STUDY ENVIRONMENT

An Agent-Based Model for Collaborative Learning to Combat Antimicrobial Resistance: Proof of Concept Based on Broiler Production in Senegal

This document includes notes for model description based on the ODD (Overview, Design concepts, Details) protocol for describing individual- and agent-based models (ABM) (Grimm et al. 2006), as updated by Grimm et al. (2020). It complements explanatory notes in the model code.

1. OVERVIEW

1.1 Purpose & patterns

The **purpose** of this model is to facilitate a process of social learning amongst and between researchers, policymakers, veterinary professionals and producer businesses by understanding dynamics and exploring scenarios in Animal Health (AH) relevant to reducing Antimicrobial Resistance (AMR). Two results are intended:

- to stimulate interactions and decisions in the immediate context of the AH sector in Senegal; and
- to inform further development of ABM as a tool in the global effort to combat AMR.

The model sets out to describe general **patterns** in simplistic, proof-of-utility terms over three levels:

(1) The *agricultural production economic system* relevant to poultry raising for meat in Senegal, supervising the growth of birds over a period until their weight is suitable for sale for food consumption.
(2) *Microbiological dynamics* representing the evolution of multiple bacterial strains over time, including factors tending to promote those that are resistant to antimicrobial medicines over those that as susceptible, and the economic relevance of these dynamics as potential vectors for morbidity and mortality.
(3) Most relevant *human behaviours* to AMR in the context of the two previous patterns and linking to globally-recognised actions relevant to combat AMR in the field of Infection Prevention & Control (IPC), namely:
    a. Treatment decision-making, ie whether and how to administer antimicrobial medicines.
    b. Hygiene practices, above all cleaning routines in the production environment.

The intention in describing these patterns is to stimulate discussions within and across numerous relevant fields of practice, including for example: within modelling communities; research into farmers' knowledge, attitudes & practice (KAP); research into agricultural value chains; agricultural extension; veterinary professional organisation and practice; surveillance system feedback improving information on AMR dynamics in research and public administration; supplier / supply chain organisation and practice; regulatory and policy initiatives; and consumer awareness and norms. 'It is imperative to analyze the emergence of AMR within low-resource settings using a systems framework to effectively address the many interactive layers.' (Hedman et al., 2020)

1.2 Entities, state variables & scales

The model describes the use case of small-scale poultry rearing enterprises, such as are typical in the Dakar and Thies regions of Senegal. It addresses chicken rearing only (to the exclusion of other poultry species), and only for meat production – broilers (not for egg production – layers). The model focuses on two types of bacteria known to present foodborne AMR transmission risk in

Human Health (HH) as well as risk of infection to the chickens themselves in AH: *Escherichia coli* and non-typhoid *Salmonella spp.* These types are also amongst the most frequently studied in AMR research, above all for poultry AH. As a local, production facility-oriented AH decision-making model, the immediate focus is on IPC-related behaviours; however more generally this may provoke discussions in the related field of Antimicrobial Stewardship (AMS) which addresses governance around the use of antimicrobial medicines.

The following **entities** are included in the model, with associated **state variables** as described in the relevant table:

- Bacterial strains, each with the same set of characteristic parameters determined stochastically at instantiation and then remaining static as global variables for the duration of a simulation run. The following table describes the initial set of six bacterial strain types used for initial model development, showing the coding system for *[strain_code]* used to assign variables to each strain:

Bacteria type	*AMR profile*	*Strain code [strain_code]*
E. Coli (Ec)	Susceptible (NR)	*EcNR*
	Resistant (R)	*EcR*
Salmonella spp. (Sa)	Susceptible (NR)	*SaNR*
	Resistant (R)	*SaR*
Others / Autres (Au)	Susceptible (NR)	*AuNR*
	Resistant (R)	*AuR*

The following table shows state variables determined for each strain:

Variable name	*Subject/unit*	*Dynamic or static*	*Type*	*Range format*
[strain_code]xm	Maximum strain growth rate[1]	Static	Number	Normal distribution
[strain_code]ec50prim / [strain_code]ec50seco	EC_{50} value, the antimicrobial concentration at which strain grows at half the maximum strain growth rate (xm) for primary (ec50prim) and secondary (ec50seco) antimicrobial medicines	Static	Integer	Uniform distribution
[strain_code]gammaprim / [strain_code]gammaseco	The 'Hill-coefficient' value, which determines the steepness of the	Static	Integer	Uniform distribution

[1] Note that Resistant strains (R) are subjected to a fitness cost penalty to their standard maximum strain growth rate. Effectively, Resistant strains tend to have comparatively poor growth rates when antimicrobials are absent, whereas their growth is comparatively good when antimicrobials are present because their growth tends to be less affected by AMU. This is the key to how AMR modelled in the Græsbøll approach: AMU can cause AMR by creating an environment in which Resistant strains have a competitive edge over Susceptible strains.

	curve around the EC_{50} value.			

- Chickens, individual bird agents living and growing in the production environment, represented as a set of state variables comprising:

Variable name	*Subject/unit*	*Dynamic or static*	*Type*	*Range*
quant[strain_ code]	Number of bacteria from each strain (see below) present in intestines	Dynamic	Number	0 - cap
Lungquant[strain_code]	Number of bacteria from pathogenic (non 'Other') strains present in lungs	Dynamic	Number	0 -
lungquantImmune	Lung population of phagocyte immune cells	Dynamic	Number	0 -
epiDamage	Proportion damage to the epithelium of the lungs	Dynamic	Number	0 - 1
cprim / cseco	Concentration of primary (cprim) and secondary (cseco) antimicrobial medicines (µg/mL)	Dynamic	Number	0, 1, 10 or 40
vax	Vaccination status	Static	[TBC]	[TBC]
EcInfect / SaInfect	Morbidity - infection status with disease caused by bacterial type (value denoting AMR status)	Dynamic	String	No, NR or R
viva	Mortality – death status	Dynamic	String	Alive or Dead
mass	Weight of chicken (g)	Dynamic	Number	0 - 2000

- Patches, representing units of physical space in the production environment with state variables as follows:

Variable name	*Subject/unit*	*Dynamic or static*	*Type*	*Range*
patch[strain_code]	Number of bacteria from each strain (see below) present on patch	Dynamic	Number	≥ 0

The observer is modelled as an individual agent production supervisor, farmer and/or vet, within the global environment who is interested in chicken state variables (notably mass as a representation of the economic value of a chicken and morbidity/mortality variables as barriers to maximum value).

Primary and secondary antimicrobial medicines are, as indicated above, represented through state variables of chicken entities (cprim / cseco concentrations).

The **scales** applicable to the model relate to space (the production enclosure as a discrete grid comprised of square patches with edges 1/16th of a square metre) and time (one tick as one hour

elapsed), with simulations run with an agent population of 500 birds raised in a production environment of 5 by 10 metres with 10 feeder units distributed at regular intervals. 500 birds in this space is understood to represent a quarter of a typical 2000-bird production unit measuring 20 by 10 metres in total. In the first stage of the rearing process (starter), chickens are confined to 'starter circles' which are used in practice to help keep chicks warm under heat lamps. The timescale of a simulation run is 1008 ticks (42 days – a standard broiler chicken rearing cycle), extended by up to 168 ticks (an additional 7 days) in cases where a significant proportion of chickens have not achieved target weight (see below on disease impact on weight gain).

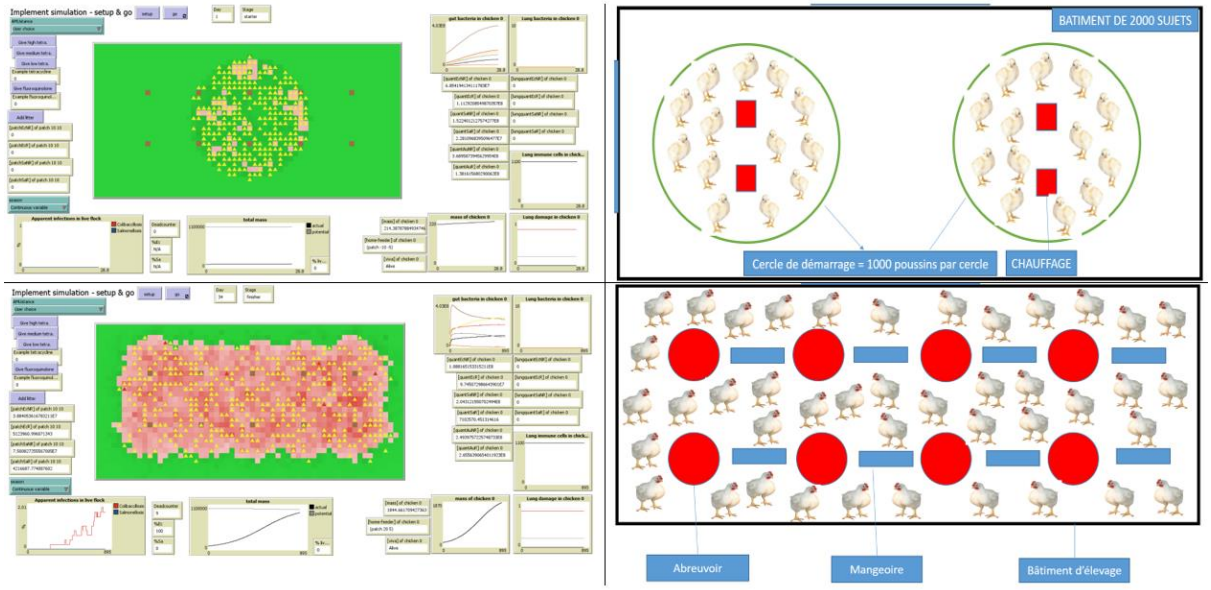


Figure 1: model observer interface (left) alongside representation of a standard semi-intensive broiler rearing facility (right). Chicks are initially reared in circular starter enclosures (top), moving to occupy the entire rearing facility for later production phases (bottom) (Source: model observer interface / Dr. Njiemessa Nsangou)

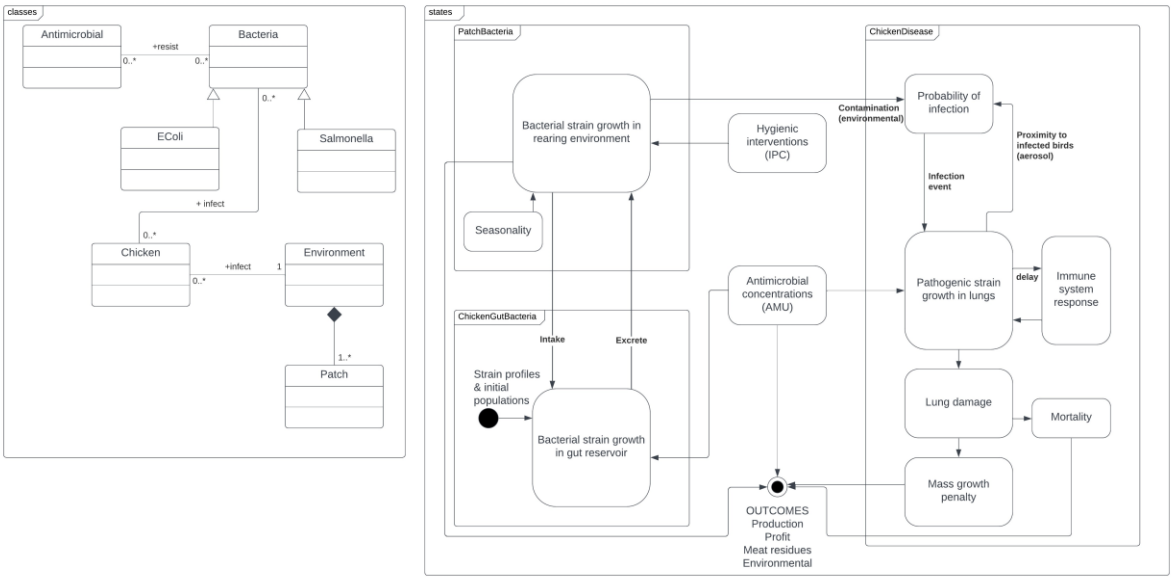


Figure 2: simplified UML class and state diagrams showing key model elements

1.3 Process overview and scheduling

The model schedule is executed at each time step as an ordered list of actions as follows:

1. Checks are implemented for conditions under which the simulation should stop.
2. Chickens execute the 'StrainsGrow' submodel, which updates chicken *quant* variables according to the bacterial strain state variables depending on factors including concentrations of antimicrobial medicines (*cprim / cseco*).
3. Chickens execute an intake procedure through which they ingest a proportion (*intakerate*) of the bacteria present on their patch (transferring from patch *patch* to chicken *quant*).
4. Chickens execute an excretion procedure through which they excrete a proportion (*excreterate*) of their patch (transferring from chicken *quant* to patch *patch*).
5. Chickens execute a strain removal procedure according to a probability that a relevant strain *quant* variable may drop to zero if its value is below a certain cutoff limit.
6. Chickens execute an infection procedure which determines whether chickens become infected, represented by non-zero values for *lungquant* variables of pathogenic bacteria populations.
7. Chickens execute an immunity response procedure in which *lungquantImmune* phagocyte immune cell populations respond to infections, determining the progress of infections in affected chickens.
8. Patches execute a growth procedure according to which *patch* variable bacterial populations in the growing environment develop according to growth rates and *season* variations in temperature and other conditions.
9. Patches and chickens change colour according to bacterial populations and infection status respectively, representing production conditions as apparent to the observer.
10. Chickens may change mortality status (*viva*) according to infection progress, with dead chickens periodically removed from the production environment.
11. Chickens execute a growth procedure according to which their *mass* changes.
12. Chickens move within space.
13. The observer initiates any treatment procedures which introduce concentrations of antimicrobial medicines into chickens (*cprim / cseco*).
14. The observer initiates any hygienic procedure which changes the number of bacteria present on patches (patch *patch* values).
15. The model updates monitor and tracker variables.
16. Time advances one tick.

The execution order is largely arbitrary in this environment since interaction between agents is only indirect. The intake procedure (2) takes place before the excretion procedure (3) to exclude within-tick feedback loops between chicken and patch bacterial strain populations.

1.4 Design concepts

i) Basic principles

At the **model level**, this environment sets out to address practical issues encountered during local efforts to combat AMR in Lower- and Middle-Income Countries (LMICs). It is generally acknowledged that antimicrobial use (AMU) in the Animal Health (AH) sector in LMIC is an important driver of AMR but one that is difficult to address. Our purpose calls for a model capable of usefully illustrating: (1)

the immediate relevance of AMR to non-specialist stakeholders in LMIC; and (2) the value of modelling in technical AMR data collection, research and evaluation efforts to inform policy.

Demonstrating the relevance of AMR to non-specialist stakeholders led us to focus on the poultry industry, considering a unit of economic production from the perspective of a farmer and/or general animal health practitioner. Especially given its importance in global efforts on poverty alleviation and economic development, including from a food security perspective, poultry production is vitally relevant to the anti-AMR agenda in this context (Hedman et al., 2020). Unfortunately, too little is known about apparent causal pathways to AMR human health burdens. However, as recognised in the FAO AMR Strategy 2021-25 (Food and Agriculture Organization, 2021), there is another more immediate and potentially compelling aspect to the AMR threat from within animal health, which is the idea that treatment failures will drive production losses and food insecurity. This aspect relates more directly to bottom-up agricultural perspectives on AMR from LMIC and the socio-technical interventions they inform, notably for example research on African farmers' knowledge, attitudes and practices (KAP) (Caudell et al., 2020, 2022). Our model seeks new ways to value existing practices and strengths, more than assuming that AMR concerns expose farmers and vets as lacking in expertise (Fortané, 2021).

Illustrating the value of modelling in this field led us to select ABM as our approach and to implement versions of state-of-the-art models within that approach. There is a lack of individual-based models in this field, especially outside human health and community settings and specifying bacteria/antibiotic (Ramsay et al., 2018). The core value of ABM in this instance lies in its ability to address complexity across multiple levels of scale (including rich depictions of within-agent mechanisms), with potential to address 'policy resistance' arising from analytical difficulties in addressing relevant complexity (Hammond, 2015). Our model seeks to support AMR and other relevant models at microbiological, host, population and market system scales simultaneously. It draws on existing modelling work for sufficient representations, in particular referring to reviews of AMR models (Birkegård et al., 2018) and seeking to develop a 'good enough' proof-of-concept model with maximum cross-disciplinary relevance and potential for future extensions. A nested approach was selected, modelling AMR spread as well as development. Stochastic elements were included. We aimed for maximum flexibility, for example including multiple strains, multiple antimicrobials and immune system representation. Useful reference models were less readily available outside microbiology and epidemiology, so for example the design economic aspects of our model relied more heavily on system descriptions (Arnoldus et al., 2021). Ideally validation of our model will potentially also support development in other directions for more direct LMIC policy relevance, for example with farms as nodes in an economic network (Steinbacher et al., 2021).

ABM also adds value in this context as a participatory modelling tool, including participatory simulation capability and therefore potential for 'serious gaming' approaches (Taillandier et al., 2019). At this proof-of-concept stage, we focused on stakeholder perspectives on a simple model (KISS) but bearing in mind that possibilities for future development depend on some degree of descriptive validation at this stage (KIDS) (Edmonds & Moss, 2005).

Our model design also set out to address an important weakness in the AMR modelling field which is lack of models originating from LMIC (Niewiadomska et al., 2019). Our proposed model also adds value as a rare example of such an approach being suggested from within the policy environment that relevant AMR efforts seek to address. Modelling was led from the Cheikh Anta Diop University (UCAD), in collaboration with the International Livestock Research Institute (ILRI), in Dakar, Senegal.

At the **agent level**, design choices targeted maximum relevance based on a general understanding of practical issues relevant to AMR in LMIC AH. Simplicity was preferred, retaining flexibility for future extensions. Particular effort was made to integrate appropriate mathematical modelling components where available. Agent design also referred to available descriptive information about AMR-relevant systems, especially in the context of poultry production in Senegal.

- *Bacterial populations.* An initial fundamental bacterial growth model was selected as a within-agent (intra-host) mechanism based on model-level principles (Græsbøll et al., 2014). This growth model represents the development of AMR as a question of the relative growth rate of strains inhabiting a competitive environment. It does not yet include other dynamics known to be important to AMR development, including for example gene transfer (Baker et al., 2016).

  Bacterial strains were selected as E. Coli and Salmonella spp. to represent types understood to be of greatest interest to microbiologists in Senegal given published research (Bada-Alambedji et al., 2006; Dieye et al., 2022; Dione et al., 2009; Fall-Niang et al., 2019; Vounba, 2019; Vounba et al., 2018, 2019). This also corresponds to our understanding that these types are of general interest to AMR investigations in a global context, with the poultry industry dynamics regarded as a priority from an epidemiological perspective in the case of E. Coli (World Health Organization, 2021) and from a food safety perspective in the case of Salmonella (Mak et al., 2022; Velasquez et al., 2018). These main strains were modelled to be pathogenic, with a further type of 'other' bacteria representing non-pathogenic strains.

- *Chickens*. Chickens perceive the environment via patches. Chickens move randomly through the environment and perceive patches. Bacteria are deposited in the environment via faeces. The basic conceptual structure of a chicken followed from the bacterial growth model, representing the intestines as a reservoir with intake/excretion to the production environment (Græsbøll et al., 2014).

  For the purposes of simplicity, we resolved to focus on broiler production since this allows for the mass variable to represent economic value (cutting out additional variables and calibration to account for eggs in layer production, for example). Growth curve modelling drew on research demonstrating the accuracy of logistic functions in representing broiler weight gain over time (Al-Samarai, 2015; Mouffok C et al., 2019).

  Infection, with associated morbidity and mortality, was established as the mechanism connecting bacterial causes to economic outcomes (in terms of weight gain implications and potential mortality). Colibacillosis and salmonellosis were noted as significant general disease types associated with our chosen pathogenic bacteria types in poultry (Kabir, 2010; Kathayat et al., 2021). Rather than seeking to address the complexity and uncertainty of relevant disease dynamics, we sought a simple mathematical model capable of simulating infection, immune response and outcomes in a general way. These considerations favoured mobilisation of an abridged version of Mochan et al's intra-host model for pneumonia in mice (Mochan et al., 2014), with the model representing the complicated pathogenesis and epidemiology of colibacillosis and salmonellosis in radically simplified terms. Infection applies to pathogenic bacterial strains only (ie only Ec/Sa strains, not Au).

Others have found our chosen bacterial growth model useful to assess infection dynamics in poultry directly (Becker et al., 2022). Elaborating distinct infection mechanisms in our model increased model complexity but increased descriptive value in conversation with AH professionals. Two causal pathways were modelled for infection, one representing environmental infection (contamination depending on the quantity of pathogenic bacteria on the chicken's current patch, and therefore indirectly representing faecal-oral as well as aerosol transmission) and one representing contact infection (depending on the presence of infected chickens on the current or surrounding patches). Modelling of chicken immune response enabled adjustment of disease impact depending on chicken age (stage of rearing process – starter, grower, finisher).

Antimicrobial agents were selected as Tetracycline and fluoroquinolones to refer to medicines understood to be commonly used in local poultry production but also frequently associated with resistance in our selected bacteria types. Colistin was originally considered as a potential secondary antimicrobial agent. In terms of general resistance rates of strains to these antimicrobial agents (ie % of strains resistant):

	AMR to tetra	**AMR to flouro**
E Coli	92% Senegal poultry 93% Togo poultry (n=29)	40% Senegal poultry 30% Togo poultry (n=29)
Salmonella	60% Mali poultry 100% Togo poultry (n=2)	25% in Senegal 2014 according to Mali poultry 62% Mali poultry 50% Togo poultry (n=2)

Senegal poultry (Vounba et al., 2019); Togo poultry (Bedekelabou et al., 2020); Mali poultry (Sidibé et al., 2019)

Helping to suggest strain profiles as follows:

	Proportions	**Tetra ec50**	**Tetra hill**	**Flouro ec50**	**Flouro hill**
EcNR	0.6 of Ec – represents Ec only NR to flouro	Low – even NR Ec is R to tetra	Gentle – small % can be NR to tetra	High – NR side of Ec	Steep
EcR	0.4 of Ec – multidrug R	Low	Steep	Low	Steep
SaNR	0.4 of Sa	High	Steep	High	Steep
SaR	0.6 of Sa	Low	Steep	Medium / high sd	Gentle

AuNR	0.8 of Au	High	Steep	High	Steep
AuR	0.2 of Au	Low	Steep	Low	Steep

- *Patches.* Farms were modelled very simplistically as isolated production environments comprised of a largely arbitrary number of patches and a largely arbitrary number of chickens approximately simulating a small-scale broiler production operation. Apart from representing a physical space in which to locate chickens, the patches were exploited as a means to represent chicken excretion to and intake from the production environment.

- *Observer.* The concept of the observer as an individual agent production supervisor, farmer and/or vet was imagined in two main ways relevant to the model interface. First, the observer was modelled as a decision-taker potentially taking IPC actions which are considered relevant in the model context. Decisions about the use of antimicrobial medicines were modelled simplistically, as directly determining relevant concentrations in all chickens at a fixed rate over a set period, but with treatment options determined to simulate understandings about typical (mis)uses in local context (including accommodation for prophylactic and metaphylactic uses which are understood to be common in local context). Second, we considered means to visualise within the environment, potentially to the exclusion of other information, those variables which would be apparent to the observer in practice and considered relevant by them.

ii) Emergence

Two main sets of results are emergent in the model:

(1) Bacterial strain development and spread.

Starting from stochastically-determined parameters (the growth/resistance profiles of strains plus per-chicken initial gut populations of each strain): development proceeds within chickens (in intestines modelled as reservoirs) depending on relative growth rates, resistance profiles, applicable antimicrobial concentrations and chickens' intake/excretion interactions with the production environment patches; and spread also proceeds in production environment patches through excretion/intake interactions with chickens.

Emergence dynamics here follow those in the Græsbøll sub-model (modified to accommodate multiple strains and antimicrobials). Bacterial strains compete with each other within a chicken's intestines, initially growing to occupy all available capacity and then moving towards equilibrium. These underlying dynamics vary according to relative strain growth profiles and also initial per-chicken strain populations. There are then two channels which alter these dynamics. First, the administration of antimicrobial agents (observer AMU interventions) works to alter the terms of competition between bacterial strains because relative resistance profiles change the *status quo* based on growth rates and fitness costs. Second, as patch bacterial populations build up their ingestion by a chicken becomes more significant in scale relative to gut population which potentially disturbs the equilibrium.

(2) Disease.

Again referring to stochastically-determined parameters (probabilities and bacterial infection loads within limits derived from the factors relevant to a specific infection pathway – see above), infection occurs through various mechanisms and causes different levels of morbidity and

mortality over time. The main relevance of disease in the model is as a factor influencing chicken mass (see below) but disease is also monitored over time / as an outcome [together with antimicrobial concentrations] as an indicator of likely human health consequences including through the food chain. See above for infection vectors in the model.

Intra-host disease dynamics follow the Mochan sub-model closely. Pathogenic bacteria populations in an infection site (simulated as the chicken's lungs) drive morbidity and potentially mortality through tissue damage. Starting with a population determined by the relevant infection event, the bacteria grow in the lungs at a proportion of the rate in which they grow in the gut. Counteracting this are responsive factors comprising: (1) mechanical clearance by mucus/cilia; and (2) the chicken's immune system, which (subject to some delay) produces phagocyte cells which destroy bacteria at some rate. Morbidity and mortality occur in individual chickens depending on the interaction of these factors over time including over successive infection events. Where bacteria are quickly overcome by the response, disease is not serious. Where bacteria quickly overwhelm the response, disease leads quickly to death. In between these extremes are more serious disease manifestations in which the bacteria-response dynamics take longer to resolve, increasing risk of infecting surrounding chickens through contact infection but also potentially equipping individuals that recover with greater immune readiness to fight future infection events. Even where high mortality is avoided, more serious disease in a simulation run is not desirable to the observer because of impact on weight gain rates.

There are two main ranges to disease emergence dynamics in the chicken population. Firstly, environmental infection acts imposes background morbidity/mortality costs, more easily controlled when patch bacteria remain within reasonable norms (especially where season limits growth and observer IPC interventions are used). Setting aside AMU interventions, stochasticity introduces a degree of chance within certain limits: observers can expect a certain proportion of chickens to get infected, and some will probably die. Secondly, contact infection – normally less relevant where relatively few chickens are seriously infected over longer periods – can take over as a dominant dynamic especially in simulations in which environmental infections are not well-controlled. Again absent AMU interventions, an epidemic-like process of negative feedback can take over to cause much higher mortality/morbidity in flocks as high prevalence drives higher rates of infection.

Otherwise all model results are relatively imposed by model rules. For example:

- Chicken mass.

Chickens gain mass over time according to a standard growth curve function, but this is influenced at the individual level by morbidity (which affects weight gain rates) and mortality (which reduces weight to zero).

- Seasonality

Bacterial growth rates are subject to a factor representing prevailing temperature, humidity etc which may encourage or inhibit a strain's proliferation.

iii) Adaptation

Model agents do not exhibit adaptive behaviour.

iv) Objectives

Model agents do not have objectives. The objectives of the model are at observer level (profit maximisation, maximum bird weight, AH).

v) Learning

Model agents do not learn.

vi) Prediction

Model agents do not engage in explicit or implicit prediction.

vii) Sensing

Model agents do not engage in sensing. Chicken movement is affected by feeder location.

viii) Interaction

In the model, chickens interact mainly with bacterial populations on patches but also with each other. There is no direct interaction of a chicken with its own gut bacterial population. However chickens emit bacteria to patches and also ingest bacteria from patches, implying an indirect interaction of a chicken with its own gut bacteria as well as with the gut bacteria of other chickens. Chickens also interact with each other through the contact infection channel.

ix) Stochasticity

The model contains both deterministic and stochastic dynamics. Main stochastic elements are identified above in notes on Emergence. Disease dynamics include some stochastic elements since the seriousness of an infection event (population of pathogenic strain bacteria introduced to a chicken's lungs) is determined using random number generation on a normal distribution with parameters set as a function of the relevant infection 'scale' and relevant infection bacteria populations (patch bacteria or surrounding chickens' lung bacteria). The movement of chicken agents is also random in the environment, although movement is relatively unlikely and chickens prefer to stay in the vicinity of a nearby feeder. During model initialization, the positions of the chicken agents are chosen at random.

x) Collectives

Collectives are not represented in the model. However chickens are modelled collectively in various respects, for example in observer AMU interventions which introduce an antimicrobial concentration for all chicken agents collectively (simulating administration though addition to water and assuming all chickens drink equally).

xi) Observation

During simulation, we observe the movement of chickens in the environment. The population dynamics of each type of bacteria are observed on one or more graphs. The evolution of the weight dynamics of each chicken is also presented on a graph as a function of the number of hours.

The model uses visual cues to simulate information that would be available to a farmer supervising broiler rearing. Chickens are yellow until showing signs of infection (>20% lung damage), at which point they become red. This may prompt observer AMU interventions. Death of a chicken (>80% lung damage) turns them black and halts movement. This also prompts simulated observer interventions, with any dead chickens automatically removed from the model environment at intervals. Patches are initially green indicating a relatively clean production environment, with colour

changes over time suggesting accumulation of bacterial strain populations (green – orange – brown – red – black) which may spur IPC intervention.

The model observer has a range of intervention decisions available, comprising AMU (administration of a specified concentration of an antimicrobial agent for a specified period) and IPC (refreshing the litter in the rearing environment). AMU influences bacterial growth rates depending on resistance profiles (see above). IPC reduces patch bacterial populations by a given proportion. The model has three modes of observer intervention: (1) no intervention – interventions disabled; (2) user choice – observer uses buttons to choose interventions depending on assessment of need during the course of a simulation run; (3) predetermined strategy – observer sets a rule for interventions algorithmically (if-then).

There are three sections to the model observer interface: (1) production environment – visualisation of the model environment, monitors summarising key variables of interest to the observer (eg total flock mass); (2) outcomes summary – a text summary of key economic, human health and environmental outcome variables which is produced upon completion of a simulation run; and (3) a parameter-setting dashboard which enables user-friendly observer calibration of main model variables through input interface items rather than through code (using a suffix naming convention '-obs').

1.5 Initialization

In the first step, the dimensions of the virtual environment are chosen and feeders located within the environment. Parameters are set for bacterial strains, comprising stochastic determination of growth rates and antimicrobial resistance (to both primary and secondary antimicrobial agents).

The following table shows the values used to set bacterial strains characteristics (see above for strain_codes / strain state variables / distributions and for supporting reasoning):

	xm			**ec50prim**		**gammaprim**		**ec50seco**		**gammaseco**	
	mean	**sd**	**max fitness cost**	**min**	**max**	**min**	**max**	**min**	**max**	**min**	**max**
EcNR	0.18	0.02		0.1	4	1	3	0.1	4	1	3
EcR	0.18	0.02	30	16	200	8	20	8	32	2	5
SaNR	0.18	0.02		0.1	4	1	3	0.1	4	1	3
SaR	0.18	0.02	30	8	100	4	10	1	128	4	10
AuNR	0.18	0.03		0.1	4	1	3	0.1	4	1	3
AuR	0.18	0.02	30	16	200	8	20	4	50	2	5

The intestinal capacity of chickens is set and an initial total bacterial population level set as a proportion of overall capacity. Model tracker variables are initialised to monitor outcomes and enable environmental conditions over time (eg AMU over a set time period). Chicken agents are randomly created and placed in the virtual environment. Patch bacterial populations are initially set to zero for all strains.

Chicken agents are initialised with the following state variables:

Variable name	***Subject***	***Initial value***
quant[strain_code]	Per chicken intestinal strain populations	See below

cap / startcap	Carrying capacity of chicken's intestines / initial total bacterial population	1.0E9 / 250000000 [ie chickens start at 25% of total capacity]
cprim /cseco	Antimicrobial concentrations	0
cutoffval / removprob	Cutoff strain population value below which removal may occur / probability of removal of a strain when below cutoff	5000000 / 0.5
excreterate	Excretion rate from intestine	0.001
intakerate	Intake rate to intestine	0.01
infectprobs (contamweight / surroundweight)	Term controlling how likely infections are to occur (weights accorded to infection probabilities)	0.01 / 1 / 1 [ie infection channel weighting not currently used]
infectscales (contamscale / surroundscale)	Term controlling scale of infections (and for specific infection vectors)	6000000 / 0.05 / 0.5 [ie higher probability of large bacterial load in contact infections]
lungquant[strain_code]	Per chicken lungs pathogenic strain populations	0 [for all strains]
lunggrowthprop	Proportion determining bacterial strains growth in lung relative to intestine	0.1
lungmechclearrate / lungphagoclearrate	Rate at which the innate immune system initially controls the bacteria in the lung respectively through: mechanical clearance via cilia and mucus; phagocytosis by alveolar macrophages	1000 / 1000000
lungquantImmune / lungimmunesteady	Per chicken lung population of phagocyte immune cells / steady-state value of lungquantImmune	1000
Ecphagorate / Saphagorate	Rate at which immune cells phagocytose pathogenic strain types, E Coli and Salmonella respectively	1.0E-7 / 5.0E-5
phagoinhib	Term for inhibition of phagocyte phagocytosis	1.0E-13
immuneinfluxrate	Rate at which phagocyte immune cells initially influx to lungs	10000
epiDamage	Damage to the epithelium of the lungs	0
damageincreaserate / damagerepairrate	Rates at which epiDamage: increase proportional to pathogenic strain	1.0E-11 / 0.1

	populations; decrease through body repair	
mass / maxmass	Chicken weight / slaughter weight towards which chickens grow [grams]	200 / 2000
vax	Vaccination status [placeholder – not used in current model version]	"No"
viva	Death status	"Alive"

Setting of specific initial gut bacteria populations for individual chickens is an important feature of model initialisation. Bacterial strain characteristics are set globally, ie growth rates, resistance profiles are standard for a strain regardless of what populations exist in chickens. But initialisation of gut bacteria populations is determined individually for each chicken agent.

Proportions of strains in the environment are set, types of bacteria according to fixed proportions and Resistant (R) strains within the relevant type stochastically within min-max ranges.

	Type proportion	**Min R as proportion of total type**	**Max R strain as proportion of total type**	**Distribution**
Ec	0.2	0.5	0.8	Uniform
Sa	0.2	0.2	0.5	Uniform
Au	0.6[2]	0.2		

This leads to each chicken having initial strain populations determined by applying these proportions to *startcap* (see above), leading to initial population ranges as follows:

	Resistant (R) - millions	**Susceptible (S) - millions**	**TOTAL - millions**
Ec	25-40	10-25	50
Sa	10-25	25-40	50
Au	30	120	150
TOTAL	65-95	155-185	250

Other initialized variables include movement probability and seasonal bacterial growth factors (*moveprob* 0.3, *seasonadjust* -20 as standard initial values).

1.6 Input data

The model does not use input data to represent time-varying processes.

[2] 1 – (proportion Ec + proportion Sa)

Instead of input, field survey data was used to calibrate simulation performance using the BehaviorSpace and BehaviorSearch tools.

Ultimately it may be possible to use input data for this model using field data (eg with Kobo).

1.7 Submodels

Mathematical models implemented in modified form in model code

- Bacteria / AMR (Græsbøll et al., 2014)
- Infection / disease (Mochan et al., 2014)

Contextual references for overall model design

- Senegal poultry value chain (Arnoldus et al., 2021; Ba et al., 2022)
- AMR OH causal pathways to outcomes (D. Emes et al., 2022; Graham et al., 2019)
- Economic models of AMR in AH (Raboisson et al., 2020)
- Wider/aggregate system models of AMR economics in Senegal poultry (Aboah et al., 2023; E. Emes et al., 2023)

Appendix – visualisations

Modelling bacterial populations in poultry production

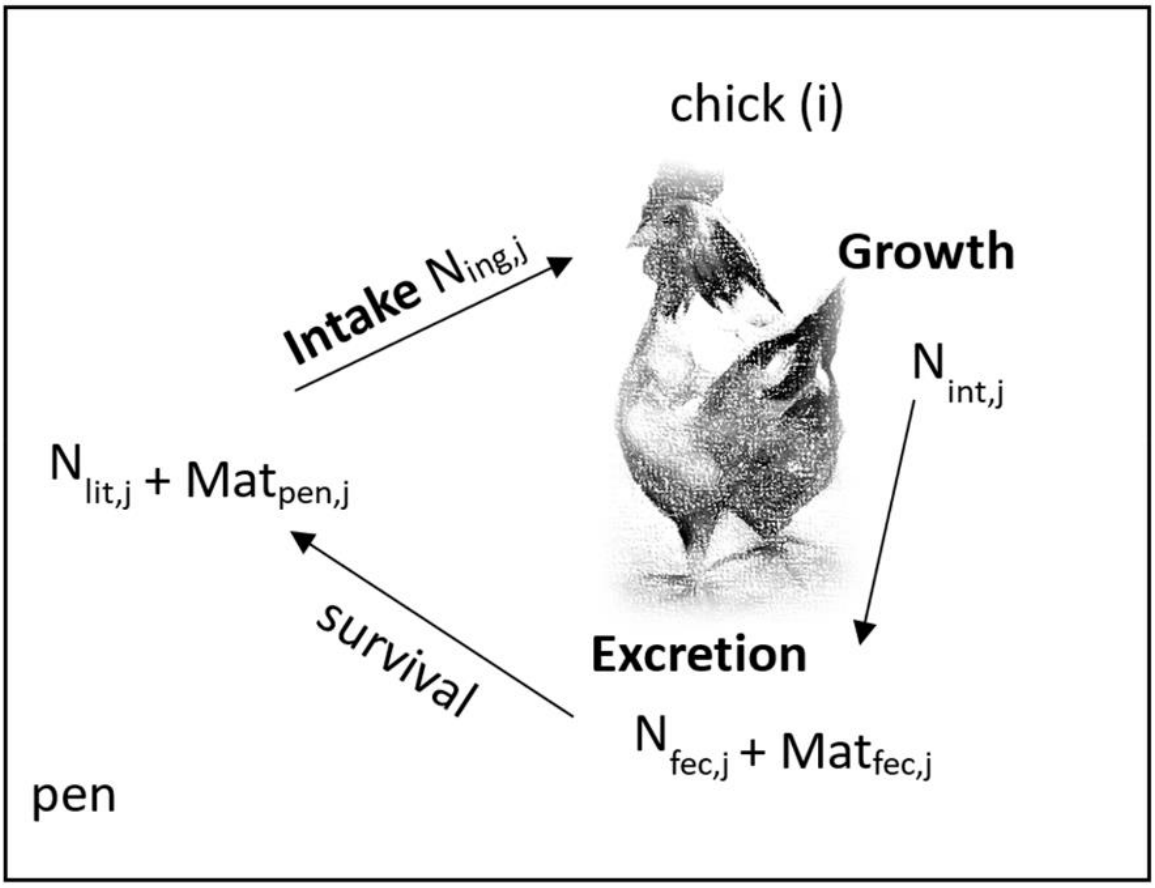


Figure 1. The model calculates the intake (N_{ing}), growth (N_{int}) and excretion (N_{fec}) of ESBL in the pen for each day (j) and chick (i). The survival of excreted ESBL (N_{fec}) in the amount of feces (Mat_{fec}) is calculated and, thus, so is the contamination of the litter mixed with feces (Mat_{pen}). These resistant bacteria present in the pen (N_{lit}) can, in turn, be picked up by the chickens.

(Becker et al., 2022)

Wider AMR systems

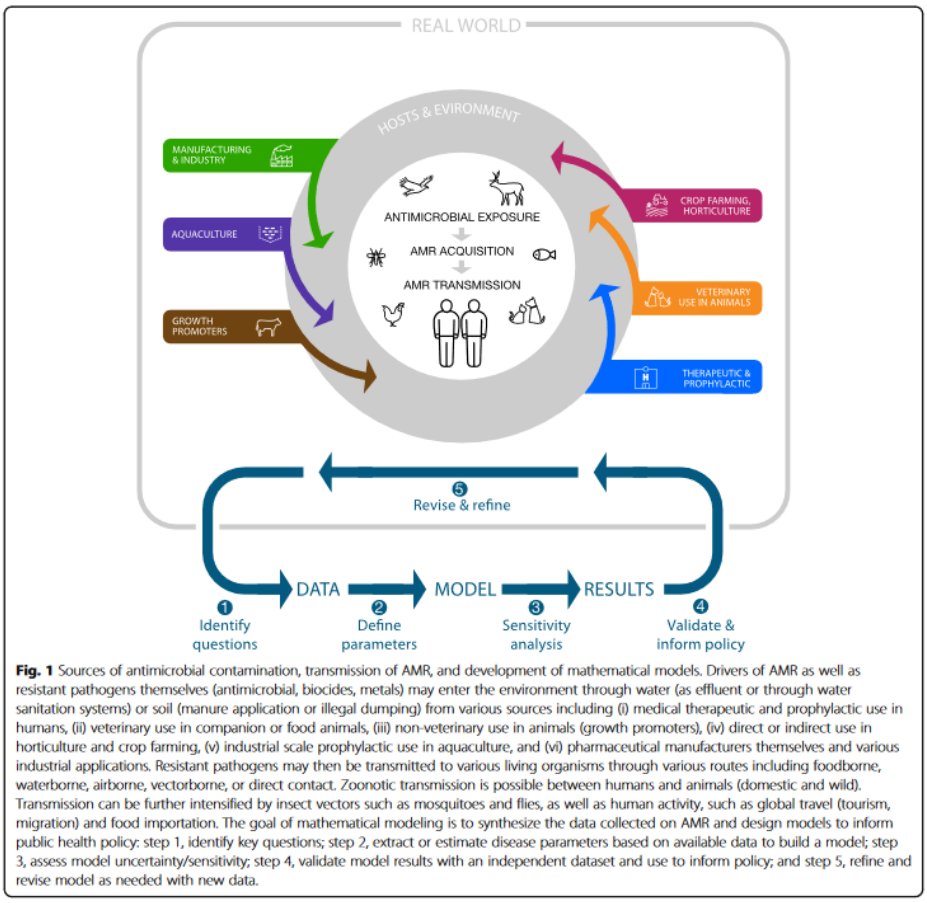
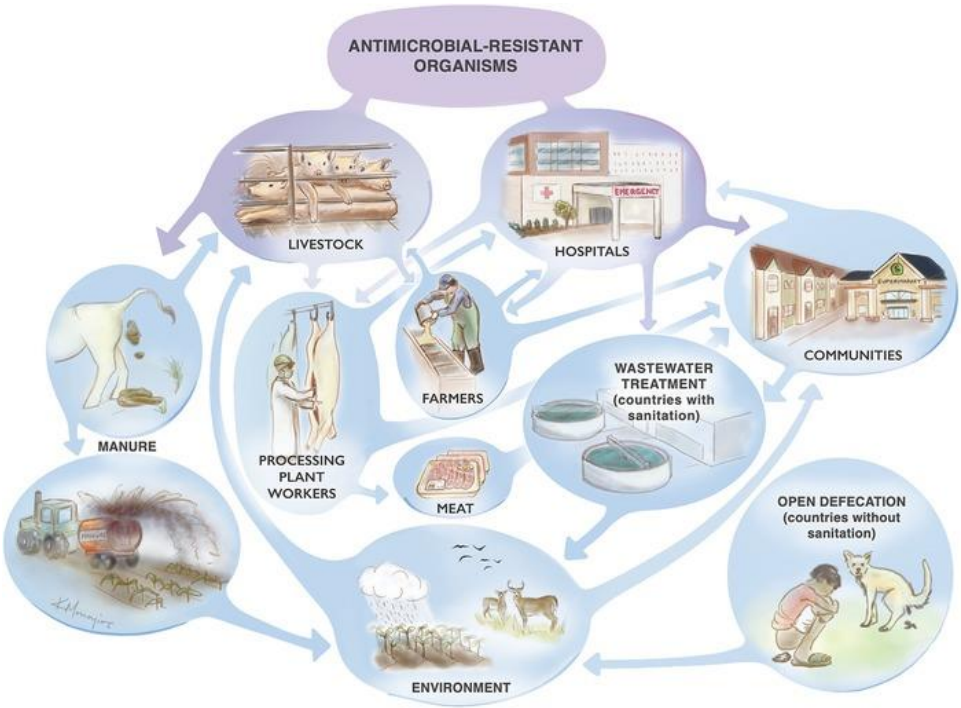
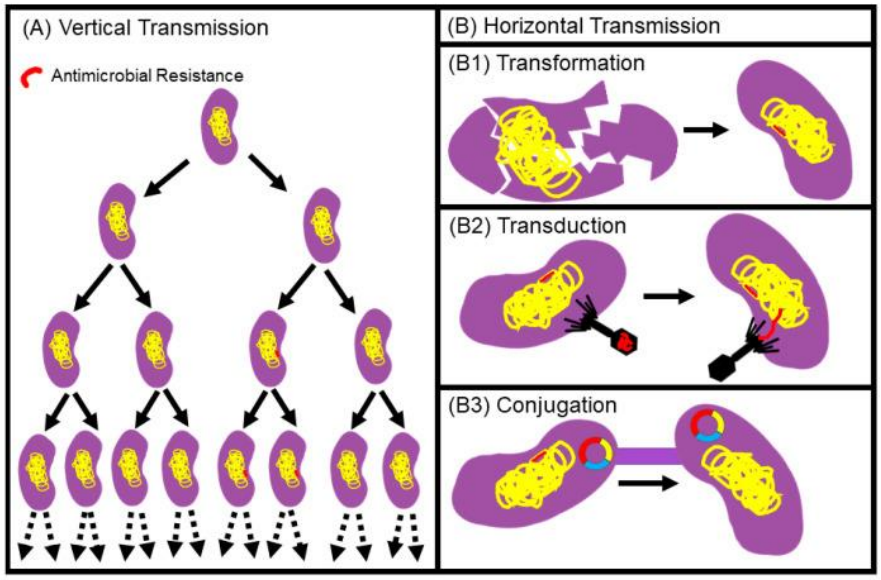


Fig. 1 Sources of antimicrobial contamination, transmission of AMR, and development of mathematical models. Drivers of AMR as well as resistant pathogens themselves (antimicrobial, biocides, metals) may enter the environment through water (as effluent or through water sanitation systems) or soil (manure application or illegal dumping) from various sources including (i) medical therapeutic and prophylactic use in humans, (ii) veterinary use in companion or food animals, (iii) non-veterinary use in animals (growth promoters), (iv) direct or indirect use in horticulture and crop farming, (v) industrial scale prophylactic use in aquaculture, and (vi) pharmaceutical manufacturers themselves and various industrial applications. Resistant pathogens may then be transmitted to various living organisms through various routes including foodborne, waterborne, airborne, vectorborne, or direct contact. Zoonotic transmission is possible between humans and animals (domestic and wild). Transmission can be further intensified by insect vectors such as mosquitoes and flies, as well as human activity, such as global travel (tourism, migration) and food importation. The goal of mathematical modeling is to synthesize the data collected on AMR and design models to inform public health policy: step 1, identify key questions; step 2, extract or estimate disease parameters based on available data to build a model; step 3, assess model uncertainty/sensitivity; step 4, validate model results with an independent dataset and use to inform policy; and step 5, refine and revise model as needed with new data.

(Niewiadomska et al., 2019)



(Graham et al., 2019)



(Hedman et al., 2020)

Agricultural value chain

TABLEAU 6:
Diagramme de la typologie des aviculteurs des secteurs 1, 2 et 3

	Caractéristiques							
Types	**Poulailler**	**Matériel d'élevage**	**Effectif**	**Système d'Alimentation**	**Cycle d'élevage**	**Zone d'élevage**	**Clientèle**	**Observations**
1. Grand élevage	Poulailler aux normes, possibilité de modernisation	Moderne, fonctionnement mécanique, ou automatique	Effectif important: supérieur ou égal à 5000 sujets	Distribution mécanique ou automatique des aliments et de l'eau	Régulier, durée du cycle est en fonction de la clientèle	Zone d'élevage, en dehors des habitations	Supermarché, restauration commune	De plus en plus abandonné, son avenir est l'intégration des différentes phases de production.
2. Élevage moyen	Poulailler acceptable	Artisanal ou moderne, adapté et suffisant	Moyen: 2000 à 4000 sujets, en moyenne 2000 sujets	Respect du programme alimentaire et d'abreuvement	Régulier, durée d'élevage normale	Zone d'élevage (Niayes, périurbaine et rurale)	Banabanas, restauration commune, hôtel	Mode de vie, résiste aux menaces de l'importation
3. Petit élevage	Poulailler plus ou moins aux normes	Artisanal, mais souvent adapté	Réduit: 1000 à 2000 sujets en moyenne 500 sujets	Respect du programme alimentaire et d'abreuvement	Ciblé aux périodes de fête, en fonction de la demande	Banlieues de Dakar et Pikine et autres villes intérieures	Banabanas, restaurateurs (gargotiers)	Menacés par l'urbanisation, doit se déplacer en zone d'élevage
4. Amateur	Pas de poulailler, poulets élevés dans des cages	Artisanal et inadapté, pas conforme	Très réduit: 50 à 100 sujets	En fonction des possibilités, pas de programme d'alimentation	Irrégulier, en fonction de la demande du marché	En milieu urbain, dans les habitations et communes rurales	Voisinage ou proches parents	Loisir, sans objectif précis en général

(Food and Agriculture Organization, 2014)

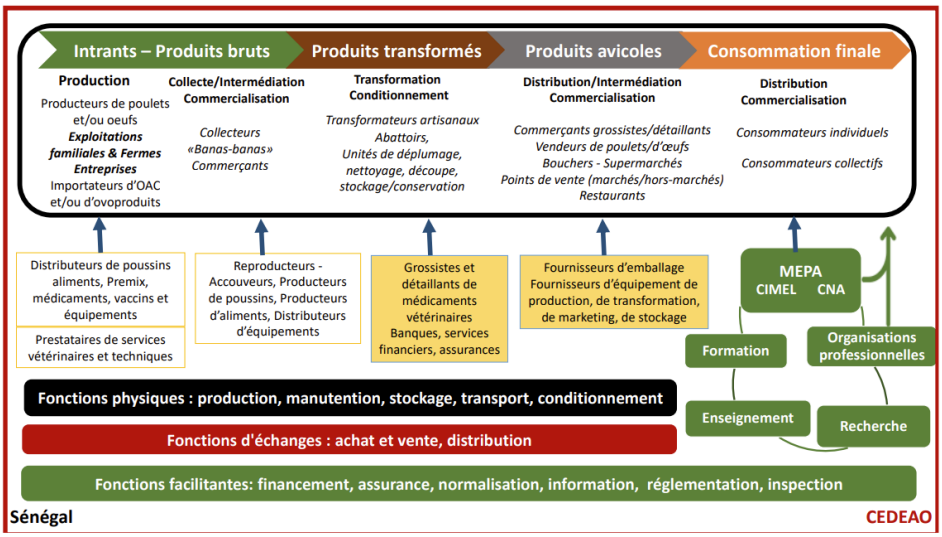
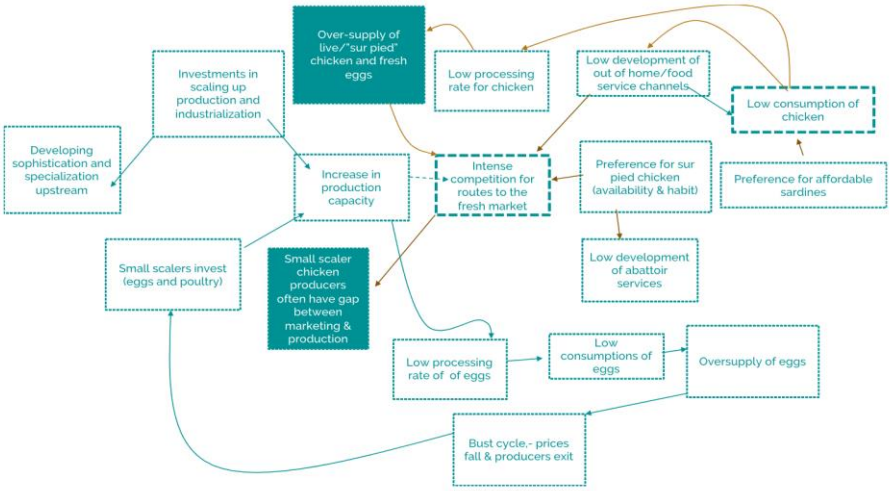


Figure 1 - Acteurs et fonctions dans la chaîne de valeur avicole du Sénégal

(LY, 2020) – Aviculture & C19

Figure 11 Critical Issues in the Poultry and Egg Chain



(Arnoldus et al., 2021)

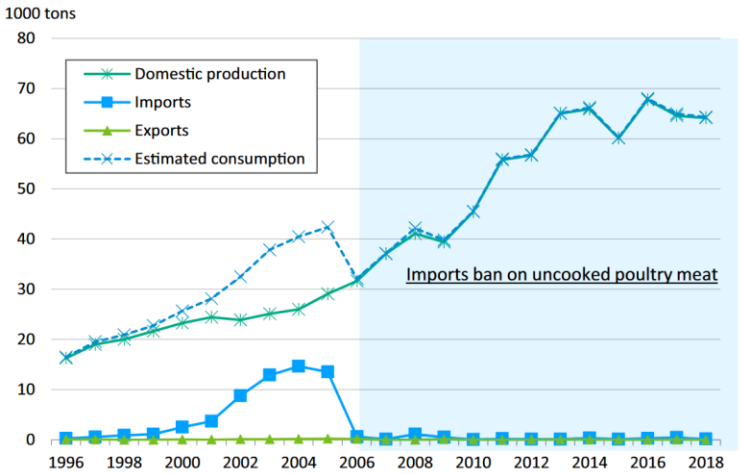
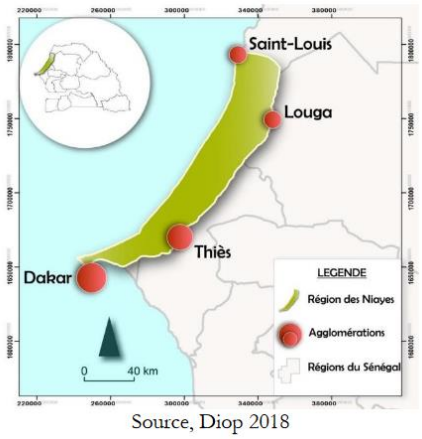


FIGURE 1 Poultry production, imports, exports, and consumption in Senegal. Source: Import and export data: UN Comtrade database (2020), Production data: FAOSTAT (2020), Consumption: based on Zamani et al. (2021)

(Boimah & Weible, 2021)

Carte 1 : Localisation de la zone des Niayes au Sénégal



Source, Diop 2018

(Ba et al., 2022)

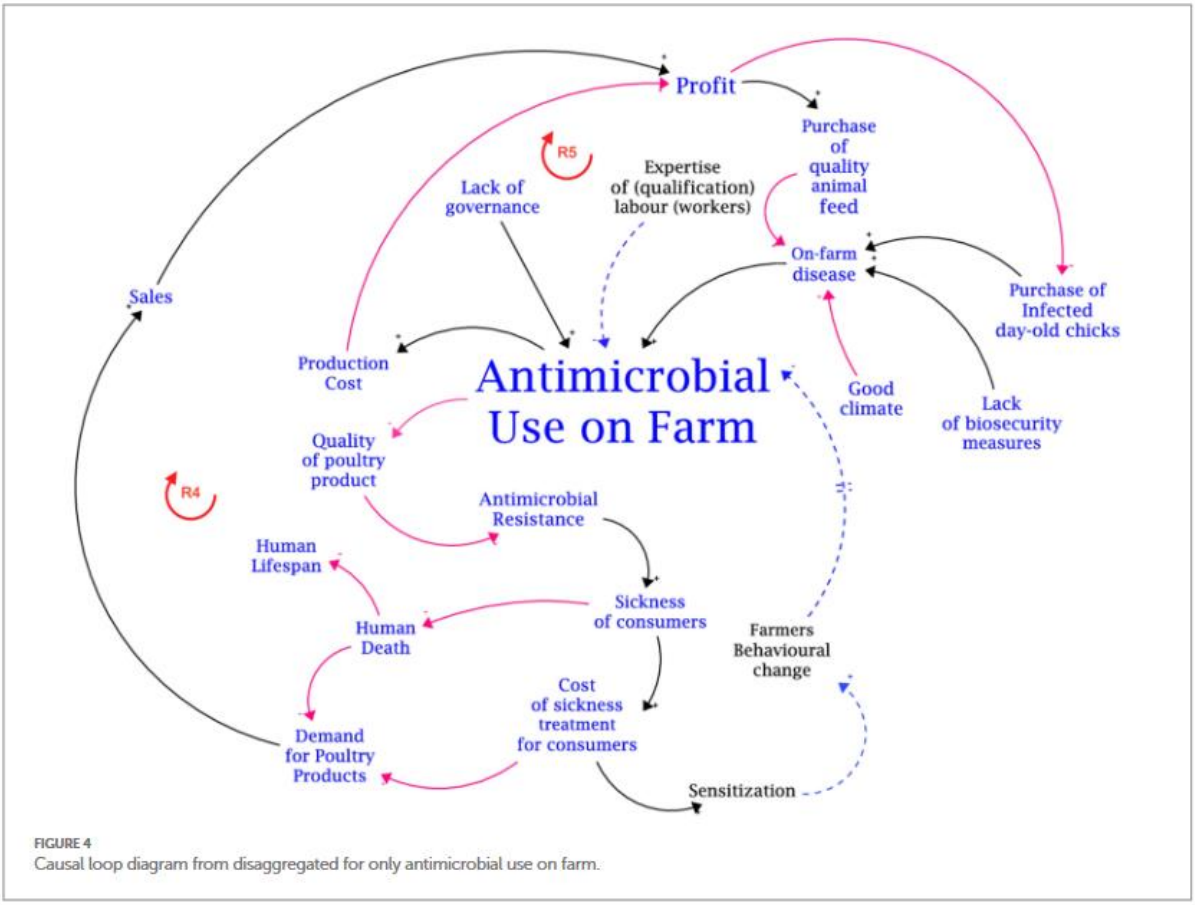


FIGURE 4
Causal loop diagram from disaggregated for only antimicrobial use on farm.

(Aboah et al., 2023)

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