Uncoordinated Human Responses During Epidemic Outbreaks

Piero Poletti, Bruno Caprile, Marco Ajelli, and Stefano Merler

Abstract Uncoordinated human behavioral responses triggered by risk perception can alter the evolution of an epidemic outbreak further and beyond control measures imposed by public authorities. In fact, spontaneous behavioral changes could develop as a defensive response during the spread of an epidemic, thereby impacting the epidemic dynamics and affecting timing and overall number of cases. In this chapter, a model coupling the classic SIR disease transmission model with an imitation dynamics process is introduced which accounts for the diffusion of different behaviors in the population as a response to the epidemic threat. A detailed analysis of the model identifies the main determinants leading to remarkable alterations in infection dynamics in both risk perception and diffusion of human behavioral patterns. Empirical evidence points to the need of incorporating human behavior in prediction models informing public health decisions.

1 Introduction

Mechanisms able to account for spontaneous behavioral changes in response to perceived risk are increasingly important as they have the potential for improving predictions about the spread of emerging epidemics. The aim of this chapter is to analyze the main determinants in both risk perception and diffusion of human behavioral patterns leading to remarkable alterations in infection dynamics.

In particular, a model accounting for human behavioral response to the risk of infection is introduced. The approach is fairy general to be applied to the description of epidemic outbreaks caused by different diseases (e.g., due to influenza, smallpox, SARS). The effectiveness of human self-protection is investigated by considering

P. Poletti (✉) • B. Caprile • M. Ajelli • S. Merler
Bruno Kessler Foundation, via Sommarive, 18 Trento, Italy
e-mail: poletti@fbk.eu; caprile@fbk.eu; ajelli@fbk.eu; merler@fbk.eu

P. Manfredi and A. d'Onofrio (eds.), *Modeling the Interplay Between Human Behavior and the Spread of Infectious Diseases*, DOI 10.1007/978-1-4614-5474-8_5,

behavioral changes during the spread of a generic, influenza-like infection. The role of the key parameters regulating the mechanism of spontaneous self-protection is analyzed along with the interplay between risk perception and the disease transmission process. As a practical application, the effect played by risk perception during the 2009 H1N1 pandemic in Italy is discussed.

1.1 Evidence of Uncoordinated Behavioral Changes

During an epidemic outbreak, individuals may change their behavior in order to reduce the risk of infection, especially when serious consequences for individual health are implied. A population-based survey reported that more than 75 % of respondents would avoid public transportation and 20–30 % would try to avoid crowded environments as precautionary actions in response to a hypothetical influenza pandemic [22]. During the 2009 H1N1 influenza, an initial high level of anxiety about the pandemic has been observed [11] and different behavioral changes triggered by the perceived risk of infection have been reported [7, 21, 23–25]. In Australia, after the first pandemic wave, individuals "reported increasing hand-washing (46 %) and covering cough and sneezes (27 %)" to reduce the risk of infection [24]. In the USA, data collected on public response to H1N1 influenza from May 2009 to June 2009 suggest that "16 to 25 % of Americans had avoided places where many people are gathered, like sporting events, malls, or public transportation and 20 % had reduced contact with people outside [their] household as much as possible" [25]. Furthermore, larger uncoordinated behavioral changes have been detected for more severe epidemics. For instance, an 80 % reduction in travel to and from Hong Kong has been reported during the 2003 SARS crisis [9]. This empirical evidence highlights that behavioral response occurs when a new infectious disease emerges, although it is hard to quantify its impact on the epidemic spread.

1.2 Evolutionary Game Theory and Epidemic Modeling

Human behavioral change in response to the risk of infection can be accounted for by modeling the diffusion of fear as a parallel infection. In this case, the "recovery from fear" occurs at a constant rate, regardless the current state of the epidemic and the behavior adopted by the individuals. However, individuals may or may not reduce risky behaviors on the basis of the current risk perception of the epidemic. The approach considered in this chapter is based on evolutionary game theory [12], which allows considering a symmetric mechanism regulating spontaneous behavioral changes. Different behaviors adopted in the population are

represented by a given set of strategies. The adoption of self-protection is assumed to be driven by the perceived convenience of different behaviors, dependent on the epidemic dynamics.

2 The Model

The disease transmission process is based on an SIR scheme, where susceptible individuals may adopt two mutually exclusive behaviors, *"normal"* b_n and *"altered"* b_a, on the basis of the perceived risk of infection. We assume that individuals adopting the *altered* behavior are able to reduce the risk of getting infected by reducing the number of potentially infectious contacts and, in turn, the force of infection to which they are exposed. This defensive response accounts for both reduction in physical contacts and, more in general, all self-prophylaxis measures which can reduce the transmission probability during these contacts. For instance, a reduction in the number of contacts can be achieved by avoiding crowded environments or by limiting travels, whereas a reduction in transmission probability can occur as a consequence of an increased wariness in common activities (e.g., the behavioral goals recommended by the WHO for reducing influenza transmission, such as washing hands frequently or respecting cough/respiratory etiquette).

In the model, spontaneous behavioral changes occur on the basis of cost/benefit considerations. This assumption perfectly fits the language of evolutionary game theory, in which behaviors adopted by individuals correspond to strategies played in a suitable game, with certain expected payoffs.

All individuals pay a cost for the risk of infection, which we assume to depend linearly on the perceived prevalence $M(t)$ and to be higher for individuals adopting the *normal* behavior (b_n) than for those adopting the *altered* behavior (b_a). However, individuals playing b_a pay an extra, fixed, cost because they are limiting their usual activities. Therefore, the payoffs associated with b_n and b_a result respectively:

$$P_n(t) = -m_n M(t), \quad P_a(t) = -k - m_a M(t)$$

The *altered* behavior gives the advantage of reducing the risk of infection ($m_n > m_a$), but the extra cost associated to it (k) implies that the *normal* behavior is the most convenient one when the perceived prevalence M is small (or in absence of disease). Which behavior is more convenient to adopt clearly depends on the status of the epidemic. The balance of the payoff between the two possible behaviors is determined by the cost associated to the risk of infection and on the perceived prevalence of infections in the population (M(t)). The latter is modeled by assuming a fading memory mechanism (such in [1, 6]) altering the perception of the risk of infection on the basis of the number of cases occurred over a certain (past) period of time.

The diffusion of strategies in the population is modeled as an imitation process [4, 12] based on the idea that individuals change strategy as they become aware that their payoff can increase by adopting a different behavior. By introducing the variables S, I, and R (describing the fraction of susceptible, infective, and recovered individuals, respectively) and by introducing the variable x (describing the fraction of individuals adopting the *normal* behavior), the system governing this process can be written as follows:

$$\begin{cases} \dot{S} &= -\beta IS[x+q(1-x)] \\ \dot{I} &= \beta IS[x+q(1-x)] - \gamma I \\ \dot{R} &= \gamma I \\ \dot{M} &= \beta IS[x+q(1-x)] - \nu M \\ \dot{x} &= x(1-x)(q\beta I - \beta I) + \rho x(1-x)(1-mM)S \end{cases} \tag{1}$$

where β is the transmission rate; $1/\gamma$ is the average duration of infectivity period (here corresponding to the generation time); q represents the reduction of the risk of infection to which individuals adopting the *altered* behavior are exposed; ν weighs the decay of the perceived prevalence; ρ essentially represents the speed of the imitation process with respect to the pathogen transmission dynamics; $m = (m_n - m_a)/k$ defines the risk threshold for determining which behavior would represent the most convenient choice.

Basically, the last equation of the system accounts for the diffusion of the two different behaviors in the population. The first term of the equation accounts for a natural selection embedded into the transmission process that favors individuals reducing the risk of infection ($q\beta I - \beta I < 0$); the second term represents the imitation process and accounts for spontaneous changes in individual behaviors, based on the balance between the payoffs associated to the two different behaviors (i.e., $1 - mM$). Behavioral change driven by the imitation dynamics occurs depending on the difference between the payoffs of the two possible behaviors, the perceived prevalence, the level of the risk threshold, and the speed of the imitation process. The latter is in general different from the speed of the disease transmission process as imitation is based on the diffusion of information. Details on the derivation of the last equation in System 1 can be found in [19] for a model comprising behavioral changes possibly occurring among infective individuals and for different symptomaticity levels of the infection.

2.1 Basic Reproduction Number

The basic reproduction number R_0 is defined as the average number of secondary infections that results from a single infectious individual in a fully susceptible population. For the System 1, R_0 can be computed using the next-generation technique [5], and it results to be $R_0 = [x+q(1-x)]\beta/\gamma$. R_0 can thus be interpreted

as a weighted sum of two basic reproductive numbers: the reproductive number for individuals adopting the *normal* behavior (namely the fraction x), i.e., $R_0^n = \beta/\gamma$ and the reproductive number for individuals adopting the *altered* behavior (namely the fraction $1-x$), i.e., $R_0^a = q\beta/\gamma$. Therefore, R_0 depends on the fraction of individuals in the population who are currently adopting either *normal* or *altered* behavior.

3 Behavioral Changes During a "Generic" Influenza-Like Infection

In this section, parameters characterizing the disease transmission process are taken from reliable estimates available for the 2009 H1N1 pandemic influenza. Specifically, R_0 is assumed to be 1.4, and the generation time is taken equal to 2.8 days [3, 10, 16].

3.1 Baseline Scenario

The effect of possible spontaneous behavioral responses to the risk of infection on the epidemic spread is investigated, starting from a *baseline* configuration and by varying one by one the parameters. This baseline represents the simple case where the perceived prevalence M is exactly the prevalence of infections I ($\gamma = \nu$) and at the beginning of the epidemic the perceived risk of infection is zero ($M(0) = 0$). Moreover, as an illustrative scenario, values of parameters related to human behavioral response are taken in such a way that (a) the adoption of the *altered* behavior reduces by 15 % the number of potentially infectious contacts, i.e., $q = 0.85$; (b) the *altered* behavior becomes more convenient when the prevalence becomes larger than the 1 % of the population, i.e., $1/m = 0.01$; (c) the delay between the time at which the *altered* behavior becomes convenient and the time at which more than 50 % of the population becomes responsive is about 5 days, i.e., $\rho = 10$. The initial conditions considered in this section are $S(0) = 1 - 10^{-3}$, $I(0) = 10^{-3}$, $x(0) = 1 - 10^{-6}$, and $R(0) = M(0) = 0$.

The resulting dynamics of System (1) is shown in Fig. 1. After an initial growth of the epidemic, the perceived prevalence reaches the prevalence threshold $1/m$ and the *altered* behavior becomes more convenient. As a consequence when the *altered* behavior became widely adopted in the population, which occurs after few days, the epidemic growth rate reduces remarkably. As the prevalence decreases below the threshold, the *normal* behavior becomes more convenient and its diffusion produces a fat tail in the infection dynamics.

The timing of the behavioral response is characterized by parameters m and ρ. The former describes how the perceived prevalence M is weighted in the payoff functions, i.e., in the balance of the cost associated to the risk of infection and the

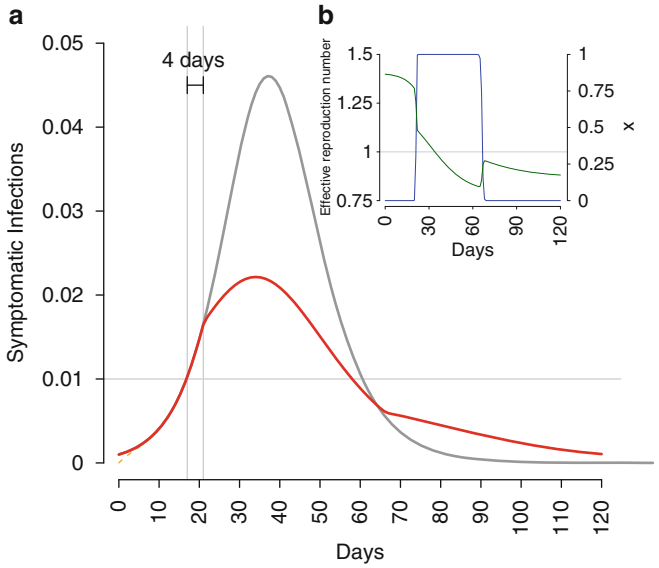

Fig. 1 (**a**) Daily prevalence of infection in the case of no responsiveness of the population ($q = 1$ *bold gray line*) and in the baseline scenario ($q = 0.85$, *bold red line*). The *horizontal gray line* represents the prevalence threshold $1/m$. The behavioral response appears about 4 days after the perceived prevalence $M(t) = I(t)$ crosses the threshold $1/m$ producing a lower increase in the prevalence of infection. (**b**) The dynamics of $1 - x$ (*blue line*, scale on the *left*) and the effective reproductive number over time (*dark green line*, scale on the *right*)

cost of a self-protection strategy. The latter represents the speed of the imitation process with respect to the disease transmission timescale. As a matter of fact, $1/m$ defines the threshold for the perceived prevalence above which individuals reducing contacts have a larger payoff; the larger m, the earlier the *altered* behavior is perceived as the most convenient choice. On the other hand, ρ drives the delay (embedded in the imitation dynamics) between the time at which a strategy becomes more convenient and the time at which the strategy is adopted by the majority of the population. In sum, the time at which the transition between the two possible behaviors occurs is driven by m, while the duration of this transition is driven by ρ; these two parameters together define the *responsiveness* of the population to an epidemic outbreak.

3.2 *Effectiveness of Human Self-protection*

The effectiveness of human self-protection is analyzed in terms of: (1) final epidemic size (defined as the total number of infections at the end of the epidemic); (2) daily peak prevalence; (3) peak day.

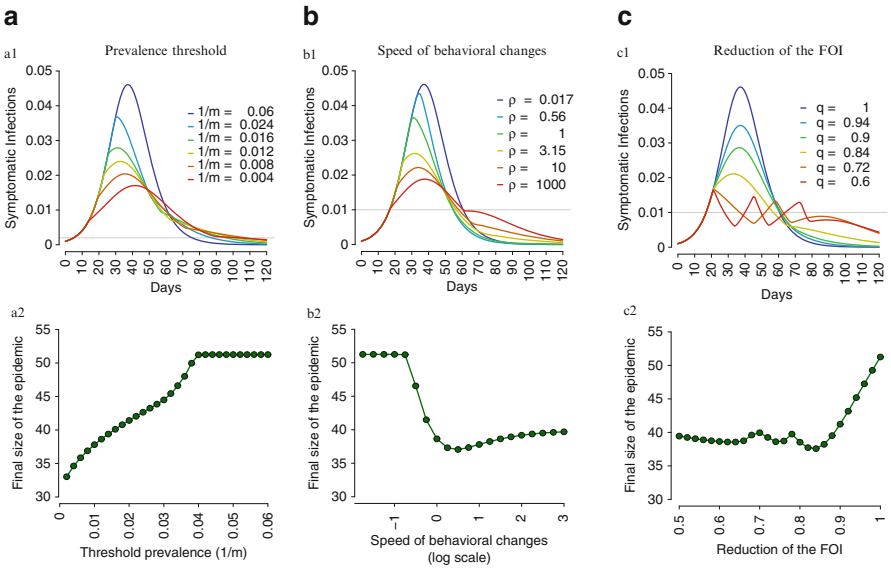

Fig. 2 (**a**) Daily prevalence of infections ($a1$), final epidemic size ($a2$) as obtained for different values of the prevalence threshold $1/m$. Other parameters as in the baseline scenario. (**b**) As (a) but for different values of the speed of behavioral changes ρ. (**c**) As (a) but for different values of the reduction factor q

As mentioned above, a major responsiveness of the population to an infection corresponds to a small prevalence threshold (large values of m) and to large values of ρ. The responsiveness of the population is related to time at which the behavioral response starts to affect the population behavior. As the population responsiveness increases, a larger reduction in the final epidemic size and in the daily peak prevalence is observed (see Fig. 2a and b). However, if the prevalence threshold $1/m$ is larger than the maximum prevalence of infections, or the imitation process is too slow (i.e., for small values of ρ), the human response never takes place and the epidemic spreads following the dynamics of an SIR model driven by R_0^n. An unreachable prevalence threshold represents the situation in which the epidemic is not perceived sufficiently severe to trigger a behavioral response of the population. This happens when $1/m$ is larger than $I^p = 1 - \frac{1}{R_0^n} + \frac{1}{R_0^n} \log \frac{1}{R_0^n}$, i.e., the largest possible daily peak prevalence, which is reached when all individuals adopt the *normal* behavior throughout the whole course of the epidemic.

The size of reduction in contagious contacts associated to the *altered* behavior has a strong impact on the epidemic dynamics. A larger reduction of the risk of infection is enacted by individuals adopting the *altered* behavior when smaller values of q are considered. As q decreases, the final epidemic size and the daily peak prevalence reduce as well (see Fig. 2c).

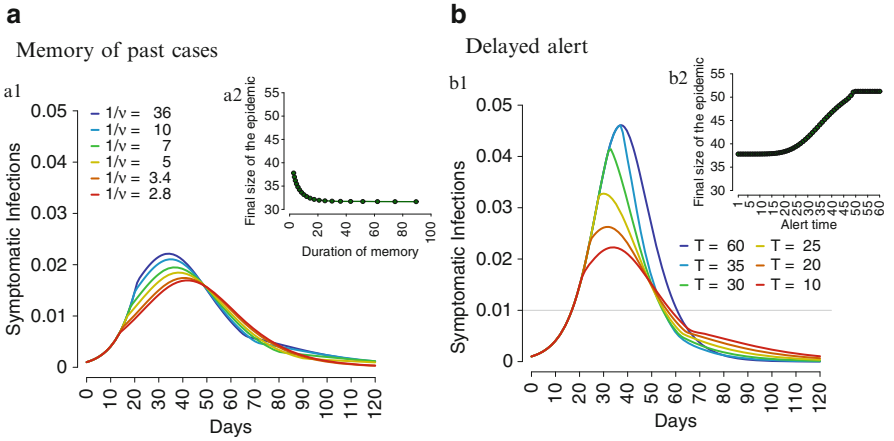

Fig. 3 (**a**) Daily prevalence of infections (*a1*), final epidemic size (*a2*) as obtained for different values of the average memory length $1/\nu$. Other parameters as in the baseline scenario. (**b**) As (a) but for different values of the alarm time T (in days)

At this point three interesting aspects are worth highlighting:

1. Even a small reduction in the number of contagious contacts enacted by the population can remarkably alter the spread of the epidemic.
2. A threshold exists for q such that for smaller values of q a larger impact of behavioral changes on the final epidemic size, the daily peak prevalence, and the peak day does not occur. Indeed, in terms of the final epidemic size and the peak day, a reduction of 100 % in the number of potentially infectious contacts (corresponding to $q = 0$, i.e., total isolation) produces the same effects obtained by considering a reduction of 25 % ($q = 0.75$).
3. For small values of q, the model accounts for multiple epidemic waves. A detailed discussion on the conditions for observing such a pattern can be found in [17].

3.3 Risk Perception and Information Diffusion

In Sects. 3.1 and 3.2 the perceived prevalence M at time t is assumed to be exactly the prevalence I at time t (i.e., $\nu = \gamma$). However, individuals may explore the convenience of different behaviors taking into account infections occurred over a (past) period of time. This case is investigated by considering $1/\nu > 1/\gamma$. As a matter of fact, the perceived risk of infection associated to every single new infection is larger when $1/\nu > 1/\gamma$ is considered. Therefore, it is not surprising that a longer memory duration leads to a larger diffusion of the *altered* behavior and implies a decrease in the daily peak prevalence and the final epidemic size, and a delay in the epidemic spread (see Fig. 3a).

A misperception of risk may occur when the population becomes aware of a new epidemic outbreak after a period of time since the emergence of the epidemic. This situation can be investigated by assuming that the perceived prevalence is initially equal to zero for a certain period of time, T. Figure 3b shows that the effectiveness of human response diminishes when a larger delay is considered. In particular, daily peak prevalence and final epidemic size increase as T increases and, no relevant effects on the outbreak can be detected when the "alert" takes place too late.

4 The 2009 H1N1 Pandemic in Italy

In March 2009, a new influenza virus emerged in Mexico giving rise to a pandemic that spread worldwide [10]. Early in the course of the pandemic, the population was very concerned about the event [15, 21]. Did this affect the behavior of the population and, consequently, alter the dynamics of the epidemic?

As most European countries, Italy experienced one single pandemic wave during fall-winter 2009 and no substantial activity was detected during the summer. However, the weekly influenza-like-illness (ILI) incidence is characterized by an initial slow exponential increase (September–mid-October 2009) followed by a sudden and sharp increase of the growth rate (mid-October). Over the whole period schools remained open [8] and only moderate mitigation measures were enacted (e.g., antiviral treatment of severe cases) [14]. This allows us to investigate an "uncontrolled" epidemic, not affected by "heavy" public health interventions or by school closure. On the other hand, since the emergence of the pandemic the Italian population was exposed to a massive information campaign on the risks possibly associated to the pandemic, which may have contributed to alter the perceived risk.

4.1 The Effect of Risk Perception During the 2009 Pandemic

Two different phases, characterized by two distinct exponential growth rates, can be appreciated in Italy (especially when data are plotted in logarithmic scale) by observing the ILI incidence as reported by the surveillance system during the 2009 H1N1 pandemic (see green points in Fig. 4a and its subpanel).

The observed pattern cannot be reproduced by a classic SIR model, unless one considers a time-dependent transmission rate, switching from a low transmission level during the first four weeks to a higher level for the rest of the epidemic. However, this model would not be able to explain the reason of the sudden change in the transmissibility potential.

On the contrary, the model introduced in this chapter perfectly fits the observed ILI incidence (see red lines in Fig. 4a and its subpanel) and provides a plausible explanation of the mechanisms responsible for the observed evolution of the ILI incidence. Indeed, the estimated parameter configuration obtained by fitting ILI

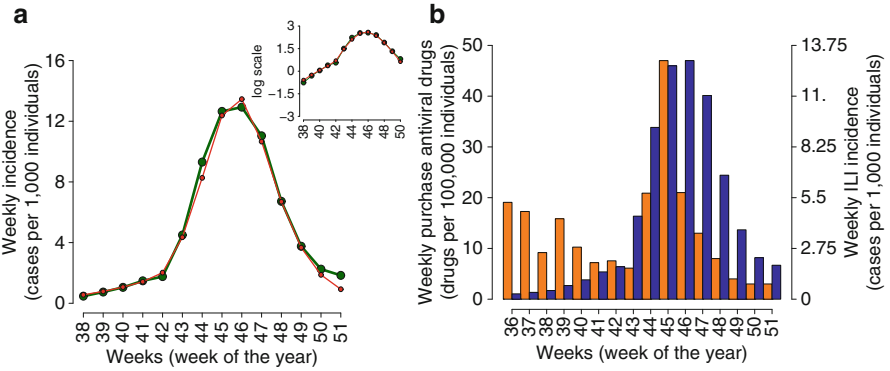

Fig. 4 (**a**) Weekly ILI incidence as reported to the surveillance system (*green*) and weekly incidence simulated by the model (*red*). Sub-panel shows the same curves in a logarithmic scale. Parameter values used in the simulation are set as follows. The generation time $1/\gamma$ is assumed 2.5 days according to [10]; $S(0) = 0.9$ according to a serological survey on the Italian population [20]; $x(0) = 10^{-8}$ and $m = 0.1$ assumed; $M(0) = 10.5$, $I(0) = 0.001243$, $\rho = 66$, $q = 0.84$, $\nu = 0.005$, $\beta = 0.59$, fitted; the estimated under reporting factor is 16.9 %, in good agreement with the range 18–20.2 % estimated in [2]. (**b**) Weekly purchase of antiviral drugs (*orange*, scale on the left axis) and weekly ILI incidence as reported to the surveillance system (*blue*, scale on the right axis) during the 2009 pandemic, in Italy

incidence entails an initial overestimation of the perceived risk (which decreases over time), along with an initial diffusion of the *altered* behavior in the population, which in turn is replaced by the *normal* behavior during the course of the epidemic. In fact, at the beginning of the pandemic, the simulated population is led to adopt the *altered* behavior by a high level of perceived risk of infection (as in the presence of a well-sustained circulation of the virus) and, as a consequence, the growth rate of the epidemic results lower than what would have been observed in a population adopting the *normal* behavior. On the other hand, a decrease in the perceived risk of infection is observed, despite the (slow) increase in the actual number of cases. In fact, the latter depends on the combination of two opposite phenomena: the increase of new infections and the decline (slowed by the memory mechanism) of the perceived prevalence, which was overestimated in the early phases of the epidemic. As the perceived prevalence goes below the risk threshold $1/m$, the *normal* behavior starts to spread quickly in the population as the most convenient strategy to be adopted through the subsequent course of the epidemic. This leads to a sudden change in the growth rate of the epidemic which is triggered by an increase of R_0. Model simulations show that the two distinct exponential growth phases observed for ILI incidence correspond to an initial diffusion of the *altered* behavior in the population, which determines an epidemic spread driven by R_0^a, and a second phase characterized by the diffusion of the *normal* behavior, where the spread is driven R_0^n. The best estimate for R_0^a is 1.24 and for R_0^n is 1.48. Estimates of R_0^n, i.e. the basic reproductive number for a population in which the normal behavior

is widely adopted, are in good agreement with those obtained for the 2009 influenza pandemic [2, 3, 10, 16].

The model explains the observed ILI incidence only if an initial (persistent) diffusion of the *altered* behavior in the population is considered. Specifically, an initial perceived risk of infection above the risk threshold, a long-lasting memory (able to keep the *altered* behavior as apparently more convenient over a relevant period of time), and a fast imitation process (enough to produce a sudden change in the force of infection) are required.

4.2 Antiviral Drugs Purchase and Perceived Risk

By fitting the model to the observed ILI incidence, our investigation identifies an initial overestimation of the risk as the main determinant of the influenza dynamics reported in Italy in the 2009. The same result is suggested by other empirical evidences, such as the temporal pattern of drug purchases.

As shown in Fig. 4b, during the fall the purchase of antiviral drugs complied with the observed ILI temporal dynamics; on the contrary, until mid-October an excess of antiviral drug purchase can be observed, suggesting an initial overestimation of the risk of infection. Specifically, when the 2009 pandemic arrived in Europe at the end of April, the weekly number of antiviral drugs sold jumped suddenly to more than 12 doses per 100,000 individuals per week [13], while the maximum weekly number of antiviral drugs sold during the 2008–2009 influenza season was less 2 doses per 100,000 individuals per week. Moreover, the purchase of antiviral drugs reached a peak of about 35 doses per 100,000 individuals per week at the end of July, despite no substantial ILI activity was detected in Italy during the summer.

The concern about the pandemic might have amplified the purchase of antiviral drugs, likely due to the information campaign about the use of antivirals for treating H1N1 infections. This example provides an empirical evidence that the Italian population have actively enacted spontaneous defensive response measures aimed at reducing the risk of infection in response to the high perceived risk. A discussion on this topic, including other (empirical) sources of information supporting the hypothesis of an initial overestimation of the risks of the pandemic, is developed in [18].

5 Conclusion

Spontaneous human behavioral changes triggered by the perceived risk of infection can remarkably alter the spread of an epidemic, leading to different epidemic dynamics. In particular, if changes in behavioral patterns are fast enough, they can

have a remarkable effect in reducing the daily prevalence of infection and the final epidemic size. In addition, human response may also lead to quite rich epidemic dynamics including, for example, the occurrence of multiple epidemic waves. Our performed investigation singles out the main determinants of human behavior and risk perception leading to remarkable alterations of the dynamics of an epidemic outbreak. First, if the perceived risk associated to an epidemic is sufficiently large, even a small decrease in the number of potentially infectious contacts can remarkably reduce the impact of an epidemic. Second, the disease spread is highly sensitive to how rapidly people adopt self-protecting behavioral patterns. Third, when the population becomes aware only late of a new epidemic outbreak, the effectiveness of human response reduces. However, when the mechanism regulating the spread of information about the disease is sufficiently fast, spontaneous social distancing is always effective.

Finally, our analysis shows that an initial overestimation of risk can delay the epidemic spread, leading to sudden changes in the transmissibility potential and, in turn, to a (somewhat unexpected) sharp increase in the growth rate of an emerging epidemic, as it might have happened in Italy during the 2009 H1N1 pandemic.

Acknowledgements This work has been partially funded by the EC-ICT contract no. 231807 (EPIWORK).

References

1. Ajelli, M., Iannelli, M., Manfredi, P., Ciofi degli Atti, M.L.: Vaccine **26**(13), 1697 (2008)
2. Ajelli, M., Merler, S., Pugliese, A., Rizzo, C.: Epidemiol. Infect. **139**(1), 68 (2011)
3. Baguelin, M., Hoek, A.J.V., Jit, M., Flasche, S., White, P.J., Edmunds, W.J.: Vaccine **28**(12), 2370 (2010)
4. Bauch, C.T.: Proc. R. Soc. B **272**, 1669 (2005)
5. Diekmann, O., Heesterbeek, J.A.P., Metz, J.A.J.: J. Math. Biol. **28**(4), 365 (1990)
6. d'Onofrio, A., Manfredi, P., Salinelli, E.: Theor. Popul. Biol. **71**, 301 (2007)
7. Eastwood, K., Durrheim, D.N., Butler, M., Jones, A.: Emerg. Infect. Dis. **16**(8), 1211 (2010)
8. European Commission. Organisation of school time in Europe, Primary and general secondary education, 2009/10 school year (2009)
9. Ferguson, N.M., Cummings, D.A., Fraser, C., Cajka, J.C., Cooley, P.C., Burke, D.S.: Nature **442**, 448 (2006)
10. Fraser, C., Donnelly, C.A., Cauchemez, S., Hanage, W.P., Van Kerkhove, M.D., Hollingsworth, T.D., Griffin, J., Baggaley, R.F., Jenkins, H.E., Lyons, E.J., Jombart, T., Hinsley, W.R., Grassly, N.C., Balloux, F., Ghani, A.C., Ferguson, N.M., Rambaut, A., Pybus, O.G., Lopez-Gatell, H., Alpuche-Aranda, C.M., Bojorquez Chapela, I., Palacios Zavala, E., Espejo Guevara, D.M., Checchi, F., Garcia, E., Hugonnet, S., Roth, C.: The WHO Rapid Pandemic Assessment Collaboration. Science **324**(5934), 1557 (2009)
11. Funk, S., Gilad, E., Watkins, C., Jansen, V.A.A.: Proc. Natl. Acad. Sci. USA **106**(16), 6872 (2009)
12. Hofbauer, J., Sigmund, K.: Evolutionary Games and Population Dynamics. Cambridge University Press, Cambridge (1998)
13. Istituto Superiore di Sanitá. FluNews Aggiornamento epidemiologico settimanale numero 14, 25–31 January 2010. (2010). (In Italian)

14. Istituto Superiore di Sanitá. FluNews Aggiornamento epidemiologico settimanale numero 22, 22–28 March 2010. (2010). (In Italian)
15. Jones, J.H., Salathé, M.: PloS One **4**, e8032 (2009)
16. Munayco, C.V., Gomez, J., Laguna-Torres, V.A., Arrasco, J., Kochel, T., Fiestas, V., Garcia, J., Perez, J., Torres, I., Condori, F., Nishiura, H., Chowell, G.: Eurosurveill **14**(32), 19299 (2009)
17. Poletti, P., Caprile, B., Ajelli, M., Pugliese, A., Merler, S.: J. Theor. Biol. **260**(1), 31 (2009)
18. Poletti, P., Ajelli, M., Merler, S.: PLoS One **6**(2), e16460 (2011)
19. Poletti, P., Ajelli, M., Merler, S.: Math. Biosci. **238**, 80 (2012)
20. Rizzo, C., Rota, M.C., Bella, A., Alfonsi, V., Declich, S., Caporali, M.G., Ranghiasci, A., Lapini, G., Piccirella, S., Salmaso, S., Montomoli, E.: Vaccine **28**(10), 3558 (2010)
21. Rubin, G.J., Amlot, R., Page, L., Wessely, S.: Br. Med. J. **339**, b2651 (2009)
22. Sadique, M.Z., Edmunds, W.J., Smith, R.D., Meerding, W.J., de Zwart, O., Brug, J., Beutels, P.: Emerg. Infect. Dis. **13**(9), 1307 (2007)
23. Schwarzinger, M., Flicoteaux, R., Cortarenoda, S., Obadia, Y., Moatti, J.: PLoS One **5**(4), e10199 (2010)
24. Seale, H., Heywood, A.E., McLaws, M., Ward, K.F., Lowbridge, C.P., Van, D., MacIntyre, C.R.: BMC Infect. Dis. **10**(1), 99 (2011)
25. SteelFisher, G.K., Blendon, R.J., Bekheit, M.M., Lubell, K.: N. Engl. J. Med. **365**, e65 (2010)