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CDC Grand Rounds: Discovering New Diseases via Enhanced Partnership Between Public Health and Pathology Experts

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Despite advances in public health, medicine, and technology, infectious diseases remain a major source of illness and death worldwide. In the United States alone, unexplained deaths resulting from infectious disease agents have an estimated annual incidence of 0.5 per 100,000 persons aged 1–49 years (*1*). Emerging and newly recognized infections, such as hantavirus pulmonary syndrome and West Nile encephalitis, often are associated with life-threatening illnesses and death (Table 1). Other infectious diseases once thought to be on the decline, such as pertussis, again are becoming major public health threats. Animals increasingly are being recognized as potential vectors for infectious diseases affecting humans; approximately 75% of recently emerging human infectious diseases are of animal origin. Increasing global interconnectivity necessitates more rapid identification of infectious disease agents to prevent, treat, and control diseases.

Surveillance and rapid response for emerging infectious diseases remain cornerstones of CDC's public health mission. There is a need for a holistic "One Health*" approach with interdisciplinary engagement, given the vital interconnectedness among humans, animals, and the environment. Fortunately, many partnerships, systems, and tools are available to use in pursuit of this goal. The strong public health partnership between CDC's Infectious Diseases Pathology Branch and forensic pathologists and medical examiners, coupled with the use of state-of-the-art technologies, has facilitated explanation of many otherwise unexplained deaths, led to the discovery of new pathogens, and enabled the monitoring of unexplained deaths and critical illnesses at the state and local levels.

* Additional information available at http://www.onehealthinitiative.com.

This is another in a series of occasional MMWR *reports titled CDC Grand Rounds. These reports are based on grand rounds presentations at CDC on high-profile issues in public health science, practice, and policy. Information about CDC Grand Rounds is available at http://www.cdc.gov/about/grand-rounds.*

The Pathologist and Public Health Partnership

Pathologists are among the first to encounter infectious disease outbreaks through their collaborative work with diverse specialists including epidemiologists, clinicians, veterinarians, and microbiologists, and are thus in an excellent position to discover emerging infectious diseases (*2*). Pathology has played a critical role in advancing the knowledge of emerging infectious diseases (*3*).

Hantavirus at the Four Corners. For example, in 1993, an unexplained respiratory illness appeared in the Four Corners

INSIDE

Continuing Education examination available at http://www.cdc.gov/mmwr/cme/conted_info.html#weekly.

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area (a region of the United States where the boundaries of Colorado, New Mexico, Arizona, and Utah meet) with reports of a influenza-like illness with high mortality rates in previously healthy young adults. The diligence of forensic pathologists in New Mexico in pursuing and performing autopsies was invaluable to the investigation (*4*). These autopsies revealed pulmonary edema and large proteinaceous pleural effusions. At the first meeting of the three joint investigators (the New Mexico Department of Health, the Office of the Medical Investigator at the University of New Mexico School of Medicine, and CDC) a list was established of the most likely causes (i.e., influenza, plague, or a possible new agent) and intensive diagnostic efforts were mounted.

TABLE 1. Emerging or newly recognized infections — worldwide, 1993–2004

Year	Disease	Country
1993	Hantavirus pulmonary syndrome	United States
1994	Plague	India
1995	Ebola hemorrhagic fever Leptospirosis	Zaire Nicaragua
1996	New variant Creutzfeldt-Jakob disease	United Kingdom
1997	H5N1 influenza (avian) Vancomycin-intermediate *Staphylococcus aureus*	Hong Kong Japan, United States
1998	Nipah virus encephalitis	Malaysia, Singapore
1999	West Nile encephalitis	Russia, United States
2000	Rift Valley fever Ebola hemorrhagic fever	Kenya, Saudi Arabia, Yemen Uganda
2001	Foot and mouth disease Anthrax	United Kingdom United States
2002	Vancomycin-resistant *Staphylococcus aureus*	United States
2003	Severe acute respiratory syndrome Monkeypox	Approximately 25 countries Midwestern United States
2004	H5N1 influenza (avian)	Eight Asian countries

The first breakthrough came via serologic testing at CDC with the detection of hantaviral antibodies in serum of patients who had succumbed to the illness (*5*). This was an unexpected finding because, at that time, there was no known pathogenic hantavirus in the United States, and all characterized pathogenic hantaviruses in other parts of the world caused renal disease with hemorrhage, unlike the pulmonary nonhemorrhagic disease observed in the Four Corners patients. Proof that this illness was caused by a hantavirus arrived rapidly through two hantavirus-specific tests developed at CDC. One test was a hantavirus-specific polymerase chain reaction (PCR) that was used to amplify the hantaviral nucleic acid sequence directly from the patient's tissues and demonstrated that the infectious agent was a novel hantavirus (*6*). The other test was an immunohistochemical test using an antibody that reacted with all known hantaviruses. Using this antibody, microscopic examination of tissues from victims of this unexplained respiratory illness enabled localization of the viral proteins to the areas of disease in the lung, specifically the pulmonary endothelial cells (Figure 1A) (*7*). Immunohistochemistry (IHC) also provided a clue as to why patients developed "pulmonary leak":

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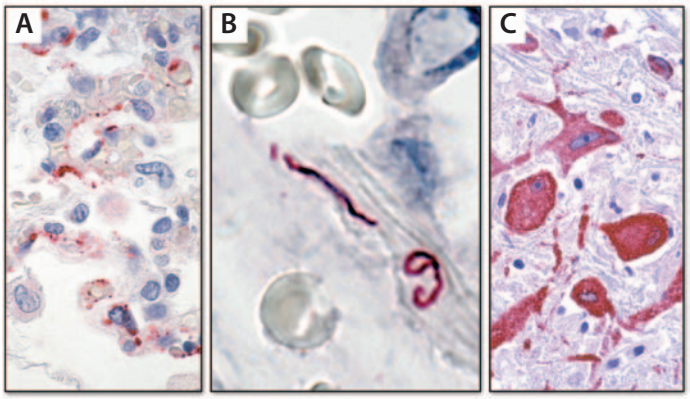
the virus damaged pulmonary vessels very much like poking holes in a pipe.

At the outset of this investigation in 1993, only one nonpathogenic hantavirus had been identified in the United States; today, 24 hantaviruses with differing levels of pathogenicity have been identified in the Americas. This recognition of New World hantaviruses, coupled with a better understanding of hantavirus pulmonary syndrome, has resulted in critical improvements in the rapid recognition and clinical management of the disease and better understanding of the natural reservoir (rodents) and mode of transmission, all of which have greatly improved the ability to implement control and prevention measures, with emphasis on the critical role of individual communities.

Leptospirosis in Nicaragua. In 1995, another pulmonary outbreak was reported, this time in Nicaragua, with several hundred cases and many deaths. An important difference with this outbreak was that instead of the clear fluid usually observed accumulating in the lungs, frank hemorrhage was detected (*8*). Initially, a viral hemorrhagic disease was suspected; however, within a few days pathologic evaluation helped solve the mystery. A novel IHC technique was used, employing several antibodies reactive against multiple strains of leptospirosis bacteria, and the etiology was confirmed (Figure 1B). The association of pulmonary hemorrhage with leptospirosis is now a well-recognized syndrome in addition to the classic hepatic and renal disease. This understanding, combined with awareness of increased transmission after intense rainfall and flooding and improved disease control and prevention efforts, resulted in better treatment, and ultimately saved lives.

West Nile virus via transplantation. Transmission of infections from a single donor to multiple recipients through organ transplantation has been detected increasingly in recent years. Some infections identified at CDC as novel associations with solid organ transplants include West Nile virus (WNV), lymphocytic choriomeningitis virus, rabies, *Balamuthia*, and microsporidiosis (*9–11*). A young female victim of an automobile crash, whose care necessitated multiple transfusions, was associated with the first of these events in 2002 (*12*). Following her death, several organs were donated, and all recipients developed a febrile illness. One of the recipients who succumbed was thought to have contracted WNV infection, but results of his serology testing were negative for WNV. However, examination of autopsy specimens at CDC showed encephalitis, with IHC clearly demonstrating WNV antigen in neurons (Figure 1C), and the negative serology was determined to be a result of the transplant immunosuppression regimen. Diagnosis of this infection led to a traceback investigation that identified the blood components the donor had received prior to her death as the source of the virus and profoundly influenced thinking about West Nile virus transmission via blood transfusion and transplants.

FIGURE 1. Immunohistochemistry for detecting pathogens in tissue*



* Red color indicates site of the pathogens: A) Hantavirus proteins can be seen in endothelial cells in the lung of a patient; B) *Leptospira* organisms are present in large blood vessels in the lung; C) West Nile virus antigens can be seen in neurons in a patient with encephalitis.

Autopsy-Based Surveillance Systems

Cause of death evaluation is an important component of the investigative process for emerging infectious diseases. When evaluating potentially infectious diseases as the causes of unexplained deaths, the use of autopsies has a number of advantages over death certificates: 1) availability of human tissues allows for enhanced diagnostic capacity and results in accurate determination of cause of death; 2) insights into pathogenesis and route of infection are gained; 3) rapid public health notification of findings is possible; and 4) recognition of additional infections not on death certificates is possible. The systematic collection and evaluation of this additional information affords an important opportunity for enhancing infectious disease surveillance. Monitoring of unexplained deaths and critical illnesses via autopsies at the state and local levels yields vital information about the actual numbers of cases of infectious diseases and provides insight into strategies for prevention.

Med-X. The New Mexico Office of the Medical Investigator created a Medical Examiner Syndromic Surveillance System (Med-X) for all fatal infectious diseases, which can be used in medical examiner jurisdictions (*13,14*). A basic principle of the Med-X system is to seek organism-specific diagnoses in all potential infectious disease deaths investigated as unexplained by medical examiners. Designed initially to provide the capacity to identify fatalities resulting from bioterrorism and infections of public health importance, the model is based on two types of information: symptoms (Box) and pathologic syndromes found at autopsy (Table 2). The lists of both symptoms and syndromes are derived from most known

BOX. Symptoms tracked — Medical Examiner Syndromic Surveillance System (Med-X), New Mexico

- Influenza-like symptoms
- Fever and respiratory symptoms
- Acute encephalopathy or new onset seizures
- Descending paralysis, polyneuropathy
- New fatal rash
- New jaundice
- Acute bloody diarrhea
- Unexpected death

bioterrorism-related illnesses. The symptom list (Box) serves to recognize and capture potential cases and drive decisions about autopsy performance; the syndrome list is used for early reporting of cases to the New Mexico Department of Health. For example, one of the 11 autopsy-based pathologic syndromes (community-acquired pneumonia and acute respiratory distress syndrome) might indicate the decedent had plague or tularemia; however, it is much more likely the decedent had influenza, pneumococcal disease, or various other more common conditions (Table 2). This information is valuable for public health officials in their decision-making regarding implementing prevention and control measures.

In New Mexico during 2000–2002, a total of 6,104 medical examiner cases were examined. Of these, 250 met entry criteria (medical examiner autopsy case with a defined symptom or syndrome), of which 141 (56%) decedents had a target pathologic syndrome and 127 (51%) were found to have an infectious disease. Three symptom sets were found to be highly predictive of infection in an otherwise unexplained death: 1) fever and respiratory symptoms (72%), 2) influenza-like symptoms (65%), and 3) encephalopathy or new-onset seizures (50%); sudden unexpected death (19%) was found to be less likely to represent an infection. Furthermore, in 81% of infectious disease cases, an organism-specific diagnosis was determined, with 58% representing notifiable conditions in New Mexico, including *Streptococcus pneumoniae* (37 cases), *Streptococcus pyogenes* (eight cases), and *Haemophilus influenzae* (five cases), as well as one case each of *Mycobacterium tuberculosis* and botulism and two cases of human immunodeficiency virus (HIV) infection. These findings indicate the value of pathologists conducting routine microbiologic testing in cases that come under their jurisdiction and have symptoms predictive of infection.

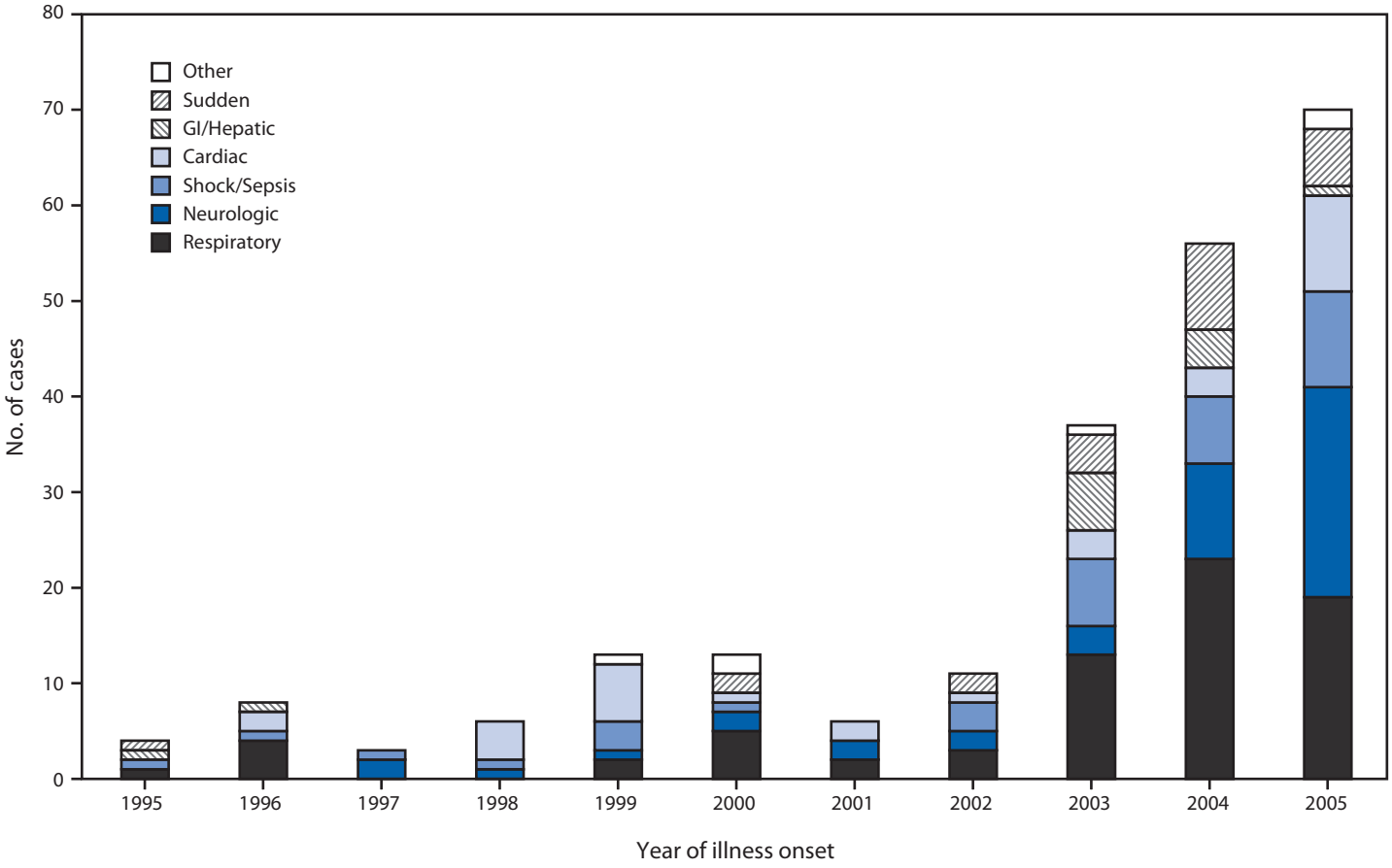
UNEX. Another surveillance system using cause of death as a tool, Surveillance of Probable Infectious Etiology for Unexplained Death (UNEX), was initiated in 1995 as part of the CDC Emerging Infections Program in California, Connecticut, Minnesota, and Oregon. The goals of UNEX are to identify novel or newly emerging pathogens; to identify sudden, unexplained deaths attributed to known pathogens; to monitor the epidemiologic features of fatal infections; and to improve diagnostic postmortem testing (*1*). In Minnesota, cases of unexplained critical illness also are included in the UNEX surveillance system. Therefore, the cases include deaths or critical illnesses unexplained by routine testing that have premortem or postmortem findings suggestive of infectious etiology such as fever, leukocytosis, cerebrospinal fluid pleocytosis, or histopathologic evidence of an infection. Although persons who were previously healthy and aged <50 years are the focus of UNEX in Minnesota, the system is not limited to this population. UNEX cases are reported by clinical partners, including infectious disease physicians, infection preventionists, and hospital pathologists, whereas the main reporters outside of acute care facilities are medical examiners (*1,15*). Sources of information include autopsy and pathology reports, medical records, scene investigation findings, and biologic specimens; results are correlated with pathologic and clinical findings to determine the cause of death. During 1995–2005, respiratory cases were the most common syndrome in most years, with the number of these cases increasing over time (Figure 2).

Med-X combined with UNEX. A Med-X surveillance system based on the New Mexico model also was initiated in Minnesota in 2006, enabling further description of infectious etiologies of death during 2006–2011. During this period, an average rate of 12 infectious deaths per 100,000 population was identified, encompassing 1,099 cases captured by UNEX and Med-X combined (723 UNEX cases, 908 Med-X cases,

TABLE 2. Example of a pathology-based syndrome with linkage to potential bioterror illnesses and to illnesses that are more likely — Medical Examiner Syndromic Surveillance System (Med-X), New Mexico

Autopsy syndrome	Potential bioterror illness	More likely illness
Community-acquired pneumonia and acute respiratory distress syndrome	Plague Tularemia Q fever Inhaled *Staphylococcus aureus* Enterotoxin B Ricin Phosgene Chlorine Other gases	Influenza Pneumococcal and other bacterial and viral pneumonias Hantavirus pulmonary syndrome

FIGURE 2. Unexplained deaths or critical Illnesses* — UNEX surveillance system, Minnesota, 1995–2005



Abbreviations: UNEX = Surveillance of Probable Infectious Etiology for Unexplained Death; GI = gastrointestinal.

* In Minnesota, in addition to deaths, cases of unexplained critical illness also are included in the UNEX surveillance system. Cases in Minnesota include deaths or critical illnesses unexplained by routine testing that have premortem or postmortem findings suggestive of infectious etiology such as fever, leukocytosis, cerebrospinal fluid pleocytosis, or histopathologic evidence of an infection.

and 532 that fit the criteria for both systems). In all three groups, males predominated, and UNEX identified 70 critical illnesses and 228 deaths in persons aged <50 years who were previously healthy and had specimens available for testing (i.e., the UNEX subgroup). Overall, during 2006–2011, the etiology for 29% of cases that had a specimen available for testing was determined. Cases with a respiratory syndrome were most commonly explained and sepsis/shock was the next most commonly explained syndrome. Examining the method of diagnosis in the explained UNEX subgroup cases revealed that, whereas most pathogens were detected by PCR (including both pathogen-specific PCR and 16S-PCR), other techniques such as culture and IHC also were very useful.

Correlating laboratory findings, clinical features, and pathologic evidence to establish a causal relationship allows for the detection of organisms that otherwise would likely be missed. However, death investigation as a surveillance tool is not without its challenges. One hurdle commonly encountered was the identification of potential pathogens that are not the primary cause of a syndrome or death. Another obstacle was the resource-intensive nature of the surveillance and additional testing and materials required of medical examiners, pathologists, and public health staffs and laboratories.

Conclusion

Effective use of basic and advanced diagnostic tools with ongoing development of new tools, a multidisciplinary approach, and vigilance by all critical partners are important in maintaining the partnership between pathology and public health. Tapping into the individual skills of clinicians, epidemiologists, microbiologists, veterinarians, pathologists, research scientists, and public health officials, especially in cases of unexplained deaths, contributes to the overarching goal of protecting the public from emerging infectious diseases and threats.

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Progress of Health Plans Toward Meeting the Million Hearts Clinical Target for High Blood Pressure Control — United States, 2010–2012

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High blood pressure is a major cardiovascular disease risk factor and contributed to >362,895 deaths in the United States during 2010 (*1*). Approximately 67 million persons in the United States have high blood pressure, and only half of those have their condition under control (*2*). An estimated 46,000 deaths could be avoided annually if 70% of patients with high blood pressure were treated according to published guidelines (*3,4*). To assess blood pressure control among persons with health insurance, CDC and the National Committee for Quality Assurance (NCQA) examined data in the 2010–2012 Healthcare Effectiveness Data and Information Set (HEDIS). In 2012, approximately 113 million adults aged 18–85 years were covered by health plans measured by HEDIS. The HEDIS controlling blood pressure (CBP) performance measure is the proportion of enrollees with a diagnosis of high blood pressure confirmed in their medical record whose blood pressure is controlled. Overall, only 64% of enrollees with diagnosed high blood pressure in HEDIS-reporting plans had documentation that their blood pressure was controlled. Although these findings signal that additional work is needed to meet the 70% target, modest improvements since 2010, coupled with focused efforts, might make it achievable.

NCQA developed HEDIS to measure the performance in care and service of health insurance plans. HEDIS measures are reported by two thirds of all U.S. health plans, representing approximately three fourths of the U.S. population receiving managed care. To account for differences in population demographics and coverage, NCQA usually collects and reports HEDIS results by Medicare, Medicaid, and commercial health plan categories. Because of differences in how health maintenance organizations (HMOs) and preferred provider organizations (PPOs) capture some data, NCQA further stratifies results by reporting plan type. This report provides aggregate national and adjusted regional estimates and rates reported by plan category and type.*

All plans that reported enrollment figures and valid CBP HEDIS measure rates† were included in the calculation of the percentage of patients seen with diagnosed hypertension.§ NCQA defines a patient with hypertension as a plan member, aged 18–85 years, who had one or more outpatient encounters in which a diagnosis of hypertension that was not pregnancy-related or complicated by end-stage renal disease was recorded¶ during the first 6 months of the measurement period. The CBP measure denominator is calculated by systematically drawing a sample of members who met the definition and had further confirmation of their hypertension diagnosis in the medical record.** The numerator is the population in the denominator who demonstrated blood pressure control (i.e., systolic pressure <140 mmHg and diastolic pressure <90 mmHg).†† Results are expressed in the context of CBP measure values for health plans 1) representing the 50th (i.e., median value) and 90th (i.e., top 10% of performing plans) percentiles for the measure, and 2) meeting the 70% control rate, with additional stratification by NCQA accreditation status.§§ Binary logistic regression was used to estimate region and accreditation status effects on the proportion of plans meeting the 70% control rate while adjusting for plan category/type and reporting year. The significance (-2 log likelihood statistic) and fit of the resulting logistic regression model (area under the curve and Hosmer-Lemeshow Goodness of Fit test) was evaluated.

In 2012, approximately 113.4 million members were covered under plans that reported valid CBP rates (Table 1). Nationally,

* Regional values are adjusted to account for differences in plan distribution across HHS regions. The reference population was the overall number of members, aged 18–85 years, in each reporting health plan category and type in 2010. Before 2010, fewer than five PPOs in each category reported valid CBP measures.

† Defined as having ≥30 patients in the target population sample (CBP measure denominator) and passing the NCQA audit review.

§ The percentage of patients seen with diagnosed hypertension is not a measure of hypertension prevalence, but describes the number of patients with diagnosed hypertension who were seen during the first 6 months of the calendar year divided by the total number of health plan members aged 18–85 years.

¶ *International Classification of Diseases, Ninth Revision, Clinical Modification* code of 401.

** To confirm the diagnosis of hypertension (HTN), the organization must find notation of one of the following in the medical record on or before June 30 of the measurement year: HTN, high blood pressure, elevated blood pressure, borderline HTN, intermittent HTN, history of HTN, hypertensive vascular disease, hyperpiesia, or hyperpiesis.

†† Based on their most recent blood pressure readings. If multiple blood pressure measurements occurred on the same date, or were noted in the medical record on the same date, the lowest systolic and lowest diastolic blood pressure readings were used.

§§ NCQA health plan accreditation includes two major components on which a plan's performance is scored: 1) standards—an evaluation of the plan's structure and processes to maintain and improve quality in five core areas, and 2) HEDIS—an evaluation of the plan's performance on process and outcomes in clinical care and member experience of care. A health plan is considered to be NCQA-accredited if it achieved "excellent," "commendable," or "accredited" status for the performance year. Additional information is available at http://www.ncqa.org/programs/accreditation.aspx.

nearly 11% of members (approximately 12.4 million) had confirmed hypertension and were eligible for the CBP measure; of those, 64% (7.9 million) had their high blood pressure under control. Adjusted control rates were ≥60% for all U.S. Department of Health and Human Services (HHS) regions,¶¶ with rates of 59.5%–68.2% across regions.

Modest improvements occurred in the 50th and 90th percentile plan-level rates from 2010 to 2012 (Table 2). In 2012, 50th percentile rates for all plan categories/types were below the clinical target of 70%, and 90th percentile rates were ≥70% for only commercial and Medicare HMOs and Medicare PPOs. Adjusted odds ratios for meeting the 70% target rate demonstrated that performance improved over time, with differences between regions and plan categories/types; NCQA-accredited plans had greater success than nonaccredited plans (Table 3).

¶¶ The HHS regions, listed with headquarters city for each, territories not included, are as follows: *Region 1* (Boston): Connecticut, Maine, Maryland, New Hampshire, Rhode Island, and Vermont; *Region 2* (New York): New Jersey and New York; *Region 3* (Philadelphia): Delaware, District of Columbia, Maryland, Pennsylvania, Virginia, and West Virginia; *Region 4* (Atlanta): Alabama, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, and Tennessee; *Region 5* (Chicago): Illinois, Indiana, Michigan, Minnesota, Ohio, and Wisconsin; *Region 6* (Dallas): Arkansas, Louisiana, New Mexico, Oklahoma, and Texas; *Region 7* (Kansas City): Iowa, Kansas, Missouri, and Nebraska; *Region 8* (Denver): Colorado, Montana, North Dakota, South Dakota, Utah, and Wyoming; *Region 9* (San Francisco): Arizona, California, Hawaii and Nevada; *Region 10* (Seattle): Alaska, Idaho, Oregon, and Washington.

Editorial Note

In 2012, HHS launched the Million Hearts initiative.*** For clinical settings, one of the Million Hearts goals is to achieve ≥70% control among U.S. adults with diagnosed hypertension by 2017. Overall, HEDIS-reporting plans were 72% more likely to have CBP measure rates meeting this target in 2012 than in 2010. However, despite these improvements, the median rates

*** HHS, in collaboration with nonprofit and private organizations, launched Million Hearts (http://www.millionhearts.hhs.gov), a combination of clinical and community evidence-based interventions and strategies aimed at preventing 1 million heart attacks and strokes during the 5-year period of 2012–2016.

TABLE 1. Blood pressure control among health plan members with diagnosed hypertension,* by plan category, type, and U.S. Department of Health and Human Services (HHS) region† — Healthcare Effectiveness Data and Information Set (HEDIS), 2012

	HEDIS reporting and membership		Patients with diagnosed hypertension			Hypertensive patients with controlled blood pressure		
				Members (%)			Controlled (%)	
Region§	Plans	Members (millions)	No. (millions)	Raw	Adjusted§	No. (millions)	Raw	Adjusted¶
National	**894**	**113.44**	**12.36**	**(10.9)**	—	**7.91**	**(64.0)**	—
Commercial HMO	193	34.54	2.94	(8.5)	—	2.03	(69.2)	—
Commercial PPO	140	53.70	4.36	(8.1)	—	2.57	(58.8)	—
Medicaid	119	13.82	0.45	(3.3)	—	0.26	(57.0)	—
Medicare HMO	310	8.16	3.30	(40.5)	—	2.25	(68.1)	—
Medicare PPO	132	3.22	1.30	(40.5)	—	0.80	(61.2)	—
HHS Region (Headquarters)								
1 (Boston)	82	7.52	0.76	(10.1)	(10.7)	0.51	(66.9)	(65.9)
2 (New York)	108	14.73	1.74	(11.8)	(11.4)	1.10	(63.2)	(62.7)
3 (Philadelphia)	123	13.10	1.72	(13.1)	(12.2)	1.09	(63.6)	(63.0)
4 (Atlanta)	164	21.05	2.86	(13.6)	(12.6)	1.69	(59.0)	(59.5)
5 (Chicago)	188	18.49	2.20	(11.9)	(10.9)	1.42	(64.5)	(65.0)
6 (Dallas)	99	9.74	1.31	(13.4)	(11.4)	0.78	(59.7)	(59.5)
7 (Kansas City)	77	4.83	0.75	(15.5)	(10.8)**	0.48	(63.6)	(64.8)
8 (Denver)	44	3.43	0.29	(8.4)	(7.3)	0.19	(67.5)	(67.6)
9 (San Francisco)	114	23.38	2.55	(10.9)	(10.0)	1.78	(69.8)	(68.2)
10 (Seattle)	66	5.15	0.49	(9.5)	(8.0)	0.30	(61.0)	(60.3)

Abbreviations: HMO = health maintenance organization; PPO = preferred provider organization.

* The percentage of patients seen with diagnosed hypertension is not a measure of hypertension prevalence, but describes the number of patients with disease meeting the hypertension case definition that were seen during the first 6 months of the calendar year divided by the total number of health plan beneficiaries aged 18–85 years.

† Listed with headquarters city for each region; territories not included. *Region 1* (Boston): Connecticut, Maine, Maryland, New Hampshire, Rhode Island, and Vermont; *Region 2* (New York): New Jersey and New York; *Region 3* (Philadelphia): Delaware, District of Columbia, Maryland, Pennsylvania, Virginia, and West Virginia; *Region 4* (Atlanta): Alabama, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, and Tennessee; *Region 5* (Chicago): Illinois, Indiana, Michigan, Minnesota, Ohio, and Wisconsin; *Region 6* (Dallas): Arkansas, Louisiana, New Mexico, Oklahoma, and Texas; *Region 7* (Kansas City): Iowa, Kansas, Missouri, and Nebraska; *Region 8* (Denver): Colorado, Montana, North Dakota, South Dakota, Utah, and Wyoming; *Region 9* (San Francisco): Arizona, California, Hawaii and Nevada; *Region 10* (Seattle): Alaska, Idaho, Oregon, and Washington.

§ Individual plans can be associated with multiple HHS regions. Within a given region, all plans associated with that region will contribute to the results for that region. Therefore, regional counts will not necessarily add up to the national counts.

¶ Regional values were adjusted to account for differences in plan distribution across HHS regions. The reference population was the overall number of members, aged 18–85 years, in each reporting health plan category and type.

** The proportion of members covered under Medicaid plans in HHS Region 7 was nearly double that of other regions, explaining why its adjusted rate is much lower than its unadjusted rate.

TABLE 2. Proportion of members with diagnosed hypertension with controlled blood pressure by health plan performance and percentage of health plans meeting the ≥70% blood pressure control target, by health plan category, type, and year—Healthcare Effectiveness Data and Information Set, 2010–2012

Plan category	Reporting plan type	Year	Plans	Hypertensive plan members with controlled blood pressure, by plan performance percentile (%)*		Plans that met the target of ≥70% blood pressure control among plan members with diagnosed hypertension (%)		
				50th	90th	Overall	Nonaccredited	Accredited
Commercial	HMO	2010	238	(65.0)	(73.0)	(23.1)	(14.9)	(25.1)
		2011	218	(65.2)	(74.1)	(21.6)	(9.6)	(25.3)
		2012	199	(66.3)	(76.2)	(28.6)	(14.0)	(32.7)
	PPO	2010	40	(49.9)	(64.8)	(5.0)	(0.0)	(16.7)
		2011	96	(56.3)	(67.6)	(5.2)	(5.6)	(5.0)
		2012	141	(59.9)	(68.2)	(7.1)	(5.0)	(7.4)
Medicaid	HMO	2010	128	(57.1)	(67.2)	(5.5)	(3.3)	(7.4)
		2011	137	(56.4)	(67.6)	(4.4)	(3.1)	(5.5)
		2012	148	(57.5)	(69.1)	(8.1)	(5.2)	(10.0)
Medicare Advantage	HMO	2010	289	(62.3)	(71.6)	(14.9)	(9.4)	(25.5)
		2011	309	(63.4)	(74.4)	(22.7)	(16.9)	(32.5)
		2012	310	(64.4)	(75.5)	(26.8)	(21.0)	(35.5)
	PPO	2010	87	(55.5)	(67.2)	(5.8)	(7.2)	(0.0)
		2011	123	(55.0)	(69.0)	(8.9)	(5.3)	(21.4)
		2012	132	(60.7)	(70.9)	(14.4)	(15.6)	(11.9)

Abbreviations: HMO = health maintenance organization; PPO = preferred provider organization.

* The controlling blood pressure (CBP) measure value of health plans at the 50th and 90th percentiles for the measure. Fifty percent of health plans had better (i.e., higher) CBP measure values than the health plan that represents the 50th percentile and 10% of plans had better values than the health plan that represents the 90th percentile.

for the measure among all plan categories/types in 2012 was below this target, and the top 10% of performing plans were barely achieving it. In particular, <15% of Medicare and commercial PPOs met the target. Commercial and Medicare HMOs were twice as likely to have met the target, but <30% were successful. NCQA-accredited plans were twice as likely to have met the 70% clinical target as nonaccredited programs, with the highest percentages occurring among accredited commercial and Medicare Advantage HMOs. The extra level of accountability taken on by accredited plans might better focus their efforts on improving blood pressure control for their members with hypertension.

The percent of patients seen with diagnosed hypertension was greatest in the southeastern states associated with the "stroke belt" (HHS regions 3, 4, and 6), a geographically identified region of high stroke morbidity and mortality (*5*). Blood pressure control was worst in the Northwest and South (HHS regions 4, 6, and 10). HHS region 10, in the Northwest, has low antihypertensive medication use among persons with self-reported hypertension (*6*). In the South, despite higher antihypertensive medication use (*6*), overall blood pressure

TABLE 3. Adjusted odds ratios for meeting the target for blood pressure control of ≥70% among health plan members with diagnosed hypertension — Healthcare Effectiveness Data and Information Set, 2010–2012

Characteristic	Comparison	Odds ratio	(95% CI)
Plan category	Medicaid versus commercial	0.21	(0.14–0.34)
	Medicare Advantage versus commercial	1.44	(1.11–1.86)
Reporting plan type	PPO versus HMO	0.30	(0.22–0.42)
Reporting year	2012 versus 2010	1.72	(1.30–2.27)
	2012 versus 2011	1.37	(1.05–1.79)
Accreditation status	"Yes" versus "no"	2.00	(1.55–2.58)
HHS Region (Headquarters)*	1 (Boston) versus others	1.76	(1.12–2.77)
	2 (New York) versus others	1.03†	(0.67–1.59)†
	3 (Philadelphia) versus others	1.26†	(0.83–1.91)†
	4 (Atlanta) versus others	0.24	(0.15–0.40)
	5 (Chicago) versus others	1.49	(1.02–2.18)
	6 (Dallas) versus others	0.12	(0.05–0.27)
	7 (Kansas City) versus others	0.63†	(0.38–1.03)†
	8 (Denver) versus others	1.32†	(0.76–2.31)†
	9 (San Francisco) versus others	1.04†	(0.66–1.63)†
	10 (Seattle) versus others	0.32	(0.16–0.63)

Abbreviations: CI = confidence interval; HHS = U.S. Department of Health and Human Services; HMO = health maintenance organization; PPO = preferred provider organization.

* Listed with headquarters city for each region; territories not included. *Region 1* (Boston): Connecticut, Maine, Maryland, New Hampshire, Rhode Island, and Vermont; *Region 2* (New York): New Jersey and New York; *Region 3* (Philadelphia): Delaware, District of Columbia, Maryland, Pennsylvania, Virginia, and West Virginia; *Region 4* (Atlanta): Alabama, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, and Tennessee; *Region 5* (Chicago): Illinois, Indiana, Michigan, Minnesota, Ohio, and Wisconsin; *Region 6* (Dallas): Arkansas, Louisiana, New Mexico, Oklahoma, and Texas; *Region 7* (Kansas City): Iowa, Kansas, Missouri, and Nebraska; *Region 8* (Denver): Colorado, Montana, North Dakota, South Dakota, Utah, and Wyoming; *Region 9* (San Francisco): Arizona, California, Hawaii and Nevada; *Region 10* (Seattle): Alaska, Idaho, Oregon, and Washington.

† Denotes no statistically significant association (p≥0.05).

What is already known on this topic?

Uncontrolled high blood pressure is a major public health problem. Focused efforts to improve blood pressure control can greatly improve health outcomes. Performance measures can be used to assess the effectiveness of health insurance plans in controlling high blood pressure among their members with hypertension.

What is added by this report?

In 2012, nearly 113.4 million members were covered under plans that reported valid Healthcare Effectiveness Data and Information Set (HEDIS) controlling high blood pressure (CBP) performance rates. Nationally, nearly 11% of plan members were eligible for the CBP measure, of whom 64% had their blood pressure under control. Adjusted control rates were ≥60% (range = 59.5%–68.2%) for all U.S. Health and Human Services regions, which was a modest improvement from 2010 rates.

What are the implications for public health practice?

Based on recent improvements measured through HEDIS, the Million Hearts clinical target of ≥70% blood pressure control among hypertensive patients by 2017 is achievable, but further work is needed to effectively identify, monitor, and treat patients with hypertension.

control is worse than in most other regions. Blacks represent a larger proportion of the population in this region compared with others (*7*), and despite being more aware of and likely to be treated for their hypertension than whites, blacks are less likely to have their high blood pressure controlled (*8*).

The findings in this report are subject to at least five limitations. First, HEDIS data are limited to those persons insured by reporting health plans. This excludes all fee-for-service Medicare members, a group with a considerable hypertension burden. Second, the CBP measure is based on a sample of plan members with diagnosed hypertension treated during the first 6 months of each reporting year; therefore, the reported percentage of patients seen with diagnosed hypertension should not be misconstrued as a prevalence estimate, because hypertension prevalence among all U.S. adults aged ≥18 years is approximately 30% (*2*). Third, the CBP measure does not capture persons who have hypertension, but have no recorded diagnosis in the medical record; therefore, it does not describe the effectiveness of plans in identifying hypertension among its members, but only the control of blood pressure among those with documented hypertension diagnoses. Control rates might be overestimated if the proportion of members with undiagnosed hypertension is high. Fourth, it was impossible to risk-adjust HEDIS results to account for population differences (e.g., chronic disease comorbidity prevalence) when comparing CBP values across category/plan types and regions (*9*). Finally, plans can be attributed to multiple HHS regions because of service area overlap; therefore, some larger plans might be overrepresented across multiple regions, potentially minimizing findings of differences by region.

Performance measures such as HEDIS are tools that can be used to promote health initiatives and assess their effectiveness. They can be used to recognize successful plans and identify areas for improvement (*10*). Additionally, public reporting on these measures and including the results in accreditation might spur providers and the plans they work with to follow evidence-based treatment guidelines and effectively track management of their hypertensive patients. Million Hearts encourages health plans to continue improvements in the identification, monitoring, and treatment of patients with hypertension. Strategies for improvement might include supporting the implementation of standardized hypertension treatment protocols and health information technology in clinical settings and modifications in health-care coverage/reimbursement (e.g., improved coverage of clinical preventive services and reduced medication copayments).

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Notes from the Field

Elemental Mercury Spill in School Bus and Residence — North Carolina, 2013

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On September 16, 2013, the North Carolina Division of Public Health was notified of an elemental (metallic and liquid) mercury spill on a school bus. An elementary student boarded the bus with approximately 1 pound (454 g) of elemental mercury contained in a film canister, which the student had taken from an adult relative who had found it in a neighbor's shed. The canister was handled by several students before the contents spilled on the bus floor. Ten passengers aboard the bus were exposed, including eight students and two staff members. Although elemental mercury is not readily absorbed from skin contact or ingestion, it does vaporize at room temperatures and inhalation of the vapor can be harmful. The bus driver promptly notified school officials. Firefighters and a local hazardous materials team directed decontamination procedures (i.e., changing clothes and washing hands and shoes) for the 10 exposed passengers. The bus was immediately taken out of service and sent for disposal because of its age and the cost of decontamination.

An Environmental Protection Agency (EPA) response team used a mercury vapor analyzer to determine mercury vapor levels at the residence from which the mercury was taken and at the three schools where the children were dropped off. The residence had mercury levels of 673 $\mu g/m^3$, which is higher than the Agency for Toxic Substances and Disease Registry's recommended levels for residential cleanup (1 $\mu g/m^3$) and evacuation (≥10 $\mu g/m^3$) (*1*). Over a 10-day period, the EPA response team remediated the contaminated residence through ventilation, removal of free mercury and mercury-contaminated items (e.g., furniture, carpet, bedding, and clothing), cleaning of surfaces with a mercury binding solution, and heating of the residence. EPA, Iredell County Emergency Management, Iredell County Health Department, American Red Cross-Greater Carolinas Chapter, and Iredell County Department of Social Services collaborated to assist the family with shelter, food, clothing, transportation, and medical needs during the response and recovery phases. Testing with a mercury vapor analyzer at the three schools potentially affected did not indicate contamination, with the exception of several pieces of carpet removed from one classroom.

To quantify human exposure and assess symptoms, the Iredell County Health Department administered a mercury exposure questionnaire to 23 persons, including the 10 exposed passengers aboard the school bus, seven family members who lived at the contaminated residence, two family members who had visited the residence 2 days before the exposure on the bus, and four firefighters. The North Carolina State Laboratory of Public Health performed blood mercury testing on 12 of the 23 persons.

Two students and three family members reported acute symptoms on the day of the exposure, including headache, cough, numbness or tingling in hands, and difficulty breathing. The student who brought the mercury aboard the bus and five family members, including two adults, had elevated blood mercury levels, ranging from 134 $\mu g/L$ to >200 $\mu g/L$. A blood mercury concentration of ≥50 $\mu g/L$ is considered the threshold for symptoms of toxicity after an acute high level exposure (*2*). Two children who had symptoms and blood mercury levels >200 $\mu g/L$ received a 19-day course of dimercaptosuccinic acid chelation therapy (*2*). Two other children with elevated blood mercury levels but no symptoms were followed every 2 weeks with urine testing until levels normalized. The two adults were referred to their physician for follow-up.

Through this investigation, six persons with blood mercury levels exceeding human health risk thresholds were identified. Two of these persons required chelation therapy. To prevent mercury spills in schools and residences, continued efforts should be made to educate school children, school employees, and the public about the dangers of possessing and handling mercury (*3*). Prompt actions by trained school personnel were critical in bringing this incident to the attention of authorities and avoiding further contamination.

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Notes from the Field

Shigella with Decreased Susceptibility to Azithromycin Among Men Who Have Sex with Men — United States, 2002–2013

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Bacteria of the genus *Shigella* cause approximately 500,000 illnesses each year in the United States. Diarrhea (sometimes bloody), fever, and stomach cramps typically start 1–2 days after exposure and usually resolve in 5–7 days.* For patients with severe disease, bloody diarrhea, or compromised immune systems, antibiotic treatment is recommended, but resistance to traditional first-line antibiotics (e.g., ampicillin and trimethoprim-sulfamethoxazole) is common. For multidrug-resistant cases, azithromycin, the most frequently prescribed antibiotic in the United States (*1*), is recommended for both children and adults (*2,3*). However, not all *Shigellae* are susceptible to azithromycin (*4–6*). Nonsusceptible isolates exist but are not usually identified because there are no clinical laboratory guidelines for azithromycin susceptibility testing. However, to monitor susceptibility of *Shigellae* in the United States, CDC's National Antimicrobial Resistance Monitoring System (NARMS) has, since 2011, routinely measured the azithromycin minimum inhibitory concentration (MIC) for every 20th *Shigella* isolate submitted from public health laboratories to CDC, as well as outbreak-associated isolates. All known U.S. *Shigella* isolates with decreased susceptibility to azithromycin (DSA-*Shigella*), and the illnesses caused by them, are described in this report.

DSA-*Shigella* is defined as a *Shigella* isolate with an azithromycin MIC >16 μg/mL (*4*). Twenty-nine DSA-*Shigella* isolates were identified through routine NARMS testing. Additional isolates from 2002–2013 were identified through a previous NARMS study (n = 3) (*4*), requests to public health officials (n = 2), and retrospective testing of available isolates with pulsed-field gel electrophoresis (PFGE) patterns indistinguishable from DSA-*Shigella* isolates (n = 21).

Among 55 patients from 17 states infected with DSA-*Shigella* (36 *S. flexneri*, 18 *S. sonnei*, one *S. boydii*), age ranged from 1 to 89 years (median: 42 years); 44 (80%) were men, and seven (13%) were children (aged <18 years). Of 35 patients for whom information was available, 23 (66%) were white, 11 (31%) were black, and one (3%) was Asian/Pacific Islander (two patients self-identified as white and Hispanic and one as Hispanic only). All but one patient resided in an urban area; one child and none of 29 adults for whom information was available reported international travel. Four patients were part of a recognized shigellosis outbreak (*5*). The median duration of illness was 11 days (n = 17). Of patients for whom information was available, 46% (12 of 26) had bloody diarrhea, 50% (16 of 32) had fever, and 45% (19 of 42) were hospitalized. Eighty-one percent (13 of 16) of men for whom information was available were human immunodeficiency virus (HIV)–positive, and 79% (11 of 14) identified as gay, bisexual, or other men who have sex with men (collectively referred to as MSM). Four men reported recent high-risk sexual practices, including anonymous sexual contact (n = 1), sexual contact without a barrier (n = 2 anal-genital; n = 1 oral-anal), and many sexual partners (n = 1); five had a history of syphilis.

All isolates harbored *mph*A or *erm*B macrolide resistance genes that are commonly plasmid-encoded. Fifty-three percent (29 of 55) were resistant to five or more classes of antibiotics, and 4% (2 of 55) were resistant to ciprofloxacin. NARMS data indicated that isolates were not susceptible to the drug used for treatment in seven of 19 patients, including three treated with azithromycin.

DSA-*Shigella* infections are occurring in the United States. Although some of the infections occurred among children, who are often treated with azithromycin for shigellosis, these data suggest that MSM, especially HIV-infected MSM, are currently at greater risk for infection with DSA-*Shigella*. Shigellosis is more common and can be more severe among HIV-infected persons with CD4 cell counts <200/mm^3 (*7*). Clinical failure of azithromycin was recently reported in a Dutch HIV-infected patient with shigellosis (*6*). Clinicians should be aware that MSM and HIV-positive persons with shigellosis might be infected with *Shigella* strains with reduced susceptibility to azithromycin. Clinicians should culture stool specimens of MSM and HIV-infected men experiencing diarrhea and determine antimicrobial susceptibility of *Shigella* to antibiotics other than azithromycin to help guide treatment, if needed. Meticulous handwashing and reducing fecal-oral exposures during sexual contact can reduce risk for infection (*7*).

The number of cases presented in this report is likely a substantial underestimate because NARMS routinely tests only 5% of *Shigella* isolates submitted to public health laboratories, and targeted testing using PFGE might miss cases because *Shigella* is highly mutable and plasmid-encoded macrolide

*Additional information available at http://www.cdc.gov/nczved/divisions/dfbmd/diseases/shigellosis.

resistance genes are mobile. Additionally, because NARMS began routinely measuring susceptibility to azithromycin in 2011, and recent isolates were more likely to be available for retrospective analysis, these data provide no information about trends. To better track illnesses and guide patient management, clinical laboratory guidelines for azithromycin susceptibility testing among *Enterobacteriaceae* are urgently needed.

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Announcement

American Heart Month — February 2014

February is American Heart Month. Cardiovascular disease (CVD), including heart disease, stroke, and high blood pressure, is the leading cause of death among women and men in the United States as well as a leading cause of disability (*1*). CVD costs the United States approximately $300 billion each year, including the cost of health-care services, medications, and lost productivity from premature death (*1*).

CVD does not affect all persons in the same way. Factors such as age, race, ethnicity, and sex can affect a person's risk for heart disease. Regardless, CVD and risk factors are largely preventable with changes in health habits, community changes to create healthier living spaces, and improvement of quality of care (*2*).

In observance of American Heart Month, CDC has published an online feature article focusing on CVD (available at http://www.cdc.gov/features/heartmonth), which includes information to help persons take control of their heart health using the "ABCS": A) take aspirin as directed by your health-care provider; B) control your blood pressure; C) manage your cholesterol; and S) don't smoke.

Additional information about CVD and heart health is available this month and throughout the year at http://millionhearts.hhs.gov/index.html.

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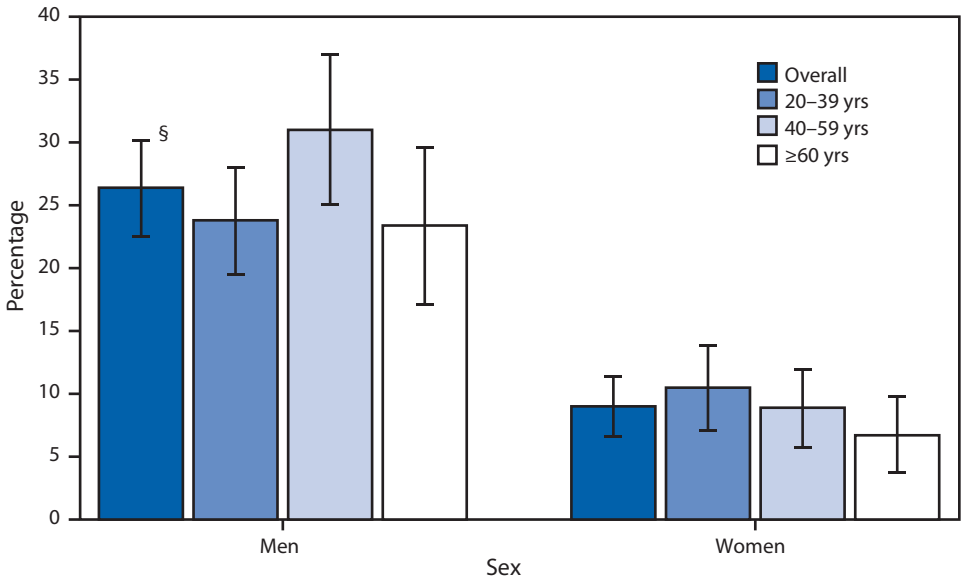
QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage of Adults Age ≥20 Years with Low Levels of High-Density Lipoprotein (HDL) Cholesterol,* by Age Group and Sex† — National Health and Nutrition Examination Survey, 2011–2012



* Low HDL cholesterol defined as serum HDL cholesterol <40 mg/dL.
† Overall estimates for men and women are age-adjusted by the direct method to the year 2000 Census population using the following age groups: 20–39, 40–59, and ≥60 years.
§ 95% confidence interval.

During 2011–2012, an estimated 26.4% of U.S. adult males and 9.0% of females aged ≥20 years had low levels of HDL cholesterol (also known as "good cholesterol"). In all age groups, a higher percentage of men had low levels of HDL cholesterol than women. A higher percentage of men aged 40–59 years had low levels of HDL cholesterol than men aged ≥60 years.

Source: Carroll MD, Kit BK, Lacher DA, Yoon SS. Total and high-density lipoprotein cholesterol in adults: National Health and Nutrition Examination Survey, 2011–2012. NCHS data brief no. 132. Hyattsville, MD: US Department of Health and Human Services, CDC; 2013. Available at http://www.cdc.gov/nchs/data/databriefs/db132.htm.

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