Information and Communication Technologies

EPIWORK

Developing the Framework for an Epidemic Forecast Infrastructure

http://www.epiwork.eu

Project no. 231807

D7.8 Yearly activity report with assessment of lesson learned

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Period covered: Month 37th - 54th	Date of preparation:
Start date of project: February 1st, 2009	Duration:
Due date of deliverable: Month 54th	Actual submission date: August 1st, 2013
Distribution: public	Status: Draft

Project Coordinator: Alessandro Vespignani
Project Coordinator Organization Name: ISI Foundation
Lead contractor for this deliverable: ISI Foundation

Work package participants

The following partners have taken active part in the work leading to the elaboration of this document, even if they might not have directly contributed writing parts of this document:

- ISI
- FGC-IGC
- TAU
- MPG
- AIBV
- SMI
- FFCUL

Change log

Version	Date	Amended by	Changes
1	01/03/12		

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1 Project objectives and implementation strategy

A fully operational, accurate and reliable epidemic forecast infrastructure nowadays faces problems related to the lack of appropriate models to understand how an infectious disease spreads in the real world, lack of extensive and accurate epidemiologically relevant data (from societal data to epidemic surveillance data), lack of understanding of the interplay among the various scales of the problem (from the host-pathogen interaction, to human-to-human transmission, to the interaction with the environment) and, most importantly, lack of communication among the different areas of research which proceed almost independently, crucially hampering a significant progress in a highly interdisciplinary field of research. The present project intends to fill this gap. *Through computational thinking, complex systems concepts and data integration tools relevant for epidemiological understanding at all levels, it will provide a set of radical, paradigm-changing results enabling a novel approach to the modelling, forecast and policy making approach to infectious diseases.* The projects overarching goals are:

- The identification of general principles and laws that characterize complexity and capture the essence of *complex epidemiological systems*.
- The development of a *collaborative information platform* enabling the production of knowledge, understanding and models from the novel *abundance of digital data in epidemic research*.
- The development of an *open, data driven, computational modelling platform* to be used in epidemic research as well as in policy making for the analysis of global epidemics, integrating and leveraging on transnational data.
- The development, deployment and validation of an *Internet-based Monitoring System (IMS) producing real time data on disease incidence and epidemic spreading*.

The project aims at exploring the following *work areas* as the major research themes directly matching the objectives of this proposal:

- ***Modelling and theoretical foundations***
- ***Data-driven computational platform***
- ***ICT monitoring and reporting system.***

The work plan is organized around six distinct scientific work packages (WP1-WP6) whose parallel scheduling of the work packages is necessary to jump-start the cycle and the Inter-WP validation. WP1 and WP2 are aimed at exploring theoretical issues in the area of epidemic modeling in complex, multi-scale systems, structured populations and in the presence of the dynamical interplay between social and technological factors, seasonality and climate, health policies implementations, WP3 and WP4 are devoted to the collection and sharing of data on a computational platform and have a two-way continuous exchange of data and algorithms with WP1 and WP2. WP5 and WP6 is aimed at the development, set-up and deployment of innovative web monitoring and data gathering tools that should provide a continuous stream of data to WP3-WP4 and be informed by constant feedback on the modeling needs in terms of data gathering by WP1 and WP2. The common research agenda of the consortium teams, which work in a coordinated way on the various tasks, favors a closer interchange of ideas and knowledge among the groups and the various components of the project in a truly interdisciplinary collective effort.

2 Assessment of the fourth year activities

In its first year of life the project this report has been a long analysis of the research and developments produced by the project and to which extent those activities did meet the schedule proposed in the initial project. As that, the report was an executive summary reporting or duplicating most of the information already contained in other documents submitted for the project. The feedback of the reviewers and the Program Manager at the review meeting made it clear that a more useful assessment report should be structured in a way that provides a guide through the material submitted for review and a discussion of specific relevant points in the life of the project and the eventual lessons learned and the measures eventually implemented to improve the work of the consortium. The second and third year we provided a report along the above guidelines that has been appreciated by the reviewers. This year we provide again a final assessment analysis structured in the following sections:

- **Executive summary and highlights of the project activities in the fourth period.**
- **Collaboration/integration within the consortium.**
- **Exemplary cases of contributions to/from Complexity science.**
- **Exploitation, sustainability and policy relevance.**
- **Problems encountered in the last year and corrective actions.**
- **Opportunities and final considerations.**

In order to avoid duplicate information that can be found in deliverables and other reporting items of the project we intend here to provide an overview of the major results of the project beyond the rigid structure of deliverables and milestones. We will therefore try to assess the actual impact of the project achievements and the outlook of the consortium activities. It is also important to stress that the above structure is meant to address the recommendations of the past year review meeting. A discussion of each specific recommendation will be placed in the corresponding section along with the corrective actions put in place to address the reviewer remarks.

3 Executive summary and highlights of the projects activities

The activity carried forward during the fourth year of the project was extremely productive and the consortium has harvested a large number of scientific results and pushed forward the development of the data and computational tools.

In particular the project has benefited from the granted extension on the lifetime of the project. This has allowed the consistent monitoring of an entire influenza season in Europe. In addition some low hanging fruits concerning developments of the computational infrastructure and in the development of modeling techniques have been achieved. Some of these results were not envisioned as possible during the writing of the project (more than 5 years ago). The scientific activity of the past four years however has allowed adding some noticeable and unexpected achievements, witnessing the effective work of the consortium beyond the initial expectations of the project.

Furthermore, the project has produced an impressive number of scientific publications (about 60) and presented at about 80 major international events. In such a landscape it is not an easy task to single out the most relevant contributions. For this reason we have carefully selected those activities that shows to integrated efforts of the consortium or explicitly show the fruitful/promising dependencies and synergies among the various WPs.

We have also selected some results that are hardly identifiable with a specific deliverable/milestone and thus may be overlooked, despite their relevance, in the conspicuous documentation provided for the review process.

The theoretical work has continued the production of an impressive number of quality scientific publications. The work performed in this area has touched upon some foundational issues such They generated impressive results built around the notion of S0, the initial population susceptibility as well as on the reinfection threshold and how real-world networks, which are the substrate upon which diseases spread on a global scale, do interact with and depend on other networks. All groups had a common interest in modelling seasonal influenza: TAU focused on surveillance data in Israel, Gulbenkian on the data collected by the web platform developed in WP5 and LSHTM on UK surveillance data, accounting for climate forcing in similar consistent ways. The results concerning seasonal influenza analysis and other diseases open the path to new development of the computational platform. In particular it is possible to envision the development of a completely automated pipeline for seasonal influenza forecast that feed the IMS data into the computational platform to perform real time analysis. This goal that is beyond the scope of the project is being pursued by means of other funding from several teams of the consortium. The WP2 has also achieved a new deliverable concerning the construction of synthetic contact patterns in European countries that has been added in the last project amendment (D2.6). This deliverable has allowed the development of a general methodology for the derivation of synthetic contact matrices, carrying information on mixing patterns by age, from routinely collected socio-demographic data. The characterization of the structure of social contacts in mathematical and computational models of infectious disease transmission is a key factor for the assessment of the impact of epidemic outbreaks. Our computational approach overcomes the difficulties associated with empirical data collection on a large scale by the simulation of a virtual society of agents through an agent based model that allows the estimate of contact matrices by age in different social settings: household, school, workplace and general community. Unlike classical agent based models of epidemic transmission and network models, aimed at characterizing the spatio-temporal spread of epidemics tagging each individual in the population with a set of social attributes, we use the same detailed information on social contacts to construct contact matrices by age in the different settings to be used in compartmental models. We obtained synthetic contact matrices by age for 26 European countries. The entire collection of European contact matrices has been made available to the community: the synthetic contact matrices by setting and the combined total matrices can be downloaded from the EPIWORK Epidemic Marketplace presented in WP3 (http://www.epimarketplace.net). The success of this techniques has spurred data collection for the derivation of synthetic contact matrices for South East Asia, United States and South America by teams of the consortium. Interestingly the study of the effect of the inclusion of contact matrices in the dynamical equations describing the epidemic evolution has pointed out very interesting non-linear effects that appears as crucial for the realistic analysis of epidemic outbreaks.

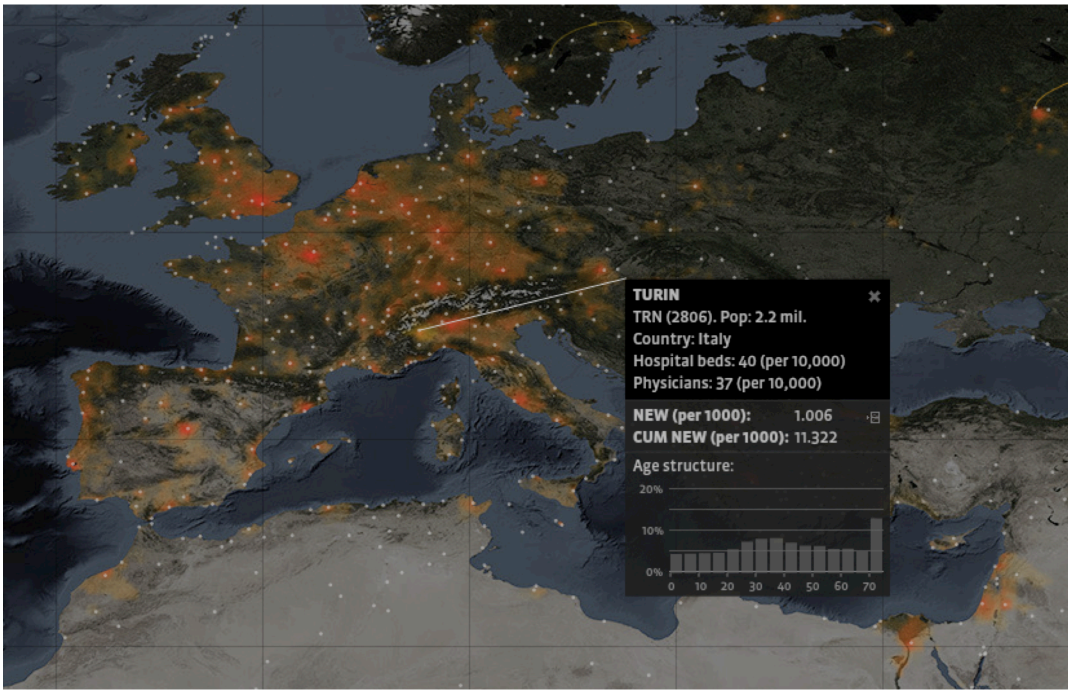

TURIN
TRN (2806). Pop: 2.2 mil.
Country: Italy
Hospital beds: 40 (per 10,000)
Physicians: 37 (per 10,000)
NEW (per 1000): 1.006
CUM NEW (per 1000): 11.322
Age structure:

Fig.1: New interface and of the Gleamviz computational infrastructure v4.2.

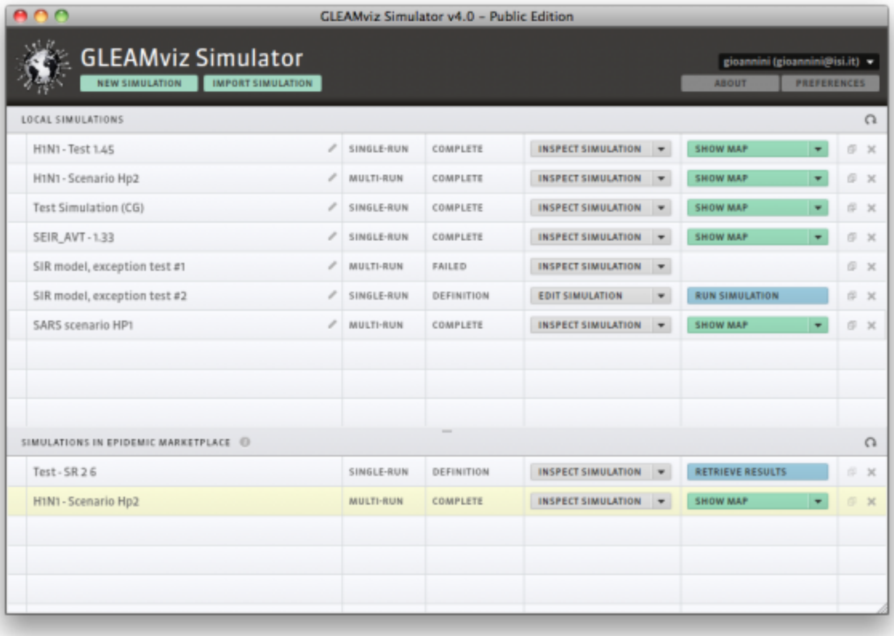
The computational and data platforms have fulfilled a complete integration and the computational platform and the epidemic marketplace (EM) are now latched and publicly available. The EM front end has been completely redesigned and its final version has been officially presented at the Epiwork workshop in Digital Epidemiology in Torino (may 2013). The computational platform GLEAMviz has reached it 4.2 public release. The new version features the following improvements and additions:

- Additional demographic and health-related information in the city info popups:
    - Average number of hospital beds per 1000 inhabitants
    - Average number of physicians per 1000 inhabitants
    - Average distribution of the population into age brackets
- Visualization of the cumulative individual transitions on the map as an alternative option to new transitions.
- Intuitive highlight of the census basins associated to each city/airport.

The integration between the GLEaMviz computational platform and the Epidemic Marketplace informational platform is bringing many advantages to the growth of the EPIWORK project. The functionalities provided by the Epidemic Marketplace in terms of annotated and searchable storage, as well in terms of data sharing and access control mechanisms, will enhance the GLEaMviz Simulator potentialities. The uploaded simulations are an additional source of epidemic resources for the informational platform; moreover, the shared user basin can help the growth of an active community interested in creating, visualizing and analyzing epidemiological simulation data, fostering the participation of pre-existing users of a platform to the other one. GLEaMviz simulator client communicates with the Epidemic Marketplace (see figure on the left) using a set of Web Services that allows it to upload simulation definitions as well as simulation's output data as searchable resources.

In the 4.0 version of the GLEAMviz computational platform, the integration with the WP3 Epidemic Marketplace data platform has been fully implemented and finalized. Existing simulations can be searched and browsed, and then retrieved and visualized within the GLEaMviz client directly from the Epidemic Marketplace.

The users of the two platforms are authenticated across a synchronized infrastructure enabling them to transparently access both systems with the same credentials. This also makes the interaction of the GLEaMviz client with the Epidemic Marketplace repository very smooth, avoiding additional user-credential requests upon interaction and therefore allowing seamless single sign-on access to both platforms. Both platforms use OpenLDAP software to manage users and credentials.



LOCAL SIMULATIONS

H1N1 - Test 1.45	SINGLE-RUN	COMPLETE	INSPECT SIMULATION	SHOW MAP
H1N1 - Scenario Hp2	MULTI-RUN	COMPLETE	INSPECT SIMULATION	SHOW MAP
Test Simulation (CG)	SINGLE-RUN	COMPLETE	INSPECT SIMULATION	SHOW MAP
SEIR_AVT - 1.33	SINGLE-RUN	COMPLETE	INSPECT SIMULATION	SHOW MAP
SIR model, exception test #1	MULTI-RUN	FAILED	INSPECT SIMULATION	
SIR model, exception test #2	SINGLE-RUN	DEFINITION	EDIT SIMULATION	RUN SIMULATION
SARS scenario HP1	MULTI-RUN	COMPLETE	INSPECT SIMULATION	SHOW MAP

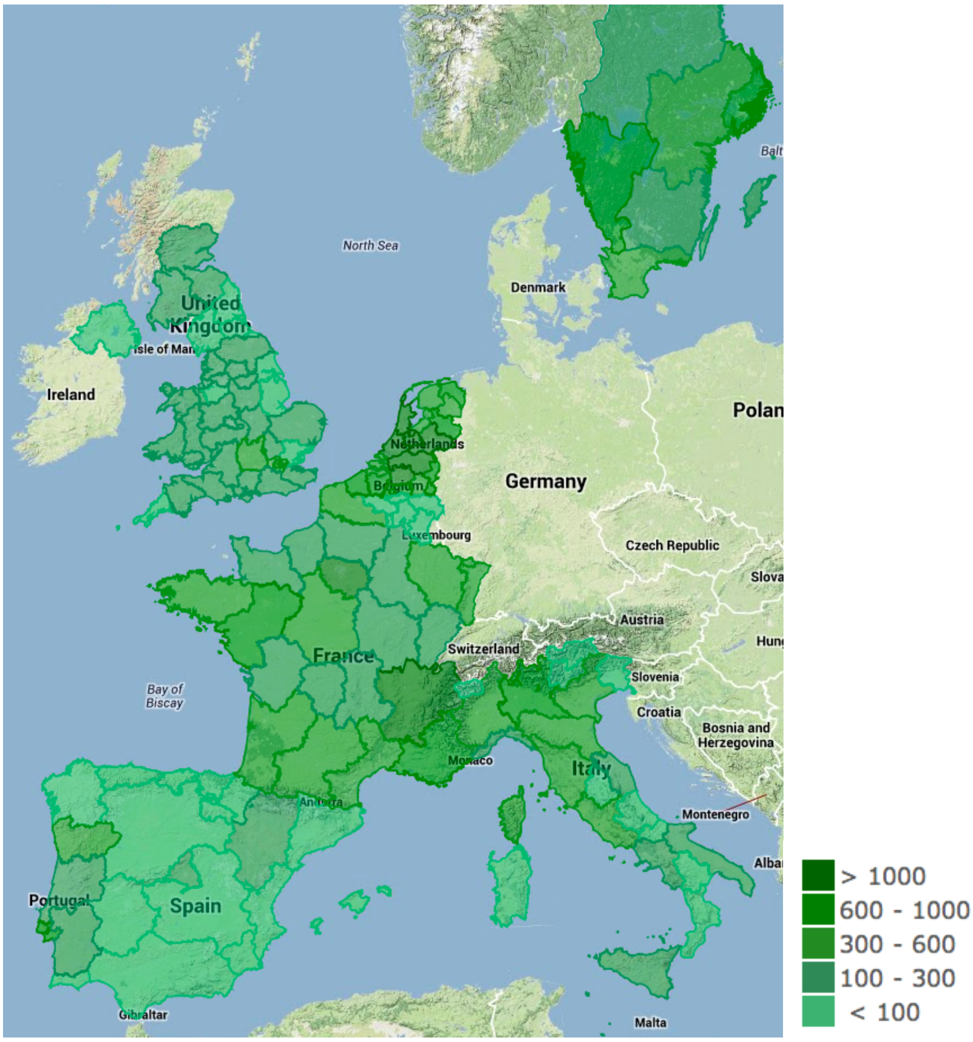
SIMULATIONS IN EPIDEMIC MARKETPLACE

Test - SR 2 6	SINGLE-RUN	DEFINITION	INSPECT SIMULATION	RETRIEVE RESULTS
H1N1 - Scenario Hp2	MULTI-RUN	COMPLETE	INSPECT SIMULATION	SHOW MAP

Fig.2: Epidemic Marketplace and computational platform integration as seen from the user of GLEAMviz.

One of the major achievements of this year is the development open access APIs for the integration of third parties Agent Based Model programs into the GLEAMviz computational platform. The goal of this integration effort is to allow the interoperability of an arbitrary country-level ABM with the Global Epidemic and Mobility model, by means of an extension of the software tool developed within the project, designed for researchers, health-care professionals and policy makers. The D4.7 is setting the technical requirements for the APIs development and models integration. We also provide a specific implementation with the ABM model developed by the FBK team. Although a fully model-independent integration is not yet possible, the delivered requirements are now used by teams of the consortium to develop the next generation of APIs and model integration requirements for other major modeling efforts in Europe and the US.

The Internet based monitoring (IMS) system comprises ten platforms in ten different countries. Influenzanet.org is operational and offers data analysis in real time as collected from the various IMS platforms. The central EpiDB is now fully functional. It has been extensively described in the previous report and in the third period Deliverable 5.5. Real-time data from the Influenzanet countries during the whole influenza seasons of 2011-12 and 2012-13 have been loaded into the EpiDB finally making possible the building of a European map:



Number of participants in the NUTS2 regions of the Influenzanet Countries

The platform was finally able to recruit a Spanish collaborator to deploy the IMS in Spain. The total number of participants is now above 45,000. Ireland and Denmark have been added to the network and will start collecting data during the next influenza season 2013-14.

The Influenzanet website: www.influenzanet.eu/ is now an established portal for health care professionals, researchers, policy makers and everybody else, interested in epidemiology, flu surveillance and modeling. Influenzanet.eu presents the project an its results in a reader-friendly way, in order to promote the concept of Internet-based Monitoring Systems in other countries, to expand scientific cooperation with colleagues all over the world and, last but not least, to show interested visitors what flu, vaccination and epidemiology is. It contains an analysis of the collected Influenzanet data so far is presented.

We are also glad to announce that CreateNet designed and implemented the iPhone and Android application to participate to the Europe-wide data collection through smartphone. The results of this activity have been documented in Deliverable D5.7, and include: (i)The design of the mobile application, including the elicitation of the requirements; (i)The implementation of the mobile application, featuring the customization of the mobile application for the various EPIWORK countries. Furthermore, we have managed the Apple Appstore and Google Play accounts for the deployment of the mobile applications in the various countries involved in the experimentation. The Android and iOS EPIWORK mobile application is available for 7 countries: Italy, Spain, Portugal, UK, Sweden, France, The Netherlands. After a pilot season in 2012-13, the data collection through mobile phones will be in full activity during the next influenza season 2013-14.

This year the project has finalized the organization of the final workshop " Digital Epidemiology" that took place in Torino on 30-31 May 2013. This workshop consisted in a major event gathering most of the relevant stakeholders interested in the Epiwork project. The workshop detailed presentation is reported in the specific deliverable D8.4.

4 Collaboration/integration within the consortium

One of the major problems in large Integrated project such as Epiwork consists in keeping a high level of interconnection and collaborations among partners. We have been working hard to keep all the communications and collaboration channels open. In summary the most evident collaboration efforts are listed below:

- ***WP1 And WP2 results have been integrated in the WP4 computational platforms.***
- ***The computational platform WP4 and the Epidemic Marketplace WP3 are fully integrated.***
- ***The IMS platforms are all integrated by the influenzanet.eu database. WP6 is integrated in WP5 by the start of the IMS Swedish Platform.***
- ***The WP1 and WP2 are starting to take advantage of the IMS platforms by using data for the development of models and forecast tools.***

This integration effort has been constant in the last three years of the project and it is witnessed by the ongoing collaborations of many teams of the consortium on other projects and joint research endeavors. . At the level of single partners the sustained level of interaction and collaboration is also witnessed by the number of joint publications and joint development activities. During 2012 and 2013, the work on the infrastructural part of the project (the three computational and web platforms) has seen the close collaboration of FBK, ISI, FFCUL and MPG. The integration of the IMS with the EM is bringing all the other teams in the effort.

5 Exemplary cases of contributions to/from complexity science

During the past years we have made a specific effort to highlight *the contribution to/from complexity science of the projec*t. The latter was one of the aim of the COSI-ICT call and we have been prompted by the reviewers to specifically report on relevant results in this area. We refer the readers to the final project report for a full account of all the contributions to complexity science. Here we want specifically to mention two recent contributions.

- ***Contact pattern heterogeneity and epidemic behavior.***

The mathematical representation of epidemics relies on the description of the transmission process that is usually modeled through the force of infection, that is the rate at which a susceptible individual acquires the infection because of the interactions with infectious individuals.

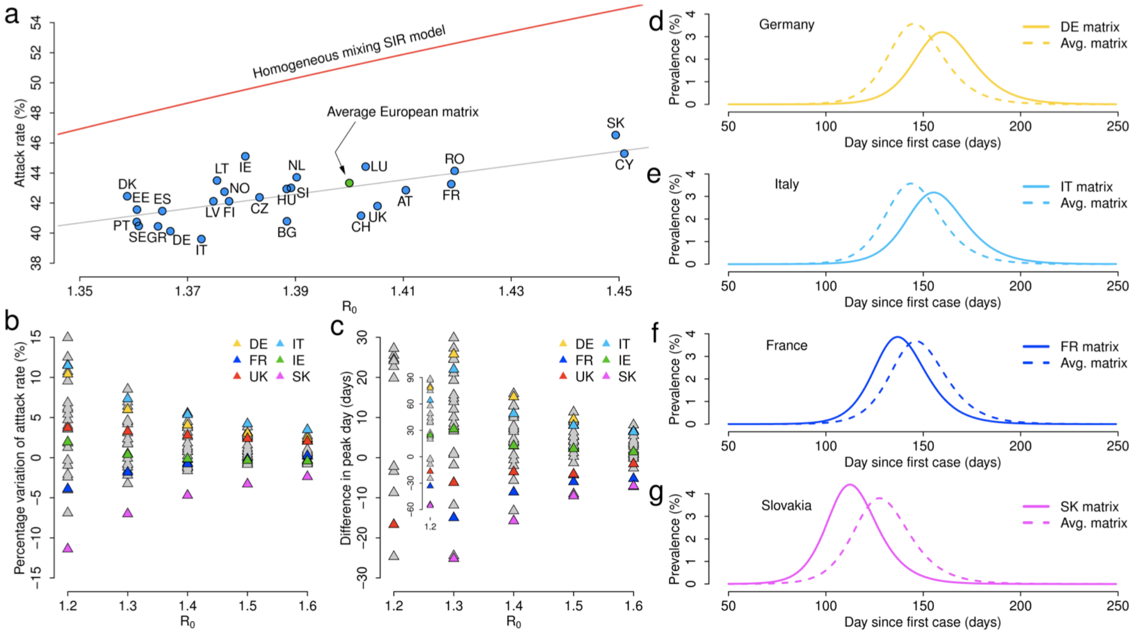


Fig 3: **a** Final infection attack rate as a function of the basic reproduction number R_0 in the different countries (blue dots) by adopting country-specific matrices and by assuming the same probability of transmission q in all countries – specifically, the value resulting in $R_0 = 1.4$ by adopting the average European matrix (green dot). The attack rate corresponding to the average European matrix is computed by assuming the average European age structure in the model. Red line represents the attack rate of the homogeneous mixing SIR model for values of R_0 in the range of variability of the basic reproduction number of country-specific matrices. Grey line represents the best fit of the linear model to data points related to the use of country-specific matrices. **b**Percentage variation of infection attack rate for increasing values of R_0 of models based on country-specific matrices with respect to models based on the average European matrix (with country-specific age structure). **c** As **b** but for the variation of the peak day. **d–g** Daily prevalence over time of models with $R_0 = 1.4$ based on either the country-specific matrix (solid lines) or the average European matrix (dashed lines, with country-specific age structure) in Germany, Italy, France and Slovakia respectively.

This quantity is proportional to the number of infectious individuals, the specific transmission probability of the infection during a contact and the overall rate of contacts of each individual with other individuals in the population. Although a vast majority of studies assumes the population as homogeneous –all individuals are equal with same average contact rate– the social and demographic structure of the population is generally reflected in heterogeneous contact patterns among individuals.

Age is obviously one of the main determinants of the mixing pattern of individuals: children tend to spend more time with children and members of their household, active adults mix with individuals in their workplace etc. Mixing patterns by age are generally defined by a contact matrix whose elements M_{ij} represent the average frequency of “adequate” contacts that an individual of age i has with individuals aged j. we propose a computational approach, based on the simulation of a virtual society of agents, allowing the estimation of contact matrices by age for 26 European countries. We validate the estimated contact matrices against those obtained by the most extensive field study on contact patterns, with data collected in eight European countries.

We have then considered a standard SIR model where all the basic parameters and scaling factors are set on the baseline yielding a basic reproduction number for the European average. For each country we used the synthetic contact matrices aggregated by one-year age brackets up to 84 years of age (so that all matrices have the same dimension). All other parameters being equal, the different contact matrices in each country define different values of R0 and different epidemic behaviors in each country. By applying to every country the average European contact matrix, large differences in terms of attack rate and peak day can be observed compared to the results obtained with the country-specific mixing patterns, especially for values of the basic reproduction number consistent with influenza epidemics as shown in Figure 3. Once more we see important non-liner effects induced by considering the heterogeneity of the population. These effects are non simply linearly related to the reproductive numbers, and once more indicate that the complex features can give rise to non-intuitive behavior. It is very important to stress that these results can be generalized to social contagion processes such as the spreading of rumors, opinion formation etc., thus having an impact in the analysis of complex systems well beyond the epidemic spreading research area.

- ***Non-linear effect of data integration.***

The sensitivity analysis of most epidemic models focuses only on the parameters describing the disease. However, in a large-scale computational model, the integration and assimilation of data on census, mobility, and other demographic factors has to deal with issues related to the quality and completeness of the data. The sensitivity analysis of the model results with regard to the incompleteness or poor quality of those 'structural' data is thus extremely important. We tested this aspect by assessing whether the full complexity of the real mobility data considered in the computational platform GLEAMviz would be essential to obtain the reliable forecast of epidemic spreading and how much considering incomplete data would be affecting the model output.

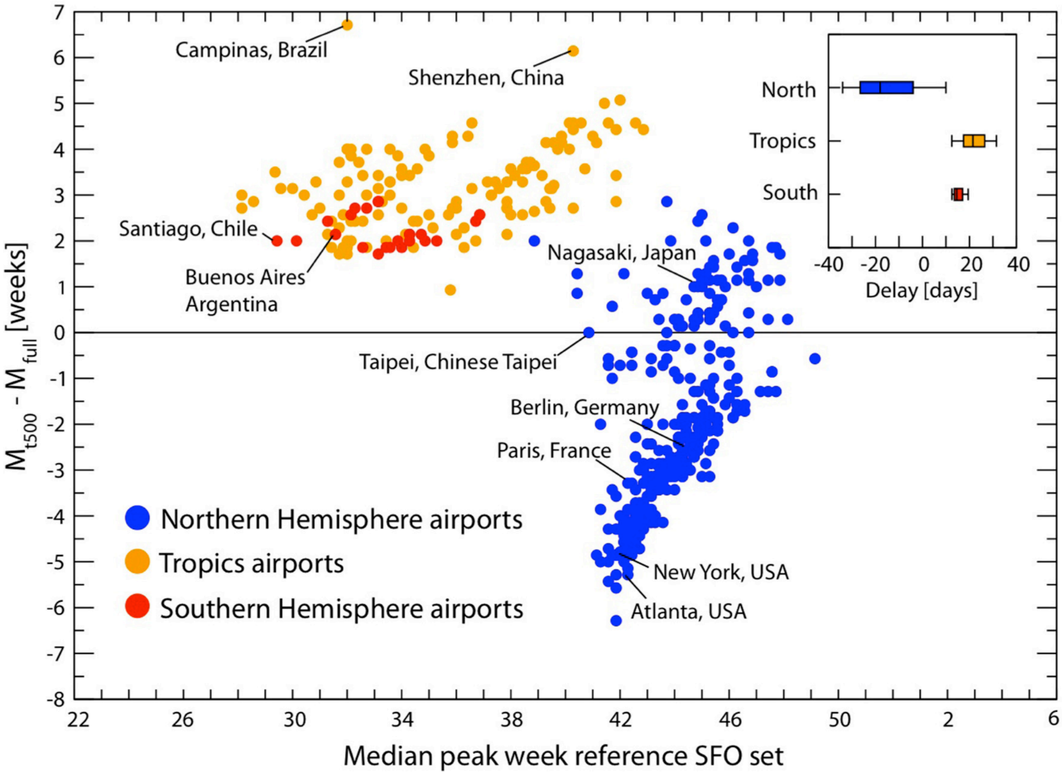


Fig.4: Difference in the median peak weeks in the reference stochastic forecast output (SFO) set, where the full mobility dataset was considered, and the top 500 scenario, for the 500 busiest airports, as a function of the median peak week in the reference SFO set. Dots are color-coded according to the corresponding airport's climate zone. In the inset, we show the box plot indicating the distribution of the differences (in days) between the peak week of the reference SFO set and the SFO set considering only the top 500 airports. The differences were considerable, with median differences of about 3 weeks.

In particular, previous approaches in the literature have considered only one transportation mode (air travel) and included a limited number of airports, ranging from 52 to 500. Although we agree with previous studies which state that considering partial datasets is informative for the overall theoretical analysis of general spreading features, we tested the performance of partial datasets in providing results concerning the evolution of the H1N1pdm according to the calibration of the GLEAM model executed in previous studies.

We considered the top 500 airports and performed the simulations of the 2009 A/H1N1 pandemic on a version of GLEAM that integrated this partial dataset. We compared these results with the data available from the simulations including the full set of airports available in the database. In particular we compared the median peak time of the epidemic in different cities and compared the results in the full and reduced dataset (see Fig. 4). Although the top 500 airports gather about 80% of the worldwide air traffic, the differences in the median peak times are clearly non-negligible. In specific places the results differs by more than 2 months, showing that a small perturbation to the dataset produces a macroscopic change in the results of the numerical system. A specific application to a real-world epidemic is thus able to show how the global backbone of the epidemic invasion can be strongly affected by the partial sampling of the mobility network, owing to the interplay of different parameters, such as the presence of loops, local connectivity, seasonal effects, and the real and effective (that is, measured on the sampled network) distance of the location from the seed of the outbreak. In addition, a limited version of the model may not be applicable to a specific real epidemic, given its partial coverage of the locations and countries in the world, as would be the case where the initial seed of the outbreak belongs to a region not included in the data integrated into the model.

6 Exploitation, sustainability and policy relevance.

As also prompted by the review panel in the past years, the consortium has always put a lot of effort exploitation and the sustainability of the tools and activities developed during the project. Also during the last years of the project the consortium made particular efforts to engage with National and International agencies and develop new collaborations. We have also been exploring opportunities to fund future developments of the tools developed in the project.

The consortium has developed collaborations and interactions with the ECDC, The JRC and the WHO and other international agencies (especially in the USA).

- We are partnering with the Joint Research Center (JRC) of the European Commission at Ispra, Italy. The Joint Research Centre is a research based policy support organization and an integral part of the European Commission.
- We have engaged in discussion with the ECDC and representatives from the ECDC were attending the final year Epiwork workshop.

- The IMS is currently developing contacts with similar initiative in the USA and Australia. The Influenzanet Consortium is indeed leading a worldwide effort consortiating all the platforms carrying out web-based influenza surveillance, i.e. the European Influenzanet (**www.influenzanet.eu**), Flu Near You (**www.flunearyou.org**) in the United States and Flu Tracking (**www.flutracking.net**) in Australia. During the 2nd International Workshop on Participatory Surveillance (IWOPS II) held in Amsterdam in April 2013 organized by the Skoll Global Threats Fund in collaboration with AIBV, aimed at mapping infectious diseases in both humans and animals, a Letter of Intent on cooperation and data exchange has been concluded between the three systems with the aim to achieve a world-wide disease radar: https://www.influenzanet.eu/en/news/2013/04/29/international-workshop-on-self-reported/

  We also plan to extend the IMS surveillance of *other than influenza contagious diseases.* Questionnaires for monitoring dengue have been developed in collaboration with a team of epidemiologists in Brazil. In collaboration with our Brazilian colleagues, the dengue monitoring system (Dengue na web) started to operate in the city of Salvador, Bahia, by October last year. This project got a lot of attention in the community of Portuguese speaking countries
- The modelling group is in contact with representative from the WHO for the development of a collaborative ffort within their activities concerning pandemic and highly pathogenic diseases.
- Members of the consortium are part of the WHO collaborating center CS4HS (Complex Systems for Health Science).

The following National Institutes have been collaborating or using the IMS and/or the modelling tools developed by the project:

- Belgian Pandemic crisis team, Belgium
- Health Protection Agency, UK (The Flusurvey data are available to the Health Protection Agency, the national body responsible for infectious disease surveillance, and they produce a weekly summary of the Flusurvey findings for their weekly influenza report)
- National Institute of health, Italy
- INSERM, France, now a subcontractor of WP5 (The Grippenet.fr data are available to the Reseau Sentinelles, the national body responsible for infectious disease surveillance, and they produce a weekly summary of the Grippenet.fr findings for their weekly influenza report)

- RIVM, the Netherlands

The computational platform has already secured funding from private foundations and other international agencies to continue development and support. At the present moment the computational platform has already funding for two more years of activity.

In summary all the components of the projects will continue to operate after the end of Epiwork and will be used as the starting point for new projects and tool development.

7 Problems encountered.

Although the project has kept sustained progress and has provided al the deliverables as scheduled, we have encountered the usual problems concerning participatory platforms and the need of High Performance computing infrastructure.

The first problems mostly concerns the use of consistent funding for the volunteer recruiting campaign. This is a long-standing problem, common also to similar projects started in the USA and Australia, that we are trying to mitigate in the future by teaming up with philanthropic foundations and individuals. Now the results coming from the IMS are solid and adopted by major Health Institute, thus shifting the resource channelling from the research side to recruiting and advertisement campaigns. Those targets are more appealing to philanthropic actors.

The issue with high performance computing is not at current time but it is a problem in the case of emergency readiness. At the moment the computational platform has more than 1,000 active users. Several national and International agencies are in contact with the consortium teams. For this reason we expect the current computational resources to be not adequate in case of a pandemic emergency. For this reason we are planning to devise a specific architecture of the computational infrastructure that will allow cloud deployment.

8 Opportunities and final considerations.

During the 4 and half years of life the project has gathered more than 100 researchers from areas as diverse as epidemiology, medicine, ICT, computer science, physics and mathematics. It proposes a multidisciplinary research effort aimed at developing the appropriate framework of tools and knowledge needed for the design of epidemic forecast infrastructures. This project thus represents a model for the initial set-up of a further development and a more general approach that includes also social contagion phenomena. It is possible then to envision a wealth of opportunities to leverage the results obtained by Epiwork to tackle new scientific questions and the development of new tools. A few among those are:

- **Enlarge the portfolio of contagion phenomena and health problems that can be addressed in the modeling, data and monitoring infrastructure.**
- **Adapt the current infrastructure to allow a scalable cloud computational architecture for health crisis management.**
- **Integrate systematically in the computational infarstructure of the social and behavioral adaptation component.**
- **Extend data integration to high quality economic determinants in order to develop predictive capabilities in problems such as Global Trade and Emerging infections.**
- **Develop a platform for the simulation of social contagion phenomena and social collective behavior that integrates data and methodologies implemented in Epiwork.**
- **Extend the participatory platforms to consider other diseases and social behavior.**

We believe that Epiwork is a successful example in the establishment of a framework for the monitoring and forecast of large scale- complex systems. Already some other European projects (see for Instance Forecasting Financial Crisis (FOC)) are mentioning Epiwork as a model of a possible route to develop predictive systems in the area of complex networks. We are looking forward to lend our expertise and tools to any future effort in this direction.

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5. Lachiany M and Stone L. A vaccination model for a multi-city system. Bulletin Mathematical Biology 74:2474-2487 (2012). [Epiwork contrib. 60%]
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