Supplementary Material

Heterogeneity of selection and the evolution of resistance REX Consortium

Table S1. Theoretical models comparing at least two strategies for delaying the evolution of resistance to two or more pesticides or drugs.

C = *Combination*, PA = *Periodic application*, M = *Mosaic* and RA = *Responsive alternation*.

Pesticide or drug	Reference	Strategies compared	Relative efficy for delaying resistance
Insecticides	[1]	C[a], PA, RA	C > PA > RA
	[2]	C, M, RA	C > M > RA
	[3]	C, PA, RA	C > PA = RA
	[4]	C[a], PA	C > PA
	[5]	C, PA, M	C > PA > M
	[6]	C, RA	C > RA
	[7]	PA, M, RA	PA = M = RA
	[8]	C, PA, M	C > PA > M
	[9]	C, RA	conditional[b]
Bacillus	[10]	C[a], PA, M, RA	conditional[b] for C but PA = M > RA

thuringiensis toxins	[11]	C, PA	C > PA
	[12]	C, RA	C ≥ RA
Herbicides	[13]	C, PA, RA	C > PA = RA
	[14]	C, PA	C > PA
	[15]	C, PA, RA	C > PA > RA
Antibiotics	[16]	PA, M	M ≥ PA
	[17]	C, PA, M	C > M ≥ PA
	[18]	C, RA	C > RA
	[19]	PA, M	M > PA
	[20]	PA, M	conditional[b]
	[21]	C, PA, M	C > M ≥ PA
Other pesticides or drugs	[22]	C, PA	C > PA
	[23]	C, PA, RA	C > PA = RA
	[24]	C, PA, M	PA = M > C

	[25]	C, RA	C > RA
	[26]	PA, M	M ≥ PA
Unspecified	[27]	C, RA	conditional[b]
pesticides	[28]	C, RA	C ≥ RA
or drugs	[29]	C, PA	C ≥ PA

[a] *Combination* is considered as a *half-dose Combination* of the pesticides or drugs; *full-dose Combination* is compared with *half-dose Combination* in [10].

[b] The ranking of the strategies depends on the setting for one or several input or output parameters.

Table S2. Empirical studies comparing at least two strategies for delaying the evolution of resistance to two or more pesticides or drugs. C = *Combination*, PA = *Periodic application*, M = *Mosaic* and RA = *Responsive alternation*.

Pesticide or drug	Reference	Strategies compared	Relative efficacy for delaying resistance	Type of study	Species	Pitfalls[c]		Specific settings[d]	
						PE	IC	HF	AR
Insecticides	[30]	C, PA, RA	C = PA > RA	Laboratory	*Blatella germanica*	√	√	√	√
	[31]	C[a], PA, RA	C = PA = RA	Field	*Bemisia tabaci*	√	√	√	
	[32]	PA, RA	PA > RA	Laboratory	*Culex quinquefasciatus*	√	√	√	
	[33]	C[a], PA, RA	PA > C > RA	Field	*Scirtothrips citri*	√	√	√	√
	[34]	C, PA, RA	C > PA > RA	Laboratory	*Musca domestica*	√	√	√	√
	[35]	PA, RA	PA > RA	Field	*Musca domestica*	√	√	√	
	[36]	C, PA, RA	C = PA > RA	Laboratory	*Haematobia irritans*	√	√	√	√

	Ref	Treatments	Results	Setting	Species	PE	IC	HF	AR
	[37]	M, RA	M > RA	Laboratory	*Musca domestica*		√	√	
	[38]	C, PA, RA	C = PA = RA	Laboratory	*Musca domestica*	√	√	√	√
	[39]	C, PA, RA	C = PA > RA	Laboratory	*Bemisia argentifolii*	√	√	√	√
Bacillus thuringiensis toxins	[40]	PA, M	PA > M	Greenhouse	*Plutella xylostella*			√	
	[41]	C, RA, M	C > RA > M	Greenhouse	*Plutella xylostella*		√	√	
	[42]	C, RA	C > RA	Laboratory	*Plodia interpunctella*	√	√	√	√
	[43]	C, RA	C > RA	Laboratory	*Culex quinquefasciatus*	√	√		√
Herbicides	[44]	C, PA	C > PA	Field	*Thlaspi arvense*			√	√
Antibiotics	[45]	PA, M	PA > M	ICU[b]	*Pseudomonas aeruginosa*	√		√	
	[46]	PA, M	M > PA	ICU[b]	*Acinetobacter baumannii*	√	√	√	

[a] *Combination* is considered as a *half-dose Combination* of the pesticides or drugs.

[b] Intensive care unit.

[c] Pitfalls: PE = problems in experimental design (lack of replicates, no randomization, confounding factors etc.) and IC = incorrect comparisons.

[d] Specific settings: HF = high frequencies of resistance before selection and AR = absence of refuges when testing *Combination*.

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