

Incidence of Lyme borreliosis in Europe: a systematic literature review

SUPPLEMENT

Table S1: Incidence (cases per 100,000 PPY) of LB in sub-national areas of Eastern European countries from literature published from 2005 to 2020

| Country (Ref) | Sub-national area | Author Year | Data source | Study Population | Cases (n) | Study design | Study period | Case definition | Incidence (95% CI) |
|--------------------|-----------------------------|-----------------------------|-------------------------------|---|-----------|---|--------------|---------------------------------------|--------------------|
| Czech Republic [1] | Regional Bohemia | Daniel 2008 | National surveillance data | Regional general population | 7,391 | Retrospective observational | 1999-2004 | NR | 12.0 (11.4-12.7) |
| Poland [2] | Bialystok North-east Poland | Toczyłowski 2020 | Hospital records | Children <18 years | 26 | Retrospective cohort, observational | 2015-2019 | Clinical with laboratory confirmation | 2.5 (1.1-6.0) |
| Poland [3] | Lubuskie | Zbrzezniak 2019 | Mandatory surveillance system | National general population except Bialystok district | 798 | Retrospective observational, surveillance | 2017 | Surveillance definition | 78.5 |
| | Dolnoslaskie | | | | 852 | | | | 29.4 |
| | Kujawsko-Pomorskie | | | | 545 | | | | 26.2 |
| | Lubelskie | | | | 1975 | | | | 92.8 |
| | Malopolskie | | | | 3322 | | | | 98.1 |
| | Mazowieckie | | | | 2216 | | | | 41.2 |
| | Opolskie | | | | 644 | | | | 65 |
| | Podkarpackie | | | | 1480 | | | | 69.6 |
| | Podlaskie | | | | 1542 | | | | 130.1 |
| | Pomorskie | | | | 1466 | | | | 63.2 |
| | Slaskie | | | | 2779 | | | | 61 |
| | Swietokrzyskie | | | | 450 | | | | 36 |
| | Warminsko-mazurskie | | | | 1302 | | | | 90.7 |
| | Wielkopolskie | | | | 655 | | | | 18.8 |
| | Zachodniopomorskie | | | | 851 | | | | 49.9 |
| | Ladzkie | | | | 637 | | | | 25.7 |
| Poland [4] | Kujawsko-Pomorskie | Paradowska-Stankiewicz 2015 | Mandatory surveillance system | National general population | 430 | Retrospective cross-sectional | 2013 | Clinical and laboratory criteria | 20.5 |
| | Lubelskie | | | | 816 | | | | 37.8 |
| | Lubuskie | | | | 350 | | | | 34.2 |
| | Malopolskie | | | | 1817 | | | | 54.1 |
| | Mazowieckie | | | | 1469 | | | | 27.2 |
| | Opolskie | | | | 431 | | | | 42.8 |
| | Podkarpackie | | | | 988 | | | | 46.4 |
| | Podlaskie | | | | 1199 | | | | 100.2 |
| | Pomorskie | | | | 507 | | | | 22.1 |

| | | | | | | | | | |
|-------------|---------------------------------------|----------------|--|--|--|--|---|-------------------------------------|---------------------------|
| | Wielkopolskie | | | | 241 | | | | 7 |
| | Zachodniopomorskie | | | | 445 | | | | 25.9 |
| | Dolnośląskie | | | | 586 | | | | 20.1 |
| | Łódzkie | | | | 291 | | | | 11.6 |
| | Śląskie | | | | 2278 | | | | 49.5 |
| | Świętokrzyskie | | | | 189 | | | | 14.9 |
| | Warmińsko-Mazurskie | | | | 736 | | | | 50.8 |
| Poland [5] | Podlaskie voivodship | Krzyzak 2019 | Provincial Sanitary-Epidemiological Station in Białystok. National bulletins | National general population | NR | Retrospective cross-sectional, surveillance | 2011-2018 | Clinical, laboratory, tick exposure | 104.2 |
| | Białystok | | | | | | | | 88.5 |
| | Sokolka | | | | | | | | 172.9 |
| | Bielsk Podlaski | | | | | | | | 198.8 |
| | Wysokie Mazowieckie | | | | | | | | 48.5 |
| | Augustów | | | | | | | | 91.6 |
| | Łomża | | | | | | | | 38.5 |
| | Grajewo | | | | | | | | 167 |
| | Siemiatycze | | | | | | | | 111 |
| | Hajnówka | | | | | | | | 200.9 |
| | Zambrów | | | | | | | | 29.8 |
| | Mońki | | | | | | | | 51.1 |
| | Kolno | | | | | | | | 60 |
| | Suwałki | | | | | | | | 154.5 |
| | Sejny | | | | | | | | 215.1 |
| Poland [7] | Lubuskie | Stefanoff 2006 | Routine epidemiological surveillance + Sero-epidemiological studies | National general population (except Białystok) | 19,052 | Retrospective surveillance, sero-epidemiological | 1999-2005 1999 2004 1999 2004 | Clinical, laboratory | 0.49 |
| | Opolskie | | | | | | | | 12.3 |
| | | | | | | | | | 1.0 |
| | | | | | | | | | 16.3 |
| Romania [8] | Mures county, central-northern region | Tilea, 2014 | 120 consecutive inpatients | Regional general population | 44 (LB) 28 (EM) 13 (LNB) 1 (LC) 76 (LB) 49 (EM) | Prospective, sero-epidemiological | 2010 2011 | CDC and EUCALB | 7.47 12.91 |

14 (LNB)
2 (LA)

| | | | | | | | | | |
|----------------------|----------------------------------|------------------|--|---|------------|-------------------------------|---|--|---|
| Russia [9] | St. Petersburg | Bogachkina 2011 | Centre of Hygiene and Epidemiology, The Directorate of the Federal Service for Surveillance on Consumer Rights Protection and Human Well-Being | General population | 487 307 | Cross-sectional, Surveillance | 2009 2010 | NR | 10.7 6.7 |
| Slovak Republic [10] | Ružomberok and Liptovský Mikuláš | Bochnickova 2012 | Medical records | Patients attending Infectious Disease Departments | 476 | Retrospective cohort | 1989-2010 1989 1990 1991 1992 1993 1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 | Epidemiological history, clinical, laboratory findings | 7.5 3.0 1.5 3 0.7 2.2 6.6 16.4 52.1 9.7 10.4 3.0 14.8 11.1 9.8 9.0 18.1 30.2 25.7 32.5 42.3 24.0 21.2 |

ACA, Acrodermatitis chronica atrophicans; CDC, the United States Centers for Disease Control and Prevention; ECG, electrocardiograph; EUCALB, European Union Concerted Action on Lyme borreliosis, EM erythema migrans; LA Lyme arthritis; LC, Lyme carditis; LNB Lyme neuroborreliosis

*Incidence *proportion* reported, rather than incidence *rate* (person-time).

Table S2: Incidence (cases per 100,000 PPY) of LB in sub-national areas of the Baltic States from literature published from 2005 to 2020

| Country (Ref) | Sub-national area | Author Year | Data source | Study Population | Cases (n) | Study design | Study period | Case definition | Incidence (95% CI) |
|----------------|-------------------|--------------------|--|------------------|-----------|-------------------------------------|-------------------|--|--------------------|
| Lithuania [11] | Vilnius district | Petruioniene, 2020 | Clinical records, Center of infectious Diseases, Vilnius | Outpatients | 7424 | Retrospective cohort, observational | 2014-2016 2016 | Clinical, laboratory, ECG, skin biopsy findings. | 85.4 101.6 |

ACA, Acrodermatitis chronica atrophicans; LB Lyme borreliosis; EM erythema migrans; LA Lyme arthritis; LC, Lyme carditis; LNB Lyme neuroborreliosis.

*Incidence *proportion* reported, rather than incidence *rate* (person-time).

Table S3: Incidence (cases per 100,000 PPY) of LB in sub-national areas of Nordic region countries from literature published from 2005 to 2020

| Country (Ref) | Sub-national area | Author Year | Data source | Study Population | Cases (n) | Study design | Study period | Case definition | Incidence (95% CI) |
|-----------------------|--------------------------------|----------------|---|--|-------------------------------------|----------------------|---------------------------|--|--------------------|
| Denmark [12] | Zealand | Dessau 2015 | Danish notification system for infectious diseases, Danish microbiology database, Danish civil registration system. | Population of Denmark | 65 | Prospective cohort | 2010-2012 | LNB | 2.6 |
| | Capital (Denmark) | | | 115 | 2.3 | | | | |
| | Southern Denmark | | | 182 | 5.1 | | | | |
| | Middle Jutland | | | 129 | 3.4 | | | | |
| | Northern Jutland | | | 35 | 2.0 | | | | |
| Denmark [13] | Funen | Andreasen 2020 | Confirmed LNB cases and controls | 10 municipalities of Funen | 401 | Case-control | 1995-2014 1998 2006 | LNB: Clinical, laboratory confirmation | 2.33 7.93 |
| Denmark [14] | Islands of Funen and Langeland | Knudtzen 2017 | University Hospital based data | LNB cases verified by positive Borrelia intrathecal antibody | 431 | Retrospective cohort | 1995-2014 | Positive CSF IgM and/or IgG | 4.7 |
| Denmark [15] | North Jutland County | Krabbe 2008 | GP medical records | Patients with LNB North Jutland County | 84 | Retrospective cohort | 1998-2006 | Detection of intrathecal antibodies | 2.0 |
| Finland [16] | Åland Islands | Sajanti 2017 | 3 Registers: Register for Primary Health Care Visits (Avohilmo); National Infectious Diseases Register (NIDR); National Hospital Discharge Register (Hilmo) | Finnish national general population | 11,793 (Avohilmo)/ 21,051 (NIDR) | Retrospective cohort | 2010-2014 | GP diagnosed EM/disseminated laboratory conformed LB | 884.6/1597.0 |
| | Southwest Finland | | | | | | | | 83.3/46.3 |
| | Helsinki and Uusimaa | | | | | | | | 63.1/34.4 |
| | Satakunta | | | | | | | | 28.4/13.2 |
| | Satakunta | | | | | | | | 17.3/3.9 |
| | Pirkanmaa | | | | | | | | 17.1/1.5 |
| | Päijät-Häme | | | | | | | | 29.9/10.8 |
| | Kymenlaakso | | | | | | | | 142.9/56.7 |
| | South Karelia | | | | | | | | 161.8/48.7 |
| | Southern Savonia | | | | | | | | 47.0/13.3 |
| | Eastern Savonia | | | | | | | | 81.0/14.7 |
| | North Karelia | | | | | | | | 66.4/15.8 |
| | Northern Savonia | | | | | | | | 47.5/14.2 |
| | Central Finland | | | | | | | | 49.7/7.8 |
| | Southern Ostrobothnia | | | | | | | | 18.2/1.8 |
| Vaasa | 40.3/31.2 | | | | | | | | |
| Central Ostrobothnia | 29.4/8.7 | | | | | | | | |
| Northern Ostrobothnia | 4.8/1.3 | | | | | | | | |
| Kainuu | 4.2/1.8 | | | | | | | | |
| Länsi-Pohja | 10.8/3.1 | | | | | | | | |
| Lapland | 5.5/3.9 | | | | | | | | |

| | | | | | | | | | |
|-------------|---|----------------|--|--------------------------------------|-------|----------------------|-----------|----------------------------|------------------|
| Norway [17] | South-Rogaland, | Tveitnes 2012 | Hospital medical and laboratory records | 62,000 children <14 years of age | 142 | Retrospective cohort | 2001-2009 | Clinical, laboratory (LNB) | 26 |
| Norway [18] | Vestfold, Telemark, Aust-Agderand Vest-Agder | Eliassen 2017 | GP medical records, surveillance data | 4 counties with highest LD incidence | 6,565 | Retrospective cohort | 2005-2009 | LB | 19.70 (8.6-30.9) |
| | | | | | | | 2005 | | 22.1 (10.9-37.8) |
| | | | | | | | 2006 | | 22.6 (6.3-42) |
| | | | | | | | 2007 | | 21.4 (8.5-37.9) |
| | | | | | | | 2008 | | 18.9 (4.4-36) |
| | | | | | | | 2009 | | 13.4 (13.1-14.3) |
| | | | | | | | 2005-2009 | EM | 448 (339-574) |
| | | | | | | | 2005 | | 353 (257-426) |
| | | | | | | | 2006 | | 552 (399-714) |
| | | | | | | | 2007 | | 450 (371-571) |
| | | | | | | | 2008 | | 455 (320-627) |
| | | | | | | | 2009 | | 431 (328-541) |
| Sweden [19] | South-East Sweden, Blekinge County | Bennet 2006 | Electronic medical records | Primary healthcare clinics | 3,437 | Retrospective cohort | 1997-2002 | EM – CDC, EUCALB | 464 |
| | | | | | | | 1997 | | 364 |
| | | | | | | | 1998 | | 400 |
| | | | | | | | 1999 | | 264 |
| | | | | | | | 2000 | | 664 |
| | | | | | | | 2001 | | 464 |
| | | | | | | | 2002 | | 632 |
| Sweden [20] | Gothenburg or Åcker, Kung, Tjrn, Stenungsund, Ale, Lerum, Partille, HÅryda, MÅlndal, Kungsbacka | Sodermark 2017 | Medical records of children (< 15 years) treated for LNB | Gothenburg and regional hospitals | 548 | Retrospective cohort | 2002-2014 | Clinical | 28 |
| | | | | | | | 2005 | | 42 |
| | | | | | | | 2010 | | 14 |

CDC, the United States Centers for Disease Control and Prevention; CI, confidence interval; CSF, cerebrospinal fluid; EM, erythema migrans; EUCALB, European Union Concerted Action on Lyme borreliosis; GP, general practices; LNB, Lyme neuroborreliosis; Avohilmo, Register for Primary Health Care Visits; NIDR, National Infectious Diseases Register

*Incidence *proportion* reported, rather than incidence *rate* (person-time).

Table S4: Incidence (cases per 100,000 PPY) of LB in sub-national areas of the UK and Ireland from literature published from 2005 to 2020

| Country (Ref) | Sub-national area | Author Year | Data source | Study Population | Cases (n) | Study design | Study period | Case definition | Incidence (95% CI) |
|---------------------|-------------------------|---------------|---|---|------------------|--|--------------|--|--------------------|
| Ireland [21] | Connemara | Vellinga 2018 | All LB tests University Hospitals Galway laboratory | 2,314,374 requests over the 5-year period | 242 | Prospective cohort | 2010-2014 | EIA and LIA for IgG or IgM. | 43 |
| | Loughrea | | | | | | | | 12 |
| | County Roscommon | | | | | | | | 11 |
| | West of Ireland overall | | | | | | | | 2 |
| Scotland [22] | Ayrshire & Arran | Mavin 2015 | National Lyme Borreliosis Testing laboratory and questionnaires from all laboratory confirmed cases within NHS Highland | Scotland national general population | 42 | Retrospective cohort, sero-epidemiological | 2008-2013 | ELISA (IgM/IgG), then immunoblot | 1.9 |
| | Tayside | | | | 223 | | | | 9.2 |
| | Dumfries & Galloway | | | | 56 | | | | 6.3 |
| | Lothian | | | | 163 | | | | 3.3 |
| | Fife | | | | 45 | | | | 2.1 |
| | Greater Glasgow & Clyde | | | | 320 | | | | 4.5 |
| | Highlands | | | | 831 | | | | 44.1 |
| | Lanarkshire | | | | 59 | | | | 1.7 |
| | Borders | | | | 21 | | | | 3.1 |
| | Western Isles | | | | 22 | | | | 13.8 |
| | Forth Valley | | | | 26 | | | | NR |
| Grampian | 57 | NR | | | | | | | |
| Scotland [23] | Highlands | Milner 2009 | Surveillance data National Lyme Borreliosis Testing Laboratory at Raigmore Hospital in Inverness. | Scotland population | NR | Cohort, Sero-epidemiological, Surveillance | 2007-2008 | LB as assessed by serology/Western blot | 43.4 |
| Scotland [24] | Highlands | Slack 2011 | National LB testing Laboratory, Medical microbiology Department at Ninewells Hospital & Medical School, Dundee | Samples from Tayside and the Highlands | 78 | Retrospective Longitudinal | 2006-2007 | Weak positive or positive Western blot | 25.4 |
| | | | | April 2001-March 2010 | 175 | | 2009-2010 | | 56.4 |
| | Rest of Scotland | | | 10 | 2001-2002 | | 2.57 | | |
| | | | | 67 | 2009-2010 | | 16.8 | | |
| | | | | - | 2005-2006 | | 0.8 | | |
| United Kingdom [25] | South West | Cairns 2019 | CPRD | 8% of the population | 248 | Retrospective | 2010-2012 | Read codes for LB, suspected and possible LB | 23.4 (20.6-26.6) |
| | London | | | 117 | 7.7 (6.3-9.3) | | | | |
| | South East England | | | 425 | 13.9 (12.9-15.3) | | | | |
| | West Midlands | | | 108 | 8.1 (6.6-9.8) | | | | |
| | | | | 70 | 6.3 (4.9-8.0) | | | | |
| | North | | | 162 | 6.3 (5.3-7.3) | | | | |

CI, confidence interval; CRPD, Clinical Practice Research Database; ELISA, enzyme linked immunosorbent assay; LB, Lyme borreliosis; LIA, line immunoassay; NR, not reported.

*Incidence *proportion* reported, rather than incidence *rate* (person-time).

Table S5: Incidence (cases per 100,000 PPY) of LB in sub-national areas of Southern European countries from literature published from 2005 to 2020

| Country (Ref) | Sub-national area | Author Year | Data source | Study Population | Cases (n) | Study design | Study period | Case definition | Incidence |
|--------------------------|--------------------------------|--------------------|--|---|-----------|---------------------------|--------------|-----------------|-----------|
| Republic of Croatia [26] | Sibensko-kninska | Mulic 2011 | Mandatory reporting to Croatian Institute for Public Health and Health | National general population | 0 | Retrospective cohort | 1999-2008 | NR | 0 |
| | Osjecko-Baranjska | | | 71 | 2.1 | | | | |
| | Viroviticko podravska | | | 57 | 6.1 | | | | |
| | Istarska | | | 58 | 2.8 | | | | |
| | Vukovarsko-Srijemska | | | 35 | 1.7 | | | | |
| | Krapina-Zagorje | | | 362 | 25.4 | | | | |
| | Zadarska | | | 2 | 0.1 | | | | |
| | Zagreb | | | 301 | 9.7 | | | | |
| | City of Zagreb | | | 992 | 12.7 | | | | |
| | Bjelovarsko-Bilogorska | | | 56 | 4.2 | | | | |
| | Koprivnicko-krizevacka | | | 255 | 20.5 | | | | |
| | Primorsko-goranska | | | 191 | 6.3 | | | | |
| | Pozesko-Slavonska | | | 35 | 4.1 | | | | |
| | Licko-senjska | | | 3 | 0.6 | | | | |
| | Karlovacka | | | 67 | 4.7 | | | | |
| | Sisacko-moslavacka | | | 65 | 3.5 | | | | |
| | Spliskot-Dalmatinska | | | 13 | 0.3 | | | | |
| | Dubrovačko-neretvanska | | | 6 | 0.5 | | | | |
| | Medimurska | | | 223 | 18.8 | | | | |
| | Varaždinska | | | 68 | 3.7 | | | | |
| Brodsko-posavska | 47 | 2.7 | | | | | | | |
| Republic of Croatia [27] | Bjelovarsko-bilogorska county | Ropac 2013 | Institute of Public Health, Bjelovar-Bilogora | 3% of the national general population | 32 | Retrospective | 2007-2011 | EM | 4.5 |
| Italy [28] | Lombardy | Zanzani 2019 | The Rare Disease Register of the Lombardy Region. | National general population | 189 | Prospective observational | 2000-2015 | Codes and | 0.124 |
| | | | | | | | | Read codes | 0.03 |
| | | | | | | | | specific to | 0.26 |
| | Lodi province Sondrio province | | | | | | 2000-2015 | Lyme disease | 0.03 |
| Spain [29,30] | Lugo Province | Vazquez-Lopez 2015 | Medical records | Persons with a positive Western Blot, inpatients with possible LB | 108 (LB) | Retrospective cohort | 2007 | CDC | 2.6 |
| | | | | | | | 2012 | | 11.6 |
| Spain [31] | Lugo Province | Vazquez-Lopez 2016 | Hospital medical records | Children (<15 years) | 10 | Retrospective cohort | 2006-2013 | CDC | 5.5 |

CDC, the United States Centers for Disease Control and Prevention; EM, erythema migrans; EUCALB, European Union Concerted Action on Lyme borreliosis; LA, Lyme arthritis; LB, Lyme borreliosis; NR, not reported.

*Incidence *proportion* reported, rather than incidence *rate* (person-time).

Table S6: Incidence (cases per 100,000 PPY) of LB in sub-national areas of Western/Central European countries from literature published from 2005 to 2020

| Country (Ref) | Sub-national area | Author Year | Data source | Study Population | Cases (n) | Study design | Study period | Case definition | Incidence (95% CI) |
|------------------|--|---------------|--|---|-----------|-----------------------------|--------------|---------------------------------------|---------------------|
| Belgium [32] | East Flanders Limburg Flemish region Walloon region Brussels Capital | Geebelen 2019 | Belgian network of sentinel GPs | National general population (inhabitants, 1.3% of the population) | 420 | Retrospective observational | 2015-2017 | EM: EUCALB | 30.9 (21.4-40.3) |
| | | | | | | | | | 390.9 (329.7-451.9) |
| | | | | | | | | | 126 (101.0-150.9) |
| | | | | | | | | | 74.2 (68.3-80.1) |
| 34.0 (28.4-39.6) | | | | | | | | | |
| France [33] | Alsace | Raguet 2018 | GP surveillance (388 GPs) | National general population | 672 (LB) | Retrospective cohort | 2014-2015 | EUCALB | 117(109-126) |
| | | | | | 530 (EM) | | | | 121 (109-133) |
| | | | | | 68 (LA) | | | | 113 (101-125) |
| | | | | | 54 (LNB) | | | | |
| | | | | | 6 (ACA) | | | | |
| | | | | | 1 (LC) | | | | |
| 1 (ophthalmic) | | | | | | | | | |
| France [34] | Limousin Alsace Pays de la Loire Provence-Alpes-Côtes-d'Azur | Septfons 2019 | National Sentinel GP network (2011-2016), national hospital discharge database (2005-2016) | National general population | 667 | Retrospective observational | 2011-2016 | Clinical with laboratory confirmation | 239 (68-410) |
| | | | | | | | | | 148 (45-251) |
| | | | | | | | | | 5 (0-27) |
| | | | | | | | | | 8 (0-20) |
| France [35] | Meuse | Beytout 2007 | Physician reports to the National Reference Center | Residents of 2 rural regions | 25 (LB) | Prospective cohort | 2003 | EUCALB | 84 (47-121) |
| | | | | | 16 (EM) | | | | |
| | | | | | 1 (LA) | | | | |
| | | | | | 49 (LB) | | | | 156 (85-227) |
| | | | | | 37 (EM) | | | | |
| | | | | | 1 (LA) | | | | |
| | 1 (LC) | | | | | | | | |
| | 35 (LB) | 106 (55-157) | | | | | | | |
| | 28 (EM) | | | | | | | | |
| | 90 (LB) | 117 (76-159) | | | | | | | |
| | 51 (EM) | | | | | | | | |
| | 1 (LA) | | | | | | | | |
| 1 (LC) | | | | | | | | | |
| 1 (LNB) | | | | | | | | | |
| 62 (LB) | 76 (38-114) | | | | | | | | |
| 33 EM) | | | | | | | | | |
| 4 (LA) | | | | | | | | | |
| 1 (LNB) | | | | | | | | | |
| France | Franche-Comté | Tessier 2018 | | | 432 (LB) | | 2010-2012 | EUCALB | 85 (77-92) |

| Country (Ref) | Sub-national area | Author Year | Data source | Study Population | Cases (n) | Study design | Study period | Case definition | Incidence (95% CI) |
|---------------|--------------------------------------|------------------|---|--|---|---|-------------------|---|---------------------------|
| [36] | | | GP-based sentinel surveillance | Regional population attending GPs | 392 (EM) 4 (LA) 31 (LNB) 3 (Lymphocytoma) 1 (ACA) | Prospective cohort | | | 73 77 100 113 |
| France [37] | Alsace | Schmitt 2006 | GP-based sentinel surveillance | Regional population attending GPs | 1,365 (LB) 891 (EM) 291 (LA) 254 (LNB) 29 (Cutaneous-secondary or tertiary) 3 (LC) | Prospective cohort | 2001-2003 | EUCALB | 180 (30-511 by canton) |
| | Limousin | | | | 217 (LB) 170 (EM) | | | | NR |
| | National | Letrilliart 2005 | French Sentinels Network: 1178 sentinel GPs | National general population | 86 | Prospective cohort | 1999-2000 | CDC, EUCALB | 9.4 (7.4-11.4) |
| France [38] | Provence-Alpes-Côte d'Azur Alsace | | | | | | | | 0 (0-7) 86 (51-134) |
| Germany [39] | Brandenburg | Fulop 2008 | Notifications to the Robert Koch Institute | Population of 6 regions where LB is notifiable | 23,394 | Cross-sectional; Retrospective surveillance | 2002-2006 2006 | EUCALB | 77.6 |
| | Berlin | | | | | | 2006 | | 5.7 |
| Germany [40] | Bavaria | Heinzinger 2017 | Sentinel Lyme Disease Incidence Study initiated in mid-2012, routine surveillance | Regional general population | 16,439 (LB) 15,797 (EM) 373 (LA) 302 (LNB) | Retrospective cohort, surveillance | 2013-2016 | EM: clinical only, LNB, LA: clinical and laboratory | 34 |

| Country (Ref) | Sub-national area | Author Year | Data source | Study Population | Cases (n) | Study design | Study period | Case definition | Incidence (95% CI) |
|---------------|-------------------------------|--------------|--|--|-------------|------------------------------------|--------------|-------------------------------|--------------------|
| Germany [41] | 6 states | Mehnert 2005 | Notifications to the Robert Koch Institute | Population of 6 regions where LB is notifiable | 3019 | Retrospective | 2002 | Clinical and/or lab confirmed | |
| | Berlin | | | | 3968 | | 2003 | | 2.0 |
| | Brandenburg | | | | | | 2002 | | 3.0 |
| | | | | | | | 2003 | | 56.7 |
| | Meckl. Vorpommern | | | | | | 2002 | | 71.7 |
| | | | | | | | 2003 | | 7.4 |
| | Sachsen | | | | | | 2002 | | 8.7 |
| | | | | | | | 2003 | | 23.8 |
| | Sachsen Anhalt | | | | | | 2002 | | 29.6 |
| | | | | | | | 2003 | | 12.3 |
| Thuringen | | 2002 | 12.9 | | | | | | |
| | | 2002 | 0.3 | | | | | | |
| | | 2003 | 10.2 | | | | | | |
| Germany [42] | All regions | Adlhoch 2010 | Notifications to the Robert Koch Institute | Population of 6 regions where LB is notifiable | 16,461 (LB) | Retrospective cohort, surveillance | 2007-2009 | | - |
| | Berlin | | | | 69 | | 2002 | LB, EM, LNB | 2.0 |
| | | | | | 103 | | 2003 | LB, EM, LNB | 3.0 |
| | | | | | 163 | | 2004 | LB, EM, LNB | 4.8 |
| | | | | | 226 | | 2005 | LB, EM, LNB | 6.7 |
| | | | | | 173 | | 2006 | LB, EM, LNB | 5.1 |
| | | | | | 137 | | 2007 | LB, EM, LNB | 4.0 |
| | | | | | 103 | | 2008 | LB, EM, LNB | 3.0 |
| | | | | | 79 | | 2009 | LB, LA, EM, LNB | 2.3 |
| | | | | | Brandenburg | | 1,467 | 2002 | LB, EM, LNB |
| | 1,860 | | | | | | 2003 | LB, EM, LNB | 72.2 |
| | 2,024 | | | | | | 2004 | LB, EM, LNB | 78.8 |
| | 2,306 | | | | | | 2005 | LB, EM, LNB | 90.1 |
| | 2,193 | | | | | | 2006 | LB, EM, LNB | 86.1 |
| | 2,048 | | | | | | 2007 | LB, EM, LNB | 80.8 |
| | 1,787 | | | | | | 2008 | LB, EM, LNB | 70.8 |
| | 1,797 | | | | | | 2009 | LB, LA, EM, LNB | 71.2 |
| | Mecklenburg-Western Pomerania | | | | | | 129 | 2002 | LB, EM, LNB |
| | | | | | 151 | | 2003 | LB, EM, LNB | 8.7 |
| | | | | | 180 | | 2004 | LB, EM, LNB | 10.5 |
| | | | | | 374 | | 2005 | LB, EM, LNB | 21.9 |
| | | | | | 453 | | 2006 | LB, EM, LNB | 26.7 |
| | | | | | 529 | | 2007 | LB, EM, LNB | 31.5 |
| | | | | | 650 | | 2008 | LB, EM, LNB | 39.1 |

| Country (Ref) | Sub-national area | Author Year | Data source | Study Population | Cases (n) | Study design | Study period | Case definition | Incidence (95% CI) |
|------------------|-------------------------------|--------------|--|--|---|----------------------|--------------|--------------------------------|--------------------|
| | | | | | 730 | | 2009 | LB, LA, EM, LNB | 43.9 |
| | Saxony | | | | 1,034 | | 2002 | LB, EM, LNB | 23.8 |
| | | | | | 1,289 | | 2003 | LB, EM, LNB | 29.8 |
| | | | | | 1,464 | | 2004 | LB, EM, LNB | 34.1 |
| | | | | | 1,636 | | 2005 | LB, EM, LNB | 38.3 |
| | | | | | 2,216 | | 2006 | LB, EM, LNB | 52.1 |
| | | | | | 1,937 | | 2007 | LB, EM, LNB | 45.9 |
| | | | | | 1,911 | | 2008 | LB, EM, LNB | 45.6 |
| | | | | | 1,668 | | 2009 | LB, LA, EM, LNB | 39.8 |
| | Saxony-Anhalt | | | | 314 | | 2002 | LB, EM, LNB | 12.3 |
| | | | | | 329 | | 2003 | LB, EM, LNB | 13 |
| | | | | | 381 | | 2004 | LB, EM, LNB | 15.3 |
| | | | | | 477 | | 2005 | LB, EM, LNB | 19.3 |
| | | | | | 531 | | 2006 | LB, EM, LNB | 21.7 |
| | | | | | 604 | | 2007 | LB, EM, LNB | 25 |
| | | | | | 576 | | 2008 | LB, EM, LNB | 24.2 |
| | | | | | 331 | | 2009 | LB, LA, EM, LNB | 13.9 |
| | Thuringia | | | | 8 | | 2002 | LB, EM, LNB | 0.3 |
| | | | | | 245 | | 2003 | LB, EM, LNB | 10.3 |
| | | | | | 265 | | 2004 | LB, EM, LNB | 11.3 |
| | | | | | 442 | | 2005 | LB, EM, LNB | 18.9 |
| | | | | | 675 | | 2006 | LB, EM, LNB | 29.2 |
| | | | | | 425 | | 2007 | LB, EM, LNB | 18.6 |
| | | | | | 541 | | 2008 | LB, EM, LNB | 23.9 |
| | | | | | 608 | | 2009 | LB, LA, EM, LNB | 26.8 |
| Germany [116] | East Germany | Wilking 2014 | Notifications to the Robert Koch Institute | Retrospective surveillance | 18,894 (LB) 18,016 (EM) 367 (LA) 630 (LNB) | | 2009-2012 | | 34.9 |
| | Mecklenburg-Western Pomerania | | | | | | 2009 | | |
| | Berlin | | | | | | 2012 | | 19.54 |
| | | | | | | | 2011 | | 74.8 |
| Netherlands [43] | Apeldoorn and Zutphen | Bierman 2019 | Hospital records of patients with facial palsy | Adults with facial palsy visiting the departments of | 26 | Retrospective cohort | 2007-2017 | LNB Clinical and laboratory | 0.9 (0.6-1.3) |

| Country (Ref) | Sub-national area | Author Year | Data source | Study Population | Cases (n) | Study design | Study period | Case definition | Incidence (95% CI) |
|------------------|---|---------------|--------------------------------|---|-----------|--------------------|--|--|--|
| | | | | neurology and/or otorhinolaryngology of Gelre hospitals | | | | | |
| Netherlands [44] | Amsterdam | Botman 2018 | Medical records | Medical records of 56,996 patients registered in 12 GPs | 2,619 | Observational | 2010- 2015 | Immunoblot confirmed cases presenting to GPs | 880 |
| Switzerland [45] | <i>All regions</i> <i>Region 1:</i> Geneva, Neuchâtel, Vaud, Valais <i>Region 2:</i> Berne, Fribourg, Jura <i>Region 3:</i> Aargau, Basel, Solothurn <i>Region 4:</i> Lucerne, Obwalden, Nidwalden, Schwyz, Uri, Zug <i>Region 5:</i> Appenzell, Glarus, St. Gallen, Schaffhausen, Thurgau, Zurich, Lichtenstein <i>Region 6:</i> Grisons, Ticino | Altpeter 2013 | National surveillance database | National general population | 864 | Prospective cohort | 2008-2011 2008-2011 2008 2009 2010 2011 2008-2011 2008 2009 2010 2011 2008-2011 2008 2009 2010 2011 2008-2011 2008 2009 2010 2011 2008-2011 2008 2009 2010 2011 | EUCALB | 67 59 60 55 93 154 184 113 123 197 130 161 170 86 105 158 154 102 127 248 156 202 151 88 185 128 168 124 96 125 |

ACA, Acrodermatitis chronica atrophicans; CDC, the United States Centers for Disease Control and Prevention; CI, confidence interval; EM, erythema migrans; EUCALB, European Union Concerted Action on Lyme borreliosis; LA, Lyme arthritis; LB, Lyme borreliosis; LC, Lyme carditis; LNB, Lyme neuroborreliosis; NR, not reported

*Incidence *proportion* reported, rather than incidence *rate* (person-time).

Table S7: Cases of LB in Eastern Europe from literature published from 2005 to 2020

| Country | National or sub-national area | Author Year | Data source | Study Population | Study design | Study period | Case definition | Number of cases |
|---------------------|--------------------------------|-------------------------------|---|--|--|--------------|---|-----------------------------|
| Bulgaria [46] | Sofia | Baymakova 2016 | Military Academy Hospital medical records | Patients with prolonged febrile syndrome | Retrospective cohort | 2006-2010 | LB | 2 |
| Bulgaria [47] | National | Deleva 2007 | 12 patients with LNB | NR | Prospective cohort | Not given | LNB: laboratory confirmed | 12 |
| Bulgaria [48] | | Trifonova 2010 | Serum samples | NR | Prospective cohort, Sero-epidemiological | 2010 | EM Disseminated LB | 68 48 |
| Czech Republic [49] | Motol | Liba 2013 | Hospital medical records | Pediatric neurology inpatients | Retrospective cohort | 2009-2011 | LNB: laboratory confirmed | 58 |
| Czech Republic [50] | National | Kriz 2017 | National Register of Hospitalised Patients | National general population | Retrospective cross-sectional, | 2003-2013 | LB: ICD-10 codes | 23,631 |
| Czech Republic [51] | Prague | Palecek 2010 | Medical records | Cardiology inpatients (N=39) | Prospective cross-sectional | 2007-2008 | LNB LB detected in endocardial biopsy (PCR or electron microscopy) | 6392 8 |
| Hungary [53] | Budapest | Lakos 2010B | Center for Tick-borne Diseases, Budapest | Pregnant women | Retrospective observational | 1986-2008 | EM: CDC, EUCALB | 97 |
| Poland [54] | Podalskie | Moniuszko 2014 | Medical Records, Department of Pediatric Orthopedics and Traumatology of the Medical University of Białystok. | | Prospective cohort | 2004-2010 | LA, laboratory confirmed | 34 |
| Poland [55] | National | Moniuszko 2020 | Serosurvey in patients with EM | Patients with EM | Prospective cohort, Sero-epidemiological | 2012-2016 | Clinical | 310 |
| Poland [56] | Krakow | Marek Kacinski 2007 | Hospital-based data | NR | Prospective cohort | 2005-2006 | LNB: laboratory confirmed | 9 |
| Poland [57] | Białystok | Krawczuk 2020 | Medical records | Inpatients with LB | Retrospective cross-sectional | 2004-2015 | LNB: laboratory confirmed | 181 |
| Poland [58] | Kuyavian-Pomeranian Voivodship | Blazejewicz-Zawadziniska 2012 | Local surveillance records | NR | Retrospective cohort | 2000-2005 | LB: confirmed by Western blot EM | 973 825 |

| Country | National or sub-national area | Author Year | Data source | Study Population | Study design | Study period | Case definition | Number of cases |
|-------------|-------------------------------|-----------------|--|--------------------------------------|-------------------------------|--------------|-----------------|-----------------|
| | | | | | | 2000 | LB | 41 |
| | | | | | | 2001 | | 59 |
| | | | | | | 2002 | | 101 |
| | | | | | | 2003 | | 195 |
| | | | | | | 2004 | | 395 |
| | | | | | | 2005 | | 218 |
| | | | | | | 2000-2005 | EM | 825 |
| | | | | | | | LA | 138 |
| | | | | | | | LNB | 53 |
| | | | | | | | LC | 2 |
| | | | | | | 2000-2005 | LB | 18 |
| | Aleksandrowski | | | | | | | 25 |
| | Brodnicki | | | | | | | 433 |
| | Bygoski | | | | | | | 10 |
| | Chełmiński | | | | | | | 15 |
| | Golubsko-dobrzyński | | | | | | | 61 |
| | Grudziądzki | | | | | | | 37 |
| | Inowrocławski | | | | | | | 3 |
| | Lipnowski | | | | | | | 14 |
| | Mogileński | | | | | | | 48 |
| | Nakielski | | | | | | | 1 |
| | Radziejowski | | | | | | | 5 |
| | Rypiński | | | | | | | 13 |
| | Sępoleński | | | | | | | 67 |
| | Świecki | | | | | | | 115 |
| | Toruński | | | | | | | 51 |
| | Tucholski | | | | | | | 19 |
| | Wąbrzeski | | | | | | | 23 |
| | Włocławski | | | | | | | 15 |
| | Zniński | | | | | | | 33 |
| Poland [59] | Białystok | Grygorczuk 2013 | Medical records of patients with disseminated LB admitted to Department of Infectious Diseases & Neuroinfections | Patients with disseminated LB (N=33) | Retrospective observational | 2012 | LB | 8 |
| | | | | | | | LNB | 17 |
| | | | | | | | LA | 5 |
| Poland [60] | West Pomeranian Province | Stawicki 2017 | Retrospective analysis of | District sanitary-epidemiological | Retrospective cross-sectional | 2005-2014 | LB | 2756 |
| | | | | | | | ACA | |

| Country | National or sub-national area | Author Year | Data source | Study Population | Study design | Study period | Case definition | Number of cases |
|--------------|-------------------------------|---------------------|---|---|-----------------------------|--------------|--|---|
| | Białogardzki | | surveillance | stations (20 units) | | | | 59 |
| | Choszczeński | | mandatory | operating in the West | | | | 73 |
| | Drawski | | notification data | Pomeranian Province | | | | 131 |
| | Goleniowski | | | | | | | 124 |
| | Gryfice | | | | | | | 146 |
| | Gryfiński | | | | | | | 182 |
| | Kołobrzeski | | | | | | | 109 |
| | Koszaliński | | | | | | | 139 |
| | Policki | | | | | | | 155 |
| | Pyrzycki | | | | | | | 19 |
| | Stargardski | | | | | | | 60 |
| | Szczecinek | | | | | | | 106 |
| | City Szczecin | | | | | | | 761 |
| | Świdwiński | | | | | | | 79 |
| | City Swinoujście | | | | | | | 140 |
| | Walecki | | | | | | | 248 |
| | Mysliborski | | | | | | | 47 |
| | Sławieński | | | | | | | 43 |
| | Łobezki | | | | | | | 40 |
| | Kamiński | | | | | | | 95 |
| Poland [61] | Lublin region | Cisak 2008 | Hospital medical records of clinical LB cases | Regional population. | Retrospective cohort | 1998-2007 | LB LA LNB Skin borreliosis | 15 11 1 3 |
| Poland [6] | Podlaskie | Czupryna 2016 | Medical records Department of Infectious Diseases and Neuro-infections, Medical University in Białystok | Patients admitted with suspected LB (N=378) | Retrospective cohort | | LA: serological confirmation LNB LA ACA EM | 193 10 4 5 207 |
| Poland [62] | Lukow | Tokarska-Rodak 2010 | Hospital-based data | Outpatients with EM Inpatients with suspected LB (N=200) | Prospective cohort | 2007-2008 | LB positive by Western blot | 100 |
| Romania [63] | County of Bihor | Constanta 2019 | Retrospective clinical archives/records | Patients attending the Infectious Diseases hospital departments | Retrospective observational | 2018-2019 | LB | 132 |
| Romania [64] | Oradea | Andrei 2019 | Emergency department medical records | NR | Prospective observational | 2015-2018 | EM with positive serology | 183 |

| Country | National or sub-national area | Author Year | Data source | Study Population | Study design | Study period | Case definition | Number of cases |
|----------------------|--|--------------------|---|---|-----------------------------|--------------|-------------------------------|--------------------------|
| Romania [65] | Cluj-Napoca | Lupse 2014 | Hospital medical Records | NR | Prospective cohort | 2011 | EM: EUCALB | 44 |
| Romania [66] | Isai | Manciuc 2019 | Hospital records | Patients with LB evaluated and treated at the hospital | Retrospective cohort | 2017 | LB: CDC | 89 |
| Romania [67] | Cluj-Napoca | Briciu 2013 | Patient interview | Patients presenting to hospital with EM | Prospective observational | 2011-2012 | EM | 40 |
| Russia [68] | Moscow | Kritchevskaya 2014 | Medical records from The Helmholtz Eye Research Institute | Patients with inflammatory eye conditions | Observational | 2013 | Ophthalmic | 3 |
| Russia [69] | Altai region Siberian Federal district | Dedkov, 2017 | Standardized questionnaire | Regional general population | Retrospective observational | 2013-2015 | IgM paired sera or IgG | 17 |
| Russia [70] | St. Petersburg | Grineva 2019 | Children Clinical Research Center of Infectious Diseases | Children (1—17 yrs) with admitted with suspected LB | Prospective cohort | 2010-2016 | LB EM | 184 142 |
| Slovak Republic [71] | Bratislava | Trnovcova 2007 | Hospital-based data | Patients with EM | Prospective cohort | 2001-2005 | EM | 25 |
| Slovenia [72] | Ljubljana | Ogrinc 2016 | Medical records University Medical Centre | Adult patients with a clinical diagnosis of Bannwarth syndrome attending the LB outpatient clinic | Prospective cohort | 2005-2013 | LNB: Bannwarth syndrome EM | 77 46 |
| Slovenia [73] | Ljubljana | Maraspin 2019 | Hospital medical records, University Medical Centre | Adults diagnosed with EM Receiving treatment with tumor necrosis factor | Prospective cohort | 2009-2018 | EM | 16 16 |
| Slovenia [74] | Ljubljana | Stupica 2011 | LB Outpatient's Clinic, University Medical Center | Adults with EM and skin biopsy | Prospective cohort | 2006 | EM: CDC | 252 |
| Slovenia [75] | Ljubljana | Stupica 2015 | LB Outpatient's Clinic, University Medical Center | Adults with EM and skin biopsy | Prospective cohort | 2010 | EM: EUCALB | 252 |
| Slovenia [76] | Ljubljana | Arnez 2011 | Dept Infectious Disease, | Consecutive children (<15yrs) with EM | Prospective cohort | 1996-2004 | EM: CDC | 1164 |

| Country | National or sub-national area | Author Year | Data source | Study Population | Study design | Study period | Case definition | Number of cases |
|---------------|-------------------------------|---------------|---|--|--------------------|--------------|-------------------------|-----------------|
| Slovenia [77] | Center Ljubljana | Maraspin 2015 | University Medical Centre Ljubljana Outpatient medical records | Adults with a hematological malignancy with EM Immunocompetent controls | Prospective cohort | 1992-2013 | EM: EUCALB | 53 |
| Ukraine [78] | National | Biletska 2008 | Serological survey | Sick people with suspected LB | Prospective cohort | 2003-2006 | LB laboratory confirmed | 1650 |

ACA, Acrodermatitis chronica atrophicans; CDC, the United States Centers for Disease Control and Prevention; CI, confidence interval; EM, erythema migrans; EUCALB, European Union Concerted Action on Lyme borreliosis; LA, Lyme arthritis; LB, Lyme borreliosis; LC, Lyme carditis; LNB, Lyme neuroborreliosis; NR, not reported

Table S8: Cases of LB in Nordic region from literature published from 2005 to 2020

| Country | National or sub-national area | Author Year | Data source | Study Population | Study design | Study period | Case definition | Number of cases |
|--------------|--|-------------------|--|----------------------|--|--------------|--|--|
| Denmark [79] | National | Christiansen 2005 | Surveillance data | Denmark population | Retrospective surveillance | 2004 | LNB: laboratory confirmed | 63 |
| | | | | | | 2005 | | 34 |
| | | | | | | 1994-2004 | | 471 |
| | | | | | | 2004-2005 | | 413 |
| Denmark [80] | National | Obel 2018 | Danish laboratories and other national registries | Denmark population | Retrospective cohort | 1985-2016 | LNB: positive intrathecal antibody test | 2067 |
| Denmark [81] | East Zealand North Zealand Southwest Zealand Funen South Jutland Mid Jutland East Northwest Jutland North Jutland Bornholm | Tetens 2020 | Danish national registries | Denmark population | Retrospective cohort | 1996-2015 | LNB: Positive intrathecal antibody test | 683 |
| | | | | | | | | 266 |
| | | | | | | | | 420 |
| | | | | | | | | 409 |
| | | | | | | | | 28 |
| | | | | | | | | 463 |
| | | | | | | | | 26 |
| | | | | | | | | 425 |
| | | | | | | | | 71 |
| | | | | | | | | 2643 |
| Denmark [82] | Copenhagen, Funen, and North Jutland | Dessau 2010 | GP survey of patients with a LB serology request | Regional populations | Cohort | 2002-2003 | LB: EUCALB EM LNB ACA LC Chronic LNB Lymphocytoma Other No current clinical symptoms | 1011 340 67 14 130 28 330 367 |
| Denmark [83] | Eastern Denmark | Gynthersen 2020 | 233 referrals of the hospital Department of Infectious Disease with suspected LB | NR | Prospective cohort, Sero-epidemiological | 2017-2019 | LB: laboratory confirmed EM LNB ACA Multiple EM LC Post-treatment LB syndrome | 45 |
| | | | | | | | | 20 |
| | | | | | | | | 14 |
| | | | | | | | | 6 |
| | | | | | | | | 4 |
| | | | | | | | | 1 |
| | | | | | | | | 12 |

| Country | National or sub-national area | Author Year | Data source | Study Population | Study design | Study period | Case definition | Number of cases |
|--------------|--|---------------|---|---|------------------------------|--------------|--|------------------------|
| Finland [84] | Helsinki | Kanerva 2013 | Computerized search within the health-care district | Patients of Department of Otorhinolaryngology, Helsinki University Central Hospital | Prospective cohort | 2007-2009 | Intra-thecal antibodies and lymphocytic pleocytosis in CSF | 14 |
| Norway [85] | South-Rogaland district | Oymar 2009 | Children admitted for possible LNB | Regional population | Retrospective cohort | 1996-2006 | LNB: laboratory confirmed | 143 |
| Norway [86] | High endemicity southern coastal areas | Ljostad 2007 | Prospective hospital-based data | Adult > 18 years inpatients with LNB | Prospective cohort | 2004-2006 | LNB: Laboratory confirmed | 43 |
| Norway [87] | Agder county | Quarsten 2017 | GP-recruited participants | 70 adults with tick bite and symptoms | Prospective cohort, GP-based | 2014-2015 | EM PCR positive | 65 |
| Norway [88] | National | Mysterud 2017 | Surveillance data | Norway population | Retrospective cohort | 1991-2015 | Laboratory confirmed since 1995 | 3424 |
| Norway [89] | South Rogaland district, Norway | Tveitnes 2007 | Prospective data collection | Children <15 years admitted with facial palsy | Prospective cohort | 1996-2004 | CSF/antibody confirmation | 142 |
| Norway [90] | Vest-Agder | Ljostad-2005 | Hospital based data | Adults admitted with facial palsy | Prospective cohort | 1997-1998 | CSF confirmed | 14 |
| Sweden [91] | Greater Stockholm | Bagger 2005 | Children treated for LNB | Regional population | Prospective case-control | 1995-1997 | LNB | 255 |
| Sweden [92] | Stockholm | Arnason 2020 | Hospital medical records | Children admitted with facial palsy | Retrospective cohort | 2014-2015 | LNB | 45 |
| Sweden [93] | Southern Sweden | Ornstein 2020 | Prospective data | 207 patients with EM and LNB | Prospective cohort | 1994-1997 | LB: CDC LNB: CDC | 75 80 |

ACA, Acrodermatitis chronica atrophicans; CDC, the United States Centers for Disease Control and Prevention; CI, confidence interval; EM, erythema migrans; EUCALB, European Union Concerted Action on Lyme borreliosis; LA, Lyme arthritis; LB, Lyme borreliosis; LC, Lyme carditis; LNB, Lyme neuroborreliosis; NR, not reported

Table S9: Cases of LB in the United Kingdom from literature published from 2005 to 2020

| Country | National or sub-national area | Author Year | Data source | Study Population | Study design | Study period | Case definition | Number of cases |
|---------|-------------------------------|-------------|--|------------------------------------|----------------------|--------------|--|-----------------|
| UK [94] | London | Dillon 2010 | The Hospital for Tropical Diseases clinical database | Patients presenting to clinics | Prospective cohort | 2002-2007 | LB: Infectious Disease Society of America definition | 65 |
| UK [95] | South west England | Lovett 2008 | Medical record | Patients with positive LB serology | Retrospective cohort | 2000-2004 | LB: serologically confirmed | 88 |

ACA, Acrodermatitis chronica atrophicans; CDC, the United States Centers for Disease Control and Prevention; CI, confidence interval; EM, erythema migrans; EUCALB, European Union Concerted Action on Lyme borreliosis; LA, Lyme arthritis; LB, Lyme borreliosis; LC, Lyme carditis; LNB, Lyme neuroborreliosis; NR, not reported

Table S10: Cases of LB in Southern Europe from literature published from 2005 to 2020

| Country | National or sub-national area | Author Year | Data source | Study Population | Study design | Study period | Case definition | Number of cases |
|------------------------|-------------------------------|----------------|--|------------------------------|-------------------------------|--------------|---|-----------------|
| Croatia [27] | Bjelovarsko-bilogorska county | Ropac 2013 | Institute of Public health in Bjelovar-Bilogora, Croatia | NR | Retrospective cross-sectional | 2007-2011 | LB | 34 |
| Croatia [96] | National | Dzelalija 2015 | Croatian National Institute of Public Health, Division of Epidemiology | Croatian national population | Retrospective cohort | 2005 | Clinical and epidemiology data, serology methods (IFA, ELISA), molecular (PCR), and culture | 220 |
| | 2006 | | | | | 301 | | |
| | 2007 | | | | | 266 | | |
| | 2008 | | | | | 439 | | |
| | 2009 | | | | | 435 | | |
| | 2010 | | | | | 492 | | |
| | 2011 | | | | | 499 | | |
| | 2012 | | | | | 434 | | |
| | 2013 | | | | | 661 | | |
| | 2014 | | | | | 470 | | |
| | 2005-2014 | | | | | 4217 | | |
| | 2005-2004 | | | | | 77 | | |
| | Bjelovarsko-bilogorska | | | | | 1383 | | |
| | Grad Zagreb | | | | | 204 | | |
| | Koprivničko-križevačka | | | | | 88 | | |
| | Virovitičko-podravska | | | | | 47 | | |
| | Požeško-slavonska | | | | | 70 | | |
| | Brodsko-posavske | | | | | 137 | | |
| | Osječko-baranjska | | | | | 52 | | |
| | Vukovarsko-srijemska | | | | | 106 | | |
| Sisa~ko-moslava~ko | 155 | | | | | | | |
| Karlovačka | 292 | | | | | | | |
| Primorsko-goranska | 5 | | | | | | | |
| Ličko-senjska | 72 | | | | | | | |
| Istarska | 3 | | | | | | | |
| Zadarska | 0 | | | | | | | |
| Šibensko-kninska | 13 | | | | | | | |
| Splitsko-dalmatinska | 7 | | | | | | | |
| Dubrovačko-neretvanska | 274 | | | | | | | |
| Međimurska | 207 | | | | | | | |
| Varaždinska | 427 | | | | | | | |
| Krapinsko zagorska | 598 | | | | | | | |
| Zagrebačka | | | | | | | | |

| Country | National or sub-national area | Author Year | Data source | Study Population | Study design | Study period | Case definition | Number of cases | | | | | | | |
|--------------|--|----------------|--|--|---|--------------|-----------------------|-----------------|--------------|--------------------------|-------------------------------------|--------------------------------|-----------|------------------------------|-----------|
| Croatia [97] | National | Mulic 2006 | Notifications to the Croatian Institute of Public Health | Croatian national population | Retrospective cohort | 1988 | LB | 4 | | | | | | | |
| | | | | | | 1989 | | 4 | | | | | | | |
| | | | | | | 1990 | | 1 | | | | | | | |
| | | | | | | 1991 | | 168 | | | | | | | |
| | | | | | | 1992 | | 96 | | | | | | | |
| | | | | | | 1993 | | 306 | | | | | | | |
| | | | | | | 1994 | | 260 | | | | | | | |
| | | | | | | 1995 | | 274 | | | | | | | |
| | | | | | | 1996 | | 335 | | | | | | | |
| | | | | | | 1997 | | 229 | | | | | | | |
| | | | | | | 1998 | | 248 | | | | | | | |
| | | | | | | 1999 | | 232 | | | | | | | |
| | | | | | | 2000 | | 235 | | | | | | | |
| | | | | | | 2001 | | 313 | | | | | | | |
| Italy [98] | National Endemic areas Friuli-Venezia Giulia, Trentino-Alto Adige, Liguria, Emilia-Romagna Non endemic areas: other regions of Italy | Esposito 2021 | Survey of 176 pediatric infectious disease physicians Registry of LD | Children with LB (N=160: 80 living in endemic and 80 in non-endemic areas) | Cross-sectional survey | 2005-2011 | EUCALB | 160 | | | | | | | |
| | | | | | | | EM | 66 | | | | | | | |
| | | | | | | | LA | 10 | | | | | | | |
| | | | | | | | LNB | 4 | | | | | | | |
| | | | | | | | EM | 64 | | | | | | | |
| | | | | | | | LA | 14 | | | | | | | |
| | | | | | | | LNB | 2 | | | | | | | |
| | | | | | | | Italy [99] | Latium | Santino 2011 | Laboratory records | Patients with serology data (N=954) | Retrospective cohort | | LB: serologically confirmed | 42 |
| | | | | | | | | | | | | | | EM | 21 |
| | | | | | | | | | | | | | | LNB | 7 |
| Italy [100] | Northeast Italy | Marangoni 2008 | Serology samples | Patients with EM | Retrospective cross-sectional, sero-epidemiological | NR | EM: Culture-confirmed | 66 | | | | | | | |
| | | | | | | | Turkey [101] | NR | Çelik 2016 | Hospital medical records | Children with LNB | Retrospective cross-sectional, | 2014-2015 | LNB: serologically confirmed | 75 |

ACA, Acrodermatitis chronica atrophicans; CDC, the United.States Centers for Disease Control and Prevention; CI, confidence interval; EM, erythema migrans; EUCALB, European Union Concerted Action on Lyme borreliosis; LA, Lyme arthritis; LB, Lyme borreliosis; LC, Lyme carditis; LNB, Lyme neuroborreliosis; NR, not reported

Table S11: Cases of LB in Central/Western Europe from literature published from 2005 to 2020

| Country | National or sub-national area | Author Year | Data source | Study Population | Study design | Study period | Case definition | Number of cases |
|---------------|---|---------------|--|--|---|--------------|---|-----------------|
| Belgium [102] | - | Linard 2007 | Sentinel surveillance data, modelled estimates | Nationwide general population (adult) | Retrospective surveillance | 1994 | Laboratory confirmed cases | ~190 |
| | | | | | | 1995 | | ~200 |
| | | | | | | 1996 | | ~250 |
| | | | | | | 1997 | | ~320 |
| | | | | | | 1998 | | ~280 |
| | | | | | | 1999 | | ~380 |
| | | | | | | 2000 | | ~400 |
| | | | | | | 2001 | | ~550 |
| | | | | | | 2002 | | ~870 |
| | | | | | | 2003 | | ~700 |
| 2004 | ~1400 | | | | | | | |
| France [103] | National | Trombert 2005 | Serosurvey in Pasteur-Cerba laboratory | Patients (N=1,330) | Retrospective cross-sectional, sero-epidemiological | 2003 | Serologically confirmed by Western blot | 425 |
| France [104] | National | Grillon 2019 | The French National Reference Center for Borrelia database | France general population | Retrospective cohort | 2010-2016 | LA: Positive PCR in synovial fluid | 37 |
| France [105] | Besancon | Voitey 2020 | Single medical center | Preferred for suspected LB | Retrospective cohort | 2015-2018 | LB: EUCALB | 48 |
| | | | | | | | LNB | 17 |
| | | | | | | | EM | 20 |
| | | | | | | | Early disseminated stage | 24 |
| Other | 7 | | | | | | | |
| France [106] | La Pitie Salpetriere Hospital, Paris | Kaminsky 2020 | Hospital-based data | Patients with LNB | Prospective cohort | 2007-2017 | LNB: laboratory confirmed | 16 |
| France [107] | National | Jacquet 2019 | Hospital medical records in Nancy | Patients referred to the hospital-based dedicated LB treatment pathway (N=468) | Retrospective cohort | 2016-2017 | LB: French Infectious Diseases Society | 69 |
| France [108] | Aquitaine, Limousin, Rhone-Alpes, Franche Comte, and Alsace | Mariet 2013 | Sentinel GP surveillance network | Regional population | Prospective observational | 2001-2012 | EM: EUCALB | 1453 |
| | | | | | | | | 41 |
| | | | | | | | | 170 |
| | | | | | | | | 335 |

| Country | National or sub-national area | Author Year | Data source | Study Population | Study design | Study period | Case definition | Number of cases |
|--------------------------|-------------------------------|-------------------------|---|---|-----------------------------|--------------|--|-----------------|
| | Franche Comte Alsace | | | | | | | 277 |
| Germany [109] | National | Lohr 2015 | German statutory health insurance company (DAK-G) | Insured DAK-G population | Retrospective observational | 2008-2011 | LB (ICD-10 A69.2 + Code M01.2 arthritis) | 630 |
| | | | | | | 2008 | | 591 |
| | | | | | | 2009 | | 512 |
| | | | | | | 2010 | | 549 |
| | | | | | | 2011 | | 511 |
| Germany [110] | Munich | Buchholz 2014 | Department of Neurology at Klinikum Grosshadern, University of Munich | Inpatients with neuroinfectious diseases (N=376) | Retrospective cohort | 2005-2009 | LNB | 35 |
| The Netherlands [111] | | Broekhuijsen-van Henten | Reports to the Dutch Paediatric Surveillance system | Children <18 y | Prospective cohort | 2006-2007 | LNB: EUCALB The Dutch Institute for Healthcare Improvement | 66 |
| The Netherlands [112] | Amsterdam | Nassar-2018 | Medical records from the Department of Medical Microbiology and Academic Medical Centre | Children (< 18 years) with a clinical suspicion of LB, referred to the AMC in The Netherlands | Retrospective cohort | 2011-2015 | LB: Clinical Dx | 38 |
| Switzerland [113] | - | Monteventi 2018 | The Swiss Neuropediatric Stroke Registry | Children with stroke | Prospective cohort | 2000-2015 | LNB: clinical and laboratory | 4 |
| | | | | | Retrospective | | Multiple EM | 545 |
| Switzerland [114] | Neuchatel | Huegli 2011 | Questionnaire and blood samples | Residents presenting after tick bite in an endemic area (N=474) | Prospective cohort | 2003-2005 | LB confirmed by Western blot EM | 12 |
| | | | | | | | | 14 |

ACA, Acrodermatitis chronica atrophicans; CDC, the United States Centers for Disease Control and Prevention; EM, erythema migrans; EUCALB, European Union Concerted Action on Lyme borreliosis; LA, Lyme arthritis; LB, Lyme borreliosis; LC, Lyme carditis; LNB, Lyme neuroborreliosis; NR, not reported

Footnote for all Supplement Tables

Incidence estimates and 95% CIs have been rounded to the first decimal to the right for consistent level of precision.

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