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# Selected Nonvaccine Interventions to Prevent Infectious Acute Respiratory Disease

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**Introduction:** Infectious acute respiratory disease (ARD) is a significant cause of worldwide morbidity, disproportionately affecting individuals living in crowded conditions, such as found at military training centers, school dormitories, and correctional facilities. Vaccines have been used to protect against ARD; however, these are not always available or effective.

**Methods:** The medical literature (1963–2004) on preventive nonvaccine ARD interventions (NOVARDIs) for infectious diseases, which addressed personal measures, administrative controls, and engineering controls, was studied during 2000 to 2004. Population-based studies in community settings (non–health care) were reviewed in detail to evaluate the effectiveness of NOVARDIs. Budgetary and logistic factors as well as acceptance were considered in formulating recommendations for implementation of NOVARDIs in military training centers.

**Results:** Thirty-eight population-based studies contained in 35 publications were examined. Three studies contained information on multiple NOVARDIs. Nine studies supported the use of personal measures relating to hand hygiene. Ten studies supported administrative controls such as cohorting military training units to reduce contact between units (4 studies), providing adequate personal space to reduce crowding (5), and cloth barriers between beds (1); and 14 studies supported the use of engineering controls such as increased indoor air dilution and ventilation (2), dust suppression (4), and air sterilization (8).

**Conclusions:** Promoting hand hygiene and reducing crowding through the provision of adequate living space and cohorting of training units may offer benefits in respiratory disease control. These interventions, along with UV lights and air dilution/ventilation, deserve further evaluation in controlled studies to assess their efficacy. NOVARDIs could benefit military and other populations living in close contact.

(Am J Prev Med 2005;28(3):305–316) © 2005 American Journal of Preventive Medicine

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## Introduction

Acute respiratory disease (ARD) of infectious origin causes substantial morbidity and mortality worldwide, and has been a frequent problem in military training centers.<sup>1</sup> Influenza caused millions of deaths in the 1918 pandemic, and continues to kill thousands each year.<sup>2</sup> More recently, severe acute respiratory syndrome (SARS) was recognized as a public health threat.<sup>3</sup> Vaccines are available for only a few pathogens, and may have limited efficacy; influenza vaccines, for example, must target circulating viral strains to be efficacious, as demonstrated recently when nearly half the crew of a U.S. Navy ship was affected

despite 95% of the sailors being vaccinated.<sup>4</sup> Other vaccines, such as those against adenovirus (ADV) types 4 and 7, were very effective in reducing ADV-associated ARD morbidity in military populations for 2 decades, until production ceased in 1996. Subsequently, pre-vaccine era morbidity (15% to 20% hospitalization rates) returned.<sup>5</sup> Replacement ADV vaccines are under development but years away from licensure. ARD vaccine arsenals currently consist of measles–mumps–rubella, meningococcal, and influenza vaccines.<sup>6,7</sup> The potential use of pneumococcal vaccines is being assessed for military use.<sup>8</sup> Despite vaccine preventive measures, military trainee and other populations living in close contact continue to suffer from respiratory disease outbreaks.<sup>5,9–13</sup>

Nonvaccine ARD interventions (NOVARDIs) have been considered since the beginning of the U.S. Army, when a 1777 regulation limiting to six the number of soldiers permitted inside a tent was enacted due to military physicians' belief that crowding caused disease.<sup>14</sup> NOVARDIs used and considered for ARD control included antimicrobials and other medications;

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herbal and dietary supplements; management of work, rest, and sleep periods; handwashing; respiratory masks; and many administrative and engineering measures to limit contact between people, and decrease the concentration of potentially harmful agents in the environment. This study focuses on prevention of communicable respiratory diseases, and NOVARDIs that would not significantly interfere with standard operating procedures for training programs nor require human-use study protocols (such as for a study of medications or herbal supplements). Feasible personal hygiene, and administrative and environmental control measures, if not cost prohibitive, could be implemented in a reasonable time or included in new building construction.

Nonvaccine ARD interventions in this study are categorized as personal measures (e.g., handwashing), administrative controls (e.g., isolating military units to limit contact between units), and engineering controls (e.g., increased indoor air dilution ventilation). Published and unpublished reports were studied to assess their potential effectiveness, the scientific rationale for their implementation, and feasibility for use in military training centers. The findings of this study may be relevant to other populations, particularly those with people living in close contact, as found in educational settings, training camps, on ships, and in correctional facilities.<sup>9-13</sup> Because the military is a defined and regimented population, it lends itself to the study of NOVARDIs. The results from military studies may be extrapolated to similar civilian settings. Furthermore, the preventive measures reviewed may have an impact on the control of other agents such as noroviruses and methicillin-resistant *Staphylococcus aureus* infections.

## Methods

Nonvaccine ARD interventions that have been used or considered were identified through communication with senior military preventive medicine officials and the study of peer-reviewed literature, military medicine textbooks, and other reports. Between 2000 and 2004, literature searches were conducted through MEDLINE (1963 to 2004) and the Technical Reports Collection on the Scientific and Technical Information Network of the Defense Technical Information Center (DTIC) (1974 to 2004). Other unpublished reports were identified by senior military officials. Bibliographies from identified articles, military publications, and studies in the Armed Forces Epidemiological Board (AFEB), Falls Church VA, archives were also reviewed.<sup>15</sup> Reviews focused on population-based studies in communities, as opposed to healthcare settings. Studies that examined other outcomes (e.g., gastrointestinal diseases), were not population-based, were in a healthcare setting, or were not in a final report form or available through DTIC, were excluded from this study. However, some excluded references served as secondary sources of information and are mentioned in the discussion section of this paper. Existing scientific data, applicability,

feasibility, and economic impact were considered for selected NOVARDIs. Recommendations were categorized using a modified classification system of the Centers for Disease Control and Prevention/Healthcare Infection Control Practices Advisory Committee (CDC/HICPAC).<sup>16</sup>

## Results

Results of the literature review are summarized in Table 1, with details on study design, population sizes, and major findings provided in Table 2. The search for hand hygiene studies yielded 12 studies (eight on handwashing with soap and water,<sup>17-23</sup> one on hand antiseptics with antimicrobial handwipes,<sup>24</sup> and three on both handwashing and hand antiseptics through hand rubs, gels, or handwipes).<sup>25-27</sup> Two of the 12 studies were conducted in elementary schools,<sup>17,18</sup> five in child daycare settings,<sup>19-21,25,26</sup> one in a senior daycare center,<sup>27</sup> and four at military recruit training sites.<sup>22-24</sup> Ten were intervention trials,<sup>17-22,24-27</sup> and two were observation studies.<sup>22,23</sup> Four of the intervention trials tested the effect of care givers' hand hygiene on the disease rates of care receivers,<sup>21,25-27</sup> while the remainder evaluated reduction in respiratory symptoms and related absences post-intervention. The intervention trials were limited in that compliance and quality of handwashing were not quantified, and two of the trials did not have concurrent control groups, but rather compared disease rates with the previous years' rates.<sup>22,27</sup> The observation studies were limited by their reliance on self-administered questionnaires to determine the extent of handwashing.<sup>22,23</sup>

Overall, nine of the 12 hand-hygiene studies reported that hand hygiene reduced the occurrence of respiratory diseases.<sup>18-24,27</sup> Three of the hand hygiene studies that showed a convincing effect among young adults were conducted at military recruit training centers. Two were done at the Naval Recruit Training Center, Great Lakes IL and published as a single paper.<sup>22</sup> The third was an Air Force study.<sup>24</sup>

The two Navy studies evaluated the same intervention.<sup>22</sup> The intervention included training given to recruits and their training staff, a mandatory policy of handwashing at least five times a day, encouragement of sink use, and emphasis on hand hygiene as a criterion for personnel inspections. The first study found that respiratory disease rates decreased by 45% compared to the previous year. A sustained effect was seen for an additional year after the study ceased. In the second study, a cross-sectional survey of a subset of recruits, self-reported respiratory illness and hospitalization rates were higher among recruits who did not wash their hands more than three times daily.

The Air Force study was a randomized, double-blind clinical trial of antimicrobial handwipes.<sup>24</sup> Recruits were given packets of handwipes and instructed to use them four times daily.<sup>24</sup> Intervention handwipes con-

**Table 1.** Interventions to prevent infectious acute respiratory disease considered for use in military training centers

Intervention category	Intervention	Number of population-based studies <sup>a</sup>			Recommendations <sup>b</sup>
		Total	Supporting intervention	Not supporting intervention	
Personal measures	Hand hygiene (handwashing or antiseptics) <sup>c</sup>	12	9	3	II and study
	Respiratory masks	0	0	0	None and study
Administrative controls	Cohorting— isolation or clustering of groups or individuals	5	4	1	II and study
	Living space allocation	5	5	0	IC and study
	“Head-to-toe” sleeping arrangement	0	0	0	II and study
Engineering controls	Barriers between beds	1	1	0	None
	Air dilution ventilation	2	2	0	Study
	Ventilation filter efficiency	0	0	0	Study
	Dust suppression (oiling floors and blankets)	5	4	1	None
	Air sterilization (glycol vapors)	1	1	0	None
	Air sterilization (ultraviolet lights)	10	7	3	Study

<sup>a</sup>In peer-reviewed literature or other documents.

<sup>b</sup>Centers for Disease Control and Prevention/Healthcare Infection Control Practices Advisory Committee system used to categorize recommendations (modified):<sup>16</sup> *Category IA*, strongly recommended for implementation and strongly supported by well-designed experimental, clinical, or epidemiologic studies; *Category IB*, strongly recommended for implementation and supported by certain experimental, clinical, or epidemiologic studies and a strong theoretical rationale; *Category IC*, required for implementation, as mandated by federal or state regulation or standard; *Category II*, suggested for implementation and supported by suggestive clinical or epidemiologic studies or a theoretical rationale; *Study*, recommended by authors for future study; *None*, interventions without sufficient evidence, strong supporting rationale, or lacking feasibility.

<sup>c</sup>Three studies involved both handwashing with soap and water and hand antiseptics.

tained parachlorometaxyleneol (PCMX) and alcohol. Control handwipes contained water and lemon juice. These were assigned randomly to training groups during the same time period. The training groups were similar in all respects but had very little contact with each other during their 6-week training period. Initial clinic visits for ARD were 33% lower ( $p=0.021$ ) and clinic visits for sore throats were 40% lower ( $p=0.009$ ) in the intervention groups.

Although evidence regarding masks as a personal protective measure is lacking, senior military preventive medicine officials reported that surgical masks had been used as a NOVARDI for military recruits. A newspaper article reported that the use of masks was associated with declining ARD rates at Fort Benning GA, and Fort Jackson SC; however, no reports were found to document or quantify the effect.<sup>28</sup>

Literature regarding administrative NOVARDIs was found on cohorting (limiting contact between defined training groups to reduce disease transmission) and reducing crowding. Five observational studies contained data that supported cohorting. However, these studies had no comparison groups and the degree of cohorting was not measured.<sup>29–32</sup> Five studies—one that included data collected at Fort Humphreys VA,<sup>33</sup> during the influenza pandemic of 1918–1919, three studies of children in other countries (including developing countries),<sup>34–36</sup> and one from a recruit ARD outbreak<sup>32</sup>—found an association between respiratory disease rates and crowded conditions. The study from Fort Humphreys had incomplete controls of confounders and incomplete density assessment. Due to the poor

living conditions, the studies of children may not be generalized to all populations. Despite these flaws, the conclusion from these studies was that reducing crowding would have a favorable impact on the occurrence of ARD. Medical literature queries on “head-to-toe” sleeping arrangements to increase the distance between personal breathing zones yielded no studies. The aforementioned study at Fort Humphreys discussed the use of cloth barriers/curtains (also called “sneeze sheets”) to form “cubicles” for separate beds; the authors attribute one group’s low incidence of influenza to the use of separation curtains. However, there was inadequate controls of other factors to assertively conclude a positive effect.

Literature regarding engineering NOVARDIs was found on indoor air exchanges, dilution ventilation, dust suppression, and air sterilization. Two studies addressing indoor air exchanges by dilution ventilation were identified. A study at Fort Benning GA, published in 1988, noted that modern, energy-efficient Army barracks had significantly higher ARD rates than drafty, older barracks at the same Army post (adjusted relative risk=1.51; 95% confidence interval=1.46–1.56).<sup>37</sup> This study, however, had little quantification of barracks’ ventilation. During an ADV type-4 outbreak at Fort Benning in 2000, lack of mechanical ventilation was significantly associated with infection in univariate analysis; however, since no cases slept in areas with operating air handlers, mechanical ventilation could not be included in the multivariate analysis.<sup>31</sup>

No population-based studies on the impact of air filter efficiency on the occurrence of respiratory disease

**Table 2.** Summary of studies of interventions to prevent acute respiratory disease

Author, year <sup>ref</sup>	Population studied <sup>a</sup>	Study type and date(s)	Variable(s) studied	Outcome measured	Result(s) <sup>b</sup>
<b>Personal protection—hand hygiene</b>					
Master, 1977 <sup>17</sup>	School children ( <i>n</i> =305)	Interventional Jan–Feb 1996	Mandatory handwashing in children	Respiratory illness absence	No significant reduction (RR=0.79, <i>p</i> =0.07)
Butz, 1990 <sup>25</sup>	Children in daycare ( <i>n</i> =108)	Interventional Jan–Dec 1988	Handwashing instruction, alcohol sanitizer use, and other practices in care providers	Respiratory illness symptoms in children	No significant reduction (OR=1.05, 95% CI=0.95–1.15)
Kotch, 1994 <sup>26</sup>	Children in daycare ( <i>n</i> =371)	Interventional May–Jul 1988	Handwashing instruction, alcohol sanitizer use, and other practices in providers	Respiratory illness in children	No significant reduction (RR=0.94, <i>p</i> >0.05)
Kimel, 1996 <sup>18</sup>	School children ( <i>n</i> =199)	Interventional Nov 1992–Feb 1993	Handwashing instruction to children	Absence due to influenza-like symptoms	Significant reduction (1.8% vs 3.8% students ill per day, <i>p</i> <0.01)
Niffenegger, 1997 <sup>19</sup>	Children in daycare ( <i>n</i> =377)	Interventional Aug 1994–Apr 1995	Handwashing instruction to children	Colds	Significant reduction (18.9 vs 27.8 colds per 100 children, <i>p</i> <0.05)
Gibson, 1997 <sup>24</sup>	Air Force recruits ( <i>n</i> =2650)	Interventional Oct–Dec 1995	Antimicrobial handwipe use in recruits	Clinic visits for respiratory illness	Significant reduction (16.2 vs 24.1 visits per 100 recruits, <i>p</i> =0.021)
Falsey, 1999 <sup>27</sup>	Seniors in daycare and providers ( <i>n</i> ~210)	Interventional Dec 1992–Mar 1996	Handwashing instruction to care providers, sanitizing foam	Respiratory illness in staff and seniors	Significant reduction in seniors compared to previous years (5.7 vs 14.5, 12.8, and 10.4 illnesses per 100 person/months, <i>p</i> <0.01)
Carabin, 1999 <sup>20</sup>	Children in daycare ( <i>n</i> =1729)	Interventional Sep 1996–Nov 1997	Handwashing instruction, other practices	Absence due to respiratory illness	Significant reduction (IRR=0.8, 95% CI=0.7–0.9)
Roberts, 2000 <sup>21</sup>	Children in daycare ( <i>n</i> =311 child-years)	Interventional Mar–Nov 1996	Handwashing instruction to care providers, other practices	Respiratory illness in children	Significant reduction in children aged <2 years (RR=0.90, 95% CI=0.83–0.97)
Ryan, 2001 <sup>22</sup>	Navy recruits ( <i>n</i> =136,225)	Interventional Oct 1995–Sep 1998	Mandatory handwashing and other measures in recruits	Respiratory illness in recruits	Significantly lower rates for 2 intervention years compared to previous year (24.3, 22.9, vs. 42.5 visits per 1000 per week, <i>p</i> <0.01)
	Subset of 136,225 recruits ( <i>n</i> =1442)	Cross-sectional Oct 1996–Sep 1998	Handwashing frequency in recruits	Self-report of respiratory illness hospitalizations	Significant increase with infrequent handwashing (OR=10.9, 95% CI=2.7–46.2)

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**Table 2.** (continued)

Author, year <sup>ref</sup>	Population studied <sup>a</sup>	Study type and date(s)	Variable(s) studied	Outcome measured	Result(s) <sup>b</sup>
Neville, 2001 <sup>23</sup>	Air Force recruits ( <i>n</i> =470)	Cross sectional May 2000	Washing hands after coughing or sneezing in recruits	Respiratory symptoms	Significant increase with infrequent washing (sneeze: OR=1.4, 95% CI=1.1–1.7; cough: OR=1.7, 95% CI=1.3–2.3))
<b>Administrative controls—cohorting</b>					
Bloom, 1964 <sup>29</sup>	Marines in training and staff ( <i>n</i> =NA)	Cohort Sep 1959–Apr 1963	Contact between training units	Adenovirus-associated respiratory illness	Lower rates in segregated units compared to units that mixed
Sanchez, 2001 <sup>30</sup>	Army recruits ( <i>n</i> =NA)	Observational May–Oct 1997	Spread of respiratory disease outbreaks	Respiratory illness hospitalizations	Clustering of illness by unit was observed
Kolavic-Gray, 2002 <sup>31</sup>	Army recruits ( <i>n</i> =678)	Cohort Oct–Nov 1998	Spread of respiratory disease outbreaks	Respiratory illness hospitalizations	Three groups followed; outbreaks in two groups did not spread to the third group (RR=2.0, 95% CI=1.3–3.1)
	Army recruits ( <i>n</i> =249)	Nested case–control Oct–Nov 1998	Military unit	Respiratory illness hospitalization	No cohort effect; military unit was not a risk factor in multivariate analysis (OR=0.6, 95% CI=0.3–1.2)
USACHPPM, 2000 <sup>32</sup>	Army recruits ( <i>n</i> =288)	Case–control Apr–May 2000	Cohorting	Respiratory illness	Cohort effect was observed; group assignment was a significant risk factor in multivariate analysis (OR=5.7, 95% CI=2.0–16.3)
<b>Administrative controls—living space allocation</b>					
Brewer, 1918 <sup>33</sup>	Army soldiers ( <i>n</i> ≈19,709)	Cohort Sep–Oct 1918	Living space per soldier	Influenza-like illness	Barracks with less crowding had lower disease rates
Tumwesigire, 1995 <sup>34</sup>	Children of Ugandan military ( <i>n</i> =152)	Cross-sectional Jan 1994	Number of persons per house	Respiratory illness	Significantly higher rates for more than five persons per house (OR=1.5, <i>p</i> =0.01)
Azizi, 1995 <sup>35</sup>	Hospitalized urban Malaysian children ( <i>n</i> =593)	Case–control Feb 1989–May 1990	Number of persons per house	Respiratory illness	More than five household members was a significant risk factor (OR=1.5, 95% CI=1.03–2.19)

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**Table 2.** Summary of studies of interventions to prevent acute respiratory disease (*continued*)

Author, year <sup>ref</sup>	Population studied <sup>a</sup>	Study type and date(s)	Variable(s) studied	Outcome measured	Result(s) <sup>b</sup>
Rahman, 1997 <sup>36</sup>	Children in Bangladesh (n=965)	Cohort Jul–Oct 1993	Household crowding	Respiratory illness	Significant increase with high-density living (38.0% vs 62.0%, <i>p</i> <0.05)
USACHPPM, 2000 <sup>32</sup>	Army recruits (n=288)	Case-control Apr–May 2000	Number of people per room	Respiratory illness	Sleeping density >50 per room was a significant risk factor (adjusted OR=5.4, 95% CI=1.5–19.8)
<b>Administrative controls—cloth barriers between beds</b>					
Brewer, 1918 <sup>33</sup>	Army soldiers (n=~19,709)	Cohort Sep–Oct 1918	Cloth barriers between beds	Influenza-like illness	Lower rates observed in barracks with barriers (25.4–74.0 vs 87.7–286.0 per 1000 soldiers)
<b>Engineering controls—increased air-dilution ventilation</b>					
Brundage, 1988 <sup>37</sup>	Army recruits (n=2,633,916 recruit-weeks)	Cohort 1982–1986	Barrack type	Respiratory illness hospitalizations	Significantly lower rates in older barracks with open window ventilation or without modern ventilation (adjusted RR=1.5, 95% CI=1.5–1.6)
USACHPPM 2000 <sup>32</sup>	Army recruits (n=288)	Case-control Apr–May 2000	Use of available mechanical ventilation in barracks	Respiratory illness	No cases in barracks with operating mechanical ventilation ( <i>p</i> =0.05)
<b>Engineering controls—dust suppression (oiling)</b>					
Anderson, 1944 <sup>38</sup>	British troops (n=~3000)	Interventional Dec 1942–Mar 1943	Oil-treated floors	Respiratory illness	Reduction in illness (7 vs 38 cases per 1000 per week)
CARD and CABI, 1946 <sup>39</sup>	Army recruits (n=~2880)	Interventional Oct 1944–Apr 1945	Oil-treated floors and blankets	Respiratory disease hospitalizations	Suggestive effect during endemic period; no effect during epidemic respiratory disease period
Schechmeister, 1947 <sup>40</sup>	Navy personnel (n=6471)	Interventional May 1945–May 1946	Oil-treated floors and blankets	Respiratory illness	Slight reduction during periods of low incidence; no effect during periods of high incidence
Miller, 1948 <sup>41</sup>	Navy recruits (n=8515)	Interventional winter 1945–1946	Oil-treated floors and blankets	Respiratory disease hospitalizations	No significant reduction (2651 vs 2549 cases per 1000 per year)
Loosli, 1952 <sup>42</sup>	Army troops (n=24,500)	Interventional Jan–Jul 1944	Oil-treated floors and blankets	Respiratory disease hospitalizations	Reduction in hospitalization (15% to 30% in two of three groups evaluated)

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**Table 2.** (continued)

Author, year <sup>ref</sup>	Population studied <sup>a</sup>	Study type and date(s)	Variable(s) studied	Outcome measured	Result(s) <sup>b</sup>
<b>Engineering controls—air sterilization (glycol vapors)</b>					
Bigg, 1945 <sup>43</sup>	Men in barracks ( <i>n</i> ≈2000)	Interventional (date not provided)	Triethylene glycol vapors	Respiratory disease hospitalizations	Reduction in hospitalizations (111 vs 126 admissions per 12-week period)
<b>Engineering controls—air sterilization (UV lights)</b>					
Wells, 1942 <sup>44</sup>	School children ( <i>n</i> =NA)	Interventional 1937–1941	UV lights in classrooms	Measles, chicken pox, and mumps	Lower risk of new cases in rooms with lights
Schneiter 1944 <sup>45</sup>	Boys in dormitories ( <i>n</i> =NA)	Interventional Jul 1941–Jul 1943	UV lights in dormitories	Hospital admissions for air-borne diseases	Small decrease with lights (2.71 vs 2.90 admissions per 1000 per day), researchers conclude no considerable difference
Wheeler, 1945 <sup>46</sup>	Navy recruits ( <i>n</i> ≈11,543)	Interventional winter/spring 1943–1944	UV lights in barracks	Respiratory disease hospitalizations	Reduction in hospitalizations (90.4 vs 114.3 admissions per 1000 per training period)
Perkins, 1947 <sup>47</sup>	School children ( <i>n</i> ≈2370)	Interventional Jan 1945–May 1946	UV lights in school	Measles	No definite effect
Miller, 1948 <sup>41</sup>	Navy recruits ( <i>n</i> =8515)	Interventional winter 1945–1946	UV lights and oiled blankets and floors vs only oiled blankets and floors	Respiratory disease hospitalizations	Significant reduction with lights (1447 vs 1790 admissions per 1000 per year, <i>p</i> <0.01)
Willmon, 1948 <sup>48</sup>	Navy recruits ( <i>n</i> =NA)	Interventional winter 1944–1945	UV lights in barracks	Respiratory disease hospitalizations	20% reduction in intervention group; researchers did not define significance
Langmuir, 1948 <sup>49</sup>	Navy recruits ( <i>n</i> =5676)	Interventional winter 1946–1947	UV lights in barracks	Respiratory disease hospitalizations	Reduction in hospitalizations (endemic: 4.9 vs 9.5 admissions per 1000 per week; epidemic period: 69.6 vs 85.6 admissions per 1000 per week)
Wells, 1950 <sup>50</sup>	Children ( <i>n</i> =2238)	Interventional Jan 1946–Jun 1949	UV lights in schools and other public areas	Measles and chicken pox	Slower spread of disease with UV lights
Gelperin 1951 <sup>51</sup>	School children ( <i>n</i> =2458)	Interventional 1948–1950	UV lights in school	Respiratory illness	No significant reduction (33.0 vs 35.0 cases per 100 children; <i>p</i> >0.05)
Menzies, 2003 <sup>52</sup>	Office workers ( <i>n</i> =771)	Interventional Jul 1999–Jul 2000	UV lights in ventilation system	Self-reported respiratory symptoms	Significant reduction (OR=0.5 95% CI=0.4–0.9)

<sup>a</sup>Population size was not always specifically stated (e.g., “approximately 70”) <sup>27</sup>; in some reports the population size was not given but could be calculated from other data provided. Population sizes not specifically defined by the author(s) are preceded by a tilde (~).

<sup>b</sup>When available, pertinent rates, ratios, and *p* values are provided.

CARD, Commission on Acute Respiratory Diseases; CABI, Commission on Air-Borne Infections; USA CHPPM, U.S. Army Center for Health Promotion and Preventive Medicine; 95% CI, 95% confidence interval; IRR, incidence rate ratio; NA, not available; OR, odds ratio; RR, relative risk; UV, ultraviolet.



were found. Five studies evaluating the impact of dust suppression were identified.<sup>38–42</sup> Oiling of floors and blankets were associated with a reduction in respiratory disease in four studies.<sup>38–40,42</sup> Oiling failed to prevent ARD outbreaks in the fifth study.<sup>31</sup>

One population-based study demonstrated a positive effect from air sterilization using glycol vapors.<sup>43</sup> Ten population-based studies of air sterilization using ultraviolet (UV) lights were identified<sup>41,44–52</sup>; Three were conducted in schools,<sup>44,47,51</sup> four in military training settings,<sup>41,46,48,49</sup> one in an entire community,<sup>50</sup> one in a dormitory,<sup>45</sup> and one in office buildings.<sup>52</sup> Seven studies supported UV lights as a means to reduce ARD rates,<sup>41,44,46,48–50,52</sup> although the measured effects in two studies were small.<sup>44,50</sup> It was concluded from the four military studies<sup>41,46,48,49</sup> that larger effects were observed only with high UV irradiation, and the effect was considered to be too low to recommend its use.<sup>48</sup>

## Discussion

### Personal Measures

There is considerable evidence to support hand hygiene as an effective intervention to prevent gastrointestinal diseases and nosocomial infections.<sup>53</sup> Handwashing is strongly recommended for control of respiratory syncytial virus (RSV),<sup>54</sup> and has been advocated by the CDC to prevent SARS in healthcare and community settings.<sup>3</sup> However, as was found in this study and as suggested elsewhere,<sup>16,55</sup> epidemiologic evidence is limited to support handwashing as a means to prevent general ARD in community settings.<sup>55</sup> Nine of 12 reviewed studies supported some form of hand cleansing, but studies with concurrent control groups that monitored compliance and quality of hand cleansing were lacking.

Hand antisepsis refers to the application or use of hand rubs, gels, foams, or premoistened towelettes (handwipes) that use various chemicals as active ingredients.<sup>16</sup> In December 2002, the CDC updated their recommendations for hand hygiene in healthcare settings to include hand antisepsis.<sup>16</sup> Use of alcohol-based hand rubs, which are effective against a variety of bacteria and viruses, are endorsed in the healthcare setting as either a supplement to traditional handwashing or as a primary means of hand hygiene if hands are not visibly soiled. These recommendations are based on well-designed experimental, clinical, or epidemiologic studies (Category IA). Authors of these recommendations point out studies that show plain soap failing to remove organisms, and the possibility of contamination of soap or soap dishes.<sup>16</sup> One study concluded that handwashing was generally less effective than hand rubs.<sup>56</sup> Another review of hand antiseptics and viruses found experimental evidence demonstrating that some formulations of hand rubs, particularly those with alco-

hol, outperformed regular handwashing.<sup>57</sup> Studies of an alcohol-based hand rub found a decrease in school absenteeism and infections in an extended care facility when hand rubs were made available; however, the effect on respiratory disease could not be determined since the studies did not analyze absenteeism by cause.<sup>58–60</sup> As demonstrated in a study of Air Force recruits, handwipes with PCMX are effective against ARD,<sup>24</sup> in spite of the CDC recommendations on hand hygiene for healthcare workers, which states that antimicrobial-impregnated wipes are not as effective as hand rubs.<sup>16</sup>

Personal protection in the form of surgical masks is recommended for isolation precautions for airborne and droplet transmission in hospitals.<sup>61</sup> For diseases transmitted by droplets, masks are recommended for susceptibles who come within 3 ft of infected patients.<sup>61</sup> These isolation precautions are not based on experimental, clinical, or epidemiologic studies, but on strong rationales and suggestive evidence. Surgical masks are used to prevent tuberculosis (TB)<sup>61</sup> transmission (worn by patients outside their isolation rooms), and masks may also be recommended in cases where the route of transmission is uncertain, such as during the SARS outbreak in 2003.<sup>3</sup> There is evidence that wearing surgical or well-fitted respiratory masks (in addition to other infection control measures) lowered the risk of SARS in healthcare settings in Hong Kong and Toronto in 2003.<sup>62–64</sup>

Filters that can capture particles as small as 1 micron in size, with a minimum filter efficiency of 95%, are used in commercial respirators tested and certified by the National Institute for Occupational Safety and Health as N95 respirators.<sup>65</sup> N95 respirators are recommended for tuberculosis, rubeola (measles), and varicella (chickenpox) control in clinical settings.<sup>61,65</sup> Susceptible people should wear an N95 respirator on entering a room with a patient known or suspected to be infected with any of these pathogens.<sup>61,65</sup>

The use of masks or respirators in military training centers to prevent ARD has not been documented. Surgical masks have been used as a NOVARDI to prevent ARD in military training; however, there are no formal reports on their efficacy.<sup>28</sup> In 1942, the AFEB's Commission on Influenza discussed the possible impact of masks on respiratory disease prevention and recommended use of a gauze-covered mask with a Canton flannel filter and flexible nose band. It is unclear how this intervention was intended to be implemented.<sup>66</sup> Today, masks are not routinely given to U.S. military trainees.

### Administrative Controls

Administrative controls do not rely on the compliance and diligence of individuals. They involve policy implementation that may be easier to enact and sustain. Cohorting, which attempts to limit transmission by

decreasing the number of susceptible individuals with whom an infected individual might come in contact, is routinely used in hospital infection control.<sup>61</sup> For patients with diseases where airborne and droplet precautions are necessary, and private rooms are not available, it is recommended that an individual patient be grouped with other patients who have the same active infection with the same microorganism, but no other infections.<sup>61</sup>

Outside a healthcare setting, identification of infected individuals is not possible. A different method of cohorting, which is practiced in military basic training centers, involves minimizing contact between training companies of approximately 100 to 200 people. Population-based evidence for the effectiveness of cohorting was observed during Marine initial entry training, but not later in advanced training, when companies had more contact with other companies.<sup>29</sup> Evidence of the effect of cohorting is suggested by the way clusters of cases occur during initial entry training. In two outbreaks in 1997<sup>30</sup> and 1998<sup>31</sup> at Fort Jackson SC, company-specific attack rates and temporal progression of ADV-associated ARD cases supported the spread of infection by cohorts. Thus, interruption of outbreaks may be possible if contact between members of separate training companies could be avoided early. In an ADV type-4 outbreak in 2000 at Fort Benning,<sup>32</sup> the involvement of only one training company, atypical of previous ADV type-4 outbreaks, may have been explained by the limited degree of interaction by members of that company with other trainees at the time. While cohorting may seem like an attractive control measure, current training structures (barracks, classrooms, dining, recreational, and medical facilities) may make it difficult to effectively isolate groups from one another for a significant amount of time.

Crowding is a fundamentally accepted risk factor in the transmission of infectious diseases,<sup>61</sup> and administrative control measures have often focused on increasing space between individuals through an increased area around beds, "head-to-toe" sleeping, fabric or other barriers between beds, and cohorting. Currently, overcrowding, especially during the summer surge when large numbers of high school graduates enter military training, may be a problem. The Army Medical Department has historically recommended adequate living space to decrease the spread of infectious diseases even though the definition of "adequate" is debatable.<sup>14</sup> Despite this long-standing concern, population-derived evidence supporting "adequate" space is lacking. Recommendations for space and ventilation dating back to 1772 are not based on controlled studies or well-designed observational studies, but rather on theory, expert or personal opinions, or limited observation.<sup>14,67</sup> In 1924, examining data from the influenza pandemic during World War I, Army Medical Department reviewers established standards of 60 ft<sup>2</sup> of floor space and 720 ft<sup>3</sup> of area per person in barracks.<sup>14,67</sup>

Data from Camp Humphreys VA, supported these recommendations, although data from other posts were less convincing.<sup>33</sup> The current space allocation guidelines specify 72 ft<sup>2</sup> of floor space per soldier, with a minimum of 55 ft<sup>2</sup> that can be reduced to 40 ft<sup>2</sup> in temporary emergency situations.<sup>14,68</sup> These requirements exceed the standards set by the American Society of Heating, Refrigerating and Air Conditioning Engineers, Inc. (ASHRAE) of 50 ft<sup>2</sup> per person.<sup>69</sup> CDC hospital guidelines for bed spacing recommend at least 3 ft between infectious and susceptible patients when private isolation rooms are not available.<sup>61</sup>

Sleeping head-to-toe, which involves alternating bed arrangements so that troops sleep in a line of bunks alternating head and foot positions, increases the distance between breathing zones. This practice makes sense and does not involve any additional cost or resources. However, there are no studies to support its efficacy.<sup>70</sup> Cloth or other barriers between beds are meant to interrupt droplet particle dispersion generated from sneezes and coughs. Cloth barriers are discussed in Army medical history, but there are no controlled studies supporting their use.<sup>70</sup>

## Engineering Controls

Engineering controls are generally considered more reliable than other intervention categories since they do not require individual compliance or enforcement of administrative policies. However, these are often resource intensive. The most practical place to implement engineering measures at training sites is in new construction of barracks and other facilities for trainees. The amount of disease agent transmission that occurs in the barracks, compared to other military training environments is unknown.<sup>70</sup> Because the occurrence of respiratory disease is thought to be related to the amount of contagion in the air,<sup>71</sup> engineering controls such as increased air dilution and ventilation, filtration, dust suppression, and air sterilization, which attempt to decrease the concentrations of microorganisms in the air, theoretically constitute effective NOVARDIs.

One of the first documented engineering preventive measures was dust suppression through oiling of wood floors and wool blankets. It was introduced during World War I, and later studies found that this practice reduced organisms in the air by 75% to 90%,<sup>15</sup> resulting in some reduction in respiratory illness.<sup>38,39,40,42</sup> Studies conducted among soldiers in 1944 to 1945<sup>39</sup> and sailors in 1945 to 1946,<sup>40</sup> however, failed to document a beneficial effect from the oiling of blankets and floors during ARD outbreaks. By comparison, investigations at Camp Carson CO found ARD reductions in some, but not all groups studied.<sup>42</sup> Later laboratory studies demonstrated that contaminated dust did not induce respiratory illness, and interest in dust suppres-

sion declined.<sup>15</sup> Floors and other surfaces in contemporary buildings should be less conducive to the accumulation of dust. Frequent thorough cleaning of environmental surfaces and personal items such as blankets should be expected to minimize airborne dust concentrations.

Optimum ventilation standards remain an item of interest. Unfortunately, the two studies that supported dilution ventilation as a NOVARDI were observational studies that did not identify a measurable standard. Increasing dilution of indoor air can be achieved by opening windows and doors or by installing effective heating, ventilation, and air conditioning (HVAC) systems. ASHRAE recommends 15 ft<sup>3</sup> of outdoor air per minute per person, and further states that indoor carbon dioxide measurements greater than 700 parts per million above outdoor air concentrations will make building occupants uncomfortable with respect to odors generated.<sup>69</sup> ASHRAE standards are comfort based, but this industry-accepted standard should be followed in the absence of health-related standards.

Decreased pathogen load in the air can also be achieved by filtration. The percentage of contaminants that can be removed by commonly used filters may be small. However, high-efficiency particulate air (HEPA) filters, which have a minimum removal efficiency of 99.97% of particles  $\geq 0.3$  microns in diameter,<sup>65</sup> could substantially sequester bacterial ARD agents, which range in size between 0.4 to 1.5 microns, and viruses, which range between 0.07 to 0.4 microns.<sup>72</sup> In experiments, HEPA filters have effectively reduced contamination.<sup>71</sup> Unfortunately, controlled, population-based studies using HEPA filters or regular filters in a non-healthcare setting were not found.

Air sterilization has been studied using two principal methods, each tested in population-based studies: glycol esters and UV lights. In the 1940s, ethylene and propylene glycol vapors were tested as methods for air sterilization.<sup>15,43,70</sup> These experiments demonstrated a significant reduction of air bacterial content when small concentrations were applied as aerosols. Additionally, studied children's hospital wards and military barracks had lower respiratory disease rates with the use of glycol vapors compared to untreated controls.<sup>15</sup> However, with today's heightened concern about chemical exposures and the possibility of harmful side effects, use of these vapors in recruit barracks is not recommended.

Ultraviolet light irradiation, an air disinfection method, has been tested and used since the 1940s,<sup>73</sup> and is recommended by the CDC for TB isolation rooms in conjunction with other control measures (e.g., negative pressure and HEPA filters).<sup>65</sup> While the documents found in this study demonstrated some effect, in most cases the effect was only slight or suggestive. Taking into consideration cost and the expected benefit, the military has not considered UV

lights to be practical.<sup>15,48</sup> A well-conducted recent study demonstrated reductions in work-related symptoms, including respiratory symptoms for office ventilation systems irradiated with UV lights.<sup>52</sup> Most military research on UV was conducted in the 1940s; thus, contemporary evaluations of UV lights in military training centers need to be undertaken.

## Conclusions and Recommendations

Despite limited population-based data regarding personal preventive measures, evidence for the use of handwashing, and hand antisepsis in cases where soap and water are not available, is encouraging. Given its proven efficacy in the healthcare industry, hand antisepsis may be justified, even with its concomitant increase in cost.<sup>16</sup> Masks or respirators vary in quality and cost, and there is inadequate evidence to recommend their use in community settings in the absence of an imminent threat. Considering the realistic possibility of an emerging infectious agent for which there is no effective vaccine or antimicrobial drug, such as a novel influenza strain, population-based studies of masking must be seriously considered.

To the greatest degree possible, inexpensive and feasible administrative controls such as cohorting should be practiced to prevent the spread of disease. Head-to-toe sleeping, despite lacking supporting studies, is a "no-cost" intervention that should be continued.<sup>70</sup> There is inadequate evidence to recommend use of cloths or similar barriers. Although population-based data on adequate sleeping space is sparse, existing standards should be followed and living space arrangements must be taken into consideration and evaluated during respiratory disease outbreak investigations.

Although theoretical support and experimental evidence exist for adequate dilution ventilation, the use of high-efficiency air filters, and air sterilization by UV lights, there is inadequate evidence to support recommendations for these controls at this time. ASHRAE standards are the accepted industry standards for indoor air quality and should still be met, but there is no evidence to justify implementation of measures beyond these standards.

This study focused on prevention interventions related to personal hygiene and administrative and environmental controls for infectious respiratory diseases. The list of potential NOVARDIs is extensive and many were not considered in this report. For example, cleansing of common surfaces and management of symptomatic personnel were not evaluated. Before the 1990s, military medical treatment facilities had liberal hospitalization policies for ARD. These policies, however, have been significantly modified in recent years with the advent of managed care. The question of whether this change influenced the spread of respiratory disease is in debate.<sup>74</sup> Other prevention interventions that were

not reviewed in this study include medications, supplements, and alternative medicine interventions (e.g., vitamin C, zinc, and Echinacea). This study reviewed and referenced some policy documents from the U.S. Army; however, instructions and policies from the other military services were not included. The literature review for this study may have also missed relevant reports due to differences in keyword search phrasing, and specificity in choosing only population-based studies. Nevertheless, it can be concluded that robust, population-based evidence is lacking for the NOVARDIs examined. Most potential methods for interrupting the transmission of respiratory disease agents are not well understood or documented. Therefore, designing studies to evaluate NOVARDIs is challenging. Complicating factors include low infecting dose,<sup>75</sup> varying degrees of communicability for different pathogens,<sup>76</sup> and multiple modes for transmission.<sup>77</sup>

Recommendations for the implementation of NOVARDIs rest on theoretical or experimental evidence, as well as on logistical and economic practicality. Logistic and economic practicality will vary based on many factors including facility infrastructure. NOVARDIs must be considered as an option for intervention, but should not detract from efforts in the military to re-establish adenovirus vaccination control policies, improve the effectiveness of influenza campaigns, implement or encourage the use or development of other vaccines for other respiratory diseases, or provide for rapid diagnostic tests that will direct prompt appropriate treatment and could limit transmission. The threat that a highly transmissible, highly virulent respiratory disease agent can present, such as SARS-associated coronavirus, and for which there is no effective vaccine or antimicrobial drug, requires both military and civilian leaders to give NOVARDIs much greater consideration in community settings than has been traditionally given. Further study of NOVARDIs, to include analysis of cost and benefits derived, is warranted.

Appreciation and thanks are extended to Megan A. Ryan, MD, MPH, Captain, U.S. Navy; Stephan Graham, CIH, CSP; and David Sliney, PhD, for their review of this work. Thanks also to Roberto N. Nang, MD, MPH, Lieutenant Colonel, U.S. Army, for his initial guidance and for "coining" the acronym "NOVARDI."

The opinions presented are those of the authors and do not necessarily reflect the opinions the U.S. Army or the U.S. Department of Defense.

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