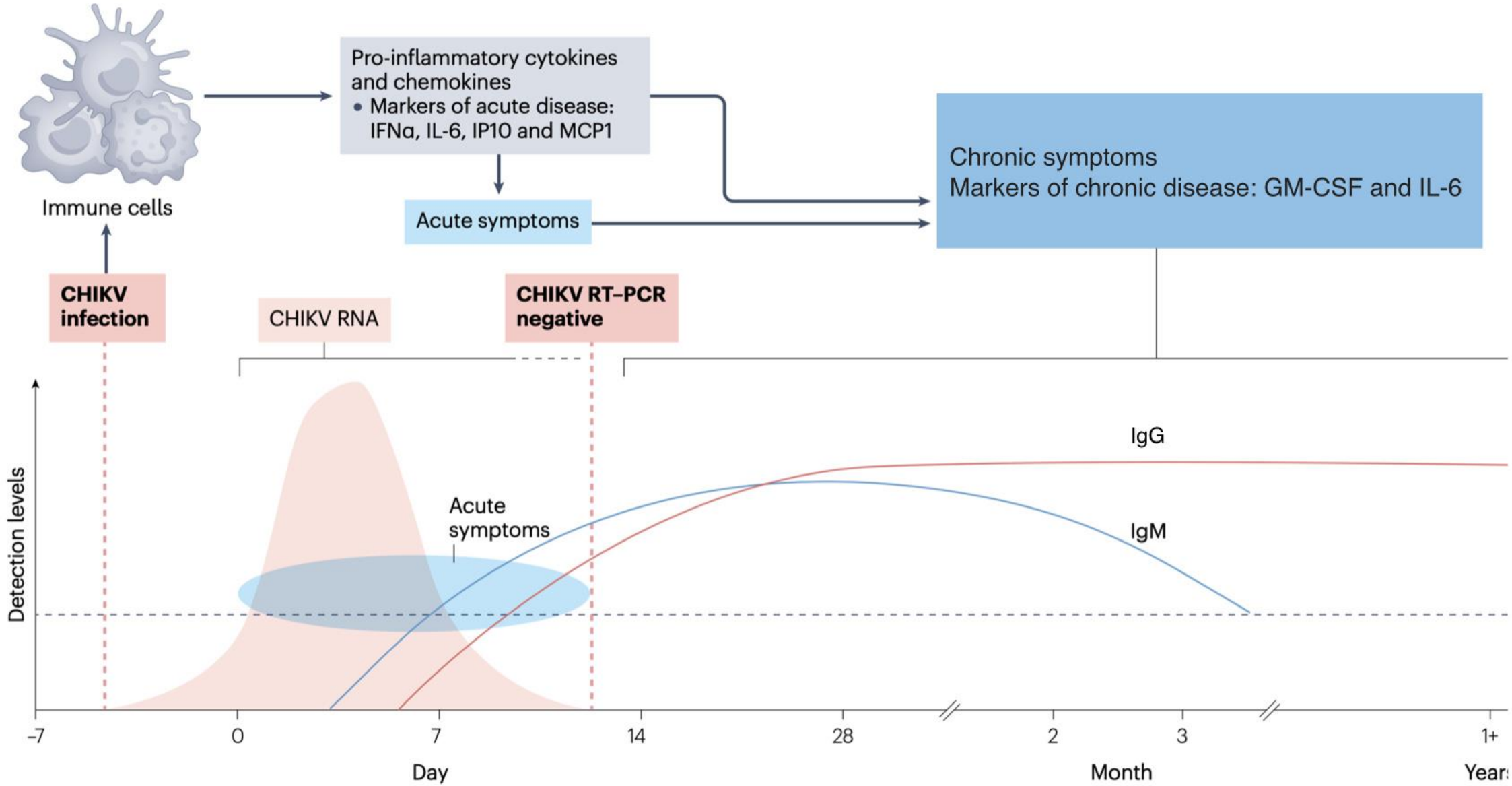




Bartholomeeuwsen K et al. Nature Reviews Disease Primers 2023;9:1

Table 2 | **Atypical symptoms of acute chikungunya**

Systems/organs affected	Percentage of hospitalized patients[10]	Manifestation examples	Refs
Neurological	40	Encephalitis	38–41,43
		Meningoencephalitis	
		Guillain–Barre syndrome	
Cardiovascular	27	Hypotension	38–41
		Myocarditis	
		Arrhythmias	
Skin	10	Hyperpigmentation	38–41
		Bullous dermatosis	
		Erythema	
Renal	26	Albuminuria	39,40,45
		Haematuria	
		Nephritis	
Respiratory	14–26	Dyspnoea	38,39,41
		Respiratory failure	
		Pneumonia	
Vascular	10	Haemorrhagic signs	39,41,205,208,209
		Bleeding gums	
		Melena	
Ocular	Less common than other atypical symptoms	Conjunctivitis	39,41,210,211
		Photophobia	
		Retinitis	
Liver	Less common than other atypical symptoms	Hepatitis	38,40,41
		Hepatomegaly	
		Altered function	

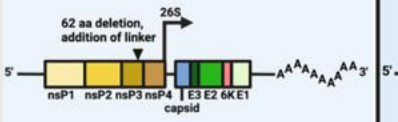

Immune cells
Pro-inflammatory cytokines and chemokines
• Markers of acute disease: IFNα, IL-6, IP10 and MCP1
Acute symptoms
Chronic symptoms
Markers of chronic disease: GM-CSF and IL-6
CHIKV infection
CHIKV RNA
CHIKV RT–PCR negative
Detection levels
Acute symptoms
IgG
IgM
–7
0
7
14
28
2
3
1+
Day
Month
Year

CHIKV - a crippling virus infection
1. *Aedes* mosquito borne alpha virus infection with **short incubation period, high attack rate and rapid onset** acute **febrile illness with debilitating polyarthralgia**
2. **Severe disease in neonates and older people** with comorbidities, possibly driven by insufficient type 1 interferon response
3. **Chronic arthritis** more likely in women, older age and severe disease
4. **Expanding geographic distribution** of four genotypes with tremendous fastly spreading and unpredictable outbreaks

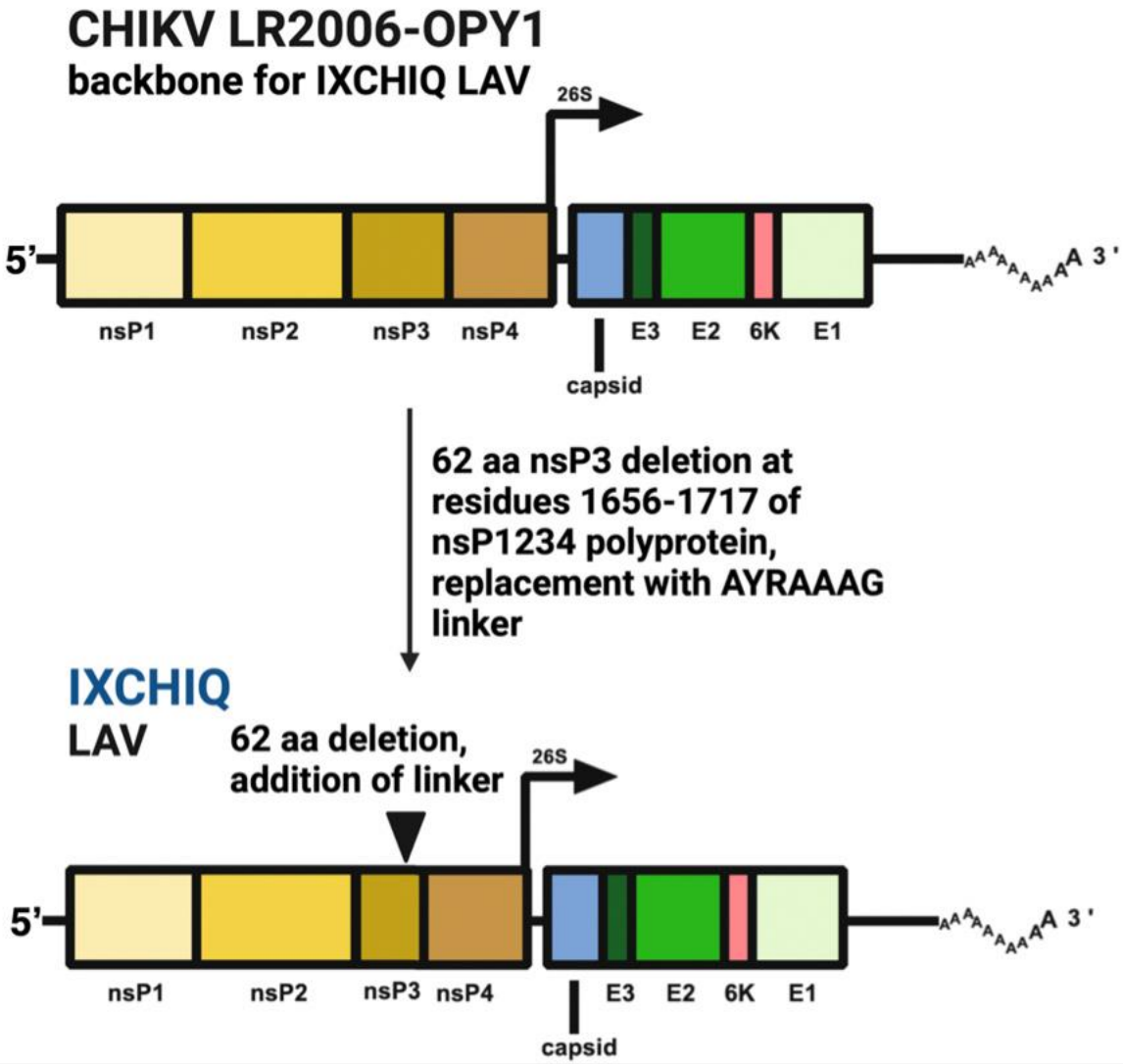
Box 1

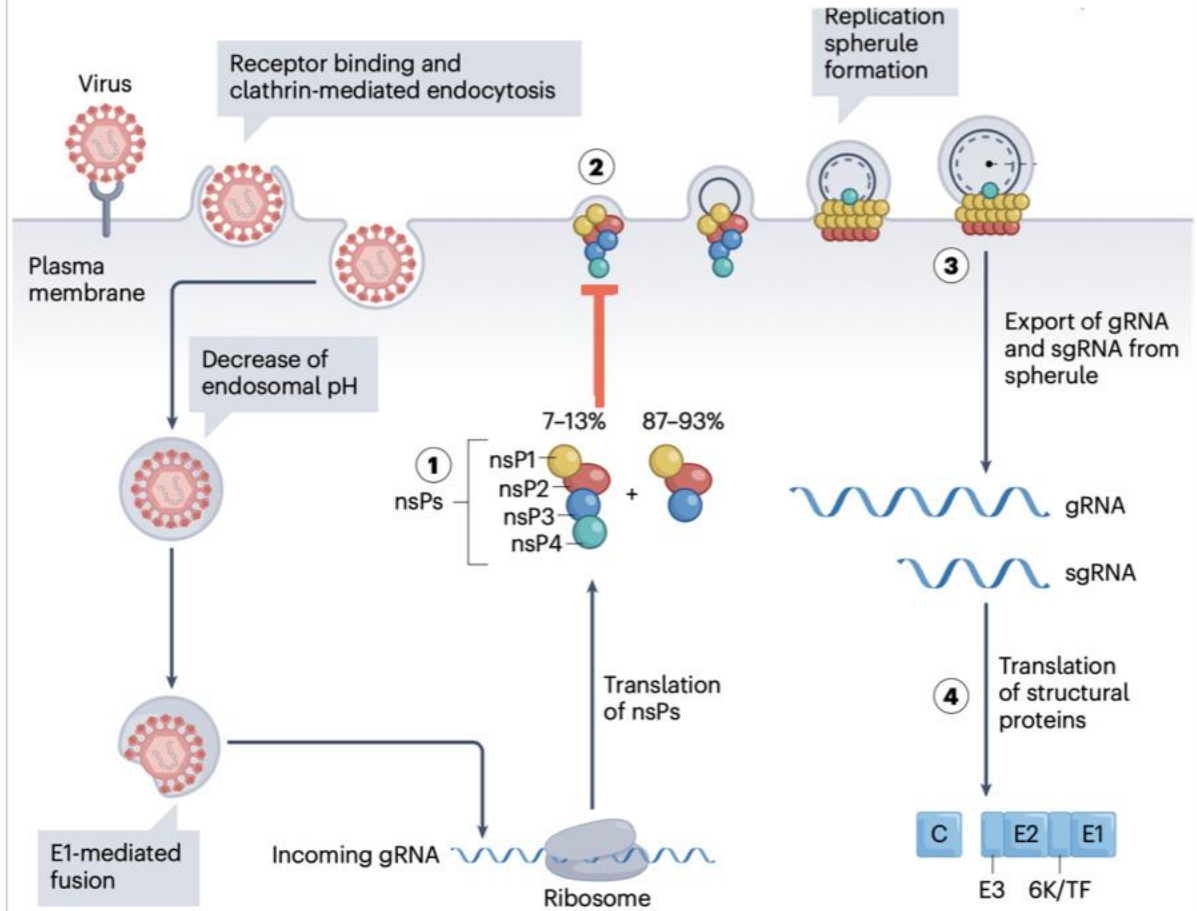
Desired features of a chikungunya virus vaccine

- Rapid onset of immunity (7–14 days)
- Durable immunity (>2 years)
- Single dose
- Protection against multiple viral strains
- Very few adverse effects and no arthritis
- Easy to store and ship
- Affordable in low-income and middle-income countries
- An established immune correlate of protection

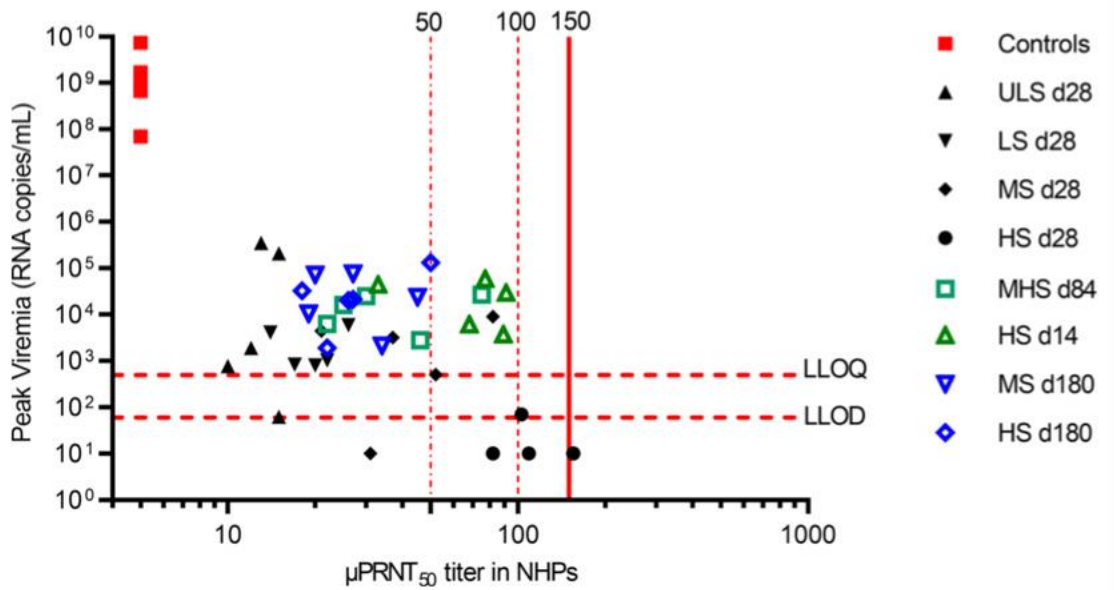
	IXCHIQ (VLA1553)	PXVX0317
PHYSICAL STRUCTURE		
GENETIC STRUCTURE		
PLATFORM	Live-attenuated (LAV)	Virus-like particle (VLP)
CHIKV STRAIN	LR2006-OPY1 (ECSA)	37997 (West African)
DOSE STORAGE	10^4 $TCID_{50}$ x 1 injection 2-8°C	20µg VLP x 2 injections 40µg VLP x 1 injection* not published
APPROVAL STATUS	U.S. FDA ✓ Health Canada ✓ European Medicines Agency ✓ Pending: Brazil	Expected 2025
ONGOING TRIALS	Phase III: Adolescents in Brazil Phase III: long-term safety / immunity in U.S.	Phase III: elderly adults in U.S. Phase III: adolescents + adults in U.S. Phase III: long-term safety / immunity in U.S.
ANTIBODY POTENCY	10^2-10^3 GMT (1 year)	10^2-10^3 GMT (1 year)
DURABILITY	2+ years	2+ years
BREADTH	CHIKV genotypes, ONNV, MAYV, RRV	CHIKV genotypes, ONNV, MAYV, UNAV, RRV
SYMPTOMS/ SIDE EFFECTS	fever 13-24% joint pain 1-18% headache 24-40% muscle pain 15-25% chills 1.5% fatigue 17-39% serious adverse events 1.2-3.7%	fever 2-4% joint pain 10-12% headache 21-27% muscle pain 21-22% chills 6-7% fatigue 16% nausea 4-14% serious adverse events 0.5-4%
VACCINE VIREMIA	Yes	No

Life-attenuated CHIK vaccine (VLA1533) - deletion of 62 amino acids in nsP3 of CHIKV reduces viral replication efficiency and fitness

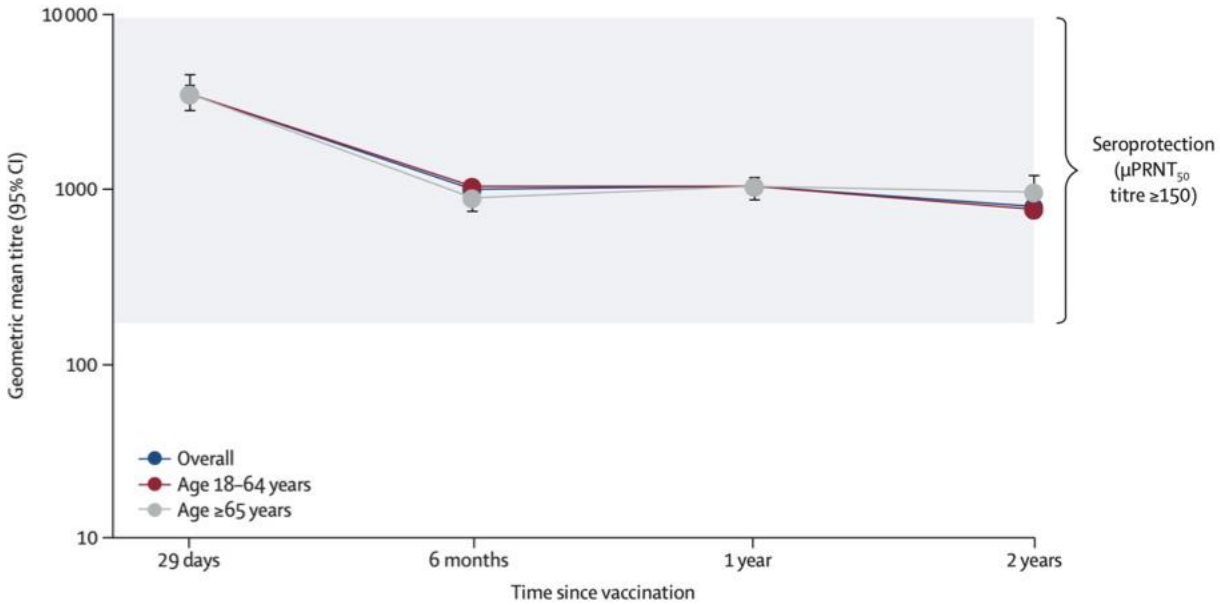




Approval VLA1553 is based on virus-neutralizing antibody correlate of protection
- real-world efficacy data are not yet available -



Roques P et al. JCI Insight 2020;7:e160173



McHanon R et al. Lancet Infect Dis 2024;August 12

Post-vaccination chikungunya-like illness preventing daily activities in 1.6% VLA1553 recipients

	VLA1553 (n=3082)	Placebo (n=1033)
Any adverse events	1926 (62·5%, 60·8–64·2) 6415	463 (44·8%, 41·8–47·9) 1071
Any related adverse events	1575 (51·1%, 49·3–52·9) 4621	322 (31·2%, 28·4–34·1) 647
Any related severe adverse events	62 (2·0%, 1·5–2·6) 70	1 (0·1%, 0·0–0·5) 3
Any serious adverse events	46 (1·5%, 1·1–2·0) 73	8 (0·8%, 0·3–1·5) 10
Any related serious adverse events	2 (0·1%, 0·0–0·2) 2	0 (0%, 0·0–0·4) 0
Any adverse events of special interest	10 (0·3%, 0·2–0·6) 26	1 (0·1%, 0·0–0·5) 2
Any adverse event with a frequency ≥10% in at least one study arm		
Headache	986 (32·0%, 30·3–33·7) 1028	160 (15·5%, 13·3–17·8) 178
Fatigue	886 (28·7%, 27·2–30·4) 893	137 (13·3%, 11·3–15·5) 139
Myalgia	750 **24·3%** 22·8–25·9) 758	82 (7·9%, 6·4–9·8) 84
Arthralgia	554 **18·0%** 16·6–19·4) 589	63 (6·1%, 4·7–7·7) 70
Injection site pain	413 (13·4%, 12·2–14·7) 519	101 (9·8%, 8·0–11·8) 122
Pyrexia	427 **13·9%** 12·7–15·1) 429	13 (1·3%, 0·7–2·1) 13
Nausea	359 (11·6%, 10·5–12·8) 364	63 (6·1%, 4·7–7·7) 64
Any serious adverse event with a frequency ≥0·2% in at least one study arm by system organ class		
Infections and infestations	9 (0·3%, 0·1–0·6) 9	3 (0·3%, 0·1–0·8) 3
Injury, poisoning, and procedural complications	8 (0·3%, 0·1–0·5) 15	1 (0·1%, 0·0–0·5) 1
Psychiatric disorders	7 (0·2%, 0·1–0·5) 8	2 (0·2%, 0·0–0·7) 4
Cardiac disorders	5 (0·2%, 0·1–0·4) 7	0 (0%, 0·0–0·4) 0

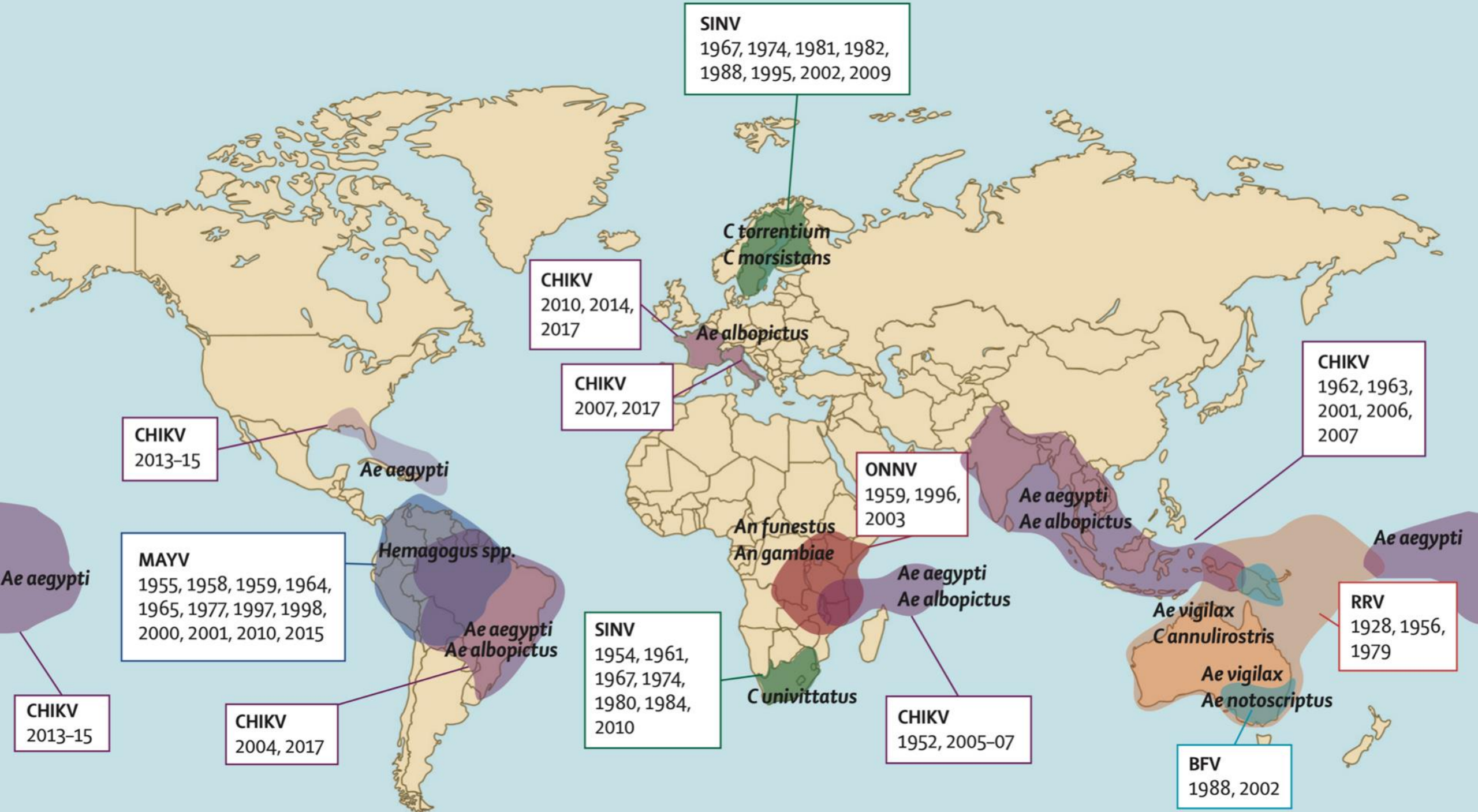
Schneider M et al. Lancet 2023;401:2138

Who is going to get it?

1. **Recommend** to travellers (≥18 yo) to territories with CHIKV outbreak
2. **Consider** in travellers 65 years and over to territories with CHIKV outbreak in last 5 years and more than 2 weeks exposure to mosquito bites
3. **Consider** in expatriates living in counties with CHIKV outbreak in last 5 years
4. **Consider** in military personnel on active duty in these areas

ACIP Recommendation February 2024

CHIKV - a crippling virus infection
1. **Expanding geographic distribution** of four genotypes with unpredictable and tremendous fastly spreading outbreaks
2. *Aedes* mosquito borne alpha virus infection with **short incubation period, high attack rate** and **rapid onset acute febrile illness with debilitating polyarthralgia** occurring in cycles of 10-18 years
3. **Severe disease in neonates** and **older people** with comorbidities, possibly driven by insufficient type 1 interferon response
4. **Chronic arthropathy** more likely in women, older age, and severe disease
5. Chikungunya **vaccines** for **travellers** to **outbreak areas,** and possibly for **older people with comorbidities, expatriates** and **military** to **areas with outbreaks last five years**


SINV
1967, 1974, 1981, 1982, 1988, 1995, 2002, 2009
C torrentium
C morsistans
CHIKV
2010, 2014, 2017
Ae albopictus
CHIKV
2007, 2017
CHIKV
2013–15
Ae aegypti
CHIKV
1962, 1963, 2001, 2006, 2007
ONNV
1959, 1996, 2003
Ae aegypti
Ae albopictus
An funestus
An gambiae
Ae aegypti
Ae albopictus
MAYV
1955, 1958, 1959, 1964, 1965, 1977, 1997, 1998, 2000, 2001, 2010, 2015
Hemagogus spp.
Ae aegypti
Ae aegypti
Ae albopictus
Ae aegypti
RRV
1928, 1956, 1979
Ae vigilax
C annulirostris
Ae vigilax
Ae notoscriptus
SINV
1954, 1961, 1967, 1974, 1980, 1984, 2010
C univittatus
CHIKV
1952, 2005–07
CHIKV
2013–15
CHIKV
2004, 2017
BFV
1988, 2002

Cross-reactive neutralising antibodies after vaccination or infection