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# Economic Burden of Reported Lyme Disease in High-Incidence Areas, United States, 2014–2016

## Appendix

### Section 1. Detailed Description of Cost Calculations for Total Patient Cost (Patient Perspective) and Societal Medical Costs (Societal Perspective)

To estimate the total patient cost, we summed self-reported medical costs, nonmedical costs, cost of productivity losses, and other related costs over all surveys. For nonmedical costs related to travel for clinician, pharmacy, or laboratory visits, the self-reported roundtrip mileage per visit was multiplied by the standard mileage rate from the Internal Revenue Service for the respective year (*1*). To calculate cost estimates for productivity losses, self-reported hours missed from work for adult participants or parents of pediatric participants were multiplied by the hourly earnings by age and sex derived from Grosse et al. (*2*), which uses the human capital approach to estimate annual market and non-market productivity from the US Census Bureau's American Community Survey and American Time Use Survey.

We calculated the societal medical cost per participant (regardless of who pays) by summing the mean cost per CPT code collected for each participant. The codes represented clinician visits, consultation and related in-office procedures, diagnostic testing, therapy, hospitalization, emergency department (ED) visits, or other procedures or relevant costs. Mean cost for each CPT code collected for participants with private insurance was extracted from IBM MarketScan Research Databases, which include national medical claims data for privately insured persons up to age 65 and their dependents. Costs for CPT codes collected for non-privately insured participants were extracted from the Physician Fee Schedule National Payment Amount File from the Centers for Medicare and Medicaid Services (CMS) (*3*). Both MarketScan and CMS costs reflect reimbursements made for charges for medical procedures and services and include the amount paid by the insurer as well as the beneficiary (such as deductibles, copays,

and coinsurance). We did not collect billing codes from pharmacies or laboratories. Therefore, we extracted the mean cost of the recommended antibiotics for Lyme disease (LD) by state and study year from MarketScan drug cost data and added this cost to each participant's total societal medical cost (*4*–*8*). Because laboratory evidence of infection is required to meet criteria for confirmed disseminated or probable disease (*9*), we added the cost of the recommended two-tiered LD diagnostic testing to the total societal medical cost for all participants in these disease categories who did not already have these CPT codes documented. We excluded from analysis participants for whom CPT code collection was incomplete due to provider nonresponse to code collection requests. We also excluded individual CPT codes deemed unrelated to LD, per consultation with an infectious disease physician, that were collected coincidentally from providers (Appendix Table 5).

## Equation 1. Multivariable Linear Regression Model Equation

We used a multivariable linear regression model to estimate the relative impact of our independent variables of interest on the total societal cost of LD per participant. As is typical for healthcare cost data, the distribution of total cost was highly skewed, resulting in heteroskedasticity of the residuals in the model (*10*). Therefore, we transformed total societal cost per participant using natural logarithms and conducted sampling-weighted least squares regression. The basic equation is as follows:

$$\log(y_i) = \beta_0 + \beta_i x_i + \varepsilon_i$$

where $Y_i$, is the dependent variable, the total societal cost of LD for patient i; $X_i$ is a vector of covariates; and $\varepsilon_i$ is a mean-zero random error. The equation is written as follows for our specific vector of covariates (i.e., independent variables of interest and potential confounders):

$$\log(y_i) = \beta_0 + \beta_1 \text{Disease category} + \beta_2 \text{Age group} + \beta_3 \text{Sex} + \beta_4 \text{State} +$$

$$\beta_5 \text{Insurance status} + \beta_6 \text{Income} + \beta_7 \text{Study year} + \varepsilon_i$$

Baseline costs came from the intercept term, $\beta_0$, which represents a patient with confirmed localized Lyme disease, female, aged <18 years, with residence in CT, without private insurance, with income <$60,000, and study year of 2014. Resulting β coefficients were back

transformed by exponentiation, interpreted as the multiplicative difference in the geometric mean of the total cost of Lyme disease for a 1-unit difference in the independent variable of interest after adjusting for confounders. For interpretability, we calculated the percent difference in cost from baseline for each level of each independent variable, excluding reference (i.e., baseline) levels (Percent difference = (Exp(coefficient) – 1) * 100). These additional costs were added or subtracted to the baseline costs for each independent variable of interest (Table 6, LINK; Appendix Table 8).

## Section 2. Description of Calculations for Extrapolation of Total Societal LD Cost Per Participant to Annual, Aggregate Total LD Cost to U.S. Society

Previous research has demonstrated that LD surveillance case numbers are likely 8–12-fold underreported (*11*,*12*), with a recent study estimating 476,000 diagnosed cases per year (*13*). The table below shows total cases by confirmed localized, confirmed disseminated, and probable disease per the proportions found in surveillance data. Case numbers by disease category are multiplied by the mean and median total cost per participant estimated from this study to get the aggregate cost per disease category (Appendix Table 9). When summed, the mean total cost of LD in the U.S. annually is approximately $968,444,834, while the median is $345,164,936 (2016 USD, Appendix Table 10). In 2020 USD, the mean cost is $1,039,260,297 using the Consumer Price Index (CPI) for all consumers and $1,078,657,584 when using the CPI for medical care (*14*), with median costs at $370,404,385 and $384,446,034, respectively (Appendix Table 10).

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**Appendix Table 1.** Cost categories and inclusion of costs dependent on perspective for economic analysis*

| | | Perspective† | |
|---|---|---|---|
| Cost categories | Examples of costs | Patient | Society‡ |
| Direct medical | | | |
| | Healthcare personnel time | Included | Included |
| | Drugs or other therapy | Included | Included |
| | Laboratory tests | Included | Included |
| | Medical devices, supplies, equipment | Not included | Included |
| Direct nonmedical | | | |
| | Administrative resources | Not included | Included |
| | Healthcare facility | Not included | Included |
| | Utilities | Not included | Included |
| | Patient's travel cost | Included | Included |
| | Hired caregiving | Included | Included |
| | Hired household help | Included | Included |
| Indirect | | | |
| | Time off work for healthcare visits | Included | Included |
| | Time off work due to symptoms | Included | Included |

*Source: adapted from Meltzer MI (*15*).
†Economic analyses are usually conducted from the following perspectives: patient, clinician, hospital, third-party payer, and/or society.
‡The societal perspective includes all costs related to an illness, no matter who pays, and is typically the sum of costs paid by the patient, clinician, hospital, and third-party payer.

**Appendix Table 2.** Participating counties from Maryland and New York

| State | County |
|---|---|
| Maryland | Anne Arundel |
| | Baltimore |
| | Calvert |
| | Carroll |
| | Cecil |
| | Frederick |
| | Harford |
| | Howard |
| | Montgomery |
| New York | Albany |
| | Rensselaer |
| | Columbia |
| | Greene |
| | Saratoga |
| | Schoharie |
| | Schnectady |
| | Washington |
| | Fulton |
| | Montgomery |
| | Ostego |
| | Delaware |
| | Dutchess |
| | Ulster |

**Appendix Table 3.** Characteristics of the subset of participants with complete patient cost and societal medical cost data, n = 613

| Characteristic | Category | No. | Unweighted % | Weighted % |
|---|---|---|---|---|
| Disease category | Confirmed localized | 273 | 44.5 | 54.4 |
| | Confirmed disseminated | 154 | 25.1 | 20.2 |
| | Probable | 186 | 30.3 | 25.4 |
| Age group, y | <18 | 173 | 28.2 | 27.7 |
| | 18–45 | 96 | 15.7 | 15.7 |
| | 46–65 | 228 | 37.2 | 37 |
| | >65 | 116 | 18.9 | 19.5 |
| Sex | Female | 262 | 42.7 | 43.0 |
| | Male | 351 | 57.3 | 57.0 |
| Race | Non-White | 45 | 7.3 | 7.1 |
| | White | 568 | 92.7 | 92.9 |
| State | CT | 128 | 20.9 | 19.3 |
| | MD | 203 | 33.1 | 33.6 |
| | MN | 191 | 31.2 | 31.1 |
| | NY | 91 | 14.8 | 15.9 |
| Income* | ≤$60,000 | 160 | 28.7 | 28.4 |
| | >$60,000 | 398 | 71.3 | 71.6 |
| Insurance | Private | 438 | 28.5 | 28.5 |
| | Other | 175 | 71.5 | 71.5 |
| Median clinician visits (range) | | 2 (1–33) | NA | NA |
| Median surveys (range) | | 3 (1–12) | NA | NA |

*Participants were not required to provide information on income; n = 558.

**Appendix Table 4.** Mean and median patient Lyme disease costs per participant, by disease and cost category, 2016 US dollars*

| | Confirmed localized disease | | Confirmed disseminated disease | | Probable disease | |
|---|---|---|---|---|---|---|
| Cost category | Median (95% CI) | Mean (95% CI) | Median (95% CI) | Mean (95% CI) | Median (95% CI) | Mean (95% CI) |
| Productivity losses | 0 (0–0) | 540 (368–712) | 0 (0–0) | 727 (359–1095) | 0 (0–0) | 627 (429–824) |
| Medical bills | 42 (31–52) | 314 (201–426) | 83 (61–145) | 628 (408–848) | 83 (62–99) | 389 (264–514) |
| Prescription medicine | 16 (11–21) | 56 (32–80) | 21 (17–21) | 79 (54–105) | 19 (16–21) | 44 (34–54) |
| Over-the-counter medicine | 0 (0–4) | 20 (13–27) | 10 (7–10) | 53 (28–78) | 5 (2–8) | 47 (21–72) |
| Transportation | 11 (10–12) | 34 (16–52) | 20 (17–23) | 55 (37–74) | 18 (14–20) | 49 (30–69) |
| Home maintenance | 0 (0–0) | 31 (7–55) | 0 (0–0) | 58 (12–103) | 0 (0–0) | 50 (4–97) |
| Other | 0 (0–0) | 40 (23–58) | 0 (0–0) | 78 (37–118) | 0 (0–0) | 51 (27–75) |
| Care for self/dependents | 0 (0–0) | 35 (0–91) | 0 (0–0) | 14 (0–28) | 0 (0–0) | 20 (0–42) |

**Appendix Table 5.** List of CPT codes removed from analyses, code description, frequency, mean cost per code (n = 30)*

| CPT code | Code description | N | Mean cost (2016 USD) |
|---|---|---|---|
| 11406 | Removal of growth (4.0 cm) of the trunk, arms, or legs | 1 | 1152 |
| 11606 | Removal of malignant growth (over 4.0 cm) of the trunk, arms, or legs | 1 | 1240 |
| 36475 | Destruction of insufficient vein of arm or leg, accessed through the skin | 1 | 3021 |
| 37609 | Tying or biopsy of temporal artery (side of skull) | 1 | 1844 |
| 42821 | Removal of tonsils and adenoid glands patient age 12 or over | 1 | 1946 |
| 42830 | Removal of adenoids patient younger than age 12 | 1 | 1854 |
| 43238 | Ultrasound guided needle aspiration or biopsies of esophagus using an endoscope | 1 | 1664 |
| 45378 | Diagnostic examination of large bowel using an endoscope | 4 | 752 |
| 45380 | Biopsy of large bowel using an endoscope | 1 | 1131 |
| 45385 | Removal of polyps or growths of large bowel using an endoscope | 2 | 2911 |
| 47562 | Removal of gallbladder using an endoscope | 1 | 4062 |
| 55700 | Biopsy of prostate gland | 1 | 679 |
| 59510 | Cesarean delivery with pre- and post-delivery care | 1 | 2893 |
| 62311 | Injections of substances into lower or sacral spine | 3 | 565 |
| 64490 | Injections of upper or middle spine facet joint using imaging guidance | 1 | 788 |
| 64491 | Injections of upper or middle spine facet joint using imaging guidance | 1 | 531 |
| 64492 | Injections of upper or middle spine facet joint using imaging guidance | 1 | 502 |
| 64635 | Destruction of lower or sacral spinal facet joint nerves using imaging guidance | 1 | 1155 |
| 64636 | Destruction of lower or sacral spinal facet joint nerves with imaging guidance | 1 | 801 |
| 66984 | Removal of cataract with insertion of lens | 3 | 2415 |
| 69436 | Incision of eardrum with insertion of eardrum tube under general anesthesia | 1 | 1802 |
| 78582 | Lung ventilation and perfusion imaging | 1 | 598 |
| 92928 | Catheter insertion of stents in major coronary artery or branch, accessed through the skin | 1 | 3530 |

| CPT code | Code description | N | Mean cost (2016 USD) |
|---|---|---|---|
| 95810 | Sleep monitoring of patient (6 y or older) in sleep lab | 1 | 1535 |
| C1725 | Catheter, transluminal angioplasty, non-laser (may include guidance, infusion/perfusion capability) | 2 | 2182 |
| C1874 | Stent, coated/covered, with delivery system | 1 | 5411 |
| C9600 | Percutaneous transcatheter placement of drug eluting intracoronary stent(s), with coronary angioplasty when performed; single major coronary artery or branch | 1 | 12616 |
| G0202 | Screening mammography digital | 14 | 490 |
| G0206 | Diagnostic mammography digital | 3 | 523 |
| J0133 | Injection, acyclovir, 5 mg | 1 | 824 |

*An infectious disease physician with subject matter expertise in Lyme disease deemed these CPT codes to be unrelated to Lyme disease; 54 instances with these 30 codes recorded were deleted from the dataset before all analyses.

**Appendix Table 6.** Twenty-five most frequently reported CPT codes, code description, and summary statistics

| CPT code | Code description | N | Proportion | MarketScan mean, median reimbursement (USD 2016) | CMS mean, median reimbursement (USD 2016) |
|---|---|---|---|---|---|
| 99213 | Established office visit | 970 | 0.1 | 100.55, 85.14 | 75.04, 74.70 |
| 99214 | Established patient office or other outpatient, visit typically 25 min | 707 | 0.07 | 144.43,120.56 | 112.68,115.18 |
| 36415 | Routine venipuncture | 579 | 0.06 | 8.40, 3.89 | 3.00, 3.00 |
| Q9967 | LOCM 300–399mg/ml iodine,1ml | 344 | 0.04 | 336.87,165.17 | 152.19,165.17 |
| 86617 | Confirmation test for antibody to Borrelia burgdorferi (Lyme disease bacteria) | 308 | 0.03 | 64.58, 32.82 | 28.49, 28.49 |
| 85025 | Complete blood cell count (red cells, leukocyte, platelets), automated test | 287 | 0.03 | 26.57, 18.03 | 14.30, 14.30 |
| 86618 | Analysis for antibody Borrelia burgdorferi (Lyme disease bacteria) | 273 | 0.03 | 42.44, 33.62 | 31.32, 31.32 |
| J3490 | Unclassified drugs | 180 | 0.02 | 489.57, 28.90 | 37.95, 28.90 |
| 97110 | Therapeutic exercises | 166 | 0.02 | 64.88, 49.72 | 33.17, 32.36 |
| J1642 | Injection, heparin sodium, (heparin lock flush), per 10 units | 130 | 0.01 | 248.86, 24.21 | 24.21, 24.21 |
| 80053 | Blood test, comprehensive group of blood chemicals | 105 | 0.01 | 40.06, 14.87 | 19.43, 19.43 |
| 97112 | Neuromuscular reeducation | 102 | 0.01 | 44.74, 25.22 | 34.03, 33.71 |
| 86140 | Measurement C-reactive protein for detection of infection or inflammation | 96 | 0.01 | 21.47, 9.49 | 9.52, 9.52 |
| 98940 | Chiropractic manipulative treatment, 1–2 spinal regions | 88 | 0.01 | 38.20, 28.00 | 29.52, 29.43 |
| 80048 | Blood test, basic group of blood chemicals | 87 | 0.01 | 33.53, 18.90 | 15.55, 15.55 |
| J0696 | Injection, ceftriaxone sodium, per 250 mg | 85 | 0.01 | 165.44, 32.76 | 44.70, 32.76 |
| A9585 | Injection, gadobutrol, 0.1 ml | 83 | 0.01 | 228.98, 90.00 | 90.01, 90.00 |
| 99212 | Established patient office or other outpatient visit, typically 10 min | 82 | 0.01 | 68.39, 51.74 | 45.35, 45.11 |
| 90471 | Administration of 1 vaccine | 78 | 0.01 | 26.87, 24.47 | 26.56, 25.52 |
| 99203 | New patient office or other outpatient visit, typically 30 min | 77 | 0.01 | 138.31,109.00 | 112.28,116.07 |
| 85652 | Red blood cell erythrocyte sedimentation rate, to detect inflammation | 76 | 0.01 | 10.53, 4.73 | 4.97, 4.97 |
| 93000 | Routine EKG using at least 12 leads including interpretation and report | 75 | 0.01 | 47.41, 38.79 | 17.95, 18.34 |
| 87880 | Strep test (Streptococcus, group A) | 70 | 0.01 | 20.26, 17.31 | 22.05, 22.05 |
| 99284 | Emergency department visit, problem of high severity | 70 | 0.01 | 532.25,411.12 | 119.94,120.87 |
| 85027 | Complete blood cell count (red cells, leukocyte, platelets), automated test | 65 | 0.01 | 23.06, 13.97 | 11.90, 11.90 |

**Appendix Table 7.** Societal Perspective: total cost of Lyme disease per participant, by demographic characteristic, n = 613

| Characteristic | Category | N | Mean (2016 US dollars) | Median (2016 US dollars) |
|---|---|---|---|---|
| Disease category | Confirmed localized | 273 | 1307 | 493 |
| | Confirmed disseminated | 154 | 3251 | 1081 |
| | Probable | 186 | 2620 | 940 |
| Age group, y | <18 | 173 | 1550 | 503 |
| | 18–45 | 96 | 2100 | 960 |
| | 46–65 | 228 | 2421 | 1136 |
| | >65 | 116 | 1926 | 521 |
| Sex | Female | 262 | 1417 | 646 |
| | Male | 351 | 2497 | 741 |
| Race | Non-White | 45 | 2188 | 774 |
| | White | 568 | 2021 | 685 |
| State | CT | 128 | 3307 | 621 |
| | MD | 203 | 1493 | 604 |
| | MN | 191 | 2112 | 1124 |
| | NY | 91 | 1470 | 434 |
| Income* | ≤$60,000 | 160 | 2159 | 685 |
| | >$60,000 | 398 | 2088 | 696 |
| Insurance | Private | 438 | 2295 | 807 |
| | Other | 175 | 1376 | 578 |

*Participants were not required to provide information on income; n = 558.

**Appendix Table 8.** Multivariable linear regression results: factors influencing total societal cost of Lyme disease per participant (n = 613)*

| Variable | Coefficient | Standard error of coefficient | Exp(coefficient)[2] | Percent difference (%) | Cost difference (2016 USD) | 95% CI for cost difference (2016 USD) | P value |
|---|---|---|---|---|---|---|---|
| Baseline (Intercept)[4] | 5.72 | 0.20 | 305.08 | NA | NA | 206.28 – 451.20 | <0.001 |
| Confirmed disseminated | 0.79 | 0.11 | 2.20 | 120 | 366.58 | 188.12 – 545.04 | <0.001 |
| Probable | 0.47 | 0.10 | 1.59 | 59 | 181.13 | 70.84 – 291.42 | <0.001 |
| 18–45 y | 0.67 | 0.15 | 1.96 | 96 | 292.99 | 107.11 – 478.88 | <0.001 |
| 46–65 y | 0.73 | 0.11 | 2.08 | 108 | 330.79 | 175.08 – 486.50 | <0.001 |
| >65 y | 0.24 | 0.17 | 1.27 | 27 | 83.65 | −27.51 – 194.81 | 0.15 |
| Male | 0.11 | 0.09 | 1.11 | 11 | 34.56 | −25.67 – 94.8 | 0.24 |
| MD | 0.00 | 0.13 | 1.00 | 0 | −0.01 | −75.98 – 75.97 | 1.00 |
| MN | 0.56 | 0.13 | 1.75 | 75 | 229.44 | 113.85 – 345.03 | <0.001 |
| NY | −0.06 | 0.17 | 0.94 | −6 | −18.52 | −118.96 – 81.91 | 0.72 |
| Privately insured | 0.24 | 0.15 | 1.27 | 27 | 82.53 | −23.22 – 188.28 | 0.11 |
| >$60,000 income | −0.06 | 0.12 | 0.94 | −6 | −18.52 | −90.11 – 53.08 | 0.61 |
| Study year 2015 | −0.07 | 0.10 | 0.93 | −7 | −21.35 | 306.05 – 427.11 | 0.48 |
| Study year 20156 | 0.50 | 0.50 | 1.65 | 65 | 197.52 | −306.37 – 668.64 | 0.32 |

*The model included independent variables of interest, i.e., disease category, age group, sex, and state, while controlling for insurance status, income, and study year. Reference levels are not shown but are described in Table **6** of main article (https://wwwnc.cdc.gov/EID/article/28/6/21-1335-T5.htm). Adjusted $R^2$ = 0.19.

†Beta coefficients were back transformed by exponentiation, interpreted as the multiplicative difference in the geometric mean of the total cost of Lyme disease for a 1-unit difference in the independent variable of interest after adjusting for confounders.

‡Percent difference = (Exp(coefficient) – 1) * 100; this represents the percent change in cost from baseline for each level of each variable, excluding reference (i.e., baseline) levels.

§Baseline cost (i.e., $e^{\beta_0}$) represents a patient with confirmed localized Lyme disease, female, aged <18 y, with residence in CT, without private insurance, with income <$60,000, and study year of 2014.

**Appendix Table 9.** Inputs for extrapolation of total Lyme disease cost per participant to aggregate total Lyme disease cost to US society

| Lyme disease category | Estimated proportion of total cases | Total cases | Mean total cost per participant* | Total aggregate cost using mean cost per participant* | Median total cost per participant* | Total aggregate cost using median cost per participant* |
|---|---|---|---|---|---|---|
| Confirmed localized | 0.547 | 260,435 | 1,307 | 340,388,077 | 493 | 128,394,278 |
| Confirmed disseminated | 0.211 | 100,278 | 3,251 | 326,004,293 | 1,081 | 108,400,689 |
| Probable | 0.242 | 115,287 | 2,620 | 302,052,464 | 940 | 108,369,968 |

*2016 USD

**Appendix Table 10.** Estimated annual total Lyme disease cost to US society

| Category | Mean | Median |
|---|---|---|
| Total (2016 USD) | 968,444,834 | 345,164,936 |
| Total (2020 USD)* | 1,039,260,297 | 370,404,385 |
| Total (2020 USD, medical CPI)† | 1,078,657,584 | 384,446,034 |

*Converted to 2020 USD using Consumer Price Index, "All items in U.S. city average, all urban consumers, not seasonally adjusted" (CPI-U, Series ID: CUUR0000SA0). 2016 annual average CPI and 2020 first half of year average CPI used. Data extracted from https://data.bls.gov/pdq/SurveyOutputServlet on 9/30/2020.

†Converted to 2020 USD using Consumer Price Index, "Medical care in U.S. city average, all urban consumers, not seasonally adjusted" (CPI-U Medical care, Series ID: CUUR0000SAM). 2016 annual average CPI and 2020 first half of year average CPI used. Data extracted from https://data.bls.gov/pdq/SurveyOutputServlet on 9/30/2020.