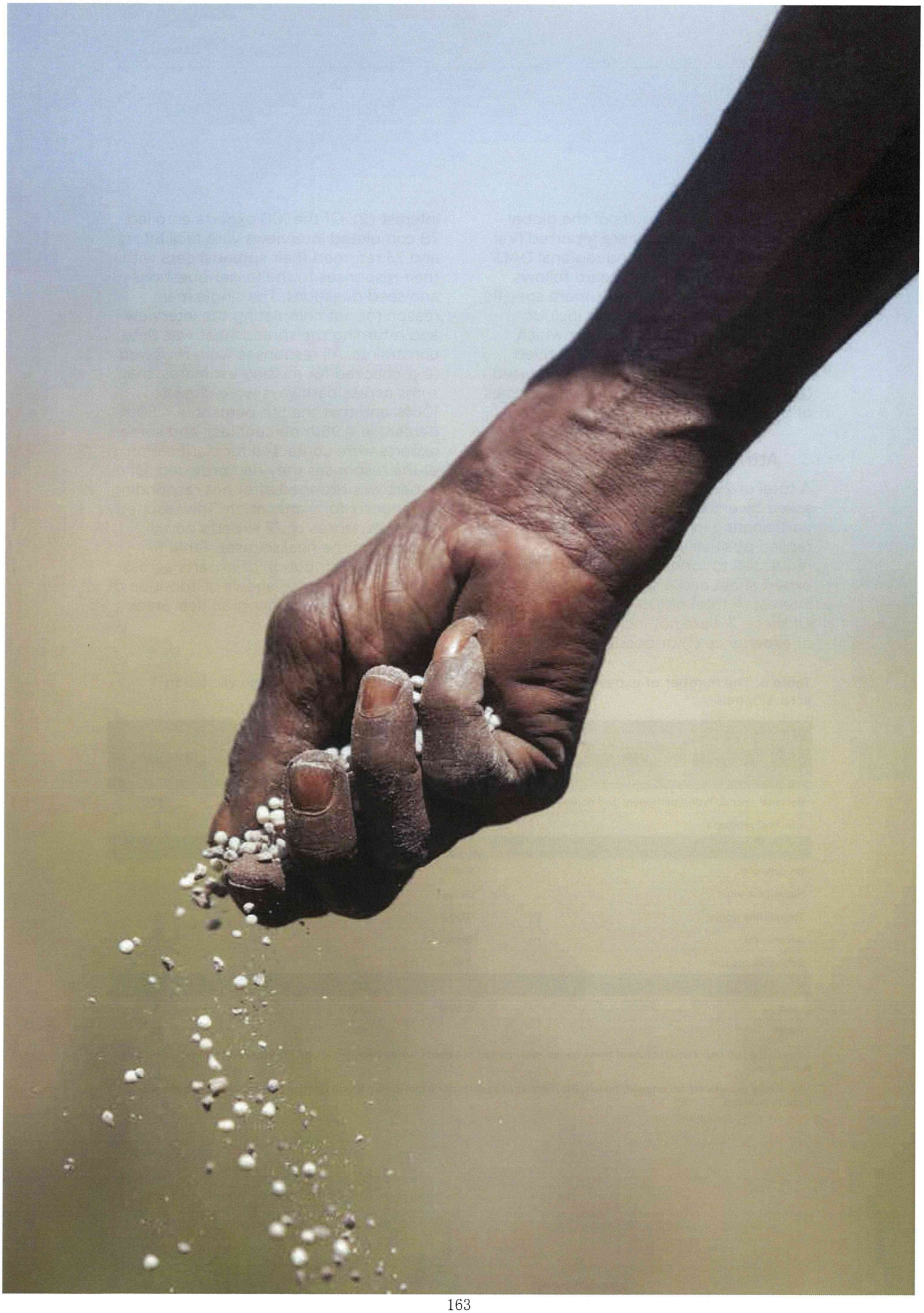
estimates were then summarized by their median and a 95% uncertainty interval defined as the 2.5th and 97.5th percentile of the distribution of estimates. Special care was taken to deal with correlated uncertainties, for instance when the disease model included "global" probabilities (e.g., when it was assumed that the probability of developing a certain health state following infection was the same for each country). In such cases, a vector of random probabilities was simulated only once and applied to the different countries, instead of incorrectly simulating a new, independent vector of random probabilities for each country.

The structured expert elicitation using Cooke's Classical Method conducted to attribute burden to different exposure routes, providing hazards-specific estimates for each exposure route per subregion [156]. This process yielded a probabilistic estimate of the proportion foodborne, in the form of an empirical cumulative density function from which random samples could be drawn. Foodborne cases, deaths, YLDs, YLLs and DALYs were then obtained by multiplying the vectors of random values for these parameters with a vector of random values for the proportion foodborne. As before, the perfect correlation of uncertainty was dealt with by simulating only one vector of random foodborne proportions per subregion, and by applying this vector to all parameters of all countries within the concerned subregion.

RESULTS 5



RESULTS

In this section, the results of the global expert elicitation study are reported first. An overview of global and regional DALY estimates according to hazard follows. Subsequent sections report more specific hazard-based estimates, and include estimates for some hazards for which global estimates could not be derived and only regional estimates are reported (peanut allergen; toxin-producing species of bacteria).

5.1 Attribution

A total of 299 potential experts were asked by email of their interest in participating in the study. Of these154 replied positively and they were requested to forward their CV, a filled-in expert sheet and a signed declaration of interest. A total of 103 did that.
Of these, 3 were not included due to lack of experience (1) or possible conflicts of interest (2). Of the 100 experts enrolled, 78 completed interviews with facilitators and 73 returned their spreadsheets with their responses to the target questions and seed questions. The single main reason for not completing the interview and returning the spreadsheet was time constraints. All responses were reviewed (e.g. checked for missing estimates, that sums across pathways were close to 100%, and that the 5th percentile < 50th percentile < 95th percentiles), and some experts were contacted for clarification of the responses they had provided. One expert was dropped after not responding to requests for clarification. This resulted in the responses of 72 experts being included in the final dataset. Table 6 shows the distribution of experts across panels, and Figure 3 shows distribution of the experts by their geographical areas of expertise.

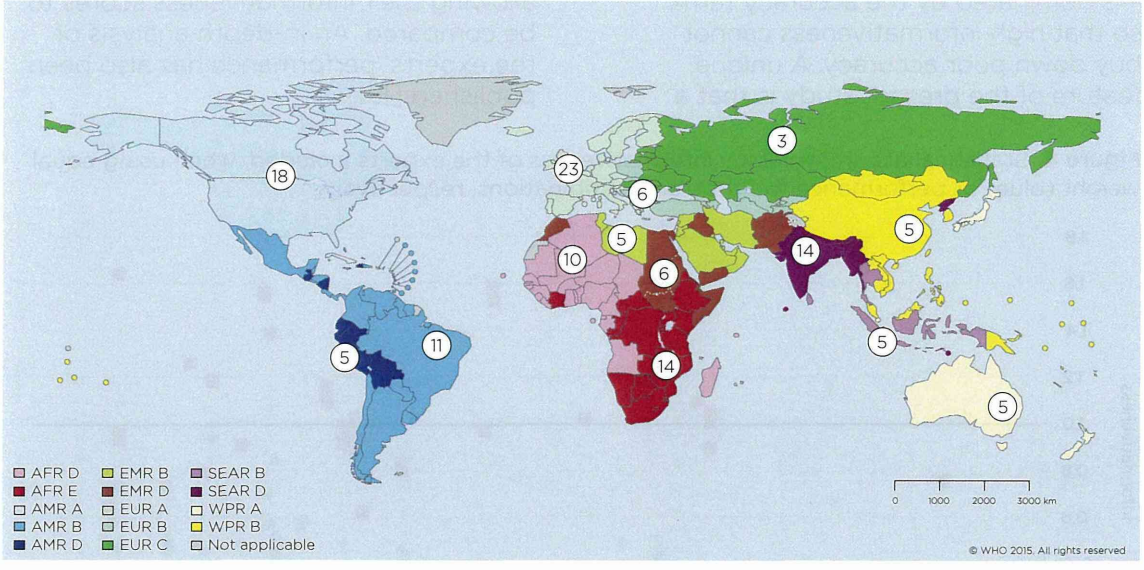
Table 6. The number of experts enrolled, interviewed and finally included in the elicitation across panels

HAZARD GROUPS		EXPERTS ENROLLED	EXPERTS INTERVIEWED	RETURNED ANSWERS
DIARRHEAL DISEASE				
Bacterial (incl. *S.* Typhi) pathogens and norovirus	Sub regional[a]	49	37	37
Intestinal protozoa	Global	12	9	9
OTHER INFECTIOUS DISEASE				
Brucella spp.	Global	10	8	7
Hepatitis A virus	Global	9	7	7
Toxoplasma gondii	Global	11	10	9
Ascaris spp.	Global	8	6	7
Echinococcus spp.	Global	7	6	6
CHEMICALS				
Lead	Global	10	9	6
Total[b]		**100**	**78**	**72**

[a] Due to the sub regional structure of these panels, the number of experts varied between 10 and 15 depending on the hazard and sub region.

[b] As several experts served on more panels, the number of experts per panel does not add up to the total number of individual experts included.

Figure 3. Geographical distribution of experts according to working experience (>3 years) per subregion. Several experts had experience in more than one subregion.



Notes: The subregions are defined on the on the basis of child and adult mortality, as described by Ezzati *et al.* [5]. Stratum A = very low child and adult mortality; Stratum B = low child mortality and very low adult mortality; Stratum C = low child mortality and high adult mortality; Stratum D = high child and adult mortality; and Stratum E = high child mortality and very high adult mortality. The use of the term 'subregion' here and throughout the text does not identify an official grouping of WHO Member States, and the "subregions" are not related to the six official WHO regions.

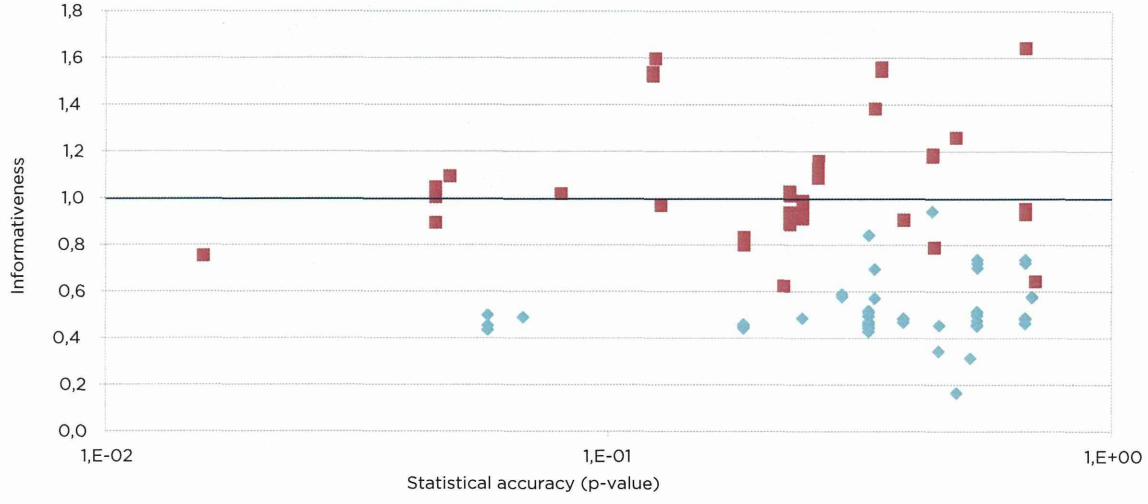
5.1.1 Expert performance

In this study, there were 115 distinct panels (i.e. panels that differed in membership or seed questions) and, overall, performance weight and equal weight combinations showed acceptable statistical accuracy. Only in the case of the panel considering lead was the *p*-value of the performance-based combination small enough to cast doubt on the usual criterion for statistical accuracy, with $p = 0.045$ (i.e. less than the 0.05 criterion). With a set of 115 panels, at least one score this low would be expected even if the performance-based combination was always statistically accurate.

Results obtained by applying equal weights pooling and performance weights pooling were compared. The equal weights solutions tended to have higher statistical accuracy than those produced by applying the performance weights. In contrast, the informativeness properties of the equal weights solutions were much lower than those provided by performance weights solutions (Figure 4). This "trade-off" between accuracy and informativeness when applying equal weights or performance weights is often seen, because the least accurate experts are typically the most informative, and their narrow 90% confidence bands often have little or no overlap. Moreover, the combined score using performance-based weights was above that of the equal weights pooling in 62% of the cases. It was therefore decided to use the performance weights combinations for constructing the joint probability distributions for the pathway attribution estimates, as long as the statistical accuracy was acceptable. It should also be noted that the weight

attributed to an expert – comprising the normalized product of their two scores – is dominated by the accuracy term, so that high informativeness cannot buy down poor accuracy. A unique feature of the present study is that a large number of experts were assessed using very similar variables, thereby allowing their informativeness scores to be compared. An in-depth analysis of the experts' performance has also been published [181].

Figure 4. Statistical accuracy versus informativeness of the experts included, when using equal weight (blue) or performance weight (red) combinations, respectively.



5.1.2 Pathway attribution results

The collective results of the performance-based weighted expert responses are shown in Appendix 7 (Table A7.1-3 for diarrhoeal disease, Table A7.4 for non-diarrhoeal parasitic disease, and Table A7.5 for lead). For most estimates there is considerable uncertainty, reflecting: (1) variations in uncertainty estimations between individual experts; (2) that, for some hazards, the values provided by experts having high performance weights in the analysis did not accord with one another; and (3) that, for some subregions or hazards, the number of contributing experts was small (<7). Thus, the broad uncertainty intervals are most likely reflecting current shortcomings in hard scientific evidence about the relative contribution to human disease from each of the transmission pathways.

Figure 5 shows the subregional estimates of the foodborne proportion for *Campylobacter* spp., non-typhoidal *Salmonella* spp., Shiga-toxin producing *Escherichia coli* (STEC), *Brucella* spp. and *Shigella* spp. For *Salmonella* spp. and *Brucella* spp., there is a clear pattern that the foodborne proportion is considered more important in the developed subregions (AMR A, EUR A and WPR A) compared with developing subregions. Although less distinct, this pattern can also be seen for *Campylobacter* spp. and STEC. For *Campylobacter* spp., *Salmonella* spp. and STEC, the foodborne transmission route was assessed by the experts to be the most important route in all subregions, followed by direct animal contact, human-to-human transmission and waterborne transmission in varying order, but generally with medians below 0.25 (Table A7.1 in Appendix 7). For *Brucella* spp., direct animal contact was considered

equally or more important than foodborne transmission in developing subregions. Human-to-human transmission was considered the most important route for *Shigella* spp. in the majority of subregions. The proportion of foodborne *Shigella* spp. infections ranged from 0.07 (95% UI 0.00– 0.46) in EUR A to 0.36 (95% UI 0.01–0.70) in WPR A (Table A7.1 in Appendix 7). Overall, foodborne transmission was assessed to be more important in South-East Asian and Western Pacific subregions than in other parts of the world. Transmission through soil or other routes was recognized by the experts to be of minor importance for these five pathogens.

Figure 6 shows the subregional estimates of the proportion foodborne for entero-pathogenic *E. coli* (EPEC), enterotoxigenic *E. coli* (ETEC), *Cryptosporidium* spp. and *Giardia* spp. The estimates for EPEC are seen to follow the same pattern as described above, with the foodborne route being assessed to be more important in developed subregions. In developing subregions in the African, American and Eastern Mediterranean regions (AFR, AMR and EMR), water was identified as the most important transmission route. For ETEC, the estimated foodborne proportions were quite similar for all subregions with medians ranging from 0.33 to 0.43 (Table A7.2 in Appendix 7), but the foodborne route was only assessed by experts to be the more important route in European subregions. For *Cryptosporidium* spp. and *Giardia* spp., the foodborne proportions were also quite similar across subregions, but generally considered less important, with medians below 0.20 (Table A7.2 in Appendix 7). Human-to-human and waterborne transmission were the more important routes for these infections in all subregions.

Figure 7 shows the subregional estimates of the proportion foodborne for *Salmonella* Typhi, *Vibrio cholerae*, *Entamoeba histolytica*, norovirus, and hepatitis A virus. Overall, foodborne infections were not assessed by the experts to be the more important routes in the majority of subregions. Exceptions were hepatitis A infections, where foodborne and human-to-human transmission were evaluated equally important in most subregions, and *S.* Typhi, where foodborne and waterborne infections were assessed equally important in SEAR and WPR regions (Table A7.3 in Appendix 7). Human-to-human transmission was identified as the main exposure route for norovirus and *E. histolytica* in most subregions, whereas waterborne transmission was estimated to be the main transmission route for *V. cholerae* infections (Table A7.3 in Appendix 7).

Figure 8 shows the subregional estimates of the proportion foodborne for *Toxoplasma gondii*, *Echinococcus multilocularis*, *Echinococcus granulosus* and *Ascaris* spp. The foodborne route was assessed by the experts to be the most important transmission route for *T. gondii* and *Ascaris* spp. in most subregions, but there was a clear tendency for soil to increase in relative importance in less developed subregions (subregions D and E) (Table A7.4 in Appendix 7). Specifically for *Ascaris* spp., the foodborne route was assessed to be particularly important in developed subregions (A subregions). There was only little geographical variation between the median estimates for each of the transmission pathways for the two *Echinococcus* species. For *E. granulosus*, animal contact was clearly believed to be the most important route, with medians just over 0.50. For *E. multilocularis*, the foodborne route was considered most important, with medians ranging from 0.43 in EMR B to 0.58 in AFR D and E, AMR B and D, and SEAR B and D, but the estimates had very large uncertainty intervals (Table A7.4 in Appendix 7).

Figure 5. Subregional estimates of the proportion of foodborne illnesses caused by *Campylobacter* spp., non-typhoidal *Salmonella* spp., Shiga-toxin producing *Escherichia coli* (STEC), *Brucella* spp. and *Shigella* spp. Indicated on the line plot are the 2.5th, 5th, 50th, 95th and 97.5th percentiles.

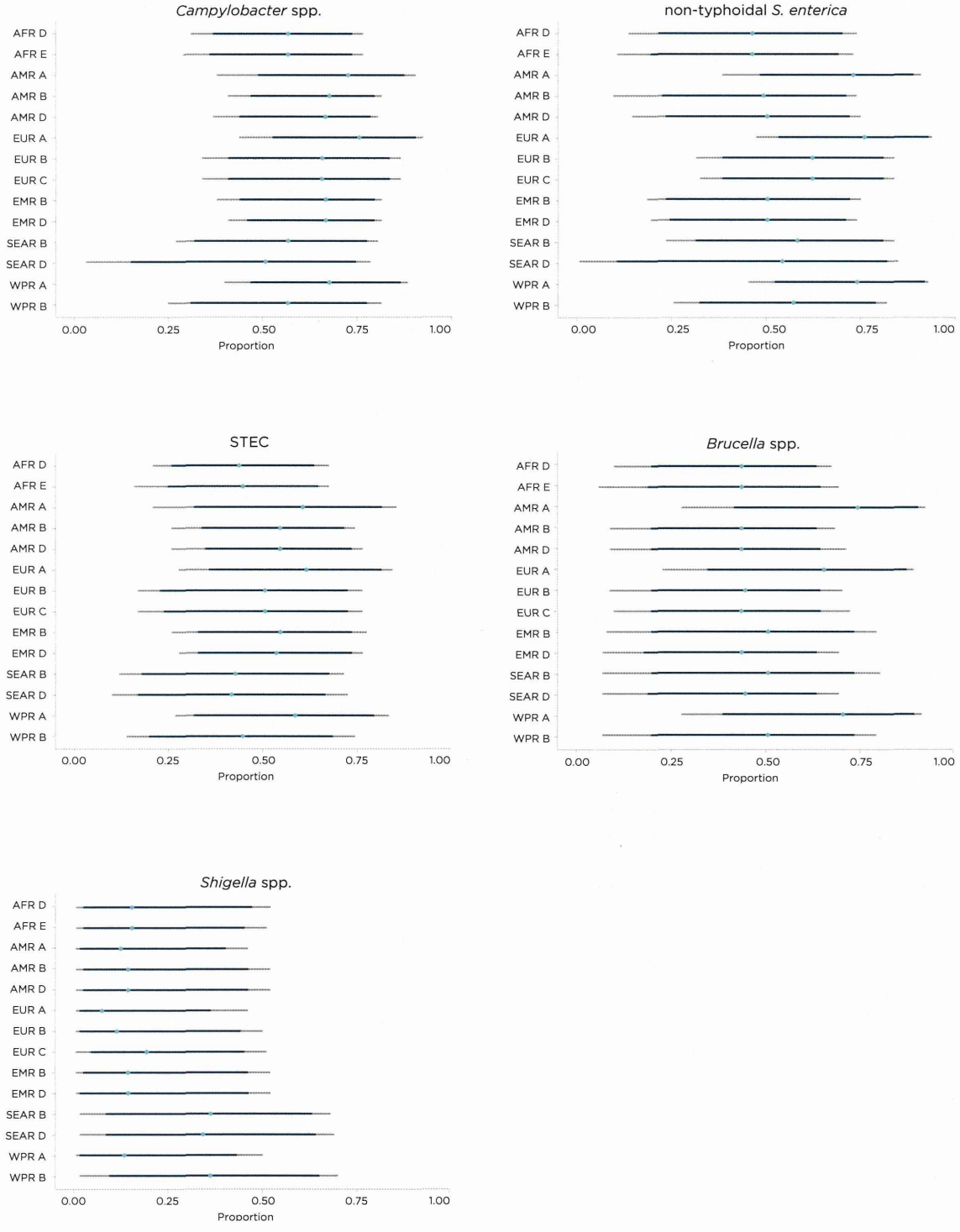
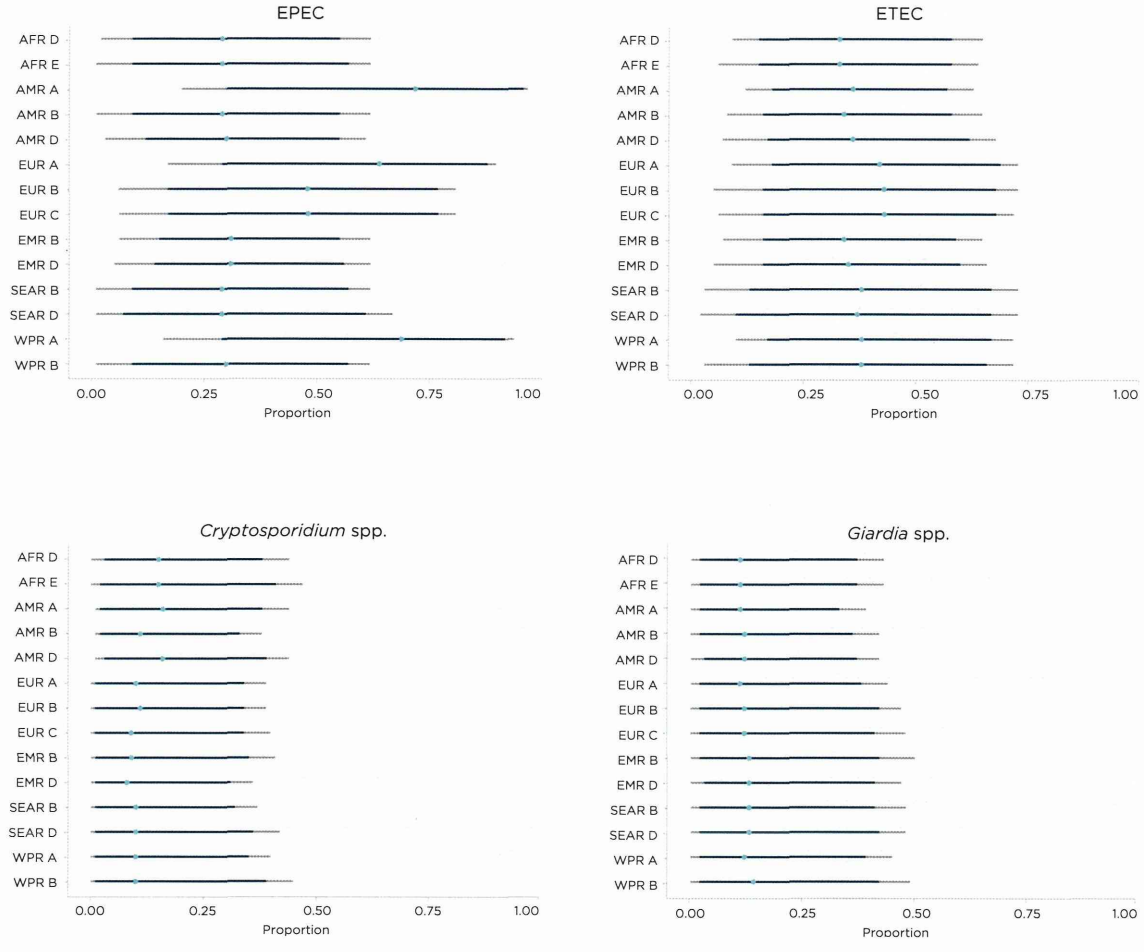


Figure 6. Subregional estimates of the proportion of foodborne illnesses caused by *enteropathogenic E.* (EPEC), *enterotoxigenic E. coli* (ETEC), *Cryptosporidium* spp. and *Giardia* spp.



Notes: Indicated on the line plot are the 2.5th, 5th, 50th, 95th and 97.5th percentiles.