



Original article

Continuing increase of tick bites and Lyme disease between 1994 and 2009



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ABSTRACT

Background: Nationwide cross-sectional retrospective studies have shown a continuous increase in general practitioner (GP) consultations for tick bites and diagnoses of erythema migrans between 1994 and 2005 in the Netherlands. In this paper, we report incidence estimates for GP consultations for tick bites and erythema migrans diagnoses in 2009, and we compare the observed increase in GP consultations to reports of tick bites in two retrospective cross-sectional surveys of the general population.

Methods: All GPs in the Netherlands were asked to complete a postal questionnaire on the number of consultations for tick bites and erythema migrans diagnoses in 2009, and the size of their practice populations. To investigate how the incidence of GP consultation rates for tick bites and erythema migrans relate to the incidence of tick bites in the general population, questionnaire data on tick bites were analyzed from two large population surveys conducted to evaluate the national immunization program in 1995/1996 and 2006/2007.

Results: The 2009 GP survey revealed a further increase, to 564 tick bite consultations per 100,000 inhabitants, and 134 erythema migrans diagnoses per 100,000 inhabitants of the Netherlands. The two population surveys from 1995/1996 and 2006/2007 exhibited an almost twofold increase of the incidence of tick bites in the general population from 4099 per 100,000 population in 1996, to 7198 per 100,000 population in 2007. People nationwide noticed approximately 1.1 million tick bites in 2007.

Conclusions: Our observation of increases in GP consultations for tick bites and erythema migrans diagnoses between 1994 and 2009 are confirmed by the parallel increase of tick bites reported by the general population, although consultation rates slightly increased. For every sixty tick bites in the general population in 2007, we observed one GP consult for erythema migrans. The increase in tick bites poses a progressive threat to public health.

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Introduction

As reporting of Lyme borreliosis is not mandatory in the Netherlands, the National Public Health Institute (RIVM) conducted nationwide cross-sectional retrospective studies among general practitioners (GP) to assess the disease incidence (De Mik et al., 1997; Den Boon et al., 2004; Hofhuis et al., 2006). These three GP surveys have shown a continuing increase between 1994 and 2005

in GP consultations for tick bites, and in erythema migrans diagnoses, the most common early manifestation of Lyme borreliosis. The incidence of tick bite consultations increased linearly from 191 per 100,000 in 1994 to 446 per 100,000 inhabitants, i.e. 73,000 GP consultations for tick bites in the Netherlands in 2005. Concurrently, the incidence of erythema migrans diagnoses increased from 39 to 104 per 100,000 inhabitants, i.e. 17,000 patients with erythema migrans seen by all GPs in the Netherlands in 2005 (De Mik et al., 1997; Den Boon et al., 2004; Hofhuis et al., 2006).

The identical methods and materials of our earlier GP surveys on 1994, 2001 and 2005, with large numbers of responding GPs, argue for the reliability of the observed increasing trend in GP consultations for tick bites and GP diagnoses of erythema migrans. Likewise, neighboring countries have reported increases of Lyme borreliosis

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during the past decades (Hubálek, 2009; Smith and Takkinen, 2006). And simultaneous to the observed increasing trend over time, there is evidence for an increase in the total number of *Ixodes ricinus* infected with *Borrelia burgdorferi* sensu lato in the Netherlands (Sprong et al., 2012). However, GP consultations for tick bites reflect an unknown fraction of tick bites in the general population, as only some people bitten by ticks will consult a physician. Whether people decide to consult a physician for a tick bite, rather than removing the tick themselves, may be influenced by media attention and public health education regarding prompt tick removal and when to visit a physician. After each GP survey, we have communicated our results to the GPs and the general population, and every time this caused a national media hype on tick bites and erythema migrans. Therefore, the question arises whether and to what extent the GP reports might be biased.

In this paper, we report incidence estimates for GP consultations for tick bites and erythema migrans diagnoses in 2009, which are in line with the earlier observed increasing trend between 1994 and 2005. We aim to confirm the increase in GP consultations for tick bites through comparison with the incidence of tick bites in the general population, as measured in two population based surveys.

Methods

GP survey on tick bites and erythema migrans in 2009

We assessed the incidence of GP consultations for tick bites and diagnoses of erythema migrans in 2009, using identical methods as for the preceding GP surveys on 1994, 2001 and 2005 (De Mik et al., 1997; Den Boon et al., 2004; Hofhuis et al., 2006). Preliminary results of the 2009 GP survey have been reported in Dutch in 2010 (Hofhuis et al., 2010). February 2010 our epidemiology group sent a pre-coded questionnaire on a postal business reply card to all 8850 GPs in our country, inquiring about the number of consultations for tick bites and diagnoses of erythema migrans in 2009 and the size of their practice population. Reminders were sent to non-responding GPs. As every person in the Netherlands is registered with only one GP, we used the practice populations of reporting GPs to calculate incidence rates and national estimates of total numbers among the population of the Netherlands. Responses to the questions were pre-coded in categories to which values were assigned based on the best fit of an assumed underlying Poisson distribution, as published by De Mik et al. (1997). Incidence rates for tick bites and erythema migrans were estimated per 100,000 GP practice population in 2009, and bootstrap 95% confidence intervals for the national incidence estimates were calculated through resampling of the GPs reports 10,000 times.

The unit of sampling in the bootstrap analysis concerned the report of a single general practice. Bootstrap resampling was required, as the 95% confidence intervals for incidence estimates should reflect the number of reporting GPs and each GPs number of consultations and practice population combined, instead of the size of the total practice population over all reporting GPs.

Tick bites in the general population compared to GP consultations

To assess the incidence of tick bites in the general population, we analyzed data from questionnaires of two highly similar nationwide cross-sectional population surveys conducted in the Netherlands in 1995/1996 and 2006/2007. The study populations of these surveys were randomly selected from 48 municipalities distributed over the country to be regionally and demographically representative of the country. The population survey proposal was approved by the Medical Ethics Testing Committee of the

foundation of therapeutic evaluation of medicines in Almere, clinical trial number: ISRCTN 20164309 (De Melker and Conyn-van Spaendonck, 1998; Van der Klis et al., 2009). These population-based seroprevalence studies were conducted primarily to evaluate the national immunization program. Both questionnaires also included one question on how many times the participant had been bitten by ticks during the preceding five years. These data were available for 9207 participants of the population survey from 1995/1996 (hereinafter referred to as 1996) and 9600 participants of the survey from 2006/2007 (hereafter 2007). The response to the question on tick bites was pre-coded in categories. To enable calculation of incidence rates and national estimates of the total number of tick bites, a value was assigned to these categories based on the best fit of an assumed underlying Poisson distribution: no tick bites' = 0; '1–4 tick bites' = 1.809; '5–9 tick bites' = 6.458; '10 or more tick bites' = 14.753. The national incidence rates and the total number of tick bites in the general population were estimated using the R package "survey" (Lumley, 2012), accounting for the age and gender distribution of the general population in the Netherlands.

To compare the number of people with a tick bite or erythema migrans who consult a GP with the number of people who do not, we calculated tick bite rates and compared these between these two groups for 1996 and 2007. Data from the 48 municipalities of the 1996 population survey were linked to the same municipalities of the 1994 GP survey (De Mik et al., 1997). Data from the 48 municipalities of the 2007 population survey were linked to those of the 2005 GP survey (Hofhuis et al., 2006). The rates for both groups (GP consulted yes or no) and both years (year 1996 or 2007) were estimated using Poisson regression with a log-link function. The number of tick bites was taken as the response variable. GP (yes or no), year (1996 or 2007), and their interaction were put in the model as explanatory variables. For the GP "no" group, the logarithm of the number of respondents to the population survey were taken as an offset, while for the GP "yes" group, the logarithm of the size of GP practice population was taken as an offset. We accounted for clustering within municipalities, by adding a random intercept to our model. Differences between the two groups are reported as rate ratios (relative rates). We call this ratio the "consultation ratio".

Additionally, we extended our analysis to high- and low-risk municipalities, using as cut-off the median incidence (150 per 100,000) of consultations for tick bites in 1994. To assess the goodness of fit of these models, we performed Pearson's chi-squared test on the residuals. Data pre-processing and statistical analyses were performed in SAS version 9.1.3, and in R version 3.0.1.

Results

GP survey on tick bites and erythema migrans in 2009

The response rate to our postal questionnaire was 51% (4480/8850) among GPs, whose practice population includes 10.7 million persons, which is 65% of the 16.5 million inhabitants of the Netherlands in 2009. Fig. 1 shows the incidence of GP consultations for tick bites and erythema migrans (EM) diagnoses per 100,000 inhabitants in 2009, as well as for the preceding GP surveys in 1994 (De Mik et al., 1997), 2001 (Den Boon et al., 2004), 2005 (Hofhuis et al., 2006). In 2009, the incidence of GP consultations for tick bites was 564 per 100,000 inhabitants of the Netherlands, and the incidence for GP diagnosed erythema migrans was 134 per 100,000 inhabitants of the Netherlands (see Fig. 1), showing a continuation of the earlier observed linearly rising trend. The large number of responses to the survey permitted a high-confidence estimate of 93,000 patients with tick bites and 22,000 patients with erythema migrans seen by all GPs in the Netherlands in 2009. Fig. 2 shows the geographical distribution of the incidence of GP consultations

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