Long-standing influenza vaccination policy is in accord with individual self-interest but not with the utilitarian optimum

Alison P. Galvani*†, Timothy C. Reluga*, and Gretchen B. Chapman‡

*Department of Epidemiology and Public Health, Yale University School of Medicine, New Haven, CT 06520; and ‡Department of Psychology, Rutgers University, Piscataway, NJ 08854

Edited by Simon A. Levin, Princeton University, Princeton, NJ, and approved January 6, 2007 (received for review August 5, 2006)

Influenza vaccination is vital for reducing infection-mediated morbidity and mortality. To maximize effectiveness, vaccination programs must anticipate the effects of public perceptions and attitudes on voluntary adherence. A vaccine allocation strategy that is optimal for the population is not necessarily optimal for an individual. For epidemic influenza, the elderly have the greatest risk of influenza mortality, yet children are responsible for most of the transmission. The long-standing recommendations of the Centers for Disease Control follow the dictates of individual self-interest and prioritize the elderly for vaccination. However, preferentially vaccinating children may dramatically reduce community-wide influenza transmission. A potential obstacle to this is that the personal utility of vaccination is lower for children than it is for the elderly. We parameterize an epidemiological game-theoretic model of influenza vaccination with questionnaire data on actual perceptions of influenza and its vaccine to compare Nash equilibria vaccination strategies driven by self-interest with utilitarian strategies for both epidemic and pandemic influenza. Our results reveal possible strategies to bring Nash and utilitarian vaccination levels into alignment.

epidemiology | game theory | mathematical modeling | psychology

Vaccination is the principal strategy for reducing the public health burden of influenza. However, a fundamental but often neglected component of implementing an optimal community vaccination program is human psychology, which influences adherence to vaccination recommendations. The utilities of vaccination decisions for individuals and for their communities are governed by the interplay between epidemiological and social systems. An individual's vaccination decisions are driven by their perceptions of the epidemiological system. Individual decisions collectively determine the level of population immunity and thus the magnitude of an epidemic.

Vaccination protects not only those who are vaccinated but also others in the community who are thereby less likely to be infected. Unmitigated pursuit of self-interest can lead to suboptimal vaccination coverage for a community (1, 2). Previous studies have applied game theory to vaccination under the assumption that individuals are fully rational decision-makers with perfect and complete knowledge (1, 2). However, our psychological data reveals that there are significant discrepancies between individuals' perceptions of influenza and its vaccine and the epidemiological facts. Here we parameterize an epidemiological game-theoretic model of influenza vaccination with empirically collected psychological data to incorporate perceptions of influenza epidemiology and vaccination (see *Methods*).

The policy of the Centers for Disease Control (CDC) has been to prioritize the elderly for influenza vaccination (3), because they are at highest risk of influenza mortality. However, most transmission occurs between children and within the adult workforce as a consequence of frequent contact with greater numbers of individuals at school and work, respectively (4–11). Thus, influenza vaccination targeted at the young can dramatically reduce community-wide transmission (4, 12, 13). Here, we show that the discordance of vaccination incentives between the young (who perpetuate epidemics) and the elderly (who are at greatest risk of influenza morbidity and mortality) obstructs utilitarian vaccination.

In a game-theoretic context, individuals seek to maximize their personal utility, which is a tradeoff between anticipated benefits and costs, discounted by the diminished value of the future relative to the present. Accordingly, survey data indicates that individuals attempt to minimize their perceived risks (14). For example, the decision to vaccinate is positively associated with perceived vaccine effectiveness and is negatively associated with perceived side effects (14, 15). People are also more likely to vaccinate if they perceive a high likelihood or severity of influenza (16). Thus, an individual's decisions may be affected by discrepancies between perceived and actual risks. Survey studies have found that people often believe that diseases are less risky than their respective vaccines (17, 18). Some parents believe that childhood vaccination is not necessary because other parents have vaccinated their children, and because childhood diseases are under control (18), indicating at least a conceptual understanding of the indirect protection that is attained from the vaccination of others via herd immunity.

We broadly define vaccine costs to include both direct costs and anticipated risks. For influenza vaccination, costs to individuals include monetary cost, opportunity costs associated with time and inconvenience of vaccine administration, and potential adverse health effects. The actual medical risks of influenza vaccination are generally minor. Potential adverse effects include arm soreness (19), rhinorrhea, nasal congestion, and fever (20). However, public perceptions of risk may be elevated beyond actual risks. There has been public concern about a reputed causative link between the influenza vaccine and Guillain–Barré syndrome, a disorder of the peripheral nervous system that can lead to paralysis and even death (22). There has also been widespread concern that thimerosal, a mercury-containing preservative, could have adverse effects, including neurodevelopmental disorders (23). Our survey data suggests that risks associated with influenza vaccination are overestimated by the public compared with actual risks estimated in epidemiological studies. Thus, we predict an effect of overestimated vaccine risks on the optimality of vaccine demand.

Without public health intervention, vaccination choices of individuals are expected to tend toward the Nash equilibrium, at which no individuals can improve their utility by switching to a different strategy (24). When driven by self-interest, an individual's utility is

---

Author contributions: A.P.G. designed research; A.P.G., T.C.R., and G.B.C. performed research; A.P.G. and T.C.R. contributed new reagents/analytic tools; G.B.C. analyzed data; and A.P.G. wrote the paper.

This article is a PNAS Direct Submission.

Abbreviation: CDC, Centers for Disease Control.

[†] To whom correspondence should be addressed. E-mail: alison.galvani@yale.edu.

This article contains supporting information online at www.pnas.org/cgi/content/full/0606774104/DC1.

Table 1. Mean responses to selected questionnaire items from the Health Promotion at Work study

Questionnaire item	Mean	SD	Epidemiological value	Symbol	*t* test; df = 594
Imagine that the flu shot is unavailable, and you are therefore unable to get the shot this fall. Given that you have had no shot, what would say is the likelihood that you will get the flu this winter?	48%	22%	15% (42)	Translated into β	50.28**
Perceived effectiveness of vaccine (relative risk reduction)	0.34	0.75	80% <65 years of age (10, 37) 60% for the elderly (38)	εv_j	−8.76**
Imagine you catch the flu from another person. How long do you think it would take from the time you were exposed to the other person until the time you got the flu?	4.4 days	2.6 days	1.2 days (39)	$1/\sigma$	30.52**
If a person gets a flu shot, for how long does the shot protect the person from the flu? That is, for how long is the shot effective?	8 months (i.e. one influenza season)	3.7 months	12 months (43)	ϕ	−25.94**
If you were to get the flu this winter, how long would it last? That is, for how many days would you experience flu symptoms?	5 days	2.7 days	4–5 days (40)	δ	3.90**

n = 595. The perceived effectiveness of vaccine (relative risk reduction) was computed from responses to the previous item and another similar item that asked about the likelihood of infection if one were to be vaccinated. **, $P < 0.0001$.

not increased by its contribution to herd immunity. However, the positive externality of herd immunity does improve the utilitarian vaccination strategy, which is defined as the strategy that achieves the highest population utility. Thus, the utilitarian strategy generates higher utilities, for both the community and the individual, on average. Nevertheless, the utilitarian strategy may not be socially stable, because at the utilitarian level of vaccination "free-riders" who do not vaccinate but benefit from herd immunity can yield a higher utility than "cooperators" who vaccinate.

Previous epidemiological game-theoretic studies have neither considered populations with heterogeneous incentives, nor influenza vaccination. Calculating mixed-strategy Nash equilibria requires determining the best response strategy for each individual in the population simultaneously, dependent on the strategy of every other individual, an operation that is recalcitrant to analytical solution. Thus, we developed a Monte Carlo algorithm for determining both Nash equilibria and utilitarian vaccination strategies. We reveal the impact of perceived vaccine cost and risk on the discrepancy between Nash equilibria and utilitarian vaccination strategies. Relative to utilitarian vaccination against epidemic influenza, we predict that much more vaccine will be desired by the elderly and much less vaccine sought by the young, at the expense of the community overall. We find that the utilitarian and Nash strategies are in closer alignment during a pandemic than during an epidemic.

To determine the likely impact of improved education about influenza and its vaccine, we compare actual epidemiological parameter values with perceived parameter values obtained from our psychological data. We reveal common misperceptions of influenza epidemiology, some of which reduce the discrepancy between utilitarian and Nash vaccination levels and others of which act against utilitarian vaccination. Interestingly, the vaccination threshold beyond which transmission is eliminated can be achieved with lower incentives if the public misestimates certain epidemiological parameters identified in our survey.

Results

Questionnaire Results. Questionnaire results are reported for 595 university employees. The questionnaire results are not necessarily a representative sample of the United States population at large.

Subjective Perceptions of Parameters. We examined whether people misperceive key epidemiological parameters for influenza. Mean responses for questionnaire items of interest are shown in Table 1, along with actual epidemiological values for each variable. Single sample *t* tests indicate whether mean perceived values differ significantly from the actual values. The data indicate that people greatly overestimate the incidence of influenza infection and underestimate vaccine efficacy. They tend to overestimate the incubation period and underestimate the duration of vaccine protection. They only slightly overestimate the duration of the infectious period.

Some questionnaire items used five-point Likert response scales, and thus it was difficult to compare participants' responses to an objectively correct value. In some cases, however, it was nevertheless possible to establish that participants misperceived parameters. One item asked, "How likely do you think it is that the flu shot would cause a person to have a severe reaction?" The mean response was 2.06 on a scale from 1 (not at all likely) to 5 (very likely). A response of 2 corresponds to "a little likely." The normatively correct response is "very unlikely," and thus the 70% of participants who gave a higher response were overestimating vaccine risk. Accordingly, we examined model output with vaccine risk elevated by varying degrees above the actual risk.

Predictors of Vaccination. Older participants were more likely to be vaccinated ($r = 0.30, n = 595, P < 0.0001$). Among participants ≥65 years of age ($n = 35$), 71% were vaccinated, compared with 47% among younger participants ($n = 560$). We asked participants how many of the adults and how many of the children (<18 years of age) in their household were vaccinated. For the 214 households with children, the average household adult vaccination rate was 0.35 (median = 0.29), compared with an average household child vaccination rate of only 0.13 (median = 0.00). The average difference within a household of adult versus child vaccination rate was 0.22 (median difference = 0.00), which was significant (Wilcoxon rank–sum test, $T = 2{,}134.5$, $P < 0.0001$, $n = 214$). Thus, the questionnaire study reveals a vaccination pattern that parallels the CDC guidelines, with high vaccination rates for the elderly, moderate rates for younger adults, and low rates for children. This vaccination pattern corresponds more closely to a Nash equilibrium than to a utilitarian strategy identified by our model. As an indication that vaccination decisions are driven by perceived risks and benefits, vaccination was positively associated with perceived likelihood of infection ($r = 0.37, n = 595, P < 0.0001$) and perceived vaccine efficacy ($r = 0.29$, $P < 0.0001$), and negatively associated with perceived adverse effects of the vaccine ($r = -0.29$, $P < 0.0001$).

Model Results

Epidemic Influenza. For the perceived parameters of epidemic influenza, the utilitarian strategy is to allocate all vaccine to the young (Fig. 1*A*). However, Nash vaccination levels for the young are much lower than those that are optimal for the community for a given vaccine cost. Conversely, vaccination demand by the elderly is much higher than that of the utilitarian strategy. Nash and

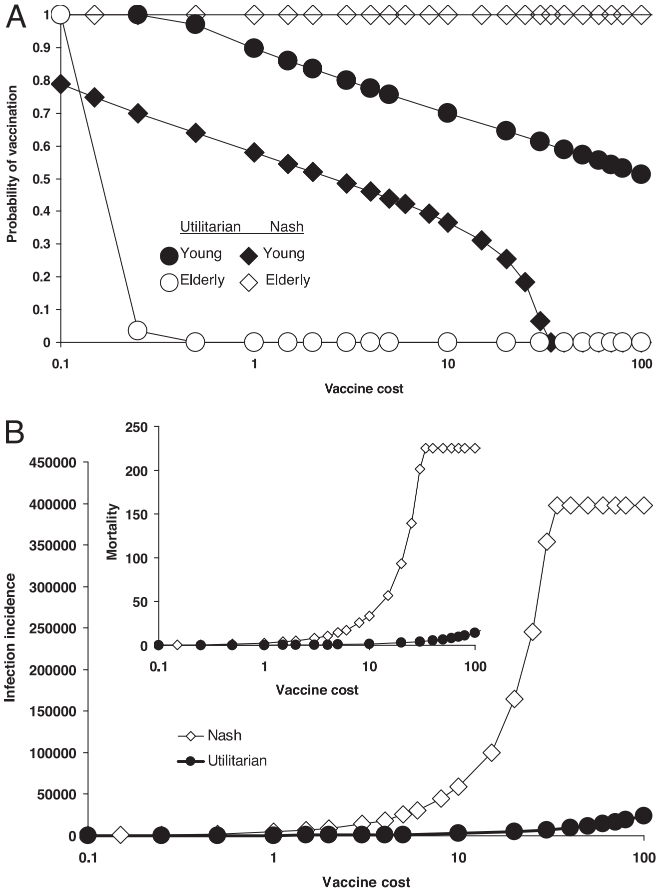

Fig. 1. Effects of vaccine cost/risk on vaccination probabilities and infection incidence for pandemic influenza. (*A*) Probability of vaccination against epidemic influenza by young and elderly when vaccination levels are at the Nash equilibrium and the utilitarian optimum for perceived parameters, with increasing vaccine relative to actual ($37.26) cost. Note that vaccine cost is on a log scale, so a value of 1 represents its actual cost. (*B*) Annual infection incidence and mortality when vaccination levels are at the Nash equilibrium and the utilitarian optimum for perceived parameters of epidemic influenza, with increasing vaccine cost.

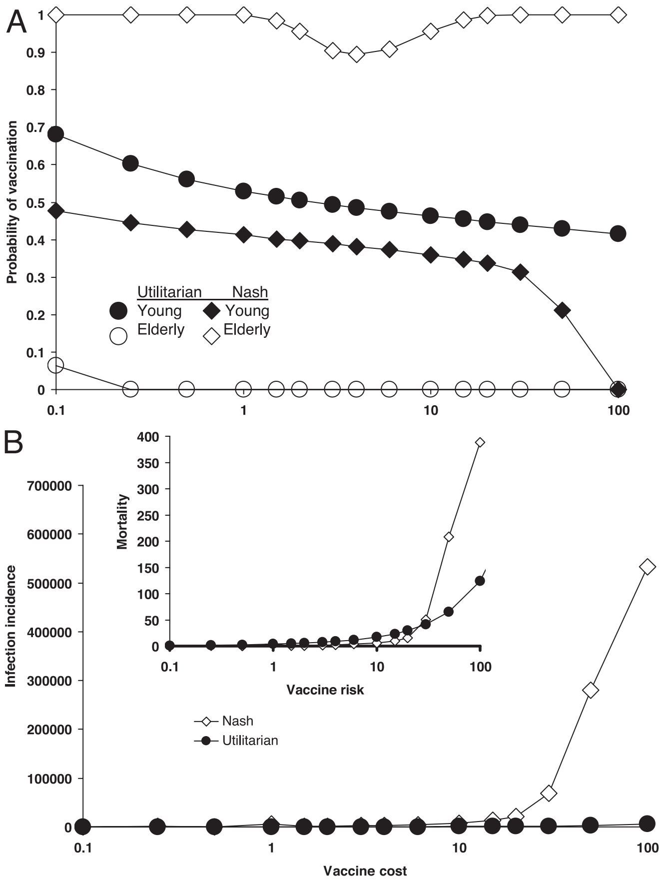

Fig. 2. Effects of vaccine cost/risk on vaccination probabilities and infection incidence for actual parameters of epidemic influenza. (*A*) Probability of vaccination against epidemic influenza by young and elderly when vaccination levels are at the Nash equilibrium and the utilitarian optimum for actual parameters, with increasing relative vaccine cost. (*B*) Annual infection incidence and mortality when vaccination levels are at the Nash equilibrium and the utilitarian optimum for actual parameters of epidemic influenza, with increasing vaccine cost.

utilitarian vaccination by the young falls exponentially with greater vaccine cost (a function of the severity and probability of all potential costs and risks), whereas Nash vaccination by the elderly is inelastic to increasing cost over the wide range examined (Fig. 1*A*).

When both age groups are vaccinated according to the Nash equilibrium, levels of disease incidence and mortality are significantly higher than when vaccination adheres to the utilitarian strategy (Fig. 1*B*). For the current vaccine cost (value of 1 on the log scale of the *x* axis of Fig. 1*B*), 170 more infections and two more deaths per million individuals occur if vaccination is guided by the Nash equilibrium than if vaccination adheres to the utilitarian strategy. If the vaccine were 10 times more risky/costly (as was the case for the swine influenza vaccine in 1976), further-reduced vaccination levels are predicted by the Nash solution that would cause 43,144 more infections and 24 more deaths per million individuals than would the utilitarian optimum.

For actual epidemiological parameters of epidemic influenza, there are also differences in vaccination levels between the utilitarian optimum and Nash equilibria (Fig. 2*A*). Furthermore, vaccination levels are lower for actual parameters than for perceived parameters, because people tend to greatly overestimate their infection probability (Figs. 1*A* and 2*A*). Nash vaccination of the elderly in Fig. 2*A* reveals the tradeoff between vaccine cost and risk of infection. At low vaccine costs, all elderly seek vaccination. However, at higher vaccine costs, the demand for vaccination drops slightly. This dip occurs until the decline in herd immunity resulting from the concomitantly falling vaccination of the young generates a rebound in vaccine demand by the elderly. The lower actual infection probability results in lower incidence and mortality than when our model is parameterized with perceived values, particularly at high vaccine costs (Figs. 1*B* and 2*B*).

Another comparison of interest is the Nash solution, based on perceived parameters (Fig. 1*A*) relative to the utilitarian solution based on epidemiological parameters (Fig. 2*B*). Because the utilitarian solution is the normatively optimal solution (often determined at a policy level), one might argue that it should be based on best estimates of epidemiological parameters. The Nash solution, in contrast, represents the self-interested behavior of individuals who act according to their own beliefs. When the Nash equilibrium is calculated by using perceived parameters, the discrepancy between the Nash and utilitarian vaccination levels is reduced. That is, in the Nash solution, the self-interest that reduces vaccination of the young is to some extent offset by the overestimation of infection risk.

Reducing vaccine cost promotes vaccination at the Nash equilibrium (Figs. 1*A* and 2*A*). Based on actual epidemiological parameters, 77% vaccination of the young would eliminate both perpetuated transmission and mortality. For perceived parameters,

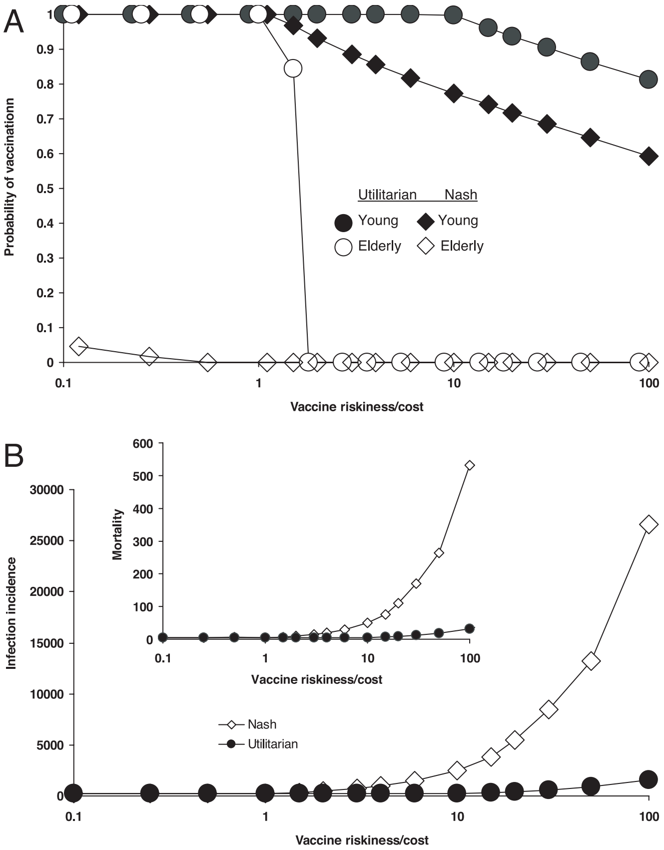

Fig. 3. Effects of vaccine cost/risk on vaccination probabilities and infection incidence for pandemic influenza. (*A*) Probability of vaccination against pandemic influenza by young and elderly when vaccination levels are at the Nash equilibrium and the utilitarian optimum, with relative increasing vaccine cost. Parameters were as in the perceived epidemic case, except that the probability of infection was assumed to be higher and biased toward the young (see *Methods*). (*B*) Annual infection incidence and mortality when vaccination levels are at the Nash equilibrium and the utilitarian optimum for pandemic influenza, with increasing vaccine cost.

this vaccination level is achieved by reducing the vaccine cost to 10% of the current cost. For actual parameters, vaccination of the young to the 77% threshold is predicted to occur at 0.9% of the current cost.

Pandemic Influenza. For pandemic influenza, as for epidemic influenza, utilitarian vaccination is achieved by vaccinating the young. The Nash and utilitarian vaccination strategies of complete vaccination for the young are in alignment over a range of lower vaccine costs (Fig. 3*A*). At both the utilitarian optimum and the Nash equilibrium, the elderly are not vaccinated, unless the vaccine cost is low. In the pandemic case, the young have more incentive to vaccinate than the elderly. The young vaccinate up to a level of herd immunity at which point the elderly have no incentive to vaccinate.

Elevations in infection incidence (Figs. 1*B* and 3*B*) at the Nash equilibrium relative to the utilitarian strategy during a pandemic are lower than those for epidemic influenza for a given vaccine cost. The greater virulence of pandemic influenza boosts incentives to vaccinate. However, pandemic influenza's higher proportion of fatal cases results in greater mortality for pandemic influenza than for epidemic influenza (Fig. 1*B* and 3*B*).

Discussion

Community-wide protection is optimally achieved by vaccinating the proportions of the population most responsible for influenza transmission, i.e., the young (4, 12, 13). However, we found that this utilitarian strategy faces obstacles in population adherence if individuals act according to self-interest, because the personal utility of vaccination is lower for the young than for the elderly.

We identified two sources of discrepancies that affect vaccination levels for both epidemic and pandemic influenza. First, discrepancies generated by discordant incentives to vaccinate between the young and the elderly lead to misalignments between Nash and utilitarian vaccination levels. For epidemic influenza, in both our model and survey results, the young tend to under-vaccinate and the elderly to over-vaccinate, relative to the utilitarian strategy, paralleling CDC recommendations. The differences between utilitarian and Nash vaccination strategies arise because the positive externalities of indirect protection by herd immunity effects are encompassed in the optimization of the utilitarian strategy, but only an individual's internalized costs and benefits come into play at the Nash equilibrium. Herd immunity is fundamental to reducing the public health burden of infectious diseases, but creates an incentive for individuals to free-ride on the vaccination of others. Consequently, the overall level of population vaccination is lower at the Nash equilibrium than at the utilitarian community optimum. Thus, the current CDC policies that focus on the elderly are reinforced by self-interest, but are not the most effective for curtailing transmission and minimizing influenza morbidity and mortality.

For a pandemic avian influenza outbreak, Nash and utilitarian strategies are in closer alignment, relative to an epidemic outbreak. During pandemics, the young are responsible for most transmission, but they also experience disproportionately more severe infection (5, 25, 26). Hence, individual and community incentives are in greater accord than for epidemic influenza. Although a pandemic vaccine will likely be of higher cost and risk than a typical influenza vaccine, the Nash vaccine demand is probably above the number of avian influenza vaccine doses that will be available during a pandemic.

A second source of discrepancy that affects vaccination levels is the difference between perceived and actual epidemiological parameters. We revealed that misperceptions of some epidemiological parameters promote vaccination, whereas others discourage vaccination. For a given vaccine cost, vaccination levels under both the Nash equilibrium and the utilitarian optimum are actually lower for realistic epidemiological parameters than for perceived parameters. People greatly overestimate influenza infection probability and vaccine risks, whereas they underestimate influenza vaccine efficacy. Thus, education about actual infection probabilities without education about actual vaccine efficacy and risks could actually expand the discrepancy between Nash and utilitarian vaccination levels.

We found that the threshold of vaccination at which perpetuated transmission is terminated could be achieved with a higher cost of vaccination for perceived parameters than for actual epidemiological parameters. For perceived parameters, vaccination of the young to this threshold is predicted to occur at 10% of the current cost. For actual parameters, the vaccine must be reduced to <1% of its current cost to achieve this critical vaccination level. Thus, for a given vaccine cost, less incentive is required (or a higher cost permitted) to promote vaccination for the inaccurately perceived parameters identified in our survey.

Achieving these reductions in vaccine costs and real or perceived risks might be accomplished in a combination of ways. Convenience of vaccination is positively associated with the decision to vaccinate (27). To make vaccination more convenient, one approach would be to provide vaccination in schools. The Advisory Committee on Immunization Practices recommends removal of administrative and financial obstacles (28). Greater vaccine availability and initiation of Medicare reimbursement are credited with increasing population vaccination levels (29).

Our survey results indicate that vaccine demand is positively correlated with perceived vaccine efficacy. However, we found that people perceive a lower influenza vaccine efficacy than is actually

Table 2. Parameterization of infection cost, if infected with epidemic influenza

Outcome	Age class	Cost of outcome, $	Relative cost of outcome	Probability (if infected and not vaccinated)	Probability (if infected and vaccinated)	Refs.	Product of relative cost and probability if not vaccinated	Product of relative cost and probability if vaccinated
Illness without medical care	Young	201	0.000192	0.57 (0.55 for pandemic influenza)	0.826	(45, 47, 48, 50)	0.000109	0.000159
	Elderly	327	0.000313	0.59	0.834		0.000185	0.000261
Outpatient visits	Young	322	0.000308	0.42	0.168	(45, 47, 48, 50)	0.000128	0.000051
	Elderly	458	0.000438	0.39	0.156	0.00017	0.000068	
Hospitalization	Young	5861	0.005607	0.011	0.0058	(46, 47, 50)	0.000063	0.000034
Elderly	7653	0.007321	0.016	0.0079	0.000116	0.000058		
Mortality	Young	1045278	1	0.000242 (0.02 for pandemic influenza)	0.000171	(46, 47, 50, 51)	0.000242	0.000171
	Elderly	1045278	1	0.00351 (0.015 for pandemic influenza)	0.0021		0.00351	0.002106
Total cost of infection if infected	Young						0.000542	0.000415
	Elderly						0.003981	0.002493

For pandemic influenza, the costs of infection are dominated by the product of the cost and the probability of mortality if infected, giving the total cost of infection as 0.02 for the young and 0.015 for the elderly (5). Vaccination reduces the severity of infection, if infected. Thus, outcomes such as illness without medical care become more likely, and mortality becomes less likely. Relative cost is the cost of the outcome divided by the cost of mortality. The probability of infection is additionally greatly reduced by vaccination. The vaccination cost includes the cost of the vaccine ($14), associated travel expenses ($4), and time cost to the individual ($16) (10).

the case. The discrepancy between utilitarian and Nash strategies is exacerbated by elevated perceptions of vaccine risk. Indeed, people report apprehension about side effects as a primary deterrent to receiving influenza vaccination (20, 30). For both epidemic and pandemic influenza, aligning the Nash and utilitarian strategies could be promoted by public education to counteract the current overestimation of vaccine risks. Additionally, replacement of thimerosal, the mercury-containing preservative, might allay concerns about vaccine safety, whether or not these concerns are overestimated.

We found that influenza vaccination driven by self-interest and promoted by current CDC recommendations compromises utilitarian programs that would minimize transmission, disease incidence and mortality for the young, the elderly and overall. We also identified discrepancies between predictions generated by using perceived and actual parameters that reveal the importance of parameterizing models of vaccine uptake with psychological data. Ultimately, policy makers must balance public health, social, economic, and ethical considerations when developing optimal public health policies (31). Assessing the interplay among biological systems, decision-making processes and social influences will generate more accurate predictions of vaccine policy adherence, which should facilitate improved interventions.

Methods

Questionnaire. To establish empirical parameters for the model, we analyzed survey responses from the Health Promotion at Work longitudinal study of university employees (15, 27, 32). Six hundred seventy-three participants indicated whether they had received a flu shot during fall 2001 and answered a variety of other questions. For a more complete description of the study and procedures, see ref. 15. The questionnaire items used in the parameterization of our model are summarized in Table 1. We compared predictions for when the epidemiological model is parameterized by using point estimates of psychological questionnaire data reflecting the perceptions that inform individuals' decisions regarding influenza vaccination with predictions for when the model is parameterized by using epidemiological estimates from published data. The epidemiological estimates are equivalent to the decisions of rational individuals with complete knowledge.

Model. Our epidemiological game-theoretic analysis consists of four main components. We first developed a population-level, age-structured, seasonal epidemiological model of influenza transmission and vaccination. The dynamics of young and elderly susceptible, vaccinated, naturally immune, latently infected, and infectious compartments of the population are described by this model. We then used infection prevalences predicted by the epidemiological model to parameterize a Markov process description (33, 34) of vaccination decisions at the level of the individual. Thirdly, we calculated expected utilities of all possible vaccination decisions, based on cost data (Table 2). Finally, a Monte Carlo algorithm parameterized with these utilities was used to determine the convergently stable Nash equilibria. Please see the supporting information (SI) for a detailed description of the model equations and methodology.

Epidemiological population model. To capture the seasonal timing of vaccination and the annual cycle of influenza epidemics, we combined a discrete-time model of vaccination with a differential equation model of a seasonal influenza epidemic (35). The population was divided into two age classes: one with all individuals <65 years of age and the other with all individuals ≥ 65 years of age, parameterized from U.S. census data (36). The older age class corresponds to the CDC's defined target group for vaccination (3). We assumed that parents make decisions in the best interest of their children.

Upon infection, individuals enter a latency period, the perceived duration of which is 4 days (Table 1), compared with an actual value of 1.2 days (39). Latently infected individuals proceed to become infectious. The perceived duration of the infectious period is 5 days (Table 1), which is close to the actual value of 4–5 days (40).

The perceived annual infection probability was 0.48 (Table 1), compared with an actual infection probability of 0.15 (42) for epidemic influenza and of 0.5 for pandemic influenza (derived from refs. 5, 25, and 26 and 1918 census data). The model incorporated the finding that younger individuals are twice as likely to transmit influenza to others (9, 10). For epidemic infection, younger and older individuals are equally likely to contract infection, whereas for pandemic influenza, the attack rate in the young is increased threefold relative to epidemic influenza (5, 25, 26). The case fatality proportion for epidemic influenza is typically 0.3% for the elderly and 0.03% for the young (5, 10). The case fatality proportion for pandemic influenza is 5% for the elderly and 2% for the young (5).

Vaccination was assumed to occur each fall, three months before transmission reaches its maximum. Because influenza rapidly evolves new antigenic variants (43), immunity tends to wane from one year to the next. People perceive that vaccine protection lasts for 8 months (Table 1), the duration of an influenza season.

Individual model of vaccination and infection. Our epidemic model describes the average population dynamics of vaccination and influenza transmission, but the infection future of an individual is stochastic. Therefore, using predicted infection prevalences from our population-level epidemic model, we parameterized a Markov process for an individual's decision dynamics. This process predicts annual probabilities of vaccination and infection for an individual within an age class.

Utility calculation. The individual-level model predicted the probability of future infection and vaccination events. We then used Markov process theory (34) to calculate an individual's expected utility by summing the products of the discounted costs and probabilities for each possible event. We assumed an annual discount rate of 3% (44).

In contrast to the CDC's analysis of infection costs (10), we assumed that all individuals value their life equally, irrespective of their age, although we also compared this result with a lower valuation of elderly life consistent with the CDC's analysis of infection costs ($74,146 versus $1,045,278) (SI). We parameterized the utility calculations with age-specific distributions of infection costs and vaccine efficacy in reducing influenza morbidity and mortality (5, 10, 37, 38, 45–60) (Table 2).

Calculation of Nash equilibria. We used our utilities of vaccination decisions to calculate convergently stable Nash equilibria of the population game in which individuals of a given age class choose vaccination rates. For some simple problems in homogeneous populations, calculations of Nash equilibria are achieved through single parameter optimization. No such simplification is available, however, for age-structured populations with two or more strategy-parameters. Other methods rely on the calculation of local derivatives, which cannot be analytically obtained in closed form for our model. Thus, we adapted a Monte Carlo algorithm (62) to calculate ρ_A and ρ_B at the Nash equilibrium.

At the Nash equilibrium, no individual can improve their expected utility by changing their vaccination probability. Thus, the utility of vaccination is equal to the utility of vaccine refusal for each age class. We found solutions to the equations through minimization of the squared difference between utilities of vaccination refusal versus acceptance for each age class over the parameter solution space. Random perturbations of the proposed vaccination probabilities were drawn sequentially for each class from triangular distributions that added or subtracted at most 0.01. For each iteration, perturbations were accepted when the ratio of the proposed to current squared difference in the specific age class was greater than uniform variates between 0 and 1. The algorithm tended to converge on the solution within ≈100 iterations. The best result from 10,000 iterations of this algorithm was considered a numerical solution. We verified the algorithm on a simplified version of our model and found that its estimate of the Nash equilibrium was the same as that determined algebraically. Additionally, solutions were examined by further manual perturbation and by starting from different initial conditions to ensure that each solution was a global rather than a local equilibrium. For any given set of parameters, only one Nash equilibrium was observed. To find the utilitarian optimum, the search procedure was the same, but the optimization criterion was the maximization of the population utility.

We thank J. Townsend, D. Thomas, S. Basu, J. Medlock, and E. Poolman for valuable comments on the manuscript. This work was supported by the James McDonnell Foundation and the John Simon Guggenheim Memorial Foundation, National Science Foundation Grants SBE-0624117 (to A.P.G.) and SBE-0624098 (to G.B.C.), and the Notsew Orm Sands Foundation (T.C.R. and A.P.G.).

1. Bauch *CT*, Galvani AP, Earn DJD (2003) *Proc Natl Acad Sci USA* 100:10564–10567.
2. Reluga TC, Bauch C, Galvani AP (2006) *Math Biosci* 204:185–198.
3. Smith NM, Bresee JS, Shay DK, Uyeki TM, Cox NJ, Strikas RA (2006) *Morbid Mort Wkly Rep* 55:1–41.
4. Brownstein JS, Kleinman KP, Mandl KD (2005) *Am J Epidemiol* 162:1–8.
5. Glezen WP (1996) *Epidemiol Rev* 18:64–76.
6. Monto AS, Ullman BM (1974) *J Am Med Assoc* 227:164–169.
7. Glezen WP, Couch RB (1978) *N Engl Med* 298:587–592.
8. Fox JP, Hall CE, Cooney MK, Foy HM (1982) *Am J Epidemiol* 116:212–227.
9. Taber LH, Paredes A, Glezen WP, Couch RB (1981) *J Hyg (London)* 86:303–313.
10. Meltzer MI, Cox NJ, Fukuda K (1999) *Emerg Infect Dis* 5:659–671.
11. Viboud C, Bjornstad ON, Smith DL, Simonsen L, Miller MA, Grenfell BT (2006) *Science* 312:447–451.
12. Monto AS, Davenport FM, Napier JA, Francis T, Jr (1969) *Bull W H O* 41:537–542.
13. Halloran ME, Longini Jr, M (2006) *Science* 311:615–616.
14. Chapman GB, Coups EJ (1999) *Prev Med* 29:249–262.
15. Chapman GB, Coups EJ (2006) *Health Psychol* 25:82–90.
16. Brewer NT, Chapman GB, Gibbons FR, Gerard M, McCaul K, Weinstein ND (2007) *Health Psychol*, in press.
17. Smailbegovic MS, Laing GJ, Bedford H (2003) *Child Care Health Dev* 29:303–311.
18. Asch DA, Baron J, Hershey JC, Kunreuther H, Meszaros J, Ritov I, Spranca M (1994) *Med Decis Making* 14:118–123.
19. Couch RB (2000) *N Engl Med* 343:1778–1787.
20. Nichol KL, Lind A, Margolis KL, Murdoch M, McFadden R, Hauge M, Magnan S, Drake M (1995) *N Engl Med* 333:889–893.
21. Ahmed F, Singleton JA, Franks AL (2001) *N Engl Med* 345:1543–1547.
22. Lasky T, Terracciano GJ, Magder L, Koski CL, Bellesteros M, Nash D, Clark S, Haber P, Stolley PD, Schonberger L, Chen RT (1998) *N Engl Med* 339:1797–1802.
23. CDC (1999) *Morbid Mort Wkly Rep* 48:996–998.
24. Nash JF (1950) *Proc Natl Acad Sci USA* 36:48–49.
25. Simonsen L, Clarke MJ, Schonberger LB, Arden NH, Cox NJ, Fukuda K (1998) *J Infect Dis* 178:53–60.
26. Reichert TA, Simonsen L, Sharma A, Pardo SA, Fedson DS, Miller MA (2004) *Am J Epidemiol* 160:492–502.
27. Capolongo MJ, DiBonaventura MD, Chapman GB (2006) *Ann Behav Med* 31:288–296.
28. CDC (1999) *Morbid Mort Wkly Rep* 48:1–15.
29. CDC (1994) *Morbid Mort Wkly Rep* 43:771–773.
30. CDC (2004) *Morbid Mort Wkly Rep* 53:1012–1015.
31. Galvani AP, Medlock J, Chapman G, *Science* 313:758–760.
32. DiBonaventura MD, Chapman GB (2005) *Psychol Health* 20:761–774.
33. Bellman R (1957) *Dynamic Programming* (Princeton Univ Press, Princeton).
34. Howard RA (1960) *Dynamic Programming and Markov Processes* (MIT Press, Cambridge, MA).
35. Reluga T (2004) *Theor Popul Biol* 66:151–161.
36. US Bureau of the Census (2000) *2000 U.S. Census–Sex by Age*.
37. Demicheli V, Jefferson T, Rivetti D, Deeks J (2000) *Vaccine* 18:957–1030.
38. Govaert TM, Thijs CT, Masurel N, Sprenger MJ, Dinant GJ, Knottnerus JA (1994) *J Am Med Assoc* 272:1661–1665.
39. Longini I, Nizam A, Xu S, Ungchusak K, Hanshaoworakul W, Cummings DAT, Halloran EM (2005) *Science* 309:1083–1087.
40. Longini IM, Halloran ME, Nizam A, Yang Y (2004) *Am J Epidemiol* 159:623–633.
41. Simonsen L, Clarke MJ, Williamson GD, Stroup DF, Arden NH, Schonberger LB (1997) *Am J Public Health* 87:1944–1950.
42. Treanor J (2004) *N Engl Med* 350:218–220.
43. Bush R, Bender C, Subbarao K, Cox N, Fitch W (1999) *Science* 286:1921–1925.
44. Gold MR, Siegel JE, Weinstein MC (2001) *Cost-Effectiveness in Health and Medicine* (Oxford Univ Press, Oxford).
45. Campbell DS, Rumley MA (1997) *J Occup Environ Med* 39:408–414.
46. US Government (1996) *The Federal Register* 61:46301–46302.
47. Haddix AC, Teutsch SM, Shaffer PA, Duet DO (1996) *Prevention Effectiveness* (Oxford Univ Press, New York).
48. Kavet J (1977) *Am J Public Health* 67:1063–1070.
49. Office of Technology Assessment (1981) *Cost Effectiveness of Influenza Vaccination* (Government Printing Office, Washington, DC).
50. Serfling RE, Sherman IL, Houseworth WJ (1967) *Am J Epidemiol* 86:433–441.
51. US Bureau of the Census (1997) *Statistical Abstract of the United States*, Washington, DC).
52. Arden NH, Patriarca PA, Kendal AP (1986) in *Options for the Control of Influenza* (Liss, New York).
53. Bridges CB, Thompson WW, Meltzer MI, Reeve GR, Talamonti WJ, Cox NJ, Lilac HA, Hall H, Klimov A, Fukuda K (2000) *J Am Med Assoc* 284:1655–1663.
54. Monto AS, Hornbrook K, Ohmit SE (2001) *Am J Epidemiol* 154:155–160.
55. Mullooly JP, Bennett MD, Hornbrook MC, Barker WH, Williams WW, Patriarca PA, Rhodes PH (1994) *Ann Intern Med* 121:947–952.
56. Neuzil KM, Dupont WD, Wright PF, Edwards KM (2001) *Pediatr Infect Dis J* 20:733–740.
57. Nichol KL, Wuorenma J, von Sternberg T (1998) *Arch Intern Med* 158:1769–1776.
58. Palache AM (1997) *Drugs* 54:841–856.
59. Patriarca PA, Weber JA, Parker RA, Hall WN, Kendal AP, Bregman DJ, Schonberger LB (1985) *J Am Med Assoc* 253:1136–1139.
60. Wilde JA, McMillan JA, Serwint J, Butta J, O'Riordan MA, Steinhoff MC (1999) *J Am Med Assoc* 281:908–913.
61. Jefferson T, Demicheli V (1998) in *Textbook of influenza*, eds. Nicholson KG, Webster RG, Hay AJ (Blackwell Science, London), pp. 541–547.
62. Johannesson H, Townsend JP, Hung C-Y, Cole GT, Taylor JW (2005) *Genetics* 171:109–117.