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Assessing potential determinants of the stagnating trend in *Salmonella Enteritidis* human infections in Europe and options for intervention: A multi-criteria decision analysis

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ABSTRACT

Background: After years of significant decline, the incidence of *Salmonella enterica* serotype Enteritidis (SE) human infections in Europe has started stagnating in recent years. The reasons for this stagnation remain largely unclear and are possibly multifactorial and interconnected in nature. We assessed and ranked several potential determinants of the stagnating SE trend in Europe, as well as different options for intervention at the level of poultry health and production, public health (infra)structure, and pathogen biology.

Methods: A Multi-Criteria Decision-Analysis (MCDA) approach based on the Analytical Hierarchy Process was used. Through two separate surveys, a European panel of *Salmonella* experts first provided weights for several pre-defined criteria and subsequently scored different potential determinants and options for intervention (i.e. alternatives) against the criteria, during 2020–21. The weighting and scoring were based on Saaty's pairwise comparisons. The final ranking of the alternatives was derived from the summation of the products of each criterion weight with the score of the corresponding alternative. Sensitivity analyses were performed to assess the impact of different methodological choices, including European regions, and domains of expertise on the ranking of the determinants and options for intervention.

Results: The first and second-ranked determinants of the stagnated trend in human SE infections were related to poultry health and production, namely "inadequacies of sampling programmes" and "premature relaxation of control measures". This ranking agreed with the ranking of the options for intervention, which were also those at the poultry health and production level, specifically "stricter biosecurity", "improving sampling", and "better/increased vaccination". Differences in rankings were observed among European regions and domains of expertise.

Conclusions: The rankings of potential determinants and options for intervention for the stagnating SE trend in Europe pointed to the level of poultry health and production. *Salmonella*-control activities in poultry in Europe are harmonized across countries since many years, but the results of this study suggest that further improvements may be necessary for some countries. A multidisciplinary collaboration among veterinarians, public health professionals, and microbiologists is needed to further understand the origins of the stagnating SE trend and to identify effective interventions in order to reverse the trend, contextually in a given country, following a One Health approach.

Abbreviations: SE, *Salmonella enterica* serotype Enteritidis; MCDA, Multi-Criteria Decision Analysis; ADONIS, Assessing Determinants Of the Non-Decreasing Incidence of *Salmonella*; RIVM, National Institute of Public Health and the Environment of the Netherlands; Sciensano, the National Institute for Health in Belgium; WBR, Wageningen Bioveterinary Research; ECDC, European Centre for Disease Prevention and Control; AHP, Analytic Hierarchical Process; AGM, Aggregated Geometric Mean; SD, Standard deviation; CR, consistence ratio; EFSA, European Food Safety Authority; CAs, Competent authorities; FBOs, food business operators; EU, the European Union.

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1. Introduction

Salmonella enterica serotype Enteritidis (SE) is a zoonotic pathogen causing mainly diarrheal disease in humans that is responsible for over half of reported human *Salmonella* infections and is often involved in foodborne outbreaks in Europe [1,2]. In 2020, 52,702 human *Salmonella* infections were reported in Europe, including 695 foodborne outbreaks, 3686 illnesses, 812 hospitalizations, and seven deaths [2]. Generally, the infection presents itself with self-limiting gastrointestinal symptoms, but can become life-threatening, especially when invading beyond the gastrointestinal tract and in immunocompromised patients [3]. Transmission of *Salmonella* from animals to humans often occurs via the consumption of contaminated food products, direct contact with animals or, although less common, via person-to-person transmission and the environment [4,5]. In Europe, the main animal and food sources of SE are poultry (laying hens and broiler chickens) and eggs, respectively [6,7].

Thanks to harmonized *Salmonella* control programmes in poultry across European countries, the incidence of SE infection in both poultry and humans has successfully declined between 2008 and 2012 [8–10]. However, this incidence has stagnated ever since [1,2,11–13], requiring further efforts to elucidate the reasons behind it. Potential factors that could explain the stagnating trend of SE can be found at three main meta-levels: 1) poultry health and production (e.g., premature relaxation of control measures, insufficient sampling efforts.) [14]; 2) public health (infra)structure and human SE infection epidemiology (e.g., changing exposure and risk factors, changes in surveillance systems and diagnostics) [13,15,16]; and 3) pathogen evolution (e.g., emergence and spread of more virulent strains) [17]. It is possible that no single factor is able to explain the observed stagnating trend in recent years, but that the reasons for these changes are multifactorial and interconnected in nature. For priority setting of the options to reverse the stagnating trend, it is important to provide indications on the relative contributions of these factors.

Multi-Criteria Decision Analysis (MCDA) is a suitable method for ranking when an intuitive approach is not pursuable because, for example, the decision is too complex to be handled intuitively, as it involves a number of different criteria and alternatives to consider, or involves multiple stakeholders with diverse views and priorities. If the problem is one that can be structured as involving a collection of alternatives that can be tested against several criteria, then the MCDA approach is a suited method. Such alternatives may be different choices, actions, strategies, or components [18,19]. In brief, MCDA provides stepping-stones and techniques for finding a compromise solution to complex issues and processes where multiple and often conflicting criteria are to be considered when assessing different options. To operationalize an assessment framework for the determinants and the options for intervention for the stagnating SE trend in recent years, these determinants cannot be weighted (as such) against one another, as they have different measurement scales. Yet, their values can be converted into comparable dimensions using MCDA techniques.

In this study, we aimed to answer the following research questions: 1) why have human SE infections stopped decreasing in Europe? and 2) What can be done to reverse this trend? To this end, we used a MCDA to rank a number of potential determinants and options for intervention to reverse the stagnating trend, from the most to the least likely to play a significant role. We considered determinants and options for intervention at the level of primary (poultry) production, changes in surveillance and epidemiological patterns of human SE infections, and pathogen evolution.

2. Methods

2.1. General methodological approach

The MCDA methodology was performed separately to rank both the determinants and the options for intervention in a European context of 2020–21. The following steps were undertaken: 1) identifying potential alternatives in terms of determinants of the stagnating SE trend and options for intervention to reverse it that encompass the aforementioned three meta-levels; 2) identifying criteria against which to assess these determinants and options for intervention; 3) identifying European experts on *Salmonella* to weight the criteria and to score the alternatives for the determinants and options for intervention; 4) weighting these criteria in terms of their relative importance using the panel of European experts (Supplementary material 1: Survey I); 5) scoring the determinants and options for intervention against the criteria by the European panel of experts (Supplementary material 2: Survey II); and 6) ranking the scored determinants and options for intervention based on their weighted score (i.e., according to their relative importance). (Fig. 1).

2.2. Identifying alternatives and criteria

The determinants possibly associated with the reversal of the stagnating trend were identified based on the hierarchical structure of the SE transmission chain and all possible interrelations between three pre-defined levels: primary poultry production, human exposure to the pathogen and pathogen characteristics. Similarly, the options for intervention were defined based on the same three pre-defined levels. The alternatives for the determinants and the interventions are described in more details in Tables 1 and 2. Next, a list of criteria was produced in which to assess these alternatives for the determinants and options for intervention, separately. The list of criteria with their definitions is given in Table 3. The alternatives and criteria for the determinants and options for intervention were determined through literature review and input from the large collaborator network provided by the *Salmonella* experts working in the research project "Assessing Determinants Of the Non-Decreasing Incidence of *Salmonella*" (ADONIS) funded through the One Health European Joint Programme by the EU's Horizon-2020 Research and Innovation Programme (https://onehealthejp.eu/jrp-adonis/).

2.3. Identification of experts

The selection of the panel of experts involved in the weighting and scoring surveys aimed at covering the different domains of expertise (poultry health and production, human *Salmonella* epidemiology, and *Salmonella* genomics), the main fields where such expertise was applied (human health, animal health and/or food safety), and European region of employment (North-, East-, South-, or West-Europe). To form a well-balanced panel of experts, those participating in the surveys were the *Salmonella* experts contributing to the ADONIS project. At least two experts per European country were recruited and the same panel of experts was considered for both surveys.

2.4. Weighting criteria and scoring the determinants and options for intervention

Two consecutive anonymous digital surveys were conducted to collect data from the panel of *Salmonella* experts. Experts (participants) were informed about the objectives and design of the study, and what their participation entailed. (Supplementary materials 3 and 4: Instructions for survey I and survey II) Both surveys were beforehand piloted internally among ten researchers from the National Institute of Public Health and the Environment of the Netherlands (RIVM), the National Institute for Health in Belgium (Sciensano), and Wageningen Bioveterinary Research (WBR) to assess their feasibility and adequacy of the completion of the surveys for the purposes of the study. As a result, minor improvements in the instructions and surveys were made. The weights of the criteria (first survey) and the scores of the determinants and options for intervention (second survey) were determined by the

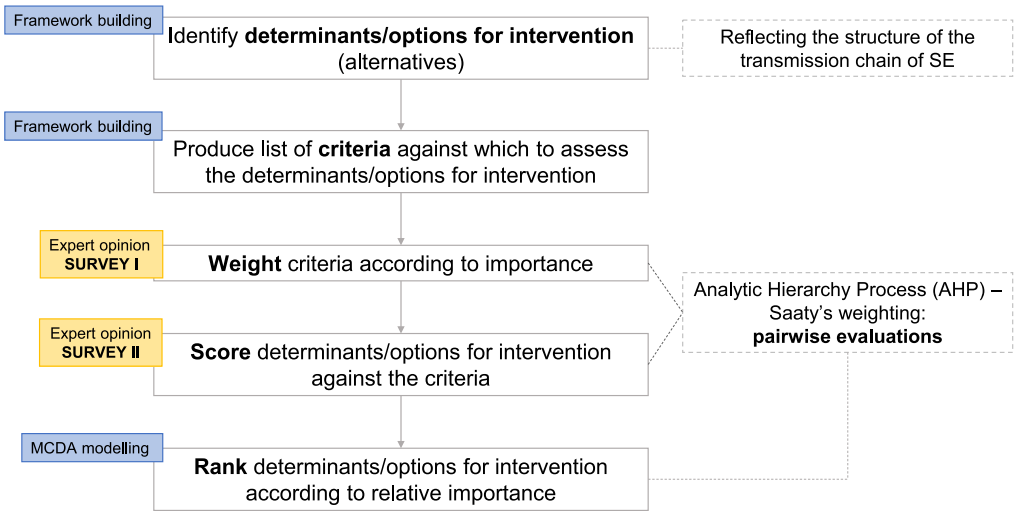

Fig. 1. Schematic overview of the Multi-Criteria Decision-Analysis (MCDA) process followed in the study. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)
Caption: The figure shows the sequential process from top to bottom.
Caption: SE: *Salmonella enterica* serotype Enteritidis.

same panel of experts, with the exception of two experts that dropped out in the second survey due to time conflicts, and five new experts were invited to participate in the second survey. Once the survey for the data collection of the weighting of the criteria was completed, the other one on the scoring of the alternatives was administered. The two surveys were therefore completed separately, following the ECDC (European Centre for Disease Prevention and Control) guidelines [20].

Experts were asked to weight the criteria (first survey) and score the alternatives (second survey), based on the Saaty's pairwise comparison scale (Analytic Hierarchical Process (AHP) method), which expresses the importance of one element over another. (Supplementary material 5: Appendix A Table 1) The AHP method decomposes multiple attributes into hierarchies or groups according to their entities and characters and compares them. Thus, it has an effect of reducing cognitive errors and can confirm the respondent's consistency with respect to the importance. As a disadvantage, seeing that all criteria and alternatives have to be compared pairwise with each other, participants had to make n*(n-1)/2 comparisons for the criteria first, and then for the alternatives for both the determinants and options for intervention as well [21], with n being 12 comparisons for the criteria and 124 comparisons for the alternatives. Instructions and examples about how to weight and score based on the AHP method were also provided when the surveys were administered. (Supplementary materials 3 and 4: Instructions for survey I and survey II) Besides the sets of criteria and possible alternatives for the determinants and options for intervention, the possibility to propose one additional criterion and one potential alternative for the determinants and options for intervention in each survey was provided. (Supplementary materials 1 and 2: Survey I and Survey II) In the second survey (scoring of alternatives), some background information on key numbers and facts on *Salmonella* was supplied to the participants to make their scoring more evidence-based and to minimize potential individual or professional bias, uncertainty, misconceptions, and cognitive heuristics, by being able to refer to recent and reliable information if/where needed [20]. (Supplementary material 6: Support information for panel of experts) Both digital surveys were designed using Adobe LiveCycle Designer ES2, version 9.0.

2.5. Data analyses

2.5.1. Criteria weights

Pairwise comparison matrices of the criteria weights for the determinants and options for intervention were obtained and analysed from the first survey, based on the nine-point semantic scale. (Supplementary material 5: Appendix A Table 1) Following Saaty's scale, a pairwise comparison matrix of $\boldsymbol{N}$ options for the $\boldsymbol{k^{th}}$ individual were obtained as:

Table 1
Alternatives for the determinants to define which factors have the strongest 'causal relationship' with the stagnation of the declining trend in *Salmonella enterica* serotype Enteritidis (SE) in humans in Europe.

Alternatives	Description
Level 1.Changes in primary (poultry) production	
Premature relaxation of control measures	Changes in husbandry practices in laying hen flocks for *Salmonella*, e.g. laxer biosecurity measures - incl. those implicitly linked to improved animal welfare like free-range hen farms and farms with outdoor access, changes in vaccination schemes, as this has become voluntary/forbidden in some countries, changes farm size, group size and stock density, etc.
Inadequacies of sampling programmes	Insufficient sensitivity of current sampling schemes, sampling protocols prone to misinterpretation/misuse, low compliance to regulations, high workload for competent authorities and/or producers, inadequate corrective/compensatory actions available for infected flocks, etc., in laying hen flocks
Level 2. Changes in (human) salmonellosis epidemiology	
Increased exposure to SE	Increased exposure to SE (through food or direct/indirect contact with animals), changes in risk factors for infection (including changes in the size/exposure of high-risk groups), and emergence of new routes of *Salmonella* transmission, e.g. changes in food patterns in the population, changes in import countries, changes in risk perception, changes in population structure, etc.
Changes in surveillance programmes	Changes in national *Salmonella* surveillance programmes and/or diagnostics, e.g. more sensitive surveillance systems and/or diagnostics, lower under-ascertainment and/or under-rereporting, increased surveillance coverage, etc.
Level 3. Changes in *Salmonella* (pathogen) itself	
Emergence of virulent strains	Emergence and spread of specific SE strains with increased fitness, e.g. increased replication capacity, virulence and/or antimicrobial resistance.

Table 2
Alternatives for options for intervention to define which is the 'most promising' target for prioritization to reverse the stagnated trend in *Salmonella enterica* serotype Enteritidis (SE) in humans in Europe.

Alternatives	Description
Level 1. To be implemented at the level of primary poultry production	
Stricter biosecurity	Stricter biosecurity measures and/or changes in husbandry practices
Better/increase vaccination	Better/increase vaccination with currently available vaccines
Improving sampling	Improving/increasing sampling schemes and/or corrective measures
Level 2. To be implemented at the level of public health infrastructure	
Improving case-reporting/ ascertainment	e.g.: more sensitive surveillance systems and/or diagnostics in order to control outbreaks more quickly, and to identify target populations for possible preventive measures, etc.
Reduce SE exposure	e.g.: increasing awareness concerning *Salmonella* infection risk, promoting changes in certain food preparation and consumption habits, etc.
Level 3. To be implemented at the level of pathogen	
Set strain-specific surveillance	–
Develop new vaccines for specific strains	–

$$\mathbf{S}_k = \begin{matrix} a_{1,1} & a_{1,2} & \dots a_{1,N} \\ a_{2,1} & a_{2,2} & \dots a_{2,N} \\ \vdots & \vdots & a_{i,j} \vdots \\ a_{N,1} & a_{N,2} & \dots a_{N,N} \end{matrix}$$

where $a_{i,j}$ represents the pairwise comparison between the option i and j. For example, if i is more important than j for 6 units, $a_{i,j} = 6$, then $a_{j,i} = \frac{1}{6}$, i.e. the reciprocal [22].

First, the weight for each criterion was calculated for each participant. Then, the weights for each criterion were aggregated over all participants. Geometric means were used for the individual and aggregated weights, which is less computationally demanding than the normalized principal eigenvector of each pairwise matrix [23] and previous research showed that they produce close results to the eigenvector method in most situations [24,25]. For the aggregated weights, standard deviations (SD) were also obtained per criterion for the determinants and options for intervention, distinctly (R package 'ahpsurvey' version 0.4.1).

2.5.2. Scoring and ranking determinants and options for intervention

The relative importance of each alternative was established through pairwise comparisons (based on the same nine-point semantic scale) of the relative performance scores for all combinations of alternatives, separately for each criterion considered in the second survey. The same procedure, involving the computation of the normalized geometric means of the pairwise comparison matrices of the alternatives (one matrix for each decision criterion considered in the analysis), was then implemented to determine the score of each alternative with reference to each criterion. Aggregated geometric means were obtained for the final score (R package 'ahpsurvey' version 0.4.1).

Finally, the overall ranking (R) of an alternative with respect to the overall of the N decision criteria was calculated by summing together the products of each criterion weight and the performance score of an alternative with respect to that criterion and this was expressed as follows [23]:

$$R(a) = \sum_{j=1}^{N} w_j{}^* x_j(a) = w_1{}^* x_1(a) + w_2{}^* x_2(a) + \dots w_N{}^* x_N(a)$$

where: $x_j(a)$ is the performance score of alternative a with reference to the j^{th} criterion; and w_j is the weight of the j^{th} criterion.

2.5.3. Sensitivity analysis: analysis scenarios

To assess the robustness on the overall ranking of the determinants and options for intervention (Scenario A), nine sub-analyses were performed to assess alternative scenarios in a sensitivity analysis. The scenarios were based on different subsets of the responses according to consistent responses, non-missing responses, European regions, and domain of expertise. (Supplementary material 5: Appendix B Table 1) These scenarios were subsequently grouped into three categories: 1) methodological choice; 2) expert's region; and 3) expert's domain. The methodological choice category consisted of the default overall analysis (scenario A), a sub-analysis only considering consistent responses (scenario B), and a sub-analysis excluding missing values (scenario C). To measure consistency in the responses for scenario B, the consistence ratio (CR) per individual for the weights and scores were calculated, where a CR higher than 0.1 was deemed to be inconsistent, according to Saaty, et al. [26]. This led to censoring 16 individual weights of the criteria for the determinants and options for intervention in the first survey. For the scores of the determinants, 16, 15, 8, and 13 individual scores with respect to "strength of evidence", "plausibility", "consistency", and "effect size", respectively, were censored. For the scores of

Table 3
List of criteria against in which to assess the determinants and options for intervention.

Criteria for the determinants (to define which has the strongest "causal relationship")	
Strength of evidence	based on rigor, type and quality of research outcomes supporting a given determinant
Plausibility	based on the general credibility/acceptability of the research outcomes and underlying assumptions supporting a given determinant
Consistency of findings	based on the amount of concordant research outcomes supporting a given determinant
Effect size	based on the magnitude of the effect: the larger the effect size in the research outcomes the stronger the causal relationship of a given determinant
Criteria for the options for intervention (to define which is the "most promising" for prioritization)	
Feasibility	based on the degree for the intervention to be easily or conveniently implemented, both financially and logistically
Public health impact	based on the expected impact that the intervention would have on the human disease burden
Cost-effectiveness	based on the expected impact that the intervention would have on the cost of illness, after considering the costs of the intervention itself
Novelty/originality	based on the degree of innovation of the intervention: something that has been experienced/tried before and has not worked well could be less promising of something that has never been tried before

the options for intervention, 17, 16, 16, and 17, individual scores with respect to "feasibility", "public health impact", "cost-effectiveness", and "novelty/originality", respectively, were censored (second survey). The command 'censorcr' from the 'ahpsurvey' package in R was used to obtain the CRs. Scenario C only considered the non-missing responses, while in the default analysis in Scenario A the missing weights or scores were replaced by 1 as a 'equally important' (a neutral value). For the experts' regions of expertise, the countries in which the experts were employed were grouped by European region as indicated in the supplementary material: Appendix C Tables 1 and 2. Scenario D consisted of responses based on the weights of the criteria and scores of the alternatives from Eastern Europe, scenario E from Northern Europe, scenario F from Western Europe, and scenario G from Southern Europe. Finally, scenarios H, I, and J were based on the main domain of expertise of the experts: 1) poultry health and production, 2) *Salmonella* epidemiology, and 3) *Salmonella* genomics, respectively. Missing values in the scenarios from the expert's region and the expert's domain were replaced with 1, the neutral value.

To visualize and compare resulting rankings from each scenario, a "bump chart" was used (packages 'ggplot2' and 'ggbump'). All analyses were done using R version 4.2.0.

3. Results

3.1. Expert panel

In total, 24 and 27 experts participated in the first and second surveys, respectively. Both surveys were completed by a well-balance panel of experts in terms of coverage of the different domains of expertise, research fields and European regions of the ADONIS project. (Supplementary material: Appendix C Tables 1 and 2) The mean years of experience in the domains of interest was 13 in both surveys. There were only two experts in the second survey who had 20 missing scores for the determinants and 3 missing scores for the options for intervention. These missing values referred to Northern Europe and the *Salmonella* epidemiology domain. No expert added any additional criterion or alternative to those proposed in both surveys.

3.2. Criteria weights

For the assessment of the determinants of the stagnating trend, the criterion that received the highest weight was the "strength of evidence" (aggregated geometric mean [AGM]: 0.30, standard deviation [SD]: 0.15), followed by "consistency of findings" (AGM: 0.24, SD: 0.15), "effect size" (AGM: 0.17, SD: 0.16), and "plausibility" (AGM: 0.13, SD: 0.10). For the assessment of the options for intervention to reverse the stagnating trend, the criterion that received the highest weight was "public health Impact" (AGM: 0.34, SD: 0.18), followed by "feasibility" (AGM: 0.26, SD: 0.13), "cost-effectiveness" (AGM: 0.17, SD: 0.14), and "novelty/originality" (AGM: 0.07, SD: 0.14). (Supplementary material: Appendix D Fig. 1).

3.3. Scoring and ranking the determinants and options for intervention

Overall, there were 40 and 84 scores from each expert to be given for the determinants and the options for intervention, respectively. For the determinants, based on all the (weighted) criteria considered, the alternatives with the highest weighted score were all related to poultry health and production, namely the "inadequacies of sampling programmes" and the "premature relaxation of control measures", followed by the only determinant related to the pathogen itself, "emergence of virulent strains". The two determinants related to (human) *Salmonella* epidemiology ranked as the least important. These were the "changes in surveillance programmes" and "increased exposure to SE". (Fig. 2).

For options for the intervention to reverse the stagnating trend, based on all the (weighted) criteria considered, the alternatives with the highest weighted score were all related to poultry health and production, namely "stricter biosecurity", "improving sampling", and "better/increase vaccination", followed by the option for intervention at the public health infrastructure level ("reduce SE exposure"), and at the pathogen level ("set strain-specific for surveillance"). The two options for intervention with the least importance were the "develop new vaccines for specific strains" and "improving case-reporting/case ascertainment". (Fig. 2).

3.4. Sensitivity analysis: alternative analytical scenarios

Nine alternative analytical scenarios were considered and their outcomes are summarized in Fig. 3.

3.5. Determinants

Within the category 'methodological choice', among the top-5 potential (poultry-associated) determinants, "inadequacies of sampling programmes" ranked first in all three scenarios (A, B, C), whereas the (poultry-associated) determinant "premature relaxation of control

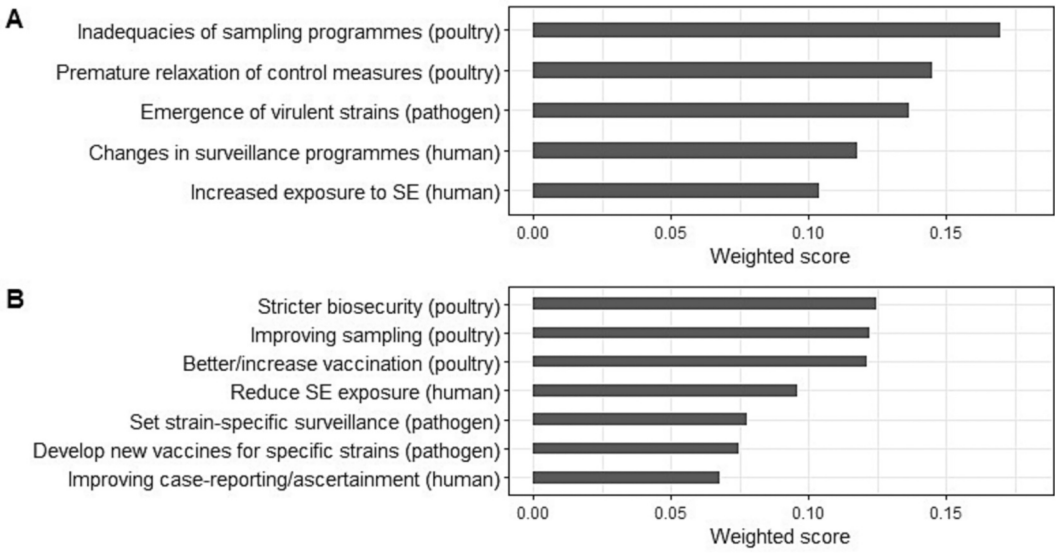

Fig. 2. Ranking of the determinants (A) and options for intervention (B) of the stagnating trend.

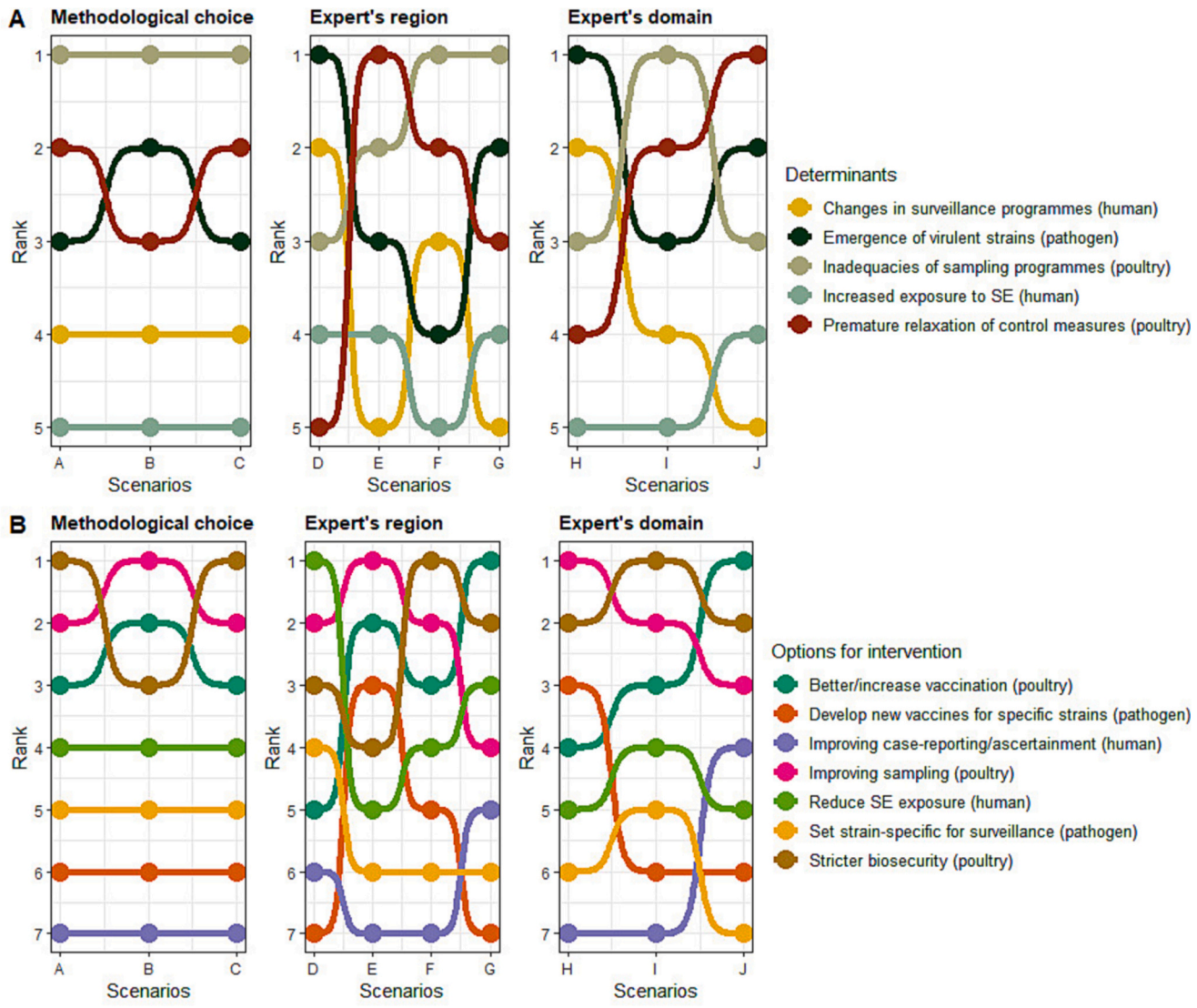

Fig. 3. Ranking scenarios of the determinants (A) and options for intervention (B) by methodological choice, expert's region, and expert's domain. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)
Caption: The 'methodological choice' were composed by the default analysis (scenario A), consistency responses (scenario B), and missing values (scenario C). For the 'expert's region', countries were categorized Eastern Europe (scenario D), Northern Europe (scenario E), Western Europe (scenario F), and Southern Europe (scenario G). Whereas scenarios H, I, and J were categorized by the domain of expertise, 'poultry health and production', '*Salmonella* epidemiology', and '*Salmonella* genomics', respectively.

measures" and the (pathogen-related) determinant "emergence of virulent strains" switched places between second and third over the three scenarios. The determinants related to (human) *Salmonella* epidemiology ("changes in surveillance programmes" and "increased exposure to SE") remained the least important in all three scenarios. (Fig. 3.A).

When considering the weighted scores by European regions (scenarios D: Eastern Europe, scenario E: Northern Europe, scenario F: Western Europe, and scenario G: Southern Europe), the ranking of the determinants varied per European region. For Eastern Europe, the top-2 determinants were the determinant related to pathogen "emergence of virulent strains" and the (human-associated) determinant "changes in surveillance programmes", respectively. In Northern Europe, the top-2 were the (poultry-related) determinants, "premature relaxation control measures" and "inadequacies of sampling programmes", respectively. Similarly, in Western Europe, the top-2 determinants were related to the poultry production. However, "inadequacies of sampling programmes" ranked as first. Finally, in Southern Europe, a determinant regarding poultry production ("inadequacies of sampling programmes") ranked as first, followed by the (pathogen-related) determinant "emergence of virulent strains". The priority of the other least determinants also varied per European region. (Fig. 3.A).

When considering the experts' domains (scenario H: poultry health and production, scenario I: *Salmonella* epidemiology, scenario J: *Salmonella* genomics), experts in poultry health and production ranked the (pathogen-associated) determinant "emergence of virulent strains" as the first one, followed by (human-associated) "changes in surveillance programmes". Experts in *Salmonella* epidemiology ranked the two (poultry-associated) determinants "inadequacies of sampling programmes" and "premature relaxation of control measures", as the first and second, respectively. Finally, experts in *Salmonella* genomics ranked as first, the (poultry-associated) determinant "premature relaxation of control measures", followed by the (pathogen-associated) determinant "emergence of virulent strains". The ranking of the other determinants also varied by domain of expertise. (Fig. 3.A).

3.6. Options for intervention

For the methodological choice scenarios (A, B, C), options for intervention at the primary poultry production ranked highest in the three scenarios, with "stricter biosecurity" ranking the highest in scenarios A and C, whereas "improving sampling", and "better/increase vaccination" being the highest in scenario B. The other least options for intervention ranked the same in all three scenarios. (Fig. 3.B).

Regarding European regions (scenarios D, E, F, G), the highest ranked options for intervention varied: for Eastern Europe, it was to "reduce SE exposure"; in Northern Europe, it was "improving sampling"; in Western Europe it was "stricter biosecurity measures"; and in Southern Europe it was "better/increase vaccination". Other options for intervention ranked differently per European region. (Fig. 3.B).

Considering the experts' domains (scenarios H, I, and J), the highest ranked options for intervention varied. However, all were related to the primary poultry production level. Experts in poultry health and production, *Salmonella* epidemiology, and *Salmonella* genomics ranked "improving sampling", "stricter biosecurity", and "better/increase vaccination" as the highest, respectively. The rest of the options for intervention ranked differently per domain of expertise. (Fig. 3.B)

4. Discussion

This study assessed the relative importance of several potential determinants of the stagnating SE trend in Europe and options for intervention at the level of primary (poultry) production, public health (infra)structure, and pathogen evolution, using expert perspectives. This was based on a recently performed (2020−21) MCDA involving a multidisciplinary group of experts within the framework of a large European project on this topic called ADONIS, following a One Health approach. The most important determinants of the stagnating SE trend were identified as those related to the poultry production level, namely "inadequacies of sampling programmes" and "premature relaxation of control measures". Accordingly, the most important options for intervention were also those referring to the poultry production level, i.e., "stricter biosecurity measures", "improving sampling", and "better/increase vaccination". In the sensitivity analyses, even after accounting for inconsistent (scenario B) and missing (scenario C) responses, the final ranking largely remained the same for the different methodological choices, except for a single change in the ranking of scenario B where the pathogen-related determinant "emergence of virulent strains" replaced the poultry-related determinant "premature relaxation of control measures" in the second position. The option for intervention "stricter biosecurity" changed to the third position in scenario B, but all others remained related to the poultry production level.

There were major differences in the ranking of the determinants and options for intervention by European region (scenarios D, E, and G) and the domain of expertise (scenarios H, I, and J). Determinants and options for intervention at the primary (poultry) production level were ranked highest by experts from Northern, Western, and Southern European countries. This is in contrast to experts from the Eastern European region who gave the highest weighted scores for the determinants and options for intervention at the level of public health (infra)structure and pathogen evolution. Concerning the rankings by the domain of expertise, experts within the domains of '*Salmonella* epidemiology' and '*Salmonella* genomics' assigned the highest rank to determinants at the level of primary (poultry) production (inadequacy of sampling programs and premature relaxation of control measures, respectively), whereas experts within the domain of 'poultry health and production' scored the emergence of virulent strains as the most important determinant. Yet, all expert's domains ranked the primary (poultry) production level as the most important option for intervention against the stagnating SE trend. These differences in ranking between sub-groups of experts highlight the importance of obtaining a well-balanced panel of experts, as the potential for 'collective views' to emerge in the results is recognized in this type of studies and was addressed here in the sensitivity analysis. Indeed, the composition of the expert group is a potential source of bias, as the under- or overrepresentation of experts from certain countries or within certain expertise domains may influence the final ranking. While this is a characteristic of the diversity of perspectives within the One Health paradigm that this study wants to capture, the results should also be interpreted in light of the representativeness of participants' expertise.

Our study indicates that inadequacies of sampling and premature relaxation of control programmes in husbandry practices in laying hen flocks for *Salmonella* were assessed to be the most important determinants of the stagnating SE trend. Although evidence for these determinants is not available in the scientific literature, some indications are present in recent EFSA (European Food Safety Authority) reports. For instance, to ensure compliance with process hygiene criteria to control *Salmonella*, competent authorities (CAs) and food business operators (FBOs) from the European Union (EU) countries conduct their own sampling and their reports are sent to EFSA independently. CAs constantly reported higher proportion of *Salmonella*-positive carcasses for poultry than FBOs in 2017–2020 and this was also the case for reported control programmes [1,2]. Even though the scopes in sampling by CAs and FBOs are different, EFSA's advice is to investigate the possible reasons for this discrepancy.

Potential options for intervention against the stagnating SE trend also referred to the poultry health and production level. This is also consistent with recent EFSA reports [1,2,12], where recommendations to control target *Salmonella* serovar, such as SE, have been mainly placed at the primary (poultry) production, such as stricter biosecurity measures, improving sampling schemes, and better/increase vaccination programmes. The combination of these measures may lead to a further decrease in the proportion of *Salmonella*-positive samples in the main food sources (eggs and poultry meat) for SE exposure in humans across European countries [2,14] Furthermore, a previous study showed that stricter biosecurity measures and vaccination programmes can synergize well [27]. However, implementing such measures has become challenging as not all EU countries have been able to meet the reduction target for all poultry populations every year since 2007 [2]. More detailed recommendations and application of the interventions to control *Salmonella* in poultry have been provided by EFSA [14].

While the MCDA allowed us to disentangle the complexity of the factors potentially contributing to the stagnating SE trend in a structured and quantitative way, addressing different meta-levels of *Salmonella* transmission to move towards potential solutions, the participation of several *Salmonella* experts from different European regions, domains of expertise and research fields, enabled us to depict a broad perspective of the issue being assessed. Besides efforts to minimize subjectivity by providing recent and reliable information for scoring, however, we cannot rule out a certain degree of subjectivity among the scores, which was unveiled in the sensitivity analyses. Although the use of AHP for the calculation of the final score is a pragmatic method to reduce multi-criteria decision-making problems into smaller groups, the reliability of the AHP has been questioned by previous studies, such as the validity of the eigenvector method, the coherence of the pairwise comparisons, and among others which were previously discussed elsewhere [23,28,29]. Additionally, due to the under-representation of certain expert groups, i.e.: the food sector, the final ranking may not be a complete reflection of experts from all EU countries and from all *Salmonella* sectors.

5. Conclusion

Several determinants of, and options for intervention for, the stagnating trend of SE human infections in Europe were identified and ranked according to their relative importance using a structured approach to priority setting. The alternatives for the determinants and options for intervention that ranked the highest were consistently those related to the level of poultry health and production. It follows, therefore, that the reversal of the non-declining SE trend is most likely to be

set if these alternatives are pursued contextually in a given country and within a multidisciplinary collaboration of different actors working on *Salmonella*, following a One Health approach.

Ethics approval and consent to participate

The present study builds on the expertise of subject matter experts. All experts (participants) were informed beforehand in writing about the aims and methods of the study and the expertise requested before they agreed to participate. Their expertise was consulted per e-mail through self-administered questionnaires. All experts were fully aware of, and agreed with, providing information for evaluating different alternatives about the stagnating salmonellosis trend in Europe and that this information would be processed anonymously to produce scientific material, including articles for publication. This type of expert elicitation study is not subject to ethical review according to the Dutch Medical Research Involving Human Subjects Act (BWBR0009408). The present study also complied with the EU General Data Protection Regulation (2016/679). All methods used in this study were carried out in accordance with the Declaration of Helsinki.

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Authors' contributions

Linda Chanamé Pinedo(LCP), Nina Van Goethem(NVG), Roan Pijnacker(RP), and Lapo Mughini-Gras(LMG) conceived and designed the study. LCP, NVG, LMG, Ewa Pacholewicz(EP) piloted the surveys and collected the data. LCP, LMG, and Panagiotis Mallioris (PM) designed the surveys and analysed the data. LCP drafted the manuscript. All authors contributed to the interpretation of the results and have substantially contributed to critically reviewing the manuscript and approved it as submitted.

Declaration of Competing Interest

The authors of the present study declare no competing interests.

Data availability

The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

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Supplementary data

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