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The burden of Lyme borreliosis expressed in disability-adjusted life years

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Background: Lyme borreliosis (LB) is the most commonly reported tick-borne infection in Europe and North America. In the last 15 years a 3-fold increase was observed in general practitioner consultations for LB in the Netherlands. To support prioritization of prevention and control efforts for LB, we estimated its burden expressed in Disability-Adjusted Life Years (DALYs). **Methods:** We used available incidence estimates for three LB outcomes: (i) erythema migrans (EM), (ii) disseminated LB and (iii) Lyme-related persisting symptoms. To generate DALYs, disability weights and duration per outcome were derived using a patient questionnaire including health-related quality of life as measured by the EQ-5D. **Results:** We estimated the total LB burden for the Netherlands in 2010 at 10.55 DALYs per 100 000 population (95% CI: 8.80–12.43); i.e. 0.60 DALYs for EM, 0.86 DALYs for disseminated LB and 9.09 DALYs for Lyme-related persisting symptoms. Per patient this was 0.005 DALYs for EM, 0.113 for disseminated LB and 1.661 DALYs for a patient with Lyme-related persisting symptoms. In a sensitivity analysis the total LB burden ranged from 7.58 to 16.93 DALYs per 100 000 population. **Conclusions:** LB causes a substantial disease burden in the Netherlands. The vast majority of this burden is caused by patients with Lyme-related persisting symptoms. EM and disseminated Lyme have a more modest impact. Further research should focus on the mechanisms that trigger development of these persisting symptoms that patients and their physicians attribute to LB.

Introduction

Lyme borreliosis (LB) is caused by *Borrelia burgdorferi* sensu lato which in Europe is predominantly transmitted by the tick *Ixodes ricinus*. LB is the most commonly reported tick-borne infection in Europe and North America.[1,2] The severity of symptoms in some LB patients, and the in recent years reported increase of LB in some countries or areas in Europe and North-America has raised questions about its public-health impact.[1–4] In the last 15 years in the Netherlands a 3-fold increase was observed in general practitioner (GP) consultations for tick bites and erythema migrans (EM)—the most frequent early LB manifestation.[5,6] Early uncomplicated infection generally responds well to antibiotic treatment, and thus the majority of LB patients have a good prognosis.[7,8] However, even after repeated antibiotic therapy, some patients report persisting symptoms like musculoskeletal pain, neurocognitive symptoms and fatigue.[1,2,8,9] Especially these persisting and sometimes disabling symptoms have great impact on the quality of life of the patients concerned.

Until now, worldwide no quantitative estimation of the disease burden of LB has been available that can be used to prioritize prevention and control efforts. Such an estimate would show which LB outcomes contribute most to the LB burden, and would make it possible to compare its burden to the public-health impact of other diseases. This study aimed to estimate the burden of LB expressed in Disability-Adjusted Life Years (DALYs), a summary measure of disease burden that aggregates the impact of mortality and morbidity in one figure.[10] Within the scope of this study we assessed the burden for the Netherlands in 2010; we also present the burden per case to facilitate estimates for other endemic countries based upon their national incidence figures.

Methods

Outcomes of LB and annual incidence per outcome

Figure 1 shows the possible health outcomes of LB, after a tick bite causing a *Borrelia burgdorferi* sensu lato infection. We distinguished three outcome categories similar as in Hofhuis et al.[11]: (i) EM— the most common clinical manifestation—an expanding skin lesion at the site of the tick bite; (ii) (early and late) disseminated LB—the more serious manifestations—which can present as a multi-system disease with skin, neurological, cardiac and musculoskeletal manifestations, especially if early infection remains untreated[1]; and (iii) persisting symptoms that patients and their physicians attribute to LB after a successfully treated infection or due to persistent infection,[1,2,9,12–14] hereafter referred to as 'persisting symptoms'.

We used a recent estimate of the LB incidence for our estimation of disease burden. In Hofhuis et al.[11], the 2010 incidence per LB outcome has been estimated for the Netherlands based on a survey among GPs: per 100 000 population 131.5 (95% CI: 127.1–136.0) diagnoses of EM, 7.7 (7.2–8.2) diagnoses of disseminated LB and 5.5 (5.1–5.8) new diagnoses with persisting symptoms which the GP

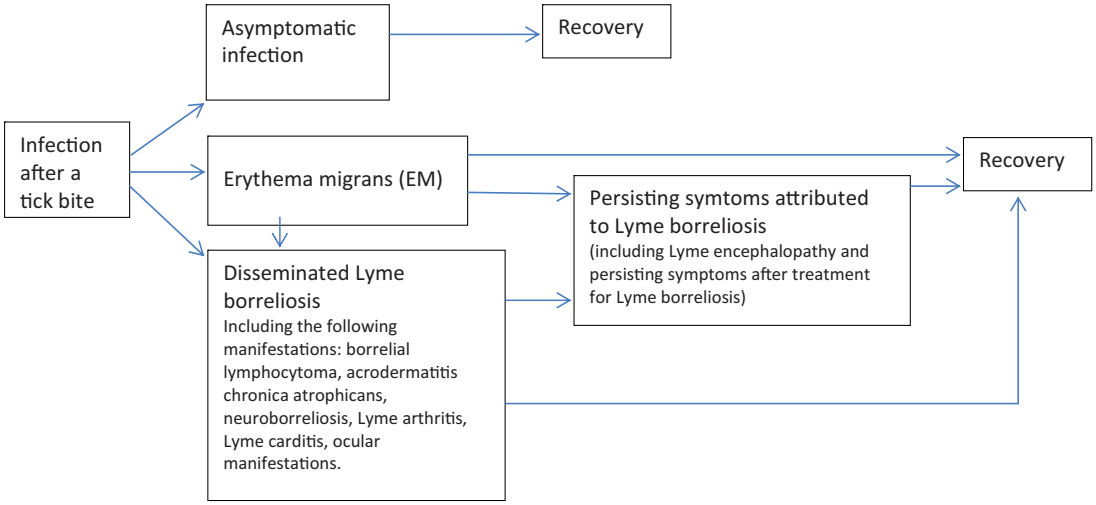

Figure 1 Outcome tree with possible health outcomes of Lyme borreliosis. After a tick bite followed by infection, we distinguished three symptomatic outcome categories: (1) EM— the most common clinical manifestation—an expanding skin lesion occurring after several days or weeks at the site of the tick bite; (2) (early and late) disseminated LB—the more serious manifestations—which can present as a multi-system disease with skin, neurological, cardiac and musculoskeletal manifestations, especially if early infection remains untreated; and (3) persisting symptoms attributed to LB—after a successfully treated infection or due to persistent infection

attributed to LB; these estimates include only (very) likely diagnoses and have been adjusted for reporting bias.[11]

Patient questionnaire

To gather data on duration of disease and severity per outcome, we developed a LB patient questionnaire. We distributed 5171 patient questionnaires by mail, of which 4702 were sent to physicians with the request to forward them to their LB patients. The Medical Ethics Review Committee of the University Medical Centre Utrecht declared that the Medical Research Involving Human Subjects Act does not apply to this study (protocol number 14-283/C, letter number WAG/om/14/015644). Patients were eligible for the study if they suffered symptoms of LB in the 12 months preceding the questionnaire.

The physicians that enrolled patients were mainly GPs, medical specialists and/or occupational physicians who responded to the incidence questionnaire by Hofhuis et al. (see Appendix A, figure A1). The remaining 469 questionnaires were sent directly to patients upon their request, mainly through the national Lyme patient association. No reminders were sent. The questionnaire included questions on demographic characteristics, diagnosed clinical manifestations of LB (based upon the case definitions used in Hofhuis et al.[11], see also figure 1), and severity and duration of disease. We also asked for co-morbidity, as adjusted from the TIC-P questionnaire.[15]

LB outcomes and severity of disease

We firstly assigned patients to 10 manifestations of LB based upon the manifestations diagnosed, as reported in the questionnaire. We subsequently assigned patients to the three outcome categories as described in figure 1 following the criteria described in Appendix A.

Following the DALY concept, we then expressed severity of disease in disability weights between 0 (representing 'full health') and 1 ('death'). In the absence of standardized disability weights for LB and because of the wide range of symptoms, we derived disability weights per LB outcome using the health states as measured by the EQ-5D in our patient questionnaire.[16,17] See Appendix B for further details.

Duration of disease

The questionnaire facilitated reporting of duration of disease both by date of onset (i.e. date of tick bite plus incubation period) and by pre-coded categories ('less than 1 week', '1–4 weeks', '1–6 months', '6–12 months', '1–5 year', '5–10 year'). To enable calculation of disease duration, a value was assigned to these pre-coded categories, based on the best fit of an assumed underlying negative binomial distribution. Since we used a cross-sectional survey, episodes of disease were right-censored for all patients that were currently ill when filling in the questionnaire. Estimates for the mean disease duration were obtained by survival analysis (see Appendix B).

Baseline DALY estimate and sensitivity analysis

We calculated the disease burden expressed in DALYs (see Appendix B). For the baseline DALY estimate we excluded the patients that were enrolled on their own request when estimating disease duration and disability weights. These patients were recruited mainly through the national patient association and therefore possibly more severely ill than the average patient.

To explore the consequences of using different estimates for the incidence, severity and duration of disease, or for possible mortality due to LB, we also calculated the DALYs for seven alternative scenarios (table 1, see also Appendix B).

Results

LB classification of patients

A total of 949 patients responded, of whom 660 patients were included in the analysis; they were assigned to the outcomes EM ($n = 88$; of which 87 (99%) enrolled through their physicians), disseminated Lyme ($n = 96$; 88 (92%) enrolled through physicians) or persisting symptoms ($n = 476$; of which 189 (40%) enrolled through physicians). See Appendix A and figure A1 for further details.

Severity, duration of disease and DALYs

No meaningful survival curve could be obtained for the Lyme-related persisting symptoms outcome because the parameter estimates of the survival distribution had very wide confidence intervals, as many participants in this group were still ill when they filled in the questionnaire (i.e. most individuals had a censored duration). Therefore, we used the censored estimate for

Table 1 Sensitivity analysis scenarios to calculate DALYs for LB based upon disease duration and severity assessed in a patient questionnaire, and incidence estimates available from Hofhuis et al.[11]

Scenarios	Criteria for included patients and parameters
Baseline estimate	–Restrict to patients that were enrolled through their physicians to estimate the disease duration and disability weights
Scenario 1: Include patients enrolled upon their own request	–Same as baseline AND include patients enrolled upon their own request—i.e. mainly through the national patient association
Scenario 2: Include less likely LB diagnoses in incidence estimates	–Same as baseline AND Use higher LB incidence estimates that also include less likely LB diagnoses[11]
Scenario 3: Exclude 5% patients with highest disease severity and duration	–Same as baseline BUT exclude per LB outcome patients with the 5% highest extreme values for disability weights and disease duration
Scenario 4: No co-morbidity	–Same as baseline BUT exclude patients with any co-morbidity.
Scenario 5: Five annual deaths due to LB	–Same as baseline AND inclusion of 5 deaths attributable to LB per year, with mean age 39 years and a residual life expectancy of 47.62 years (as derived from the GBD 2010 standard life table[22])
Scenario 6: Adjust for censored disease duration in the persisting symptoms patients.	–Same as baseline AND raise the disease duration for persisting symptoms patients with 25%.
Scenario 7: Combine scenario 2,3,4, 5 & 6	–Same as baseline AND scenario 2,3,4, 5 & 6

the mean duration for this particular outcome—i.e. 4.6 years, similar to the 3–6 years reported in earlier studies.[9,18]

Table 2 shows the disability weights, duration of disease and DALYs per LB outcome in the Netherlands in 2010 for the baseline estimate. The total burden due to LB was estimated at 10.55 DALYs per 100 000 population (95% CI: 8.80–12.43) and thus for the entire 16.6 million population at 1749 DALYs (95% CI: 1458–2060). For EM, we estimated the lowest disease burden per patient—i.e. a disability weight of 0.047, disease duration 5 weeks, and thus 0.005 DALYs per patient—reflecting its relatively mild condition. Because of the relatively high EM incidence, the total disease burden due to EM was nevertheless 0.60 DALYs per 100 000 population (and 99 DALYs for the total population). For disseminated LB the disease burden of 0.113 DALYs per patient was 23 times higher, reflecting its more severe condition, with a disability weight of 0.262 and disease duration of 22.5 weeks. Yet, because of the lower incidence compared with EM, the total disease burden due to disseminated LB was only 1.4 times higher: 0.86 DALYs per 100 000 population (143 for the total population). The outcome persisting symptoms had the highest disease burden per patient: an average disability weight of 0.364, disease duration 4.568 years, and thus 1.661 DALYs per patient. Although the incidence of persisting symptoms is lower than the incidence of disseminated LB, this high disease burden per patient leads to the highest disease burden per outcome: 9.09 DALYs per 100 000 population (1506 for the total population). This accounts for 86% of the total DALYs due to LB.

Sensitivity analysis

Table 2 and figure 2 show the disease burden per LB outcome for the baseline and the seven scenarios in the sensitivity analysis. The total burden due to LB ranges from 7.58 DALYs (scenario 3) to 16.93 DALYs (scenario 1) per 100 000 population. The high estimate in scenario 1, which included patients enrolled upon their own request, is mainly due to a significantly higher disease duration of these patients compared with the patients enrolled through physicians (ANOVA; $P < 0.0001$). In scenario 4, differences in disability weights and disease duration were not significant between patients with and without co-morbidity (ANOVA: $P = 0.08$ and $P = 0.87$).

In all scenarios, the outcome persisting symptoms is the biggest contributor to the total disease burden—ranging from 76–91% of total DALYs by LB. All scenarios showed the per patient disease burden to be highest for persisting symptoms and lowest for EM.

Discussion

We assessed the disease burden expressed in DALYs of Lyme borreliosis, the most commonly reported tick-borne infection in Europe and North America. Using available incidence estimates from Hofhuis et al.[11] and a patient questionnaire to assess severity and duration of disease, we estimated the burden due to LB in the Netherlands. The total disease burden for 2010 was 10.55 DALYs per 100 000 population (95% CI: 8.80–12.43) and thus for the entire population 1749 DALYs (95% CI: 1458–2060). The vast majority of this burden due to LB was caused by patients with persisting symptoms attributed to LB (9.09 out of 10.55 DALYs per 100 000 pop.; i.e. 86%), whereas EM and disseminated LB have a more modest impact of 1.46 DALYs (0.60 and 0.86 DALYs per 100 000 pop.). Per individual LB case, the DALY estimate was also highest for persisting symptoms attributed to LB (1.661 DALYs per patient), moderately high for disseminated LB (0.113) and modest for EM (0.005).

We thus found a substantial disease burden due to LB, which calls for continued prevention and control efforts. However, its major impact is caused by patients with persistent Lyme-related symptoms, whereas both in Europe and North-America it remains debated to what extent persisting symptoms attributed to LB are actually due to a present or preceding infection.[1,2,12,19–21] Our patient questionnaire and the incidence survey applied by Hofhuis et al.[11] cannot discriminate whether LB actually caused the reported Lyme-related persisting symptoms. Nevertheless, our results reflect the very substantial disease burden due to persisting symptoms that patients and their physicians attribute to LB. This calls for further research to the causal mechanisms of developing these symptoms—whether or not due to past or present *Borrelia* infection—to be able to develop better prevention and treatment strategies for patients at risk for persistence of symptoms.

This is to our knowledge worldwide the first DALY estimate for LB; it adds to other studies estimating the burden of infectious diseases,

Table 2 Estimation of disease burden of LB in the Netherlands 2010: baseline estimate and sensitivity analysis

Scenario	LB outcome	Enrollment	Disability weight (95%CI[a])	Duration of disease in years[b] (95%CI[a])	DALY per patient (95%CI[a])	Annual numbers (16.6 million pop.)[11] (95%CI[a])	Annual incidence per 100 000[11] (95%CI[a])	DALYs per 16.6 million pop. (95%CI[a])	DALYs per 100 000 population (95%CI[a])
Baseline estimate	**EM**	(*n* = 87)	0.047(0.033–0.064)	0.096(0.072–0.130) i.e. 5.0 wks (3.7–6.8)	0.005(0.003–0.007)	21 802(21 064–22 545)	131.5(127.1–136.0)	99(61–148)	0.60(0.37–0.89)
	Disseminated Lyme	(*n* = 88)	0.262(0.205–0.325)	0.432(0.304–0.656) i.e. 22.5 wks (15.8–34.1)	0.113(0.072–0.178)	1268(1186–1353)	7.7(7.2–8.2)	143(91–223)	0.86(0.55–1.34)
	Persisting symtoms	(*n* = 189)	0.364(0.326–0.397)	4.568(3.919–5.234)	1.661(1.372–1.967)	905(845–966)	5.5(5.1–5.8)	1506(1226–1796)	9.09(7.40–10.84)
	All LB							**1749(1458–2060)**	**10.55(8.80–12.43)**
1. Include patients enrolled upon their own request	**EM**	(*n* = 88)	0.047(0.033–0.065)	0.097(0.074–0.131)	0.005(0.003–0.007)	21 802(21 064–22 545)	131.5(127.1–136.0)	100(64–151)	0.60(0.39–0.91)
	Disseminated Lyme	(*n* = 96)	0.270(0.218–0.328)	0.422(0.298–0.609)	0.114(0.075–0.170)	1268(1186–1353)	7.7(7.2–8.2)	145(95–219)	0.87(0.57–1.32)
	Persisting symtoms	(*n* = 476)	0.385(0.362–0.408)	7.337(6.793–7.966)	2.826(2.528–3.119)	905(845–966)	5.5(5.1–5.8)	2561(2247–2876)	15.45(13.56–17.35)
	All LB							**2806(2488–3151)**	**16.93(15.01–19.01)**
2. Include less likely LB diagnoses in incidence estimates	**EM**	(*n* = 87)	0.047(0.033–0.064)	0.096(0.072–0.130) i.e. 5.0 wks (3.7–6.8)	0.005(0.003–0.007)	21 802(21 064–22 545)	131.5(127.1–136.0)	99(61–148)	0.60(0.37–0.89)
	Disseminated Lyme	(*n* = 88)	0.262(0.205–0.325)	0.432(0.304–0.656) i.e. 22.5 wks (15.8–34.1)	0.113(0.072–0.178)	1386(1296–1479)	8.4(7.8–8.9)	157(100–243)	0.95(0.60–1.47)
	Persisting symtoms	(*n* = 189)	0.364(0.326–0.397)	4.568(3.919–5.234)	1.661(1.372–1.967)	1137(1061–1214)	6.9(6.4–7.3)	1892(1540–2256)	11.41(9.29–13.61)
	All LB							**2147(1788–2530)**	**12.96(10.79–15.26)**
3. Exclude 5% patients with highest disease severity and duration	**EM**	(*n* = 66)	0.036(0.025–0.048)	0.081(0.064–0.101)	0.003(0.002–0.004)	21 802(21 064–22 545)	131.5(127.1–136.0)	63(39–92)	0.38(0.23–0.56)
	Disseminated Lyme	(*n* = 68)	0.217(0.169–0.270)	0.332(0.237–0.466)	0.072(0.047–0.111)	1268(1186–1353)	7.7(7.2–8.2)	92(59–142)	0.55(0.36–0.86)
	Persisting symtoms	(*n* = 158)	0.337(0.304–0.371)	3.615(3.189–4.049)	1.218(1.019–1.425)	905(845–966)	5.5(5.1–5.8)	1101(913–1309)	6.64(5.51–7.90)
	All LB							**1256(1067–1474)**	**7.58(6.44–8.89)**
4. No co-morbidity	**EM**	(*n* = 39)	0.053(0.025–0.085)	0.082(0.054–0.124)	0.004(0.002–0.008)	21 802(21 064–22 545)	131.5(127.1–136.0)	93(40–171)	0.56(0.24–1.03)
	Disseminated Lyme	(*n* = 40)	0.237(0.160–0.316)	0.353(0.223–0.604)	0.084(0.042–0.147)	1268(1186–1353)	7.7(7.2–8.2)	106(54–191)	0.64(0.32–1.15)
	Persisting symtoms	(*n* = 75)	0.329(0.280–0.387)	4.706(3.583–6.164)	1.547(1.118–2.077)	905(845–966)	5.5(5.1–5.8)	1402(998–1888)	8.46(6.02–11.39)
	All LB							**1602(1217–2091)**	**9.66(7.34–12.62)**
5. Five annual deaths due to LB	**EM**	(*n* = 87)	0.047(0.033–0.064)	0.096(0.072–0.130)	0.005(0.003–0.007)	21 802(21 064–22 545)	131.5(127.1–136.0)	99(61–148)	0.60(0.37–0.89)
	Disseminated Lyme	(*n* = 88)	0.262(0.205–0.325)	0.432(0.304–0.656)	0.113(0.072–0.178)	1268(1186–1353)	7.7(7.2–8.2)	143(91–223)	0.86(0.55–1.34)

(continued)

Table 2 Continued

Scenario	LB outcome	Enrollment	Disability weight (95%CI[a])	Duration of disease in years[b] (95%CI[a])	DALY per patient (95%CI[a])	Annual numbers (16.6 million pop.)[11] (95%CI[a])	Annual incidence per 100 000[11] (95%CI[a])	DALYs per 16.6 million pop. (95%CI[a])	DALYs per 100 000 population (95%CI[a])
	Persisting symtoms	(*n* = 189)	0.364(0.326–0.397)	4.568(3.919–5.234)	1.661(1.372–1.967)	905(845–966)	5.5(5.1–5.8)	1506(1226–1796)	9.09(7.40–10.84)
	Assumed nr of Deaths	n/a	1	47.62 (i.e. mean 47.62 yrs life expectancy for mean 39 yrs of age)	47.62	5	0.03	238.1	1.44
	All LB			–	–			**1987(1696–2299)**	**11.99(10.23–13.87)**
6. Adjust for censored disease duration in the persisting symptoms patients.	**EM**	(*n* = 87)	0.047(0.033–0.064)	0.096(0.072–0.130)	0.005(0.003–0.007)	21 802(21 064–22 545)	131.5(127.1–136.0)	99(61–148)	0.60(0.37–0.89)
	Disseminated Lyme	(*n* = 88)	0.262(0.205–0.325)	0.432 (0.304 0.656)	0.113(0.072–0.178)	1268(1186–1353)	7.7(7.2–8.2)	143(91–223)	0.86(0.55–1.34)
	Persisting symtoms	(*n* = 189)	0.364(0.326–0.397)	5.708 (4.897 6.541)	2.075(1.714–2.459)	905(845–966)	5.5(5.1–5.8)	1882(1532–2245)	11.35(9.24–13.54)
	All LB			–	–			**2124(1767–2505)**	**12.82(10.66–15.11)**
7. Combine scenario 2, 3, 4, 5 & 6	**EM**	(*n* = 28)	0.027(0.011–0.046)	0.065 (0.047 0.090)	0.002(0.001–0.004)	21 802(21 064–22 545)	131.5(127.1–136.0)	40(14–77)	0.24(0.08–0.47)
	Disseminated Lyme	(*n* = 36)	0.196(0.130–0.271)	0.301 (0.191 0.485)	0.060(0.030–0.115)	1386(1296–1479)	8.4(7.82–8.92)	83(42–158)	0.50(0.25–0.95)
	Persisting symtoms	(*n* = 66)	0.314(0.266–0.365)	4.589 (3.783 5.455)	1.445(1.085–1.854)	1137(1061–1214)	6.9(6.40–7.32)	1644(1227–2122)	9.92(7.40–12.80)
	Assumed nr of Deaths	n/a	1	47.62(i.e. mean 47.62 yrs life expectancy for mean 39 yrs of age)	47.62	5	0.03	238.1	1.44
	All LB			–	–	–		**2004(1599–2503)**	**12.09(9.64–15.10)**

For each scenario in the sensitivity analysis the table shows the included disability weights, the duration of disease and DALY estimates based on the annual incidence per LB outcome.
[a]We estimated 95% CIs using a bootstrap procedure with 1000 iterations while including missing values; for all 660 included patients an (un)censored duration of illness had been recorded; 51 had missing values for disability weights (12 for EM, 6 for disseminated Lyme and 33 for persisting symptoms).
[b]For EM and disseminated patients the uncensored duration of disease was estimated using survival analysis, for the persisting symptoms patients we used the mean censored duration of disease

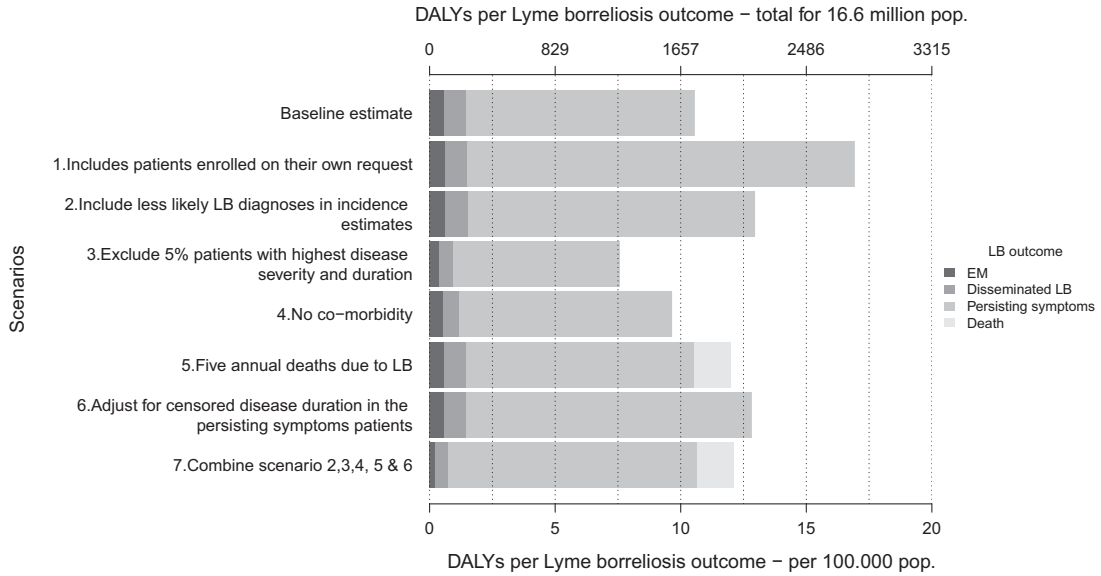

Figure 2 Sensitivity analysis: DALYs per LB outcome for baseline and seven scenarios. We performed a sensitivity analysis with seven alternative scenarios, exploring the consequences of using different estimates for the incidence, severity and duration of disease, or for possible mortality due to LB (table 1). On the *y*-axis, the baseline estimate and the seven alternative scenarios are indicated. The upper *x*-axis presents the DALYs per outcome for the entire population of the Netherlands (16.6 million), the lower *x*-axis DALYs per 100 000 population

and facilitates LB burden estimates for endemic countries in Europe and North-America based upon our DALY estimates per case and their national incidence figures. Compared with many non-communicable diseases, the LB burden is limited—like for most infectious diseases especially in western countries.[22–24] Nevertheless the burden of LB, as for many infectious diseases, can be decreased by public-health measures focusing on prevention of pathogen transmission and timely treatment of infection, and would likely increase without such measures. This calls for continuous priority setting in public-health.

The current study shows that in the Netherlands LB has the 12th highest disease burden, compared with the comprehensive DALY estimates for 32 other infectious diseases largely based upon the 'Burden of Communicable Disease in Europe' (BCoDE) project[25,26,27]; LB is preceded by hepatitis C and Q-fever, and followed by norovirus and *Salmonella* spp. with a somewhat lower burden. If we restrict our estimate to the disease burden attributed to EM and disseminated Lyme (together 1.46 DALYs per 100 000 pop.), LB has still the 20th highest burden, preceded by hepatitis B and *H. influenza*, and followed by *Shigella* spp. and *Listeria* spp.

In addition, DALYs per case can also be used to compare disease burden at the individual level. Per case, the burden of Lyme-related persisting symptoms is the 11th highest compared with the 32 above mentioned pathogens, preceded by tuberculosis and *Listeria* spp., and followed by hepatitis B and tetanus. Disseminated LB and EM have the 19th and 31st highest disease burden respectively.

Finally, disability weights per disease can be used to compare the severity of diseases. Our disability weights based upon the patient questionnaire are within the range of the Global Burden of Disease (GBD) study 2010 disability weights for acute episodes and post-acute consequences of infectious diseases.[28] For EM and disseminated LB the disability weights are very similar to the GBD disability weights for respectively moderate and severe episodes of acute infectious diseases. Lyme-related persisting symptoms and the GBD disability weight for post-acute consequences of infectious disease have overlapping confidence intervals (the GBD point estimate is 30% lower). Compared with non-infectious chronic diseases, our disability weight for Lyme-related persisting symptoms is somewhat higher than Crohn's disease and moderate Parkinson's disease, and somewhat lower than moderate multiple sclerosis and a moderate episode of a major depression.[28]

In our sensitivity analysis, the high impact due to Lyme-related persisting symptoms was consistent in all scenarios. Patients who enrolled in the study on their own request (scenario 1) clearly had a higher disease burden than patients enrolled through their physician. Since these patients predominantly enrolled through the national patient association, it seems plausible that more severely ill patients have been more likely to join this association, and thus these patients were probably not representative for the impact of LB in the general population. This further supports our decision to exclude these patients from the baseline and other scenarios.

When using the incidence estimates that include less likely LB diagnoses (scenario 2), the disease burden increased with 23%, illustrating that under-ascertainment may have led to substantial underestimation of the disease burden. Among the patients enrolled through their physician, the 5% most severely ill had a relatively high impact (28%) on the disease burden (scenario 3). Although this may be representative for LB in the general population, it also illustrates to what extent our estimates could be influenced by selection bias; i.e. if more severely ill cases have been more likely to be enrolled for the study through their physicians.

The influence of co-morbidity on our total disease burden estimate was at most modest (8%), and the observed difference may be due to other co-variables (scenario 4). Sporadic mortality due to LB would moderately increase the disease burden (14% with five annual deaths, scenario 5). We were not able to adjust for censoring in the patient group with persisting symptoms, but our censored estimate for the disease duration was similar to earlier reported durations of Lyme-related persisting symptoms.[9,18] Nevertheless using the censored estimate may have substantially influenced our estimates, as raising our censored estimates with 25% proportionately increases the total disease burden with 22% (scenario 6). On the other hand, we also showed that if we combined this and all other scenarios based on physician enrolled patients, the disease burden converges towards the baseline (scenario 7): 15% above the baseline.

For reasons described in[25,26], in the BCoDE project a pathogen-based incidence approach was developed to derive DALYs for infectious diseases, rather than a prevalence based approach. We similarly derived DALYs using a pathogen-based incidence approach including long-term disease outcomes. However, instead of extrapolating the impact of long-term disease outcomes from the

incidence of initial infections, we used the available incidence estimates for long-term disease outcomes in 2010.[11] Although incident cases of long-term disease outcomes in 2010 originate from initial infections in 2009, this was no problem since the incidence of initial infections was the same for 2009 and 2010 (both ~22000 EM cases for 16.5 million pop.); the 2010 incidence for long-term outcomes is thus expected to be proportionate to the incidence of initial infections in 2010.

Age, sex and other covariates were not taken into account; studies with higher number of patients would facilitate further analysis of the influence and possible bias of such covariates. Furthermore, since unused questionnaires distributed through physicians were mostly not returned, we do not have insight into the non-response to validate to what extent our study population was representative. As an alternative validation, we compared the age and sex distributions of our study population and people acquiring tick bites.[29] The two age distributions both show peaks around 10–14 years of age and around 50 years of age, although elderly people seem to be overrepresented in our study population; as a result the mean age of our study population was 52 years of age, whereas the mean age of people acquiring tick bites was 39 years. The sex distribution of our patients enrolled through physicians was similar to people acquiring tick bites—50% vs. 58% male respectively.

Conclusion

Lyme borreliosis has a substantial disease burden of 10.55 DALYs per 100 000 population (95% CI: 8.80–12.43) based on the incidence of LB in 2010 in the Netherlands (16.6 million pop.). This is the first estimate in DALYs of the public-health impact of LB, which will facilitate LB burden estimates for other countries. The disease burden is predominantly due to patients with persisting symptoms attributed to LB (9.09 DALYs per 100 000 pop.), and to a lesser extent due to patients with EM (0.60 DALYs) and disseminated LB (0.86 DALYs). Further research should focus on evaluating the effectiveness of prevention and control measures to reduce the disease burden, and especially on the mechanisms of developing persisting symptoms that patients and their physicians attribute to LB.

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Key points

- We estimated the disease burden of Lyme borreliosis in the Netherlands expressed in Disability-Adjusted Life Years (DALYs), using available incidence estimates and a patient questionnaire to assess severity and duration of disease.
- This is the first DALY estimate of the public-health impact of Lyme borreliosis, which makes our results relevant for public-health prioritization in all countries where the disease in endemic.
- We found that the disease burden is substantial compared with a comprehensive list of 32 other infectious diseases, which is predominantly due to Lyme-related persisting symptoms.
- The observed disease burden due to Lyme-related persisting symptoms calls for further research to the mechanisms that cause these symptoms—whether or not due to past or present *Borrelia* infection—to be able to develop better prevention and treatment strategies for this patient group.

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Routine testing for blood-borne viruses in prisons: a systematic review

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Background: People in prison have a higher burden of blood-borne virus (BBV) infection than the general population, and prisons present an opportunity to test for BBVs in high-risk, underserved groups. Changes to the BBV testing policies in English prisons have recently been piloted. This review will enable existing evidence to inform policy revisions. We describe components of routine HIV, hepatitis B and C virus testing policies in prisons and quantify testing acceptance, coverage, result notification and diagnosis. **Methods:** We searched five databases for studies of both opt-in (testing offered to all and the individual chooses to have the test or not) and opt-out (the individual is informed the test will be performed unless they actively refuse) prison BBV testing policies. **Results:** Forty-four studies published between 1989 and 2013 met the inclusion criteria. Of these, 82% were conducted in the USA, 91% included HIV testing and most tested at the time of incarceration. HIV testing acceptance rates ranged from 22 to 98% and testing coverage from 3 to 90%. Mixed results were found for equity in uptake. Six studies reported reasons for declining a test including recent testing and fear. **Conclusions:** While the quality of evidence is mixed, this review suggests that reasonable rates of uptake can be achieved with opt-in and, even better, with opt-out HIV testing policies. Little evidence was found relating to hepatitis testing. Policies need to specify exclusion criteria and consider consent processes, type of test and timing of the testing offer to balance acceptability, competence and availability of individuals.

Introduction

The prison estate in England and Wales holds approximately 84 000 people with almost 200 000 passing through the system each year.[1,2] People in prison tend to have both a higher burden of disease and poorer access to healthcare.[3] Infection with blood-borne viruses (BBVs) is higher than the general population largely due to higher levels of injecting drug use.[4] At any given time in the UK detention estate, there are approximately 40 000 problematic drug users with 55% of new prisoners testing positive for Class A drugs.[5] People who inject drugs (PWIDs) are also repeatedly incarcerated with more than 40% having been in prison at least five times.[5] Further, there is a risk of amplification of infectious disease in prisons because of overcrowding, the high prevalence of BBVs, a lack of knowledge among prison staff, limited facilities for diagnosis and treatment, large turnover and high-risk activity such as unprotected sex.[6]

In 2010, out of 6750 new HIV diagnoses in the UK, only 2.4% (160) were infected through injecting drugs.[2] Prevalence data are limited but suggest a higher rate of HIV infection in the prison population: 0.22% versus 0.14% in the UK as a whole.[2] An anonymous testing study in eight prisons across England and Wales in 1997–98 reported a prevalence of 0.4%, based on 82% uptake.[7] The 2001 National Sexual Health and HIV Strategy highlighted that people in prisons have particular HIV prevention requirements.[8] More recently, Public Health England (PHE) has focused on expanding HIV testing to reduce late diagnoses and recommends routine HIV testing for all general medical admissions in areas of high prevalence (estimated prevalence of undiagnosed HIV >= one per 1000 population aged 16-59 years).[9]

Sentinel surveillance in England for 2010 showed that a higher proportion of people in prison tested positive for hepatitis C than in all community health settings except for drug dependency services.[3] In England in 1997/98, 7% of people in prison were positive for