微生物学的リスク評価事例

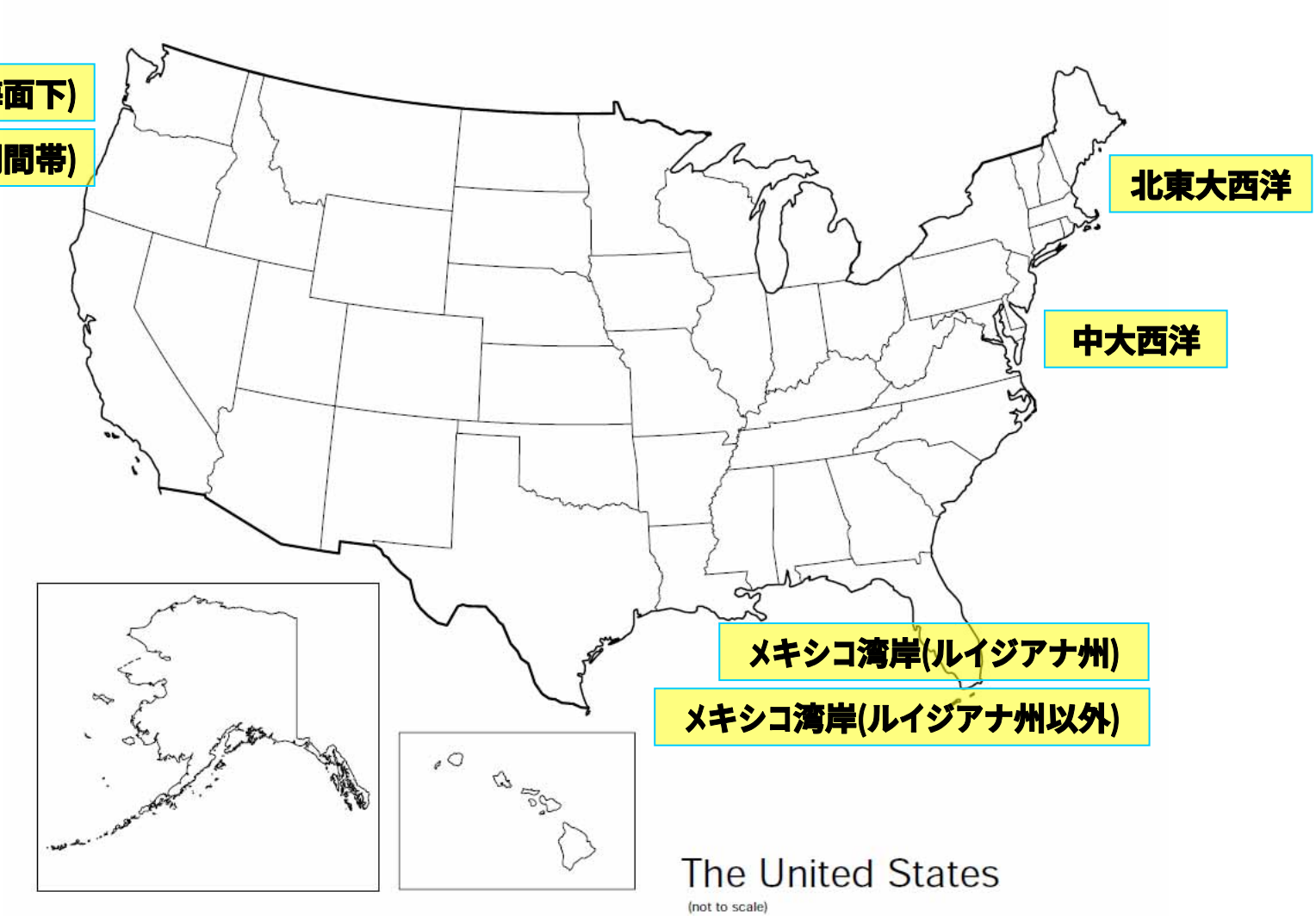
米国Food and Drug Administration (FDA)の “Quantitative Risk Assessment on the Public Health Impact of Pathogenic *Vibrio parahaemolyticus* in Raw Oysters”の紹介

米国FDAの“Quantitative Risk Assessment on the Public Health Impact of Pathogenic *Vibrio parahaemolyticus* in Raw Oysters”は、

生かきの摂食に関する*V. parahaemolyticus*の公衆衛生上のリスクに影響する因子を明らかにするための定量的リスク評価

1999年1月	作業開始
2000年12月	草稿公表 “Draft Risk Assessment on the Public Health Impact of *Vibrio parahaemolyticus* in Raw Molluscan Shellfish”
2005年7月	改訂版公表 “Quantitative Risk Assessment on the Public Health Impact of Pathogenic *Vibrio parahaemolyticus* in Raw Oysters”

全米を6つの地域･採捕方法に分け、それぞれに春夏秋冬を考慮

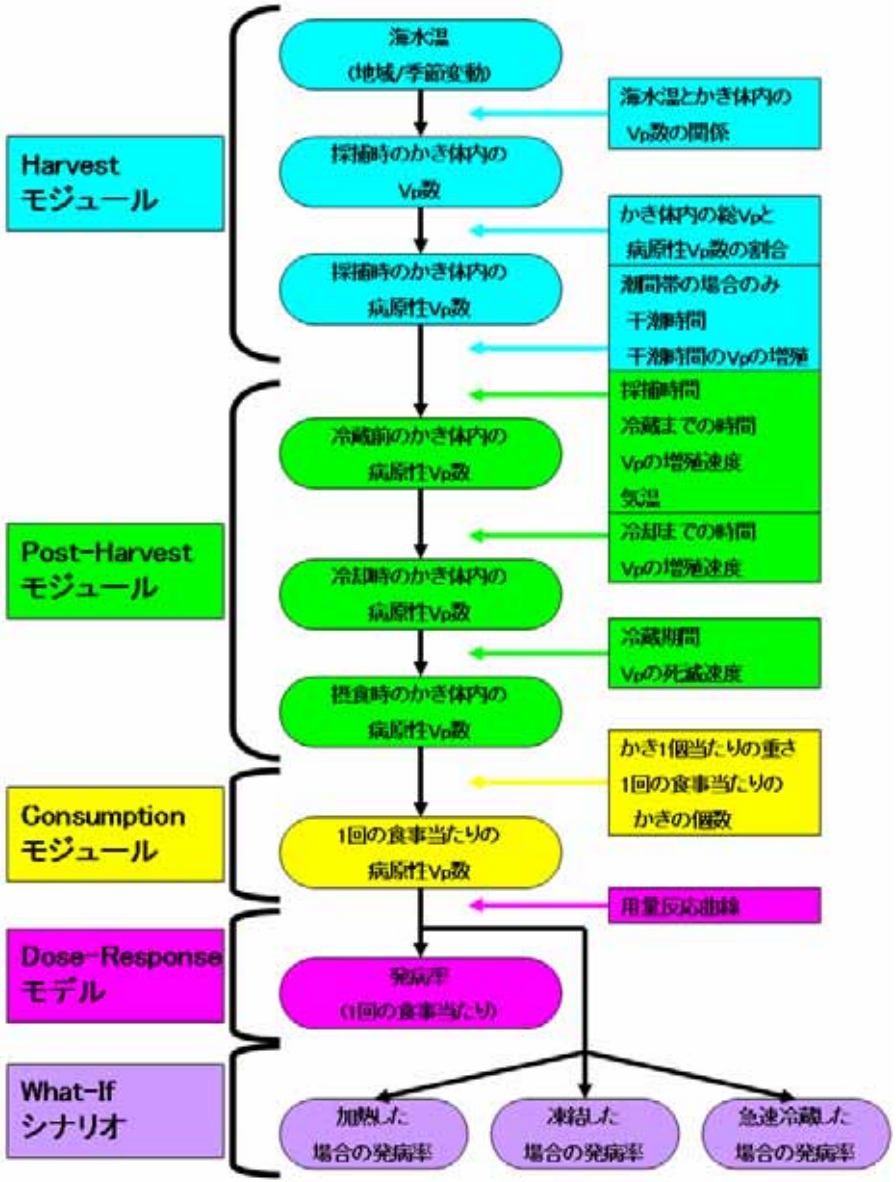


6つの地域･採捕方法×春夏秋冬＝24通りのシミュレーション

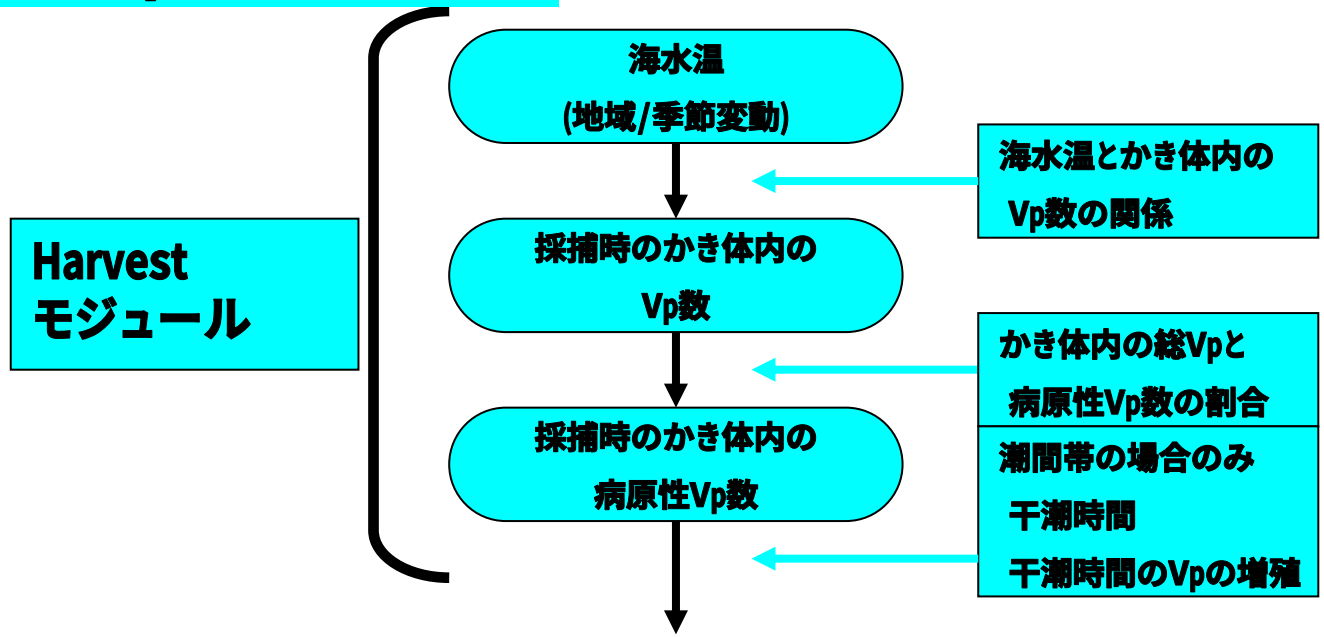
FDAのリスクアセスメント・モデルの主要部分
(メキシコ湾岸(ルイジアナ州)の夏)

	A	B	C	D	E	F	G	H	I	J	K	L	M	N
1	Gulf Coast	Louisianna			Light green cells contain the 'no mitigation' calculation.									
2	Summer													
3	3				No mitigation				Water and Vp density		Parameters			
4		Water parameters							a_w	0.985				
5		mean m			28.80128				b	0.0356				
6		mean s			1.537398				c	0.34				
7		Water temperature			28.80128		degrees C		T_min	278.5	degree K			
8		Temperature->Vp statistics							T_max	319.6	degree K			
9		intercept			-0.46834				a_w_min	0.921				
10		slope			0.093791				a_w_max	0.998				
11		sigma			0.724242				d	263.64	degree K			
12									lag	0	hours			
13									max density	6	log cfu/gram			
14					**total Vp**	**pathogenic Vp**								
15						0.001895	% pathogenic at harves		max density	3.277705	log cfu/gram			
16		Log Vp level density at harvest			2.232971	-0.489324								
17		Log Vp level in environ. Trunc			2.232971	-0.489324	log counts/g	170.99	0.32	0				
18		Time on flat					hours	temp increase on flat						
19		estimated growth rate							degrees C					
20		outgrowth on flats				0	log counts/g	sqrt(max growth rate)						
21		Log Vp level on flats				-0.489324	log counts/gram							
22		Harvesting parameters												
23		min time on water			5									
24		likely time on water			9							axenic to c	4.693387	
25		max time on water			11							landings	2,854,000	lbs
26		Time on the water			8.666667		hours					Oysters pe	13	
27		Time unrefrigerated			4.833333		hours					**total raw s**	**3,236,436**	
28		Air temperature parameters												
29		μ			-1.66									
30		σ			1.33							Fraction pa	0.001895	
31		Ambient air temp			27.14128		degree C							
32												counter	0	
33		sqrt(max growth rate)			0.191458	0.191458							244.1564	
34												alpha	0.52	
35		Estimate growth rate in oysters			0.203514	0.203514	log counts/hr					beta	97862872	
36														
37		outgrowth1			0.983651	0.983651		6716.82	12.73	0			5.31E-09	
38		Predicted counts at 1st refrigerat			3.216622	0.494327	log counts/gram			rapid cool				
39		Duration of cooldown			5		hours	Heat	Freeze	mitigation				
40		outgrowth2			0.610542	0.610542		treatment	treatment					
41		Predicted counts after cooldown			3.827164	1.104868		four.five log	two log	0.121218				
42		Length of refrigeration time			7.7		days	reduction	reduction					
43														
44		Predicted level after die off			3.330364	0.608068	log counts/	-3.891932	-1.391932	-0.375582				
45					2139.75	4.06	0							
46		Grams oysters consumed			188.5006		grams							
47														
48		Vp exposure per meal			403344.9	764.5064	mean count	0.024176	7.645064	79.38356				
49		Pathogenic Vp consumed				765	counts	0	8	79				
50						2.883381	log mean counts							
51		probability of illness				4.06E-06		0	4.25E-08	4.2E-07				
52														
53														
54														

リスクアセスメント・モデルの構造



採捕時の病原性 *Vp*数を求める



採捕時の総 *Vp*数[*1]×総 *Vp*に対する病原性 *Vp*の割合

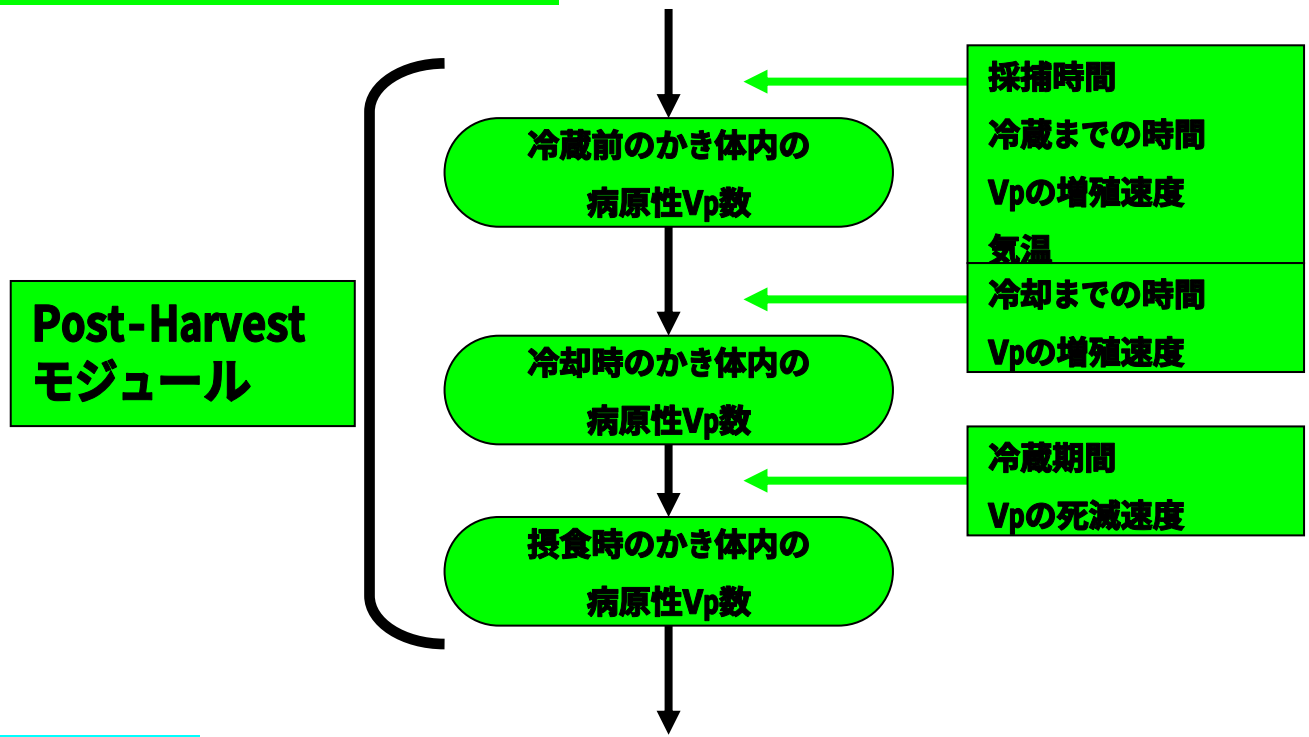
[*1]採捕時の総 *Vp*数は海水温に比例

北西太平洋(潮間帯)の場合のみ、
上記＋干潮中の病原性 *Vp*数の増殖[*2]

[*2]総 *Vp*の増殖速度[*3]×(干潮時間＋1)×総 *Vp*に対する病原性 *Vp*の割合

[*3]総*Vp*の増殖速度は気温に依存

摂食時の病原性*Vp*数を求める



採捕時の病原性*Vp*数＋冷蔵前の病原性*Vp*の増加[*3]＋冷却中の病原性*Vp*の増加[*4]－冷蔵中の病原性*Vp*の死滅[*5]

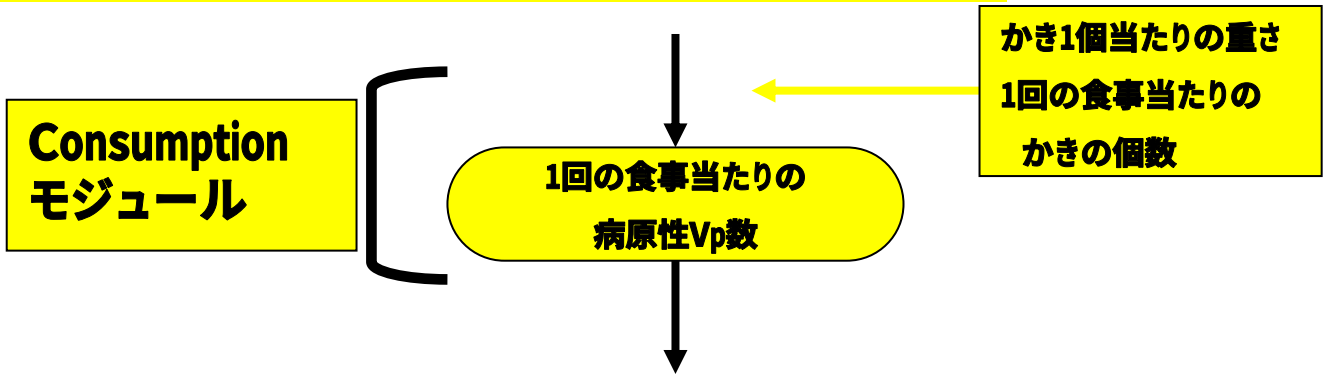
[*3]総*Vp*の増殖速度×採捕時間×総*Vp*に対する病原性*Vp*の割合

[*4]総*Vp*の増殖速度×(冷却時間＋1)/2×総*Vp*に対する病原性*Vp*の割合

[*5]総*Vp*の死滅速度×冷蔵時間×総*Vp*に対する病原性*Vp*の割合

北西太平洋(潮間帯)の場合、採捕時間から干潮時間を引いて計算

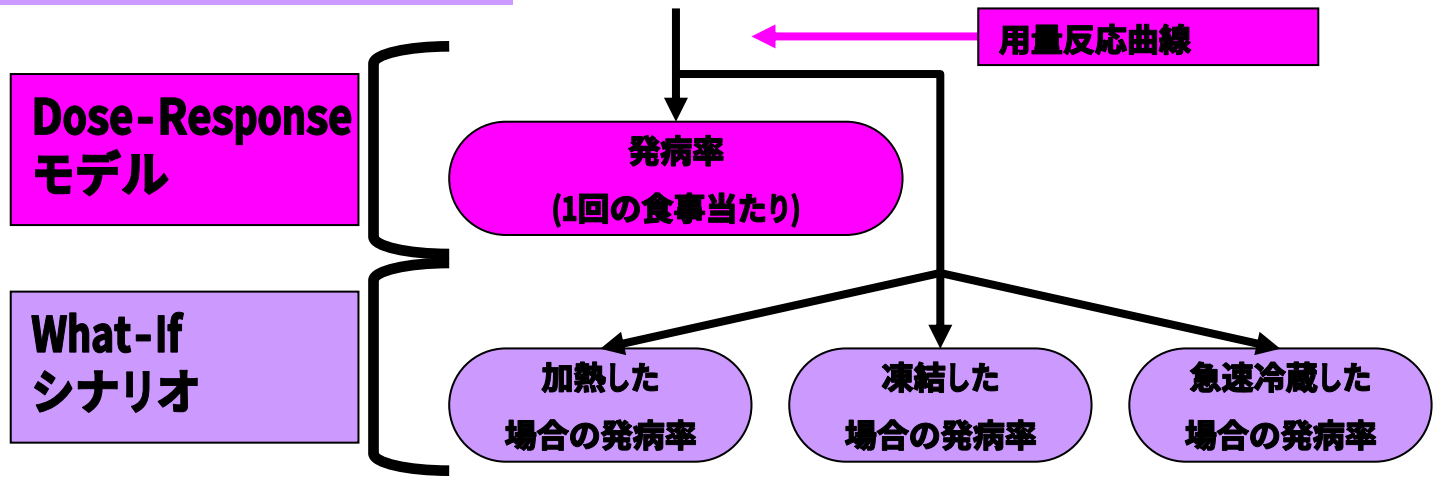
1回の食事で摂取される病原性*Vp*数を求める



摂食時の病原性*Vp*数×1回の食事当たりの生かきの個数×かき1個当たりの身の重量

実際の発病率を求める

シナリオ上の発病率を求める



1回の食事で摂取される病原性*Vp*数から1回の食事当たりの発病率を推定

加熱した場合(総*Vp*数が$10^{4.5}$減少)
凍結した場合(総*Vp*数が10^{2}減少)
採捕後、すぐに冷蔵した場合(冷蔵前の総*Vp*の増加を考えない)
の1回の食事当たりの発病率を推定

それぞれの地域･採捕方法、季節における胃腸炎発症者数の予測
(発病率×採捕量で計算)

Region	Mean Annual Number of Illnesses[a]				
	Summer (July to Sept)	Fall (October to December)	Winter (January to March)	Spring (April to June)	Total
Gulf Coast (Louisiana)	1406 (109, 4435)	132 (6, 468)	7 (0.2, 26)	505 (36, 1624)	2,050
Gulf Coast (Non-Louisiana)[b]	299 (22, 985)	51 (2, 180)	3 (<0.1, 11)	193 (13, 631)	546
Mid-Atlantic	7 (0.36, 25)	4 (<0.1, 17)	<0. 1 (<0.01, <0.1)	4 (0.2, 15)	15
Northeast Atlantic	14 (0.6, 53)	2 (0.1, 7)	<0.1 (<0.01, <0.1)	3 (<0.1, 12)	19
Pacific Northwest (Dredged)	4 (<0.1, 16)	<0.1 (<0.01, <0.1)	<0.1 (0, <0.01)	0.42 (<0.1, 2)	4
Pacific Northwest (Intertidal)[c]	173 (4, 750)	1 (0.01, 4)	<0.01 (<0.01, 0.01)	18 (<0.1, 81)	192
TOTAL	1,903	190	10	723	2826

[a] Mean annual number illnesses refers to predicted annual number of illnesses (gastroenteritis alone or gastroenteritis followed by septicemia) in the United States each year. Values in parentheses are the 5th and 95th percentiles of the uncertainty distribution. Note: Actual values for the illness predictions are provided in Appendix 7.

[b] Includes oysters harvested from Florida, Mississippi, Texas, and Alabama. The typical time from harvest to refrigeration of oysters for these states is shorter than for Louisiana.

[c] Oysters harvested using intertidal methods are typically exposed to higher temperature for longer times before refrigeration compared with dredged methods.

それぞれの地域･採捕方法、季節における発症敗血症者数の予測
(胃腸炎から敗血症に進行する確率を0.0023と推定した場合)

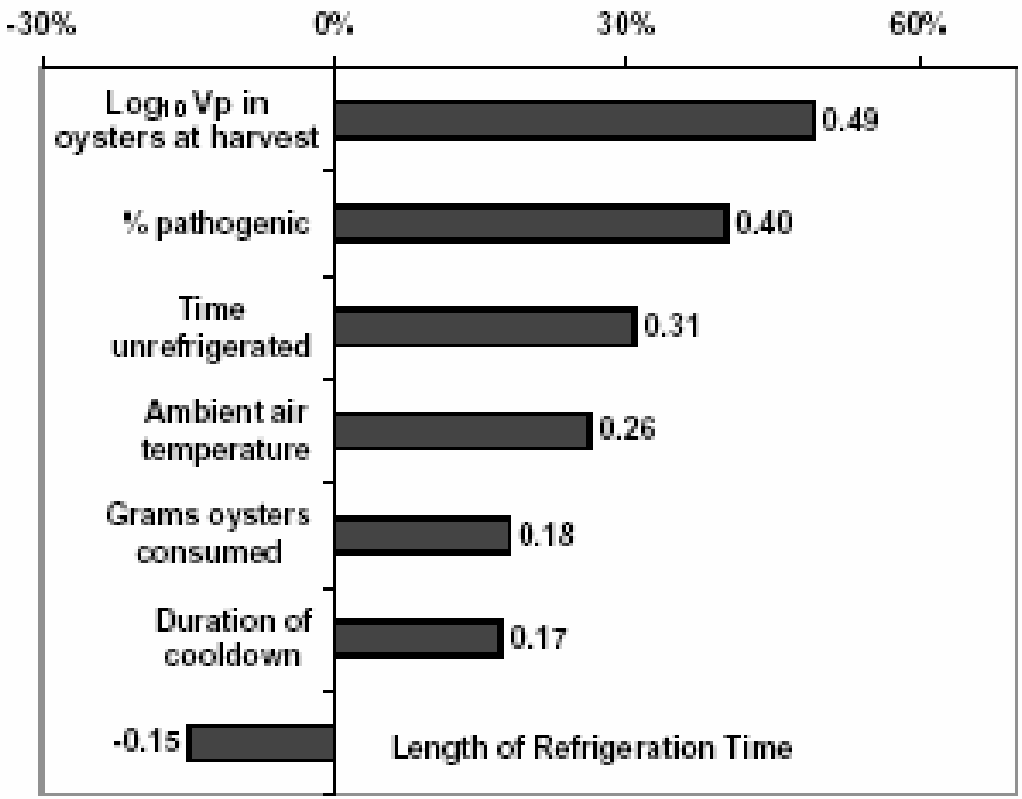
Region	Mean Annual Cases of Septicemia[a]				
	Summer (July to Sept)	**Fall** (October to December)	**Winter** (January to March)	**Spring** (April to June)	**Total**
Gulf Coast (Louisiana)	3	<1	<1	1	4
Gulf Coast (Non-Louisiana)[b]	<1	<1	<1	<1	1
Mid-Atlantic	<1	<1	<1	<1	<1
Northeast Atlantic	<1	<1	<1	<1	<1
Pacific Northwest (Intertidal)[c]	<1	<1	<1	<1	<1
Pacific Northwest (Dredged)[c]	<1	<1	<1	<1	<1
TOTAL	4	<1	<1	2	7

[a] Calculated by multiplying the estimated probability of septicemia (0.0023; Table III-4) by the mean predicted number of illnesses (Table V-2). Note: Actual values for septicemia cases shown as <1 are provided in Appendix 7.

[b] Includes oysters harvested from Florida, Mississippi, Texas, and Alabama. The typical time from harvest to refrigeration of oysters for these states is shorter than for Louisiana.

[c] Oysters harvested using intertidal methods are exposed to higher temperature for longer times before refrigeration compared with dredged methods.

変動性因子の感度分析結果(tornado plot)
(メキシコ湾岸(ルイジアナ州)の夏の場合)



採捕時の総*Vp*数 ＞ 総*Vp*に対する病原性*Vp*の割合 ＞ 非冷蔵の時間 ＞ 気温 ＞ 1回の食事当たりの生かきの重量 ＞ 冷却にかかる時間 ＞＞ 冷蔵時間

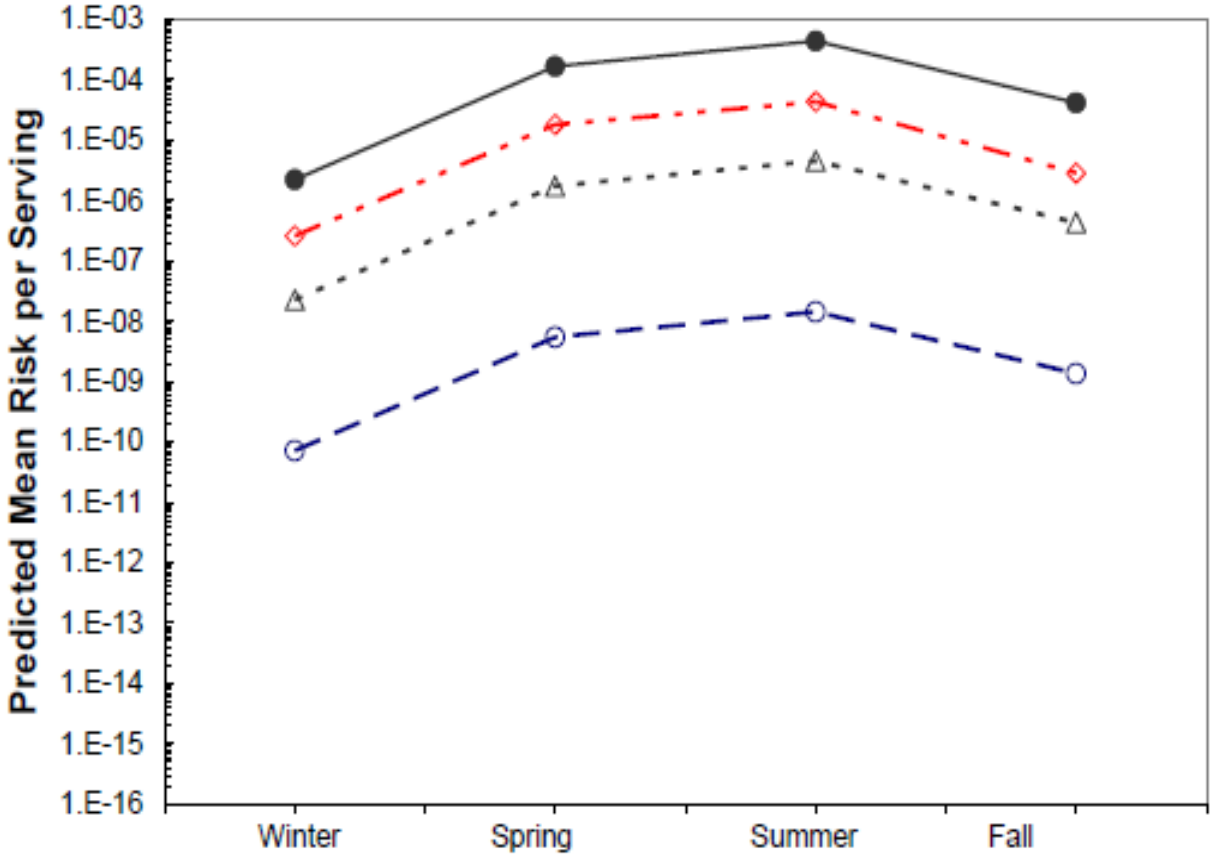
不確実性因子の感度分析結果
(メキシコ湾岸(ルイジアナ州)の夏の場合)

Uncertainty Factor	Conditional Variance[a]	Importance[b]
Dose-response model	5.23×10^{-8}	75.4%
Percentage pathogenic	1.77×10^{-7}	16.5%
Growth rate in oysters	1.83×10^{-7}	13.8%
Relationship of total *V. parahaemolyticus* levels and water temperature	1.89×10^{-7}	11.1%
Year-to-year water temperature variation	2.08×10^{-7}	2.0%

[a] Conditional variance refers to the variance of the uncertainty distribution of the mean risk per serving conditional on the specified uncertainty factors being fixed to nominal (mean) values, one at a time.
[b] Importance is based on a comparison to an unconditional variance of 2.12×10^{-7} for the distribution of mean risk per serving from a simulation in which all uncertainty factors vary.

Dose-Responseモデル ＞＞ 総*Vp*に対する病原性*Vp*の割合 ＞ *Vp*の増殖速度 ＞ 採捕時の総*Vp*数と海水温の関係 ＞ 海水温の年による変動

*Vp*数を減少させる対策を取った場合の胃腸炎発症率の変化 (メキシコ湾岸(ルイジアナ州)の場合)



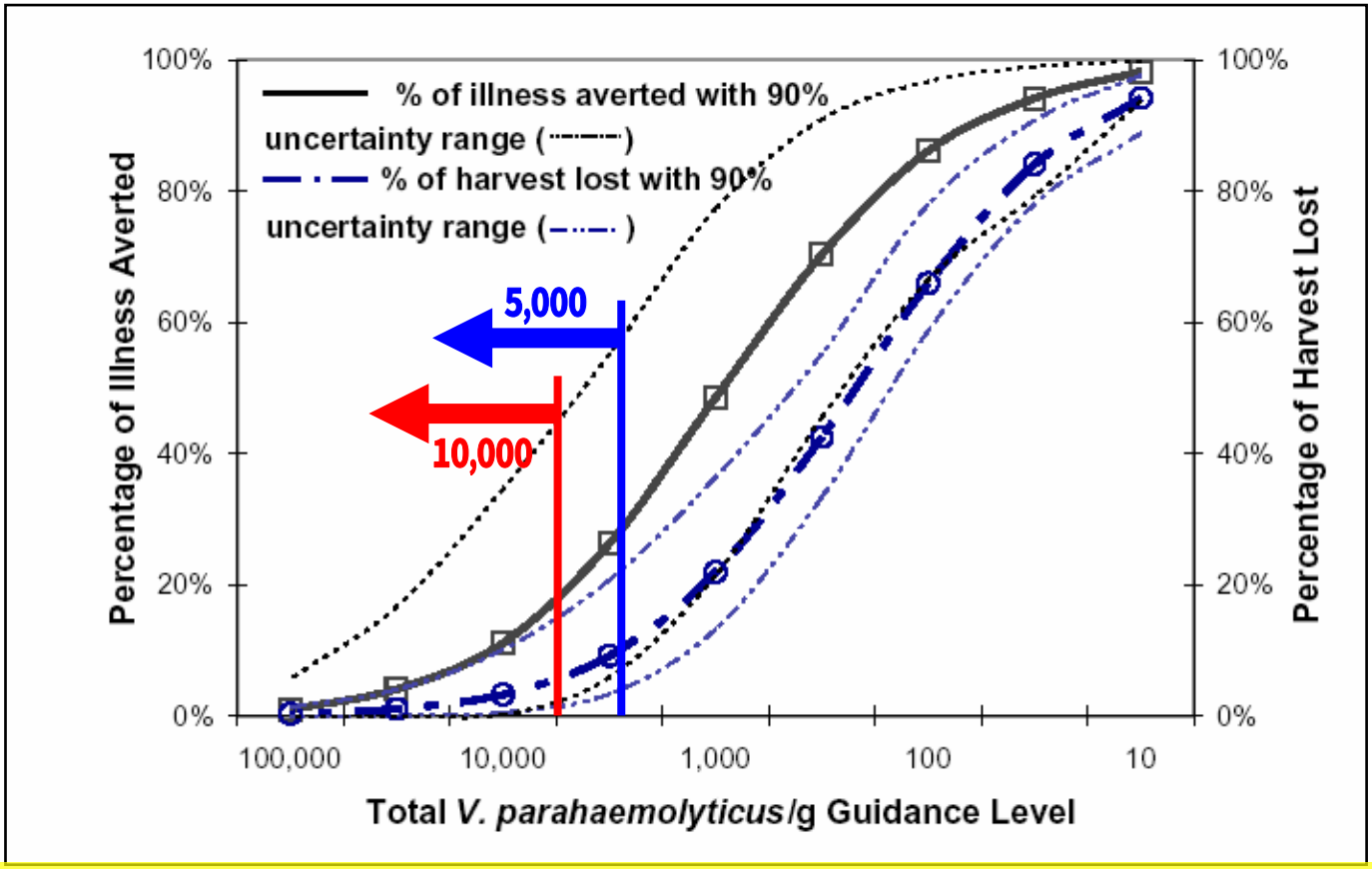
[No mitigation (●); immediate refrigeration upon harvest (◊); treatment resulting in a 2-$\log_{10}$ reduction (Δ); treatment resulting in a 4.5-$\log_{10}$ reduction (○).]

それぞれの地域･採捕方法、季節における *Vp*数を減少させる対策を取った場合の発症者数の変化

Region	Season	Predicted Mean Number of Illnesses per Annum[a]			
		Baseline	Immediate Refrigeration[b]	2-$\log_{10}$ Reduction[c]	4.5-$\log_{10}$ Reduction[d]
Gulf Coast (Louisiana	Spring	505	54	5.2	<1.0
	Summer	1,406	139	15	<1.0
	Fall	132	8.8	1.3	<1.0
	Winter	6.7	<1.0	<1.0	<1.0
Gulf Coast (Non-Louisiana)	Spring	193	29	2.0	<1.0
	Summer	299	42	3.1	<1.0
	Fall	51	7.7	<1.0	<1.0
	Winter	2.9	<1.0	<1.0	<1.0
Mid-Atlantic	Spring	4.4	<1.0	<1.0	<1.0
	Summer	6.9	<1.0	<1.0	<1.0
	Fall	3.8	<1.0	<1.0	<1.0
	Winter	<1.0	<1.0	<1.0	<1.0
Northeast Atlantic	Spring	3.0	<1.0	<1.0	<1.0
	Summer	14	1.7	<1.0	<1.0
	Fall	1.7	<1.0	<1.0	<1.0
	Winter	<1.0	<1.0	<1.0	<1.0
Pacific Northwest (Dredged)	Spring	<1.0	<1.0	<1.0	<1.0
	Summer	3.9	<1.0	<1.0	<1.0
	Fall	<1.0	<1.0	<1.0	<1.0
	Winter	<1.0	<1.0	<1.0	<1.0
Pacific Northwest (Intertidal)	Spring	18	10	<1.0	<1.0
	Summer	173	96	2.1	<1.0
	Fall	1.0	<1.0	<1.0	<1.0
	Winter	<1.0	<1.0	<1.0	<1.0

[a] Values rounded to significant digits. See Appendix 7 for actual values of numbers presented as <1.0.
[b] Represents conventional cooling immediately after harvest; the effectiveness of varies both regionally and seasonally and is typically approximately 1-log reduction.
[c] Represents any process which reduces levels of *Vibrio parahaemolyticus* in oysters 2-log, e.g., freezing.
[d] Represents any process which reduces levels of *Vibrio parahaemolyticus* in oysters 4.5-log, e.g., mild heat treatment, irradiation, or ultra high hydrostatic pressure.

採捕時の総*Vp*数に基準を設けた場合の発症者数の変化とかきの排除率(メキシコ湾岸(ルイジアナ州)の夏の場合)

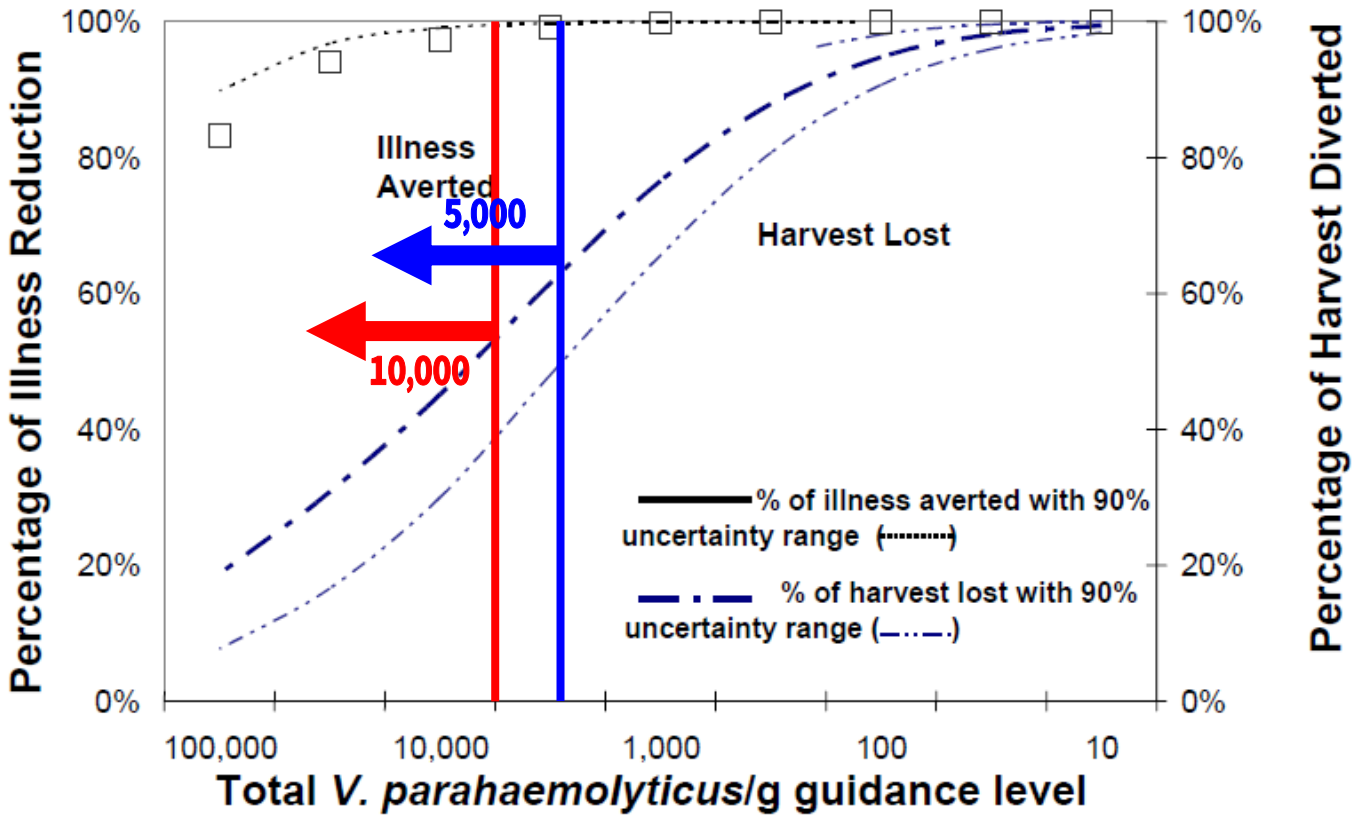


10,000個/g以上のかきを排除・・・発症者数16%減少、かきの廃棄率3%

5,000個/g以上のかきを排除・・・発症者数28%減少、かきの廃棄率6%

採捕後に*Vp*数が著しく増加することも少なくないため、効果は限定的

摂食時の総 *Vp* 数に基準を設けた場合の発症者数の変化とかきの排除率(メキシコ湾岸(ルイジアナ州)の夏の場合)



10,000個/g以上のかきを排除・・・発症者数99%減少、かきの廃棄率43%

5,000個/g以上のかきを排除・・・発症者数ほぼ100%減少、かきの廃棄率70%

採捕時の規制よりも発症者数は著しく減少するが、同時にかきの廃棄率も著しく増加する