Arbovirus Risk Assessment

Forum on Microbial Threats
National Academies of Sciences, Engineering and Medicine

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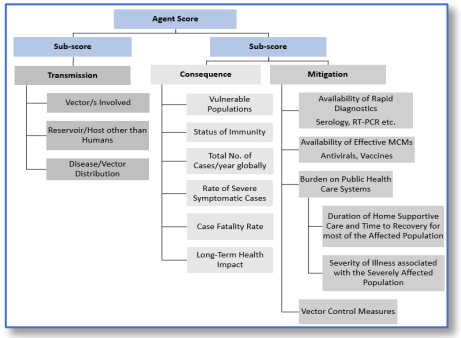
Note: This work is currently in-progress and subject to modifications per SME review and feedback

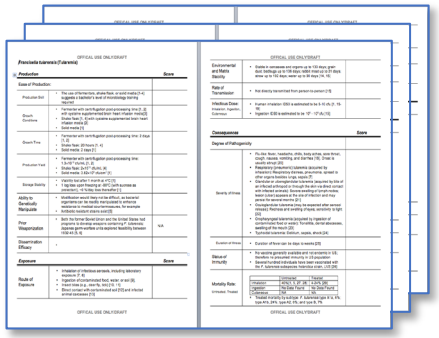
Arbovirus

- More than 25% of human infectious diseases globally are vector-borne diseases.
- This results in more than 2.5 million annual deaths globally.
- Mosquitoes and Ticks are the main vectors along with Sandflies and Midges.
- Around 550+ arboviruses are already described worldwide with about 50 or so causes disease in domestic animals and wildlife and more than a 130 or so causes infections and diseases in humans, animals, and wildlife.

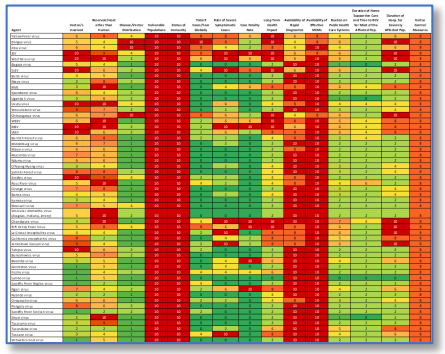
Overall Process for Arbovirus Risk Assessment



Defining the Factors and Criteria for scoring



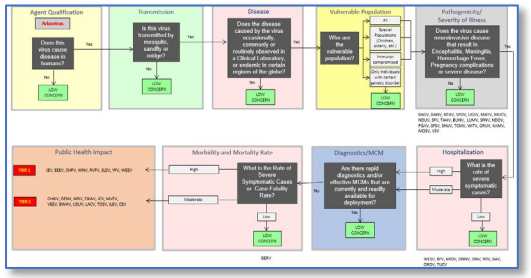
Data collection



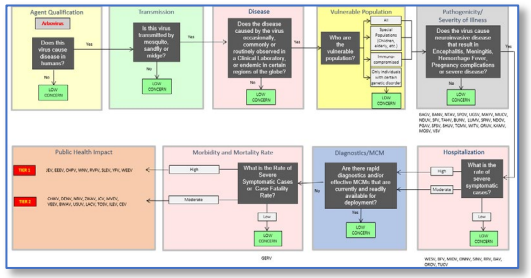
Scoring results

Factor	Criteria	Weight
Transmission	Vector/s involved	1
	Reservoir/Vertebrate Host other than Humans	2
	Disease/Vector Distribution	2
Consequence	Vulnerable Populations	1
	Status of Immunity	1
	Total Number of Cases/year globally	3
	Rate of Severe Symptomatic Cases	3
	Case Fatality Rate	3
	Long-Term Health Impact	3
Mitigation	Availability of Rapid Diagnostics	1
	Availability of Effective Medical Countermeasures	1
	Burden on Public Health Care System	2
	Vector Control Measures to reduce Disease Persistence	1

Apply criteria weighting



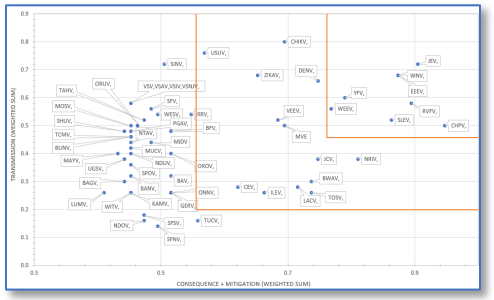
Conceptualizing the DSF Framework and Logic Tree approach



Applying the Concept

Decision Support Framework		Multi-Criteria Decision Analysis (MCDA) Approach							
Logic Tree Approach		1D, Unweighted		1D, Weighted		2D, Unweighted		2D, Weighted	
Tier 1	Tier 2	Tier 1	Tier 2	Tier 1	Tier 2	Tier 1	Tier 2	Tier 1	Tier 2
JCV	CHIKV	JCV	NRIV	JCV	JCV	JCV	CHIKV	JCV	CHIKV
EEEV	DENV	EEEV	ZIKAV	EEEV	ZIKAV	EEEV	DENV	EEEV	DENV
CJPV	NRIV	CJPV	JCV	CJPV	MVEV	CJPV	WEEV	CJPV	NRIV
WNV	ZIKAV	WNV	MVEV	WNV	VEEV	WNV	NRIV	WNV	ZIKAV
RVFV	JCV	RVFV	VCDV	RVFV	BWAV	RVFV	ZIKAV	RVFV	JCV
SLEV	MVEV	SLEV	BWAV	SLEV	TOSV	SLEV	VEEV	SLEV	MVEV
YFV	VEEV	YFV	USUV	YFV	LACV	YFV	JCV	YFV	VEEV
WEEV	BWAV	WEEV	LACV	WEEV	USUV		MVEV	WEEV	BWAV
	USUV		DENV		DENV		BWAV		USUV
	LACV		CHIKV		NRIV		TOSV		LACV
	TOSV		CEV				ILEV		TOSV
	ILEV		SINV						ILEV
	CEV								CEV

Compare results using two methods



2-D Results

Arboviruses subjected to Risk Assessment

Flaviviridae (14)		Vector
Yellow Fever virus	YFV	Mosquito Ae
Dengue virus	DENV	Mosquito Ae/An/Ar/Cx
Zika virus	ZIKAV	Mosquito Ae/An/Cx/Ar
Japanese encephalitis virus	JEV	Mosquito An/Ae/Ar/Cx
West Nile virus	WNV	Mosquito Ae/An/Ar/Cx/ Cu
Bagaza virus	BAGV	Mosquito Ae/Cx/Midges
St. Louis encephalitis virus	SLEV	Mosquito Ae/Cx
Banzi virus	BANV	Mosquito Cx
Ntaya virus	NTAV	Mosquito Cx
Murray Valley encephalitis virus	MVEV	Mosquito Cx
Spondweni virus	SPOV	Mosquito Ae/Cx
Uganda S virus	UGSV	Mosquito Ae
Usutu virus	USUV	Mosquito Ae/An/Cx/V
Wesselsbron virus	WESV	Mosquito Ae/Cx

Togaviridae (13)		Vector
Chikungunya virus	CHIKV	Mosquito Ae/Cx
Western Equine encephalitis virus	WEEV	Mosquito Ae/An/Cx/Cu
Eastern Equine encephalitis virus	EEEV	Mosquito Ae/Cx/Cu
Venezuelan Equine encephalitis virus	VEEV	Mosquito Ae/Cx/Cu
Barmah Forest virus	BFV	Mosquito Ae/Cx
Middelburg virus	MIDV	Mosquito Ae
Mayaro virus	MAYV	Mosquito Ae/Cx/H
Mucambo virus	MUCV	Mosquito Cx
Ndumu virus	NDUV	Mosquito Ae/Cx
O'Nyong-Nyong virus	ONNV	Mosquito Ae/An
Semliki Forest virus	SFV	Mosquito Ae
Sindbis virus	SINV	Mosquito Ae/Cx
Ross River virus	RRV	Mosquito Ae

Reoviridae (2)		Vector
Orungo virus	ORUV	Mosquito Ae/An
Banna virus	BAV	Mosquito Ae/An/Cx Ticks

Rhabdoviridae (4)		Vector
Kamese virus	KAMV	Mosquito Cx
Mossuril virus	MOSV	Mosquito Cx
Vesicular stomatitis virus (Alagoas, Indiana, Jersey)	VSV VSAV VSIV VSNJV	Sandfly/Black flies/Midges/ Mosquito V
Chandipura virus	CHPV	Sandfly

Key for Mosquito species

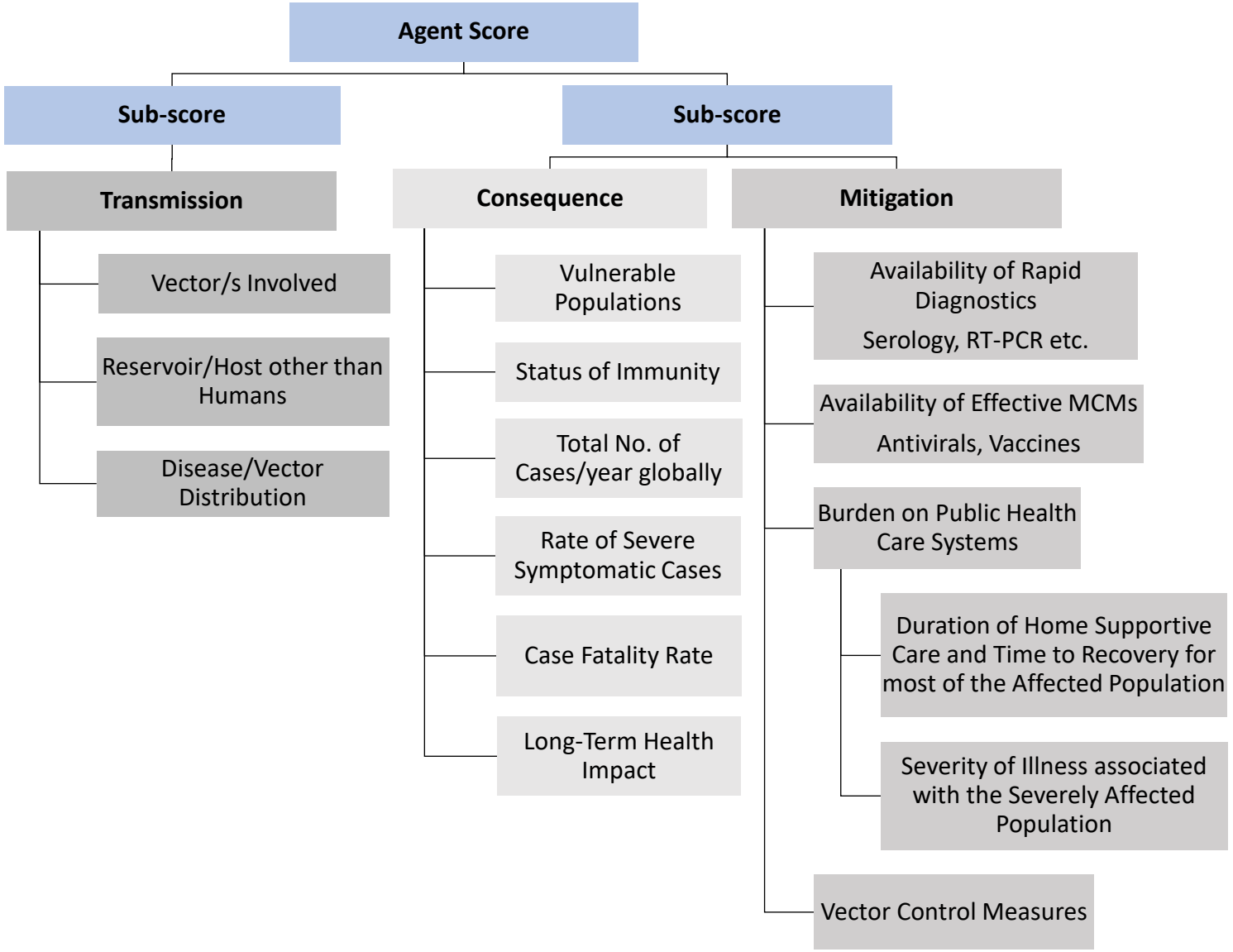
Ae – Aedes sp.
An – Anopheles sp.
Ar – Armigeres spp.
Cx – Culex sp.
Cu – Culiseta spp.
H – Haemagogus sp.
V – Various sp.

Bunyaviridae (21)		Vector
Rift Valley Fever Virus	RVFV	Mosquito Ae/V/Cx
La Crosse encephalitis virus	LACV	Mosquito Ae
California encephalitis virus	CEV	Mosquito Ae
Jamestown Canyon virus	JCV	Mosquito Ae
Tahyna virus	TAHV	Mosquito Ae/Cx
Bunyamwera virus	BUNV	Mosquito Ae/An
Bwamba virus	BWAV	Mosquito Ae/An
Germiston virus	GERV	Mosquito Cx
Ilesha virus	ILEV	Mosquito An
Lumbo virus	LUMV	Mosquito Ae
Sandfly Fever Naples virus	SFNV	Sandfly
Ngari virus	NRIV	Mosquito Ae/An
Nyando virus	NDOV	Mosquito An
Oropouche virus	OROV	Mosquito Ae Midge
Pongola virus	PGAV	Mosquito Ae
Sandfly Fever Sicilian virus	SFSV	Sandfly
Shuni virus	SHUV	Mosquito Cx
Tacaiuma virus	TCMV	Mosquito An
Tucunduba virus	TUCV	Mosquito An/Cx
Toscane virus	TOSV	Sandfly
Witwatersrand virus	WITV	Mosquito Cx

Arboviruses not included in the Risk assessment

- Hartland virus, Severe fever thrombocytopenia syndrome virus, Crimean Congo Hemorrhagic Fever virus, Omsk Hemorrhagic Fever virus, Kyasanur Forest Disease virus, Tick-borne encephalitis virus, Powassan virus, Bourbon virus, Colorado tick fever virus and other arboviruses transmitted by fleas or ticks.
- Arboviruses transmitted by mosquito, sandflies and midge that does not cause disease in humans e.g., Getah virus, Potosi virus, etc..

Methodology uses a Multi-Criteria Decision Analysis Approach to Derive the Agent Risk



Framework Provides Scoring Definitions, Bins and Weights; Straight forward Math Provides Overall Priority

- Scoring:
  - Criteria are scored on a 0-10 scale
  - Each criteria is assigned a weight
  - Higher-level scores are calculated by summing the weighted scores

- Additional considerations for criteria selection:
  - Independence
  - Data quality and availability for scoring
  - Agent-specific criteria that are critical for Risk Assessments

Case Fatality Rate	
0	Close to 0%
2	1 – 9%
4	10 – 14%
6	15 – 19%
8	20 – 24%
10	25% or greater

Criteria Bins for Scoring

TRANSMISSION

Vectors Involved in Transmission – The number and type of vectors that can contribute to the transmission of disease to human:

0 0-1 species of mosquitoes or flying insects
2 2-3 species of mosquitoes or flying insects
4 4-5 species of mosquitoes or flying insects
6 6-7 species of mosquitoes or flying insects
8 8-9 species of mosquitos or flying insects
10 10 or more species of mosquitos or flying insects

Reservoir/Host other than humans– The number of other potential host or carriers of the disease that can contribute to enhance transmission:

0 None
2 Only humans
4 1-2 host species
6 3-4 host species
8 5-6 host species
10 7 or more host species

Disease/Vector Distribution – Number of countries impacted by the disease and vectors

0 Less than 9 countries
2 10 to 24 countries
4 25 to 49 countries
6 50 to 74 countries
8 75 to 99 countries
10 More than 100 countries

CONSEQUENCE

Vulnerable Populations – The portion of the population susceptible to disease, more severe form of the disease and/or complications from the disease:

0 None
2 Small subset or group (e.g., rare genetic disorder)
4 Only immunocompromised
6 Immunocompromised and pregnant females
8 Immunocompromised, pregnant females and children or elderly
10 All

Status of Immunity – The extent to which the population may have immunity to the disease due to previous exposure or vaccination:

0 Close to 90-100%
2 Significant (>60-90%) of population have immunity
4 Moderate portion (30-60%) of population have immunity
6 Previous vaccines or exposure may have reduced impact in about 10-30%
8 Small subset (<10%) have immunity (e.g., from vaccination or previous exposure)
10 No presumed immunity to disease in majority of the global population

Number of Clinical Cases per year globally– Number of individual infected per year

0 Less than 1K
2 1K – 10K
4 10K – 100K
6 100K – 1M
8 1M – 10M
10 10M or higher

Rate of Severe Symptomatic Cases – Individuals requiring hospitalization and supportive care

0 Close to 0%
2 1 – 9%
4 10 – 14%
6 15 – 19%
8 20 – 24%
10 25% or higher

Case Fatality Rate – The number of deaths from the disease per 100 diagnosed cases (or number of known cases):

0 Close to 0%
2 1 – 9%
4 10 – 14%
6 15 – 19%
8 20 – 24%
10 25% or greater

Long-Term Health Effects – The extent to which a portion of the affected population may incur disability or require additional medical care beyond treatment for acute illness (sequelae):

0 None and/or unknown due to too few cases
2 Little to no long-term effects
4 No functional effects, but follow-up medical care required
6 Persists to a chronic stage for years and/or acute disease can reoccur
8 Long-term functional impacts (e.g., flaccid paralysis, neurological)
10 Some level of permanent incapacitation, requiring long-terms care (e.g., long term brain damage, liver damage)

MITIGATION

Availability of Rapid Diagnostics – The availability of rapid diagnostics that can be rapidly deployed in response to a public health emergency:

0 No need to deployed rapid diagnostics due to low morbidity and mortality
2 Widely available and easy to deploy efficiently (e.g. lateral flow immunoassays)
4 Available with some limitation to deploy widely (e.g. Real-Time PCR testing) due to lack of validation or availability of technology/reagents
6 Available but difficult to deploy widely (e.g. Serological testing) due to lack of validation, expertise or availability of technology/reagents
8 Available only at limited institutions (e.g., EUA required) or only approved outside the U.S.
10 No Rapid Diagnostics currently available

Availability of Effective Medical Countermeasures – The availability of efficacious medical treatments/countermeasures and extent to which they can be rapidly deployed in response to a public health emergency:

0 No MCMs required or would be deployed or needed due to low morbidity or mild illness
2 Over the Counter MCM to treat or minimize the symptoms
4 Widely available and easy to deploy efficiently (e.g. Antiviral oral tablets/capsules)
6 Widely available but difficult to deploy efficiently (e.g. intravenous-only drugs) or lacks efficacy
8 Approved treatment or vaccine available in limited quantities
10 No treatment beyond supportive care available

Burden on Public Health Care Systems – The potential burden to public health during and after an event, as measured by duration of medical countermeasure treatment and duration of hospitalization.

Duration of Home Supportive Care and Time to Recovery – The length of time for home supportive care required for most of the affected population and the time to recovery:

0 1-6 days
2 7-14 days
4 15-21 days
6 22-28 days
8 29-35 days
10 >36 days

Illness Severity – The type of illness associated with infection in severe cases:

0 No illness or mild illness
2 Fever (flu-like)
4 Fever with other complications (paralysis, seizures, back pain, joint pain, myalgia etc.)
6 Hemorrhagic Fever or Aseptic meningitis
8 Neurological (encephalitis or meningitis)
10 Neurological (encephalitis or meningitis) + Hemorrhagic Fever or other serious complications

Vector Control measures to reduce Disease Persistence – The potential extent remediation efforts are effective to reduce vector persistence in the environment to reduce disease persistence in the population.

0 No vector control measures required as disease is least likely to persist
2 There are vector control measures that will eliminate disease persistence.
4 There are vector control measures that are highly effective.
6 There are vector control measures that are moderately effective
8 There are vector control measures that have limited effectiveness
10 There are no effective vector control measures

Scoring Results

Agent	Vector/s Involved	Reservoir/Host other than Human	Disease/Vector Distribution	Vulnerable Populations	Status of Immunity	Total # Cases/Year Globally	Rate of Severe Symptomatic Cases	Case Fatality Rate	Long-Term Health Impact	Availability of Rapid Diagnostics	Availability of Effective MCMs	Burden on Public Health Care Systems	Duration of Home Supportive Care and Time to RCV for Most of the Affected Pop.	Duration of Hosp. for Severely Affected Pop.	Vector Control Measures
Yellow Fever virus	6	8	4	10	10	8	8	6	10	6	8	4	2	6	8
Dengue virus	5	4	10	10	10	10	8	2	10	4	8	6	2	10	8
Zika virus	6	4	10	10	10	8	4	2	8	4	10	4	2	6	8
JEV	10	9	4	10	10	8	10	10	10	6	8	6	2	10	8
West Nile virus	10	10	2	10	10	6	10	6	10	6	10	6	2	10	8
Bagaza virus	5	4	1	10	10	0	0	0	2	10	10	1	0	2	8
SLEV	10	6	2	10	10	4	10	8	10	6	10	6	2	10	8
Banzi virus	4	5	1	10	10	0	0	0	2	10	10	2	2	2	8
Ntaya virus	2	8	2	10	10	0	0	0	2	10	10	2	2	2	8
MVE	3	10	1	10	10	0	4	6	8	8	10	6	4	8	8
Spondweni virus	6	4	2	10	10	0	0	0	2	10	10	2	2	2	8
Uganda S virus	3	6	2	10	10	0	0	0	2	10	10	1	0	2	8
Usutu virus	10	10	4	10	10	0	6	0	4	8	10	4	4	4	8
Wesselsbron virus	9	7	2	10	10	0	2	0	2	10	10	3	2	4	8
Chikungunya virus	6	7	10	10	10	8	6	2	10	4	8	6	2	10	8
WEEV	6	10	1	10	10	2	6	6	10	8	10	6	4	8	8
EEEV	10	10	2	10	10	2	10	10	10	6	10	6	4	8	8
VEEV	10	6	2	10	10	2	6	2	8	8	10	6	4	8	8
Barmah Forest virus	6	8	1	10	10	2	2	0	4	8	10	3	4	2	8
Middelburg virus	6	7	1	10	10	0	2	0	2	10	10	2	2	2	8
Mayaro virus	6	6	1	10	10	0	0	0	2	8	10	2	2	2	8
Mucambo virus	7	6	1	10	10	0	0	0	2	10	10	2	2	2	8
Ndumu virus	6	6	1	10	10	0	0	0	2	10	10	2	2	2	8
O'Nyong-Nyong virus	3	4	1	10	10	0	2	0	4	10	10	3	2	4	8
Semliki Forest virus	8	8	2	10	10	0	0	0	4	10	10	3	2	4	8
Sindbis virus	10	9	4	10	10	2	2	0	4	8	10	2	2	2	8
Ross River virus	5	10	1	10	10	4	2	0	4	8	10	4	6	2	8
Orungo virus	7	8	1	10	10	0	0	0	2	10	10	3	2	4	8
Banna virus	4	5	1	10	10	0	2	0	4	10	10	3	2	4	8
Kamese virus	3	4	1	10	10	0	0	0	2	10	10	2	2	2	8
Mossuril virus	7	5	4	10	10	0	0	0	2	10	10	2	2	2	8
Vesicular stomatitis virus (Alagoas, Indiana, Jersey)	5	10	2	10	10	0	0	0	2	10	10	2	2	2	8
Chandipura virus	3	10	1	10	10	4	10	10	10	10	10	7	4	10	8
Rift Valley Fever Virus	5	8	4	10	10	8	6	10	10	8	10	6	2	10	8
La Crosse encephalitis virus	4	4	1	10	10	2	10	0	8	8	10	6	2	10	8
California encephalitis virus	8	2	1	10	10	0	4	2	8	8	10	5	2	8	8
Jamestown Canyon virus	9	4	1	10	10	2	10	2	8	8	10	6	2	10	8
Tahyna virus	10	6	2	10	10	2	0	0	2	10	10	2	2	2	8
Bunyamwera virus	5	7	2	10	10	0	0	0	2	10	10	2	2	2	8
Bwamba virus	3	5	1	10	10	0	4	10	6	10	10	4	2	6	8
Germiston virus	1	5	1	10	10	0	4	0	2	10	10	2	2	2	8
Ilesha virus	1	4	2	10	10	4	4	4	6	10	10	2	2	2	8
Lumbo virus	1	5	1	10	10	0	0	0	0	10	10	0	0	0	8
Sandfly Fever Naples virus	1	2	1	10	10	4	0	0	2	10	10	2	2	2	8
Ngari virus	7	4	2	10	10	2	6	10	8	10	10	4	2	6	8
Nyando virus	2	2	1	10	10	0	0	0	4	10	10	2	2	2	8
Oropouche virus	6	6	1	10	10	2	2	0	4	8	10	3	2	4	8
Pongola virus	8	6	2	10	10	0	0	0	2	10	10	2	2	2	8
Sandfly Fever Sicilian virus	1	2	2	10	10	2	0	0	2	10	10	2	2	2	8
Shuni virus	2	10	1	10	10	0	0	0	2	10	10	1	0	2	8
Tacaiuma virus	3	9	1	10	10	0	0	0	2	10	10	2	2	2	8
Tucunduba virus	2	2	1	10	10	0	2	0	6	10	10	5	2	8	8
Toscane virus	3	4	1	10	10	4	10	0	8	10	10	4	2	6	8
Witwatersrand virus	1	5	1	10	10	0	0	0	2	10	10	2	2	2	8

Lessons Learned form Select Agents and Toxins Risk Assessment – Support Biennial Review.

1 D Plots

- Top agents remain on the top.
- Bottom agents tends to fall in the bottom.
- Agents that fall in the middle seem to have low fidelity.

2 D Plots

- Gave better discrimination between the agents.
- Provided reason behind the risk ranking:
  - Where the agent falls in terms of Consequence.
  - Where the agent falls in terms of our current response capability or status

Criteria Weights

- Not all criteria used are of equal value.
- Some criteria are more critical than others.
- Benefit of assigning weights allowed for better segregation/separation of agents in the risk assessment

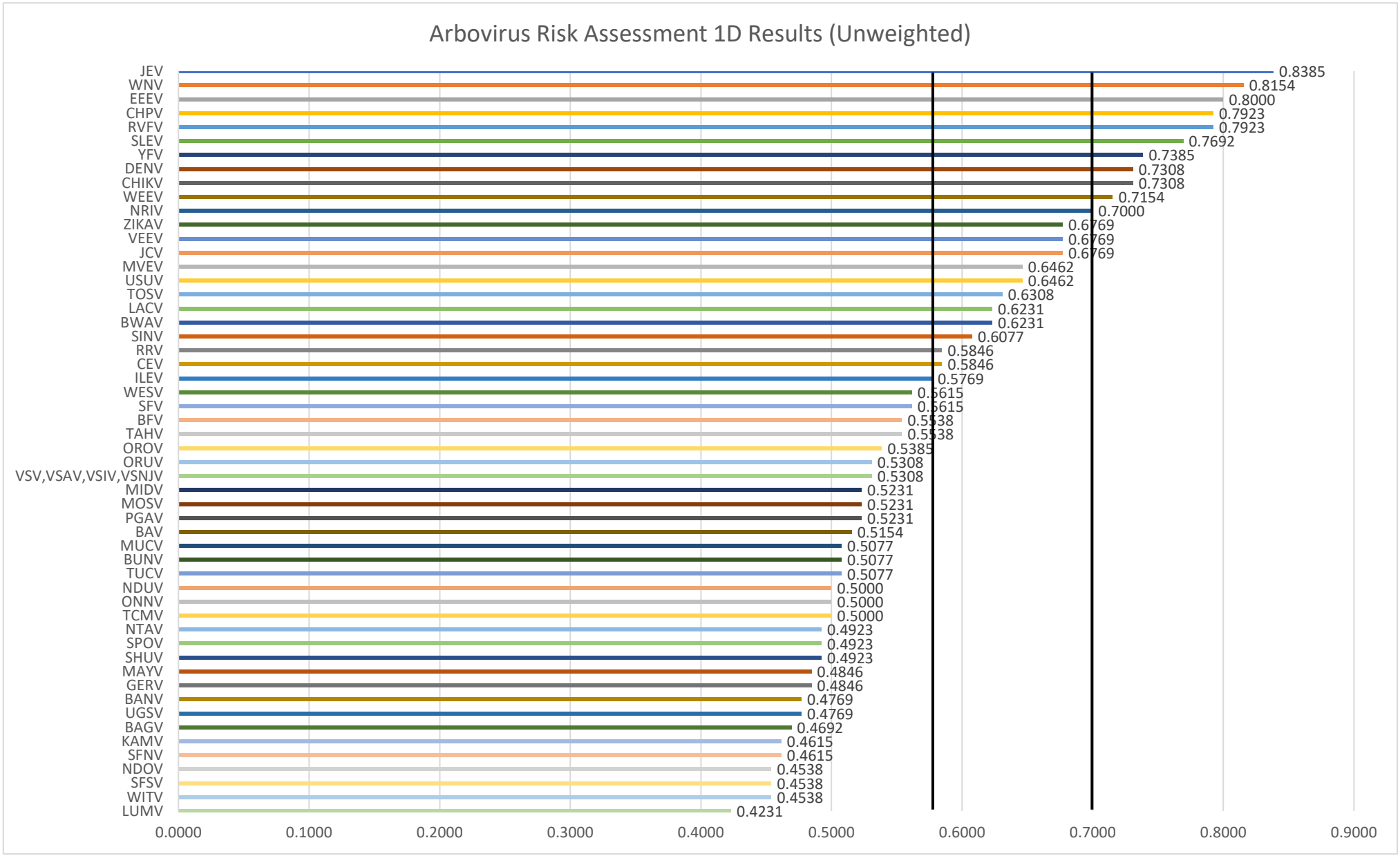
Weights Assigned for Criteria Ranking Results

Factor	Criteria	Weight
Transmission	Vector/s involved	1
	Reservoir/Vertebrate Host other than Humans	2
	Disease/Vector Distribution	2
Consequence	Vulnerable Populations	1
	Status of Immunity	1
	Total Number of Cases/year globally	3
	Rate of Severe Symptomatic Cases	3
	Case Fatality Rate	3
	Long-Term Health Impact	3
Mitigation	Availability of Rapid Diagnostics	1
	Availability of Effective Medical Countermeasures	1
	Burden on Public Health Care System	2
	Vector Control Measures to reduce Disease Persistence	1

Key for assigning Weights:

Criteria's that will not make a big difference in the score for all the agents are assigned a weight of 1x.
Criteria's that will have some impact on the different agents are assigned a weight of 2x.
Criteria's that are critical to understanding the risk of agents with significant impact are assigned a weight of 3x.

Scoring Results



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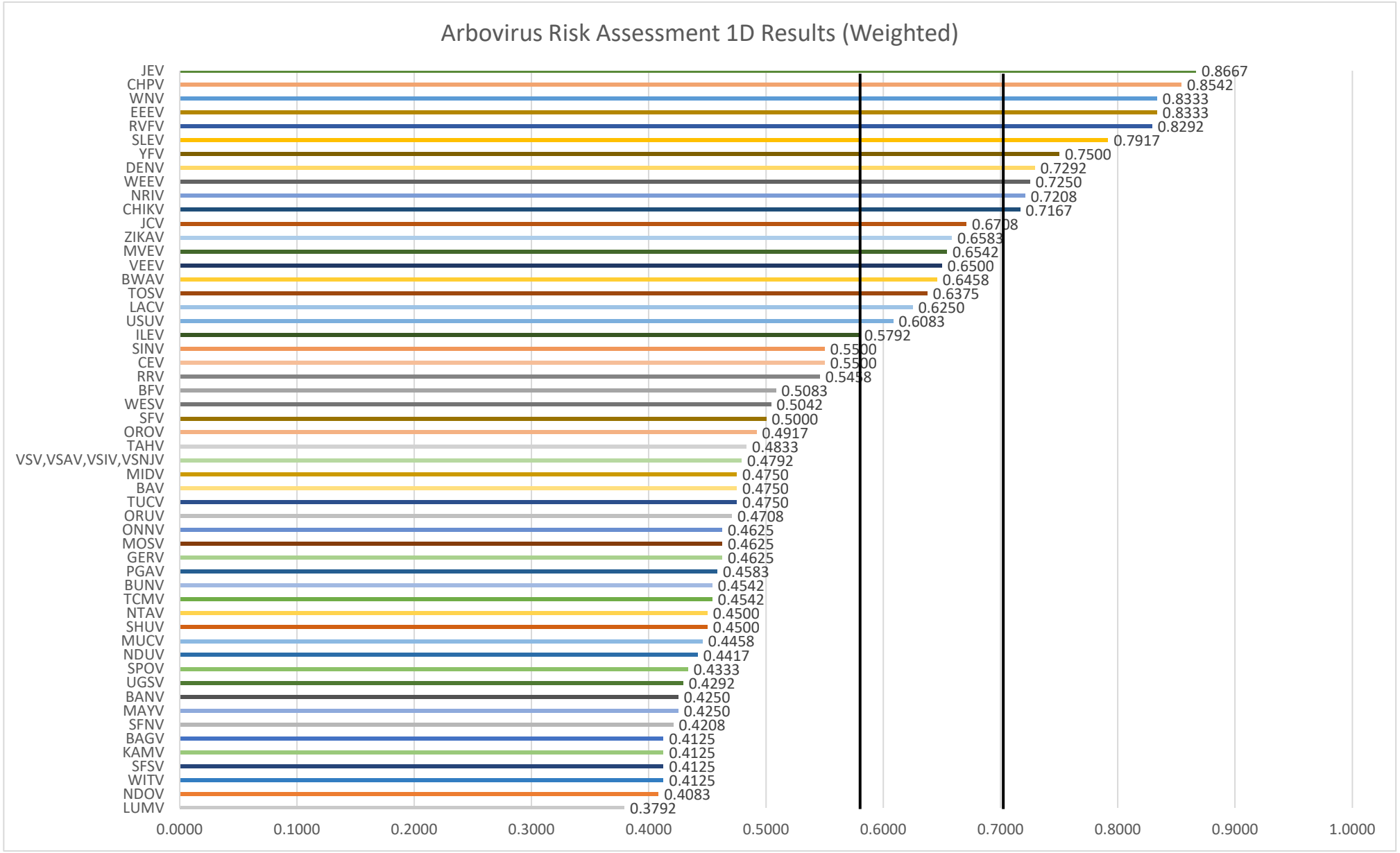

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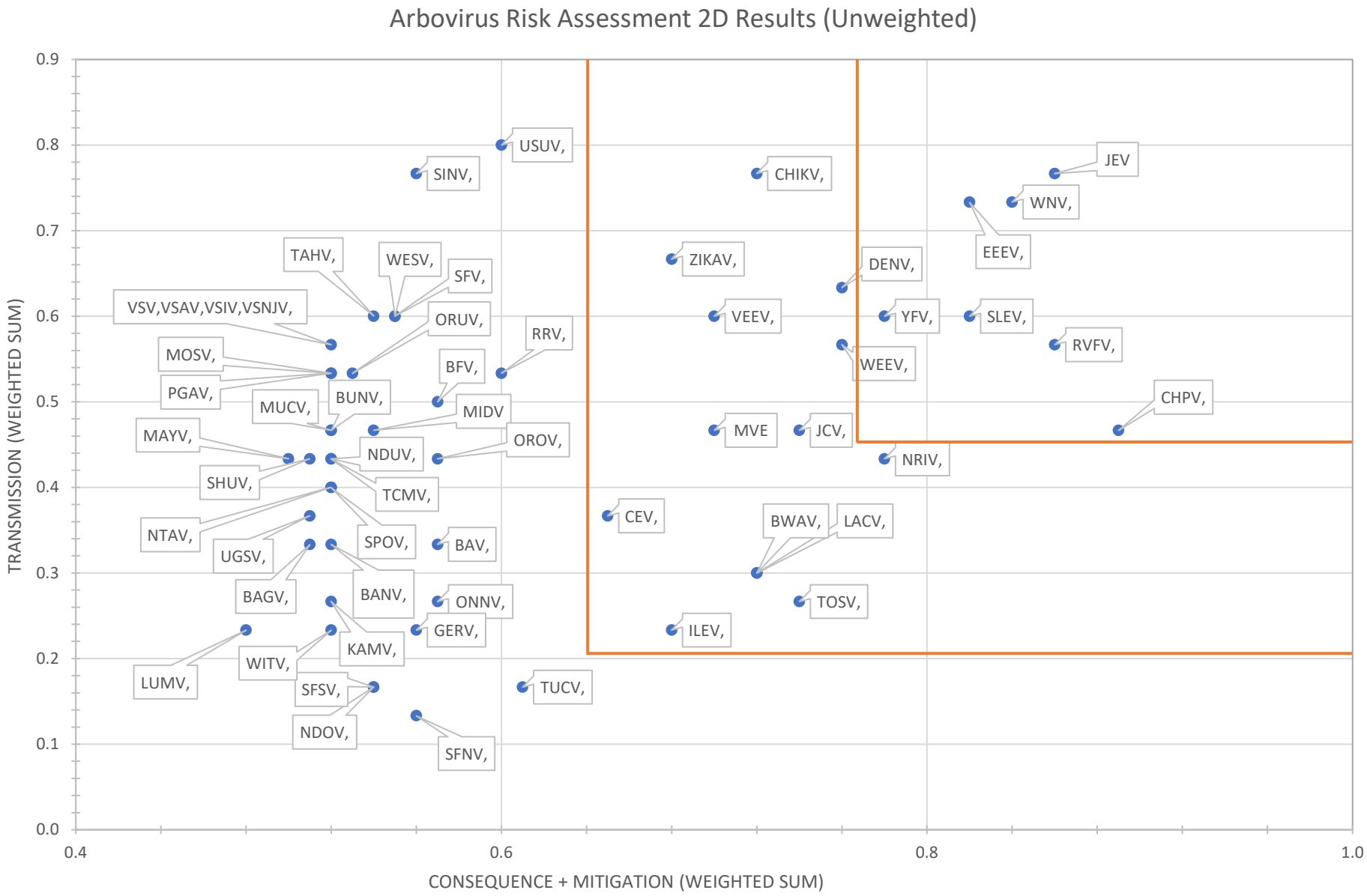

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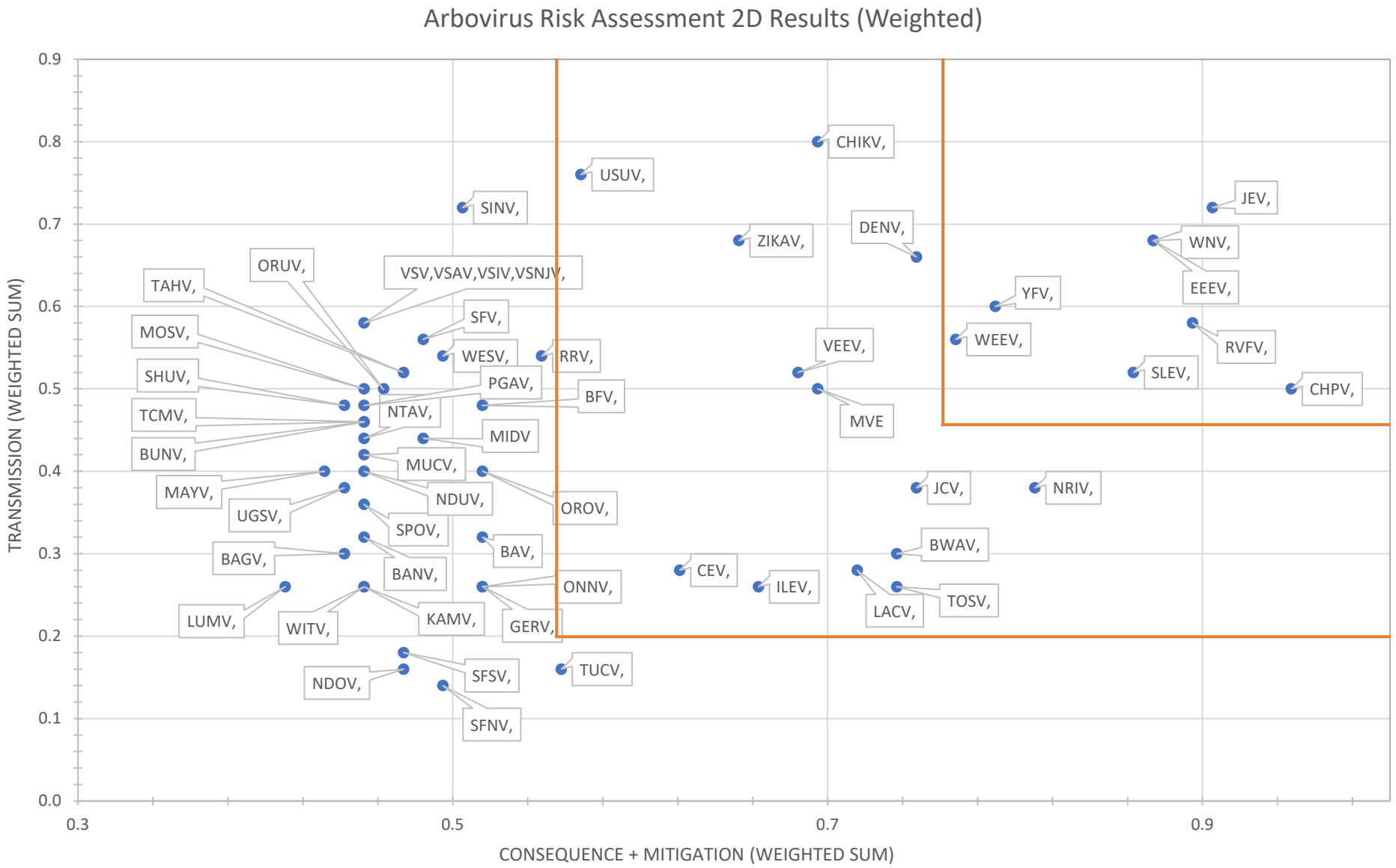
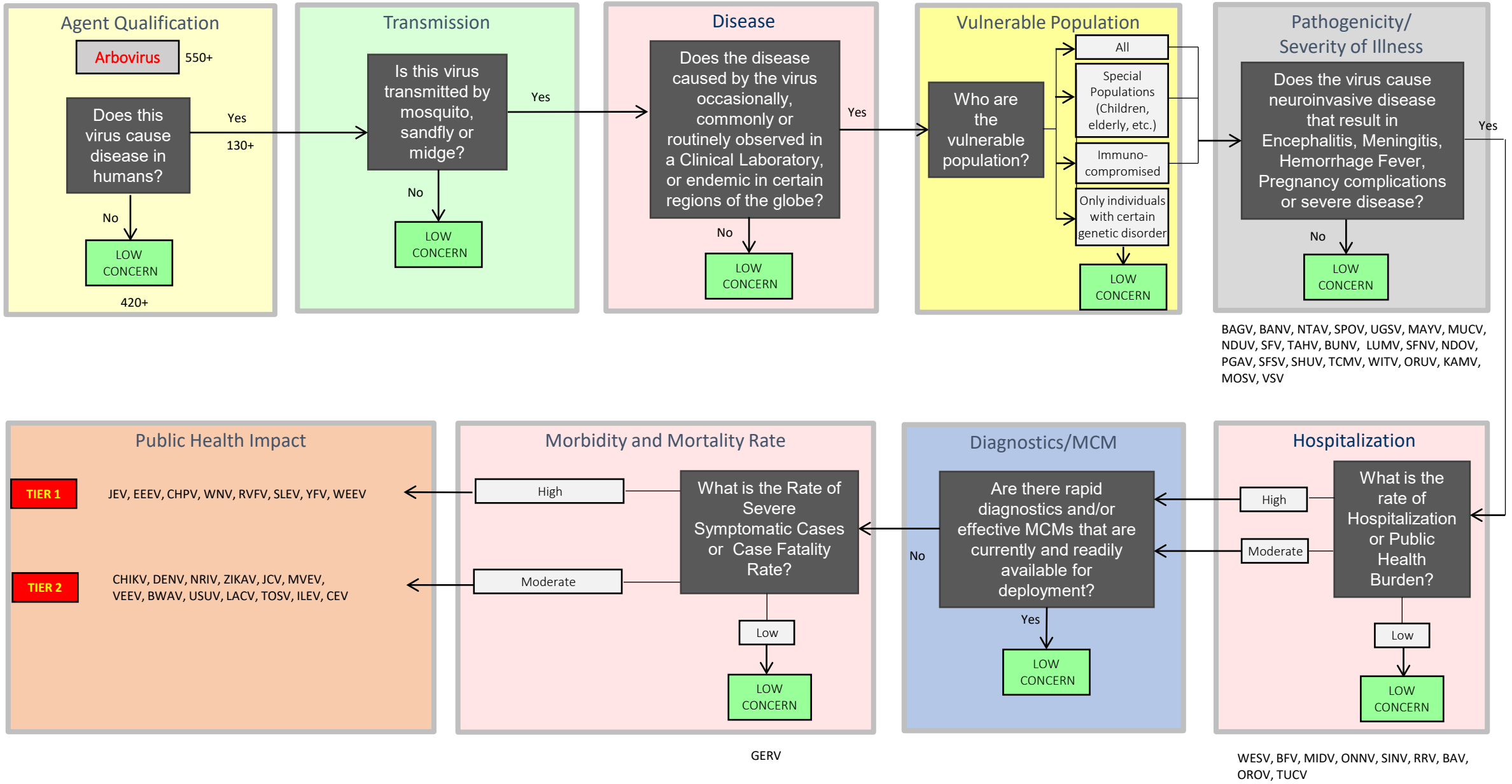


Decision Support Framework Results



Comparison of Results Using the Decision Support Framework and MCDA Approach

Decision Support Framework		Multi-Criteria Decision Analysis (MCDA) Approach							
Logic Tree Approach		1D, Unweighted		1D, Weighted		2D, Unweighted		2D, Weighted	
Tier 1	Tier 2	Tier 1	Tier 2	Tier 1	Tier 2	Tier 1	Tier 2	Tier 1	Tier 2
JEV	CHIKV	JEV	NRIV	JEV	JCV	JEV	CHIKV	JEV	CHIKV
EEEV	DENV	EEEV	ZIKAV	EEEV	ZIKAV	EEEV	DENV	EEEV	DENV
CHPV	NRIV	CHPV	JCV	CHPV	MVEV	CHPV	WEEV	CHPV	NRIV
WNV	ZIKAV	WNV	MVEV	WNV	VEEV	WNV	NRIV	WNV	ZIKAV
RVFV	JCV	RVFV	VEEV	RVFV	BWAV	RVFV	ZIKAV	RVFV	JCV
SLEV	MVEV	SLEV	BWAV	SLEV	TOSV	SLEV	VEEV	SLEV	MVEV
YFV	VEEV	YFV	USUV	YFV	LACV	YFV	JCV	YFV	VEEV
WEEV	BWAV	WEEV	LACV	WEEV	USUV		MVEV	WEEV	BWAV
	USUV	DENV	TOSV	DENV			BWAV		USUV
	LACV	CHIKV	RRV	CHIKV			TOSV		LACV
	TOSV		CEV	NRIV			ILEV		TOSV
	ILEV		SINV				CEV		ILEV
	CEV								CEV