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Cost-effectiveness of One Health intervention to reduce risk of human exposure and infection with non-typhoidal salmonellosis (NTS) in Nigeria

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ABSTRACT

Background: Non-typhoidal *Salmonella* infection (NTS) is an important foodborne zoonosis with underappreciated health and economic burdens, and low case fatality. It has global prevalence, with more burdens in under-resourced countries with poor health infrastructures. Using a cohort study, we determined the cost-effectiveness of NTS in humans in Nigeria for the year 2020.

Methods: Using a customized Excel-based cost-effectiveness analysis tool, structured (One Health) and unstructured (episodic intervention against NTS) in Nigeria were evaluated. Input data on the disease burdens, costs surveillance, response and control of NTS were obtained from validated sources and the public health system.

Results: The non-complicated and complicated cases were 309,444 (95%) and 16,287 (5%) respectively, and the overall programme cost was US$ 31,375,434.38. The current non-systematic episodic intervention costed US$ 14,913,480.36, indicating an additional US$ 16,461,954 to introduce the proposed intervention. The intervention will avert 4036.98 NTS DALYs in a single year. The non-complicated NTS case was US$ 60/person with significant rise in complicated cases. The cumulative costs of NTS with and without complications far outweighed the program cost for One Health intervention with an incremental cost-effectiveness ratio (ICER) of -US$ 221.30).

Conclusions: Utilising structured One Health intervention is cost-effective against NTS in Nigeria, it carries additional mitigative benefits for other diseases and is less costly and more effective, indicative of a superior health system approach. Identified limitations must be improved to optimize benefits associated and facilitate policy discussions and resource allocation.

1. Introduction

Non-typhoidal Salmonellosis (NTS) is an important foodborne zoonosis globally with significant but underappreciated health and economic burdens. In low-and-middle income countries (LMICs), especially in under-resourced, unplanned and underserved areas, humans and animal live in close proximity and often share the environmental resources, hence, NTS infection and transmission may be acquired through the environment [1]. A critical evaluation and profiling of the food systems in Nigeria, and in particular, the animal sourced food (poultry), revealed an additional risk of NTS in Nigeria [2,3]. Specifically, the country's poultry meat production is approximately 0.3 million tons per annum, but poultry meat demand is in excess of 1.5 million tons [3,4]. In addition, the country imposed an import ban on

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live poultry (except for day-old chicks) and frozen poultry products since 2003 [5,6]. To meet the shortfalls of approximately 1.2 million tons annually, poultry meat and poultry products are being smuggled into Nigeria almost on daily basis, especially from the neighbouring Benin Republic [4,6]. These unscrupulously smuggled poultry and its products are non-assessed, unregulated and non-standardized and end up in the human food chain in Nigeria [5,7], with high likelihood of risk of salmonellosis.

In addition, workers in the poultry value chain and consumers of poultry and products that evade pre-slaughter and post-slaughter inspection and hygienic processing procedures, are considered as high-risk groups [1,8]. In Nigeria, the NTS is prevalent, and is an often-underdiagnosed persistent disease in both humans (≤ 16.3%) and animals (≤ 48.3%), particularly in poultry [7,9,10]. Human and poultry cases of NTS are complicated by the phenomenon of antimicrobial resistance, which is linked to underdiagnoses, ease of access to antimicrobials, antibiotic misuse, abuse and overuse in order to treat infections [7,11,12].

The disease spectrum and economic burden of non-typhoidal *Salmonella* infections is broad and often underestimated [8,13,14]. In a recent estimate of social and economic burdens of NTS in Nigeria, approximately 325,731 cases with 1043 deaths and 324,689 survivors, as well as an estimated DALYs of 13,391 were directly associated with NTS at a human cost of approximately US$ 473,982,068.00, apart from similar livestock related costs [8]. Worse still, the World Health Organization in its Global Health Estimates listed diarrhoeal disease in the top four causes of disability-adjusted life year (DALY) in Nigeria for the year 2019, and the country ranked in the top slot globally for DALYs, years of life lost from mortality (YLL) and years of healthy life lost due to disability (YLD) for diarrhoeal diseases [15]. In another modeled economic evaluation, which considered full, partial and no deployment in cases of mild and severe (complicated) invasive NTS, decision to use point of care diagnostic- tests fast-track identification and differentiation between the resistant and non-resistant strains, and shorted time to treatment and patient outcomes [1]. Previous workers have also confirmed that *Salmonella*-associated gastroenteritis had a high incidence, medium to high mortality, high population burden, low individual burden but a difficult to estimate disease specific incidence in the European Union [16]. Furthermore, the age specific population burden of gastro-intestinal salmonellosis was higher in adult >65 years, but the disease is reported more in children under 15 years and ranked as medium to high both in terms of notification rate and DALYs per 100,000 individuals in the world [16].

Furthermore, in low- and middle-income countries (LMICs), empirical data to support decision to guide evidence-based local action in public health is scarce. Hence, making cases for increased investment by governments and resource partners in the areas of intervention and surveillance systems difficult [17]. In this situation, modeling techniques are needed to bridge such statistical, economic and data gaps. One such tool is the cost effectiveness analysis (CEA) tool [18,19]. The cost effectiveness analysis is an objective measure that compares intervention costs against common outcome(s) of interest, for instance DALYs, or number of lives saved [18,19]. It assisted in the selection of the most cost-effective intervention for this outcome while evaluating the programme costs. The CEA is particularly useful when health benefits are difficult to calculate or convert to monetary terms [18,19]. The objective of the current work is to use the customized cost-effectiveness analysis model to demonstrate the benefit of structured but systematic One Health approach to disease surveillance and control against non-typhoidal salmonellosis (NTS) versus allowing the current episodic non-systematic intervention based on the previously estimated burden of NTS in Nigeria (≤ 325,731 cases and 1043 human deaths in a fixed year, 2020 and assuming that the utilization of One Health makes health system 50% more effective) [8]. The outcome should contribute to and supports empirical decisions on investment in national One Health approaches in tackling food-borne zoonoses like salmonellosis specifically, but also the agrifood system and other One Health challenges in Nigeria.

2. Materials and methods

2.1. Definition of One Health Intervention against non-typhoidal salmonellosis and input parameters

2.1.1. Data collection and management

Based on previously validated and published data [1–3,8], we defined One Health intervention against non-typhoidal salmonellosis (NTS) as all interventions carried out by the public and animal health sectors towards mitigating the risk of NTS in humans and animals in Nigeria for the year 2020. This will be inclusive of investigations, responses (epidemio-surveillance and laboratory) and control activities aimed at NTS [8]. It was estimated that these activities were aimed at 325,731 human cases of NTS, which was estimated to occur in the year 2020 and a human mortality of 1043 with a disability-adjusted life year (DALYs) of 37,321 [8]. In addition, a total of 43,662,085 poultry (chickens) were involved in the 2020 outbreaks from January–December 2020 with 15,841,044 deaths, 20,574,302 salvage slaughters, 5,713,152 culls and 1,533,587 chickens whose destinations were difficult to trace [8]. The total cost of these outbreaks in humans and poultry was a cumulative of US$ 930,887,379. Input parameters were collected from various sources including peer-reviewed literature, experts' opinions and field surveys. These were summarized in Table 1. Additional parameterisation and assumptions were detailed in Supplementary Table 1 and Supplementary material 2.

2.2. Study design

A decision tree analysis model was developed in Microsoft Excel v2016 (Microsoft Corporation, Redmond, USA) to evaluate the cost-effectiveness of investments in structured multisectoral One Health interventions against NTS in humans in Nigeria from a health systems perspective (Supplementary material 2). The model followed a cohort of 325,731 individual cases of NTS from a Nigerian human population of 208,327,405 for the year 2020. These values were representative of all individuals infected with non-typhoidal *Salmonella* organisms in the year 2020, with hospitalization or no hospitalization including 16,287 (5%) that proceeded to severe/complicated illnesses and 1043 (0.32%) whose death were associated with NTS in the year. We estimated intervention and treatment pathways, costs and health gains. Typical symptoms of NTS are self-limiting acute gastroenteritis with the sudden onset (6–72 h) of headache, fever, nausea, vomiting, abdominal cramps, dehydration and infectious diarrhoea, usually for up to 5–7 days [20,21]. The 5% of individuals who have severe/complicated illnesses are expected to develop symptoms associated with bacteremia or focal invasive infection (e.g., osteomyelitis, meningitis, endovascular infection, septic arthritis) [22,23]. The inclusive criteria for the economic data used in this analysis included: 1) Relevance to research objectives, 2) Accuracy and reliability of the data or associated verification system with the national or subnational health system, 3) Completeness and consistency of the data, 4) Timeliness of the data, 5) Accessibility and availability, where possible, data were accessed directly from the health authorities, 6) Granularity and details – we utilized published peer-reviewed documents and grey literature to verify our data, and 7) Consistency with theoretical frameworks fitting into our current economic analysis.

We excluded poor quality data and those with questionable integrity, extremely large or incomparably small data (Outliers and anomalies), redundant dataset, those that did not contribute directly to the objectives of the study, those subject to bias, and those that were deemed not representative or cannot be cross verified.

Table 1
Input Parameters for the Cost-Effectiveness Analysis for Non-typhoidal salmonellosis in Nigeria, 2020.

Variable	Value	Notes and Source*
Epidemiological, surveillance and laboratory test variables		
Prevalence of NTS in humans	0.1563%	Calculations, See Supplementary Table 1
Prevalence of NTS in humans (with 50% case reduction with One Health inputs)	0.07815%	
Accuracy of test kit (rapid stool antigen test)	82.92%	
Accuracy of test kit (Widal's antigen test)	43.00%	
Mortality rate of NTS (among human cases only)	0.320202867%	
Cost of laboratory testing	US$9.73	
Proportion of NTS cases hospitalized	5%	
Proportion of NTS death hospitalized	60%	
Duration of mild illness (NTS)	5 days	
Duration of severe (complicated) illness (NTS)	15 days	
Proportion of cases that proceed to severe illnesses	0.00781777	
Costs and budgeting		
Annual national budget for health, 2019	US $980,126,753.51	See Supplementary Table 1
Total programme cost for diarrhoeal diseases (1.3% of annual budget)	US $12,741,647.80	
Mean Health Expenditure (National)	0.516241	
Mean Health Expenditure (Sub-national)	0.483759	
Multisectoral Coordination Mechanisms (MCM) at the National Level		
Annual programme cost	US$6,577,238.59	See Supplementary Table 1. The costs for national and subnational were based on partial attribution of diarrhoeal diseases and annual health budget (see the footnotes).
Personnel salaries	US$5,492,678.96	
Overhead (training, administrative, secretarial and communication)	US$77,146.29	
Laboratory supplies, consumables and medications	US$1,007,413.34	
Subnational (State and Local Government) One Health Units and clinics		
Annual programme cost	US$6,164,409.20	See Supplementary Table 1.
Personnel salaries	US$5,147,923.44	
Overhead	US$72,304.10	
Laboratory supplies, consumables and medications	US$944,181.67	
Treatment cost/patient	US$60	See Supplementary Table 1.
Vaccination cost	0	Humans are not vaccinated against NTS in Nigeria
NTS cost to death	US$50,000	See Supplementary Table 1.
Socio-demographic data		
GDP per capital, Nigeria, 2020	US$2074.61	See Supplementary Table 1.
Human population, 2020	208,327,405	
Life expectancy, 2020	53 years	
Birth rate in Nigeria, 2020	37/1000	
Death rate in Nigeria, 2020	13/1000	
Minimum wage in Nigeria, 2020	US$78.89	
Annual wage increment	12%	
Epidemiological models		
NTS DALYs	37,321	See Supplementary Table 1.
YLD	632	
DALY weight	0.21	
YLL	36,690	
Mean infection age	19 years	
Number of survivors	324,688	
Associated mortality (humans)	1043	
Number of NTS cases (humans)	325,731	
Value of life lost	446,749.49	
Mean number of cases/ day (human)	892.41 cases/day	
Mean number of deaths/ day (human)	2.858 deaths/day	
Human deaths avoided/day due to One Health intervention	1.429 deaths/day	

* Details of references and sources of the values are available in Supplementary Table 1. Note that overhead costs is inclusive of training, indirect administrative costs and communication costs and miscellaneous costs. Attributable budgets of 51.62% and 48.38% for the national and subnational systems is based on the details from the Federal Ministry of Health (See Supplementary Table 1). Only 1.3% of the annual budget is spent on diarrhoeal diseases.

2.3. Model structure

Two different strategies were compared including the systematic and intentional One Health approach to disease control measures against NTS (Strategy 1) and the current episodic non-systematic interventions in Nigeria (Strategy 2) (Fig. 1; Supplementary material 2). Strategy 1 is defined as an enhanced investment in the investigation, management and control of NTS with the aim to make it intentional and effective, empirical administration of antimicrobials and laboratory activities (Supplementary Fig. 3). Strategy 2 is defined as the current level of episodic investment in NTS investigation, management and control. Both national and subnational coordination was considered with the Nigeria Center for Disease Prevention and Control (NCDC) leading the surveillance, the National Primary Health Care Development Agency (NPHCDA), and the primary, secondary, and tertiary level healthcare facilities among others contributing to the surveillance system for humans and the Federal and States' Ministries of Health (F/SMoH) coordinating the related matters. Human-level data were also cross-validated, where necessary with the Surveillance Outbreak Response Management and Analysis System (SORMAS), a tool being used by the Surveillance unit of the FMOH (Supplementary Fig. 4) [24].

2.4. Measurement of effectiveness and cost-effectiveness

The model's primary outcome measure is the cost per disability adjusted life years (DALYs) averted using One Health intervention in structured One Health interventions against NTS in humans in Nigeria from a health systems perspective. DALYs were calculated as the sum of years of life lost (YLL) and years of life with disability (YLD). We used standard methods to compute DALYs [15]. Years lost due to premature death (YLL) is calculated from the number of deaths at each age multiplied by a global standard life expectancy for the age at which death occurs (Table 1). To estimate YLD for a particular cause for a particular time period, the number of incident cases in that period is multiplied by the average duration of the disease and a weight factor that reflects the severity of the disease on a scale from 0 (perfect health) to 1 (dead). The DALYs were calculated using a discount rate of 3%, age weighting, Nigeria's life expectancy of 53 years [25], and assumed an average duration of illness of 5 days. The applied disability weight for mild, moderate and severe diarrhoea were: Mild 0·074 (0·049–0·104); Moderate 0·188 (0·125–0·264) and Severe 0·247 (0·164–0·348), as obtained from the Global Disease Burden Study 2013 [26].

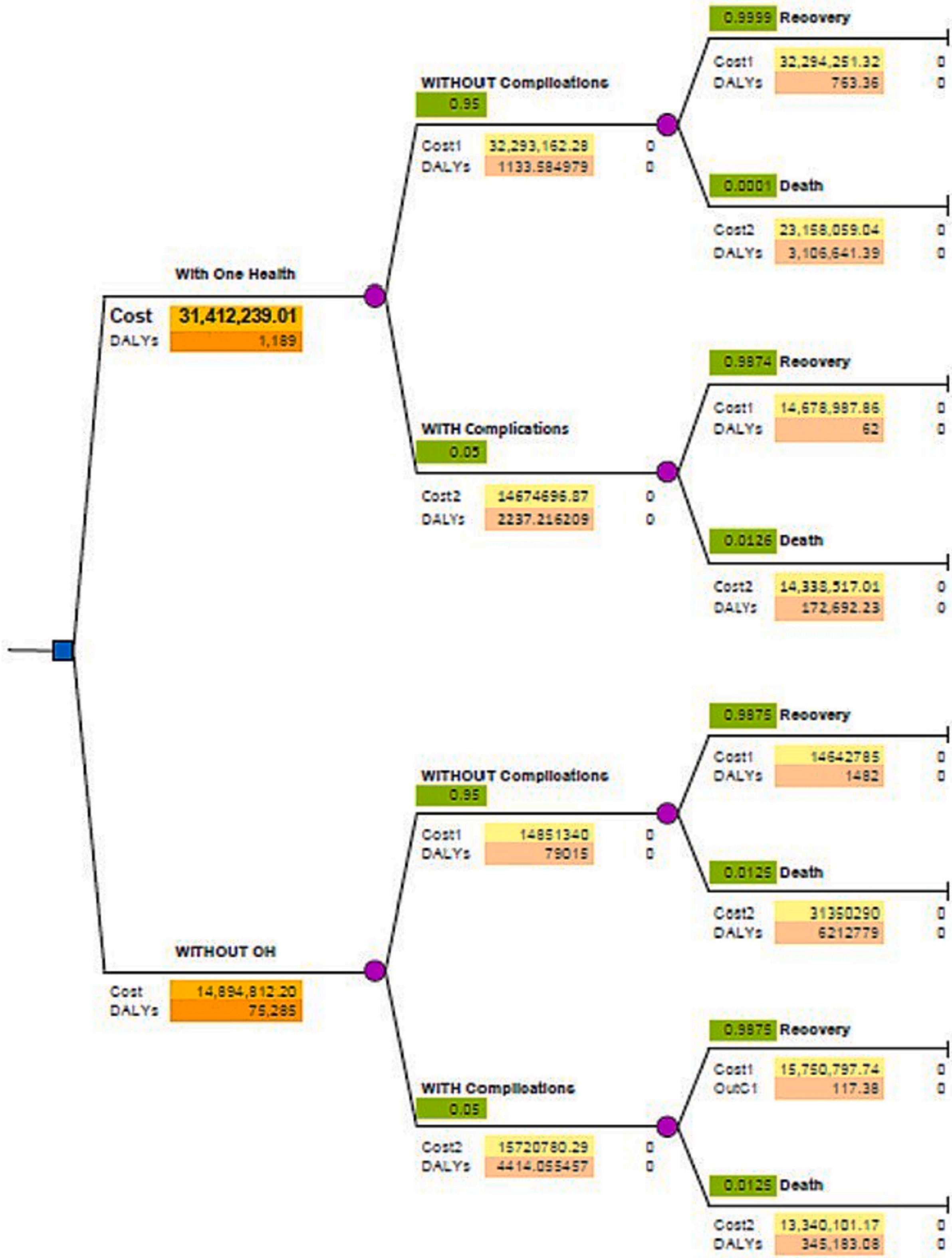

Fig. 1. Framework of schematic decision tree to assess cost-effectiveness of One Health approach versus episodic non-systematic interventions against non-typhoidal salmonellosis in Nigeria, 2020.

2.5. Calculation of disability adjusted life years (DALYs) and incremental cost-effectiveness ratio

Using the formula:

$$\text{DALY} = \text{Years of life lost to premature death (YLLs)} + \text{Years lived with disability (YLD)}.$$

Where, for a single individual: YLL = life expectancy – age at death, and in a population: YLL_x = number of deaths at age_x, X standard years of life lost was put at age 20, and YLD = Incidence of cases x average duration x disability weight.

The number of deaths and incident cases were obtained from the line previous findings of Sanni et al. [8], and population estimates were obtained from the *United Nations, Department of Economic and Social Affairs, Population Division* estimates [27]. The average duration of illness for NTS is 5 (mild) – 15 (severe/complicated) days (Table 1), hence, these values were annualized by dividing the values by 365 to get them on a year scale. These calculations were made with reference to the Microsoft Excel template developed by World Health Organization was used for computation of YLL, YLD and DALYs respectively.[15]

The incremental cost-effectiveness ratio (ICER) was the measure of cost-effectiveness calculated as the net change in total costs and DALYs averted between providing One Health interventions compared with maintaining the current intervention and management system against NTS. The ICER was calculated as:

$$\text{ICER} = (\text{CNTS}_{\text{OH}} - \text{CNTS}_{\text{nOH}})/(\text{DALYs}_{\text{OH}} - \text{DALYs}_{\text{nOH}}),$$

where the $CNTS_{OH}$ is the total cost of One Health interventions against NTS for mild and severe (complicated) cases and $CNTS_{nOH}$ is the total of cost of non-One Health interventions against NTS for mild and severe (complicated) cases. The ICER was compared with the opportunity cost based on the Nigeria cost-effectiveness threshold (US$1037.31) (50% of the per capita GDP (US$2074.61)) for the year 2020 [28].

2.6. Sensitivity analysis and dealing with uncertainty

Sensitivity analysis was assessed using a one-way sensitivity analysis (deterministic) and a probabilistic sensitivity analysis (PSA). The one-way sensitivity analysis was conducted across selected parameters to assess the effect of selected changes on the ICER (Table 3; supplementary material 2). Using the increase or decrease of parameters without confidence bounds, the output values in the determination analysis model were compared with deterministic and probabilistic values at the lower and upper range of each output (Table 3). However, where possible, ranges for sensitivity analysis were based on upper and lower confidence intervals or IQR found within the systematic literature review (supplementary material 2 – Sensitivity analysis). The PSA (Monte Carlo simulation) was performed to explore the effect of uncertainty across our model parameters using 1000 iterations. The key parameters

Table 2
Outputs from the decision tree pathways, with termination in recovery or death.

Cost variables*	US$
Programme costs with OH	31,375,434.38
Programme costs WITHOUT OH	14,913,480.36
Additional costs spent on implementing OH programme	16,461,954.02
DALYs of NTS with One Health	1229.70
DALYs of NTS WITHOUT One Health	75,618.47
Incremental DALYs	74,388.77
ICER ($/DALY)	−221.30
Treatment costs of NTS per patient (hospitalization)	60
Vaccination cost against NTS	–
Cumulative Cost of NTS to deaths	50,000
Cost of NTS with complications that progress to Recovery (if OH is implemented)	14,678,987.86
Cost of NTS with complications that progress to Recovery (if OH is not implemented)	15,750,797.74
Cost of NTS WITHOUT complications that progress to Recovery (if OH is implemented)	32,294,251.32
Cost of NTS WITHOUT complications that progress to Recovery (if OH is not implemented)	14,642,785.00
Cost of NTS with complications that progress to Death (if OH is implemented)	14,338,517.01
Cost of NTS with complications that progress to Deaths (if OH is not implemented)	13,340,101.17
Cost of NTS WITHOUT complications that progress to Deaths (if OH is implemented)	23,158,059.04
Cost of NTS WITHOUT complications that progress to Deaths (if OH is not implemented)	31,350,290.00
DALYs	
DALYs of NTS with complications that progress to Recovery (if OH is implemented)	46
DALYs of NTS with complications that progress to Recovery (if OH is not implemented)	91
DALYs of NTS WITHOUT complications that progress to Recovery (if OH is implemented)	890
DALYs of NTS WITHOUT complications that progress to Recovery (if OH is not implemented)	1780
DALYs of NTS with complications that progress to Death (if OH is implemented)	283,429
DALYs of NTS with complications that progress to Deaths (if OH is not implemented)	566,857
DALYs of NTS WITHOUT complications that progress to Deaths (if OH is implemented)	5,108,829
DALYs of NTS WITHOUT complications that progress to Deaths (if OH is not implemented)	10,217,658
Incremental cost-effectiveness ratio (ICER)	-US$,221.30

* This table is supported by details from Fig. 1 and Supplementary material 2. The baseline DALYs (WITHOUT One Health) was 75,512. With One Health, an additional 74,389 DALYs was averted. NTS = non-typhoidal salmonellosis; DALYs = Disability-adjusted life years; OH = One Health; ICER = incremental cost-effectiveness ratio.

included the per day costs for severe (complicated) and critical patients, DALYs, length of stay, and the transition probabilities with defined distributions prevalence of NTS without One Health, prevalence of NTS with One Health, screening accuracy of NTS test Kit (Pen side test) [29], mortality rate associated with NTS in Nigeria, probability of NTS with and without complications that progress to Recovery (if OH is implemented or not implemented), probability of NTS with and without complications that progress to Death (if OH is implemented or not implemented) (online supplementary material 2). The analysis randomly sampled each parameter in our model simultaneously from their probability distribution and repeated this 1000 times to generate CIs around our estimates of cost per DALY averted. The confidence intervals (CIs) or variation of parameters and the effect on the cost-effectiveness were also evaluated. Finally, the PSA was run, and estimates were presented in Table 3 with details in supplementary material 2.

Table 3
One way sensitivity analysis for cost-effectiveness analysis for non-typhoidal salmonellosis in Nigeria, 2020.

Variables	Value in the model	Deterministic value	Probabilistic Value	Lower	Upper	SE
Probabilities						
Prevalence of NTS without One Health	0.0016	0.0016	0.0015	0.0015	0.0016	0.0000
Prevalence of NTS with One Health	0.0008	0.0008	0.0007	0.0007	0.0008	0.0000
Screening accuracy of NTS test Kit (Pen side test)	0.8292	0.8292	0.8565	0.7877	0.8707	0.0007
Mortality rate associated with NTS in Nigeria	0.0370	0.0370	0.0353	0.0352	0.0389	0.0000
Probability of NTS with complications that progress to Recovery (if OH is implemented)	0.9454	0.9454	0.9875	0.8981	0.9926	0.0007
Probability of NTS with complications that progress to Recovery (if OH is not implemented)	0.9454	0.9454	0.9873	0.8981	0.9926	0.0007
Probability of NTS WITHOUT complications that progress to Recovery (if OH is implemented)	0.9995	0.9995	0.9999	0.9495	0.9999	0.0004
Probability of NTS WITHOUT complications that progress to Recovery (if OH is not implemented)	0.9454	0.9454	0.9875	0.8981	0.9926	0.0007
Probability of NTS with complications that progress to Death (if OH is implemented)	0.0546	0.0546	0.0522	0.0519	0.0574	0.0000
Probability of NTS with complications that progress to Deaths (if OH is not implemented)	0.0005	0.0005	0.0005	0.0005	0.0005	0.0000
Probability of NTS WITHOUT complications that progress to Deaths (if OH is implemented)	0.0005	0.0005	0.0005	0.0005	0.0005	0.0000
Probability of NTS WITHOUT complications that progress to Deaths (if OH is not implemented)	0.0005	0.0005	0.0005	0.0005	0.0005	0.0000

Costs (US$)	Value in the model (US$)	Deterministic value (US$)	Probabilistic value (US$)	Lower (US$)	Upper (US$)
Cost of NTS with complications that progress to Recovery (if OH is implemented)	14,716,351.41	14,716,351.412	14,727,785.36	11,773,081.13	17,659,621.69
Cost of NTS with complications that progress to Recovery (if OH is not implemented)	15,666,871.41	15,666,871.412	15,651,174.69	12,533,497.13	18,800,245.69
Cost of NTS WITHOUT complications that progress to Recovery (if OH is implemented)	32,327,851.41	32,327,851.412	32,252,834.64	25,862,281.13	38,793,421.69
Cost of NTS WITHOUT complications that progress to Recovery (if OH is not implemented)	14,642,687.80	14,642,687.796	14,668,199.93	11,714,150.24	17,571,225.35
Cost of NTS with complications that progress to Death (if OH is implemented)	14,331,111.41	14,331,111.412	14,294,956.26	11,464,889.13	17,197,333.69
Cost of NTS with complications that progress to Deaths (if OH is not implemented)	13,306,927.80	13,306,927.796	13,291,166.50	10,645,542.24	15,968,313.35
Cost of NTS WITHOUT complications that progress to Deaths (if OH is implemented)	23,103,801.41	23,103,801.412	23,134,527.01	18,483,041.13	27,724,561.69
Cost of NTS WITHOUT complications that progress to Deaths (if OH is not implemented)	31,367,587.80	31,367,587.796	31,244,429.14	25,094,070.24	37,641,105.35

Outcomes	Value in the model	Deterministic value	Probabilistic Value	Lower	Upper
DALYs of NTS with complications that progress to Recovery (if OH is implemented)	45.57	45.57	62	28	63
DALYs of NTS with complications that progress to Recovery (if OH is not implemented)	91.15	91.15	118	55	127
DALYs of NTS WITHOUT complications that progress to Recovery (if OH is implemented)	890	889.96	863	541	1239
DALYs of NTS WITHOUT complications that progress to Recovery (if OH is not implemented)	1779.92	1779.92	1409	1082	2478
DALYs of NTS with complications that progress to Death (if OH is implemented)	283,428.71	283,428.71	172,766	172,325	394,533
DALYs of NTS with complications that progress to Deaths (if OH is not implemented)	566,857.41	566,857.41	345,189	344,649	789,066
DALYs of NTS WITHOUT complications that progress to Deaths (if OH is implemented)	5,108,828.81	5,108,828.81	3,106,691	3,106,168	7,111,490
DALYs of NTS WITHOUT complications that progress to Deaths (if OH is not implemented)	10,217,657.63	10,217,657.63	6,212,817	6,212,336	14,222,979

NTS = non-typhoidal salmonellosis; DALYs = Disability-adjusted life years; OH = One Health; SE = Standard Error.

3. Results

The results of the costs, DALYs and the ICER associated with the two options are shown in Table 2. The overall programme cost using a structured and comprehensive One Health intervention was US$ 31,375,434.38, whereas the continuation of the current non-systematic episodic intervention was US$ 14,913,480.36, an indication that an additional US$ 16,461,954.02 will be needed to implement the structured systematic One Health surveillance system (including diagnosis) in combating the burden of NTS in Nigeria (Table 2). The One Health intervention may avert 74,221 NTS DALYs in 2020. Approximately US$ 60 is needed to treat a case of non-complicated NTS, but this cost may rise significantly with complications. Ordinarily, the Cost of NTS WITHOUT complications that progress to recovery (if OH is implemented) (US$ 32,294,251) outweighed the program cost for One Health for the year 2020 (US$ 31,375,434.38) (Table 2). In addition, the cost of NTS WITHOUT complications that progress to Deaths (if OH is implemented) amounted to US$ 23,158,059 in the single year. Other costs are detailed in Table 2.

The Incremental cost-effectiveness ratio (ICER) (-US$ 221.30) was lower than the cost-effectiveness threshold for Nigeria (US$ 1037.31), confirming that it is cost-effective (Table 2; Supplementary material 2).

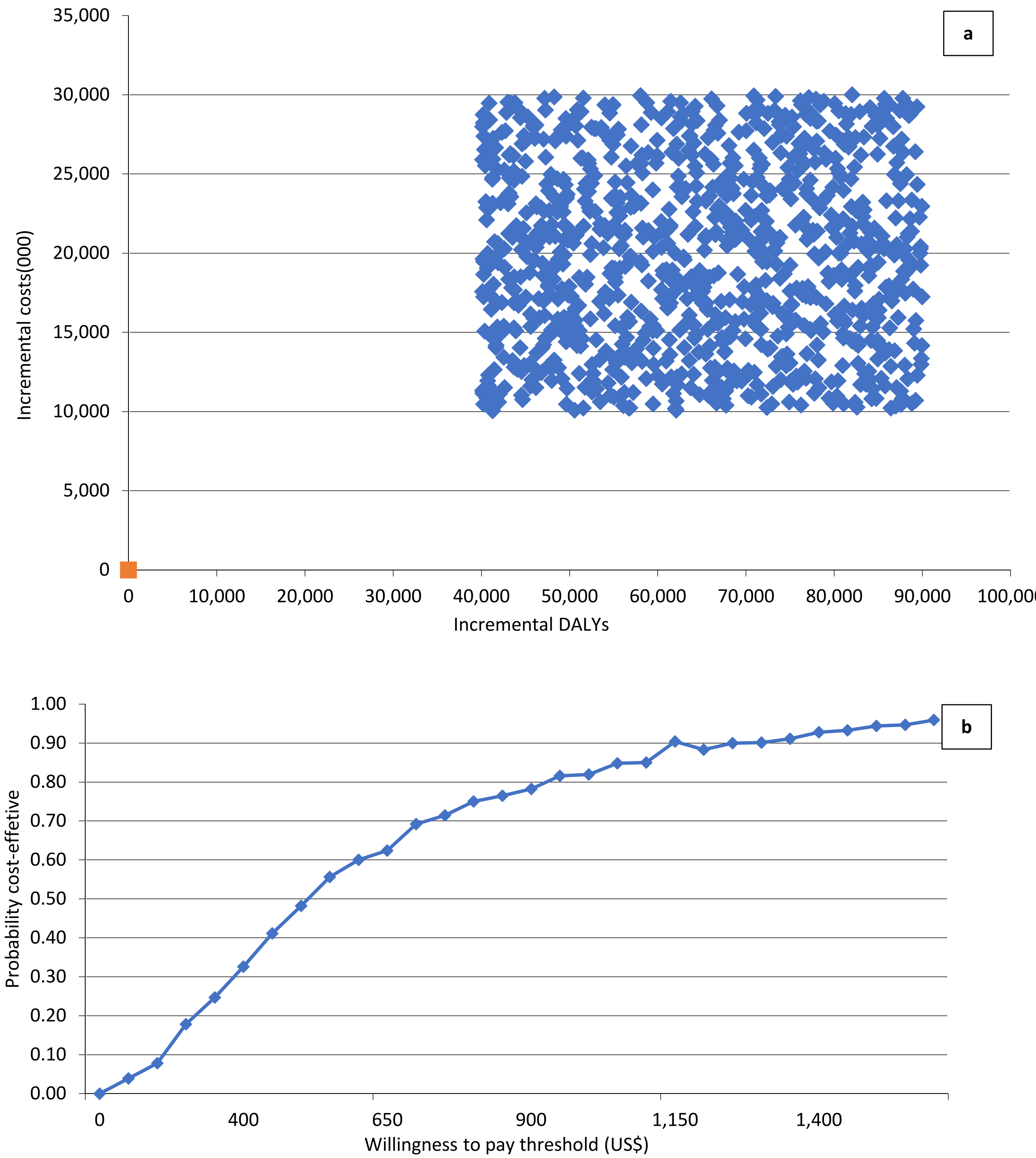

Fig. 2. a The cost-effectiveness plane based on sensitivity analysis; **2b**. Willingness to pay threshold for cost-effectiveness analysis for non-typhoidal salmonellosis in Nigeria, 2020.

Basically, non-complicated and complicated cases were 309,444 (95%) and 16,287 (5%) respectively, making a cumulative total of 325,731 human cases. Of the total recoveries, 309,290 were from the non-complicated cases and only 15,397 presented with complications. An estimated 155 non-complicated cases proceeded to death whereas 889 cases proceeded to death from the complicated cases (Supplementary material 2).

3.1. Cost-effectiveness of baseline and additional costs spent

Whereas the baseline (without OH approach) cost was US$ 14,913,480.36 came with the associated disability adjusted life years (DALYs) (≈ 75,618), an additional spending on One Health to the tune of US$ 16,461,954.02 will avert ≈ 74,389 DALYs. Cumulatively, the years of life lost (YLL) with and without One Health was 17,209.50 and 34,419.00 respectively (Supplementary material 2).

3.2. Sensitivity analysis

The probability evaluations in sensitivity analysis produced variations in costs and DALY outcomes as outlined in Table 3. Based on the cost-effectiveness plane, incremental costs ranging from over US$10 million to US$30 million will produce incremental DALYs of approximately 40,000 to over 90,000 by implementing One Health intervention against non-typhoidal *Salmonella* in Nigeria (Fig. 2a). As willingness to pay thresholds for One Health intervention against non-typhoidal salmonellosis increases, the probability for cost-effectiveness increases correspondingly, peaking at a willingness to pay threshold of US$1600 at a probability cost-effectiveness of 0.96 (Fig. 2b).

In summary, with the average probabilistic runs and at 95% confidence limit, the total DALYs with One Health was 1230 and without One Health was 75,618 at total costs of US$ 31,375,434 and US$ 14,913,480 respectively (Supplementary material 2). Comparing the baseline results with the average probabilistic runs, whereas the original incremental DALYs shifted from 74,389 to 65,311 (95% confidence interval: CI95%: 64,538–66,085), the incremental costs shifted from US$ 16,461,954 to US$ 20,007,081 (CI95%: 19,698,379–20,315,783) and ICER shifting from 221 to 322 (CI95%: 195.90–448.50) (Supplementary material 2).

4. Discussion

Currently, it costs an estimated US$ 60 to treat non-complicated NTS in this study but estimate for the complicated cases was difficult to obtain due to different treatment pathways and health outcomes [30]. This treatment cost may differ based on political geography, health systems' pricing and the country's GDP; for instance, such cost range between US$ 8.96 and 39.11 in Ethiopia [14], and in mild to complicated cases of NTS, it may vary between US$ 399 and US$ 760 ($CI_{95\%}$: 201–1285) (Hong Kong) [31], or more than US$ 3375 (Spain), and up to US$ 7400 (USA) [13]. We established that the cost of NTS WITHOUT complications that progress to recovery (if OH is implemented) outweighed the program cost for One Health in the single year, 2020. If the additional costs associated with NTS with and without complications, and those that proceeded to deaths or recovery (if OH is implemented) are added, the investment cost is worthwhile. This should provide justification for political economy and investment in structured One Health in NTS surveillance and control with unintended mitigative benefits for other diseases.

In this analysis, the annual allocation of the initial set-up cost was included in the One Health interventions, versus the non-One Health intervention. Debate on whether it should be annualized, and the subjectivity in determining the estimated total of start-up cost, and whether such costs and capital costs should be expensed as incurred cost remained [32]. This debate should make CEA complex, but we considered it as part of capital costs, and annualized it in the analyses. We generated a negative ICER of - US$ 221.30. Such negative ICER can mean two things, either that the new intervention is more costly and less effective, in which case the comparator is superior, and the new intervention should be rejected, or that the new intervention is less costly and more effective, in which case the new intervention is superior for adoption [33,34]. In our case, the second position subsisted because the structured One Health intervention averted the DALYs worth 74,388.77 at a top-up cost of ≈ US$ 16,461,954. Our DALYs for One Health intervention (17,687) is much lower than WITHOUT (35,356), which is a positive outcome, hence the current analysis is suggested for implementation (Supplementary material 2).

This study is subject to a number of limitations. First, it has been reported previously that some diarrhoeal diseases, for instance salmonellosis typically have a comparative high notification rate in children - due to a testing bias including more regular tests, relative reduced immunity in the young and higher chances of exposure to infectious agents, and pattern of hospital-seeking behaviour [16,35,36], however, we did not conduct an age-segregated analysis in this study. Perhaps, we have underestimate or overestimate the age specific or overall burden of NTS. Secondly, we estimated the CEA for a year and did not apply the multi-year time-discounted factor used in economic studies, however, with the understanding that program implementation in health system with future implications typically have multi-year benefits, thus additional maintenance costs and benefits may attend this analysis. Thirdly, the difference between national assembly- approved (allocated) and released (performance) budget may have significant impact on the outcome of the analysis in varied widely. In addition, we utilized the whole of capital and set up cost for the One Health interventions in the analysis, whereas we did not utilize the same for non-One Health interventions (due to non-committal spending associated with episodic non-systematic interventions), with implication on potential overcosting for inputs in One Health. Furthermore, Widal's test (for agglutinating antibodies detection against the O and H antigens) is widely used in Nigeria, similar to in other LMICs, for the diagnosis of gastrointestinal form of salmonellosis and typhoid fever, but it is not sufficiently sensitive, specific or reliable enough to be an optimal diagnostic assay for typhoid fever and it does not aid in the diagnosis of paratyphoid (NTS) fever, as the antibodies are not cross-reactive against *S. paratyphi* A, B and C antigens. Hence, a false-negative Widal's test may result from the assay being performed early in the course of illness and a false-positive Widal's test is more likely in an area of high endemicity where antibodies may represent past infection [9,30]. This observation makes NTS specific attribution of burden of illness quite difficult and may lead to test-sensitive underestimation or overestimation of cases. Finally, the health authorities in Nigeria and globally typically cluster NTS together with other gastrointestinal health challenges as part of the diarrhoeal diseases programmes; and other Enterobacteriaceae, as well as other diseases such as malaria can create further complexities with antigenic determinants that cross-react with *S. typhi*; hence, where a baseline was not established previously, as is the case in most LMICs due to additional health costs, interpreting test results may be complicated. It is encouraged that more sensitive methods like ELISA should be employed or used in combination with Widal's test [30].

5. Conclusion

This evaluation has produced empirical evidence suggesting that structured surveillance and control intervention against NTS in humans is cost-effective despite the low prioritization of the disease in Nigeria and similar LMICs. One Health intervention attracts enormous costs initially. However, 'structured?' One Health interventions are effective in preventing costs associated with DALYs and costs associated with illnesses and deaths. The ICER was US$ 221.30./ Based on outcomes One Health intervention for NTS is less costly and more effective in the long run. It has the potential to prevent additional illnesses and deaths. The output should support discussions with policy makers, funders and resource allocators in robust funding of surveillance and control efforts in health. The outputs also produce data for further discussion on the burden of NTS.

Collaborators

Alexander R. Jambalang.

Disclaimer

The contents of this paper are solely the responsibility of the authors and do not necessarily represent the official views of the institutions mentioned in the work.

Ethical statement

Written consent was obtained from participants, or oral consent for telephone participants. All key informants were informed of their rights as participants and their right to discontinue participation at any time. The protocol for the work was part of the protocol approval from the Federal University of Technology, Minna's Ethical Review Committee approval number: 000030, May 2022, and concurrently got additional ethical approval of the Research Ethics Committee of the Faculty of Veterinary Science, University of Pretoria, with ethical approval number REC 142–22 (July 2023).

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CRediT authorship contribution statement

Abdullahi O. Sanni: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Annelize Jonker:** Conceptualization, Supervision, Writing – original draft, Writing – review & editing. **Vincent Were:** Investigation, Methodology, Resources, Software, Writing – review & editing. **Olubunmi G. Fasanmi:** Conceptualization, Methodology, Writing – original draft, Writing – review & editing. **Oluwawemimo O. Adebowale:** Data curation, Formal analysis, Investigation, Writing – review & editing. **Aminu Shittu:** Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing – review & editing. **Abdurrahman H. Jibril:** Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. **Folorunso O. Fasina:** Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Declaration of competing interest

None.

Data availability

All the data utilized in this work are available as supplementary materials 1–5 or are publicly available in public databases.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.onehlt.2024.100703.

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