The global burden of listeriosis: a systematic review and meta-analysis

Charline Maertens de Noordhout, Brecht Devleesschauwer*, Frederick J Angulo, Geert Verbeke, Juanita Haagsma, Martyn Kirk, Arie Havelaar, Niko Speybroeck*

Summary

Background **Listeriosis, caused by *Listeria monocytogenes*, is an important foodborne disease that can be difficult to control and commonly results in severe clinical outcomes. We aimed to provide the first estimates of global numbers of illnesses, deaths, and disability-adjusted life-years (DALYs) due to listeriosis, by synthesising information and knowledge through a systematic review.**

Methods **We retrieved data on listeriosis through a systematic review of peer-reviewed and grey literature (published in 1990–2012). We excluded incidence data from before 1990 from the analysis. We reviewed national surveillance data where available. We did a multilevel meta-analysis to impute missing country-specific listeriosis incidence rates. We used a meta-regression to calculate the proportions of health states, and a Monte Carlo simulation to generate DALYs by WHO subregion.**

Findings **We screened 11 722 references and identified 87 eligible studies containing listeriosis data for inclusion in the meta-analyses. We estimated that, in 2010, listeriosis resulted in 23 150 illnesses (95% credible interval 6061–91 247), 5463 deaths (1401–21 497), and 172 823 DALYs (44 079–676 465). The proportion of perinatal cases was 20·7% (SD 1·7).**

Interpretation **Our quantification of the global burden of listeriosis will enable international prioritisation exercises. The number of DALYs due to listeriosis was lower than those due to congenital toxoplasmosis but accords with those due to echinococcosis. Urgent efforts are needed to fill the missing data in developing countries. We were unable to identify incidence data for the AFRO, EMRO, and SEARO WHO regions.**

Funding **WHO Foodborne Diseases Epidemiology Reference Group and the Université catholique de Louvain.**

Introduction

Listeriosis is caused by the Gram-positive ubiquitous bacterium *Listeria monocytogenes*, which was first recognised as a foodborne pathogen in the early 1980s.[1] Since its discovery, it has been identified as a cause of major foodborne outbreaks. Unlike most other foodborne pathogens, *L monocytogenes* can grow in food with fairly low moisture content and high salt concentration. Most importantly, *L monocytogenes* grows at refrigeration temperatures, by contrast with many other foodborne pathogens. This ability to persist and multiply in the food environment makes *L monocytogenes* especially difficult to control.[2]

Clinical listeriosis mainly occurs in particular at-risk groups: pregnant women, elderly people, immunocompromised people, unborn babies, and neonates (through vertical transmission from the mother or, more rarely, at birth by ascending colonisation from the vagina).[3] In healthy people, *L monocytogenes* infections might cause febrile gastroenteritis, which is usually mild and self-limiting. Mainly in patients with impaired cell-mediated immunity, listeriosis can lead to severe illnesses, including severe sepsis, meningitis, or encephalitis, and thereby cause lifelong consequences and even death.[4–6] Infection during pregnancy can result in spontaneous abortions or stillbirths.[7] Preterm birth is also a common consequence of listeriosis in pregnant women.[8,9]

Most cases of listeriosis are sporadic and have been reported in high-income countries, where incidence is quite low but fatality rate is high.[10] Important outbreaks have also occurred—for example, an outbreak of listeriosis from cantaloupes in Colorado, USA, in 2011 resulted in infection of 147 people and 33 deaths, making it the deadliest recorded US foodborne outbreak since the US Centers for Disease Control and Prevention (CDC) began tracking outbreaks in the 1970s.[11–13]

Listeriosis often results in admission to intensive-care units, which makes *L monocytogenes* the third most costly foodborne pathogen in the USA per case in 2010, after *Clostridium botulinum* and *Vibrio vulnificus*.[14] Ivanek and colleagues[15] estimated that the annual cost of *L monocytogenes* in the USA was US$2·3 billion to 22 billion, and the annual benefit of *listeria* food safety measures was $0·01 billion to 2·4 billion.

Only a few countries have assessed the listeriosis burden in terms of disability-adjusted life-years (DALYs),[16–18] and the global burden of listeriosis has never been estimated. However, DALYs can be used to

Lancet Infect Dis 2014; 14 1073–82

Published Online September 16, 2014 http://dx.doi.org/10.1016/S1473-3099(14)70870-9

See Comment page 1027

*These authors contributed equally

Institute of Health and Society (IRSS), Université catholique de Louvain, Brussels, Belgium (C Maertens de Noordhout MSc, B Devleesschauwer MSc, Prof N Speybroeck PhD); **Department of Virology, Parasitology and Immunology, Faculty of Veterinary Medicine, Ghent University, Ghent, Belgium** (B Devleesschauwer); **Division of Global Health Protection, Center for Global Health, Centers for Disease Control and Prevention, Atlanta, GA, USA** (F J Angulo PhD); **Interuniversity Institute for Biostatistics and Statistical Bioinformatics, Katholieke Universiteit Leuven, Leuven, Belgium** (Prof G Verbeke PhD); **Department of Public Health, Erasmus MC, Rotterdam, Netherlands** (J Haagsma PhD); **National Centre for Epidemiology and Population Health, The Australian National University, Canberra, Australia** (M Kirk PhD); **National Institute for Public Health and the Environment, Centre for Infectious Disease Control, Bilthoven, Netherlands** (Prof A Havelaar PhD); **and Institute for Risk Assessment Sciences, Faculty of Veterinary Medicine, Utrecht University, Utrecht, Netherlands** (Prof A Havelaar)

Correspondence to: Charline Maertens de Noordhout, Institute of Health and Society (IRSS), Université catholique de Louvain, Clos Chapelle-aux-Champs, Brussels, 1200 Belgium **charline.maertens@uclouvain.be**

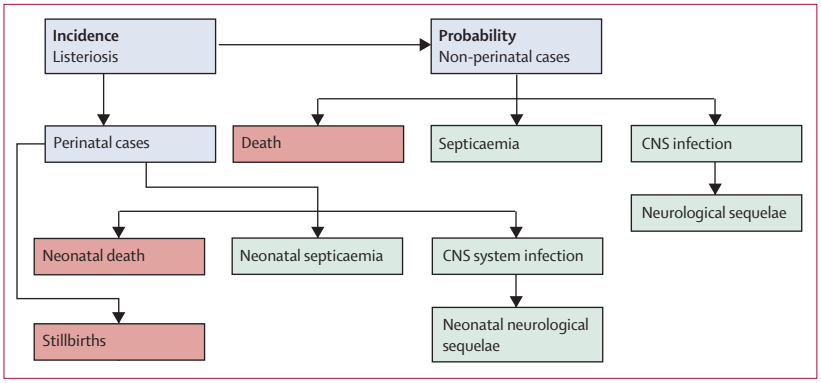

Figure 1: **Outcome tree for perinatal and non-perinatal listeriosis**
Each block represents a node in the computational disease model, and arrows represent transition probabilities between nodes. Red boxes contribute years of life lost caused by premature death (YLLs), green boxes contribute years lived with disability (YLDs), and blue boxes have no contribution to the disability-adjusted life-years. In addition to this baseline model, we did a scenario analysis in which stillbirths were excluded from the burden estimates.

	Disability weight (95% CI)
Perinatal or non-perinatal septicaemia	
(A) Infectious disease: acute episode (severe)—disability weight used for septicaemia	0·210* (0·139–0·298)
Perinatal or non-perinatal CNS infection	
(A) Infectious disease: acute episode (severe)	0·210*
(B) Intellectual disability (severe)	0·126*
(C) Epilepsy (severe and treated, with recent seizures)	0·488*†
(D) Motor impairment (moderate)	0·076*
(A) and (B)	0·340‡
(A) and (C)	0·540‡
(A) and (D)	0·270‡
(B) and (C)	0·553‡
(B) and (D)	0·192‡
(C) and (D)	0·527‡
(A) and (B) and (C)	0·646‡
(A) and (B) and (D)	0·362‡
(B) and (C) and (D)	0·626‡
(A) and (B) and (C) and (D)	0·673‡
Disability weight used for CNS infection	0·426§ (0·368-0·474¶)
Perinatal or non-perinatal neurological sequelae	
(A) Hearing loss	0·047*†
(B) Vision loss	0·087*†
(C) Stroke: long-term consequences	0·303*†
(A) and (B)	0·130‡
(B) and (C)	0·364‡
(A) and (C)	0·336‡
(A) and (B) and (C)	0·394‡
Disability weight used for neurological sequelae	0·292§ (0·272–0·316¶)

*GBD 2010.[26] †Averaged disability weight. ‡Multiplicative methodology. §Using expert elicitation. ¶Bootstrap analysis.

Table 1: **Disability weights used to calculate the global burden of listeriosis**

See Online for appendix

compare diseases and health conditions, and thereby help policy makers to allocate resources. To understand the global burden of foodborne diseases, including listeriosis, WHO therefore established an advisory body, the Foodborne Disease Epidemiology Reference Group (FERG).[19] The aim of our study was to estimate the annual global number of illnesses, deaths, and DALYs due to listeriosis, to contribute to the FERG initiative. We synthesised existing information and knowledge through a systematic literature review and meta-analysis, which was incorporated into calculations of the disease burden.

Methods

Search strategy and selection criteria

We did a systematic review to identify all relevant information about the global burden of listeriosis. We searched PubMed, WHOLIS, Sciverse Scopus, CAB abstracts (BIDS), OpenGrey, and Conference proceedings citation index (Web of knowledge) for references published between Jan 1, 1990, and May 21, 2012. We did not set any language restrictions. Papers in languages we could not read were translated by native speakers. For one report in Malay, no native speakers could be identified, so we used Google Translate.

We developed the search terms in accordance with the Medical Subject Headings thesaurus, using a combination of test searches and via collaboration between independent researchers and knowledge users. Search terms were designed to capture a range of terms and outcomes associated with listeriosis (appendix). The appendix summarises further details on the databases and Boolean operators that were checked.

Additionally, for each of the member states of WHO for which we did not identify incidence data, we reviewed national surveillance data where available, via national websites. We identified the national websites and surveillance data through a Google search in French, Dutch, English, or the official language of the country using Google Translate (if no website was identified in French, Dutch, or English). The appendix summarises the search terms. We contacted countries for which we did not identify websites or national surveillance data by contacting the ministry of health or health professionals in the country.

Finally, for each of the WHO subregions for which we did not identify incidence data, we consulted the WHO Collaborating Centre for Foodborne Listeriosis to assist in filling of data gaps. After deleting duplicates, we screened titles, abstracts, or entire articles for exclusion criteria. Screening was done independently by two authors (CMN, BD). Any disagreement about eligibility between reviewers was resolved by a third author (NS). The first two authors extracted data from included papers using a data extraction form reviewed by the other co-authors (appendix), and we excluded incidence data from before 1990 from the analysis. We hand-searched bibliographies of included documents for additional references. Our procedures accorded with the PRISMA guidelines for reporting systematic reviews (appendix).