CRMVT
Centre de Référence des Maladies Vectorielles liées aux Tiques
Région Grand Ouest

Best of MVT

Dr Sorya Belaz
Parasitologue - Service de mycologie et parasitologie au CHU Pontchaillou Rennes
Dr Sophie Blanchi
Infectiologue - Service de Maladies Infectieuses CH Le Mans
CRMVT Grand Ouest/CCMVT Le Mans

Guérin *et al. BMC Microbiology* (2023) 23:204
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Lyme borreliosis diagnosis: state of the art of improvements and innovations

Mickaël Guérin[1], Marc Shawky[2], Ahed Zedan[3], Stéphane Octave[1], Bérangère Avalle[1], Irene Maffucci[1] and Séverine Padiolleau-Lefèvre[1*]

- Revue de la littérature : Sérologie
  - Bonne Se et Sp de la stratégie 2 ELISA comparée à la stratégie classique ELISA WB

Table 1 Sensitivity and specificity for STTT

Symptoms / Stage of the disease	Europe		
	Sensitivity	Specificity	References
Erythema migrans or early Lyme borreliosis *Acute phase[c] (AP)*	23–55%	75–99%	[34, 58–61]
Erythema migrans or early Lyme borreliosis *Convalescent phase[d] (CP)*	30–67%	95%	[61]
Acute-phase neurologic or cardiac involvement	69–97%	98–99%	[58, 61]
Arthritis or late neurologic involvement	78–100%	98–99%	

Table 2 Examples of sensitivity and specificity for MTTT in America and in Europe

Methods used		Symptoms / Stage of the disease	Patient's localization				
			America			Europe	
First test	Second test		Sensitivity	Specificity	References	Sensitivity	Specificity
VlsE C6-ELISA	na	Erythema migrans or early Lyme borreliosis *AP*	29%	96%	[68]	65–68%	91–92%
		Erythema migrans or early Lyme borreliosis *CP*	56%	96%		80–82%	
		Acute-phase neurologic or cardiac involvement	98–100%	96%		94–100%	
		Arthritis or late neurologic involvement	98–100%	96%		94–100%	
Enzygnost-2®	C6-ELISA	Erythema migrans or early Lyme borreliosis	na			78%	96%
Whole-Cell Sonicate ELISA	C6-ELISA	Erythema migrans or early Lyme borreliosis *AP*	38–58%	98–100%	[20, 34]	na	
		Erythema migrans or early Lyme borreliosis *CP*	76–79%	98–100%			
Borrelia DotBlot G®	na	nd	93%	35%	[69]		
MarDx® EIA	na		100%	92%			
VIDAS®	na		100%	90%			
VlSE1-IgG	pepC10-IgM	Erythema migrans or early Lyme borreliosis *AP*	46%	96%	[54]		
		Erythema migrans or early Lyme borreliosis *CP*	89%				
		Acute-phase neurologic or cardiac involvement	100%				
		Arthritis or late neurologic involvement	100%				
VlsE1-pepC10	C6-ELISA	Erythema migrans or early Lyme borreliosis *AP*	na			51%	94–95%
		Erythema migrans or early Lyme borreliosis *CP*				67%	
		Acute-phase neurologic or cardiac involvement				88%	
		Arthritis or late neurologic involvement				90%	

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- Revue de la littérature : Sérologie
  - Bonne Se et Sp de la stratégie 2 ELISA comparée à la stratégie classique ELISA WB
  - Amélioration de l'ELISA? iPCR se 69%-sp 98%

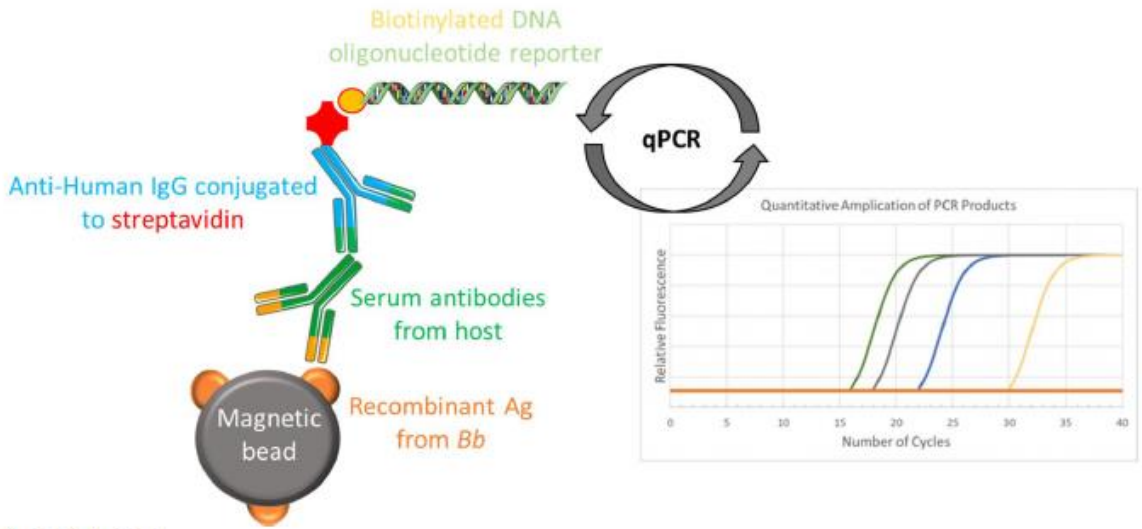

Fig. 4 iPCR principle

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- Revue de la littérature :
  - TDR
    - Se très faible sauf avec un « Reader »
    - Existe un test « multi TBP » xVFA
  - Système micro fluidique
  - Tests de la réponse cellulaire
    - Sp et ou Se : Faibles ➔ faux positifs et faux négatifs, non adaptés à la pratique clinique

Table 3 Sensitivity and specificity for emerging but not yet accredited laboratory tests

Classification	Tests	Sensitivity	Specificity
Microfluidics, lateral and vertical flow immunoassay	mChip-Ld	84%	92%
	Lyme IgM and IgG	26%	85%
	Keul-o-test Borreliose Complete IgM and IgG test	32%	88%
	ReaScan + C6 LYME IgG	83%	91%
	Multiplexed vertical flow assay (xVFA)	86%	96%
Luminex	Paramagnetic bead-based multiplex assay and INTELLIFLEX System	94%	97%
ELISpot and cells-based approaches	iSpot LymeTM	54—84%	54 – 94%
	QuantiFERON-Lyme	70%	na
	Spirofind	43%	82%
	LTT-MELISA	30%	53%
	TCR sequencing	56%	99%

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- Medium Enriched for Newly Synthesized Antibodies : Evaluation de la réponse humorale

PLOS ONE

Circulating antibody-secreting cells are a biomarker for early diagnosis in patients with Lyme disease

Natalie S. Haddad[1], Sophia Nozick[1], Shant Ohanian[1], Robert Smith[2], Susan Elias[2], Paul G. Auwaerter[3], F. Eun-Hyung Lee[1,4‡], John L. Daiss[1*]

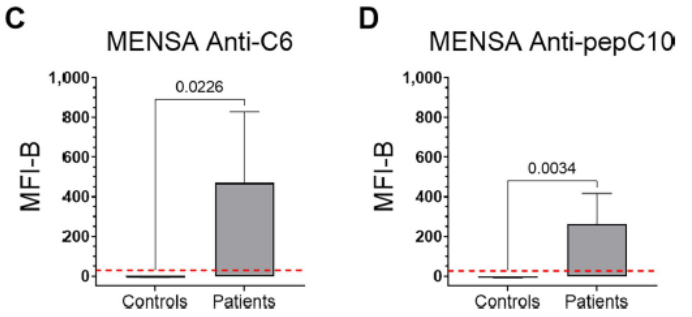

Fig 3. The Newly Diagnosed Lyme Disease Patient population has significantly higher MENSA and serum anti-C6 and anti-pepC10 antibody levels than the Control population. Average net MFI values were calculated for A) serum

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- Revue de la littérature : Dg direct par PCR
  - Se surtout dans les lésions cutanées et articulaire
  - Mais ADN persistant?

Table 4 Sensitivity of culture detection and PCR assays depending of the origin of clinical sample

Methods	Origin of clinical sample	Sensitivity range
Culture of *B. burgdorferi*	Skin biopsies from EM	40 – 90%
	Skin biopsies from ACA	20 – 60%
	Skin biopsies from Borrelial lymphocytoma	24 – 32%
	Synovial fluid/biopsy	< 1%
	Cerebrospinal fluid	10 – 26%
	Blood	5 – 40%
	Urine	nd
Traditional PCR assays	Skin biopsies from EM	30 – 89%
	Skin biopsies from ACA	20 – 100%
	Skin biopsies from Borrelial lymphocytoma	67.5%
	Synovial fluid/biopsy	40 – 96%
	Cerebrospinal fluid	5 – 30%
	Blood	10 – 20%
	Urine	nd

Nd not detectable

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- Revue de la littérature : Dg direct par PCR
  - Se surtout dans les lésions cutanées et articulaire
  - Mais ADN persistant?
  - Intérêt d'une PCR sur les bactériophage de Bb

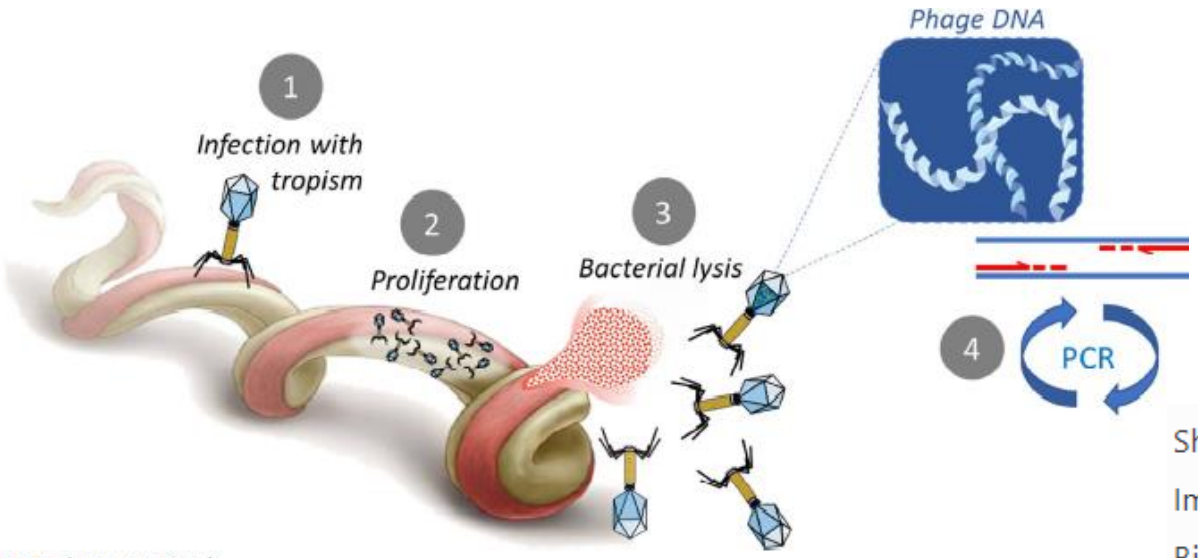

Fig. 5 Phage PCR principle

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BMC Public Health

Spatial multi-criteria decision analysis for the selection of sentinel regions in tick-borne disease surveillance

C. Guillot[1,2,3*], C. Aenishaenslin[1,3], E. S. Acheson[1,4], J. Koffi[1,5], C. Bouchard[1,4] and P. A. Leighton[1,3]

Canada :

- 143➔3000 cas de maladie de Lyme entre 2010 et 2021
- Surveillance passive de la population de tiques en place depuis 1990, débordée par leur augmentation et stoppée en 2021
- Comment remettre en place une surveillance plus uniforme sur le territoire en tenant compte des particularités du pays ?

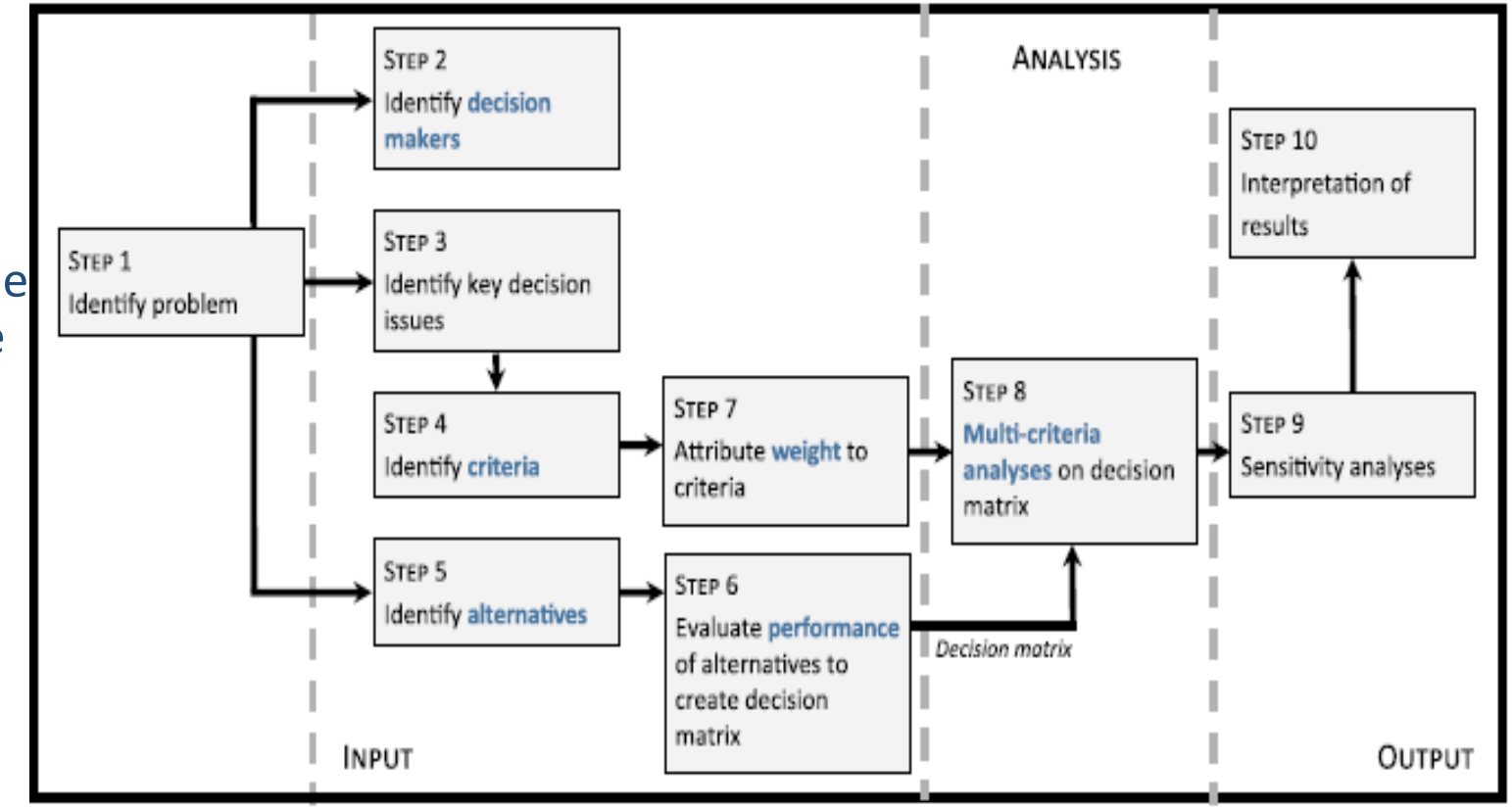

Fig. 1 Diagram of general steps in multi-criteria analysis

Approche Multicritère : Multi Criteria Decision Analysis

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No.	MCDA criteria	Performance measure
1)	Maximize the human population reached within the units of the study zone	Logarithm of the population taken from Statistics Canada's Census 2016 data
2)	Document risk of disease due to the presence of appropriate vector within the sentinel region	Number of passive tick submissions from federal passive surveillance system from 2010 to 2015 standardized by the logarithm of the population
3)	Determine ecological suitability for the presence of the vector, *Ixodes* spp. ticks	Habitat suitability indication for *Ixodes* spp. ticks using the product of the percentage of deciduous or mixed forest cover and temperature in the form of accumulated degree days above 0 °C
4)	Identify logistical constraints	Distance traveled between the nearest CLyDRN collaboration center (i.e. main address of sampling teams) to the center of the sentinel region in kilometers

- Poids des 4 critères évalué par les spécialistes de chaque province ➔

Criteria	Weight	Standard deviation
Acarological risk	40	9.81
Log of the population	25	7.34
Environmental index	25	8.86
The distance from collaborating research centers	10	3.08

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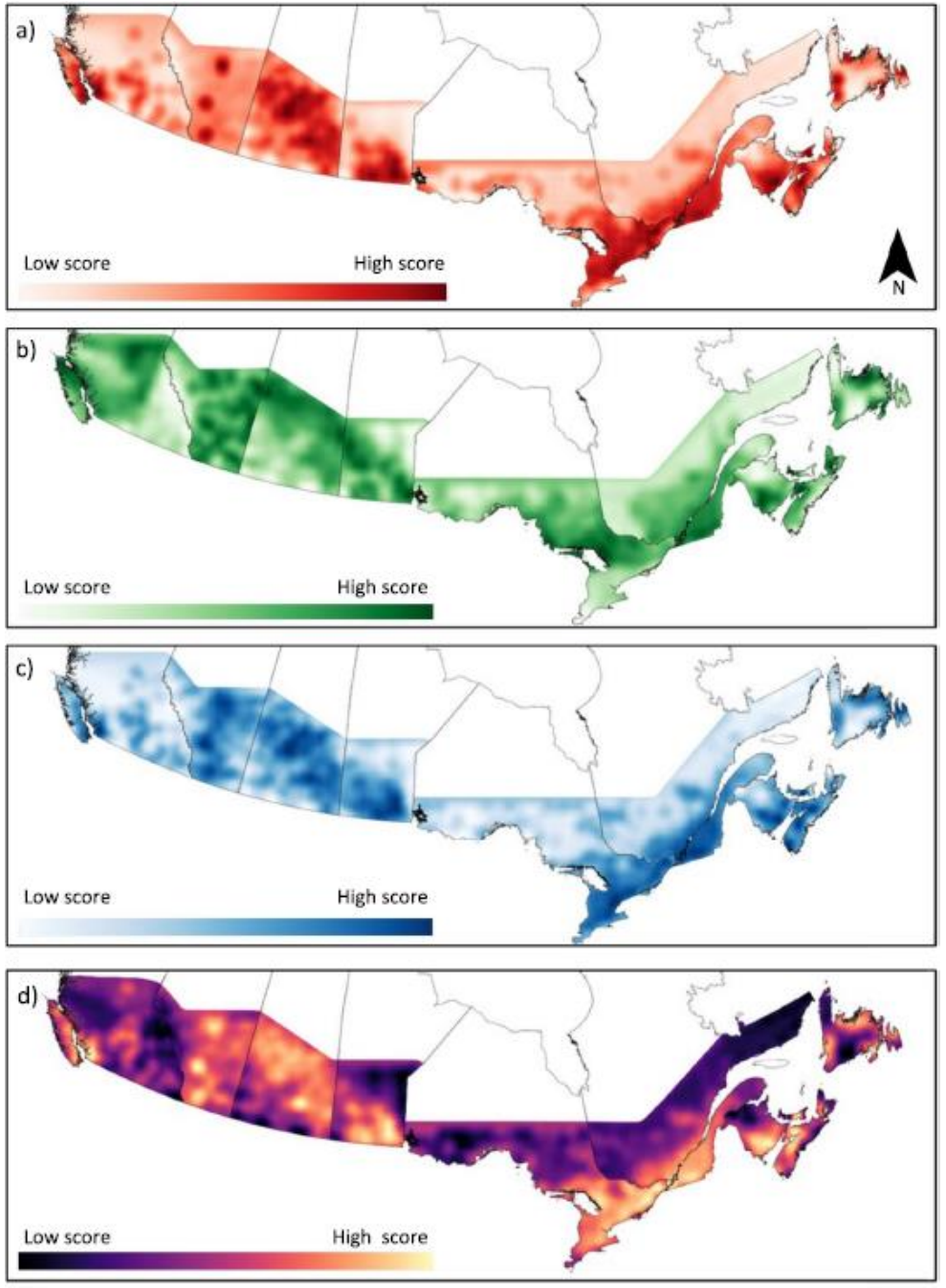
- Phi score pour les différentes alternatives :
  - Risque de maladie de Lyme (a)
  - Population (b)
  - Risque acarologique (c)
  - ➔Risques pondérés (d)



Maps projecting MCDA Phi scores from scenario **a**) risk-based, **b**) population, **c**) environment, and **d**) weighted. The shading indicates

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Table 4 Stability levels for results of Prince Edward Island for weighted scenario, with levels for all ranking to remain the same, and levels for half of the rankings to remain the same

Criteria	Weight	Stability intervals[a] for rankings to remain the same		Stability intervals for 50% of rankings to remain the same	
		Min weight	Max weight	Min weight	Max weight
Risk	40	29.4	42.9	29.4	46.3
Environment	25	17.8	34.8	17.8	34.8
Population	25	18.9	44.4	0	44.4
Distance	10	7.7	21.7	3.1	21.7

[a] Stability intervals refer to range in which the weight of a criterion can be modified without affecting the ranking for a given scenario

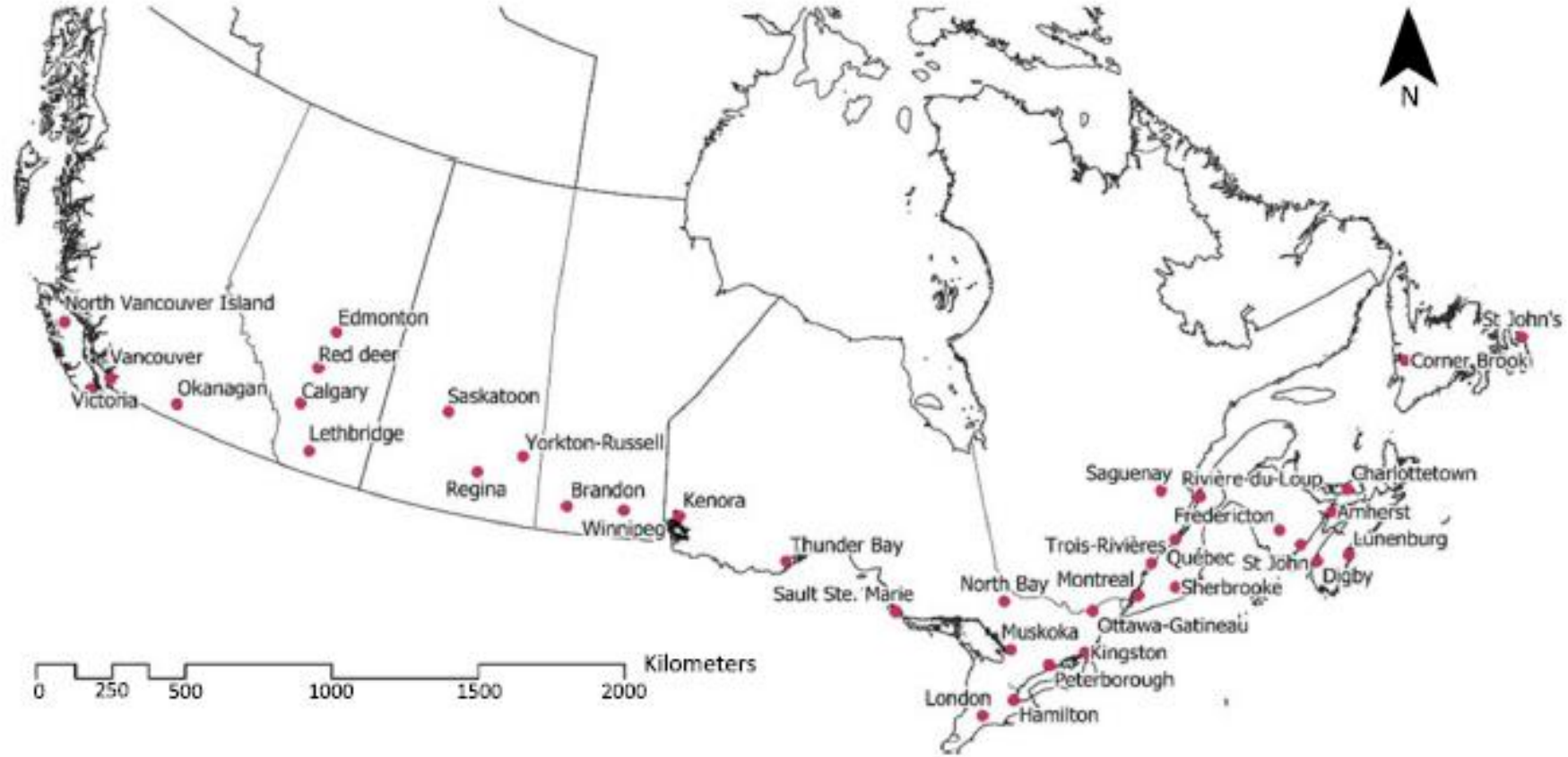

Fig. 3 Sentinel regions ($n = 37$) for the Canadian Lyme Sentinel Network (CaLSeN) (pink dots)

In vitro acaricidal activity of essential oils and their binary mixtures against *ixodes scapularis* (Acari: Ixodidae)

Luís Adriano Anholeto [a], Sophia Blanchard [b], Haozhe Vincent Wang [a], Ana Carolina de Souza Chagas [c], Neil Kirk Hillier [b], Nicoletta Faraone [a,*]

- Résistance aux acaricides synthétiques
- Nécessité de trouver des produits moins polluants et moins néfastes pour les pollinisateurs
- Améliorer l'efficacité des Huiles essentielles (HE) en les associant

➔Evaluation HE citronnelle, géranium, thym et sarriette

Compound*	No. C atoms	RT[†]	% abundance ± SEM			
			LG	G	ST	WT
phenylethyl alcohol	8	13.42	–	6.22±0.12	–	–
α-phellandrene	10	8.39	–	–	2.01±0.01	1.27±0.14
α-pinene	10	8.60	–	–	4.11±0.16	1.62±0.23
camphene	10	9.08	–	–	6.58±0.21	–
β-myrcene	10	10.26	–	–	–	1.33±0.10
α-terpinolene	10	10.99	–	–	–	1.47±0.10
o-cymene	10	11.20	–	–	10.71± 0.42	20.89±1.45
limonene	10	11.33	3.52 ± 0.126	–	–	–
α-terpinene	10	12.09	–	–	–	9.13±0.79
linalool	10	13.12	–	6.10±0.16	5.71±0.05	4.09±0.10
trans-rose oxide	10	13.37	–	1.35±0.06	–	–
camphor	10	14.25	–	–	0.97±0.02	–
L-menthone	10	14.45	–	2.98±0.11	–	–
isomenthone	10	14.66	–	1.29±0.05	–	–
borneol	10	14.84	–	–	24.63±0.36	–
terpinen-4-ol	10	15.02	–	–	1.31±0.18	–
α-terpineol	10	15.34	–	–	4.05±0.18	–
citronellol	10	16.01	–	54.38±0.26	–	–
neral	10	16.25	40.59±0.15	–	–	–
geraniol	10	16.50	–	9.80±0.54	–	–
nerol	10	16.50	1.32±0.02	–	–	–
geranial	10	16.87	48.36±0.14	–	–	–
thymol	10	17.34	–		1.73±0.13	53.26±2.31
carvacrol	10	17.51	–		26.05±0.38	1.96±0.48
R-citronellene	10	18.47	–	1.38±0.04	–	–
citronellyl formate	11	16.95	–	11.20±0.29	–	–

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- LC_{50} de HE seule ou en association
  - Meilleure HE seule Thym
  - Meilleure association : Thym/citronnelle

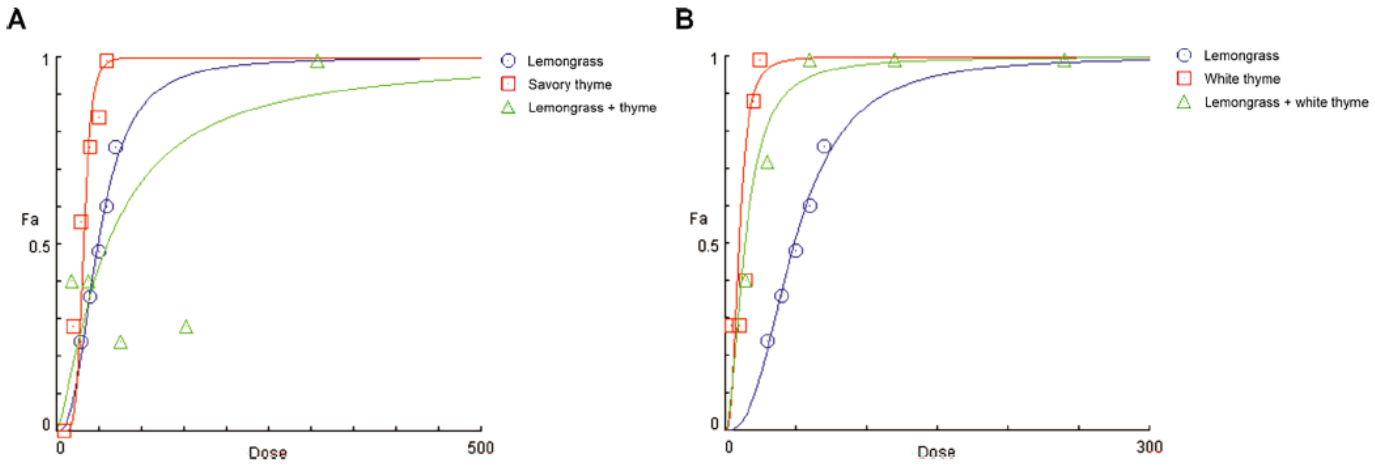

Fig. 2. The dose-effect curve for combinations with lemongrass and savory thyme (A) and lemongrass and white thyme (B) essential oils on unfed *Ixodes scapularis* adult females. Fa= fraction affected (percentage of mortality). The dose is expressed in µg/µL.

Table 3
Toxicity (LC_{50}) of single and combined essential oils against unfed *Ixodes scapularis* adult females under laboratory conditions.

Essential oil(s)	Total no. of ticks tested	Slope	LC_{50} (µg/µL)	95 % confidence interval
Lemongrass	150	3.7 ± 0.93	49.0	41.7–58.0
Geranium	150	7.24 ±0.98	39.7	36.1–43.1
Savory Thyme	150	5.06 ±0.73	28.0	24.3–31.5
White Thyme	150	3.10 ±0.54	11.1	8.6–14.4
Lemongrass + Geranium	150	3.7 ± 0.57	65.3	53.1–79.8
Savory Thyme + White Thyme	150	1.99 ±0.34	58.3	18.8–1096.5
Lemongrass + Savory Thyme	150	0.93 ±0.28	95.4	43.4–210.0
Lemongrass + White Thyme	150	3.87 ±0.86	18.5	13.6–22.8
Geranium + Savory Thyme	150	3.19 ±0.47	66.8	53.7–82.9
Geranium + White Thyme	150	1.98 ±0.33	36.9	26.4–49.5

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- Effet majoritairement antagoniste des associations d'huiles essentielles

Table 4
Effects of essential oil (EO) binary combinations on unfed *Ixodes scapularis* adult females.

EO Binary combinations	Ratio* [$(LC_{50})_1/(LC_{50})_2$]	Concentrations (µg/µL)	% Mortality	Combination index	Effect
Lemongrass + Geranium		22.2	4	1.29821	Antagonism
		44.4	36	1.20858	Antagonism
	1.2:1	88.7	52	2.01856	Antagonism
		177.4	100	1.33038	Antagonism
		354.8	100	2.66076	Antagonism
Savory Thyme + White Thyme		9.75	12	0.83072	Synergism
		19.5	20	1.41850	Antagonism
	2.5:1	39.0	28	2.53261	Antagonism
		78.0	36	4.61233	Antagonism
		156.0	100	2.78082	Antagonism
Lemongrass + Savory Thyme		18.9	40	0.51576	Synergism
		38.5	40	1.05302	Additive
	1.75:1	77.0	24	2.60400	Antagonism
		154.0	28	4.90520	Antagonism
		308.0	100	2.47315	Antagonism
Lemongrass + White Thyme		15.0	40	0.61214	Synergism
		30.0	72	0.75994	Synergism
	4.5:1	60.0	100	0.42161	Synergism
		120.0	100	0.84322	Synergism
		240.0	100	1.68644	Antagonism
Geranium + Savory Thyme		17.0	0	3.02030	Antagonism
		34.0	27	1.14061	Antagonism
	1.4:1	68.0	42	2.05148	Antagonism
		136.1	80	3.13259	Antagonism
		272.2	100	3.77747	Antagonism
Geranium + White Thyme		12.7	24	0.72898	Synergism
		25.4	32	1.31702	Antagonism
	3.6:1	50.7	60	1.97153	Antagonism
		101.5	73	3.41447	Antagonism
		203.0	100	2.97051	Antagonism