ORIGINAL RESEARCH

Two Aircraft Carriers' Perspectives: A Comparative of Control Measures in Shipboard H1N1 Outbreaks

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ABSTRACT

Background: The USS George Washington (GW) and the USS Ronald Reagan (RR), 2 US Navy aircraft carriers, experienced almost simultaneous outbreaks of novel H1N1 influenza A in the summer of 2009. We compared the respective epidemic control measures taken and subsequent lessons learned.

Methods: Data were collated from both outbreaks to assess various elements including attack rate, isolation/quarantine protocols, and treatment methods. The respective duration of each outbreak was compared with survival curve analysis. The number of personnel affected in each outbreak was compared using χ^2 analysis.

Results: Differences were found in the protocols used on the 2 ships. The GW treated about two-thirds of the patients with oseltamivir through day 14 and quarantined all patients meeting case definition throughout the outbreak. Face masks were used throughout. The RR used oseltamivir and quarantined many fewer patients (through days 5 and 3, respectively). No face masks were used after day 5. The outbreaks were similar in duration (GW = 25 days, RR = 27 days, $P = .38$), but the RR had significantly more cases (n = 253 vs 142, $P < .0001$). A portion of each group had samples that were confirmed H1N1 by polymerase chain reaction.

Conclusions: GW's protocol, including aggressive oseltamivir treatment of two-thirds of the cases and quarantine throughout the duration decreased the overall number of personnel affected, likely reducing the overall control reproduction number. Both outbreaks were similar in duration. Even though the GW expended significantly more resources than the RR, if the 2009 pandemic H1N1 strain had been as clinically severe as the 1918 pandemic, a more stringent treatment protocol may have been the only way to prevent significant operational impact. *(Disaster Med Public Health Preparedness*. 2013;7:29-35)

Key Words: H1N1, influenza, pandemic, isolation, outbreak, naval vessel, aircraft carrier, treatment protocol, operational impact, infection containment

Displacing 100 000 tons and carrying crews of approximately 5000 sailors, Nimitz class aircraft carriers are the centerpiece of the US Navy's maritime doctrine. These ships are designed to operate for extended periods of time at sea, leaving their crews in a physically (and consequently medically) isolated environment. However, part of the mission of these ships is to show the US presence at various port visits, creating point exposures to less-controlled environments throughout their deployments. In the summer of 2009, 2 Nimitz class carriers were operating in the western Pacific Ocean. The USS George Washington (GW), whose home port is Yokosuka, Japan, is the only permanently forward-deployed aircraft carrier in the US Navy. The GW left home port in mid-May of 2009. She entered port in Perth, Australia, for a 5-day visit on July 2, 2009. The home port of the USS Ronald Reagan (RR) is San Diego, California. The RR also began a summer patrol in mid-May of 2009, sailing across the Pacific en route to the Arabian Sea, where the ship would be operating in support of Operation Enduring Freedom in Afghanistan. On route to the Arabian Sea, RR entered port in Singapore on June 24, 2009, for a 5-day visit.

This period was also significant for a World Health Organization (WHO) level 6 pandemic of novel H1N1 influenza A (H1N1), which by its conclusion would infect roughly 16% of the world's population[1] and lead to more than 18 000 deaths.[2]

Earlier that year, on March 18, 2009, surveillance began recording cases of influenza-like illness in the Federal District of Mexico. On April 24, 2009, the US government reported 7 confirmed cases of human swine influenza A/H1N1, while Mexico had 18 cases.[3] A level 6 pandemic is defined as an outbreak of an infectious agent affecting at least 2 WHO countries in

at least 2 WHO regions.[4] The H1N1 outbreak was active throughout the western Pacific, and cases had been reported to WHO in both Perth, Australia, and Singapore. On May 9, 2009, Australia reported its first case of confirmed H1N1. In Western Australia, the first reported swine flu case was May 24, 2009. Between June 1 and June 23, the effective reproductive number in Western Australia was well below 1. However from June 24 onward, calculated values for the effective reproductive number ranged from 1 to 1.4 throughout July, consistent with a self-sustaining pandemic of H1N1 swine flu.[5] This reproductive number was similar to figures calculated earlier with the outbreaks in Mexico and the United States.[5,6] The basic reproductive number (R0) is defined as the number of cases a single case causes over its lifespan in a completely susceptible population. Further, the effective reproductive number, or R, is the real-time reproductive number as a population's susceptibility changes with time. The control reproductive number is defined as the number of cases caused by a single case with control measures in place.

Around the time both ships left port, both the GW and RR experienced outbreaks of a respiratory illness that were treated as and eventually confirmed to be H1N1. The unique environment aboard naval vessels presents particular epidemiological advantages and challenges. Some interventions that have been shown to decrease spread of disease such as social distancing[7] are not feasible in such a closed environment. The majority of crew members live in open-bay berthing, sleeping in 2-or 3-stack bunk beds with no ability to isolate one living/sleeping space from another. During normal ship operation, ventilation is operated in series, so ventilated air from one berthing space is reconditioned and then blown into subsequent berthing spaces. For these reasons, medical personnel aboard the ships must make rapid decisions about containment measures when outbreaks of infectious diseases are identified. In addition, the ships operate in medically austere environments, so conservation of resources is equally important. An example of this is the different approach to pharmacotherapy and chemo-prophylaxis applied on board the 2 ships.

Aggressive use of antiviral drugs has been shown to affect attack rate.[8] On board GW, medical personnel initiated pharmacotherapy and chemoprophylaxis immediately on identifying the outbreak; they ultimately treated almost two-thirds of their cases. On board RR, medical personnel rapidly decided to withhold pharmacotherapy and chemoprophylaxis soon after the start of the outbreak. We compared the outbreaks on board the GW and RR, with attention to the differences in the protocols and attack rates on the 2 ships.

METHODS

The duration of outbreak was calculated from the first case to the last day a new case was diagnosed. Kaplan-Meier survival curve analysis was used to calculate the statistical difference in the duration of the 2 outbreaks. The total number of personnel affected was tracked, and χ^2 analysis was used to calculate the statistical significance in the number of cases during both outbreaks.

USS George Washington Clinical Protocol

All active-duty personnel serving aboard GW had received the annual seasonal trivalent influenza vaccinations (FluMist® influenza vaccine live, 2009-2010 formula, Medlmmune, LLC; Fluzone influenza virus vaccine, suspension for intramuscular injection, 2009-2010 formula, Sanofi Pasteur Inc) in the fall of 2008.

Patients who presented to sick call were asked about symptoms of influenza like-illness (ILI). Those who answered yes to 2 or more symptoms (rhinorrhea, nasal congestion, pharyngitis, myalgias, chills, or cough) were evaluated on the ILI protocol. A full set of vital signs (temperature, pulse, respirations, and blood pressure) was measured, and the symptoms were reviewed. The presumptive diagnosis of H1N1 was assigned if the patient demonstrated a core body temperature over 37.7°C, with 2 or more indicated symptoms. As guidance was still being formulated at WHO and the Centers for Disease Control and Prevention, and no formal case definition was available, this definition was deliberately designed to maximize sensitivity even at the expense of specificity.

Patients with a positive screen were evaluated by a primary care provider. Each patient was assessed for severity of disease and options for symptomatic treatment (antipyretics, decongestants, analgesics) were discussed. Patients were placed in respiratory isolation. During the initial period of the outbreak, patients were isolated on the medical ward. The capacity of the medical ward was overwhelmed on day 8, so some patients were moved to a berthing area that had been converted into an isolation area. Initially patients were maintained in quarantine for a full 5 days. Ultimately, due to space restrictions, the isolation release criteria were modified so that patients who had been afebrile for 48 hours and who had minimal residual respiratory symptoms were released from quarantine and maintained their respiratory precautions with an N95 mask in regular berthing spaces. All patients were required to maintain precautions for at least 8 days after diagnosis (whether quarantined or wearing a mask in berthing). The precautions were continued for a longer period if respiratory symptoms persisted.

Initially, patients who met the clinical definition for H1N1 were treated with oseltamivir phosphate (Tamiflu®, Roche Laboratories Inc), 150 mg daily, for 5 days. However, as the outbreak expanded the decision was made (on day 14) to discontinue oseltamivir treatment to preserve stock for severe cases and mission-critical personnel.

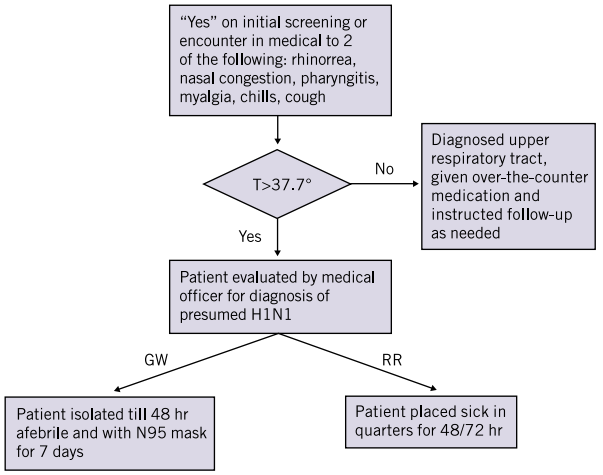
USS Ronald Reagan Clinical Protocol

As on GW, all active duty personnel serving aboard the RR had already received the annual seasonal trivalent influenza vaccinations in the fall of 2008. RR also used the same

https://doi.org/10.1001/dmp.2012.53 Published online by Cambridge University Press

FIGURE 1

USS Ronald Reagan (RR) vs USS George Washington (GW) Isolation/Face Mask Protocols.



Screening was similar, but after day 5 the GW continued to isolate and use face masks, whereas the RR did not.

criteria for the presumptive diagnosis of ILI (2 or more of rhinorrhea, nasal congestion, pharyngitis, myalgias, chills, or cough plus a core body temperature higher than 37.7°C). Patients received the same evaluations and symptomatic treatment as GW patients.

Initially, RR quarantined patients who met ILI criteria, but on day 5, its quarantine capacity was exceeded. Rather than expand its quarantine facilities, patients were isolated by placing them on "sick in quarters" (SIQ) status in their berthing spaces. The RR had limited supplies of face masks, so patients were directed to remain in their berthing spaces, but no face masks were issued.

Initially, RR treated patients who met the clinical definition for H1N1 with oseltamivir phosphate, 150 mg daily, for 5 days. However, the decision was made much earlier (day 3) to discontinue routine treatment and to preserve supplies for severe cases and/or mission-critical personnel (Figure 1).

RESULTS

USS George Washington

Ultimately, 142 patients met the case definition following the port call and were treated per GW protocol (Table 1). With an approximate total crew of 4600 on board the GW, this equated to a 3% attack rate. Before the decision was made to reserve remaining doses, 84 patients were treated with oseltamivir.

The sentinel case of novel H1N1 (later confirmed by polymerase chain reaction [PCR]) aboard GW presented on July 6 (day 1), one day before the ship left port from Perth. By day 11, new cases of presumed H1N1 were prevalent throughout the ship. The peak number of cases occurred on day 14, with 21 new cases identified and 55 patients in isolation. On July 30 (day 25), the last epidemic patient was diagnosed with presumed H1N1. One more patient presented 4 days later, but was considered an outlier and not included in these calculations. No additional cases of presumed H1N1 were identified for the balance of the deployment, in spite of a port visit to Singapore on August 6 and to a variety of other ports.

Based on discussions with the operational chain of command on the GW, no degradation in mission capability of the ship was noted during the period of the outbreak.

USS Ronald Reagan

Ultimately, 253 patients met the case definition following the port call and were treated per RR protocol. With an approximate total crew of 4600 on board the RR, this equated to a 5.5% attack rate. Twelve patients were treated with oseltamivir before the decision was made to reserve the remaining doses.

The sentinel cases of novel H1N1 aboard RR presented on June 28 (day 1), when the ship left port from Singapore. The peak number of new cases occurred on day 9, with 23 new cases. RR did not isolate or quarantine its patients after day 5. Patients were sent to their berths (SIQ) and told to limit their time out of bed. Thus, the total number of SIQ patients did not directly correlate with new diagnoses or with patient isolation. On July 24 (day 27), the last epidemic patient was diagnosed with presumptive H1N1 (Figure 2, Table 2). No additional cases of presumptive H1N1 were identified for the balance of the deployment, in spite of a port visit to Jebel Ali, United Arab Emirates, on August 10, and to various other ports.

Based on discussions with the operational chain of command on the RR, no degradation in mission capability of the ship was noted during the period of the outbreak.

Viral Testing

Both ships tested a sample of their patients to confirm the presence of H1N1. Neither ship had point-of-care testing capability, so samples were obtained and shipped to the Naval Health Research Center in San Diego, California, for analysis. Due to the logistics of being on cruise, samples were not obtained for all affected patients.

Specimens from 32 GW patients and 50 RR patients were submitted for analysis. There was no difference in the percentage of patients meeting case definition that were tested between the 2 ships (GW = 22.5% vs RR = 19.8%, $P = .52$ by Fischer's exact test). Of the samples tested, 17 from GW and 42 from RR were positive or equivocal for H1N1.

https://doi.org/10.1001/dmp.2012.53 Published online by Cambridge University Press

TABLE 1

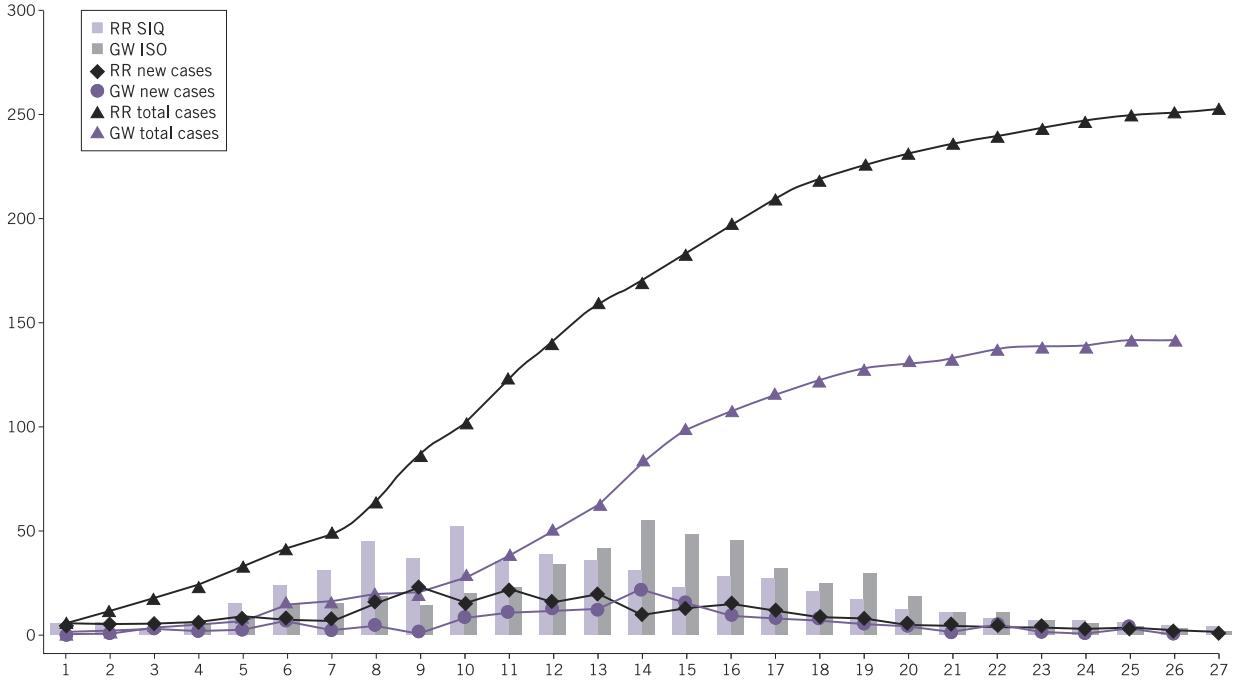
Demographics of the USS George Washington with Relevant Attack Rates[a]

Characteristics	Ship's Population	Isolated (Presumed H1N1)	Attack Rate, %	*P*
Officers				
Male	368			
Female	24			
Enlisted				
Male	3542			
Female	662			
All cases	4596	142	3.09	
Male	3910	129	3.30	.05
Female	686	13	1.90	
Rank				
Enlisted	4204	134	3.19	
Officer	392	8	2.04	.21

[a]Data for the USS Ronald Reagan were unavailable, but reasonably can be assumed to be the same; all crews of US Navy aircraft carriers are drawn from the same heterogeneous, cross-sectional population. Total number of male and female officers and enlisted personnel embarked on board. Patients were isolated by sex, rank, and age groups. Enlisted includes both junior and senior personnel.

FIGURE 2

USS Ronald Reagan (RR) vs USS George Washington (GW) Outbreak Timelines.



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27
RR SIQ	6	6	6	6	15	24	31	45	37	52	37	39	36	31	23	28	27	21	17	13	11	8	7	7	6	5	4
GW ISO	1	2	5	7	9	15	15	19	14	20	23	34	42	55	48	45	32	25	30	19	11	11	7	6	4	3	
RR new cases	6	6	6	6	9	9	7	15	23	15	22	16	20	10	13	15	12	9	8	5	5	3	4	3	3	2	1
GW new cases	1	1	3	2	2	7	1	4	0	8	10	12	12	21	15	9	8	7	5	4	1	5	1	0	3	0	
RR total cases	6	12	18	24	33	42	49	64	87	102	124	140	160	170	183	198	210	219	227	232	237	240	244	247	250	252	253
GW total cases	1	2	5	7	9	16	17	21	21	29	39	51	63	84	99	108	116	123	128	132	133	138	139	139	142	142	

The two outbreaks are compared day by day for a number of variables including total number affected, number of new cases, and number either on "sick in quarters" (SIQ) status or in isolation (ISO).

The percentages of samples that were positive or equivocal were significantly different between the 2 ships (GW = 53.1% vs RR = 84%, $P = .005$ by Fischer's exact test). The percentages of total patients who had positive or equivocal swabs were not different (GW = 12.0% vs RR = 16.6%, $P = .24$ by Fischer's exact test) between the 2 ships.

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TABLE 2

USS George Washington (GW) vs USS Ronald Reagan (RR) Outbreak Statistics[a]

	GW	*RR*	P-*value*
Total No. of crew	4596	4600[b]	
No. of persons affected	142	253	<.0001
No. of tests positive/equivocal/negative	13/4/15	39/3/8	.003
Percentage of cases confirmed	13/142	39/253	.077
No. of patients receiving oseltamivir	84	12	<.0001
No. of patients quarantined	142	39	<.0001
No. of patients receiving respiratory isolation	142	0	<.0001
Duration of epidemic, d	25	27	

[a]Number of persons affected were diagnosed with presumed H1N1 and treated per protocol. Number of tests summarized the results of probes submitted, followed by confirmed cases as a proportion of those affected. Number of patients receiving respiratory isolation were required to wear face masks.

[b]Exact number of RR could not be obtained but is assumed to be similar, as both vessels were in a deployed operational status.

GW and RR tested similar proportions of their cases with real-time (rRT) PCR (22.5% vs 19.8%). There was no difference in the case definition used to clinically identify those presumptively diagnosed with H1N1, and no apparent sampling bias was found in the way the 2 ships selected patients to be tested. While the percentage of total patients who had positive or equivocal swabs was not different (GW = 12.0% vs RR = 16.6%, $P = .24$ by Fischer's exact test), the percentage of total swabs that were positive or equivocal was (GW = 53.1% vs RR = 84% $P = .005$ by Fischer's exact test).

COMMENT

Overall morbidity from these influenza outbreaks was low. No patients required ventilator support, intensive care unit admission, or medical evacuation. No fatalities or unforeseen complications were encountered in either group.

GW and RR had relatively low attack rates (3% and 5.5%, respectively). These rates compared favorably with those on 2 other ships reporting epidemics during the same time. A Peruvian navy vessel with a crew of 355 experienced an outbreak in June and July 2009; they reported 78 confirmed cases of H1N1 during a 22-day period (attack rate = 22%).[9] The USS Iwo Jima (IJ), an amphibious ship with a crew of approximately 1100, experienced an outbreak in May and June 2009; 135 patients over a 3-week period met diagnostic criteria (attack rate of 12%).[10] While GW, RR, and IJ relied on clinical criteria for diagnosis (limited rRT-PCR results confirmed the presence of H1N1 only after the outbreaks had essentially run their course), the Peruvian ship used H1N1 rRT-PCR to confirm the diagnosis. If the Peruvian ship had relied on clinical criteria alone, it is possible that its attack rate would have been higher.

The attack rate appears to be inversely proportional to the size of the ship, although it may be thought that a smaller crew should have a lower attack rate, as based on lower population density and less likelihood of contact intimate enough to spread respiratory droplets. However, the smaller crews are on smaller ships. GW and RR are the largest warships afloat—it is possible for large segments of the crew members to never meet each other during the course of a 3-year tour. On smaller ships, given less space and fewer crew members, it is likely that the whole crew knows and interacts with each other on a daily basis.

The differing outbreak control measures on the 4 ships described here, when correlated with outbreak duration and the total number of individuals affected, provide some insight into what impact, if any, these measures may have. The 4 ships had significantly different attack rates. As discussed, the differences between the attack rates on the smaller ships and the aircraft carriers were likely explained by the differences in the physical size of the ships and the number of the crew. However, the aircraft carriers were identical with respect to both physical size and crew size. So, the differences in attack rates may be better explained by the different outbreak control measures.

The major differences between the control measures were the higher use of oseltamivir and the more extensive use of quarantine measures on the GW. It was likely that both of these interventions affected the attack rate. It was unclear whether oseltamivir decreases the rate of viral shedding,[11,12] which would be a possible explanation for the lower number of cases on the ship that used oseltamivir to a greater extent (GW). Logically, the use of respiratory isolation contributed to the lower number of cases, by removing individuals from the general population while they were shedding virus. On the ship using both of these control measures, there were 40% fewer cases. While other factors may have contributed, these 2 control measures likely accounted for a significant portion of this reduction.

The R0 for the 2009 H1N1 outbreak has been estimated at between 1.4 and 1.6. The R for the Western Australia outbreak

https://doi.org/10.1001/dmp.2012.53 Published online by Cambridge University Press

ranged from 1 to 1.4 during the time frame the GW was exposed to the virus during its port call. Although not calculated, the control reproductive number for the GW likely was smaller, given the significantly decreased number of cases experienced during the outbreak, in spite of the other similarities (ie, same ship design, same crew numbers, and layout.).

Fortunately the fatality rate for the 2009 H1N1 strain was very low (<1%) compared to the virus's infection rate. One could argue that had the novel strain been more virulent, a more stringent treatment protocol would have likely minimized fatalities and impact on mission capabilities.

In spite of the significantly different attack rates, no significant difference in the duration of the outbreaks was found between the GW and the RR. In fact, little difference in the duration on any of the 4 ships, despite attack rates ranging from 3% to 22%, was noted. This finding raises the question of why factors affecting the attack rate would not affect the outbreak duration. A possible explanation is the closed and isolated nature of the ships. Once a military vessel goes to sea, there is very little movement of personnel on or off the ship. Thus, very limited numbers of new (virus-naïve) individuals enter the system.

In almost all outbreaks, medical personnel acknowledge that a small cadre of personnel either did not quite meet the case definition or simply did not feel sick enough to seek medical attention. It is possible that some or all of these individuals represent subacute cases of viral infection. If these individuals are acquiring immunity from subacute episodes and the actual epidemic patients are acquiring immunity from their full-blown cases, then a critical level of immunity may be reached on board the ship in which "herd" immunity develops and the virus cannot propagate further. This result is only possible in the closed, isolated nature of shipboard populations. Further research would be required to confirm this, but this hypothesis would indicate that a predictable duration to an outbreak of any given immunity-inducing infection is possible, if it occurs in an isolated population. The only way this predictable duration could be exceeded would be if a regular injection of infection-naive individuals were allowed to continue propagation of the outbreak.

This hypothesis is further supported by the fact that both ships continued to operate in the area of the WHO epidemic without subsequent cases. In fact, GW had a port visit to Singapore, the source of RR's outbreak shortly after the end of the outbreak. While there is no objective evidence to indicate that sailors were exposed to H1N1 during these subsequent visits, it is naive to assume that they were not, as their behavior would not differ from that which produced the initial outbreaks on the 2 ships. Thus, it is reasonable to believe that some factor prevented infection during subsequent exposure. It can be reasonably assumed that the outbreak conveyed resistance not just to local but to regional strains.

Although the differences in percentage of positive swabs might raise the question of multiple organisms or more or less strict adherence to case definitions, the fact that there was no difference in the percentage of positive patients should help mitigate that concern.

Limitations

This study was limited by several factors. First, unlike the Vera et al study, only 20% of patients who met criteria for ILI on both ships were actually tested for H1N1. Further, because of the lag between obtaining samples and receiving results, all patients were treated clinically, leading to the inclusion of significant numbers of H1N1-negative patients in the outbreak population. Certainly, a proportion of personnel tested were negative for H1N1, suggesting seasonal flu or another etiology in spite of prior flu vaccination. Of the 3178 notifications for pandemic and seasonal influenza in Western Australia between May 22 and September 11, 2009, only 87.9% were confirmed to have the pandemic 2009 H1N1 subtype.[13] Swabs were not conducted for the entire duration of the outbreak. If this had been done, it is possible that an earlier or later end date for the outbreak might have been assigned.

Second, the GW was exposed to H1N1 in Perth, Australia, while the RR's outbreak was triggered by its visit to Singapore. In addition to being geographically separated, these 2 cities have different populations and population densities; further, the prevalence of H1N1 at the time of the ship visits was not the same in the 2 cities. While it is assumed that the strain of a virus that has propagated during this kind of an outbreak is the same in all geographic areas, it is possible that subtle differences existed in the behavior of the virus contracted in the 2 different regions.

Third, most of the US sailors are young and they enjoy and actively seek time away from the ship. It is very likely that many affected personnel were hesitant to report to sick call from fear of being put in isolation or being held back from liberty in port. The clinical screen is as accurate as the input from those completing it. Just as there were a substantial number of false-positive results on the clinical screen, there were likely many false-negative results from those who either obfuscated their answers or had such low-grade symptoms that they never presented for evaluation or were misdiagnosed. Thus, the actual attack rate was probably underestimated on both ships.

Fourth, demographic information for the RR was not as readily available as it was for the GW while preparing this manuscript. For the purposes of this report, however, both ships had a full complement of operational personnel that theoretically would be very similar (ie, same enlisted/officer ratios, same medical screening process, same physical readiness requirements).

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Finally, this study was ecological in nature. It was not a randomized controlled study, and thus we cannot assess the effectiveness of any of the interventions in individual patients.

However, this weakness is perhaps also the greatest strength of this study. The strength of an ecologic study is its ability to look at population-wide interventions and assess their overall impact, without being concerned with the specific impact on a single individual. The data were robust enough to show both the areas in which the 2 ships intervened differently and in which their populations responded differently.

It was a rare opportunity to observe 2 similar populations that were exposed in similar ways, in similar regions of the world, at similar times, and with similar resources at their disposal that approached the same problem in different ways. This situation yielded some valuable insight into the impact that the different approaches might have.

CONCLUSIONS

In spite of their large populations, confined spaces, and different treatment protocols, the GW and RR were able to contain their outbreaks to approximately 3% and 5.5% of their overall population, respectively. These populations, consisting of young, healthy people, suffered little morbidity and had no mortality from the outbreak. Aggressive screening, early intervention with isolation, and appropriate post discharge respiratory and hygiene precautions appeared to have limited GW's attack rate vs that of RR's. The differing approaches, producing different intermediate results (different attack rates) but similar endpoints (preservation of operational capability) highlight the fact that stringent control measures on outbreak containment may not necessarily improve the ultimate outcome. Many times resource utilization, operational necessity, and logistic concerns need to take precedence over absolute infection control. More conservative infection control measures appear to be effective at lowering the attack rate, but they also exhaust more resources as prevalence increases. However, had this strain of H1N1 been more virulent, a more stringent protocol may have been the only way to maintain operational capability. Therefore, all factors, including minimizing disease burden, potential operational impact, and optimizing resource utilization should be factored into outbreak control plans instituted on board military ships. Oseltamivir and respiratory isolation did appear to be helpful public health measures to mitigate the overall attack rate of the outbreak.

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Received for publication December 10, 2010; Accepted May 2, 2012.

Published online: October 19, 2012. doi:10.1001/dmp.2012.53

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