APPENDIX

Section 1. Distributions used for individual level characteristics

All 100,000 individuals entering the model simulation are assigned an age, sex, and whether or not they live in endemic area (i.e., high-risk) for Lyme disease through random sampling from distributions. These individual characteristics are stochastic and affect probability of Lyme disease infection, Lyme disease progression (testing, sequelae) and health state utility values (subsequently quality-adjusted life years).

Age is randomly sampled for each individual from a normal distribution created using a mean age of 37.62 and a standard deviation of 22.67 years. This is representative of the age distribution in Ontario, Canada.

Sex and **endemicity** are both randomly sampled for each individual from separate uniform distributions where the lower bound = 0 and upper bound = 1. The sampled number is compared with the probability of being assigned as female (p_Female = 0.51) and the probability of being assigned as residing in an endemic area (p_Endemic = 0.63) to assign both individual characteristics.

Appendix 1, as supplied by the authors. Appendix to: Mac S, Evans GA, Patel SN, et al. Estimating the population health burden of Lyme disease in Ontario, Canada: a microsimulation modeling approach. *CMAJ Open* 2021. DOI:10.9778/cmajo.20210024.

Section 2. Model inputs of 2017 Lyme disease incidence rates in Ontario by age and sex

	Female		Male	
AGE GROUPS	**Reported cases**	**Incidence rate***	**Reported cases**	**Incidence rate***
≤ 14	41	0.000029	71	0.000050
15 to 49	108	0.000075	199	0.000139
50 to 65	143	0.000100	181	0.000126
≥ 65	94	0.000066	121	0.000085

* *Adapted from:* Nelder MP, Wijayasri S, Russell CB, Johnson KO, Cronin K, Johnson S. The continued rise of Lyme disease in Ontario , Canada: 2017. Can Commun Dis Rep. 2018;44:231–6. (1)

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Section 3. Methods of matched retrospective cohort study in Ontario to identify probability of sequelae for individuals with laboratory-confirmed Lyme disease infection*

We used a previously created LD cohort of laboratory-confirmed cases between Jan 1, 2006 and Dec 31, 2013 from provincial laboratory and reportable diseases databases, linked to population-based health administrative data. Infected subjects were hard-matched 1:3 to uninfected subjects on age ±1 year, sex, index date ± 30 days, and the logit of the propensity score from a regression on rurality, neighbourhood income quintile, and comorbidities 2-years prior to index date. We used ICD-10 and Ontario Health Insurance Plan billing codes to identify emergency department visits, physician billings and hospitalizations related to LD sequelae: skin rashes, carditis, arthritis, facial palsy, cognitive sequelae, polyneuropathy or meningitis, and physical sequelae (e.g. myalgia, arthralgia, nausea and vomiting, headaches, vertigo). We looked back 1-year pre-index date to exclude sequelae reported prior to confirmed LD infection, and followed subjects until March 31, 2017. We compared proportion of sequelae using a chi-square test, and calculated relative risk (RR) ratios.

**Adapted from:* Mac S, Jung J, Kopp A, Evans G, Pullenayegum E, Patel SN, et al. Estimating Health Burden Attributable to Laboratory-Confirmed Lyme Disease in Ontario, Canada: A Population-Based Matched Cohort Study Using Health Administrative Data. Med Decis Mak. 2019;40(1):E102–3.

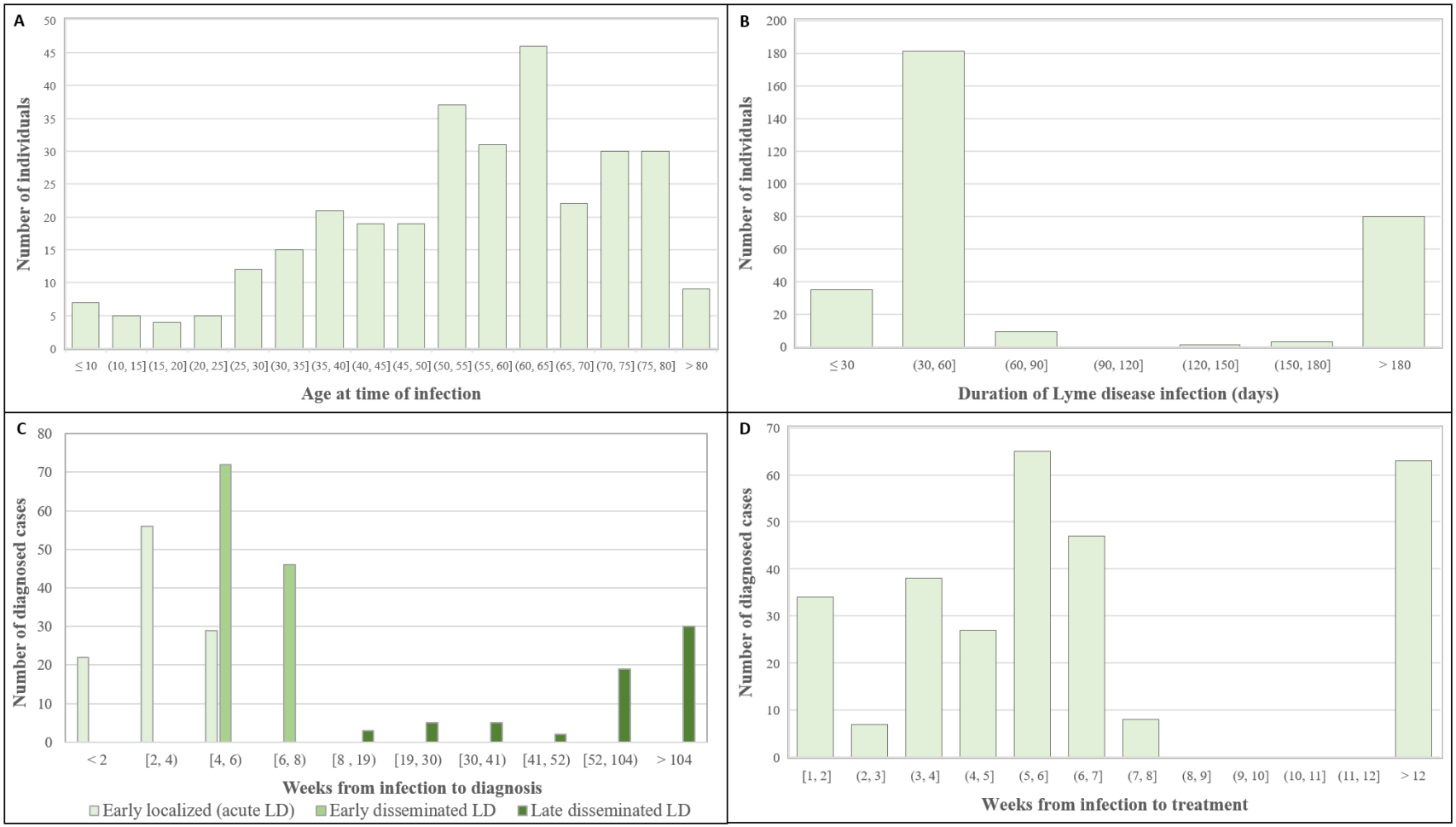
Appendix 1, as supplied by the authors. Appendix to: Mac S, Evans GA, Patel SN, et al. Estimating the population health burden of Lyme disease in Ontario, Canada: a microsimulation modeling approach. *CMAJ Open* 2021. DOI:10.9778/cmajo.20210024.

Section 4. Scenario analysis descriptions and results by descending health burden

Scenario	Description and Rationale	QALYs Lost
A. Underreporting (factor of 10)	Estimate of possible underreporting in United States. Rationale: To explore true burden if underreporting factor is as concluded by Kuehn 2013 (2)	881.30
B. Underreporting (factor of 3)	Rough estimate of possible underreporting in Canada. Rationale: To explore true burden if underreporting factor is as concluded by Ogden 2019 (3)	257.48
C. LD incidence Increasing for 10 years	Increase by 1 per 100,000 for each age group (by sex), in each of the next 10 years before becoming stable over the lifetime of all individuals. Rationale: To explore increasing risk areas	165.51
D. Assuming persistent symptoms for those undiagnosed for LD	This scenario assumes that undiagnosed individuals may experience persistent symptoms similar to PTLDS, but are not captured since they cannot be diagnosed with PTLDS without an appropriate diagnosis and treatment for LD. Rationale: To explore possible burden when including those who are undiagnosed.	85.29
E. Increased awareness for EM being diagnostic	Probability of clinical diagnosis in the presence of EM rash of 90% in all areas (high and low-risk). Rationale: To explore increase in early clinical diagnosis in high risk and low risk exposure areas.	68.64
F. Ontario: 1 M individuals, 1 year risk of LD infection	Burden for 1 million Ontarians over 1 year of risk of LD infection, discounted at 1.5%	19.38

Appendix 1, as supplied by the authors. Appendix to: Mac S, Evans GA, Patel SN, et al. Estimating the population health burden of Lyme disease in Ontario, Canada: a microsimulation modeling approach. *CMAJ Open* 2021. DOI:10.9778/cmajo.20210024.

Section 5. Description of Lyme disease infections from cross-sectional cohort of 100,000 individuals. A) Age at time of infection B) Distribution of duration of active Lyme disease infection C) Distribution of time from infection to diagnosis D) Distribution of time from infection to treatment



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Section 6. Health outcomes for scenario F (1 million people with 1-year risk of LD infection)

Outcomes	Incidence per 100,000, n (%)
Total LD infections	53
Diagnosed cases	47 (88.7%)
Early localized	21 (39.6%)
Clinically diagnosed	7 (13.2%)
Lab-confirmed	14 (26.4%)
Early disseminated	20 (37.7%)
Late disseminated	6 (11.3%)
Undiagnosed cases	6 (11.3%)
Re-infections	0 (0)
Sequelae	
Arthritic	4 (7.5%)
Cardiac	0 (0)
Cognitive	0 (0)
Cranial nerve palsy	0 (0)
Multiple erythema migrans	2 (3.8%)
Neurological (meningitis, polyneuropathy)	2 (3.8%)
PTLDS	4 (7.5%)
QALYS	
Discounted (1.5%)	19.38

LD, Lyme disease; LY, Life years; PTLDS, post-treatment Lyme disease syndrome; QALY, quality-adjusted life years

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1. Nelder MP, Wijayasri S, Russell CB, Johnson KO, Cronin K, Johnson S. The continued rise of Lyme disease in Ontario , Canada: 2017. Can Commun Dis Rep. 2018;44:231–6.

2. Kuehn BM. CDC estimates 300000 US cases of lyme disease annually. JAMA. 2013;310(11):1110.

3. Ogden NH, Bouchard C, Badcock J, Drebot MA, Elias SP, Hatchette TF, et al. What is the real number of Lyme disease cases in Canada? BMC Public Health. 2019;19(1):1–12.