

DECISION SUPPORT SYSTEM FOR A REGIONAL SPREADING OF A/H1N1 INFLUENZA VIRUS

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KEYWORDS

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ABSTRACT

The evaluation of the impact of the recent inter-human A/H1N1 influenza spreading on a regional health system has been achieved using a Decision Support System. The latter includes two models: first, a stochastic model composed of a multi-agents system linked to a Geographical Information System; second, a deterministic model using the main parameters of a virus spreading. Both models have been designed in collaboration with doctors (of medicine?). The simulation software has been tested with the data available for Corsica Island and the results have been presented to the local authorities. Small experimental plans, with the main spreading parameters, help in predicting various indicators for the regional health system, such as the number of medical consultations, the number of doctors needed in the different medical areas... The final aim of this support system is for it to be used for local public health decisions, and possibly be adapted to other regions.

INTRUCTION

Since 2005, the probability of a new influenza pandemic virus was close to 1. In order to be reactive enough, we started to work on decision-aid software able to study the inter-human spreading of the H5N1 strain. Indeed, at that time, Asian countries suggested a probable person-to-person transmission of avian influenza H5N1 (Ungchusak et al. 2005). In 2008, a Chinese group even presented a probable case of inter-human contamination (Wang et al. 2008). In the meantime we were able to propose simulation software, designed by a multi-disciplinary team, including doctors in computer technology (Hill et al. 2008). The simulation was an individual based model, using current data on the existing medical areas of Corsica. The proposed software was dedicated to the H5N1 strain, and combined a Geographical Information Systems (GIS) and a Multi-Agent System (MAS) with a small world like communication between agents. This model could be viewed as a self-organizing system with an important focus on spatial distribution as a key point for the decision

aspects. However, in the proposed individual model, the main purpose was to provide indicators for the health system, thus emergent properties were not looked for and the system was too simple to look for dynamic structures at runtime.

After this first software development, we wanted to propose a more generic application. First, we had enough information to customize the software for any kind of virus (including sanitary measures and barriers). Second, we wanted to provide an easy and fast entry point for any region with spreadsheet data as input file in addition to the geographical information system link. Third, we wanted to offer the opportunity to include a basic comparison of the simulation results obtained with the spatial multi-agent simulation with a more classical deterministic model for pandemic spreading. With this last point we wanted to be able to launch a basic experimental plan with a variation of the pandemic factors (mainly the virus attack rate). Indeed, since the beginning of computer simulation, experimental design has been an active research field for improving the effectiveness of simulated systems (Kempthorne 1952) (Zeigler 1976; Kleijnen 1987; Balci and Sargent 1989).

In the first semester of year 2009, the emergence of A/H1N1 surprised many specialists (Linea 2009) and the question of a pandemic was raised (Sim and Mackie 2009). We are now certain of the pandemic but of course the future virulence and evolution is still unknown. When many factors are imprecise, simulation is a good exercise. Experimental design is then a valuable technique in the decision-making context (Kleijnen and Groenendaal 1992; Hill 1996; Amblard et al. 2003).

Since 2004, many models have been built with the avian flu in mind (Longini et al. 2004, 2005) (Fergusson et al. 2005) (Carrat et al. 2006) (Colizza et al. 2007) (Hill et al. 2008) (Das et al. 2008) and (Iwami et al. 2009). Regarding A/H5N1, model proposals are of course currently limited. A markovian model has been proposed for parameter estimation (Ross et al. 2009). The latter has been used for infectious data from an outbreak of 'Russian influenza' (A/USSR/1977 H1N1) in an educational institution. More recently, a generic serious game has been released; it has been developed by the medical center of the Erasmus University (Rotterdam) and the Ranj Serious Games company (it is even possible to play online:

http://www.thegreatflu.com/). Concerning our proposal, the inclusion of two simulation models (a classical deterministic model and a spatial stochastic multi-agents simulation) sharing a common set of parameters led to the

design of a Decision Support System (DSS hereafter) including the main sanitary measures (vaccination, prophylaxis, masks and quarantine enforcement).

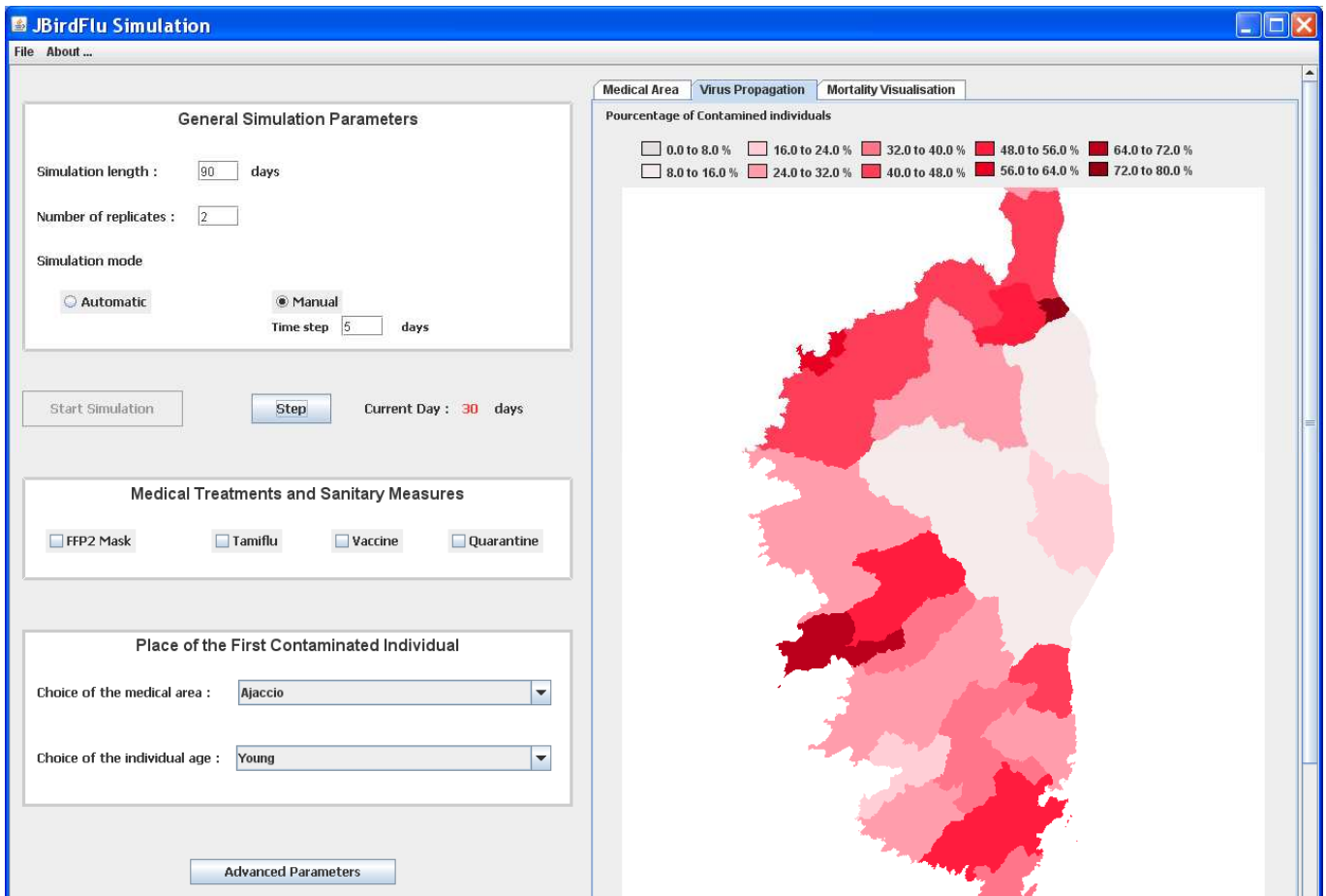


Figure 1: Graphical Result of the Interface with the Local Geographical Information System - Spatial Stochastic Simulation (Using a Multi-Agent System with A 25% Attack Rate as Main Parameter)

DESIGN OF THE DECISION SUPPORT SYSTEM

Figure 1 above presents a sample output of the interactive simulation software we developed in 2008. As mentioned in the introduction, this software was a stochastic multi-agents system connected with a Geographical information system, it is fully described in (Hill et al. 2008). The development was done using an object-oriented analysis and design with a Java implementation. We wanted to enhance this first modular software to obtain a more complete DSS intended to help decision makers in case of intensive flu virus spreading. Our system is a Model-driven DSS, compiling useful information and parameters provided by users to assist decision makers in analyzing a pandemic situation. Using two different models and personal knowledge, this tool will help identifying potential problems and thus participate in the local decision process (support is provided for medical groups, medical organizations or local medical authorities). As in many DSS we have 3 main components:

1. The data base, which includes geographical data, but also territorial and medical data.
2. The model (2 models in this DSS: the stochastic spatial multi-agent system and the deterministic model).
3. The user interface enabling doctors and specialists to run simulations and sets of experiments, thereby helping them in the decision process.

Despite the fact that one of our models uses agents representing individuals with social relationships, we do not deal with cognitive decision-making functions, i.e. we have not introduced artificial intelligence in our DSS – it would have been called an Intelligent Decision Support System (IDSS). The main UML classes of our DSS are presented in figure 2. The data base is composed of four elements: maps, statistic, territory and parameter. These are used by the simulator, which is in charge of handling the model component. Finally, the interactions with the user are obtained through the GUI, configuration and test classes.

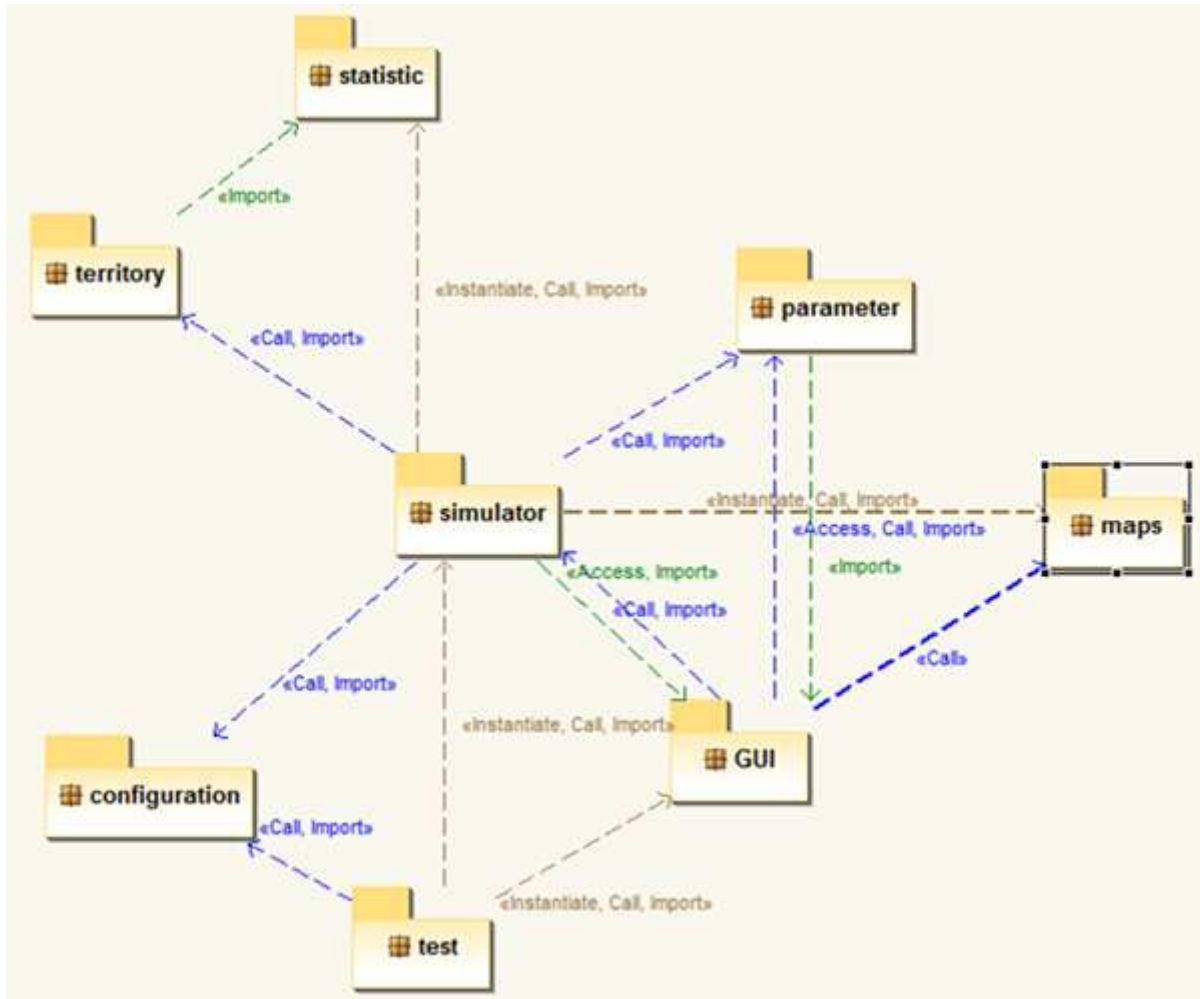


Figure 2: UML Diagram of the Main Classes (Generated from the DSS Software with eUML2)

INPUT DATA AND PARAMETERS AND DETERMINISTIC MODEL

Figure 1 showed that we have different local maps with contour for the different medical areas of Corsica. In addition, among a set of raw data we also have at our disposal for each medical area:

- The number of doctors and nurses.
- The number of inhabitants – with the number of individuals for 3 age groups: junior (below 20 years old), adult (between 20 and 60 years old) and senior.

Regarding the models parameters, both kinds of model share an XML file mapped with the XStream library to instantiate the parameter class. The file structure is as follows: the first parameter is the attack rate: `<attackRate>0.30</attackRate>`

Then, the file is split in two parts, the first one describing the characteristics of the first wave of a pandemic virus and the second one dealing with the

second wave, statistically more serious than the first wave (we have not considered more than 2 waves).

```

<firstWave>
  <ratioVirus>
    <double>0.4</double> // Junior factor
    <double>0.5</double> // Adult factor
    <double>0.1</double> // Senior factor
  </ratioVirus>
  <ratioConsultation>
    <double>3.0</double> // Junior
    <double>3.0</double> // Adult
    <double>3.0</double> // Senior
  </ratioConsultation>
  ...
</firstWave>
  
```

With this parameter set we specify for each age group: its sensitivity to the virus, the number of consultations if an individual has contracted the virus, the probability of a hospitalization and the death probability in case of hospitalization. This set of parameters is given twice, for the first and second wave.

With this approach the deterministic model can easily compute how many people are concerned in each age

group for both waves. To obtain the number of persons infected in a medical area, we simply apply the attack rate to the number of adults present in a medical area. Then the reduction factor of its age group applies (modeling the resistance), it is thus easy to specify that adults below 60 years old are more susceptible to be infected by the virus (which is a common signature for pandemic viruses). For each infected person we apply the mean consultation factor to obtain a number of medical consultations imposed by the new virus. Knowing the number of doctors in a medical area and its average number of consultations, we can determine if we need to reassign doctors in areas poorly equipped in human medical resources.

For the spatial stochastic model we have many specific parameters such a contact matrix depending on the age group (implementing a contact network), the incubation duration time (between 2 and 7 days in the case of H1N1), and so on.

An advanced parameter window (figure 4) enables the testing of sanitary measures: pre-vaccine and pandemic vaccination, antiviral drugs (prophylaxis), masks (chirurgical and FFP2). The quarantine is also considered.

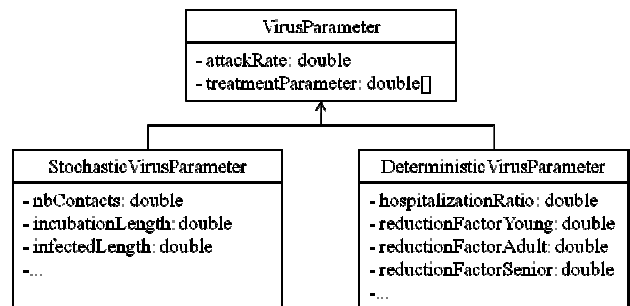


Figure 3: Subclassing of the Main Parameter Class to Facilitate the Handling of Both Model Types

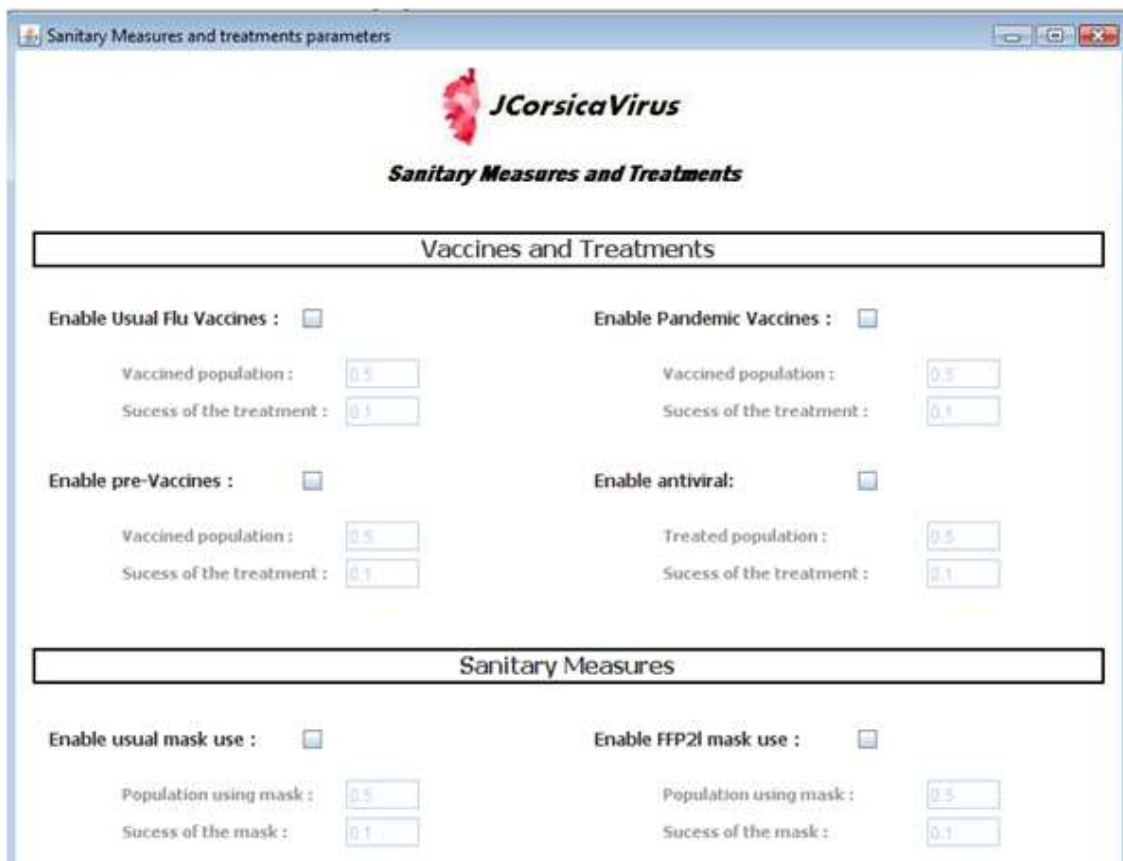


Figure 4: Parameter Window for Sanitary Measures Including: Pre-vaccines, Pandemic Vaccine, Masks (Chirurgical Masks and FFP2 Masks - and Quarantine Enforcement is also Considered but only in the Spatial Stochastic Model

TEST AND RESULTS FOR CORSICA

Our approach consists of three interdependent levels:

1. The Modeling level: This is the longest phase (following an analysis, design, verification and validation cycle.) Through a deterministic global

simulator: modelers evaluate the impact of *global parameters* (attack rate and sanitary measures) on the number of infected people. Through an individual-based stochastic simulator: They evaluate the impact of *individual-based parameters* (social network, latent and infection periods) on the number of infected people. Finally, a rough comparison between both

models allows calibrating both global and local factors.

2. Engineering level: Results of the modelling level (e.g., the number of consultations) are compared with resources (e.g., consultations achievable by doctors.)

3. Decision level: Depending on the result of the comparison of both usage and availability of resources, these resources (doctors) can be reallocated in local medical areas.

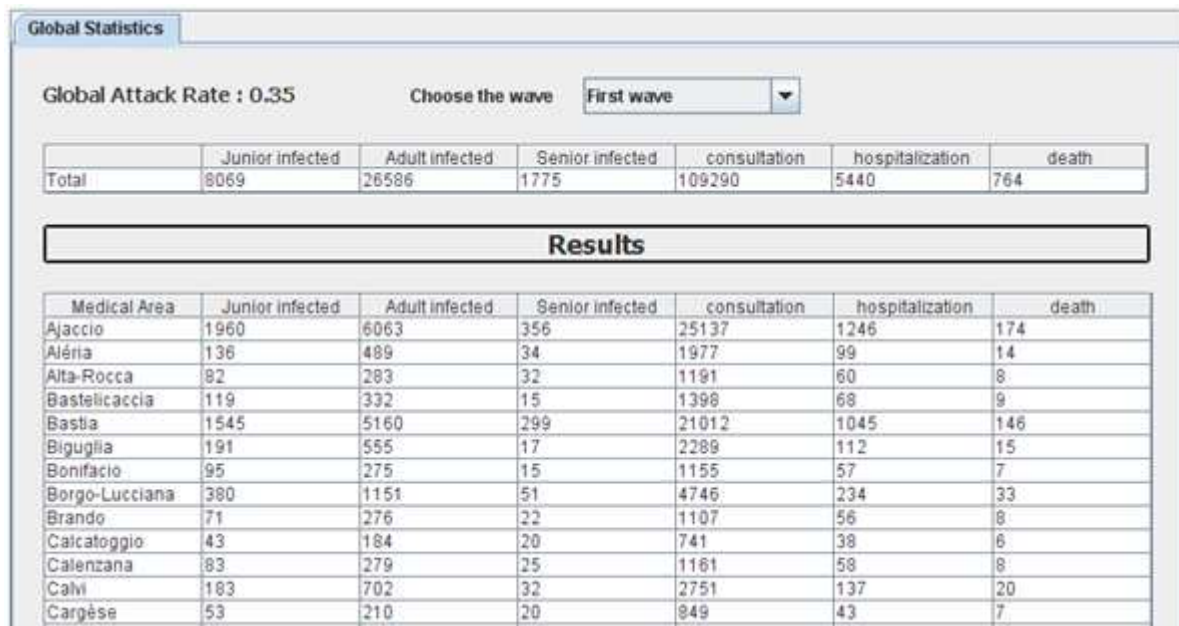


Figure 5: Results of the Deterministic Model for all the Medical areas in Corsica with a Unique Attack Rate (35%)

The modelling level

Using the deterministic model, the main parameter is the attack rate. It was easy to run quasi-instantly many scenarios. Figure 5 above presents a simulation for all the medical areas of Corsica (with an attack rate at 35% and a very strong lethality of 2% for a first wave, which is considered as an extremely severe case (almost like the Spanish Flu). Fortunately, the A/H1N1 virus is currently much less virulent, but we have to test the worst cases to determine if the local medical system can cope with the pandemic.

During the testing phase of the spatial stochastic model, we realized that the individual-based parameters (number of contacts by age categories, latent and infection periods, etc.) as well as the duration of infection largely influence the results.

Although the deterministic model provides quickly exploitable results, the spreading is more realistic in the spatial stochastic simulation. In the latter, we can really and finely observe the difference between attack rates and of course the spatial impact is much more evident (cf., Figure 6). For instance, we can notice that some medical areas are less affected by the virus (in particular in the centre of Corsica and in areas with fewer inhabitants). Indeed the population is much less concentrated and the population density is also a factor used in our multi-agent system in addition to the connection matrix.

Finally, a calibration of stochastic parameters (cf. Figure 7) can be achieved by comparing both stochastic and deterministic results.

For both models, the most effective medical measures are the wearing of masks as well as the setting in quarantine. Indeed, with sanitary measures, it is possible to strongly limit the propagation speed of the disease.

The engineering level

The number of consultations, hospitalizations and deaths are used as indicators and do not have to be considered as prediction. However, they can be used to test probable propagation scenarios, and thus evaluate the safeness of the healthcare network.

Figure 8 depicts such a comparison. *Required consultations* by infected people, *consultations achieved* by doctors, and *consultation margins* (i.e., the number of *Required consultations* minus the number of *consultations achieved*) are depicted. We can notice that for attack rates above 45%, the consultation margin is negative. That is to say that the number of doctors assigned to this medical area is not sufficient.

Decision level

Using the knowledge acquired on the previous engineering level, new policies can be developed. For example, the consultation margin can be carefully noticed in medical

areas. For medical areas with a large consultation margin, we can consider the reassignment of some cases to other medical areas with a poor or negative margin.

According to the number of infected persons, the impact on society organization can also be inferred. Hence, the number of infected adults corresponds

approximately to the number of work stoppages (subtracting naturally the number of people who do not work). New organization policies can then be developed for maintaining a minimum activity level for administrations, businesses and industries.

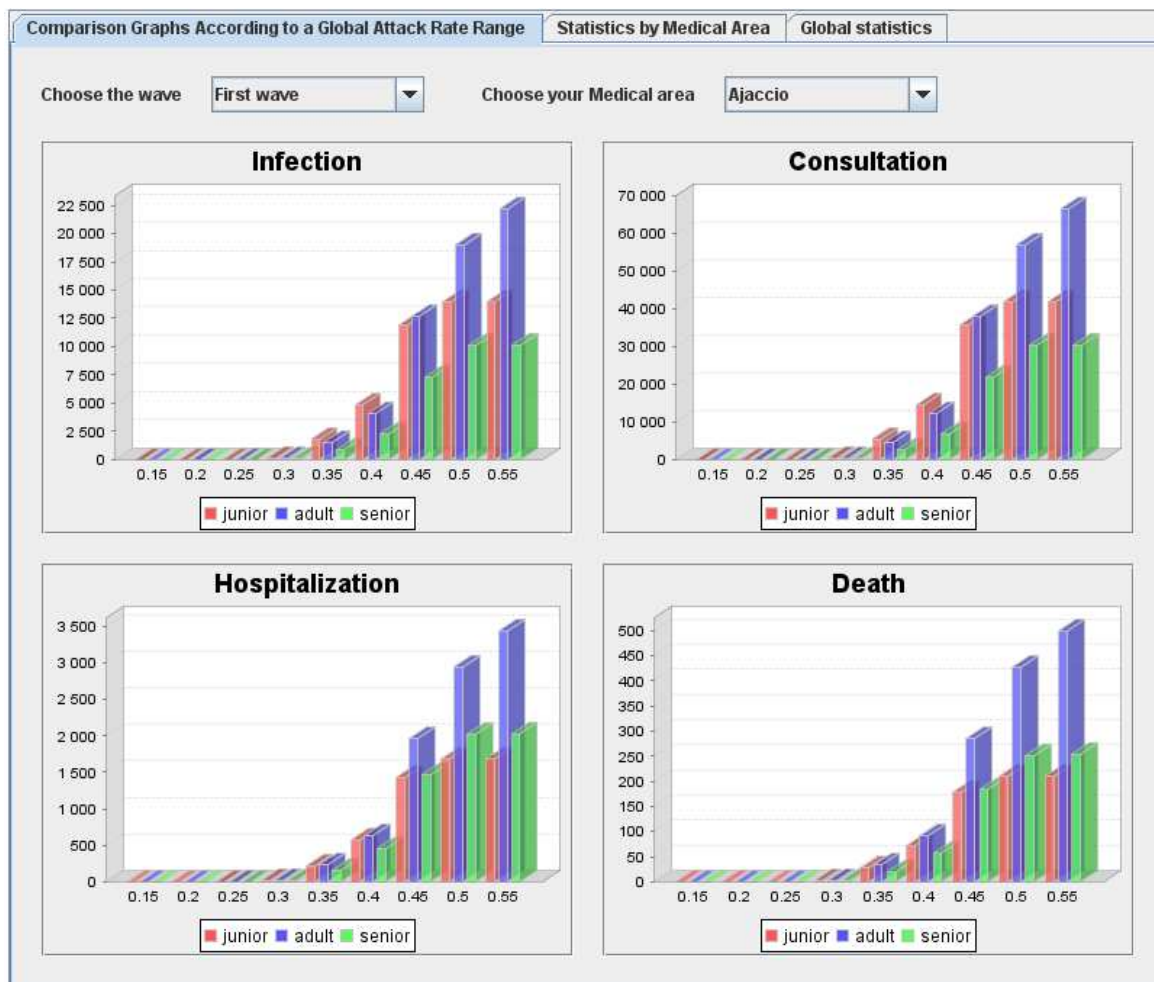


Figure 6: Results of the Spatial Stochastic Simulation with a Simple Experimental Plan (with an Attack Rate Varying from 15 % to 55 % in the Ajaccio Medical Area)

DISCUSSION AND CONCLUSION

The main goal of our Decision Support System was to provide the user with a modular tool, enabling him to specify the main parameters influencing the propagation of a pandemic on the island of Corsica. It is a classical application of DSS without particular technical innovations. The object-oriented software proposed uses text configuration files (in XML) and a graphical interface to test the results of two models. The first one is a spatial stochastic multi-agent system (individual based) linked to a Geographical Information System providing maps and valuable data for all the Corsican medical areas. Its study needs replications and the production of confidence intervals (Hill et al. 2008). The second simulation model is deterministic and applies the main factors of flu propagation to all the medical areas. A command line

version also exists and enables the use of parallel computing – mainly on computing clusters or small SMPs – for further statistical studies following specific design of experiments. For the stochastic multi-agents simulation, we can also specify scenarios of propagation with ASCII files (mainly to test the impact of various occurrence of flu in the different medical areas). A confidence interval is of course computed when we run the stochastic model, thus a direct comparison between a unique stochastic run and the deterministic model has a limited interest.

Even if we use this kind of statistical technique, no one can propose accurate predictions for a pandemic flu. The main problem of simulation software for prediction is the lack of reliable statistics. This point has been strongly underlined by the World Health Organization. This does not mean that decision support systems are useless, but our point of view is that we need to run experimental plans

with a wide range of values for the most sensitive parameters such as the attack rate (or R_0 for the stochastic multi-agent model) and the lethality factor. The latter, for instance, ranges from 0,002% to 0,7% if we observe the current data with more than thousands of cases from different regions of the World. Therefore, all the speculative estimates can only serve to test scenarios. The variation of the main model factor (virus attack rate) has even been proposed directly in the decision support software without having to run another dedicated statistical tool. For the sake of generality, we need to leave aside

useful information about some medical areas, which could increase the accuracy of the simulation results. For instance, the presence of a local University in the centre of Corsica (Corti) and the fact that many young students plus teachers and scientists are travelling from Bastia or Ajaccio to Corti will make a significant change in the results of the corresponding medical area. The closure of the university could also be considered. Without data about schools we have not introduced this parameter, which, like a kind of quarantine, will have a significant impact over the speed of virus spreading.

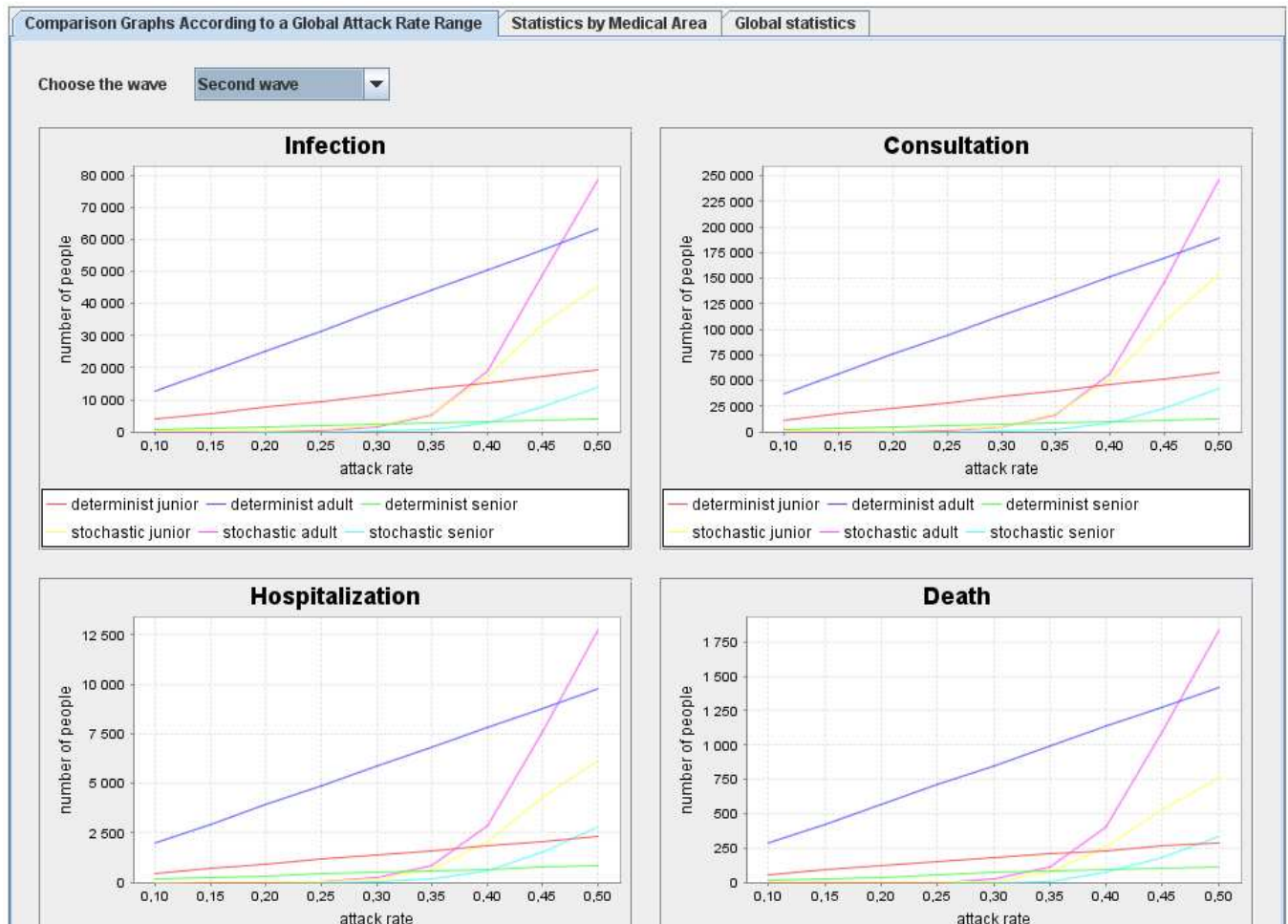


Figure 7: Visualization of Results of the Spatial Stochastic Simulation with the Deterministic Model for a Second Wave of the Virus Spreading over the whole Corsican Population (Attack Rate Varying from 10 % to 50 %) In the Case of the Stochastic Model, the Attack Rate Corresponds to the Probability of Infection per Person

Among the possible evolutions of this decision support system, a major change could be to add a dynamic link to geographical data. Currently, we have a very limited link with geographical data since bitmap data exported from a Geographical System are post-processed by a separate program before being loaded in memory at the beginning of the simulation. Various techniques can be deployed; in the past, we have deployed many (Coquillard et al. 1995) of them but this would imply much more software development not directly connected with the main aim of this decision support system. However, more essential

improvements could be made if we could also have reliable data concerning the remaining stockpile of vaccine, of prophylactic (antiviral) drug, as well as vaccine and prophylactic drug administration capacity. As in (Das et al. 2008), it could also be interesting to consider the duration of hospital stay to combine this model output with the regional hospital bed capacities. A variant of the quarantine enforcement can be to consider only the school and university closure. The current computing performances are satisfactory using Java; they have been tested and profiled to work on a regular personal computer. Moreover, we

could adapt the input files and parameters to handle larger areas, from countries to a worldwide simulation. Large experimental designs are planned to be run on computing

clusters and not on personal computers. Finally, we think that the current decision support system is flexible enough to be adapted to other viruses.

Choose the wave		Choose your Medical area						
First wave		Ajaccio						
Attack rate	Junior infected	Adult infected	Senior infected	Required Con...	Hospitalization	Death	Consultations achieved	Consultation Margin
0.15	840	2598	153	10773	535	75	30150	19377
0.2	1120	3464	204	14364	712	100	30150	15786
0.25	1400	4331	254	17955	890	124	30150	12195
0.3	1680	5197	305	21546	1069	150	30150	8604
0.35	1960	6063	356	25137	1246	174	30150	5013
0.4	2240	6929	407	28728	1424	200	30150	1422
0.45	2520	7795	458	32319	1602	224	30150	-2169
0.5	2800	8661	509	35910	1780	250	30150	-5760
0.55	3080	9527	560	39501	1959	274	30150	-9351

Figure 8. Consultation margin for Aiacciu, with attack rates from 15% to 50%, with 3 consultations per contaminated people.

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