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U.S. airport entry screening in response to pandemic influenza: Modeling and analysis

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Summary *Background:* A stochastic discrete event simulation model was developed to assess the effectiveness of passenger screening for Pandemic Influenza (PI) at U.S. airport foreign entry. *Methods:* International passengers arriving at 18 U.S. airports from Asia, Europe, South America, and Canada were assigned to one of three states: not infected, infected with PI, infected with other respiratory illness. Passengers passed through layered screening then exited the model. 80% screening effectiveness was assumed for symptomatic passengers; 6% asymptomatic passengers. *Results:* In the first 100 days of a global pandemic, U.S. airport screening would evaluate over 17 M passengers with 800 K secondary screenings. 11,570 PI infected passengers (majority asymptomatic) would enter the U.S. undetected from all 18 airports. Foreign airport departure screening significantly decreased the false negative (infected/undetected) passengers. U.S. attack rates: no screening (26.9%–30.9%); screening (26.4%–30.6%); however airport screening results in 800 K–1.8 M less U.S. PI cases; 16 K–35 K less deaths (2% fatality rate). Antiviral medications for travel contact prophylaxis (10 contacts/PI passenger) were high – 8.8 M. False positives from all 18 airports: 100–200/day.
Conclusions: Foreign shore exit screening greatly reduces numbers of PI infected passengers. U.S. airport screening identifies 50% infected individuals; efficacy is limited by the asymptomatic PI infected. Screening will not significantly delay arrival of PI via international air transport, but will reduce the rate of new US cases and subsequent deaths.

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Introduction

Concepts of operational plans for pandemic influenza (PI) screening of arriving international air travelers at the 18 major U.S. airports have been developed and more detailed plans are in progress at the local level. A stochastic discrete event simulation was created to assess screening efficacy, identify cost effective processes, and minimize passenger delays. Discrete event simulations involve probability distributions of a chronological sequence of events and are utilized to improve customer service queues. Diagnostic and treatment options for infected arriving passengers and prophylaxis of plane and traveling companions were also integrated into the simulation. The overall goal of airport screening of internationally arriving passengers is to minimize the peak of pandemic illness (flatten the epidemic curve) within the country, thereby decreasing surge demands on the medical care system and allowing additional time for vaccine development and distribution. In a pandemic with a global world economy, entry of disease into countries is inevitable, but cost effective control measures are certainly possible. The integrated discrete event simulation model is adaptable to other nations with international air terminals and unique flight schedules.

Materials and methods

The probability of a passenger being infected with pandemic influenza (*Pip*) in the first 100 days of a global epidemic was calculated upon the assumption that the initial cases originate in the Asian continent with a reproductive rate (Ro) value of 3 (Fig. 1). Ro value assumptions for other regions as follows: Europe = 2.4, Latin America = 2.1, Canada and U.S. = 2.0. Ro values were derived from Center for Disease Control and Prevention, Division of Global Quarantine and Migration, scenarios and Models of Infectious Disease Agent Study (MIDAS) calculations.[1]

The integrated stochastic discrete event passenger process simulation involved probabilities of infected states of passengers over time (not infected, infected with PI, infected with other respiratory illness), number and originating location of international air flights arriving to the 18 U.S. airport ports of entry, and screening process decision points (Fig. 2). Additional detailed methodology on the simulation is available.[2] The arriving international passenger screening process for U.S. airports utilized in this study is detailed in Fig. 3. The time period of 100 days from the initial start of the global pandemic was chosen for greatest efficacy of screening; once the epidemic has been significantly established within a country, continuing to supply extensive resources to screen international travelers for a relatively low number of newly arriving cases will not significantly affect the epidemic curve within a country.

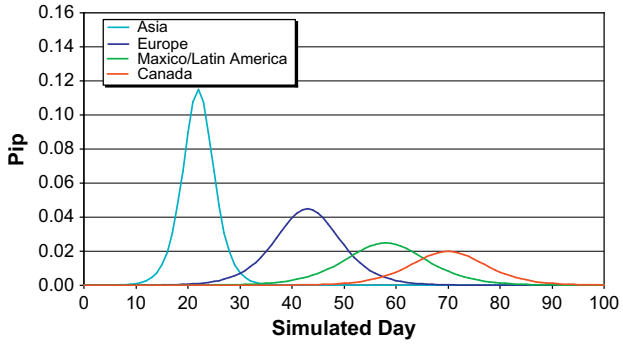

Figure 1 Probability of a passenger being infected with pandemic influenza *Pip* as a function of simulation day by region of origin.

Three scenarios were chosen based upon the likelihood of an individual's decision to travel when ill. In scenario 1, 50% of passengers predicted to be possibly infected with pandemic or other respiratory illness attempt to embark on international flights. High detection rates (80%) for symptomatic individuals with fever, cough, myalgia, exist at various screening layers, most importantly at the point of embarkation. This scenario results in significant number of ill passengers being identified and prevented from traveling at origin, resulting in more true positives (TP) infected with pandemic influenza detected upon U.S. arrival than false negatives (FN). False negative pandemic influenza infected but undetected asymptomatic travelers have no or minimal symptoms and only 6% are identified in the screening process.

In scenario 2, 100% of passengers predicted to be possibly infected with pandemic or other respiratory illness elect to travel when ill or incubating PI, ignoring regulations for isolation and quarantine. They attempt to embark on flights and high detection rates (80%) exist at various screening layers. More total pandemic and other infected passengers are introduced into system than in scenario 1, therefore more TPs and FNs exist at U.S. screening ports of entry.

In scenario 3, 50% of passengers predicted to be possibly infected with PI or other respiratory illness embark on flights with significantly reduced detection rates (<50%) especially at embarkation points. The same amount of pandemic infected passengers is introduced into the system as in scenario 1, but since less infected passengers are identified at origin, there are more TPs and FNs identified at U.S. entry screening.

The predicted false negative (pandemic influenza infected but undetected) passengers were then entered into EPICAST (Epidemiological Forecasting model design and parameterization) for prediction of epidemic diffusion in the United States with resulting morbidity and mortality.[3] True Positives, passengers with pandemic influenza identified at arrival screening, are treated and isolated, thereby removed as a transmission source within the U.S. but after exposure to passengers, travel companions, and aircrew during their travel.

Results

The total numbers of passengers infected with pandemic influenza on inbound international flights for all 18 U.S. international airports per the three scenarios are graphed in Fig. 4. The graph is bimodal, a majority of the passengers in the first peak are from Asia where the pandemic initiates; a majority of passengers in the second peak originate in Europe. The second peak is larger as many more international flights to the United States originate in Europe.

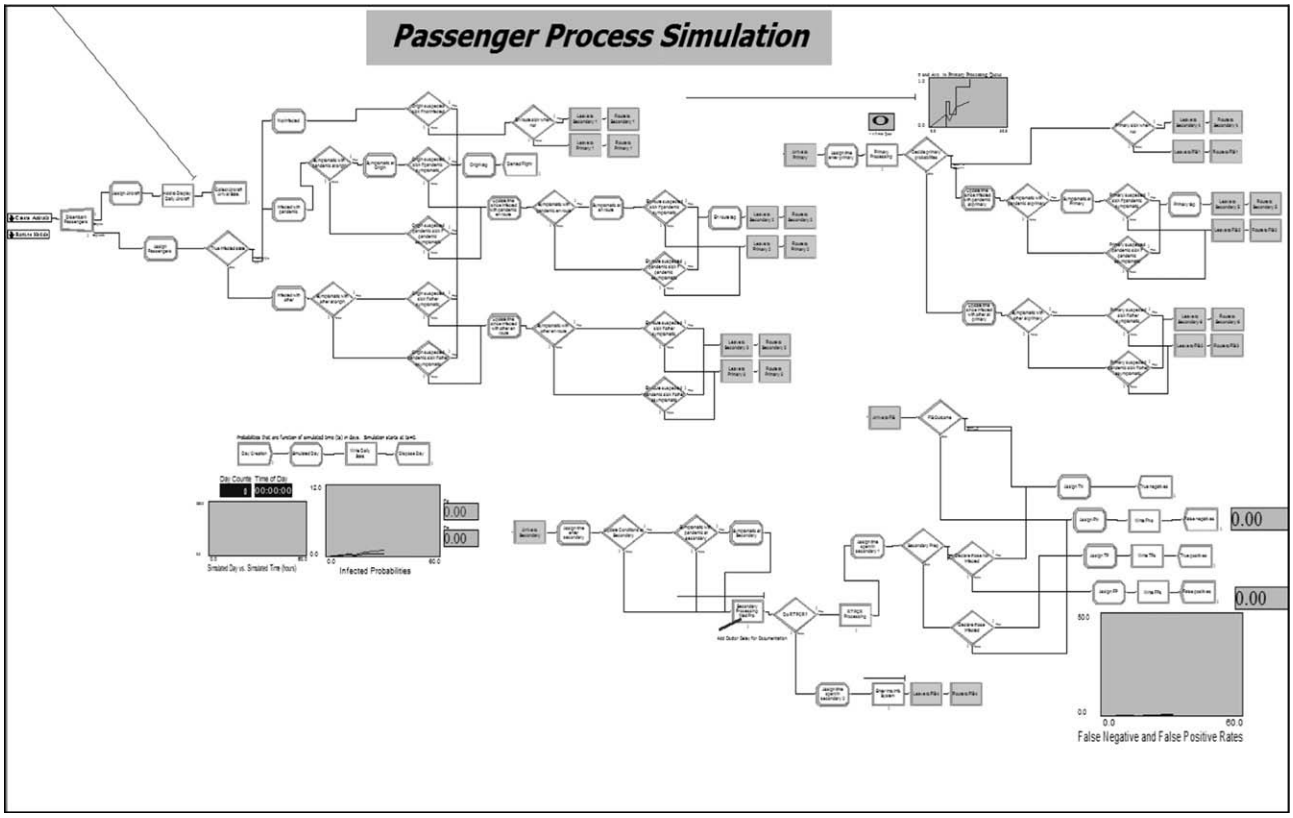

Figure 2 Stochastic discrete event passenger process simulation.

Scenario 3 has the highest number of infected arriving passengers due to reduced detection rates (<50%) at the point of embarkation. More infected passengers (includes true positives and the highest number of false negatives) are introduced into the system — (peak day 45—1600 arrive), even if only 50% of the predicted infected population of passengers carrying virus elect air travel, attempting compliance with isolation and quarantine guidelines. Scenario 2 with a higher prevalence (100%) of possibly infected passengers traveling due to no effective isolation and quarantine with a high (80 %) embarkation screening for symptomatic passengers results in decreased peak days 24 and 45 by approximately 200 individuals but otherwise a fairly similar curve. Scenario 1 with 80% detection rates for symptomatic passengers, most importantly at the point of origin, and even if only 50% compliance with isolation and quarantine, has the lowest number of arriving infected passengers (peak days 45—980). The number of infected arriving passengers is reduced by nearly 40% in scenario 1.

The numbers of passengers detected and actually infected with PI (true positives) at the 18 U.S. airport screening stations are depicted in Fig. 5. In scenario 1, the high detection rate of symptomatic individuals at embarkation results in the lowest number of true positives identified at U.S. airport ports of entry. Total positives for scenarios 2 and 3 are essentially the same. Scenario 2 has a higher efficacy of screening (80%) but less compliance with isolation and quarantine travel restrictions (100% possibly infected fly); therefore more infected passengers enter the system. In scenario 3, screening effectiveness at embarkation point is relatively low (<50%), resulting in more infected passengers enroute, despite 50% compliance with isolation and quarantine guidelines with a decreased number of potentially infected electing not to fly. Even though screening efficacy is lower at the point of U.S. entry in scenario 3, more infected passenger board planes for travel to the U.S. and the distribution of true positives is similar.

As with most contagious respiratory infections, infected individuals who are not incapacitated and do not appreciate the significance of their illness or their ability to disseminate disease are the source of spread in a population. In pandemic influenza, the infected/undetected — false negatives (FN) — are of greatest concern as they are not isolated and treated, thereby spreading infection upon arrival. Also their travel companions and airplane contacts during the confined 8—12 h long transcontinental air flight are not identified for prophylaxis and quarantine. The ability to identify FN passengers is realistically low (only 6%) in our model as passengers would have to voluntarily self-identify themselves as having a known high risk exposure after commencing travel. Fig. 6 depicts the false negatives by scenario with a similar bimodal peak to the total number of PI infected arriving international passengers. The significantly reduced <50% detection ability (low sensitivity) in scenario 3 results in a higher number of false negative passengers. The high 80% detection rates for symptomatic individuals in scenarios 1 and 2 result in similar curves, with scenario 2 having more individuals due to a higher prevalence (100% of passengers that could be infected with PI or other respiratory illness) embarking for transcontinental air travel.

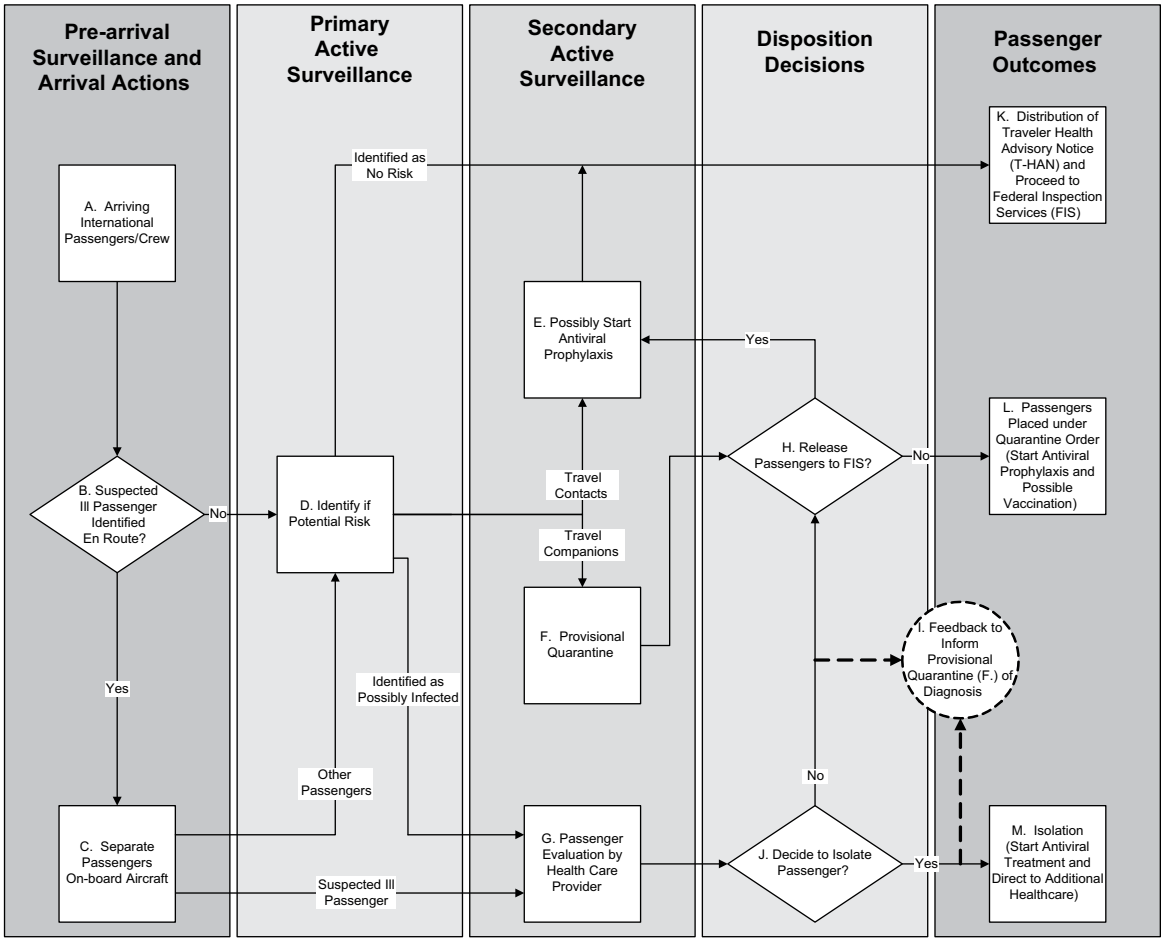

Figure 3 Proposed U.S. airport international arriving passenger screening process.

The false negative passenger numbers predicted were transferred to the EpiCast simulation model to identify impact of untreated and not isolated passengers on the diffusion of the epidemic within the U.S. The impact of screening of arriving international travelers at U.S. airports by scenario is detailed in Table 1. The impact of a 45-day delay in the epidemic due to early and accurate airport screening, allowing an effective vaccine to be developed and distributed, is also depicted. In scenario 1, with high (80% symptomatic) detection rates and 50% compliance with isolation and quarantine restrictions for international travelers, the U.S. attack rate is reduced from 30.7% to 30.4% — this represents an estimated 867,000 fewer people becoming ill in the U.S. population and 17,000 fewer deaths, assuming a 2% case-fatality rate. With the possibility of a 45-day delay in this scenario allowing for development of an effective vaccine, there are 1.3 million fewer cases and 25,800 fewer deaths in 100 days of the epidemic.

The reduction in cumulative incidence of U.S. pandemic influenza cases for scenario 1, the ''best case'' with lowest number of false negatives that disseminate disease within the country is depicted in Fig. 7. Early in the epidemic, with a 5—7 day estimated incubation period for influenza, there are some new cases attributable to international travelers, but the cumulative incidence is difficult to visually identify in the graph, therefore the figure is truncated and commences at day 40. The graphs for the other scenarios are very similar. In our model, the cumulative incidence of U.S. infection eventually increases to over 85,000,000 cases indicating an attack rate of over 30%, reflecting the suggested values in the *Federal Pandemic Influenza Strategic Plan*.[4] A 45-day delay for effective vaccine production could reduce the cumulative incidence by approximately 10 million cases.

Significant resources are required to implement the layered screening program as described in Fig. 3. Based on 2006 flight data, over 17 million international passengers arrive at all 18 U.S. airport ports of entry during the first

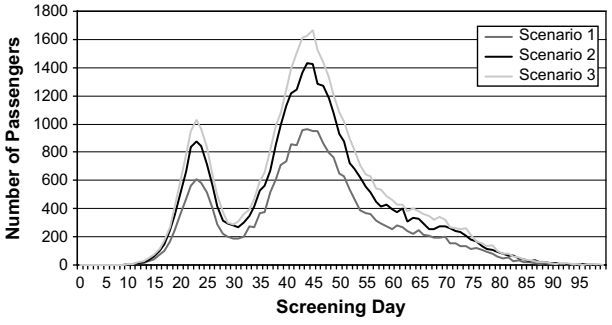

Figure 4 Total number of passengers infected with pandemic influenza on inbound international flights for all 18 U.S. airports per day.

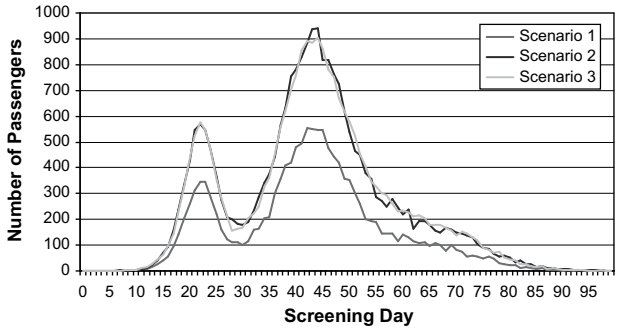

Figure 5 Number of passengers detected and actually infected with pandemic influenza — true positives (TP) — total for all 18 U.S. international airports per day.

100 days of the epidemic, 1.7 million inbound international passengers each day. Although severe reductions (30%) of international air travel passengers may result from the pandemic, significant decrements are unlikely in the first 100 days, and an increase in returning passengers may occur from the several million U.S. citizens residing in foreign countries. Table 2 identifies the number of passengers processed into secondary screening requiring a healthcare professional evaluation and final definitive testing by Reverse Transcriptase Polymerase Chain Reaction (RT-PCR). For example, San Francisco (SFO) International airport has about 10,000 international arriving passengers per day. Given scenario one, 4.6% of the passengers (average of 440 per day) would be directed to secondary active surveillance for a medical evaluation. For the 18 U.S. airports over 100 days, this percentage corresponds to almost 800,000 passenger evaluations and 170,000 RT-PCR laboratory tests, as 22% of those in secondary screening are tested to meet an 80% detection rate.

False positive (FP) passengers, those erroneously diagnosed during the layered screening process as infected when they in fact are not, and their contacts, would be subjected to considerable stress. Such passengers would be placed in isolation, provided unnecessary medications, and their contacts quarantined and provided prophylactic medications. Of the 190,000 daily arriving international passengers, approximately 170 arriving passengers per day are erroneously diagnosed at U.S. airports as having pandemic influenza in scenarios 1 and 2 and 100/day in scenario 3 (Fig. 10). Scenario 3, with only 50% of predicted passengers flying with a respiratory illness due to compliance with travel guidelines, and reduced screening detection rates with decreased utilization of RT-PCR testing results in the lowest number of false positives. The 99% sensitivity/specificity of the RT-PCR laboratory test is unchanged in the three scenarios.

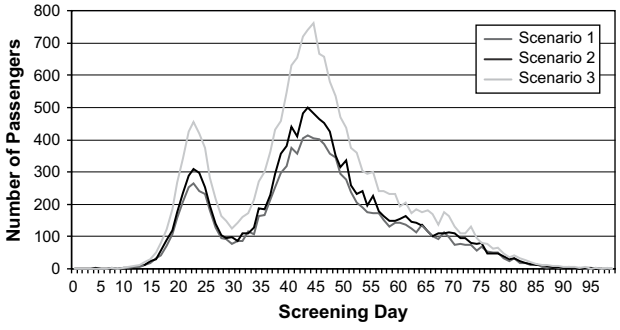

Figure 6 Number of passengers infected with pandemic influenza that are not detected — false negatives (FN) — total for all 18 U.S. international airports per day.

An estimate by scenario of pandemic influenza antiviral medication usage over the initial 100 days of the pandemic is pictured in Fig. 8. Effective antiviral drug utilization for treatment of passengers identified as being infected — both true positives (TP) and false positives (FPs) — and prophylaxis of travel companions and plane contacts (including aircrew) is a significant intervention in this mitigation strategy. Estimates of plane contacts were calculated at 10 and 30 per infected passenger, based on available information for influenza spread in airplanes. One intention of this model is to reduce passenger delays by not detaining and supporting infected or exposed passengers in isolation and quarantine areas in nearby airport facilities. Such facilities would also have to be quite large and capable of handling a myriad of patient health and family issues. Fig. 9 estimates the number of healthcare workers required to operate the screening stations at each U.S. international airport facility based on passenger volumes and projected waiting times. All airport screening and health professionals involved in primary and secondary active surveillance also receive antiviral prophylaxis (approximately 8000 weekly doses for 730 individuals for 12 weeks).

Discussion

Effective screening of international passengers arriving to the 18 U.S. international airports for pandemic influenza is a daunting task. Approximately 1.7 million air travelers arrive daily on nearly 5000 flights, with each large jet carrying over 300 individuals including flight crews. Flights frequently arrive in early morning hours and require intense resourcing during brief periods to prevent long passenger delays. A layered screening process with primary and secondary active surveillance was developed for appropriate sensitivity and specificity (Fig. 3). For the first 100 days of a pandemic, the stochastic discrete event simulation produced bimodal curves of passengers predicted to be infected with influenza. In our assumption, the outbreak originated in Asia and then spread to Europe. The second peak of the total number of passengers infected with pandemic influenza on inbound international flights is larger due to more U.S. arriving air flights and passengers from the European continent. A subtle analysis revealed that the initial cases of Asian origin passengers may arrive to the U.S. through departure from European air terminals to East Coast U.S. cities, not necessarily from direct transpacific flights.

European flights are a larger threat for pandemic influenza entry into the U.S. due to more arriving flights and passengers. Although flights from the Southern Hemisphere and Canada to the U.S. can contain PI infected passengers, the smaller number of flights and also the lower predicted prevalence of influenza in the area populations in the first 100 days of a global pandemic originating in Asia resulted in fewer PI infected passengers (Fig. 1). The African Continent

Table 1 Impact of international airport entry screening, U.S. population attack rate and number of deaths.

National health impact of entry screening					
		Scenario	1	2	3
Reference case	Attack rate	w/o screening	30.7%	30.8%	30.9%
		With screening	30.4%	30.5%	30.6%
	Fewer Ill		867,000	996,000	801,000
	Fewer deaths[a]		17,000	19,900	16,000
45-day shift	Attack rate	w/o screening	26.9%	27.1%	27.2%
		With screening	26.4%	26.5%	26.7%
	Fewer Ill		1,290,000	1,760,000	1,430,000
	Fewer deaths[a]		25,800	35,200	28,500

[a] Assuming a 2% case-fatality rate.

was not specifically considered as a majority of transcontinental U.S. air travel from this continent connects through major European cities. The first 100 days of global pandemic were modeled as airport screening was not expected to produce a significant difference in the U.S. epidemic spread once infection was firmly established within the country.

The ''worst case'' scenario 3 with a low (<50%) detection for PI at foreign port embarkation and the 18 U.S. screening stations and a low 50% compliance with isolation and quarantine policies had the highest number of arriving PI infected passengers (Fig. 4). As expected with a low detection ability (sensitivity) and high prevalence of disease, scenario 3 had the highest number of infected and undetected (false negative) passengers missed by the airport screening procedures (Fig. 6). Scenario 3 subsequently has a slightly higher attack rate to the U.S. population (no screening 30.9%, screening 30.6%) and screening results in slightly lower numbers of 801,000 infections and 16,000 fewer deaths (Table 1). In the ''best case'' with scenario 1 of an 80% detection of those symptomatic with PI and a 50% compliance by passengers with isolation and quarantine restrictions, a significant number (peak day 45–400) of undetected and infected passengers entered the U.S. to disseminate infection. The effectiveness of screening is limited by those that are incubating the virus infected but not symptomatic with fever, cough, and myalgias. Detection of influenza in children is especially challenging.

The ability to identify incubating or minimally affected passengers (i.e. headache and mild myalgia early in clinical infection) is realistically low (6%) as passengers would have to voluntarily self-identify to known high risk exposure after commencing travel. To increase self-identification, a one page questionnaire for in-flight completion searching for high risk exposure was developed emphasizing the potential for personal treatment with antivirals for infected passengers and prophylaxis of travel companions. This may be an incentive for voluntary identification, even if resulting in isolation and quarantine.

Airport screening of international arriving travelers predicted by this model reduced the number of infected passengers entering country, but could not prevent entry. A significant finding of this computer modeling is that airport entry screening could reduce the number of people infected in the U.S. by 800,000–900,000, with up to nearly 20,000 fewer deaths (Table 1) in an epidemic infecting 30% of the 300 million U.S. population. Also, if the entry of infected passengers could be delayed by 45 days, then the reduced number of cases in the U.S. could range from 1,290,000 to 1,760,000 with 25,000 to 35,000 fewer deaths, assuming the possibility to produce and distribute an effective pandemic influenza vaccine (Fig. 7). In an emergency situation, approximately 4 months are currently estimated to produce significant vaccine quantities.

As for passengers incorrectly identified as having pandemic influenza infection, scenario 3 has the lowest number of false positives (FPs) due to decreased mid-level probabilities of pandemic influenza detection (Fig. 10). Scenario 3 averages approximately 100 false positives per day, well below by nearly half the other two scenarios. The lower detection probabilities of scenario 3 lead to a lower FP number, but also, a higher number of infected passengers (FN) entering the U.S. population and a worsening of the U.S. pandemic (Fig. 4).

In scenario 2, where 100% of potentially infected passengers with pandemic influenza or other respiratory illness embark (i.e. no isolation and quarantine compliance) with high (80%) detection rates for symptomatic individuals, the prevalence of symptomatic passengers is

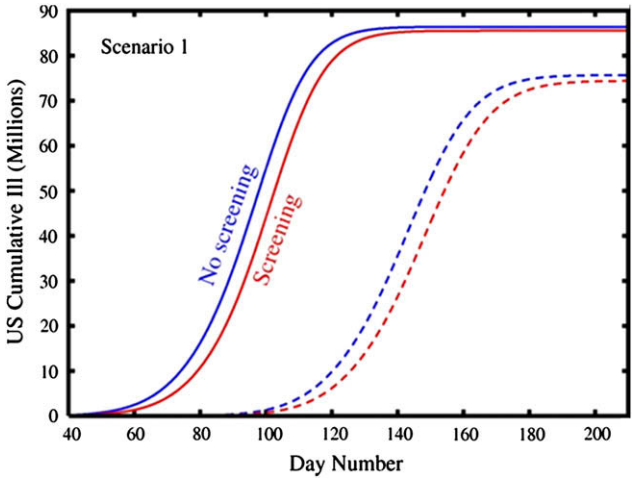

Figure 7 Impact of international passenger airport screening on U.S. pandemic influenza cumulative incidence. Dashed curves – effect of 45-day entry delay with effective vaccine development.

Table 2 Number of passengers screened — 18 U.S. International Airports — 100 days duration.

Outcome	Observations	# To Secondary	# PCR tested
Scenario 1			
FN	11,570	1,397	273
TP	13,962	13,962	13,962
FP	17,194	17,194	17,194
TN	17,093,545	759,102	137,599
Totals	17,136,271	791,655	169,028
		Percent PCR Tested of Those Going to Secondary	21.35%
Scenario 2			
FN	13,253	2,172	505
TP	23,523	23,523	23,523
FP	18,513	18,513	18,513
TN	17,347,604	817,271	147,633
Totals	17,402,893	861,479	190,174
		Percent PCR Tested of Those Going to Secondary	22.08%
Scenario 3			
FN	19,139	2,081	503
TP	23,499	23,499	23,499
FP	9,367	9,367	9,367
TN	17,521,211	415,833	75,257
Totals	17,573,216	450,780	108,626
		Percent PCR Tested of Those Going to Secondary	24.10%

doubled that in Scenario 1 where only 50% of the passengers possibly infected with pandemic influenza or other respiratory illness embark on flights with similar high (80%) detection rates. Scenario 2 subsequently has a higher number of infected passengers peaks (day 24—820, day 45—1400) compared to scenario 1 peaks (day 24—580, day 45—820) as in Fig. 4. Scenario 2 also has a slightly greater number of infected and undetected false negatives (peaks day 24—50 more; day 45—100 more) compared to scenario 1, due to a higher prevalence of disease (Fig. 6). The FN curve of scenarios 1 and 2 is nearly identical due to similar 80% detection rates, and still much less FN activity than ''worst case'' scenario 3. In scenario 2, as the prevalence of ill passengers is greater, a greater number (861,477) enters secondary screening but are appropriately identified with the highest utilization of RT-PCR requiring 190,173 tests (Table 2).

False positive (FP) passengers with a common respiratory illness (seasonal influenza, rhinovirus, mycoplasma) are diagnosed with pandemic influenza despite a >99% specificity for confirmatory pandemic influenza testing. Respiratory specimens are obtained by healthcare workers per the passenger screening flow diagram (Fig. 3). False positive tests can result from incorrect specimen labeling or laboratory cross-contamination. In our model the FP rate is

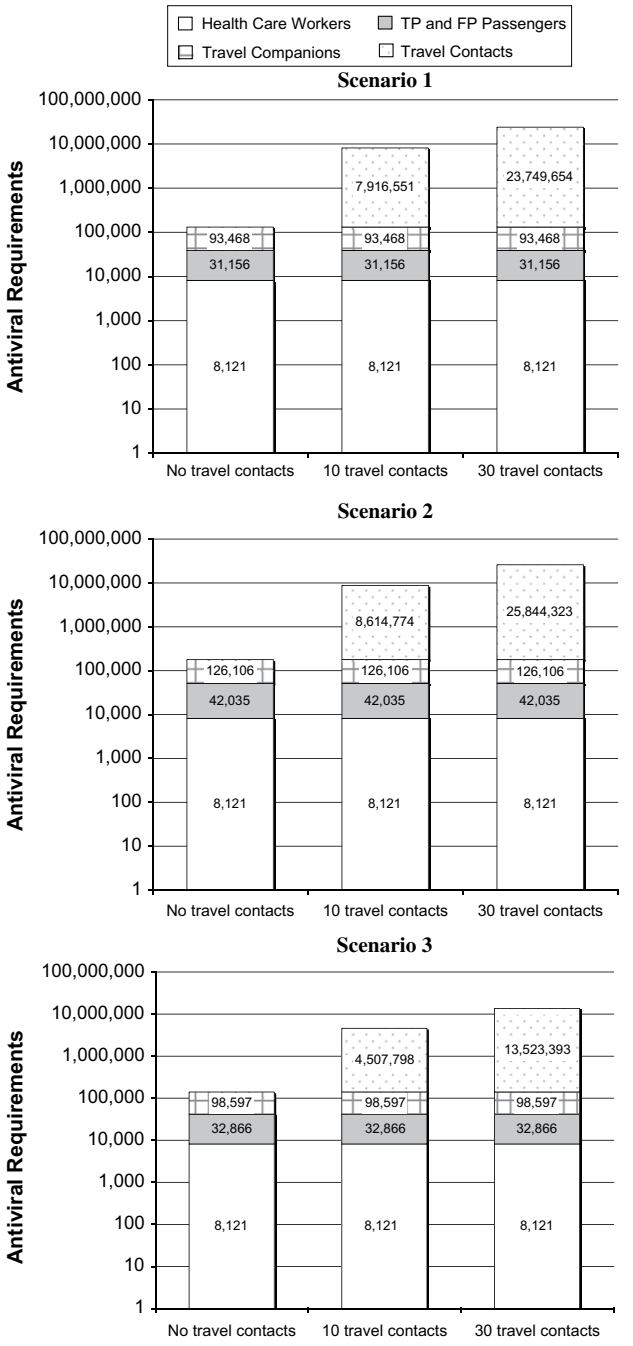

Figure 8 Potential antiviral requirements initial 100 days — 18 U.S. International Airports.

very low (scenario 3 — 100/day; scenario 1 and 2—170/day), due to the >99% specificity of the RT-PCR laboratory test, but with the high number of passengers being screened (1.7 million per day) and low prevalence of actual disease, a noticeable 100—200 FP number results.

The number of FP in Scenario 2 (100% of predicted potentially PI infected with respiratory illness travel, 80% detection rates for symptomatic) on most days is slightly greater than Scenario 1, (50% of predicted potentially infected passengers with respiratory illness travel, 80% detection rates for symptomatic) although the scenarios are nearly similar (Fig. 10). The reason for similar FP is the

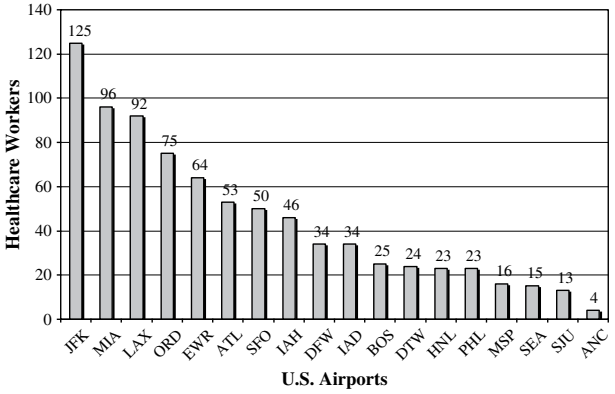

Figure 9 Healthcare worker requirements for screening — 18 U.S International Airports.

little difference between the two scenarios in the number of non-pandemic influenza infected passengers, and the slightly higher number of false positives in scenario 2 can be related to the 20,000 more RT-PCR tests performed.

The large amount of antiviral medication, which currently implies oseltamivir therapy, for treatment and prophylaxis during the 100-day period was an unexpected finding (Fig. 9). Scenario 2 with high (80%) detection rates and no passenger compliance with isolation and quarantine subsequently showed the highest prophylaxis requirement — 25 million week long antiviral courses at 30 contacts per identified infected passenger and 8.8 million week long courses at 10 travel contacts. Along with personal protective equipment including N95 masks, professional healthcare workers in the airport screening environment, especially those obtaining respiratory specimens, should be on antiviral prophylaxis; 8000 week long courses are estimated for prophylactic coverage of 736 individuals staffing 18 airports for 12 weeks (Fig. 9). Prioritization of these healthcare workers for receiving an effective pandemic vaccine may minimize the need for antiviral prophylaxis.

Our model included pandemic influenza antiviral prophylaxis for 30 contacts per identified infected air passenger. Those that are infected, especially symptomatic with cough and fever, and elect to travel in spite of isolation and quarantine policies, are of great concern for disease spread to fellow travelers and aircrew during the confined 8—12 h long transcontinental air flight.

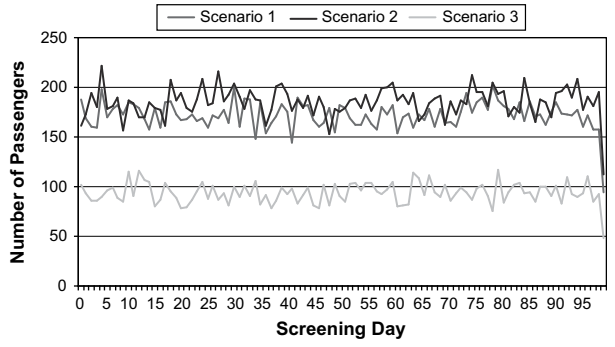

Figure 10 Number of passengers who do not have pandemic influenza but erroneously diagnosed — False Positives (FPs) — total for all 18 U.S international airports per day.

Transmission of influenza virus is by aerosol or direct contact. Inhalation of as few as three infective particles can transmit infection and young children are most likely to be infected and spread disease.[5] Actual data on the risk of influenza transmission in airplanes is sparse and primarily provided by several outbreaks. In 1979, an airplane undergoing ventilation system repairs was grounded on the tarmac and 54 passengers were confined for several hours with the doors closed and no ventilation.[6] A 72% influenza attack rate occurred from 1 infected passenger and the secondary attack rate in families of passengers within 2 weeks was estimated to be 20%. Although this case involved older airplane ventilation technology, the high transmission rate was attributed to the 3 h delay while an inoperative ventilation system underwent repair with passengers confined and doors closed. In today's congested air travel system, several hours of tarmac delays occur with varying procedures that decrease cabin ventilation by not operating fuel consuming jet engines. In October 2008, of 554,325 total U.S. carrier flights for the month, of those that were finally cancelled or diverted, three had tarmac delays of over 4 h and 9 of more than 3 h.[7]

An air travel outbreak of Influenza A was reported among military members at a U.S. Naval Air Station in 1989. Passenger transmission occurred on the ground and aboard two DC 9 aircrafts with a 37% attack rate among a 114 person air squadron.[8] In 1999 with more modern aircraft, 20 passengers were infected with influenza like illness on a 3 h flight in a 75-seat passenger jet in Australia.[9] Although 9 cases were clustered within 3 rows of the index case that coughed and sneezed throughout the flight, cases were noted in the first and last rows of the passenger compartment and in a passenger that circulated selling raffle tickets. With the 2003 SARS coronavirus, a passenger with fever and cough on a 737—300 with nearly completely full capacity of 120 people during a 3 h flight probably infected 22 individuals, 8 were seated within three rows of the patient, but cases were diffused throughout the plane including two flight attendants.[10] The number of secondary cases may have involved over 300 individuals.

The above outbreaks do not follow the typical example of in-flight transmission of airborne pathogens involving droplets with a 6-foot radius of transmission. Tuberculosis exposure evaluation of passengers with active disease in flights over 8 h is recommended to include the two adjacent rows front and back of the suspected case.[11,12] Droplet transmission requiring close contact is commonly cited for influenza, but more diffusing airborne transmission of smaller virus particles is certainly possible, especially in closely confined spaces, hence the requirement for N95 masks for healthcare workers. Modern commercial airliners with ceiling to floor air flow patterns create very strong counter rotating air currents in cross-section along the rows and minimize air flow in a longitudinal direction within the plane.[13] This results in 20—30 Air Changes per Hour (ACH) — typical indoor environment is 5 ACH — with High Efficiency Particulate Air (HEPA) filtered air that removes 99.97% of particles. The recirculated air has a very low humidity of 10—20%, which is conducive to highly efficient influenza virus transmission.[14]

Advanced Computational Fluid Dynamic (CFD) models have delineated transmission of infectious respiratory

particles across an entire airplane row within 16 s of a sneeze or cough due to the strong cross-sectional counter rotating air flows.[15] CFD modeling of airborne transmission on a longitudinal axis throughout the airplane is much more difficult as significant variations in local airflows result in local contaminant spread.[16] Infected passenger locations and seating patterns have little impact on longitudinal contamination, specifically; longitudinal patterns in business and economy are similar, while first class is highly variable due to different seating designs resulting in asymmetric flow patterns. Galleys have a major effect on longitudinal flow.

Although respiratory transmission is most common, influenza can exist on surfaces for 24–48 h and the low humidity (10–20%) is generally beneficial for viral growth.[18,19] Data on potential influenza transmission from surface contact, especially in small multiple use airplane lavatories, is minimal.[20] Careful epidemiologic investigations to understand the frequency and relative importance of different modes of transmission for specific pathogens utilizing advanced multiplexing PCR assay techniques are necessary.[21]

Aircrews are at greater risk for influenza like illness than the general population. Brazilian aircrews had a 33% attack rate in influenza unvaccinated individuals (compared to 10% of the general population) and vaccinated aircrew members had 40% fewer episodes of influenza like illness.[17] The risk of influenza to flight attendants in close passenger contact is most likely elevated; in the reported outbreaks, several flight attendants were infected. Pilots on large transcontinental planes have a dedicated separate cockpit air supply and usually minimal passenger contact. To maintain their operational status and minimize potential for spreading influenza to their native country, select international airline crews may be candidates for early receipt of pandemic influenza vaccine.

The spectrum of viruses and atypical bacteria in intercontinental air travelers with symptoms of acute respiratory infection is significant. For example in 2003, passengers fulfilling the case definition for SARS with symptoms of fever and cough or difficulty breathing and stay in an affected area or close contact with a suspected patient were evaluated with highly specific PCR testing of respiratory samples.[22] Of 172 passengers arriving on 146 international flights to Germany, a pathogen was identified in 67 travelers (43%); 30% were positive for influenza and parainfluenza viruses; 2.6–4.8% for adenovirus, human metapneumovirus, coronavirus, rhinovirus; and less than 1% for *Legionella*, *Mycoplasma*, *Chlamydophilia* species.

The consumable costs of screening are driven by the difficulty of discriminating pandemic influenza cases from common respiratory infections, i.e. the specificity of the laboratory testing methods. The specificity of a test is the probability that the test will be negative among passengers who do not have the disease; mathematically stated specificity = TN/TN + FP. The denominator is the number of healthy passengers; minimizing the false positives will increase the specificity and a highly specific laboratory test will nearly eliminate the chance of pandemic influenza in passengers tested. Our model utilized the 99% specific RT-PCR laboratory test, subsequently a low number of FPs 100–170/day was generated in a population of 17 million evaluated.

A high sensitivity of the screening process is demanded by a system responding to a contagious and potentially fatal disease. The goal is to detect the largest amount of passengers with pandemic influenza and prevent spread. The sensitivity of a test is the probability that the test is positive when given to a group of patients with the disease; mathematically stated at sensitivity = TP/TP + FN. The denominator is the number of patients with the disease, minimizing the FNs in the denominator will increase the sensitivity. Our model realistically assumed an 80% chance of identifying pandemic influenza in passengers with symptoms and only 6% identification of asymptomatic infected passengers; therefore a large number of false negative passengers (highest peak day 45–400 to 800) were generated.

In an attempt to increase the sensitivity of screening in a cost effective manner with little passenger disruption, some countries are considering implementing thermal imaging cameras that require minimal space and personnel. Thermal imaging cameras were implemented in SARS with mixed effectiveness.[23] Technologic improvements in cameras continue to increase their sensitivity to detect those with fever of 101 F (38.3 °C) but a high false negative rate will continue for infected passengers without a temperature elevation at the time of passing through the device. Thermal imaging cameras may have an additional deterrence effect and encourage compliance with isolation and quarantine travel guidance. Sensitive and specific rapid diagnostics for pandemic influenza are certainly required. Effective handheld tests for proteomic biomarkers of infection prior to symptoms are far future goals.

The model identified significant variability in the estimated average delay times for passengers in primary active surveillance. Passenger delays depend on resourcing, but due to the compressed times of flight arrivals, passenger queues will form. Personnel, equipment, and space should be planned for maximum and not mean passenger demands. Using San Francisco Airport as an example, average delay times were estimated to be up to about 17 min. In Scenarios 1 and 2, the average delay times among passengers who only undergo primary active surveillance, and not secondary active surveillance, are about the same. In Scenario 3, with significantly reduced detection rates at embarkation screening, fewer ill passengers are identified at pre-departure. Consequently, more passengers remain to be screened at secondary surveillance. Delay times for RT-PCR testing were estimated at 8–12 h as specimens require transport to specialized laboratories. On site PCR testing could minimize the delay time to several hours.

Additional personnel to augment the small CDC Division of Global Quarantine and Migration staff at each of the 18 U.S. International Airports should be scalable and maximally staffed for peak international arrival times to minimize passenger delays. Groups such as the Medical Reserve Corps, Disaster Medical Assistance Teams (DMAT), and U.S. Military – Army, Navy, and Air Force Medical Reservists could provide trained and certified healthcare and administrative workers who are also covered for malpractice issues under Federal tort claims law. With minimal prior notice of a global pandemic, contracting a local workforce of civilian healthcare professionals to

assemble immediately for a potential 3-month employment period to identify contagious patients with a potentially life threatening illness is an unlikely alternative.

As an additional benefit, the screening procedure will identify pandemic influenza cases from their global points of origin for epidemiological purposes. The respiratory diagnostic specimens obtained will allow tracking for pandemic influenza variants including medication resistant and vaccine variable strains. In addition, a pandemic influenza international air traveler screening program is also of value in preparing for other emerging infectious disease outbreaks or bioterrorism scenarios. The efforts may also maintain confidence in the air-travel system and mitigate isolationist agendas.

After establishment of the epidemic in a country with the expected surge in demand for healthcare, airport screening assets will be more appropriately utilized in patient care and epidemic control within the country. If the epidemic progresses significantly more slowly in the U.S. than outside the country, the bulk of new pandemic influenza cases may be caused by international air travelers for a greater period of time. Land border crossings may also become a dominant source of influenza cases, negating the value of screening international air travelers. Infected individuals that enter across land borders or by ship would not have the impact in speed of nation-wide spread as those rapidly traveling to internal destinations by plane and mixing at intensely crowed airports.

With any model, initial assumptions are based on best available data and drive conclusions while providing limitations. In our model, the outbreak initiated on the Asian continent with an Ro value of 3, and with an incubation period of 5–7 days. Initiation of pandemic influenza in another continent with alternate airline patterns would provide different epidemiologies although unlikely to change the conclusion of screening effectiveness. Obviously, onset of pandemic influenza within the U.S. would mitigate the effectiveness of arriving passenger screening, but emphasize the importance of U.S. exit screening. The ability to successfully identify 80% of symptomatic and 6% of asymptomatic pandemic influenza infected passengers with a 99% RT-PCR test accuracy was chosen based on subject matter expertise, but other sensitivities and specificities are possible. The prevalence of disease in a population, as determined by the extent of the global pandemic, coupled with passenger compliance with isolation and quarantine restrictions, will have the greatest impact for significance of air passenger screening. The virulence of the virus, summarized by a case-fatality rate assumed to be 2%, a frequently cited figure, may vary and reflect different conclusions on efficacy. The study was based on 2006 air passenger data. During an epidemic, air travel, especially involving outbreak areas, may greatly decrease, and vary the impact of passenger screening. Although based on the large influx of 17 million passengers over 100 days to 18 U.S. Airports, the generalization of the study to smaller nations with fewer international passenger arrivals is possible.

Air travel is the avenue for the most rapid spread of a human to human contagious disease, but in a global economy no nation can be an isolated island economically or politically for any extended period of time. The more aggressive and effective the screening, the greater number of infected people detected, but also greater expenditure of resources, passenger delays, and false positive results. A meaningful impact on the spread of the disease throughout a nation can be brought about by efficacious airport screening measures.

In conclusion, departure screening of air travelers for pandemic influenza, with emphasis on isolation of the ill and quarantine of the exposed, will minimize international spread by air travel in the initial 100 days of the pandemic. U.S. entry screening can identify more than 50% of infected travelers, but is limited by the inability to identify the asymptomatic and infected. Entry screening will lower the predicted U.S. pandemic influenza attack rate by less than 1%; this results in 800,000–1,800,000 fewer infections and 16,000–35,000 fewer deaths. Antiviral requirements for prophylaxis and treatment for airports could be orders of magnitude greater than expected. Effective screening activities will require substantial resources in healthcare personnel, equipment, and highly valuable airport space. Passenger delays will depend on resourcing, but due to the compressed times of flight arrivals, passenger queues will form. Requirements should be planned for maximum and not mean passenger demands. U.S. Airport port of entry screening for pandemic influenza is an effective measure to reduce the total number of U.S. cases and associated deaths but will not delay the day when the initial infected individual enters the country.

Conflict of interest

There are no conflicts of interest to declare.

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