



Nerve Agent ChE Operational Impact from Dermal Exposures

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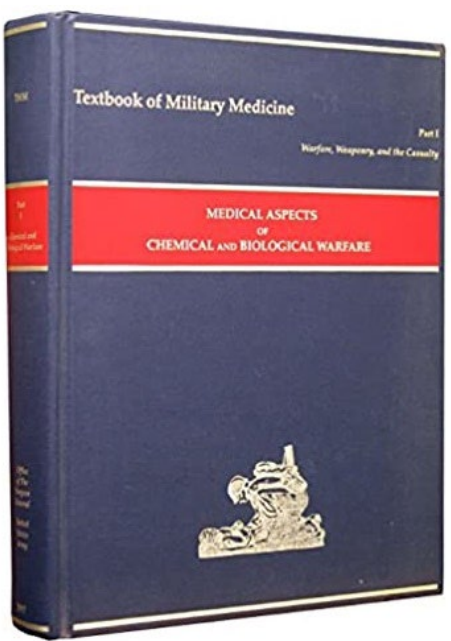


THE CHALLENGE

The Chemical and Biological Defense community is tasked to protect the warfighter from chemical and biological threats. New equipment for detection, protection or decontamination is frequently evaluated against health based metrics in order to ensure chemical or biological exposures do not impair the warfighter from completing their mission. For nerve agents these evaluations require a linkage between commonly measured toxicological endpoints (cholinesterase depression) and symptomology that would impact military operations.

MEDICAL NERVE AGENT SEVERITY GUIDANCE

The US Army Office of the Surgeon General has published guidance on assessing nerve agent dermal exposures on a general severity scale.



Level	Effects	Time to effect
Mild	Increased sweating at site Muscular fasciculation at site	Effects may be precipitant in onset after an asymptomatic interval of up to 18 hours
Moderate	Mild effects + Nausea Diarrhea Generalized weakness	
Severe	Moderate effects + Loss of consciousness Convulsions (seizures) Generalized fasciculations Flaccid paralysis Apnea Generalized secretions Involuntary micturition/ defecation possible with seizures	Effects may be precipitant in onset after a 2-30 min asymptomatic interval

Score	Symptoms	Operational relevance
0	No signs	No operational impact
1 (mild)	Local sweating or itching, dreams, headache, nightmares	No operational impact
2 (moderate)	Nausea, vomiting, weakness, dizzy	Operational degradation
3 (severe)	Paralysis, profuse vomiting	Loss of operational capability

Using this guidance an ordinal rubric was developed to assign scores to symptomology recorded in toxicological studies



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TOXICOLOGICAL STUDIES

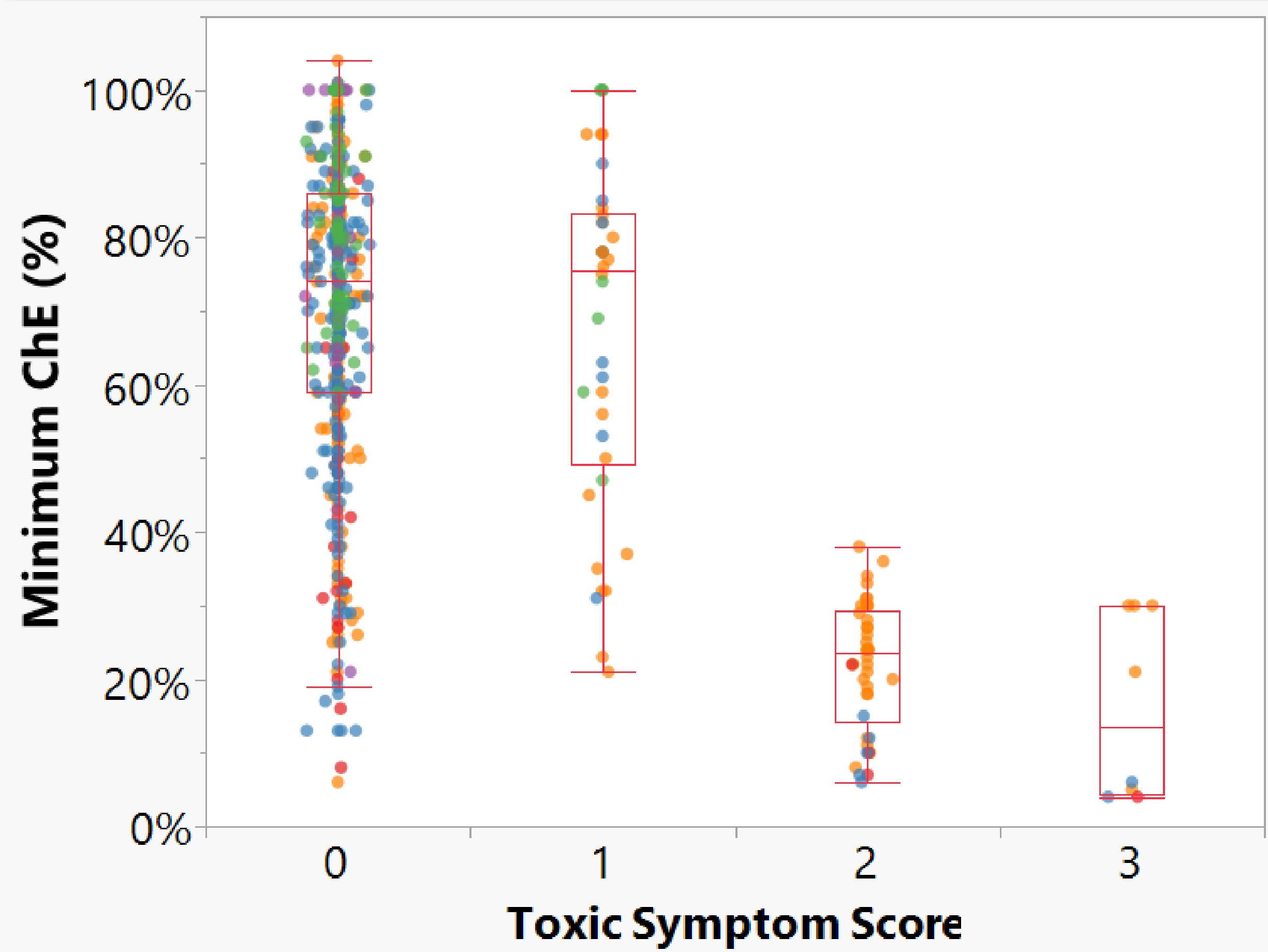
Multiple studies were identified that provided both cholinesterase measurements and symptomology for multiple nerve agents.

Quantitative			
Source	Exposure Route	# Trials	Minimum ChE
Sim 1962	PC Liquid	156	5%
Sidel 1965	IV	31	4%
McGrath 1951	PC Vapor	14	31%
Bramwell 1963	IH Vapor	19	30%
Bramwell 1963	PC Vapor	35	30%
Cullumbine 1953	PC Liquid	260	4%
Neitlich 1965	PC Liquid	37	47%

Qualitative			
Source	Route	# Trials	Min ChE
Bertino 1957	Multiple	16	11%
Reutter-Cristy et.al 2010	PC and IV	96 Rabbit 64 minipig	0%
McGrath 1951			
Sim 1962			

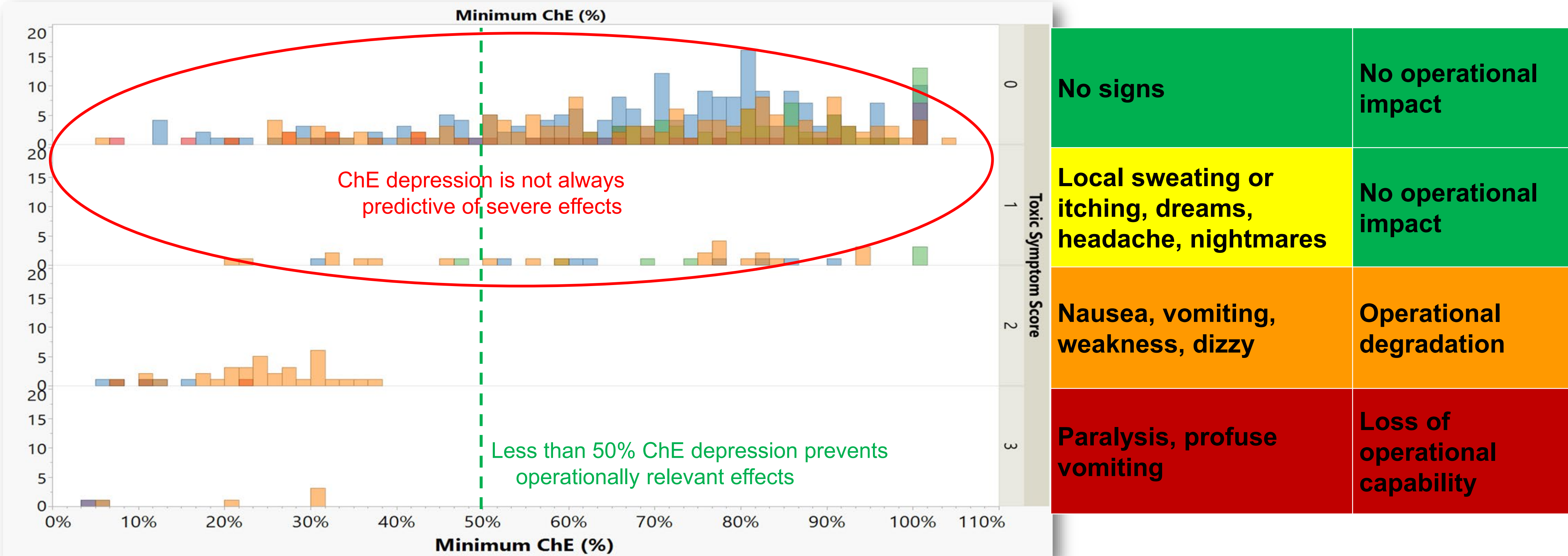
SYMPTOMOLOGY SCORE VS CHE DEPRESSION

Using the symptomology scoring rubric, each subject’s symptomology was scored and plotted against the measured ChE depression from the toxicological studies

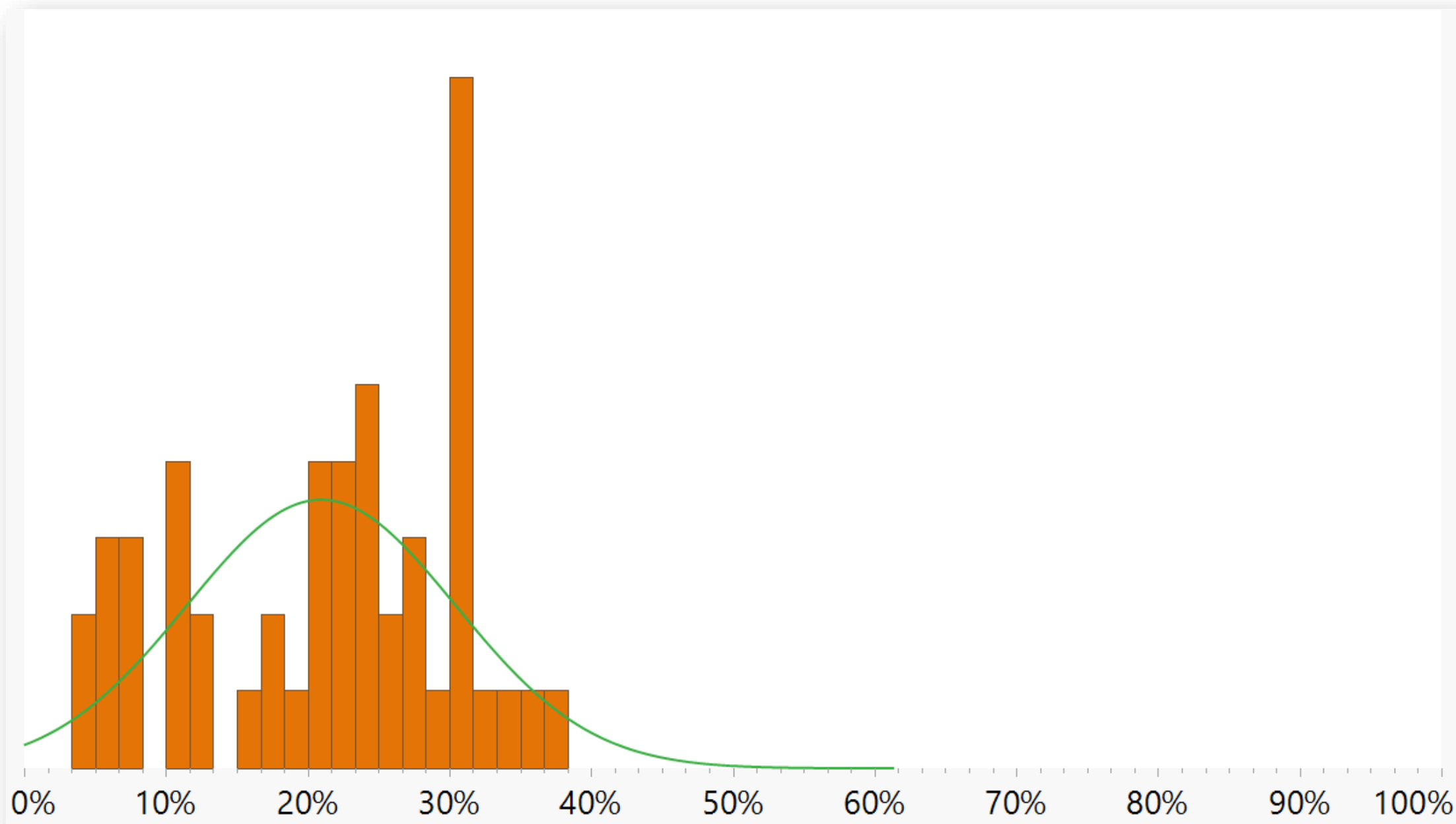


RESULTS

The linkage between ChE depression and symptomology, specifically using ChE depression to predict symptomology was considered unfeasible due to observations of subjects with almost complete ChE depression and no symptomology. However, in this analysis we show the reverse is possible. i.e. the ability to link severe symptomology to a ChE depression level.



There were fewer measurements of ChE depression associated with severe symptomology, however fitting a distribution to the data that was available indicated that selecting a value of 50% ChE depression has less than a 1% chance of causing severe symptomology in an exposed population.



CONCLUSIONS

Preventing >50% ChE depression from exposure to nerve agents should limit health effects to mild, reversible effects and prevent operationally relevant symptomology in the warfighter.

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