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Research Note—

Added Value of Avian Influenza (H5) Day-Old Chick Vaccination for Disease Control in Egypt

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SUMMARY. The immunity profile against H5N1 highly pathogenic avian influenza (HPAI) in the commercial poultry value chain network in Egypt was modeled with the use of different vaccination scenarios. The model estimated the vaccination coverage, the protective seroconversion level, and the duration of immunity for each node of the network and vaccination scenario. Partial budget analysis was used to compare the benefit-cost of the different vaccination scenarios. The model predicted that targeting day-old chick avian influenza (AI) vaccination in industrial and large hatcheries would increase immunity levels in the overall poultry population in Egypt and especially in small commercial poultry farms (from <30% to >60%). This strategy was shown to be more efficient than the current strategy of using inactivated vaccines. Improving HPAI control in the commercial poultry sector in Egypt would have a positive impact to improve disease control.

RESUMEN. *Nota de investigación-* Utilidad de la vacunación contra la influenza aviar (H5) en pollos de un día de edad para el control de la enfermedad en Egipto.

El perfil de la inmunidad contra el virus de la influenza aviar altamente patógena H5N1 en la red de la cadena de la avicultura comercial en Egipto fue modelada con el uso de diferentes escenarios de vacunación. El modelo estima la cobertura de vacunación, el nivel de seroconversión de protección, y la duración de la inmunidad para cada nodo de la cadena y escenario de vacunación. Se utilizó el análisis de presupuesto parcial para comparar el costo-beneficio de los diferentes escenarios de vacunación. El modelo predijo que la vacunación contra la influenza aviar en pollos de un día de edad en incubadoras comerciales aumentaría los niveles de inmunidad en la población avícola total en Egipto y sobre todo en las pequeñas granjas avícolas comerciales (de <30% a >60%). Esta estrategia ha demostrado ser más eficiente que la estrategia actual de utilización de las vacunas inactivadas. Mejorar el control de la influenza aviar de alta patogenicidad en el sector avícola comercial en Egipto tendría un impacto positivo para un mejor control de la enfermedad.

Key words: avian influenza, vaccination, immunity, hatchery, network, model, Egypt, benefit-cost

Abbreviations: AI = avian influenza; B/C = benefit-cost; BR = breeders; Bro = broilers; CLEVB = Central Laboratory for Evaluation of Veterinary Biologicals; DOC = day-old chick; FAO = Food and Agriculture Organisation of the United Nations; GOVS = Government Veterinary Services; GP = grandparent; H = hatcheries; HI = hemagglutinin inhibition; HPAI = highly pathogenic avian influenza; HVT = herpes virus of turkey; Ic = cumulated incidence; Lay = layers; LE = Egyptian pound; NLQP = Reference Laboratory for Veterinary Quality on Poultry Production; Sc = scenario.

H5N1 highly pathogenic avian influenza (HPAI) viruses emerged in Egypt in early 2006. During the first wave of outbreaks, only stamping out (within 3 km of the initial outbreak), quarantine surveillance, and some movement control (within a 7-km radius from the outbreak location) measures were implemented in an attempt to contain the disease, with only limited success. Initially, emergency vaccination was used to protect grandparent and parent flocks. However, the disease spread to most Governorates within a few weeks and the country was declared endemic in July 2008. The veterinary authorities considered vaccination to be the most efficient tool in controlling this infectious disease. In March 2006, the decision was taken to vaccinate all commercial flocks, followed by mass vaccination of household poultry, starting in May 2007. An assessment study performed by the Food and Agriculture Organisation of the United Nations (FAO) has highlighted substantial limitations in current immunization practices, which have not curbed the spread of infection or improved public health safety (14,20).

Vaccination against avian influenza (AI) is currently being implemented worldwide, mostly using inactivated vaccines that are not applicable to day-old chicks (DOCs) (15). Since the start of vaccination efforts against H5N1 HPAI, the need for a suitable hatchery-level vaccination administered to day-old chicks (DOCs) and day-old ducklings has been raised in order to ensure adequate implementation of vaccination, earlier onset of immunity despite the presence of maternally derived antibodies, and protection of a large proportion of poultry populations while ultimately lowering the financial burden for the government and producers (7,9,11). Since November 2012, a recombinant HVT (herpes virus of turkey) AI

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Table 1. Description of the vaccination scenarios and related protocols tested by the study model.

DOC source	Integrated hatcheries		Nonintegrated hatcheries		
DOC destination	Integration (Sector 1)	Clients (Sector 2 and 3)	Large farms (Sector 2)	Medium farms (Sectors 2 and 3)	Small farms (Sector 3)
Scenario 1	Farm vaccination[A]	Farm vaccination	Farm vaccination	Farm vaccination	Farm vaccination
Scenario 2	Hatchery[B]	Farm vaccination	Farm vaccination	Farm vaccination	Farm vaccination
Scenario 3	Hatchery	Hatchery	Farm vaccination	Farm vaccination	Farm vaccination
Scenario 4	Hatchery	Hatchery	Hatchery	Farm vaccination	Farm vaccination
Scenario 5	Hatchery	Hatchery	Hatchery	Hatchery	Farm vaccination
Scenario 6	Hatchery	Hatchery	Hatchery	Hatchery	Hatchery

[A]Farm vaccination = birds older than 7 days old are vaccinated at the farm with inactivated vaccines.
[B]Hatchery vaccination = DOCs are vaccinated with rHVT vaccine in the hatchery.

vaccine has been commercialized and applied in some industrial hatcheries in Egypt (8,9). However, the use of inactivated vaccines remains the most common vaccination strategy currently in place in Egypt.

Network analysis approaches (6,21) have been developed to study complex socioeconomic interactions such as influence or knowledge spreading. The analysis is based on the network paradigm, which states that emergent properties appear from the study of a network of individuals that will not be observed by looking at each individual separately. The principle of network analysis is to study the interactions between the nodes of the networks, which could be actors or group of actors (in our context groups of poultry farming/production types). Those interactions are called *links* or *edges* and could represent social contact or exchange of goods (e.g., animals). Network analysis has been widely applied in animal production/health to study movements of animals along the value chains (18). Recent studies have looked at the combination of animal movement network and infectious models to study the spread of animal diseases through the value chain (16). Analysis of nodes and network properties could provide essential information on the role of each node in terms of animal movement or disease spread, and therefore help identify critical control points to target disease surveillance or control measures in the network (16).

In this study we proposed to combine network analysis of poultry production systems with an immunity model to study the profile of avian influenza immunity through the commercial poultry production network in Egypt according to different vaccination strategies. The objective of this study was to compare the cost effectiveness of different vaccination scenarios (and schedules) based on the vaccine types currently registered in Egypt: inactivated AI vaccines and HVT-AI vaccine. This study was performed independently as a request from the General Organisation of Veterinary Services (GOVs) in Egypt and the FAO to assess the added value and feasibility of implementing AI DOC vaccination in hatcheries of the different production sectors in Egypt and to draw recommendations on the integration of this approach in the next national vaccination strategic plan.

MATERIALS AND METHODS

Poultry network organization data collection. A cross-sectional survey was carried out from May to July 2013 in a set of randomly selected farms in each of the branches of the poultry production tree. Data collection followed an ego-centric approach whereby all in-going and out-going bird movements between the selected and contact farms were recorded. Then a snowball approach was applied to collect similar information in randomly selected contact farms. With respect to the destination of DOCs from breeder farms and hatcheries, only Governorate-level information was available. Random sampling of small broiler and layer farms was performed in order to fill the data gaps. Data were collected from a total of 140 farms, including all the grandparent farms ($n = 4$), all breeder (broiler and layer) farms ($n = 19$), and 15% of the commercial layer and broiler farms ($n = 119$). In addition, interviews with key actors from the poultry production network ($n = 10$, public institution employees, and private vaccine manufacturers), were performed.

With the use of structured questionnaires, demographic and production information (type of poultry production[s], farm total capacity per year, total volume of DOC production per year, origin and destination of the DOCs) were collected. Information on AI vaccination strategy (vaccine coverage, vaccine type, vaccination protocol, and perception of AI vaccination [including DOC vaccination]) was also collected. Data on the organization of the poultry production network in Egypt were also collected from peer-reviewed scientific literature and grey literature provided by GOVs, private poultry companies, and private vaccine suppliers (GOVs census, 2012; CEVA poultry database, 2013) (12).

Vaccine efficacy data collection. Quantitative data on avian influenza vaccine efficacy were collected from peer-reviewed scientific and grey literatures (reports on laboratory and field evaluation in Egypt) provided by GOVs, the reference laboratory for veterinary quality on poultry production (NLQP) and the central laboratory for evaluation of veterinary biologicals (CLEVB) (CLEVB, internal reports on inactivated vaccine batch release testing in Egypt, 2013) (2,3,4,7,8,9,13,15,17,19).

Network construction. A model of the Egyptian poultry production network, based on the type of poultry production (i.e., grandparents, breeders, layers, or broilers) and production sectors (Sectors 1–4) aggregated at the national level and for a period of 1 yr, was developed with the use of a social network analysis approach (12). A primary model was developed based on literature data and information gathered through key informant interviews in the various poultry production sectors. This model was then completed and validated with data obtained from the cross-sectional survey conducted at farm levels. Each node represented a type of poultry production; each link represented either the movement of eggs (between breeder farms and hatcheries) or the movement of DOCs (between hatcheries and commercial broiler/layer farms). All the links were directed; that is, the links between the nodes showed the direction in which DOCs were moved from one node to another. Furthermore, directed-weighted matrices were developed based on the direction and volume of exchange of DOCs between nodes. Attribute tables were generated to provide information on the type of production (grandparent [GP], breeder [BR], hatchery [H], layer [Lay], or broiler [Bro]), the production sector (1–4), farming type (integrated, semi-integrated, or nonintegrated), and the number of birds (heads) on the farms.

Network analysis. Centrality indices such as out-degrees (number of outgoing links, i.e., number of nodes that receive DOC from a specific node); in-degrees (number of incoming links, i.e., number of nodes that send DOC to a specific node) and betweenness (number of shortest paths between nodes that a node is connected to, i.e., the intermediary position of a node in the network in terms of DOC movements) were calculated to assess the role of each node in the DOC distribution network (6,21). The network centralization index was used to measure how far the network departs from a network where all nodes have the same degree (an index of 0) and to identify whether highly connected nodes are present, which could possibly be targeted for DOC vaccination (6).

Analysis of network connectivity with the use of the cut-point analysis was performed to assess the structure of the network and to identify nodes that have a key role in distribution of DOC through the network, independent of their centrality level, i.e., to assess critical nodes for which removal would increase the number of subcomponents in the network. Structural

Table 2. Vaccine coverage parameters used in the model and estimated by expert opinion elicitation.

Type of production	AI vaccine type	Vaccination protocol	Vaccine coverage, mean % (Ic 95%)	Statistical distribution
Grandparents (GP) Breeder integrated	Inactivated	Four to five doses before egg-laying age	97 (96–98)	Triangle (95;98;100)
Breeder large Breeder medium		Three doses before egg-laying age and one to two doses during egg-production phase	97 (96–98)	Triangle (95;98;100)
	rHVT and inactivated (prime boost)	One dose of rHVT in DOC and one dose of inactivated vaccine at the age of 20 wk	97 (96–98)	Triangle (95;98;100)
Broiler integrated Broiler large farms	Inactivated	One or two doses	97 (96–98)	Triangle (95;98;100)
Broiler medium and small farms	Inactivated	One dose	40 (36–44)	Triangle (20;40;60)
All broilers	rHVT	One dose	97 (96–98)	Triangle (95;98;100)
	rHVT and inactivated (prime boost)	One dose rHVT One dose inactivated	97 (96–98)	Triangle (95;98;100)

equivalence was performed with the use of the Euclidian distance to identify clusters of nodes in the network with interchangeable positions (6). The structural-equivalence clustering coefficient measures the average proportion of connections that exist among neighbors of a node, divided by the number of possible connections that could have existed (6). Network connectivity and structural equivalence analysis were used to define the different DOC vaccination scenarios to be tested in the study.

Vaccination scenarios. Six vaccination scenarios were identified based on centrality and connectivity analysis of the structure of the poultry production network and age at vaccination (vaccination of birds >7 days old and/or DOCs; Table 1). DOC vaccination of long-cycle birds (breeders and layers) was only considered as a prime-boost strategy (vaccination at day old in hatcheries and boost at 20 wk in farms); whereas DOC broiler vaccination was considered as one single shot of vaccine.

Modeling the immunity distribution. A stochastic simulation model was developed in an Excel spreadsheet (Microsoft Corp.) and the Excel 'add-in' software @Risk (Palisade Corp.) was used to estimate the vaccine coverage (proportion of vaccinated birds from the total population, i.e., birds that received a shot of vaccine), the protective seroconversion level (proportion of birds with hemagglutinin inhibition [HI] titers greater than $4\log_2$) and the duration of immunity (number of weeks where more than 70% of the birds had a protective seroconversion level) for each nodes and according to each vaccination scenarios (10).

Model parameters. The parameters considered in the model were type of vaccines used, vaccination coverage per poultry production component (node), efficacy of the vaccine used (in terms of seroconversion and duration of protection), number of vaccine doses used, vaccination schedule (time interval between doses) and cost per 100 doses of a vaccine. A probability distribution was initially defined *a priori* and fit to each parameter of the model as explained in the next subsection. Detailed accounts of the parameters used in the model are provided in Tables 2–4.

Parameter estimations. Probability distributions were assigned to each model parameter with the use of published data, field data, or expert opinions. When limited information was available, uniform and triangular distributions were considered. Triangular distributions were used when the most likely minimum and maximum values were known. Gamma distribution, the most frequently used distribution to model dynamic variables such as time, was used to model the duration of immunity. Data on vaccination coverage were retrieved from the correlation of the total number of vaccine doses released in the country and data collected during the field study on the level of vaccine coverage applied in different types of production (Table 2). For inactivated vaccines, an error margin of 5% was applied to account for mortality and logistical errors during the vaccination process. For the rHVT vaccine, the parameter value was fitted to the data collected from field experimentation of the vaccine. Data from laboratory and field vaccine trials on different types of vaccines were provided by FAO and NLQP and were used to estimate the vaccine efficacy parameters (proportion of seropositive birds [HI titer$>4\text{Log}_2$]) and duration of immunity following vaccination. Opinions of a panel of experts ($n = 27$): NLQP ($n = 5$), CLEVB ($n = 4$), GOVs ($n = 4$), and private poultry producers ($n = 14$) were obtained in an expert opinion elicitation workshop organized by FAO. Briefly, estimates of parameters and distributions were presented to the panel and group discussions ($n = 3$) were carried out. The outcomes of the three group discussions were combined. When discrepancies were noticed, they were presented back to the panel for discussion and consensus (1).

Table 3. Seroconversion parameters used in the model and estimated by expert opinion elicitation.

Type of production	AI vaccine type	Vaccination protocol	Seroconversion (HI titer $>4\text{Log}_2$), mean % (Ic 95%)	Statistical distribution
Grandparents (GP)	Inactivated	Four to five doses before egg-laying age	92 (91–93)	Uniform (90;95)
Breeder integrated Breeder large Breeder medium		Three doses before egg-laying age and one to two doses during egg-production phase	92 (91–93)	Uniform (90;95)
	rHVT and inactivated (prime boost)	One dose of rHVT in DOC and one dose of inactivated vaccine at the age of 20 wk	92 (91–93)	Uniform (90;95)
Broiler integrated	Inactivated	One dose	43 (40–46)	Triangle (30;40;60)
Broiler large farms		Two doses	92 (91–93)	Uniform (90;95)
Broiler medium and small farms	Inactivated	One dose	43 (40–46)	Triangle (30;4;60)
All broilers	rHVT	One dose	92 (91–93)	Uniform (90;95)
	rHVT and inactivated (prime boost)	One dose rHVT One dose inactivated	92 (91–93)	Uniform (90;95)

Table 4. Duration of seroprotection parameters used in the model and estimated by expert opinion elicitation.

Type of production	AI vaccine type	Vaccination protocol	Duration of immunity (weeks), mean % (Ic 95%)	Statistical distribution
Grandparents (GP)	Inactivated	Four to five doses before egg-laying age	48 (38–56)	Gamma (6;8)
Breeder integrated Breeder large		Three doses before egg-laying age and one to two doses during egg-production phase	72 (57–77)	Gamma (6;12)
Breeder medium	rHVT and inactivated (prime boost)	One dose of rHVT in DOC and one dose of inactivated vaccine at the age of 20 wk	72 (57–77)	Gamma (6;12)
Broiler integrated	Inactivated	One dose	1 (0.5–2.5)	Gamma (1;2)
Broiler large farms		Two doses	12 (8–16)	Gamma (2;6)
Broiler medium and small farms	Inactivated	One dose	1 (0.5–2.5)	Gamma (1;2)
All broilers	rHVT	One dose	2.9 (1.6–4.4)	Gamma (1;3)
	rHVT and inactivated (prime boost)	One dose rHVT One dose inactivated	4 (2–6)	Gamma (1;4)

Model outputs. For each vaccination scenario and for each node of the network, the model calculated 1) the proportion of vaccinated birds (vaccination coverage), 2) the proportion of seroprotected birds (seroconversion), 3) the number of protected weeks (duration of immunity), and 4) the cost of vaccination. These values were calculated for each node of the network according to the vaccination protocols applied both in the node and its adjacent nodes and to the strength of links between the nodes (volume of DOC exchange and immune status of DOCs). Analysis was then performed to compare outputs between the different vaccination scenarios.

Model simulation and sensitivity analysis. Monte Carlo simulations were performed with 10 runs of 10,000 iterations each; i.e., 10,000 data points were generated from each run to calculate the output variables. The simulations provide a mean and a standard deviation for each variable for each vaccination scenario.

Sensitivity analysis was performed to assess the importance of each input parameter on the outputs of the model. The influence of the stochastic distributions assigned to the model input parameters was also assessed.

Spatial analysis. Spatial analysis of the distribution of the immunity according to the different vaccination scenarios was performed to account for spatial clustering of the different poultry production types (e.g., GP production is concentrated in three Governorates; 80% of the breeders are located in six Governorates; 70% of the layers in five Governorates; 60% of the broilers, and the total poultry population is concentrated in four Governorates). Poultry census data at the Governorate level (GOVs census, 2012) was used for the spatial analysis in point density. Data were aggregated according to the five production types (GPs, breeder broilers, breeder layers, and large and small broiler farms). For each vaccination scenario the percentage of vaccine coverage, protective seroconversion, and duration of immunity (model outputs) were weighted according to the poultry density (for each production type) per Governorate for each poultry category. From these data 18 maps were produced to represent the density of vaccine coverage, protective seroconversion, and duration of immunity according to the different vaccination scenarios.

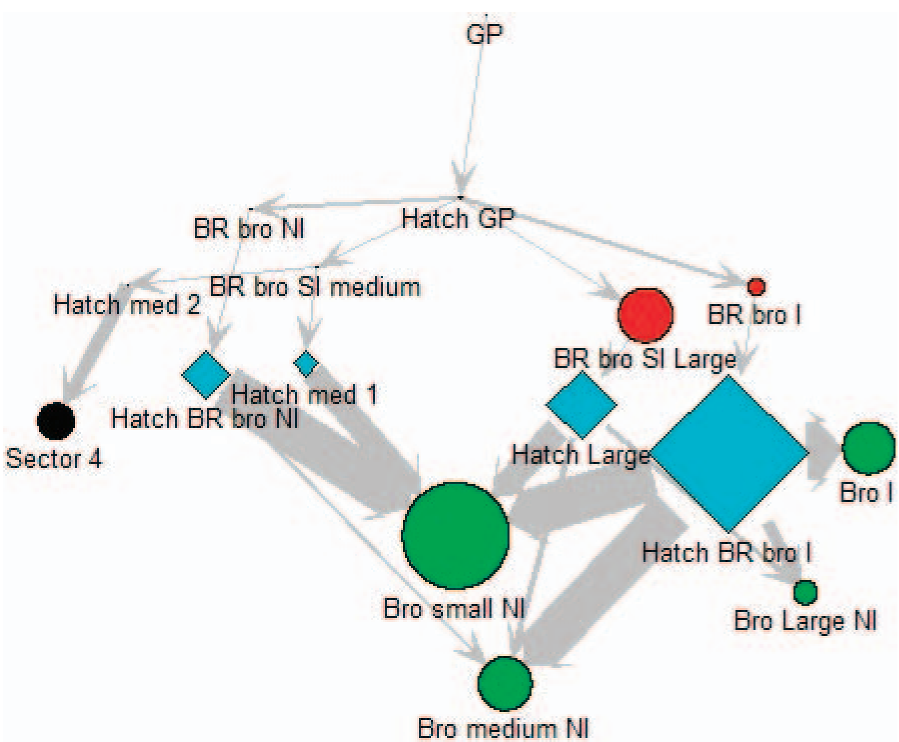

Fig. 1. Model of Egypt poultry production network. The types and colors of nodes represent the different types of productions (integrated [I], semi-integrated [SI], or not integrated [NI]), grandparents (GP) and breeders (BR) (red circles), hatcheries (Hatch) (light blue diamonds), commercial broilers (Bro) (green circles), and sector 4 (black circle). The size of the nodes represents the number of birds per nodes. The arrows represent the movement of eggs or DOC between the nodes and the size of the arrows the volume of eggs or DOC for each movement.

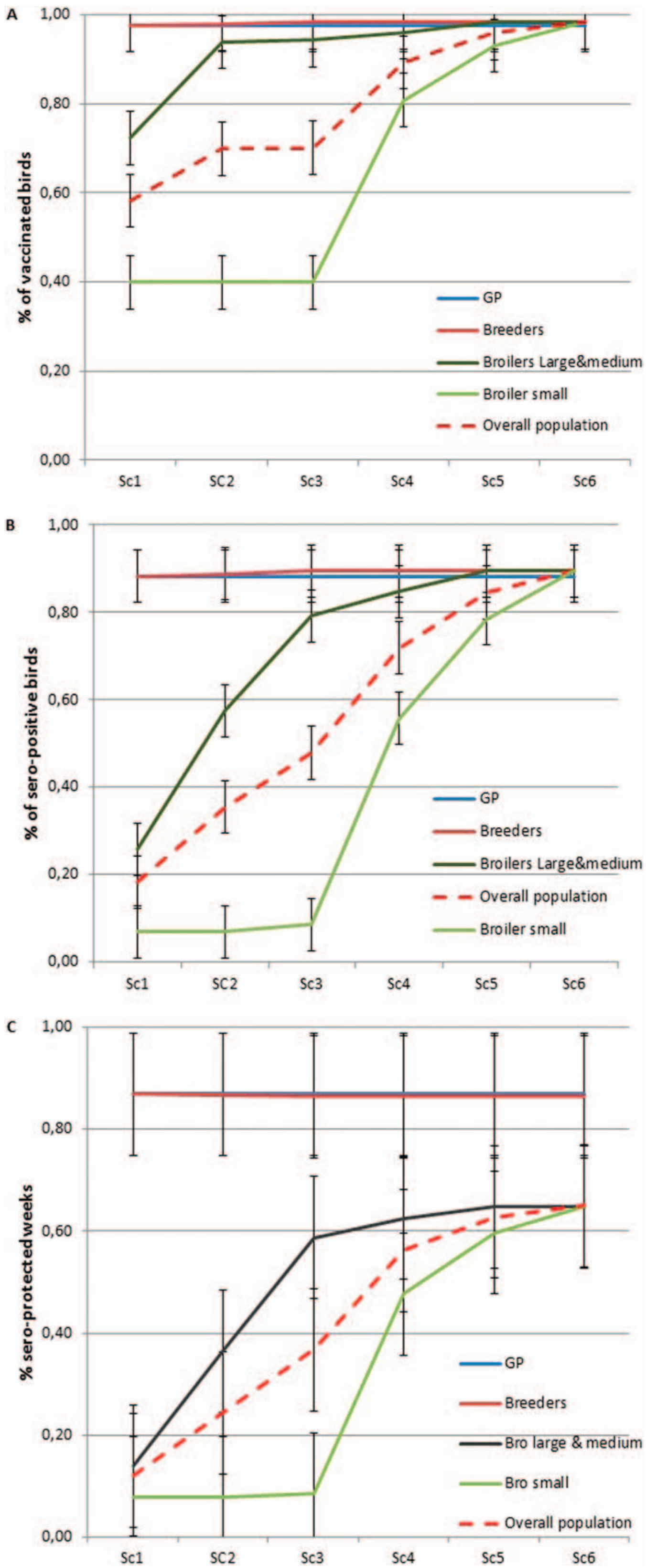

Fig. 2. Evolution of the vaccine coverage rate (A), the positive seroconversion rate (B), and the duration of immunity (rate of seroprotective weeks as defined as the number of weeks with >70% seropositive birds and a geometric mean titer (GMT) ≥20) (C), expressed as a percentage of the bird population per poultry production type and according to the different vaccination scenarios tested in the model: farm vaccination only with inactivated vaccine (Sc1); vaccination of DOC in integrated farms, Sc1 for the other productions (Sc2); Sc2 plus DOC vaccination of integration clients (Sc3); Sc3 plus DOC vaccination in large breeder hatcheries (Sc4); Sc4 plus DOC vaccination in medium breeder hatcheries (Sc5); DOC vaccination across all sectors (Sc6).

Cost-effectiveness, benefit-cost, and break-even analysis. Analysis of the cost effectiveness of the different vaccination scenarios was conducted with the use of seroconversion rate and duration of protection as effectiveness measures. The cost was estimated for each scenario with the use of vaccination costs of 28 Egyptian pounds (LE) and 31 LE for inactivated and rHVT vaccines, respectively, based on revision of initial estimates made by Hinrich (5). Benefit-cost analysis was done with the use of partial budget analysis to estimate the B/C ratio for each vaccination scenario and poultry production type. The benefits were limited to the value of the avoided production losses in the vaccinated population and calculated for a disease cumulated incidence (Ic) of 3.5% (minimum level observed in Egypt from surveillance data). The costs were defined as the vaccination costs and the value of the losses in the nonvaccinated population. The production losses due to AI infection were a function of the risk of infection at a certain point of time (Ic) and the vaccine efficacy in terms of seroprotection rate and duration of protection. A break-even analysis was then performed to estimate the threshold level of disease Ic where vaccination would no longer be cost effective (B/C ratio >1).

Acceptability study. A qualitative survey on the acceptability and feasibility of AI DOC vaccination in hatcheries was carried out based on field data (n = 20 farmers) and expert elicitation workshop involving 13 experts and 14 poultry producers. Participants were asked to provide their perception on the advantages and limitations of AI DOC vaccination along with their interest in this strategy. They were asked to provide arguments supporting their respective answers. From the answers provided by participants, four categories of topic were defined (immunity, application, cost, and strategy). The results were analyzed with the use of these aggregated categories.

Data analysis. All data collected were entered into an Access database (Microsoft Access 2007). Network development and analysis were performed with the use of the "R" software version 2.1, sna package (Butts, C. T. [2010], "sna: Tools for Social Network Analysis", R package version 2.1). The immunity model was developed with the use of the @Risk software (Vose Palissade Corp.) application within Excel spreadsheet (Microsoft Excel 2007). This application also allowed setting distribution of parameters and performing simulation and sensitivity analysis. ArcGIS 9.1 (ESRI, Redlands, CA, USA) was used to generate maps. Acceptability study data were analyzed with the use of Microsoft Excel 2007 software.

RESULTS

Network analysis of the Egyptian poultry value chain. Over 770 million of commercial DOCs are produced every year in Egypt from five different categories of breeder farms and distributed to eight different types of production farms based on size and biosecurity levels (Fig. 1). Broiler birds represent 95% of the total commercial poultry in Egypt (665 million heads). About 50% of the total DOCs are produced by integrated breeder hatcheries (i.e., farms that integrate all the production from breeders to commercial broilers and sometimes GPs, and provide feed and technical support to all their farms). About 4.5% of commercial DOCs were distributed to sector 4 (equivalent to 35% of the total poultry population size in this sector).

Small commercial broiler farms were the most connected type of production in the network and received DOCs from breeders in all production sectors. About 50% of the small commercial broiler farms

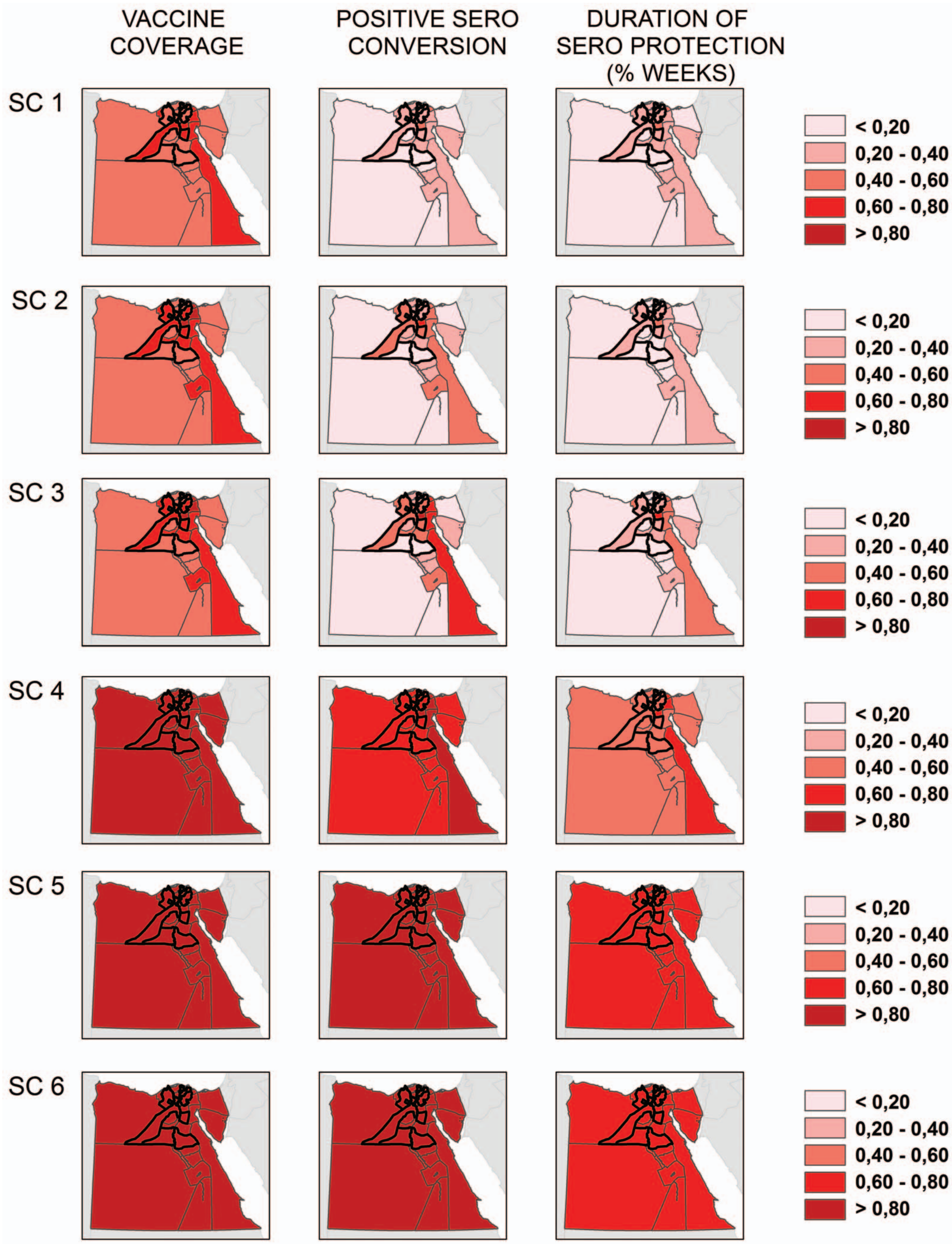

Fig. 3. Spatial distribution of the bird population immunity against AI according to the different vaccination scenario tested in the model: farm vaccination only with inactivated vaccine (Sc1); vaccination of DOC in integrated farms (Sc2); Sc2 plus DOC vaccination of integration clients (Sc3); Sc3 plus DOC vaccination in large breeder hatcheries (Sc4); Sc4 plus DOC vaccination in medium breeder hatcheries (Sc5); DOC vaccination across all sectors (Sc6). For each scenario the percentage of vaccine coverage, protective seroconversion, and duration of immunity (model outputs) were weighted according to the poultry density (for each production type) per Governorate for each poultry category. The six Governorates classified at high risk of HPAI infection are highlighted in bold (Menofia, Behera, Sharkia, Dakahlia, Menia, and Giza).

buy DOCs from large (18%) and large integrated (32%) breeder farms (Fig. 2). Network analysis demonstrated that most of sector 3 commercial poultry farms relied on DOC supply from sector 1 and sector 2 hatcheries. Only 20% of sector 3 farms receive their DOCs from sector 3 breeder hatcheries. Moreover, the connection between the commercial poultry network and sector 4 was very limited, with only 35% of sector 4 poultry being supplied by the commercial sector. These results thus highlighted the fact that all the nodes, except from the GP hatchery, could be reached by more than one alternative pathway in the network. Vaccination scenarios were developed based on the analysis of these pathways (Table 1).

Immunity distribution profile against AI within the poultry production network. The model predicted that targeting DOC AI vaccination in industrial and large hatcheries (scenario 4 [Sc4]) would be sufficient to increase the immunity in the overall poultry population up to 80%. The vaccine coverage in the broiler population would especially increase above the critical threshold levels of 80%. The immunity levels in this type of production would increase above

Table 5. Comparative cost-effectiveness and benefit-cost analysis of vaccination strategies with the use of only inactivated or rHVT-H5 and inactivated vaccines (prime-boost) according to the different type of poultry production.

Type of poultry production	Vaccination protocol (scenario)	Vaccination effectiveness: seroprotected birds (%)	Vaccination costs (Egyptian pound) for 100 doses of vaccine (3)	Benefit-cost[A] ratio (B/C) of vaccination for Ic[B] = 1%	Break-even point (level of Ic for which B/C < 1)[C]
Grandparents	Inactivated vaccines only (Three to five doses) (Sc1)	0.92	84–140	1.2	0.015
Breeders/layers	Inactivated vaccines only (Three to five doses) (Sc1)	0.92	84–140	1.2	0.015
	Prime with rHVT-H5 (DOCs) and boost with inactivated vaccine (7 days old) (Sc)	0.92	59.5	3.7	0.007
Broilers	One dose of inactivated vaccine at 7 days of age	0.1–0.33[D]	28	0.1–0.4[D]	B/C always <1 (for Ic = 1; B/C = 0.43)
	One dose of rHVT-H5 vaccine (DOCs)	0.7–0.8[D]	31.5	1.5–2[D]	0.005–0.01
	Prime with rHVT-H5 (DOCs) and boost with inactivated vaccine (7 days old)	0.7	59.5	1.3	0.01

[A]Benefit reduced to the monetary value of the number of avoided production losses thanks to vaccination effectiveness;
[B]Cumulated incidence.
[C]Using the minimum cost of vaccination for inactivated vaccines (with the use of three doses of vaccine = 84 EPD).
[D]Range varies according to the production sector (lower value = small broiler farms; higher value = integrated broilers).

60% both for seroprotection and duration of protection (2,3,4,19). This would contribute toward improving the control of HPAI in the poultry population in Egypt. This strategy would also improve the duration of protection in long-cycle birds (GP, parent/breeder and commercial layers) by 20%, which would contribute to the reduction of risks of disease introduction within this type of production system. Additional vaccination of DOCs in medium breeder hatcheries (Sc5) was sufficient to increase the duration of protection over 60% for all production types. The spatial distribution profile of AI immunity was heterogeneous across Governorates, which reflected the spatial cluster distributions of the different poultry production types. However, the spatial analysis outputs for the six Governorates classified at high risk (i.e., Menofia, Behera, Sharkia, Dakahlia, Menia, and Giza) were similar to the homogeneous population model outputs described above (Fig. 3).

Cost-effectiveness and benefit-cost analysis of the different vaccination scenarios against AI. The results of the cost-effectiveness study highlighted the fact that implementing DOC vaccination either as prime-boost strategy with one boost of inactivated vaccine or as single-dose vaccination will be cost effective (in terms of vaccine coverage, seroprotection, and duration of seroprotection) both for long-cycle and broiler birds irrespective of the vaccination protocol used (from three doses of inactivated vaccine onwards) (Table 5). The results of the benefit-cost and break-even analysis highlighted the limitation of the current vaccination of broilers with inactivated vaccine. Indeed, this strategy was found inefficient (B/C <1) even if the risk of infection was 100% (Table 5). The strategy using rHVT-vectored vaccines would be efficient in the broiler production system even at low cumulated disease incidence (Ic) levels (1%). This criterion will be easily met under the current Egyptian avian influenza epidemiological situation (Ic levels were estimated between 3.5 and 9% during low- and high-risk periods, respectively) (GOVs national surveillance database, 2006–2013).

Acceptability of DOC versus farm vaccination strategy. Results of the acceptability study of DOC AI vaccination showed high interest in DOC vaccination strategy (81% of participants); however, 19% of the participants referred to implementation issues linked to this strategy. Of the respondents, 81% believed that DOC vaccination would improve vaccine coverage and protection of the birds against HPAI. The second important advantage mentioned by the participants (38%) was about the application of DOC vaccination, which reduces the stress and mortality rate during the vaccination process and reduces the biosecurity risk associated with the vaccinator team (19%). However, 19% of the participants mentioned implementation issues in DOC vaccination. Acceptability of mass hatchery vaccination (24%) and interference of AI DOC vaccination with other vaccines (31%) were the most important constraints mentioned by the participants. Acceptability was mentioned both at the hatchery level (40%) because of the high-tech process, and at the client level (29%) because of trust issues on the implementation of the vaccination ("how can I be sure that my DOCs are vaccinated as specified by the supplier"). This study also highlighted the fact that knowledge on the technical advantages and limitations of DOC vaccination was variable. There is a need to raise awareness both for animal health practitioners and poultry farmers on DOC AI vaccination processes. Additional field validation of these vaccines was also highlighted as a prerequisite to ensure its application. Further study on the feasibility and acceptability of DOC vaccination in nonintegrated and traditional hatcheries is required in order to decide the expansion of DOC vaccination into small-holder and backyard sectors (sectors 3 and 4).

DISCUSSION

This study demonstrated the interest of combining network analysis and immunity model to assess the efficacy of AI vaccination scenario in Egypt. The model predicted that targeting DOC AI vaccination in sector 1 and 2 hatcheries would increase immunity levels in the overall poultry population in Egypt, and especially in sector 3 small commercial poultry farms, up to sufficient levels to improve HPAI disease control in Egypt. This strategy was shown to be more efficient than the strategy using inactivated vaccines. However, this strategy could face implementation issues, as DOC AI vaccination requires specific training and cold chain equipment (e.g., liquid nitrogen). These practical issues could be addressed by promoting a private–public partnership and collaboration with the vaccine distributors, who can provide equipment and specific training for application of HVT-AI vaccines in hatcheries. This will be a requirement if expansion of this practice is to happen. Moreover, because of the current limited knowledge on the efficacy of those vaccines to provide a long-term protective immunity, a prime-boost strategy is still recommended. This study has demonstrated the added value of this prime-boost strategy both in long- and short-cycle commercial chickens. In long-cycle birds, the number and timing of booster doses need to be based on serosurveillance monitoring data if less than 70% of the birds have positive seroconversion rate. A recent study has shown long-term seroprotection of layers with the use of a prime-boost schedule of HVT-AI and inactivated H5N1 at DO and 19 wk of age, respectively (8).

This approach would have only marginal impact on immunity levels in sector 4 household poultry. Additional studies on the organization of the baladi (native) chicken and duck production networks would be required to assess the feasibility of introducing DOC vaccination in this production sector (which represents most of sector 4 poultry production). However, improving HPAI control in the commercial poultry sector in Egypt is expected to reduce the environmental viral load and therefore have positive spillover effect on the disease situation in the household sector (sector 4). An assessment of the impact of DOC vaccination strategy on disease control in commercial poultry could be done in pilot areas in Egypt where this vaccination is already in place in sector 1 and 2 hatcheries. This would also allow field validation of the metapopulation immunity model presented here. Moreover, the impact of commercial DOC AI vaccination on HPAI epidemiological situation in sector 4 could be assessed through increased surveillances in live bird markets in areas where AI DOC vaccination is practiced or vaccinated chicks distributed.

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