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Distribution of Influenza Vaccine to High-Risk Groups

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Vaccine distribution programs have historically targeted individuals at high risk of complications due to influenza. Despite recommendations from the Advisory Committee on Immunization Practices, vaccination coverage among high-risk populations has been generally low. This review systematically summarizes the recent literature evaluating programs in different settings, from within medical settings to venue-based and community-based approaches, in an effort to identify successful program components. The published literature was identified by using the MEDLINE database from 1990 to 2006 covering studies that reported on interventions or programs aimed at vaccinating high-risk populations. The authors reviewed 56 studies. In the United States, the Healthy People 2010 goals included 90% vaccination coverage for adults aged ≥65 years and 60% for high-risk adults aged 18–64 years. Only a handful of the studies reviewed managed to meet those goals. Interventions that increased vaccination coverage to Healthy People 2010 goals included advertising, provider and patient mailings, registry-based telephone calls, patient and staff education, standing orders coupled with standardized forms, targeting of syringe exchange customers, and visiting nurses. Few studies evaluated the impact of vaccination programs by race/ethnicity and socioeconomic status. Few studies targeted individuals outside of the health-care and social services sectors. Given the growing disparities in health and health-care access, understanding the way in which interventions can remedy disparities is crucial.

adult; aged; child; immunization; influenza, human; review; vaccination

INTRODUCTION

Influenza is associated with significant morbidity and mortality in the United States. Between the 1990–1991 and 1998–1999 influenza seasons, the rate of influenza-related primary respiratory and circulatory hospitalizations ranged from 62.6 to 159.1 per 100,000 person-years; the rate for primary pneumonia and influenza hospitalizations specifically ranged from 31.0 to 71.4 per 100,000 person-years (1). During the same interval, the influenza-related morality rates were 19.6 per 100,000 person-years for all causes, 13.8 for underlying respiratory and circulatory deaths, and 3.1 for underlying pneumonia and influenza deaths (2). The highest rates of influenza-related mortality are seen among individuals aged 65 years or older: 132.5 per 100,000 person-years for all-cause deaths, 98.3 for underlying respiratory and circulatory deaths, and 22.1 for underlying pneumonia and influenza deaths (2).

Vaccine distribution programs have historically targeted individuals at high risk of complications due to influenza (3). Mathematical modeling suggests that focusing influenza control efforts on high-risk groups (high risk in terms of both susceptibility and contagiousness) can offer a considerable advantage in terms of reduction of infectious disease compared with interventions that target more general populations (4). Most current recommendations suggest prioritizing vaccination for individuals at high risk of complications due to influenza virus infection. The Advisory Committee on Immunization Practices classified high-risk groups to include, but not be limited to, adults aged 65 years or older, children aged 6–23 months, pregnant women, and individuals with chronic medical conditions, especially pulmonary or cardiovascular disorders (5).

Given the higher risk of morbidity and mortality among high-risk groups, the Healthy People 2010 initiative has set an influenza vaccination goal of 90 percent coverage for noninstitutionalized adults aged 65 years or older and 60 percent for noninstitutionalized high-risk adults aged 18–64 years (6). However, data from the 2003 Behavioral Risk

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Factor Surveillance System study suggest that vaccination coverage is lower: coverage among adults aged 65 years or older was 69.9 percent and among adults aged 18–64 years was 34.0 percent for those with asthma and 49.0 percent for those with diabetes (7). During the 2004–2005 influenza season, when there was a significant vaccine shortage, vaccination coverage was estimated to be 62.7 percent among adults aged 65 years or older and 25.5 percent among adults aged 18–64 years with a high-risk condition (8). Furthermore, influenza vaccination coverage is not evenly distributed. Data from the National Health Interview Study revealed significant differences in influenza vaccination coverage among elderly adults by race/ethnicity, with rates being higher among Whites, followed by Hispanics and Blacks (66 percent vs. 50 percent and 46 percent, respectively) (9).

Rates of vaccination have been low despite recommendations. A variety of settings and approaches have been utilized in the effort to increase vaccination rates among individuals at high risk of complications due to influenza infection. This review systematically summarizes the recent literature evaluating programs in different settings, from within medical settings to venue-based and community-based approaches, in an effort to identify the features of such programs that are most successful and that may guide efforts to increase vaccination rates nationwide. We also considered limitations in the current body of literature, focusing on areas for further research and program development.

REVIEW OF THE LITERATURE

The potential scope of the literature that may be considered relevant to the distribution of influenza vaccination is vast. In light of recent reviews examining immunization delivery methods that have included much of the older literature (10–12), we chose to limit the focus of our review to studies conducted after 1990. Given the large numbers of studies that allude to vaccine delivery methods, we limited our review to studies that were explicitly, at least in part, concerned with evaluating an intervention or program to either distribute or increase uptake of influenza vaccine among individuals at high risk.

The published literature was identified by using the MEDLINE database (National Library of Medicine, Bethesda, Maryland) from 1990 through early 2006, covering both US and international studies that reported on interventions or programs aimed at vaccinating high-risk populations. We considered randomized controlled trials, pre- and postintervention evaluation studies, and simple evaluations with and without controls. The search was limited to English-language studies in biomedical research. Keywords and terms used for the search included primarily the following: influenza, vaccination, intervention, program, distribution, elderly, children, pregnant, diabetes, cardiovascular, cardiovascular disease, chronic obstructive pulmonary disease, asthma, chronic lung disease, and HIV.

FINDINGS

In this review, we move from the medical setting out into community settings and discuss influenza vaccine distribution in five different contexts: 1) hospital/tertiary-care settings, 2) primary-care settings, 3) venue-based (e.g., nursing homes) targeted delivery, 4) large-scale regional programs, and 5) community-based distribution programs. Table 1 provides details for each study, including year of publication, location, setting, sample size and study type (i.e., randomized controlled trial, pre-post evaluation, and simple evaluations with and without controls), intervention content, and study findings.

Hospital/tertiary-care settings

Hospital- and tertiary-care-based programs for increasing influenza vaccination coverage generally focused on the provider and included standing orders for influenza vaccination and reminders to hospital staff. Two studies evaluated the impact of standing orders on vaccination coverage. One study of 761 elderly patients in a tertiary-care hospital that implemented a standing order for influenza vaccination reported that vaccination coverage increased from 45 percent prior to admission to 67 percent after the inpatient intervention; almost 40 percent of unvaccinated patients were vaccinated (13). In a 10-year evaluation of a vaccination program in a veterans' hospital that implemented standing orders and standardized forms, vaccination coverage increased from 79 percent to 86 percent (14).

Reminder systems have also been evaluated. Dexter et al. (15) assessed a computerized reminder system by using a randomized controlled trial among 6,371 patients representing all patients discharged from six general medicine wards in an urban hospital during an 18-month period. Four general medicine teams were randomized to the intervention team and four were randomized to the control team. Vaccination coverage was 51.4 percent among eligible patients in the intervention group compared with 1.0 percent in the control group. Bloom et al. (16) evaluated fax reminders to primary care physicians encouraging vaccination before discharge among 103 physicians serving 153 patients aged 65 years or older; the vaccination rate before discharge was less than 2 percent. Common reasons physicians gave for not vaccinating before discharge included the following: patient vaccinated prior to hospitalization (85 percent), patient discharged prior to completion of treatment (47 percent), and acute-care setting not appropriate to give vaccinations (40 percent). Claims data did not corroborate the reports of past vaccination; for only 24 percent of patients whom physicians identified as previously being vaccinated for pneumococcus or influenza was there a claim in the system of notation in their hospital medical record. However, the authors noted that claims data may have been lagged or physicians may have billed for vaccinations separately and thus no claims were submitted. Despite the limitations of the claims data, the authors concluded it was unlikely that the rate of influenza vaccination prior to admissions was as high as the physician reports suggested.

The structured setting of hospitals and tertiary-care facilities provides an important opportunity for vaccination. Standing orders and reminders appear to improve vaccination rates, but there are two problems. First, while the rates were higher in the intervention groups, they still did not

TABLE 1. Key studies that evaluated programs and interventions aimed at increasing influenza vaccination coverage, 1990–2005

Study, year (reference no.)	Location	Target group	Setting	Sample	Study type	Intervention	Findings	Result
				Hospitals and tertiary care				
Nichol, 1998 (14)	Minneapolis, Minnesota	Elderly and high-risk adults	Veterans' hospital	500 elderly and high-risk patients per year	Prospective evaluation	Standing orders, standardized forms, patient mailing	For all inpatient respondents, rates increased from 79% in 1990–1991 to 86% in 1996–1997.	$p < 0.001$
Bloom et al., 1999 (16)	New York and New Jersey	Elderly	Managed-care organization serving a large Medicare population	106 primary-care physicians treating 153 patients aged ≥65 years	Prospective evaluation, retrospective claims analysis	Reminders to primary-care physicians requesting vaccination before discharge	Vaccination rate before discharge was 1.96%. Physicians identified 85% as being vaccinated before admission. Claims data did not corroborate past vaccination reports.	Not reported
Lawson et al., 2000 (13)	Edmonton, Alberta, Canada	Elderly	Tertiary-care hospital	761 patients aged ≥65 years	Prospective cohort	Standing order	Vaccination coverage increased from 45% before admission to 67% after intervention. 39.9% of unvaccinated adults received influenza vaccine. 33% refused vaccine.	Not reported
Dexter et al., 2001 (15)	Indianapolis, Indiana	Hospitalized patients	Urban hospital	6,371 patients in general medicine service	RCT*	Computerized reminder vs. computerized standing order	Vaccine was administered to 42% in the standing-order group and 30% in the reminder group.	$p < 0.001$
				Primary care				
Barton and Schoenbaum, 1990 (22)	Boston, Massachusetts	Elderly and high-risk outpatients	Health maintenance organization	647 patients aged ≥65 years and 198 high-risk patients aged <65 years	Pre/post* and RCT of postcards to diabetics	Mailing, computer reminder to physicians, feedback to physicians and service chiefs	Vaccination coverage increased among elderly and high-risk patients after the intervention. Among diabetic patients, vaccination coverage was higher among those who received a reminder (55.9% vs. 27.9%, respectively).	Not reported
Nichol et al., 1990 (24)	Minneapolis, Minnesota	High-risk outpatients	Veterans' hospitals	1,375 outpatients	Cross-sectional with controls	Vaccination by a nurse without a physician's order, chart-based reminders, mailing	Vaccination coverage in the intervention hospital was 58.3% vs. 28.4–31.4% in controls. For each high-risk subgroup (age ≥65 years, lung or heart disease, diabetes, other), coverage was better in the intervention hospital than in controls.	$p < 0.001$

Knoell and Leeds, 1991 (36)	San Francisco, California	Elderly	Ambulatory-care facility	433 patients aged ≥65 years	Pre/post with historical controls	Staff/patient education and vaccination clinic	47% of the historical controls had been offered vaccine vs. 71% of the intervention group. The vaccination rate for the intervention group was 62%.	$p < 0.001$
Spaulding and Kugler, 1991 (18)	Fort Lewis, Washington	High-risk outpatients	Military hospital family practice department	1,068 high-risk patients, excluding those aged ≥65 years without other risk factors	RCT	Mailing	25.2% of the intervention group received influenza vaccine compared with 9.1% of the control group. The group with higher military rank (proxy for socioeconomic status) was more likely to be vaccinated.	$p < 0.001$
Margolis et al., 1992 (25)	Minneapolis/ St. Paul, Minnesota	Elderly	Health maintenance organization	600 people aged ≥65 years	Pre/post with controls	Standing order	Postintervention vaccination rates were 70–72% in intervention clinics vs. 54–60% in control clinics. The differences in vaccination rates pre- and postintervention were significant in only 1 intervention clinic.	$p = 0.01$
Herman et al., 1994 (37)	Cleveland, Ohio	Elderly	Ambulatory medical clinic	1,202 patients aged ≥65 years	RCT	Staff and patient education, flow sheet/ standing order	Influenza coverage was 41.7% in the control group, 44.6% in the group that received education only, and 55.1% in the group that received education and the flow sheet/standing order.	$p < 0.001$
Hutchinson and Norman, 1995 (19)	Seattle, Washington	High-risk outpatients	Family medicine clinic	327 patients at high risk for influenza	Prospective	Mailing	72% of respondents reported receiving an influenza vaccination that year. Of those who did, 72% received it from the family practice clinic; the mailing prompted 26% to get vaccinated.	Not reported
Ohmit et al., 1995 (46)	South-central and southwestern lower Michigan	Elderly	Community public health program	Medicare beneficiaries: 1,333 cases aged ≥65 years with a pneumonia/ influenza admission and 2,978 community controls	Case-control	Physician education, patient mailings, targeted advertising	Influenza vaccine coverage increased from approximately 40% to 56%. The intervention increased vaccination among community controls in years 1 and 2 and hospitalized cases in year 2.	Significant

Table continues

TABLE 1. Continued

Study, year (reference no.)	Location	Target group	Setting	Sample	Study type	Intervention	Findings	Result
Satterthwaite, 1997 (20)	Auckland, New Zealand	Elderly	15 general practitioners	2,791 patients aged ≥65 years	RCT	Mailing with or without offer of free vaccine	Vaccination coverage was 17% in the control group, 27% in the group that received an invitation without promise of a free vaccine, and 45% in the group that received an invitation with a promise of a free vaccine.	$p < 0.001$
Nichol, 1998 (14)	Minneapolis, Minnesota	Elderly and high-risk adults	Veterans' hospital	500 high-risk patients (including elderly) per year, except 1 year for which there were 400	Prospective	Mailings, walk-in clinics, standing orders, standardized forms	Vaccination coverage increased among outpatients from 58% in 1987–1988 to 84% in 1996–1997. The highest rates were observed among elderly in the general internal medicine clinic.	$p < 0.001$
Kerse et al., 1999 (47)	Melbourne, Australia	Elderly	Metropolitan general practices	42 general practitioners plus 267 of their patients aged ≥65 years	RCT	Physician education program	Vaccination coverage was 63% in the intervention group and 70% among the controls.	Not significant
Dalby et al., 2000 (41)	Stoney Creek, Ontario, Canada	Elderly	Primary-care practice	142 adults aged ≥70 years at risk for sudden deterioration in health	RCT	Visiting nurse	Influenza vaccine was administered to 90.1% of the visiting nurse group vs. 53.0% of the usual care group. Home visits did not improve death or hospital admission rates.	$p < 0.001$
Jans et al., 2000 (45)	The Netherlands	Patients with asthma or chronic obstructive pulmonary disease	General practices	607 patients aged 16–70 years with asthma or chronic obstructive pulmonary disease in 19 general medical practices	Pre/post	Quality system including barrier identification, documentation, education, feedback, and peer review	Vaccination coverage was higher in the intervention practices compared with the control practices (61% vs. 50%).	Not significant
Kellerman et al., 2000 (32)	Salina, Kansas	Elderly	Rural family practice center	475 patients aged ≥65 years	Pre/post	Mailing and telephone reminders	Overall, 28% of the population was vaccinated compared with 18% the previous year. 78% were vaccinated after receiving the initial postcard. Telephone reminders did not significantly improve coverage.	$p < 0.001$
Arthur, 2001 (40)	Leicestershire, England	Elderly	Rural practice	389 patients aged ≥75 years	Cross-sectional with controls	Health assessment and vaccine offer	Those who received the health assessment were more likely to be vaccinated during the study period compared with those who did not (63.7% vs. 34.9%).	$p = 0.001$

Gaglani et al., 2001 (26)	Temple, Texas	Children with asthma or reactive airway disease	Health-care delivery system with ~160,000 enrollees	925 asthma or reactive airway disease patients aged ≥6 months–<19 years	Pre/post	Computerized mailing and autodial telephone message	Overall, the vaccination rate went from 5.4% to 32.1%. Autodial resulted in vaccination of 15% of those contacted.	$p < 0.001$
Van Amburgh et al., 2001 (38)	Altamont, New York	Elderly and high-risk outpatients	Rural primary-care clinic	657 high-risk patients	Pre/post	Patient education packet and posters in waiting areas	Vaccination coverage increased from 28% to 54% for patients with indications for vaccination and 38% to 42% for patients aged ≥65 years.	$p < 0.05$
Arthur et al., 2002 (27)	Leicestershire, England	Elderly	Large, rural general practice	2,052 patients aged ≥75 years	RCT	Home-based health examination vs. mailing	74.3% of the health examination arm received influenza vaccine vs. 67.9% of those who received the personal letter.	$p < 0.001$
Birchmeier et al., 2002 (28)	Lausanne, Orbe, and Neuchâtel, Switzerland	Elderly	Medical outpatient clinic and family physician practices	401 outpatients, 195 regularly followed outpatients, and 598 family practice patients, all aged ≥65 years	Prospective	Physician education, mailing, medical student vaccine offering	Vaccine coverage was 83% in family practice patients and 85% in the outpatient clinic. Among outpatient clinic vaccinees, 52% were advised by a medical student, 26% went to the nurse, and 19% were advised by a physician. There was a 58% relative increase in vaccination coverage.	Not reported
Hull et al., 2002 (34)	East London and Essex, England	Elderly	Three general practices with an inner-city, mobile, multiethnic population	1,206 low-risk patients aged 65–74 years	RCT	Telephone appointments	50% of the intervention group received vaccination compared with 44% of controls. The effect was achieved during a national media campaign and mailed reminders for all eligible persons from the health authority.	$p = 0.026$
Humair et al., 2002 (44)	Geneva, Switzerland	Elderly	Primary-care clinic	520 clinic patients aged ≥65 years	Pre/post	Clinic advertisements, walk-in clinics, physician education and feedback, medical record reminders, standardized procedures	Vaccination coverage increased from 21.7% preintervention to 51.7% postintervention. Intervention had a strong impact on patients at higher risk because of chronic diseases.	Significant

Table continues

TABLE 1. Continued

Study, year (reference no.)	Location	Target group	Setting	Sample	Study type	Intervention	Findings	Result
Nuttall, 2003 (29)	Lancashire, England	Elderly	General practice	90 patients aged 65–90 years	RCT	Mailing and/or home visit	Vaccination coverage was 27% in the letter group, 23% in the leaflet group, and 40% in the home visit group.	Not significant
Weaver et al., 2003 (42)	United States	Veterans with spinal cord injury	Veterans Affairs spinal cord injury centers	2,284 veterans at 8 spinal cord injury centers	Quasi-experimental with controls	Patient and provider mailing, clinic advertising	Vaccination coverage was higher in the intervention group than in the controls (60.5% vs. 54.3%). Barriers included refusal and feeling that the vaccine was not worth the trouble or would not prevent influenza.	$p < 0.001$
Ahmed et al., 2004 (31)	Denver, Colorado	High-risk adults	Three managed-care organizations	505 employers, with 3,996 employees	RCT	Patient mailing and employer tool kit	The overall vaccination rate was 69%. A second postcard or tool kit did not increase vaccination coverage for those aged 18–49 years. Two postcards increased vaccination coverage 6% among adults aged 50–64 years.	$p < 0.05$
Daley et al., 2004 (21)	Denver, Colorado	Children with chronic medical conditions	Private pediatric practices	1,851 children aged 6–72 months with a high-risk condition	RCT	Mailing	Overall, 42% of the intervention group was vaccinated compared with 25% of the control group.	$p < 0.001$
Pappano et al., 2004 (39)	Rochester, New York	High-risk patients or their household members	Pediatric emergency department or fast-track area	337 families (625 subjects) that included a high-risk patient	RCT	Education and information and/or on-site vaccination	67% in the intervention arm were vaccinated compared with 35% in the education-only arm.	Significant
Patel et al., 2004 (43)	Chicago, Illinois	Adults and children with asthma	Large medical group practice	451 baseline and 427 follow-up visits; adults and children with asthma	Pre/post	Patient registry, asthma therapy assessment, case management, physician education	The study showed reductions in hospitalizations and emergency department visits (the primary goals), but vaccination coverage decreased from 24.2% at baseline to 15.0% at follow-up.	$p < 0.001$
Kempe et al., 2005 (35)	Denver, Colorado	Children aged <2 years	Five pediatric practices	5,193 children aged 6–21 months	RCT	Registry-based telephone call	62.4% in the intervention group were vaccinated compared with 58.0% of controls. Media coverage of the epidemic blunted the intervention effect but increased immunization rates early on.	$p = 0.001$

Crawford et al., 2005 (33)	Philadelphia, Pennsylvania	Elderly	Managed-care organization	22,984 persons aged ≥65 years who were managed-care organization members	Case-control, with those who did not receive the call acting as controls	Telephone-based interactive voice response reminder system	6.9% of those who received the reminder calls were vaccinated compared with 3.2% of those who did not.	$p = 0.0001$
Nowalk et al., 2005 (23)	Pittsburgh, Pennsylvania	Children aged <2 years	5 inner-city health centers	1,534 children aged 6–23 months	Pre/post with historical and concurrent controls	Varied by site; patient-, provider-, and system-oriented components	For all 5 sites combined, vaccination rates increased from a mean of 6.5% to 38.5% for the first dose and from 1.9% to 13.2% for the second dose.	$p < 0.01$
				Targeted				
Schluter et al., 1999 (48)	Colorado	Elderly	Long-term-care facilities	1,030 long-term-care-facility residents	Prospective	Patient and staff education and advertising, study information including baseline results	Influenza vaccination increased from 84% to 89%.	$p = 0.006$
Krieger et al., 2000 (30)	Seattle, Washington	Elderly	Senior center	1,246 persons aged ≥65 years residing in 5 contiguous zip codes served by the senior center	RCT	Mailings, telephone calls to unvaccinated persons by senior volunteers, computerized vaccination tracking	Among those who did not receive the influenza vaccine in the previous year, 50% in the intervention group were vaccinated vs. 23.0% in the control group. The overall influenza vaccination rate was 82%.	$p < 0.001$
Stancliff et al., 2000 (51)	New York, New York	Injection drug users	Syringe exchange program	199 injection drug users	Cross-sectional, no comparison group	Influenza vaccine made available at syringe exchange programs during a 1-month period	181 people were eligible for influenza vaccine; 86% accepted it. Of 48 people reporting a chronic medical condition, 87% accepted vaccination.	Not reported
Hutt et al., 2004 (50)	Denver, Colorado	Elderly	Nursing homes	78 health maintenance organization patients in 6 nursing homes with signs and symptoms of pneumonia	Pilot test	Organizational change (immunization and emergency antibiotic policies) and education	Significant improvement in vaccination coverage was observed within the intervention facility (14% to 52%).	$p = 0.01$
Bardenheier, et al., 2005 (49)	United States	Elderly	Long-term-care facilities in 14 states	20 long-term-care facilities	RCT	Promotion of standing orders by state quality improvement organization	20% of the facilities increased influenza vaccination by at least 10%.	Not significant
				Regional				
Black et al., 1993 (52)	Ontario, Canada	Elderly	Regional public health program	359 public health clients aged ≥65 years	RCT	Home visits	No significant differences in vaccine uptake among the intervention group vs. the control group (56.1% vs. 56.6%).	Not significant

Table continues

TABLE 1. Continued

Study, year (reference no.)	Location	Target group	Setting	Sample	Study type	Intervention	Findings	Result
Bennett et al., 1994 (56)	Monroe County, New York	Elderly	Public-private collaboration	88,811 Medicare enrollees aged ≥65 years	3-year evaluation, with 2 RCTs of a physician tracking poster and physician financial incentives	Expanded program to many settings, physician tracking poster, financial incentives	Influenza vaccination coverage increased from 40.5% in 1989 to 74.3% in 1991. Poster program physicians vaccinated 66% of patients compared with a rate of 50% among those not in the program. Physicians receiving financial incentives vaccinated 73.1% of their patients compared with 55.7% of those who did not.	$p < 0.001$
Centers for Disease Control and Prevention, 1995 (55)	Montana and Wyoming	Elderly	Regional Medicare program	190,000 Medicare beneficiaries	RCT	Mailing	Vaccination coverage was 6.1% higher in the intervention vs. the control group.	Not significant
Honkanen et al., 1997 (53)	Northern Finland	Elderly	Regional public health program	41,500 persons aged ≥65 years	Controlled trial	Free vaccine with and without mailing targeting by age or disease	The vaccination rate was highest for the age-based program with personal reminders (82.4%) compared with the age-based program without reminders (49.5–56.2%) and the disease-based program (19.0–21.8%).	Significant
Barker et al., 1999 (91)	Monroe and Onondaga counties, New York	Elderly	Community-wide intervention	85,000 Medicare enrollees in Monroe County and 58,000 in Onondaga County	Program evaluation	Multimedia public service announcements, targeting to minority communities, mailings, physician monitoring of vaccination coverage	Vaccination rates increased from 40.5% in year 1 to 60.2% in year 2 and 74.3% in year 3. A modest increase in vaccination rates was observed in Onondaga County (46% to 57%).	Not reported
Kumar et al., 1999 (57)	Louisiana	Elderly	Statewide program	1,917 physicians and their Medicare patients aged ≥65 years	RCT	Mailing	Between 1996 and 1997, vaccination coverage increased among both the intervention and control groups (48.5% to 53.3% and 48.5% to 52.6%, respectively).	$p = 0.03$
Smith et al., 1999 (58)	Indiana	Elderly	10 randomly selected counties	10,000 Medicare beneficiaries	RCT	Mailing	Vaccine coverage was estimated to be 69.0% among the intervention group and 64.2% among the control group.	Not significant
Christenson et al., 2001 (54)	Stockholm, Sweden	Elderly	Regional public health program	259,627 adults aged ≥65 years	Prospective	Mailing, media, physician office advertising	38% received influenza vaccine alone or with pneumococcal vaccine.	Not applicable

Grabenstein et al., 2001 (63)	Oregon and Washington	Elderly and high-risk adults	Urban chain pharmacies	1,261 adults aged ≥65 years	Pre/post with comparison group	Vaccination by a pharmacist	Vaccination coverage increased in Washington from 76.5% to 81.2% among those aged ≥65 years between 1997 and 1998; coverage remained at 83.8% during both years in Oregon. Vaccination coverage increased in Washington from 56.9% to 66.1% among those aged <65 years between 1997 and 1998; in Oregon, coverage was 59.3% in 1997 and 57.9% in 1998.	Not significant for elderly; significant. for high-risk adults
Chan et al., 2002 (59)	Washington	Elderly	Washington State physiatrists participating in Medicare	44 physicians and 13 practitioner groups with approximately 4,300 patients	Randomized crossover trial	Physician mailing	In year 1, the mailing was associated with an increased likelihood of having medical billing documentation for vaccination services for patients of both solo and group practitioners.	Not significant
Luthi et al., 2002 (64)	Vaud, Switzerland	Elderly	Regional public health program	2,933 persons aged ≥65 years	Pre/post	Informational meetings and media	Influenza coverage was 58.0% and 58.4% before and after the intervention, respectively. Among those aged 65–69 years, coverage increased significantly (40.5% to 47.0%).	Not significant
McCaul et al., 2002 (60)	North Dakota	Elderly	Statewide program	23,733 Medicare beneficiaries	RCT	Mailing	Type of reminder letter was not associated with changes in vaccination coverage; however, letters framed in terms of loss or gain resulted in higher vaccination coverage than no message (28.2% vs. 19.6%).	$p < 0.01$
Steyer et al., 2004 (62)	United States	Elderly	16 states	Adults aged ≥65 years participating in the Behavioral Risk Factor Surveillance Survey	Cross-sectional with comparison group	Vaccination by a pharmacist	Between 1995 and 1999, vaccine coverage increased from 57.7% to 68.4% in states where pharmacists could administer vaccine and from 61.2% to 64.7% in states where they could not. The difference between years and states in 1999 was significant.	$p < 0.01$

Table continues

TABLE 1. Continued

Study, year (reference no.)	Location	Target group	Setting	Sample	Study type	Intervention	Findings	Result
Hannah et al., 2005 (61)	West Virginia	Elderly	Statewide program	Hospitalized Medicare beneficiaries (sample size not reported)	Evaluation	Education, audit and feedback, tool kits and training meetings for hospitals and long-term-care facilities	During the first 3 years of the program, influenza vaccination at discharge went from near zero to 63%.	Not reported
				Community-based				
Hanna et al., 2001 (66)	Far North Queensland, Australia	At-risk indigenous adults	Regional program	17,345 indigenous adults aged ≥15 years who received their first dose of influenza vaccine	Retrospective	Indigenous public health officers recruited for program promotion and development of materials, key stakeholders involved in early planning and promotion	Greater uptake of pneumococcal vaccine during the first 2 years may reflect effectiveness of client pamphlet. When more balanced materials and emphasis was used, influenza uptake increased.	Not reported
Zimmerman et al., 2003 (69)	Pittsburgh, Pennsylvania	Elderly	Faith-based neighborhood health centers	Inner-city adults aged ≥50 years	Comparison of community-selected interventions	Both centers: free/low-cost vaccines for indigent, examination room posters, staff education, chart reminders, standing orders; center A: mailings; center B: off-site vaccination clinics and community advertisement	Vaccination rates were 59% for center A and 49% for center B; this difference was not significant. Vaccination coverage in center A increased from 24% to 30% among adults aged 50–64 years and 45–53% among adults aged ≥65 years.	$p < 0.001$
Weatheril et al., 2004 (67)	Vancouver, Canada	Community sites in a 10-square-block area	Community sites in a 10-square-block area	Estimated population of 16,000	Program evaluation	Vaccination offered in nontraditional settings (e.g., streets, alleys, single room occupancy hotels)	Influenza vaccines were distributed to 8,043 people in 1999, 3,718 in 2000, 5,175 in 2001, and 4,131 in 2002.	Not reported
Zimmerman et al., 2004 (68)	Pittsburgh, Pennsylvania	Children aged <2 years	Urban health centers	1,534 children aged 6–23 months	Pre/post	Site-selected interventions from strategies proven to increase vaccination rates	Vaccination coverage increased from 6.5% to 38.5% for the first dose and from 1.9% to 13.2% for the second dose compared with preintervention.	$p < 0.001$

* RCT, randomized controlled trial; pre/post, pre- and postintervention evaluation.

meet the Healthy People 2010 goals, with one exception (14). Second, and perhaps more importantly, these approaches were limited to people hospitalized during the influenza season. In 2003, 13.2 million people aged 65 years or older were discharged from short-stay hospitals (17), representing approximately 38 percent of the US population aged 65 years or older. These facilities have limited ability to reach high-risk individuals.

Primary-care settings

Primary care was the most common setting for studies of mostly multicomponent vaccination programs for high-risk populations, and interventions were directed at the patient, provider, and organization levels. Of 30 studies evaluating interventions in primary-care settings, patient-level components were included in more than 75 percent of interventions. Patient mailings were among the most frequent patient-level program components either alone (18–21) or in combination with other intervention components (14, 22–31). A variety of other patient-level interventions have been evaluated, including telephone reminders (23, 26, 32–35), patient education (36–39), home visits (27, 29, 40, 41), clinic-based advertising (23, 38, 42), vaccination offers during office visits (28), and case management (43). Twelve studies included components aimed at improving provider performance. Provider-level components included provider reminders (22–24, 44), feedback to physicians and staff (22, 44, 45), provider education (23, 28, 36, 37, 43–47), provider mailings (42), and provider e-mails (23). Nine studies used organizational components including nurse-administered vaccines with physicians' order (24), standing orders (14, 25, 37, 46), standardized documentation (14, 45), vaccination clinics (14, 36, 39), and patient registries (43).

Because most programs included multiple components, disentangling the independent effect of specific components is challenging. In studies with a comparison group (e.g., pre-post evaluation or controlled trial), interventions that included only patient mailings increased vaccination coverage by 10–17 percent (18, 20, 21). For example, one randomized controlled trial examined the impact of mailings to parents of children with high-risk conditions that strongly encouraged influenza vaccination for their child (21). For those children who were not vaccinated after the initial letter, a reminder letter was mailed 4 weeks later and a postcard 4 weeks after that. Overall, vaccine coverage was 42 percent among the intervention group and 25 percent among controls ($p < 0.001$). In studies with a comparison group, vaccination coverage improved by 10–18 percent with standing orders (25), by 7 percent with provider education (47), and by 38 percent with a visiting nurse (41). Three studies evaluated interventions with telephone reminders alone (33–35) or in combination with patient mailings (26, 32), which resulted in 4–6 percent and 10–27 percent increases in vaccination coverage over the comparison groups, respectively. One study examined the impact of home health assessments, where vaccination was offered, and found that those persons who accepted the home health assessment were significantly more likely to have been vaccinated than those who refused the home health assessment (63.7 percent vs. 34.9 percent, $p = 0.001$) (40).

Most studies contained two or more intervention components. For example, Ahmed et al. (31) used up to two mailed reminders to managed-care organization patients and provided an influenza tool kit to employers, which included educational messages to employers, advertising material targeted to staff (e.g., flyers, newsletter articles, payroll stuffers), and tips and a checklist for employer-sponsored vaccination clinics at work sites. The authors observed only a 4 percent increase in vaccination coverage for two postcards compared with one among adults aged 50–64 years.

Although significant improvements were observed in 24 studies, one exception is noteworthy. Patel et al. (43) evaluated a multidisciplinary asthma disease management program that included a patient registry, asthma therapy assessment, case management, and physician education. A written home treatment plan was provided, which included reminders for influenza vaccination. Although not a primary target of the intervention, influenza vaccination was recommended for individuals with chronic lung disease. The study demonstrated reductions in hospitalizations and emergency department visits (the primary goals); however, vaccination coverage significantly decreased from 24.2 percent at baseline to 15.0 percent at follow-up ($p < 0.001$). No explanation was provided for the decrease.

Venue-based targeted delivery

An efficient method for vaccinating individuals at high risk of influenza is to target venues frequented by high-risk groups. While there is some overlap with respect to nursing homes, we distinguish these venues from the previously discussed primary- or tertiary-care settings based on location. Primary- and tertiary-care settings were either hospital based or situated in clinics or physician practices. Venues frequented by high-risk groups included nursing homes, which are specialized tertiary-care facilities, as well as senior centers and community-based organizations such as syringe exchange programs. Five such studies were published (30, 48–51) between 1990 and 2006, four of which focused specifically on long-term-care facilities and senior centers (30, 48–50). In a study among the elderly, influenza vaccination was offered to all residents in a nursing home, resulting in an increase in vaccination coverage from 14 percent to 52 percent (50). Kreiger et al. (30) reported on an intervention that utilized a senior center in Seattle, Washington. When patient mailings, telephone calls to the unvaccinated by peers, and computerized vaccination tracking were used, 50 percent of the intervention group that had not been vaccinated the previous year was vaccinated compared with 23 percent of the control group. Patient advertising, including a videotape about the benefits of the influenza vaccination featuring a Colorado First Lady, and patient education increased vaccination coverage from 85 percent to 89 percent in long-term-care facilities (48).

Although not explicitly designated as a group at high risk for influenza complications according to the Advisory Committee on Immunization Practices recommendations, injection drugs users are generally at high risk for a variety of

chronic conditions. One study evaluated influenza vaccine distribution at a syringe exchange program in New York City (51). Among 181 people eligible for influenza vaccine, 86 percent accepted and received vaccination. Forty-eight people reported a chronic medical condition, and 87 percent of them were vaccinated.

Large-scale regional programs

Fourteen studies have evaluated large-scale regional vaccination interventions in different populations using a variety of approaches alone or in combination. Thirteen focused on the elderly, and one focused on the elderly and adults with high-risk conditions. Settings included regional public health programs (52–54), targeting of Medicare beneficiaries in a specific region (46, 55–61), and pharmacy-based vaccine distribution (62, 63). In terms of approaches, six studies have used mailings to the target population either alone (53, 57, 60, 64) or in combination with an educational insert or brochure (55, 58) or a media campaign (46, 54). Letters alone increased vaccination coverage 5–33 percent in those studies that had a comparison group (46, 53, 55, 57–60); however, mailed reminders were not always effective in improving coverage (58, 59).

Multicomponent programs were among the most successful at vaccinating high-risk individuals. One study reported on an effort to expand an existing influenza vaccination program by adding urban outreach clinics as well as open clinics at proprietary homes and senior nutrition centers and by enrolling area nursing homes, local hospitals, local home health agencies, and primary-care physicians (56). Special arrangements were made with the local health maintenance organization and individual practice association to enable participation. This demonstration project resulted in an immunization rate of 74.3 percent among 88,881 Medicare beneficiaries aged 65 years or older.

Two studies examined the effectiveness of pharmacy-based vaccination programs in the United States. Grabenstein et al. (63) compared urban chain pharmacies in Washington, where pharmacists could legally administer influenza vaccines, with similar pharmacies in Oregon, where pharmacists could not vaccinate. Although no significant differences were reported, vaccination coverage in Oregon remained stable and increased by 4.7 percent in Washington between 1997 and 1998. Steyer et al. (62) compared vaccination coverage in eight states where pharmacists could administer vaccine with eight states where they could not. Between 1995 and 1999, vaccine coverage increased by 10.7 percent in states where pharmacists could administer vaccine and 3.5 percent in states where they could not. The difference between years was significant, as was the difference between states in 1999.

One study evaluated the impact of home visits to the elderly by a public health nurse on vaccination coverage (52). There were no significant differences in vaccine uptake among the intervention group versus the control group (56.1 percent vs. 56.6 percent). However, significantly more people in the intervention group reported talking about immunization with the public health nurse (42.2 percent vs. 18.2 percent of controls).

Immunization distribution programs involving active community engagement

Program descriptions thus far have been medicine or public health directed. Another approach involves community–academic–local health department partnerships. Partnerships between researchers and community representatives that facilitate participation in defining the research problem, interpreting the data, and applying the findings can help address trust issues and translation of research into practice and policy (65). Four studies have used community engagement techniques to implement vaccination programs (66–69). In their program aimed at increasing influenza vaccination coverage among indigenous adults in Australia, Hanna et al. (66) involved key stakeholders in early planning and promotion and recruited indigenous public health workers to promote the program and develop materials.

Community-wide programs are less commonly reported. Weatherill et al. (67) evaluated a large-scale vaccination ''blitz'' in an inner-city neighborhood of 10 square blocks with 12,000 injection drug users who lived or spent time there. The researchers held an informational stakeholder meeting, which included local agencies, physicians, clinic representatives, and large businesses, to apprise the community of the program. Resident volunteers were recruited for distribution. Distribution sites included single room occupancy hotels, soup kitchens, food banks, community agencies, needle exchanges, drop-in centers, pubs, medical clinics, jails or pretrial centers, parks, streets, and alleys. Influenza vaccines were distributed to 8,043 people in 1999, 3,718 in 2000, 5,175 in 2001, and 4,131 in 2002. A decrease in emergency department visits for pneumonia was noted in 2000, although this reduction was confounded by differences in the timing and magnitude of the 1999 and 2000 influenza epidemics.

Two studies used a more community-directed approach. Working with faith-based neighborhood health centers, Zimmerman et al. (69) evaluated interventions aimed at vaccinating inner-city adults aged 50 years or older. The researchers offered a selection of intervention components derived from the US Task Force on Community Preventive Services (70) to two faith-based centers. Centers chose components that best suited their particular circumstances. Both centers selected examination room posters, free or low-cost vaccines for indigent adults, staff education, chart reminders, and standing orders. One center (center A) also chose to use mailings, while the other (center B) chose community advertisement and off-site vaccination clinics. There were no significant differences in vaccination rates before and after the intervention. Vaccination rates were 59 percent for center A and 49 percent for center B; this difference was not statistically significant. Adults aged 65 years or older were significantly more likely to be vaccinated compared with those aged 50–64 years (65 percent vs. 47 percent). In a similar study, Zimmerman et al. (68) worked with urban health centers to target children less than 2 years of age for the recommended initial two doses of influenza vaccine. The researchers again asked their community partners to choose intervention components that best suited their needs. Postintervention vaccination coverage increased from 6.5

percent to 38.5 percent for the first dose and from 1.9 percent to 13.2 percent for the second dose compared with preintervention. Including influenza vaccine did not delay receipt of other childhood vaccines.

LIMITATIONS OF THE CURRENT LITERATURE

In evaluating interventions to vaccination, several methodological issues, limitations, and gaps should be considered. Methodologically, we note that enumerating the target group and collecting data on vaccination rates is challenging. In epidemiologic studies, clear enumeration of the target group is necessary for estimating vaccination coverage. Studies conducted in health-care settings, or with the use of governmental lists (e.g., Medicare recipients and municipal records) are able to accurately determine vaccination coverage insofar as these lists are complete. However, a number of important subpopulations may not be reflected in these enumerations, including the homeless and undocumented immigrants. Studies that use community settings are often challenged by the need to precisely enumerate their target populations.

Another methodological challenge is accurate documentation of vaccination rates. For studies involving medical claims data, these data may be lagged and physicians may bill for vaccinations separately, as reported earlier (16). Other studies have relied on patient or parent self-report. Zimmerman et al. (71) demonstrated that these methods can be problematic: sensitivity was 98 percent and specificity was 38 percent for self-reported influenza vaccination among elderly outpatients and was 85.7 percent and 66 percent, respectively, among parents of children aged 6–23 months (72).

The current literature is limited with respect to comprehensive coverage of high-risk groups and key subpopulations. Of 56 studies examined, 40 (71.4 percent) targeted the elderly, 14 (25.0 percent) were directed at adults with high-risk conditions, and five (8.9 percent) targeted children. More than half of the studies ($n = 30$) occurred in primary-care settings, 14 (25.0 percent) were large-scale regional programs, four (7.1 percent) were in tertiary-care facilities or hospitals, four (7.1 percent) were targeted to nursing homes or long-term-care facilities, three (5.4 percent) included active community engagement, and two (3.6 percent) were targeted to specific communities. Thus, most studies examined vaccination within the context of primary-care settings or large-scale regional programs. An important limitation of these types of approaches is their inability to reach those people not engaged in the health-care system. Given the number of Americans without health insurance, the need for alternative methods for providing influenza vaccinations is clear. Beyond lack of health insurance, a variety of other personal and structural barriers may limit appropriate vaccination coverage, including mistrust of modern medicine or the government, availability, convenience, and concern about side effects (73–77).

Targeted efforts to deliver influenza vaccine to high-risk groups have resulted in higher influenza vaccination rates among persons who are most at risk of influenza compared with the general population; however, vaccination rates in these target groups are not optimal. There are substantial disparities between and within high-risk groups. For example, data from the 1999 National Health Interview Survey reveal that Black adults with high-risk conditions such as diabetes, chronic heart disease, and cancer, compared with White adults with the same conditions, had a significantly lower prevalence of influenza vaccination (78). Although increasing attention has been given to racial/ethnic and socioeconomic status disparities in health and health-care access, only seven of 54 studies reviewed considered race/ethnicity or socioeconomic status characteristics with respect to vaccination uptake. One study presented influenza immunization data for the United States and for Louisiana by race but did not examine it as a correlate of vaccine uptake in their intervention (57). Three studies reported no difference in vaccination status by race (62, 69, 79), and one study showed a decreased likelihood for vaccination among Blacks (62). Weaver et al. (42) found that vaccine recipients were significantly more likely to be White, but possible explanations for the differences were not reported. Zimmerman et al. (68) reported differences in vaccine uptake by race/ethnicity in their study of inner-city children, but they were cautious in drawing conclusions because race/ethnicity was not available for a substantial number of study participants.

Only one study examined socioeconomic status in terms of vaccination uptake. Spaulding and Kugler (18) found that enlisted military beneficiaries were less likely than officers to be vaccinated. Our review of the literature suggests that there is a substantial gap in the literature with respect to reporting vaccination rates for interventions by race/ethnicity and/or socioeconomic status. Given that disparities in vaccination continue to be documented, understanding how programs address, or do not address, the needs of these groups is essential.

Low vaccination coverage among minorities and persons living in and near poverty is a persistent problem. Although there is a paucity of empiric evidence in this regard, previous infectious disease epidemics have been accompanied by concerns about the possible spread of disease through populations with relatively low vaccination rates. In the last smallpox epidemic in the United States (1901–1903 in Boston, Massachusetts), there were 1,596 recorded cases of smallpox (with a case fatality rate of 17 percent). A concerted effort by public health officials to forcibly vaccinate all homeless persons in Boston, while controversial, preceded resolution of the smallpox epidemic at the time (80). Vaccination rates for most vaccine-preventable diseases are particularly low among marginalized, difficult-to-reach (or ''hidden'') populations (e.g., injection drug users, elderly shut-ins) within disadvantaged urban communities (81–83). Few studies have made concerted attempts to vaccinate difficult-to-reach populations for influenza, such as the homeless, substance users, elderly shut-ins, and undocumented immigrants. With few notable exceptions, the interventions we reviewed engaged people already formerly connected to health-care or social services. Two studies stand out: Stancliff et al. (51) offered vaccine at a syringe exchange program, and Weatherill et al. (67) offered vaccine in a variety of nontraditional settings.

Most interventions that we reviewed were not community based but relied on programs that were professionally directed and administered. However, community-based participatory research is emerging as one of the more effective methods for addressing health disparities (84). Recent reviews of intervention studies have overwhelmingly concluded that population-level intervention research should include an expanded appreciation of social, environmental, and health policy components of health promotion (85, 86). New directions that have been suggested for community intervention studies consist of involving a diverse team including community members in program planning and implementation (87). We reviewed five studies that involved the community, all of which occurred after 2000. Moving forward, we anticipate that more programs will begin to use community-based participatory research as a powerful tool to improve health.

SUMMARY AND FUTURE RESEARCH

Between 1990 and 2006, a number of studies examined interventions to increase influenza vaccination among high-risk populations. In the United States, a goal has been set to ensure 90 percent vaccination coverage for adults aged 65 years or older and 60 percent for high-risk adults aged 18–64 years (6). Only a handful of the studies we reviewed managed to meet that goal for their target populations. Interventions that increased vaccination rates to the goals outlined by Healthy People 2010 included advertising (42, 48), provider (42) and patient (14, 42) mailings, registry-based telephone calls (35), patient and staff education (48), standing orders coupled with standardized forms (14), targeting of syringe exchange customers (51), and visiting nurses (41).

During the 2004–2005 influenza season, coverage was estimated at 62.7 percent for people aged 65 years or older and 25.5 percent for people aged 18–64 years with a high-risk condition (8), which was lower than for the 2003 influenza season, where coverage was 69.9 percent among adults aged 65 years or older and, among adults aged 18–64 years, 34.0 percent for those with asthma and 49.0 percent for those with diabetes (7). Although there was a substantial influenza vaccine shortage in 2004–2005, those coverage rates highlight the effort still needed to meet national goals.

This review has focused on those at high risk of complications from influenza; however, those at high risk of transmitting influenza are also an important target group for vaccination programs. For example, epidemiologic models (88) and several Japanese studies have suggested that vaccinating schoolchildren for influenza can reduce morbidity and mortality among adults (89, 90). The Advisory Committee on Immunization Practices does not currently recommend influenza vaccination for healthy schoolchildren (5).

There are two primary areas in which future research can make a valuable contribution. First, there is a paucity of research that evaluates the impact of vaccination programs by race/ethnicity and socioeconomic status. Given the growing disparities in health and health-care access among racial/ethnic minorities and individuals with low socioeconomic status attainment, understanding the way in which interventions can remedy these differences is crucial. Second, few studies have targeted individuals outside of the health-care and social services sectors. To reach those who do not have health insurance and are not connected to social services, interventions that move away from these settings are needed.

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