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Original Article

Evidence-Based Semiquantitative Methodology for Prioritization of Foodborne Zoonoses

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Abstract

Objectives: To prioritize an extended list of food- and water-borne zoonoses to allow food safety authorities to focus on the most relevant hazards in the food chain.
Methods: An evidence-based semiquantitative methodology was developed. Scores were given by 35 scientific experts in the field of animal and public health, food, and clinical microbiology and epidemiology to 51 zoonotic agents according to five criteria related to public health (severity and occurrence in humans), animal health (severity of disease coupled with economic consequences and occurrence in animals), and food (occurrence in food). The scoring procedure was standardized and evidence-based as experts were provided, for each zoonotic agent, a same set of up-to-date help information data related to the five criteria. Independently, the relative importance of the five criteria was weighted by seven food chain risk managers. The zoonotic agents were ranked based on overall weighted scores and were grouped in four statistically different levels of importance.
Results: The following foodborne zoonotic pathogens were classified as "most important": *Salmonella* spp., *Campylobacter* spp., *Listeria monocytogenes*, and verocytotoxigenic *Escherichia coli*. A second group of "significant importance" included *Toxoplasma gondii*, the agent of bovine spongiform encephalopathy, *Clostridium botulinum, Staphylococcus aureus, Cryptosporidium parvum, Mycobacterium bovis, Echinococcus granulosus, Streptococcus* spp., *Echinococcus multilocularis, Yersinia enterocolitica, Mycobacterium avium, Fasciola hepatica, Giardia intestinalis*, and Rotavirus.
Conclusions: This methodology allowed to rank 51 zoonotic agents with objectivity and taking account of a combined input from risk assessors and risk managers.
Applications: These results support food safety policy makers to establish the multiannual monitoring program of foodborne zoonoses. They also enable to identify knowledge gaps on specific zoonotic agents and to formulate key research questions. Principally, this method of prioritization is of general interest as it can be applied for any other ranking exercise and in any country.

Introduction

Numerous foodborne zoonotic pathogens threaten the health of the consumer every day. A cost-effective control policy by food safety agencies requires to focus on the most relevant hazards. It is therefore crucial for risk managers to be informed, on a scientific basis, about the respective importance of foodborne zoonotic pathogens. Food safety

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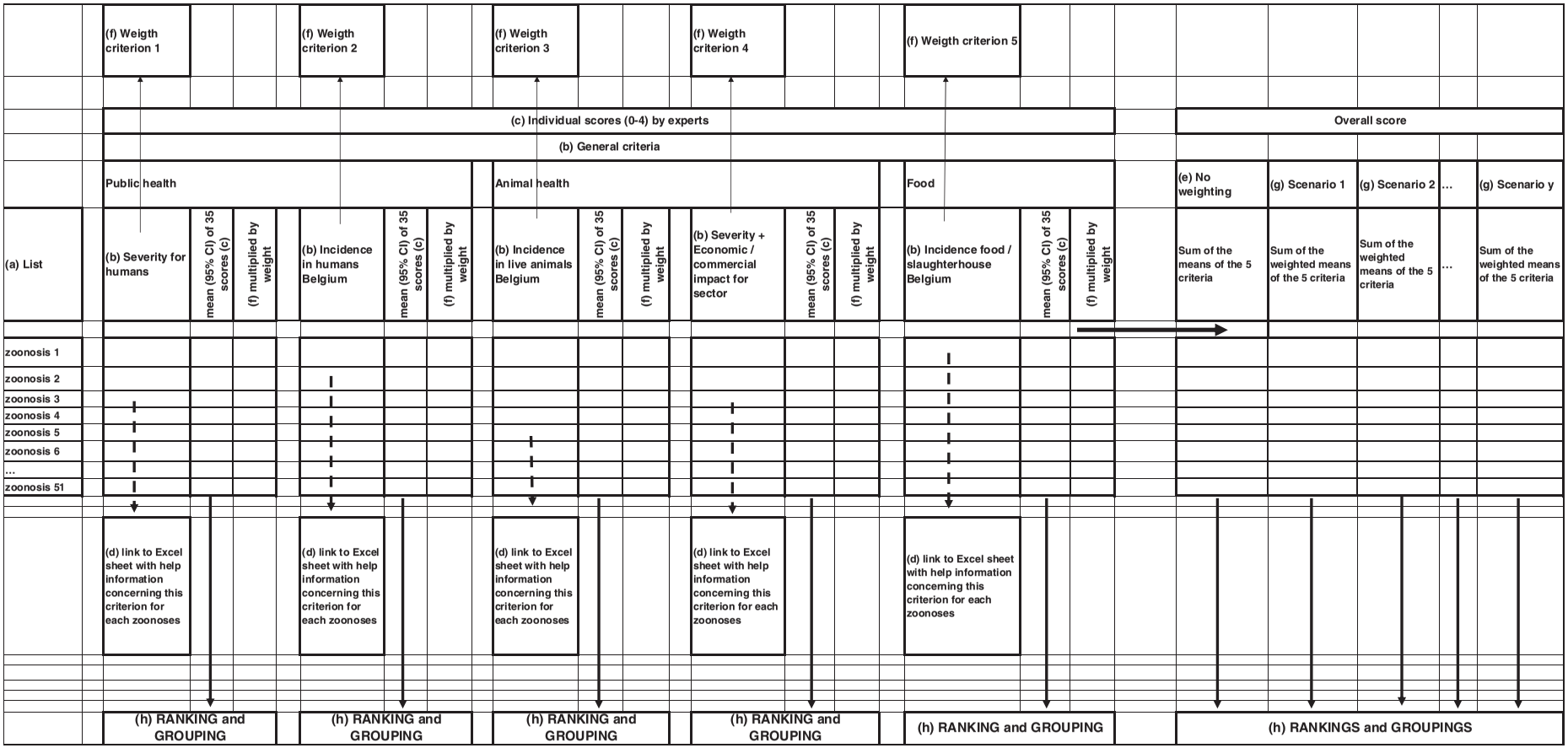
(f) Weigth criterion 1
(f) Weigth criterion 2
(f) Weigth criterion 3
(f) Weigth criterion 4
(f) Weigth criterion 5
(c) Individual scores (0-4) by experts
Overall score
(b) General criteria
Public health
Animal health
Food
(e) No weighting
(g) Scenario 1
(g) Scenario 2
...
(g) Scenario y
(a) List
(b) Severity for humans
mean (95% CI) of 35 scores (c)
(f) multiplied by weight
(b) Incidence in humans Belgium
(b) Incidence in live animals Belgium
(b) Severity + Economic / commercial impact for sector
(b) Incidence food / slaughterhouse Belgium
Sum of the means of the 5 criteria
Sum of the weighted means of the 5 criteria
zoonosis 1
zoonosis 2
zoonosis 3
zoonosis 4
zoonosis 5
zoonosis 6
...
zoonosis 51
(d) link to Excel sheet with help information concerning this criterion for each zoonoses
(h) RANKING and GROUPING
(h) RANKINGS and GROUPINGS

monitoring and control programs established by risk managers are generally applied on risk-based approaches by risk assessors (Maudoux *et al.*, 2006). In this study, an evidence-based standardized semiquantitative method to prioritize food- and water-borne zoonoses was developed to give recommendations to risk managers for establishing control programs in the food chain.

Several qualitative (Valenciano *et al.*, 2001), semiquantitative (Carter, 1991; Petersen *et al.*, 1996; Rushdy and O'Mahony, 1998; Doherty, 2000; Horby *et al.*, 2001; Ross and Sumner, 2002; Sumner and Ross, 2002; Sumner *et al.*, 2005; Krause *et al.*, 2007; McKenzie *et al.*, 2007), and quantitative (Kemmeren *et al.*, 2006; Fosse *et al.*, 2008) rankings of communicable diseases and zoonoses have been performed.

A semiquantitative method was adopted in this study to circumvent the problems usually encountered in quantitative methods, such as the lack of data (Batz *et al.*, 2005; Kemmeren *et al.*, 2006) and in qualitative methods, such as subjectivity and unreliability (Cox *et al.*, 2005).

The semiquantitative approach described in this article has two major improvements compared to existing semiquantitative studies. First, it is based on an evidence-based and up-to-date set of help information data that enabled to standardize, to objectify, and to make more accurate the scoring process by scientific experts. This help information also compensated for an eventual lack of ready knowledge of the experts for all of the 51 zoonoses. Second, an independent weighting process of the criteria by food chain risk managers allowed a combined implication of policy priorities of risk managers and of scientific expertise of risk evaluators (scientific experts) in the final ranking.

The developed method by itself can be applied for other ranking exercises than foodborne zoonoses, for example, animal diseases, and zoonoses other than foodborne.

As the list of zoonotic pathogens presented in this article is exhaustive, including exotic and rare agents, and as the methodology described is reproducible, the developed method is applicable worldwide. In this article, Belgian data were used as a model with the aim to give examples of output (rankings), but information data of any country can be used to obtain specific rankings.

Materials and Methods

The method is schematized in Fig. 1.

Establishment of an exhaustive list of (potential) food- and water-borne zoonotic pathogens

An exhaustive list of 51 food- and water-borne zoonoses was established based on a literature review (Acha and Szyfres, 2005) and on the opinion of a working group of scientific experts (Table 1, column A). To establish the list, the following definition of "zoonosis" was applied: "disease or infection naturally transmissible from animals to humans and vice versa" (Toma *et al.*, 1991). The scope of the list was restricted to zoonotic pathogens transmitted by food and/or water with the concern to work exhaustively in the food chain domain and to work with prioritization criteria specific to this route of transmission. The term "water-borne" includes drinking water, but also water susceptible to come into contact with foodstuff (e.g., rinsing water for vegetables). Drinking water is defined as food in the Regulation (EC) Nr 178/2002.

Each zoonosis was defined by its etiologic agent(s) (Table 1, column B). In a concern of simplification, some etiologic agents were grouped in species (e.g., *Salmonella* spp.). In a concern to be exhaustive, potential zoonotic pathogens (transmission from animal to humans or transmission via food not yet fully proven) and rare pathogens were included in the list.

Despite their possible food or water transmission, *Bacillus cereus, Ascaris suum*, and the tropical *Entamoeba histolytica* were not included in the list because food or water is, in these cases, only contaminated via an infected environment.

Selection of relevant criteria

The prioritization exercise was based on the scoring of the impact of the 51 zoonotic pathogens to five relevant criteria, cited in Tables 1 and 2. Two criteria concerned public health: the severity of the disease in humans and the occurrence of the disease in the human population between 2003 and 2006. Two criteria dealt with the animal production sector: occurrence of the disease in the concerned animal population between 2003 and 2006, and severity of the disease for animals combined with economic and commercial considerations of the disease for the sector. A fifth criterion considered the importance of food as source of transmission of the zoonotic pathogens to humans and was related to the occurrence of these zoonotic agents in the food and/or on carcasses.

The criterion "severity of the disease for animals" was coupled with an evaluation of economic and commercial impact of the disease for the sector. Socioeconomic impact of the disease for the society was indirectly included in the help information related to the criterion "severity of the disease for humans" (see next point).

Constitution of an evidence-based "help" information database

For each of the 51 zoonoses, a set of "help" information data related to the five criteria were collected and provided to the experts. This help information consisted of up-to-date quantitative and/or qualitative national and international data

FIG. 1. Stepwise methodology for prioritization. After (**a**) establishment of an exhaustive list of (potential) food- and water-borne zoonotic agents and (**b**) identification of five relevant prioritization criteria, 35 scientific experts were invited to give (**c**) individual standardized scores based on (**d**) help information. (**c**) The mean of the 35 expert scores per zoonotic agent and per criterion was calculated with a confidence interval of 95% (normal distribution). The (**e**) overall score of each zoonotic agent was calculated as the sum of the bootstrapped mean scores of the five criteria. After (**f**) weighting of the five criteria by seven risk managers, individual bootstrapped weighted scores per criterion and (**g**) several scenario's of weighted overall scores were calculated. (**h**) Rankings and grouping were performed on the several scenario's (individual scores per criterion and overall (weighted) scores. Finally, the aim of the study was to give recommendations to risk managers after comparison of the overall score(s) with existing control measures.

Table 1. Exhaustive List of Food- and Water-Borne Zoonoses (Column A) with Their Etiologic Agent(s) Alphabetically Classified (Column B) and Individual Standardized Expert Scores for the Five General Criteria

A	B	C	D	E	F	G
		Mean expert scores (± standard error) for five general criteria				
		Public health impact		*Animal health impact*		*Food impact*
Zoonoses	*Agents*	*Severity for humans*	*Occurrence in humans*	*Occurrence in live animals*	*Severity + economic and commercial impact for sector*	*Occurrence in food/slaughter-houses*
Bacteria						
Aeromonosis	*Aeromonas* spp.	1.16 ± 0.10 (*n* = 32)	0.71 ± 0.12 (*n* = 21)	0.43 ± 0.20 (*n* = 7)	0.37 ± 0.09 (*n* = 27)	0.71 ± 0.29 (*n* = 7)
Arcobacteriosis	*Arcobacter butzleri*	1.33 ± 0.12 (*n* = 30)	1.46 ± 0.16 (*n* = 28)	2.15 ± 0.34 (*n* = 13)	0.81 ± 0.15 (*n* = 27)	1.82 ± 0.38 (*n* = 11)
Anthrax	*Bacillus anthracis*	3.61 ± 0.11 (*n* = 33)	0.27 ± 0.08 (*n* = 33)	0.60 ± 0.10 (*n* = 25)	2.44 ± 0.24 (*n* = 32)	0.21 ± 0.21 (*n* = 14)
Bovine brucellosis	*Brucella abortus*	2.84 ± 0.09 (*n* = 32)	0.42 ± 0.09 (*n* = 31)	0.16 ± 0.08 (*n* = 31)	2.81 ± 0.16 (*n* = 31)	0.10 ± 0.07 (*n* = 21)
Caprine and ovine brucellosis	*Brucella melitensis*	2.88 ± 0.10 (*n* = 32)	1.00 ± 0.13 (*n* = 32)	0.13 ± 0.06 (*n* = 31)	2.77 ± 0.17 (*n* = 31)	0.13 ± 0.09 (*n* = 16)
Campylobacteriosis	*Campylobacter coli* and *jejuni*	1.94 ± 0.11 (*n* = 33)	3.45 ± 0.14 (*n* = 33)	3.30 ± 0.25 (*n* = 20)	1.55 ± 0.18 (*n* = 31)	3.39 ± 0.13 (*n* = 31)
Vibriosis	*Campylobacter (vibrio) fetus* subsp. *fetus* and *venerealis*	2.29 ± 0.21 (*n* = 31)	0.97 ± 0.06 (*n* = 29)	1.12 ± 0.12 (*n* = 25)	1.65 ± 0.17 (*n* = 26)	0.25 ± 0.16 (*n* = 8)
Botulism	*Clostridium botulinum*	3.52 ± 0.13 (*n* = 33)	1.00 ± 0.05 (*n* = 31)	1.40 ± 0.12 (*n* = 30)	1.94 ± 0.16 (*n* = 32)	1.00 ± 0.13 (*n* = 19)
Food toxi-infection with *Clostridium perfringens*	*Clostridium perfringens*	1.69 ± 0.12 (*n* = 32)	1.27 ± 0.12 (*n* = 30)	2.10 ± 0.25 (*n* = 21)	1.90 ± 0.12 (*n* = 30)	1.29 ± 0.14 (*n* = 24)
Corynebacteriosis	*Corynebacterium ulcerans*	1.38 ± 0.14 (*n* = 29)	0.19 ± 0.11 (*n* = 27)	0.78 ± 0.28 (*n* = 9)	0.92 ± 0.31 (*n* = 12)	0.25 ± 0.25 (*n* = 4)
Corynebacteriosis	*Corynebacterium bovis*	1.27 ± 0.12 (*n* = 30)	0.15 ± 0.09 (*n* = 26)	1.22 ± 0.43 (*n* = 9)	1.08 ± 0.34 (*n* = 12)	0.25 ± 0.25 (*n* = 4)
Q fever	*Coxiella burnetii*	2.63 ± 0.11 (*n* = 32)	1.45 ± 0.14 (*n* = 31)	1.53 ± 0.19 (*n* = 17)	1.86 ± 0.15 (*n* = 29)	0.33 ± 0.21 (*n* = 6)
Hemolytic-uremic syndrome	*Verocytotoxigenic E. coli*	3.48 ± 0.10 (*n* = 33)	1.91 ± 0.14 (*n* = 32)	1.89 ± 0.17 (*n* = 28)	1.61 ± 0.17 (*n* = 31)	1.52 ± 0.12 (*n* = 31)
Tularemia	*Francisella tularensis*	3.12 ± 0.12 (*n* = 33)	0.84 ± 0.07 (*n* = 31)	0.86 ± 0.08 (*n* = 28)	1.25 ± 0.20 (*n* = 28)	0.25 ± 0.16 (*n* = 8)
Helicobacteriosis	*Helicobacter* spp.	2.30 ± 0.15 (*n* = 30)	1.82 ± 0.31 (*n* = 17)	1.77 ± 0.32 (*n* = 13)	1.11 ± 0.17 (*n* = 28)	0.71 ± 0.29 (*n* = 7)
Leptospirosis	*Leptospira* spp.	2.70 ± 0.12 (*n* = 33)	1.16 ± 0.07 (*n* = 31)	1.46 ± 0.15 (*n* = 24)	1.58 ± 0.14 (*n* = 31)	0.38 ± 0.18 (*n* = 8)
Listeriosis	*Listeria monocytogenes*	3.39 ± 0.11 (*n* = 33)	1.76 ± 0.11 (*n* = 33)	1.45 ± 0.15 (*n* = 22)	2.06 ± 0.14 (*n* = 31)	2.34 ± 0.13 (*n* = 29)
Bovine tuberculosis	*Mycobacterium bovis*	3.09 ± 0.13 (*n* = 33)	1.15 ± 0.10 (*n* = 33)	0.90 ± 0.07 (*n* = 31)	2.91 ± 0.14 (*n* = 32)	1.00 ± 0.07 (*n* = 30)
Avian tuberculosis	*Mycobacterium avium* subsp. *avium*	2.50 ± 0.21 (*n* = 32)	1.00 ± 0.11 (*n* = 27)	1.50 ± 0.17 (*n* = 28)	2.32 ± 0.18 (*n* = 31)	0.88 ± 0.30 (*n* = 8)
Paratuberculosis	*Mycobacterium avium* subsp. *paratuberculosis*	2.54 ± 0.21 (*n* = 26)			2.61 ± 0.15 (*n* = 31)	1.25 ± 0.25 (*n* = 8)
Salmonellosis	*Salmonella enterica*	2.58 ± 0.12 (*n* = 33)	3.42 ± 0.12 (*n* = 33)	3.23 ± 0.12 (*n* = 31)	2.69 ± 0.12 (*n* = 32)	2.97 ± 0.11 (*n* = 31)
Staphylococcosis	*Staphylococcus aureus*	2.09 ± 0.14 (*n* = 32)	1.97 ± 0.18 (*n* = 31)	2.28 ± 0.20 (*n* = 29)	1.65 ± 0.13 (*n* = 31)	1.68 ± 0.10 (*n* = 28)
Streptococcosis	*Streptococcus* spp.	2.06 ± 0.16 (*n* = 33)	1.36 ± 0.22 (*n* = 25)	2.53 ± 0.27 (*n* = 19)	1.75 ± 0.18 (*n* = 28)	1.86 ± 0.51 (*n* = 7)
Cholera	*Vibrio cholerae*	2.94 ± 0.14 (*n* = 33)	0.56 ± 0.10 (*n* = 32)	0.06 ± 0.06 (*n* = 17)	1.00 ± 0.19 (*n* = 22)	0.25 ± 0.16 (*n* = 8)
Food toxi-infection	*Vibrio parahaemolyticus*	1.66 ± 0.14 (*n* = 32)	0.45 ± 0.14 (*n* = 29)	0.56 ± 0.18 (*n* = 9)	0.55 ± 0.14 (*n* = 20)	0.86 ± 0.10 (*n* = 22)
Yersiniosis	*Yersinia enterocolitica*	2.06 ± 0.11 (*n* = 33)	2.36 ± 0.11 (*n* = 33)	2.00 ± 0.23 (*n* = 20)	1.07 ± 0.15 (*n* = 29)	1.32 ± 0.09 (*n* = 28)
Pseudotuberculosis	*Yersinia pseudotuberculosis*	2.24 ± 0.12 (*n* = 33)	1.09 ± 0.07 (*n* = 33)	1.38 ± 0.29 (*n* = 13)	1.31 ± 0.14 (*n* = 26)	0.75 ± 0.16 (*n* = 8)

TABLE 1. (CONTINUED)

A	B	C	D	E	F	G
		Mean expert scores (± standard error) for five general criteria				
		Public health impact		*Animal health impact*		*Food impact*
Zoonoses	*Agents*	*Severity for humans*	*Occurrence in humans*	*Occurrence in live animals*	*Severity + economic and commercial impact for sector*	*Occurrence in food/slaughter-houses*
Viruses and prions						
Lymphocytic choriomeningitis	Lymphocytic choriomeningitis virus	1.65 ± 0.19 ($n = 31$)	0.57 ± 0.11 ($n = 21$)	0.20 ± 0.20 ($n = 5$)	0.13 ± 0.09 ($n = 16$)	0.00 ± 0.00 ($n = 5$)
Norovirus viral gastroenteritis	Norovirus	1.61 ± 0.14 ($n = 33$)	1.87 ± 0.22 ($n = 30$)	1.00 ± 0.39 ($n = 10$)	0.73 ± 0.15 ($n = 22$)	1.58 ± 0.21 ($n = 24$)
Central European tick-borne encephalitis Vorou *et al.* (2007)	Central European tick-borne encephalitis virus	3.06 ± 0.13 ($n = 33$)	1.17 ± 0.12 ($n = 29$)	0.19 ± 0.11 ($n = 21$)	1.00 ± 0.25 ($n = 21$)	0.00 ± 0.00 ($n = 6$)
Avian influenza	Avian influenza virus H5N1	3.28 ± 0.14 ($n = 32$)	0.07 ± 0.05 ($n = 30$)	0.10 ± 0.06 ($n = 29$)	2.94 ± 0.21 ($n = 31$)	0.06 ± 0.06 ($n = 18$)
Hepatitis A	Hepatitis A virus	2.55 ± 0.14 ($n = 33$)	2.36 ± 0.14 ($n = 33$)	0.11 ± 0.07 ($n = 19$)	0.96 ± 0.18 ($n = 26$)	0.50 ± 0.13 ($n = 22$)
Hepatitis E	Hepatitis E virus	2.69 ± 0.16 ($n = 32$)	1.25 ± 0.37 ($n = 8$)	0.00 ± 0.00 ($n = 5$)	0.65 ± 0.19 ($n = 17$)	0.17 ± 0.17 ($n = 6$)
Rotavirus infection	Rotavirus	1.66 ± 0.13 ($n = 32$)	3.09 ± 0.20 ($n = 32$)	2.00 ± 0.30 ($n = 17$)	1.71 ± 0.20 ($n = 24$)	0.19 ± 0.11 ($n = 21$)
Bovine spongiform encephalopathy	Prion protein	3.84 ± 0.08 ($n = 32$)	0.27 ± 0.09 ($n = 32$)	0.94 ± 0.06 ($n = 32$)	3.28 ± 0.14 ($n = 32$)	1.03 ± 0.06 ($n = 32$)
Parasites						
Anisakiasis	*Anisakis simplex*	1.64 ± 0.11 ($n = 33$)	0.64 ± 0.13 ($n = 14$)	1.69 ± 0.29 ($n = 13$)	1.28 ± 0.16 ($n = 25$)	1.00 ± 0.39 ($n = 10$)
Balantidiosis	*Balantidium coli*	1.10 ± 0.11 ($n = 31$)	0.14 ± 0.07 ($n = 28$)	0.50 ± 0.22 ($n = 6$)	0.50 ± 0.15 ($n = 12$)	0.25 ± 0.25 ($n = 4$)
Chlonorchiasis	*Clonorchis sinensis*	1.79 ± 0.15 ($n = 29$)	0.56 ± 0.12 ($n = 32$)	0.10 ± 0.10 ($n = 10$)	0.25 ± 0.18 ($n = 12$)	0.00 ± 0.00 ($n = 5$)
Cryptosporidiosis	*Cryptosporidium parvum*	1.69 ± 0.11 ($n = 32$)	2.28 ± 0.12 ($n = 32$)	2.50 ± 0.27 ($n = 16$)	1.89 ± 0.15 ($n = 27$)	1.67 ± 0.49 ($n = 6$)
Dioctophymosis	*Dioctophyma renale*	1.90 ± 0.15 ($n = 29$)	0.50 ± 0.17 ($n = 10$)	0.60 ± 0.40 ($n = 5$)	0.78 ± 0.32 ($n = 9$)	0.00 ± 0.00 ($n = 4$)
Diphyllobotriosis	*Diphyllobothrium*	1.00 ± 0.10 ($n = 31$)	0.64 ± 0.09 ($n = 28$)	0.20 ± 0.20 ($n = 5$)	0.50 ± 0.22 ($n = 10$)	0.00 ± 0.00 ($n = 4$)
Echinococcosis/ Hydatidosis	*Echinococcus granulosus*	3.22 ± 0.12 ($n = 32$)	1.10 ± 0.07 ($n = 30$)	1.10 ± 0.14 ($n = 20$)	2.07 ± 0.18 ($n = 29$)	1.04 ± 0.11 ($n = 28$)
Echinococcosis/ Hydatidosis	*Echinococcus multilocularis*	3.52 ± 0.11 ($n = 31$)	1.08 ± 0.13 ($n = 26$)	1.42 ± 0.19 ($n = 19$)	1.54 ± 0.21 ($n = 28$)	0.38 ± 0.14 ($n = 13$)
Fasciolosis	*Fasciola hepatica*	2.36 ± 0.13 ($n = 33$)	1.13 ± 0.11 ($n = 30$)	1.91 ± 0.21 ($n = 22$)	1.90 ± 0.13 ($n = 31$)	1.58 ± 0.26 ($n = 12$)
Giardiasis (Lambliasis)	*Giardia intestinalis*	1.52 ± 0.11 ($n = 33$)	2.67 ± 0.15 ($n = 33$)	2.25 ± 0.31 ($n = 16$)	1.00 ± 0.22 ($n = 23$)	1.43 ± 0.37 ($n = 7$)
Pentastomosis	*Linguatula serrata*	0.86 ± 0.13 ($n = 29$)	0.33 ± 0.21 ($n = 6$)	0.43 ± 0.20 ($n = 7$)	0.09 ± 0.09 ($n = 11$)	0.00 ± 0.00 ($n = 5$)
Sarcosporidiosis	*Sarcocystis suihominis*	1.16 ± 0.10 ($n = 31$)	0.43 ± 0.20 ($n = 7$)	2.21 ± 0.26 ($n = 14$)	1.50 ± 0.17 ($n = 30$)	1.16 ± 0.15 ($n = 25$)
Sarcosporidiosis	*Sarcocystis bovihominis*	1.03 ± 0.12 ($n = 32$)	0.96 ± 0.10 ($n = 23$)	2.43 ± 0.29 ($n = 14$)	1.59 ± 0.19 ($n = 22$)	1.55 ± 0.23 ($n = 22$)
Bovine cysticercosis	*Taenia saginata*	1.06 ± 0.16 ($n = 28$)	1.61 ± 0.31 ($n = 18$)	1.76 ± 0.19 ($n = 21$)	2.13 ± 0.16 ($n = 30$)	1.65 ± 0.15 ($n = 31$)
Ovine and caprine cysticercosis	*Taenia* spp. (other than *T. saginata*)	1.04 ± 0.20 ($n = 28$)	0.40 ± 0.16 ($n = 10$)	1.13 ± 0.30 ($n = 8$)	1.69 ± 0.17 ($n = 29$)	0.86 ± 0.07 ($n = 28$)
Toxoplasmosis	*Toxoplasma gondii*	3.03 ± 0.10 ($n = 33$)	1.50 ± 0.10 ($n = 32$)	2.04 ± 0.17 ($n = 28$)	1.69 ± 0.16 ($n = 32$)	1.36 ± 0.20 ($n = 11$)
Trichinellosis	*Trichinella* spp.	2.58 ± 0.14 ($n = 31$)	0.86 ± 0.08 ($n = 29$)	0.50 ± 0.12 ($n = 24$)	2.00 ± 0.16 ($n = 29$)	0.72 ± 0.09 ($n = 25$)

The potential zoonoses and the zoonoses for which food has not been proven as source of transmission are in italic (column A). Columns C to G present the five general criteria and the average together with its standard error (35 experts) of the individual standardized expert scores.

Table 2. Description of the Help Information (Column B) Corresponding to the General Criteria (Column A) and Results of the Weighting of the Criteria by Risk Managers (Column C)

A	*B*	*C*
Five general criteria	*Help criteria (Belgian data)*	*Weighting (mean ± standard error)*
Public health		
1. Severity of the disease for humans	Clinical signs Risk of mortality Necessity for hospitalization Absence of treatment/vaccine Necessity for medical intervention Possibility of complications (after effects) Possibility of grouped cases Existence of YOPI's (young, old, pregnant, immunodeficient) Duration of illness Classification of the disease in regional decrees	6.57 ± 0.53
2. Occurrence of the disease in the Belgian population	If searched, number of registered cases in 2003, 2004, 2005, and 2006 Presence of the disease in Europe Incidence of the disease in the world	4.29 ± 0.52
Animal health		
3. Occurrence in live animals in Belgium	Number of registered cases in 2003, 2004, 2005, and 2006, or prevalence of the disease in Belgium Epidemiological form of the disease (sporadic, enzootic, epizootic, emergent, exotic, country [officially] free) Geographical repartition of the disease in Europe (or another continent), in the Northern (or Southern) hemisphere and in the world; and characteristics of the repartition (cosmopolite, industrial countries, etc.)	3.14 ± 0.40
4. Severity of the disease for animals and commercial and economic impact of the disease for the sector	Classification of the disease in regional decrees Contagiousness of the disease between animals Existence of an animal reservoir Existence of multiple animal species (multispecies disease) Important economic consequences for the sector Existence of a risk at importation	2.57 ± 0.43
Food		
5. Occurrence of the agent in food or in carcasses	Number of positive samples in foodstuffs (all food matrixes merged) or in carcasses in slaughterhouses in 2003, 2004, and 2005	3.43 ± 0.37

originated from different official sources, in regard to 23 topics (Table 2). The experts were encouraged to consult these information data for attributing their individual scores to the five criteria (see next point).

Belgian occurrence data were used to illustrate possible outputs of this ranking exercise. However, data specific to any country can be used if a country-specific ranking is to be obtained.

Data on the severity of the zoonotic diseases in humans and in animals were collected from scientific literature (Acha and Szyfres, 2005), regional decrees (Decree of the Flemish Region, 2004; Decree of the Walloon Region, 2002; Decree of the Brussels-Capital Region, 2001), and Directive 2000/54/CE. Data on economic and commercial impact of the disease were collected by expert opinion. Data on the occurrence in humans were found in annual reports on infectious diseases (Ducoffre, 2007), in the scientific literature (Acha and Szyfres, 2005), in Handistatus II, and in the World Animal Health Information Database interface of the OIE (WAHID). Data on occurrence in animals were collected from Trends and Sources reports on zoonotic agents (2003, 2004, and 2005), from Handistatus II and WAHID, from the scientific literature (Acha and Szyfres, 2005), and from Internet sites of official institutions and organizations. Finally, data on the occurrence in food origi-

nated from results 2003–2005 of the control program of the Belgian Federal Agency for the Safety of the Food Chain. Occurrence data in Belgium presented in the scientific literature [e.g., *Sarcocystis bovihominis* (Vangeel *et al.*, 2007), cryptosporidiosis (Geurden *et al.*, 2007), giardiasis (Geurden *et al.*, 2008), and paratuberculosis (Boelaert *et al.*, 2000)] were also used. To help the experts, quantitative occurrence data were always accompanied by estimations of the epidemiological situation of the disease in Belgium, in Europe, and in the world and by the geographical distribution of the disease. Occurrence data concerning exotic diseases were noted as "imported cases." In case no data were available, expert opinions by human and veterinarian epidemiologists provided additional information to complete the set of help information data.

Owing to the abundance of the information and the specificity to Belgium, these detailed information data are not presented in this article but may be obtained for scientific use on request to the corresponding author.

Establishment of standardized scores by scientific experts

Thirty-five scientific experts (risk assessors), affiliated with different scientific institutions or universities, and with a medical, veterinary, agrochemical, or biological background were asked to participate in the scoring exercise. The experts individually scored the impact of the 51 zoonoses on each of the five criteria, after having read detailed instructions and having been encouraged to use the help information data (Table 2).

The impact of each zoonotic agent on the five criteria was scored on a scale from 0 to 4, according to instructions (Table 3). The experts had the possibility to write "ND" (not determined) if no data were available or to write a question mark ("?") if they did not agree with the available data or if the scoring was impossible to their opinion. In case of absence of help information data, the experts were invited to give a score based on own data or literature.

It was also explained to the experts that the provided help information (in particular occurrence data) had to be interpreted as indicative rather than as an accurate description of the true situation for several reasons, such as underestimation caused by well-known underreporting problems, variation of the sources of information, and impossibility to obtain detailed occurrence data for several subspecies of zoonotic agents because of analytical limitations in species identification (e.g., *Mycobacterium avium* subspecies *avium* [Avian tuberculosis] and subspecies *paratuberculosis* [Paratuberculosis], which were therefore considered simultaneously and should not be considered in the ranking).

Table 3. Instructions Provided to the Experts for Attributing the Scores

Individual scores[a]	*Occurrence criteria (criteria 2, 3, and 5)*	*Severity criteria (criteria 1 and 4)*
0	Zero (absence)	Benign
1	Rare	Weak
2	Moderate	Moderate
3	Significant	Severe
4	High	Lethal/no treatment
ND	No data available (not determined, not searched, not analyzed)	
?	Expert does not agree with data; scoring not possible	

Framework used by experts for the semiquantitative scoring to assess the impact of the foodborne zoonoses as a basis for prioritizing.

[a]Experts were asked to attribute a score on a scale 0–4, following instructions provided in this table and in accordance with the data provided in the help information. There was a possibility to write "ND" (not determined) if no data were available or to write a question mark if experts did not agree with the available data or if the scoring was not possible.

Calculation of individual and total scores and quantification of the uncertainty

The individual scores of the 35 experts were used to calculate, for each zoonosis, an average individual score per criterion (scale from 0 to 4 points) together with its standard error reflecting interexpert heterogeneity (Table 1, columns C to G). In case "ND" or "?" values were given, the average score was calculated based on the remaining expert scores (indicated as "*n*" value in Table 1), which increased the uncertainty.

The average total scores were calculated in R (R; www.r-project.org/) using a clustered bootstrap. The bootstrap was set up in such a way that the same experts were sampled for all criteria (results not shown). The bootstrapped analysis allowed a correct estimate of the variance of the total score, overcoming the problem of the missing scores resulting from the fact that some experts attributed "ND" or "?" values. Absence of bias was ascertained by comparing the calculated (non-bootstrapped) averages with the bootstrapped averages.

The R code used is shown in Appendix 1.

For each zoonotic agent, a total score (from 0 to 20 points) was calculated as the sum of the bootstrapped average scores per criterion. Uncertainty was measured by estimating (through bootstrapping in R) the 95% confidence intervals for the total scores.

The average individual expert scores of each of the five criteria (Table 1) were used to analyze the impact of each of the criteria on the total scores of the zoonotic pathogens and to evaluate which criterion(a) is (are) responsible for the relative position of each pathogen in the ranking.

Weighting of the five criteria by food chain risk managers

The relative weighting of the five criteria is aimed at emphasizing the importance of specific criteria in accordance to policy priorities. Seven food chain risk managers were asked to independently distribute a total of 20 points between the five criteria using the Las Vegas methodology (Gore, 1987). This resulted in the attribution of a relative weight to the criteria that was introduced in the calculations of the total scores, making the total weighted scores dependent on the priorities of the risk managers.

Ranking and grouping of the zoonoses

The zoonotic pathogens were ranked according to their total (weighted) scores in Excel.

Different groups of importance were identified by Classification and Regression Tree (CART—Salford Systems; www.salford-systems.com) analysis using the mean total scores per disease as input. This methodology, developed by Breiman *et al.* (1984), can be used to analyze either categorical (classification) or continuous data (regression). In this article, regression tree models were used as the target variable "zoonotic importance" is a continuous variable (Saegerman *et al.*, 2004) with the aim to obtain subgroups with minimal within-variance (grouping zoonoses with similar importance) using a technique called cross-validation (Speybroeck *et al.*, 2004). The default settings of the software, described in Steinberg and Colla (1995), were used to develop the regression tree.

Comparison of the total scores with existing surveillance measures and recommendations

Information concerning the presence (or absence) of three types of specific national control measures was collected for each of the 51 zoonoses: first, the existence of national or European legislation (e.g., Directive 2003/99/CE, Royal Decree of 22th May 2005, Regulation [EC] No 853/2004, Regulation [EC] No 854/2004); second, the existence of an official control program, and/or of a herd, exploitation or country qualification system; and third, the existence of an official surveillance or monitoring program at primary production level (live animals), in slaughterhouses (carcasses, cutting plants, etc.) and/or in retail points (foodstuffs).

This information was directly compared with the total (weighted) scores and with the importance group of the zoonoses to identify inadequacies (e.g., absence of surveillance measures for a highly important zoonosis) and to give recommendations to the food chain risk managers and policy makers to implement or to adapt (e.g., increase in the number of analyses) the monitoring program of zoonotic agents.

Identification of knowledge gaps

Knowledge gaps on zoonoses were identified by the presence of "ND" values in the help information and by high numbers of "ND" or "?" filled out by experts, reflected by high confidence intervals.

Results

Standardized individual expert scores

Table 1 (columns C to G) shows the averages of the 35 individual expert scores per criterion and per zoonosis together with their standard errors and the number of experts having given a score (n).

The means of the individual expert scores of the 51 zoonotic agents were calculated for each of the five criteria (between 0 and 4 points) and compared. The criterion "severity of the disease for humans" (2.19 points) had the highest impact on the total scores and thus contributed the most to the final position of the zoonoses in the ranking. It was followed by the criteria "severity for animals coupled with economic consequences" (1.49 points), "occurrence in live animals" (1.22 points), "occurrence in humans" (1.14 points), and "occurrence in food" (0.84 points).

Weighting of the criteria

In the absence of weighting, the five criteria are equally important. By the weighting process, it is possible for policy makers to express a preference. Several rankings based either on weighted scores or unweighted scores become possible. The weights given by seven food chain risk managers were moderate and showed a relatively good homogeneity (see Table 2, column C). The highest importance was attributed to public health and particularly to the criteria "severity of the disease in humans," which had also the highest impact on the total expert scores (point 3.1).

Total (weighted) scores, rankings, and groupings

The relative importance of the zoonoses was determined by ranking the 51 zoonotic agents based on the total non-weighted (Fig. 2) or weighted (Fig. 3) scores. Four statistically different groups of importance were identified by CART and are indicated by thresholds in Figs. 2 and 3.

Low confidence intervals were observed in the rankings, indicating that few subjective interpretation problems existed or that individual discordances were diluted among the high number of experts.

The individual expert scores (Table 1) allowed to explain the individual impact of the five criteria on the total scores and the position in the ranking of each zoonosis. For example, the high score of bovine spongiform encephalopathy (BSE) is because of the high impact of the severity of the disease in humans and to the important economic consequences of the disease for the animal sector in case of outbreak. When considering the criteria "occurrence in humans, in animals and in food," the most important zoonoses were campylobacteriosis and salmonellosis.

The results of the rankings are in accordance with the Directive 2003/99/EC, which also includes *Salmonella enterica, Campylobacter coli* and *jejuni, Listeria monocytogenes*, and verocytotoxigenic *Escherichia coli*. Despite they had not exactly the same scope and methodology, the results are also in accordance with results of other studies (Sumner *et al.*, 2005; Kemmeren *et al.*, 2006; Krause *et al.*, 2007; Fosse *et al.*, 2008).

Concordantly, most of the rare zoonotic pathogens, such as *Dioctophyma renale, Clonorchis sinensis, Lymphocytic choriomeningitis* virus, *Balantidium coli, Diphyllobotrium latum*, and *Linguatula serrata*, which were included in the list in a concern to be exhaustive, are of low importance.

The second group (significant importance) contains many parasites, which are monitored less frequently than for example bacteria, mainly because of a lack of routinely available detection methods.

Comparison of the total scores with existing surveillance measures and recommendations

The result obtained by weighted ranking was compared with existing official national control measures to identify inadequacies and to give recommendations to the risk managers of the competent authority for the official monitoring/control program. The results of this comparison have been described in a scientific advice of the Scientific Committee

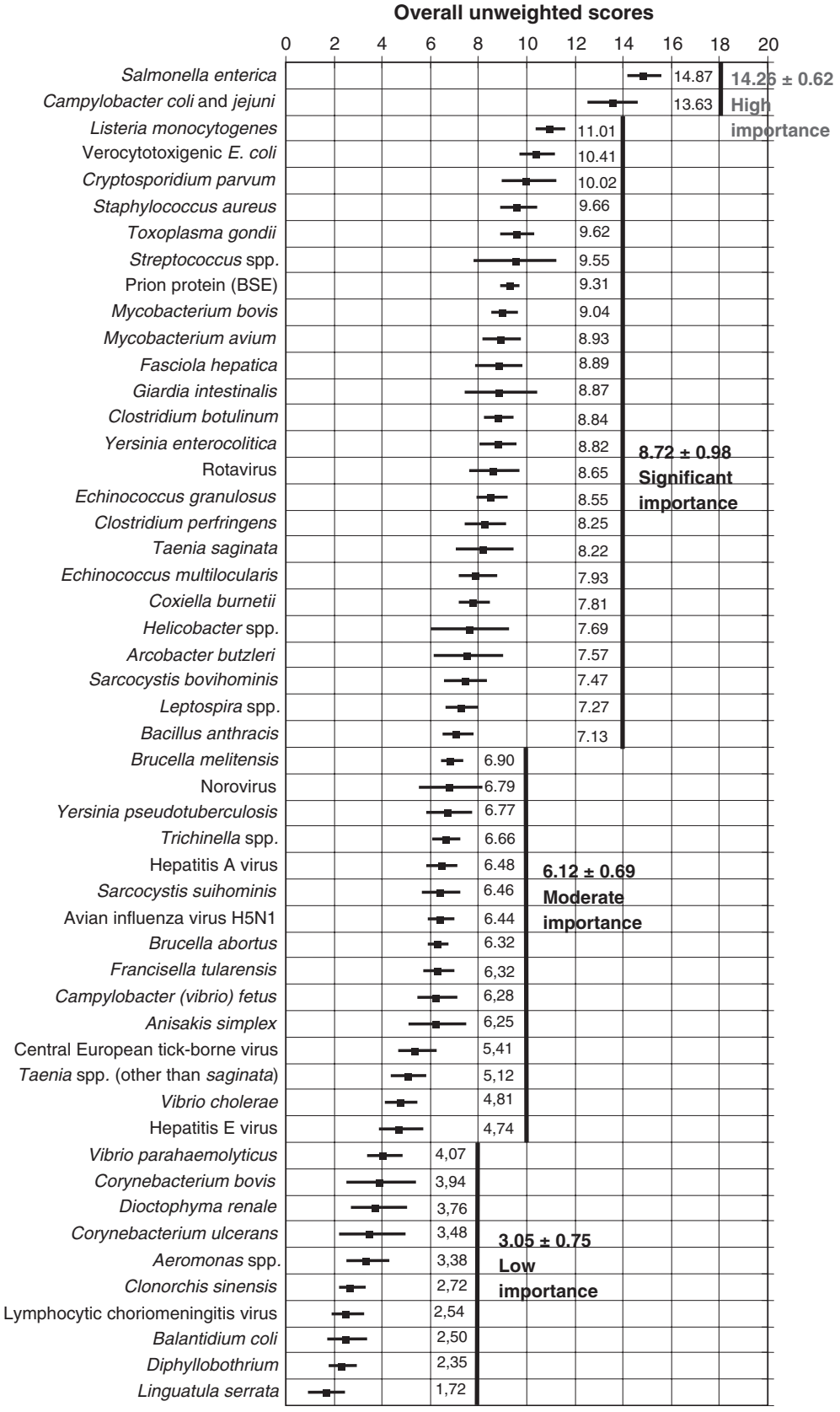

FIG. 2. Results of the ranking of foodborne zoonoses following bootstrapped overall scores without weighting. The means (■) are presented with 95% confidence intervals (—■—) and value labels. Four groups of statistically different importance were identified by Classification and Regression Tree analysis and are represented by the means of the groups ± the standard deviations calculated on basis of the population.

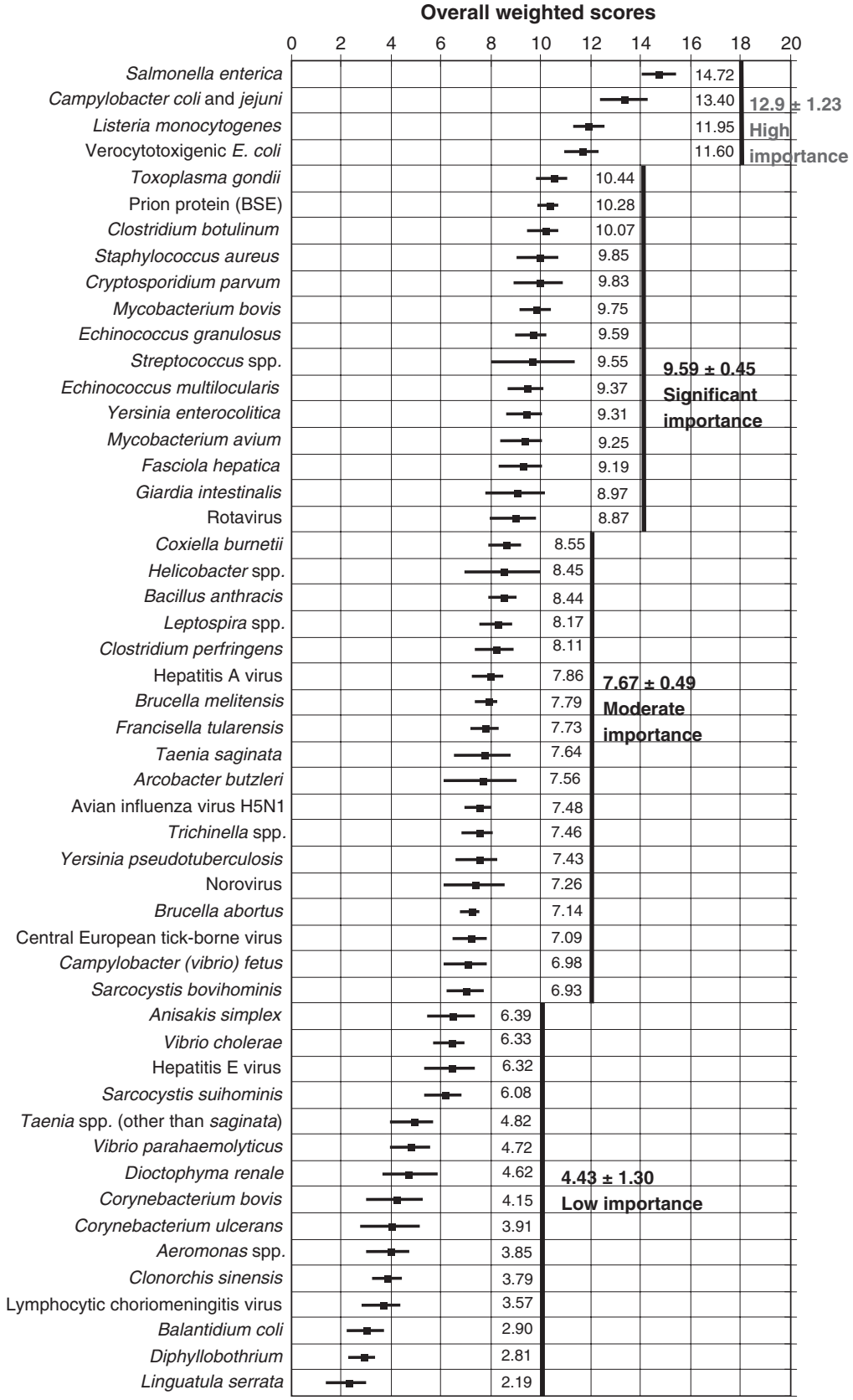

FIG. 3. Results of the ranking of foodborne zoonoses following bootstrapped weighted overall scores based on the weighting mean of the five criteria by seven risk managers. The means (■) are presented with 95% confidence intervals (—■—) and value labels. Four groups of statistically different importance were identified by Classification and Regression Tree analysis and are represented by the means of the groups ± the standard deviations calculated on basis of the population.

(www.favv-afsca.fgov.be/comitescientifique/avis/2008.asp) addressed to the food chain risk managers of the Belgian Federal Agency for Safety of the Food Chain. Examples of such recommendations are the introduction of an official control for *Toxoplasma gondii* in carcasses in slaughterhouses, an increase in the number of analyses of *L. monocytogenes*, and the implementation of a control plan for *Campylobacter* spp.

Identification and analysis of knowledge gaps and recommendations for key research

For some zoonoses with a high or important score, gaps in occurrence data were identified, reflected by high standard error in the individual expert scores and low "n" values (Table 1). For these zoonoses, recommendations for prevalence studies (screenings) eventually accompanied with applied research (e.g., to set up appropriate routine detection methods in animals, food, or water) were made (R; www .favv-afsca.fgov.be=comitescientifique=avis=2008.asp). This was the case, for example, *T. gondii* in carcasses of ruminants and in food, *Coxiella burnetii* (Q fever) in ruminants and in milk, *Leptospira* spp. in cattle, *Anisakis* spp. in raw fish, *Arcobacter* spp. in poultry carcasses, *Helicobacter* in food, *Echinococcus* spp. in wild fruit, *Fasciola hepatica* in cress, *Cryptosporidium parvum* in animals, in food and in water, and *Giardia intestinalis* in food and water.

Concerning potential zoonoses, recommendations for key research were made, that is, to investigate the zoonotic character (e.g., *M. avium* subsp. paratuberculosis) or the foodborne transmission (e.g., avian influenza virus H5N1).

Discussion and Conclusions

The objective of this study was to develop an evidence-based semiquantitative method for prioritization of food- and water-borne zoonoses to allow food safety authorities to focus on the most relevant hazards.

The choice for a semiquantitative rather than for a quantitative approach was justified because of the aim to work with an exhaustive list of 51 foodborne zoonoses and with five criteria, for which no complete data set was available. A quantitative approach, can only be applied to a restricted number of diseases for which an exhaustive quantitative database is available (Kemmeren *et al.*, 2006; Fosse *et al.*, 2008).

A qualitative approach is considered to be too subjective and to be unreliable (Cox *et al.*, 2005), and a semiquantitative approach is therefore less dependent on arbitrary choices. The developed methodology circumvented the disadvantages of qualitative approaches by two main actions. First, by the standardized and evidence-based manner the experts had to give their individual scores, with the use of the help information, and second, by the consultation of a high number (35) of experts resulting in a dilution of the effect of individual subjectivity and misinterpretation. The fact that the experts had to use help information data made their scores "evidence based," less subjective, and more accurate. This help information also enabled to circumvent eventual lack of ready knowledge of the experts for all these 51 zoonoses.

A clear distinction was made between risk assessment and risk management, according to the definition of the risk analysis. The developed ranking methodology respected this distinction by restricting the judgment of the risk assessors (in this case, the expert group) to the scoring of the hazards (the zoonotic agents) and the judgment of the risk managers (in this case, the risk managers) to the weighting of the criteria. Another characteristic of this prioritization method is thus the combined input from risk assessors and risk managers, respectively, for scoring the impact of the hazards and for weighting the criteria. In this way opinions of both branches of the risk analysis process were taken into account resulting in total weighted scores and a weighted ranking list, allowing to make relevant recommendations for the control program.

Despite the existence of multiple ways of transmission of zoonoses, this study was limited to those transmitted by food and water with the concern to use specific criteria for foodborne transmission and to work exhaustively in the food chain matter. Table 1 shows a list of all possible food- and waterborne zoonotic agents, including potential and rare zoonotic pathogens, and can be used as starting point for other or similar studies with data from any country.

The choice of the criteria was made from the viewpoint to have a well-balanced representation of public and animal health criteria and to add a criterion "food" to comply with the aim of the study. Socioeconomic aspects in relation to public and animal health were also taken into consideration. There is a trend to present "disease burden" for public health as a major tool for priority setting (Kemmeren *et al.*, 2006). In the present study, this criterion was included in the help information for the criterion "severity for humans," by the inclusion of help information about the risk of mortality, the possibility of complications, etc. (Table 2). Several other evaluation criteria such as the risk perception by the consumer or the impact of media were not considered because of their subjective nature.

In several studies, rankings are performed according to more than five criteria (Valenciano *et al.*, 2001; Krause *et al.*, 2007). In the present study, the number of criteria was limited to five relevant ones. A large number of other criteria were described more thoroughly in the 23 topics of the help information (Table 2). This was done in a concern of simplification of the work of the 35 experts, to observe more significant differences between the 51 zoonoses in the ranking, and to evaluate the impact of the five relevant criteria on the total scores. The rankings are mainly influenced by a higher impact of the criterion "severity of the disease in humans."

In this article, only two ranking scenarios were presented, but the weighting of the criteria enabled various other scenarios, depending on the way the weights are distributed among the criteria. For example, when only the public health criterion "severity for humans" was taken into account, the two most important zoonotic agents were the prion protein (BSE) and *Bacillus anthracis*, both causing death in humans. When considering only the public health criterion "occurrence in humans," or only the criterion "occurrence in live animals," or "occurrence in food/slaughterhouses," the two most important zoonotic agents were *C. jejuni* and *coli* and *S. enterica*. When considering only the criterion "severity in animals + economic and commercial impact for the animal sector," the two most important zoonotic agents were the prion protein (BSE) and avian influenza virus H5N1, probably because of the eradication policy associated with these diseases. It is

also possible to exclude some criteria from the rankings, such as the two animal health criteria, when the objective is to consider only public health criteria.

Since the results presented in this article are specific to Belgium, they are not discussed profoundly in this article. They are given as example to illustrate the results of the ranking. Information data from any country can be used, and the developed model is applicable worldwide.

In conclusion, the presented methodology provides a reproducible, standardized, and transparent prioritization of pathogens with minimal distortion by individual expert opinion. Further applications of this study may be threefold. First, periodically updating the occurrence data can help to account for trends or emergence of zoonoses. Second, this methodology can be applied for prioritization of zoonoses other than foodborne (e.g., vector-borne or directly transmissible zoonoses), or of other nonzoonotic pathogens (animal or human diseases), with other appropriate criteria. Finally, this exercise can be universally performed with data of any country. Food Safety Agencies could ask their advisory committees to perform such prioritization exercises to apply cost-effective policy.

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(Appendix follows →)

Appendix 1. R Code Used for Bootstrapped Total Score

```
setwd("/. . .")
diseases <- 51; experts <- 35; criteria <- 5
samplesize <- 1000
results <- array(0.0, c(samplesize, diseases))
output <- array(0.0, c(diseases,4))
number_NA <- array(0, diseases)

wght <- 0 ## 0 = unweighted, 1 = expert weighted
ifelse(wght, weighting <- c(1.6425,1.0725,0.7850,0.6425,0.8575), weighting <- c(1,1,1,1,1))

c1 <- as.matrix(read.table("c1.txt", na.strings="?"))
c2 <- as.matrix(read.table("c2.txt", na.strings="?"))
c3 <- as.matrix(read.table("c3.txt", na.strings="?"))
c4 <- as.matrix(read.table("c4.txt", na.strings="?"))
c5 <- as.matrix(read.table("c5.txt", na.strings="?"))
ccc <- array(c(c1, c2, c3, c4, c5), c(diseases, experts, criteria))
for (i in 1:diseases) number_NA[i] <- sum(is.na(ccc[i,,]))
for (i in 1:samplesize)
{
  booty <- sample(1:experts, experts, replace=T)
  for (j in 1: diseases)
  {
    for (k in 1:criteria)
          results[i,j] <- results[i,j] + mean(ccc[j,booty,k], na.rm=T) *
  weighting[k]
    }
  }
for (i in 1:diseases)
{
  output[i,1] <- i
  output[i,2] <- mean(results[,i], na.rm=T)
  output[i,3] <- quantile(results[,i], probs=0.025, na.rm=T)
  output[i,4] <- quantile(results[,i], probs=0.975, na.rm=T)
  }
output2 <- t(output)
ii <- order(output2[2,],output2[3,],output2[4,])
output3 <- t(rbind(output2[1,],output2[2,],output2[3,],output2[4,])[,ii])
plot(c(output3[1,3],output3[1,4]),c(1,1),type="l", ylim=c(0,diseases),
xlim=c(0,max(output[,4], na.rm=T)), xlab="", ylab="")
lines(c(output3[1,2],output3[1,2]),c(0.5,1.5))
text(output3[1,3]-0.25,1+0.2,output3[1,1])
for (i in 2:diseases)
      {
          lines(c(output3[i,3],output3[i,4]),c(i,i))
          lines(c(output3[i,2],output3[i,2]),c(i-0.5,i+0.5))
          text(output3[i,3]-0.25,i+0.2,output3[i,1])
          }
```