



Epidemiology and surveillance of human (neuro)cysticercosis in Europe: is enhanced surveillance required?

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Abstract

OBJECTIVES To report on relevant national surveillance systems of (N)CC and taeniasis (the infection with the adult tapeworm) in the European Union/European Economic Area and to assess the magnitude of (N)CC occurrence by retrieving information on cases for the period 2000–2016.

METHODS (N)CC cases were retrieved via national reporting systems, a systematic literature search, contact with clinicians and a search for relevant ‘International Statistical Classification of Diseases and Related Health Problems’ (ICD)-based data.

RESULTS Mandatory notification systems for (N)CC were found in Hungary, Iceland and Poland. Ten cases were reported in Poland and none in Hungary and Iceland. Through the systematic literature review and information given by clinicians, 263 individual and 721 aggregated (N)CC cases from 19 European countries were identified. ICD-based data were obtained from five countries. From 2000 to 2016, a total of 3489 cases (N)CC cases were coded: 832 in Italy, eight in Latvia, 357 in Portugal, 2116 in Spain and 176 in Sweden.

CONCLUSION Despite being classified as a possible eradicable disease, (N)CC is still diagnosed across Europe, yet its true extent and impact remain unclear.

keywords neurocysticercosis, Europe, epidemiology

Sustainable Development Goals (SDGs): SDG 3 (good health and well-being), SDG 17 (partnerships for the goals)

Introduction

Human (neuro)cysticercosis (N)CC is a neglected tropical parasitic disease caused by the metacestode larval stage of the zoonotic tapeworm *Taenia solium*. The parasite has a complex life cycle involving both humans and pigs, causing two distinct diseases in humans, namely taeniasis and (N)CC, and (N)CC in pigs. Taeniasis is the intestinal infection with the adult *T. solium* tapeworm resulting from consumption of undercooked infected pork, whereas the infection with the metacestode larval stage is called cysticercosis (CC) and is due to faecal–oral ingestion of *T. solium* eggs. When the central nervous system is affected, it is referred to as neurocysticercosis (NCC) [1–3].

Cysticerci can persist in the brain for several years before patients become symptomatic, or patients can remain asymptomatic [2–4]. Symptoms and signs often result from degeneration of cysticerci and the associated host immune reaction and are pleomorphic [1–3]: the most common symptoms are epileptic seizures, various types of headaches, focal neurological deficits and signs of increased intracranial pressure [5]. Neurological manifestations depend on the number (single or multiple), size, location (e.g. intraparenchymal and extraparenchymal) and stage of the cysticerci (viable or calcified) and on the host's immune response [3].

Taenia solium taeniasis/(neuro)cysticercosis (TSTC) is a preventable and potentially eradicable disease complex [6]. Despite this, *T. solium* still has a considerable health and economic impact worldwide, being ranked first among food-borne parasites worldwide by the Food and Agriculture Organization of the United Nations (FAO) and WHO [7,8]. In endemic areas, (N)CC accounts for around one-third of epilepsy cases [9]. The global burden of human CC was estimated to be 1.61 million DALYs in 2017 [10].

A possible re-emergence of (N)CC in Europe has been discussed by experts in recent years, as several risk factors such as human travel and migration, importation of pigs/pork, changes in pig rearing and meat inspection practices as well as possible ongoing autochthonous transmission could favour the spread of the parasite [11–18]. Other high-income countries (e.g. USA, Canada) have reported a recent increase in (N)CC cases, thus raising the question as to whether an increase of TSTC cases in Europe could be detected in a timely manner [19,20].

Surveillance of infectious diseases is key to their sustained control, elimination and eradication. The European Centre for Disease Prevention and Control routinely collects data on 56 communicable diseases and related health issues from the European Union Member States

and from Iceland, Norway and Liechtenstein, the three participating countries of the European Economic Association/European Free Trade Association [21,22]. TSTC is not part of the indicator-based surveillance by ECDC, but that does not exclude surveillance at national level. However, no comprehensive compilation of existing national surveillance systems regarding (N)CC is available to date.

The aim of the present study was, therefore, to report on current surveillance systems for TSTC implemented in Europe and to assess the magnitude of (N)CC occurrence in Europe. This study was embedded in CYSTINET (European Network on taeniasis/cysticercosis, COST Action TD 1302), a network aiming to improve knowledge and understanding of this zoonotic disease complex in Europe.

Methods

Mandatory reporting of *Taenia solium* taeniasis/cysticercosis and registries

First, countries with a mandatory notification for TSTC in Europe were identified through an online search for national laws on infectious disease control, a questionnaire for CYSTINET members; experts from the European Creutzfeld-Jakob Disease Surveillance Network, who provided missing information on the infectious disease control laws of respective countries; and through personal contacts [23]. Included countries were the EU member states plus Iceland, Norway, Liechtenstein, the Republic of North Macedonia, Serbia and Switzerland. Information on registries for TSTC was also collected through a questionnaire distributed among participants at the CYSTINET international conference in Belgrade, Serbia (3–4 November 2015).

Data collection regarding (neuro)cysticercosis cases

Subsequently, data on (N)CC were retrieved via extraction of notified cases from countries with a mandatory notification system for (N)CC, a systematic literature search of (N)CC case reports/case series and observational studies (including the search of grey literature), a collection of unpublished (N)CC case reports/aggregated data through clinicians and laboratories, and country-level data based on International Statistical Classification of Diseases and Related Health Problems (ICD) codes.

The study protocol for the literature search was based on the PRISMA-P statement [24] and was registered at PROSPERO (CRD42016050729). Institutional Review Board approval for retrospective analysis of anonymised

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patient data was obtained from the Technical University of Munich.

Data based on mandatory reporting of *Taenia solium* taeniasis/cysticercosis and registries

Data on notified (N)CC cases from countries with previously identified mandatory notification systems were extracted from pertinent publications [25–27].

Systematic literature search

For the systematic literature search, only studies reporting on neurocysticercosis cases (case report/case series or aggregated data) in Europe were considered. Europe was defined as all EU/EEA member states, candidate countries for EU membership (except Turkey as most of its territory belongs to Asia), potential candidates, all Schengen countries and other small European countries. Further predefined inclusion and exclusion criteria are listed in the Appendix S1. No language restrictions were applied. Literature published between January 1st, 1990 and November 20th, 2016 was included; however, for data extraction, we considered literature published from January 1st, 2000.

The following databases were used: PubMed, EMBASE, Web of Science, Global Index Medicus (limited to Regional Databases LILACS, AIM, WPRIM, IMSEAR, IMEMR), Global Health (CABI), as well as OAIster and Open Grey. The search terms and date of search are described in Appendix S1. Additionally, reference lists from other reviews were checked for relevant records [11,13,17] and CYSTINET-Europe members searched grey literature in their respective countries.

Regarding the online-published literature, four independent reviewers screened the search results from PubMed, EMBASE, Web of Science, Global Index and Global Health by means of the Covidence tool (AA, JB, PS, CU) [28]. Two independent votes from any of the reviewers were necessary for inclusion/exclusion of literature. In case of disagreement and where a decision could not be taken after referring to the inclusion/exclusion criteria, another expert was asked.

As the first step, publications worldwide were included or excluded based on title and abstract. Then a geographical restriction was applied: all previously included case reports/series and observational studies were imported in an Excel file with information on title and abstract and filtered by European country names and other related terms (Appendix S1) and further included. These publications were then screened in full.

A pilot of the study selection process was undertaken by all the reviewers to check accuracy and applicability

of these criteria and to get familiar with the work. No masking or blinding (journal, author, institution etc.) was performed, as those were considered unlikely to influence the search. Grey literature, comprising papers in local languages, conference abstracts and doctoral theses, was identified by searching OAIster and Open Grey and with the help of CYSTINET members. All presentations at all CYSTINET meetings (2014–2017) were also systematically searched for relevant information.

Collection of unpublished data

For the search of unpublished data and additional grey literature, a questionnaire was distributed among the participants at the CYSTINET international conference in Belgrade (2015). CYSTINET members from 29 participating countries were asked to provide or indicate sources of information, contact details of local experts and data on patients [29]. In Romania and the United Kingdom, institutional approval was necessary and obtained. Participants were reminded of this project by email and at all following CYSTINET meetings and conferences over the next three years (2015–2017).

Data based on ICD codes

Data based on ICD codes were requested from respective national authorities or searched online at the respective institutes' homepages.

Data extraction and analysis

Publications eligible for data extraction were further restricted on time (1st of January 2000 to the 20th of November 2016), as the aim of the study was to give an overview of recent data and previous publications had already dealt with older data. Data from publications were extracted in an Excel sheet by five researchers (AA, MK, RM, DS, AF) and checked for plausibility and consistency (AA, DS). All variables and response possibilities were predefined. For the data analysis, R (3.5.1) and EMMA (ECDC map maker; a mapping application created by ECDC) were used [30,31].

Results**Mandatory reporting of *Taenia solium* taeniasis/cysticercosis and registry**

Information regarding mandatory notification of TSTC was identified for 29 of the 34 included countries (information could not be obtained from Czech Republic,

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Cyprus, Liechtenstein, Lithuania and Slovakia) [23]. An overview of these results is presented in Table 1. Solely laboratory-based reporting of these diseases cannot be excluded.

Notification of (N)CC is mandatory in Hungary, Iceland and Poland, and notification of taeniasis is mandatory in Hungary, Slovenia, Croatia and the Republic of North Macedonia. When looking in detail into the infectious disease control legislation in Hungary, (N)CC was mentioned in the taeniasis section. Therefore, we assumed that both diseases must be notified there. In Portugal, the Taeniasis and Cysticercosis Observatory is being implemented aiming at a One Health-based national disease surveillance system for sustainable health protection. This is the only registry in Europe for (N)CC.

(Neuro)cysticercosis cases in Europe: Results of the systematic literature search

A total of 13 777 publications were retrieved by searching PubMed, EMBASE, Web of Science, Global Index and Global Health (CABI). Another 54 publications were identified by searching OAIster, Open Grey, CYSTINET presentations and through personal communication.

After deduplication, 10 037 publications remained. Of these, 1756 case reports/series and observational studies on (N)CC worldwide were selected based on title and abstract screening. The internal search to limit the results geographically revealed 296 publications. The full text of those publications was screened, and 210 publications were included. After restricting to publications from the year 2000 onwards, 134 publications (see Appendix S2 and Appendix S3) reporting on individual cases or smaller case series (in which data on individual patient level was reported) and 22 publications with aggregated data on (N)CC cases and two serological based studies were finally included, and data extracted. Figure 1 shows the flow chart on the screening process for publications.

Results of individual patient data – published and unpublished

A total of 263 cases were identified from published and unpublished literature: 198 individual cases from the 134 included papers and 65 unpublished cases (34 cases from England and Wales (2001–2017) and 31 cases from Romania (2000–2014)). Among these cases, 106 were male and 134 female (not known: 24) with a mean age of 37±18 years. Clinical details of 26 UK cases between 2001 and 2015 have since been published as a case series [49].

Table 1 Mandatory surveillance for *Taenia solium* taeniasis/cysticercosis

EU/EEA states	Reporting for (N)CC	Reporting for taeniasis
Austria	No*,†	No*
Belgium	No†	No†
Bulgaria	No**	No**
Cyprus	-	-
Croatia	No**	Yes**
Czech Republic	-	-
Denmark	No*	No*
Estonia	No**	No**
Finland	No†	No†
France	No†	No†
Germany	No*,†	No*,†
Greece	No†	No†
Hungary	Yes†	Yes†
Iceland	Yes†	No†
Ireland	No†	No†
Italy	No*,†	No*,†
Latvia	No‡	No**
Liechtenstein	-	-
Lithuania	-	-
Luxembourg	No†	No†
Malta	No†	No†
Netherlands	No†	No†
Norway	No*	No*
Poland	Yes†	No†
Portugal	No*	No*
Romania	No**	No**
Slovakia	-	-
Slovenia	No*	Yes*
Spain	No*	No*
Sweden	No†	No†
United Kingdom	No*	No§
Additional countries from CYSTINET		
North Macedonia	No*	Yes
Serbia	No*	No*,‡
Switzerland	No	No†

Overview of mandatory reporting for TSTC in Europe based on results from the questionnaire within CYSTINET network, results from the online search on national laws on infectious disease control and information through personal contact as well as ECDC [23,32–47]. -: not available.

*Results from the questionnaire within CYSTINET network.

†Results from the online search.

**Information through personal contact and ECDC.

‡Taeniasis was notifiable in Serbia between 1997 and 2004.

§*Taenia* infections are to be reported based on the 'Laboratory reporting to Public Health England' (England, Wales and Northern Ireland).[48]

Of all published individual cases, 11 were autochthonous, that is, defined as cases without a migration background where a travel history outside the patient's country was excluded. Among the unpublished cases, 29

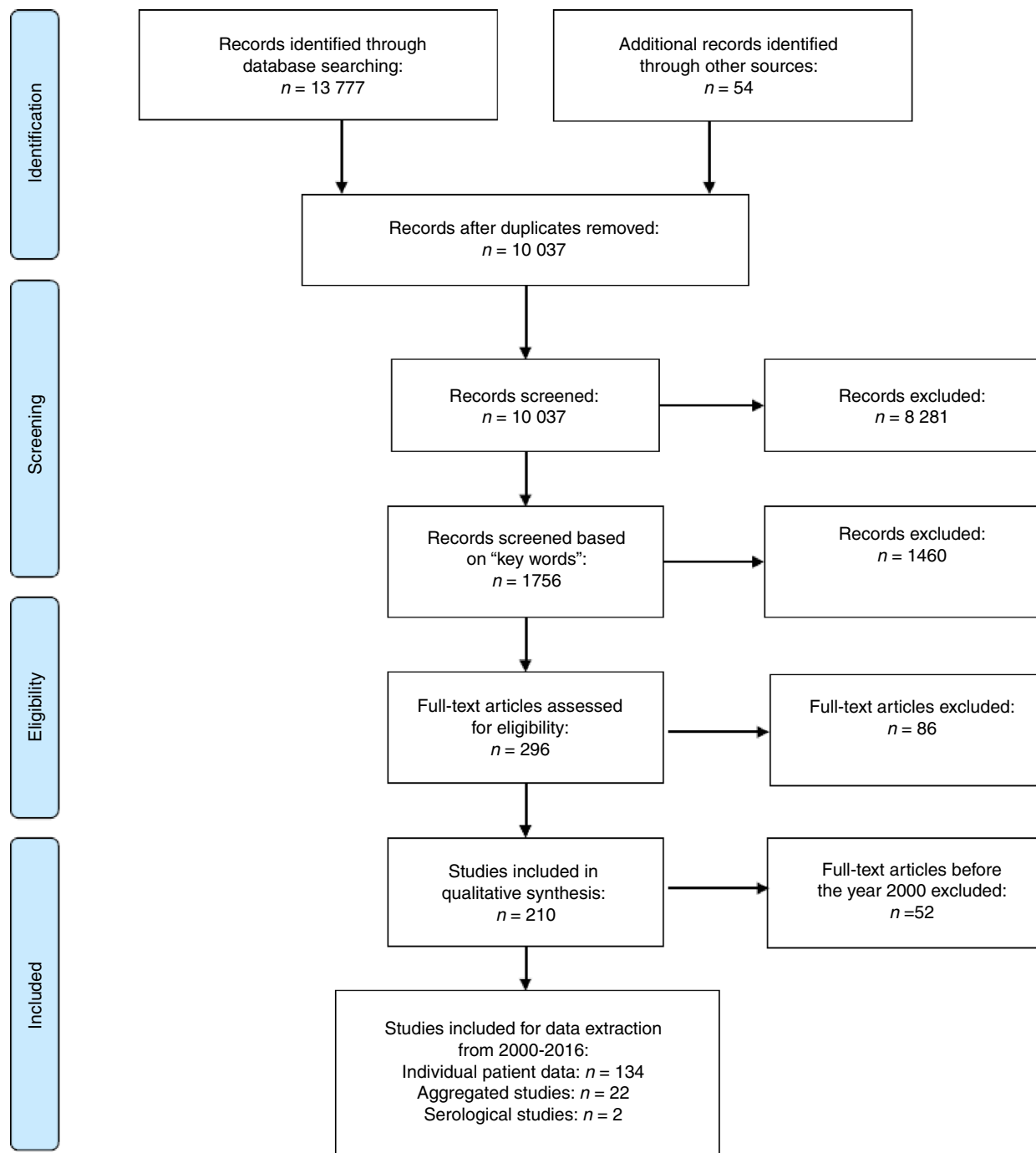


Figure 1 Results of the literature search. Systematic literature search for individual (N)CC patient data and aggregated data. [Colour figure can be viewed at wileyonlinelibrary.com]

cases from Romania were classified as autochthonous [50–59]. Most published case reports mentioned a travel and/or migration background, mostly from Latin America

(37%), Africa (26%), Asia (23%), Europe (8%) and elsewhere (7%). Regarding the unpublished cases, in Romania two cases were related to travel history, whereas all

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patients from England and Wales had a travel and/or migration background.

The most common clinical presentations were headache (52%), epileptic seizures(s) (42%) and focal neurological signs (38%).

Results of the aggregated data

Two types of aggregated data were identified: hospital-based and serological studies. Through 22 hospital-based studies (including studies with inpatient and outpatient services), a total of 721 (N)CC cases were identified [60–81]. Ten of these studies were performed in Spain, six in Serbia and two in Portugal. Diagnostic criteria were often not reported (17 studies); one study used the criteria published by Carpio *et al.* [65] and four studies mentioned the Del Brutto criteria [67,70,79,81]. Furthermore, serology and imaging were not always described in sufficient detail to permit reassessment of the cases according to current diagnostic criteria.

Of the 721 (N)CC patients, 266 were males and 287 females (for the other patients, no information was provided). The main risk factors for (N)CC reported by patients were travelling and migration to and from highly endemic regions [62,73,78,80,81]; other risk factors were previous *T. solium* taeniasis [62,65], close contact with a *T. solium* tapeworm carrier [65,75], low socio-economic conditions [67], working in the food industry, contact with pigs and living in rural areas [71]. An overview of the included studies is presented in Table 2.

Five additional serology-based studies were identified [82–86]; two of them are summarised below, while the other three studies reported on individual patient data and were, therefore, summarised together with the other (N)CC case reports/series [84–86]. Gomez-Morales and colleagues from the Istituto Superiore di Sanità in Rome – the European Union Reference Laboratory for Parasites – used an enzyme-linked immunoelectrotransfer blot (EITB) assay to identify 59 CC-positive serum samples for *T. solium* among 1247 sera tested (4.7%) between 2001 and 2014. The sera came from patients with neurological symptoms/signs or with lesions compatible with NCC [82].

Mestrovic *et al.* (2012) retrospectively analysed sera of 770 Croatian patients with diagnosed epilepsy who were referred to the Croatian National Institute of Public Health between 2005 and 2009. A commercial qualitative enzyme immunoassay, plus a Western blot technique as a confirmatory test, yielded 11 samples (1.5%) with *T. solium* CC antibodies [83].

Mandatory notification of (N)CC in Europe

Data from all the three countries where (N)CC is mandatorily notifiable were identified for the period of 2000 to 2016. (N)CC seems to be either absent (Hungary and Iceland) or only sporadic, as in Poland in the past years: 1 case in 2006, 2008 and 2015; 2 cases in 2010 and 2011 and 3 cases in 2013.

ICD-based data

ICD-based data for (N)CC were obtained for five countries: Italy (832), Latvia (8), Portugal (357), Spain (2116) and Sweden (176) for the time period 2000–2016 (Table 3/Figure 2) [17,89–94]. The data sources varied by country (Table 3).

Discussion

An objective of this study was to assess the frequency of (N)CC cases in the EU between the years 2000 and 2016 based on various sources. Cases were consistently reported across a wide range of countries: 198 individual published (N)CC cases, 65 individual unpublished (N)CC cases, 721 (N)CC cases from hospital-based data, 70 cases from serological studies, 3489 (N)CC cases from ICD-based data and 10 (N)CC cases from mandatory notification systems. Cases were mostly travel and migration-related with a mean age of 37 and a slightly higher female proportion (56%) among the published and unpublished case reports where this information was available. Autochthonous cases were also identified. These results are in line with previous findings, raising the question as to what extent the full life cycle of *T. solium* is still completed in Europe [11–13,15–18].

In our study, we combined data from various sources, which differentiates this manuscript from recently published literature reviews on CC in Europe, thereby making the assessment more comprehensive [15,18]. However, the following limitations remain: (i) Due to restrictions to full text access to publications, some (N)CC case descriptions could not be retrieved. Neither were all cases published in the past (publication bias). (ii) The search for published literature focused exclusively on NCC patients and did not include CC patients. NCC patients present with more severe symptoms and constitute the majority of cases, but the integration of CC patients would have added to complete the picture of disease transmission. (iii) Regarding unpublished cases and ICD-based cases, data collection is highly dependent on research cooperations and therefore incomplete. (iv) Data reliability is often difficult to assess, as the data are retrospective and originate from heterogeneous

A. Abraham *et al.* Human neurocysticercosis in Europe**Table 2** Overview of aggregated data. Hospital-based studies identified through literature search and personal contacts

Author and year	Country/ Continent	Study period	Number of (N)CC cases	Male	Mean/(median) age at diagnosis	Migrants
Studies identified through literature search						
Terraza <i>et al.</i> 2001 [80]	Spain	1990–2000	10	4 (40%)	-	7/10 (70%)
Overbosch <i>et al.</i> 2002 [62]	Europe†	1996–2000	45	-	-	-
Lobo <i>et al.</i> 2003 [69]	Spain	1998–2002	16	6 (38%)	30	15/16 (94%)
Pérez-López <i>et al.</i> 2003 [75]	Spain	2000–2001*	8	4 (50%)	27	8/8 (100%)
Roca <i>et al.</i> 2003 [78]	Spain	1992–2002	23	13 (57%)	33‡	17/23 (74%)
Esquivel <i>et al.</i> 2005 [65]	Spain	1990–2002	20	7 (35%)	37	17/20 (85%)
Ferreira <i>et al.</i> 2006 [67]	Portugal	1996–2003	14	4 (29%)	10‡	13/14 (93%)
Fernandez-Dominguez <i>et al.</i> 2007 [66]	Spain	1996–2006	38	-	-	15/38 (40%)
Más-Sesé <i>et al.</i> 2008 [70]	Spain	1997–2005	23§	14 (61%)	30‡	20/23 (87%)
Milovanovic <i>et al.</i> 2008 [71]	Serbia	2005–2006*	12	4 (33%)	56	-
Parra <i>et al.</i> 2009 [74]	Spain	1990–2008	19	-	39	13/19 (68%)
Cruz <i>et al.</i> 2010 [61]	Switzerland	–*,¶	6	2 (33%)	-	4/6 (67%)
Ramos <i>et al.</i> 2011 [77]	Spain	2001–2010*	10	-	-	10/10 (100%)
Ruiz <i>et al.</i> 2011 [79]	Spain	1996–2009	35**	24 (69%)	30	35/35 (100%)
Januário <i>et al.</i> 2015 [87]	Portugal	–*,††	15	9 (60%)	-	-
Zammarchi <i>et al.</i> 2015 [81]	Italy, Spain	1980–2013	81	33 (41%)	30	66/81 (81%)
Pagès <i>et al.</i> 2016 [73]	France	2010–2015*	58	27 (47%)	44	10/53 (19%)
Studies identified through personal contacts						
Doder <i>et al.</i> 2002 [63]	Serbia	1997–2001	13	8 (62%)	49	-
Nikolic <i>et al.</i> 2006 [72]	Serbia	2000–2004*	60	-	-	-
Poluga <i>et al.</i> 2013 [76]	Serbia	2006–2010*	22	10 (46%)	51	-
Dulovic <i>et al.</i> 2014 [64]	Serbia	2006–2013*	25	11 (44%)	52	-
Bobic <i>et al.</i> 2015 [60]	Serbia	1990–2014	168	86 (51%)	46	-

(N)CC, (neuro)cysticercosis; -, not available.

*Data entered for calculating results for the map.

†Austria (1), France (8), Germany (6), Norway (1), The Netherlands (14), Spain (9), Switzerland (1), Czech Republic (3) and the UK (2).

‡Median age.

§23 according to the Del Brutto criteria [88], 5 patients definitive cases, 18 probable cases.

¶Last 10 years.

**Del Brutto definitive criteria of disease [88]: 12 patients (34.28%), probable diagnosis: 21 patients (60%) and two patients (5.72%) did not meet sufficient criteria (only coming from areas endemic and presented cystic lesions suggestive of NCC by imaging criteria).

††The last five years.

sources over many years. (v) It is to be assumed that not all (N)CC cases have been correctly classified/diagnosed. (vi) ICD-based data are dependent on the health system in place and the statistics used to aggregate it; thus, comparison of these data between countries is difficult. Moreover, the use of ICD codes for retrieval of TSTC cases was shown to be far from faultless in a study in Belgium [95]. Some authors took measures to ensure higher quality: Vilhena *et al.* (2017), for example, checked ICD-based data manually if the supporting diagnostic code was consistent with neurological disease manifestations such as epilepsy [91].

Due to all these limitations, we consider our data – even though we used a holistic approach for data acquisition – to be just the tip of the iceberg, neither allowing for accurate prevalence/incidence measures nor making a definite statement as to whether or not (N)CC is re-

emerging in Europe due to migration and travel patterns. Yet our review is the most comprehensive data collection on (N)CC in Europe to date.

Is enhanced surveillance of the disease complex *Taenia solium* taeniasis/cysticercosis required in Europe?

Considering that (N)CC is a disease with an important global health impact, that it is potentially eradicable, that tools exist to take public health action and that (N)CC is present in Europe (albeit in low numbers), the question arises whether enhanced indicator-based surveillance for TSTC is required in the EU/EEA. To answer this question, we refer to the criteria listed by the European Commission for the ‘selection of communicable diseases of special areas to be covered by epidemiological surveillance within the network’:

Table 3 Overview of (neuro)cysticercosis cases reported through ICD-based data from 2000 to 2016. ICD-based data were available for Italy, Latvia, Portugal, Spain and Sweden

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	Total
Italy	-	54	59	43	60	43	60	61	50	58	52	55	73	44	38	43	39	832
Latvia	0	0	0	1	1	2	2	1	0	0	1	0	0	0	-	-	-	8
Portugal	-	-	-	-	-	-	52	35	55	39	52	42	43	39	-	-	-	357
Spain	64	117	129	135	149	153	159	169	169	160	148	136	140	117	92	79	-	2116
Sweden	5	14	14	11	17	11	12	6	14	8	6	7	3	10	18	9	11	176
Total																		3489

Italy: Number of hospitalisations for cysticercosis (ICD-9-CM, code 123.1). Repeated admissions of the same patient in the same year were excluded. Source: Italian Ministry of Health, Direzione Generale della Programmazione Sanitaria-Banca dati SDO. **Latvia:** Data have been collected and reported to the Centre for disease control and Prevention of Latvia (regulated by the Cabinet rules No 90 from 31st of January, 2012). **Portugal:** ICD-9-CM code 123.1, hospitalisations, records were manually checked for supporting diagnostic or procedural code consistent with a manifestation of relevant neurological disease, all included patients had procedural codes of neuroimaging studies (CT/MRI), duplicates due to readmission or hospital transference were removed. **Spain:** ICD-9-CM code 123.1, hospitalisations. **Sweden:** Diagnoses in hospitalised patients and primary care, B69 Cysticercosis, Sweden in total.

- Diseases that cause, or have the potential to cause, significant morbidity and/or mortality across the Community, especially where the prevention of the diseases requires a global approach to coordination.
- Diseases where the exchange of information may provide early warning of threats to public health.
- Rare and serious diseases which would not be recognised at national level and where the pooling of data would allow hypothesis generation from a wider knowledge base.
- Diseases for which effective preventive measures are available with a protective health gain and
- Diseases for which a comparison by Member States would contribute to the evaluation of national and Community Programmes' [96].

The question as to whether these criteria apply to TSTC in Europe needs to be considered with care. Although TSTC is a preventable and possibly eradicable disease complex, significant associated morbidity and mortality mainly due to NCC (criterion 1) remain worldwide. NCC is estimated to have caused 1.61 million DALYs in 2017 [7,10]. In Europe, however, NCC is in 10th place based on the criteria of WHO/FAO's worldwide ranking of food-borne parasites [97]. Overall, the limited available data do not seem to support the applicability of criterion 1 in this case at the moment. However, new challenges like migration from and travel to endemic areas as well as uncontrolled backyard slaughtering or organic pig farming with free-roaming pigs might increase the number of infections [98].

Taenia solium tapeworm carriers can spread a large number of infectious eggs of *T. solium* for a relatively long period of time without experiencing symptoms themselves; thus, even in the absence of locally infected pigs, (N)CC cases can arise after human-to-human faecal-oral transmission [1]. Therefore, early warning based on improved diagnostic techniques and laboratories, and ideally through cross-national collaboration and pooling of data to improve knowledge of (N)CC epidemiology [99] could lead to preventive action (referring to criteria 2 and 4 from the list above). Such action could include strict hygienic measures for close contacts of *T. solium* tapeworm carriers, safe disposal of infective material and increased public health measures both in the human (screening programmes of high-risk populations, etc.) and veterinary sector (enhancing meat inspection in pigs with outdoor access, etc.). These criteria are at least partially applicable for the TSTC disease complex.

In Europe, (N)CC is considered a rare disease (defined as fewer than 1/2000 people [100]) and as such 'hypothesis generation from a wider knowledge base' (criterion 3),

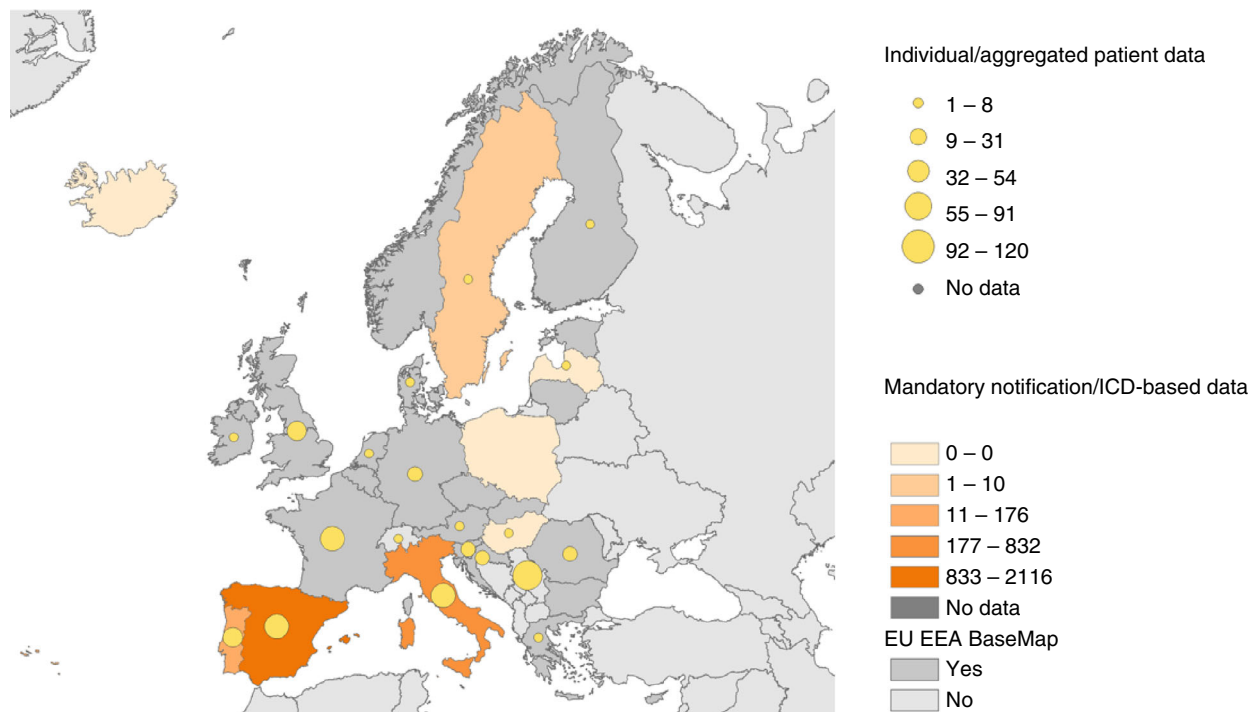


Figure 2 Mapping of ICD-based data and mandatory notification cases on cysticercosis as well as individual and aggregated patient data on (N)CC.

would be an asset. Even if a wider knowledge base were available through the high number of cases worldwide, it cannot be ruled out that there are specific characteristics of (N)CC cases in Europe, for example, due to environmental, genetic or sociocultural risk factors. Applicability of criterion 3 can, therefore, not be dismissed, even if a strong collaboration with experts in endemic regions is certainly very important.

Possible advantages of a mandatory notification would have to be balanced against disadvantages. In particular, the added value of information on TSTC gained through reporting needs to outweigh the necessary intrusion of patients' privacy and additional resources needed for reporting and monitoring such as money, time and effort involved in mandatory notification.

Additionally, there are some characteristics of the disease complex that render surveillance challenging: Patients infected with the adult *T. solium* tapeworm often present without or with only mild symptoms. In NCC, a delay between infection and presentation of symptoms of up to several years makes it difficult to assess time, place and source of infection; also, infected persons may stay asymptomatic. NCC is often misdiagnosed, as none of the symptoms/signs are pathognomonic and therefore cannot unequivocally be linked

to NCC. This aspect is especially challenging in a setting where NCC is rare and health personnel may not be familiar with the disease. Relapses of symptoms/signs and chronicity may be frequent, making it difficult to determine whether the patient was already counted. Availability and quality of serological tools to correctly identify (N)CC cases are often insufficient, as is the expertise to correctly interpret those results. There is ongoing scientific controversy about NCC case definitions; and the control of (N)CC would involve experts from various scientific disciplines including veterinarians, medical doctors and other experts at an animal–human–ecosystem interface ('One Health approach'), which can be difficult to achieve.

To conclude, despite some of the EU surveillance criteria being fully or partially fulfilled, more conclusive evidence would be needed to justify the introduction of a mandatory surveillance system for TSTC in Europe, including a more profound analysis and assessment of potential risk factors for acquisition of (N)CC in Europe. Irrespective of the question of surveillance, some measures are advisable, such as improvement of the quantity and quality of data on prevalence and incidence of (N)CC and the provision of capacity and expertise for accurate diagnosis and treatment of cases in both humans and

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animals. For an evidence-based prioritisation of diseases for surveillance, experts from various backgrounds, actors using surveillance data on a regular basis and different stakeholders must work together.

Conclusion

This work contributes to a better understanding of the epidemiology and surveillance of (N)CC in Europe, demonstrating the occurrence of (N)CC cases throughout Europe over a period of 16 years. Given that reporting mechanisms are not uniform, data are fragmented and reliable incidence/prevalence measures for (N)CC in Europe are not available, firm conclusions about the actual disease burden are impossible. Further research on how to use ICD-based data reliably or on other ways to obtain good-quality data in a cost-effective way is needed. While most (N)CC cases are associated with travel to or migration from an endemic area, the potential for autochthonous transmission from *T. solium* carriers seems to coexist. Therefore, and because disease transmission dynamics might change, a more profound analysis and assessment of potential risk factors for acquiring (N)CC in Europe is needed.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Search terms and inclusion and exclusion criteria of the systematic literature search.

Appendix S2. Citations of included studies.

Appendix S3. Individual patient data.

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