BIOTHERAPEUTICS QUARTERLY

Diagnostic and Pharmaceutical News for You and Your Medical Practice

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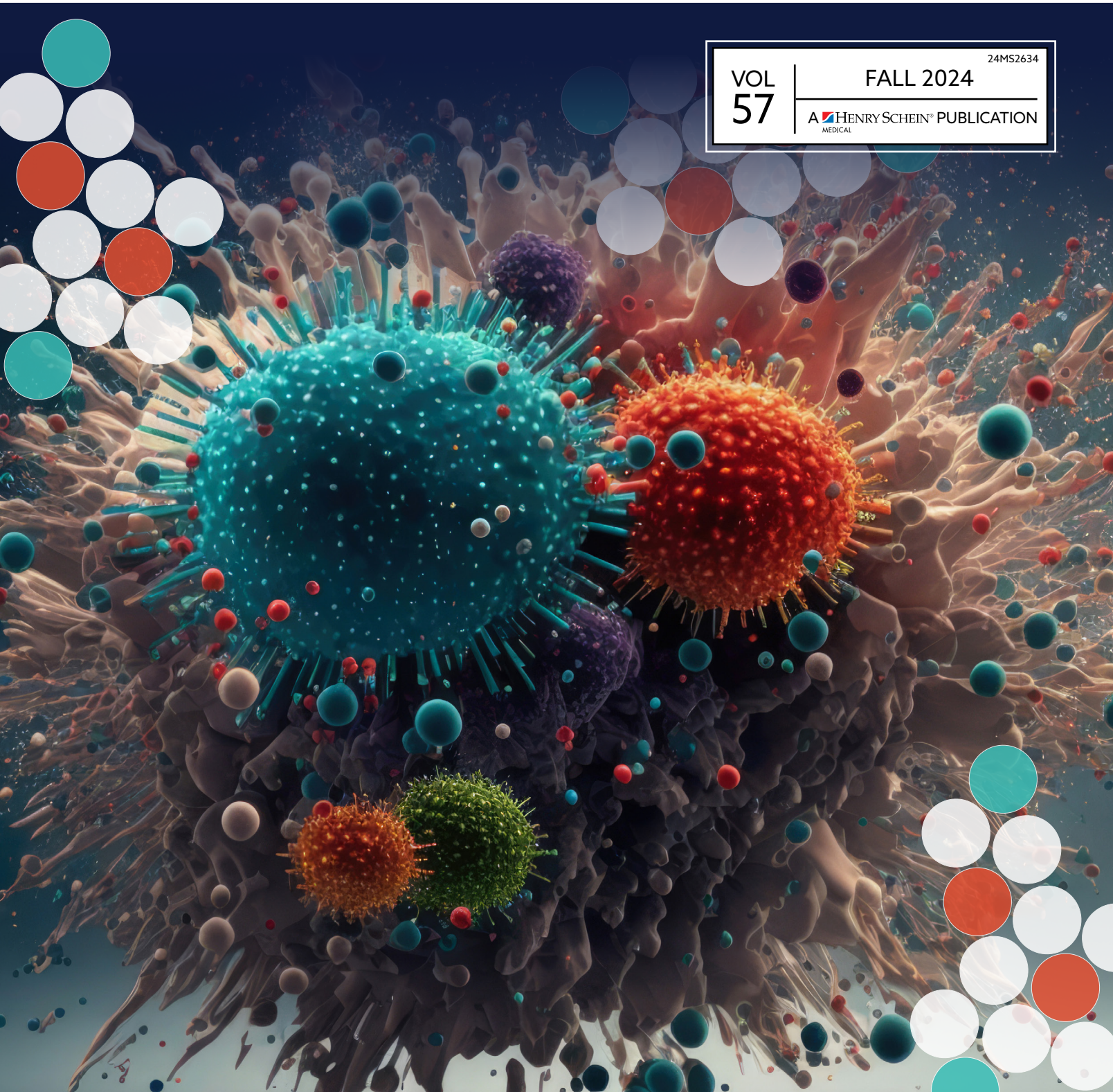

2023 **CARES** REPORT

SUSTAINABILITY AND CORPORATE CITIZENSHIP REPORT

Henry Schein's 2023 Sustainability & Corporate Social Citizenship Report **AVAILABLE NOW!** Titled "2023 CARES Report," this year's report shows how we envision a future where our innovation, leadership, and trusted partnerships inspire and generate positive impact across health care, ensuring a sustainable and healthier future for generations to come. This year's report reflects the many ways we advance health care access, accelerate environmental sustainability, advance policies and solutions for global health equity, and foster a culture of care and support to deepen relationships and cultivate trust with our five constituents especially **YOU** the customer. Simply put, Henry Schein Cares.

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BIOTHERAPEUTICS QUARTERLY

Diagnostic and Pharmaceutical News for You and Your Medical Practice

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New DRUG APPROVALS

CAPVAXIVE™ (pneumococcal 21-valent conjugate vaccine) Injection—formerly V116
Date of Approval: June 17, 2024
Company: Merck
Treatment for: Pneumococcal Disease Prophylaxis
Capvaxive (pneumococcal 21-valent conjugate vaccine) is a 21-valent pneumococcal conjugate vaccine indicated for active immunization for the prevention of invasive disease and pneumonia in adults 18 years of age and older.

OHTUVAYRE™ (ensifentrine) Inhalation Suspension
Date of Approval: June 26, 2024
Company: Verona Pharma plc
Treatment for: COPD, Maintenance
Ohtuvayre (ensifentrine) is a selective dual inhibitor of the enzymes phosphodiesterase 3 (PDE3) and phosphodiesterase 4 (PDE4) indicated for the maintenance treatment of chronic obstructive pulmonary disease (COPD) in adult patients.

KISUNLA™ (donanemab-azbt) Injection
Date of Approval: July 2, 2024
Company: Eli Lilly and Company
Treatment for: Alzheimer's Disease
Kisunla (donanemab-azbt) is an amyloid beta-directed antibody indicated for the treatment of early symptomatic Alzheimer's disease.

ZUNVEYL® (benzgalantamine) Delayed-Release Tablets - formerly ALPHA-1062
Date of Approval: July 26, 2024
Company: Alpha Cognition Inc.
Treatment for: Alzheimer's Disease
Zunveyl (benzgalantamine) is an acetylcholinesterase inhibitor indicated for the treatment of mild to moderate dementia of the Alzheimer's type in adults.

neffy® (epinephrine) Nasal Spray
Date of Approval: August 9, 2024
Company: ARS Pharmaceuticals, Inc.
Treatment for: Anaphylaxis
neffy® (epinephrine) is an intranasal epinephrine formulation for the emergency treatment of allergic reactions (Type 1), including anaphylaxis, for adults and children ≥30 kg.

Notes from the Field

Health Monitoring, Testing, and Case Identification Among Persons Exposed to Influenza A(H5N1) — Michigan, 2024

Joseph Coyle, MPH[1]; Natasha Bagdasarian, MD[1]; Seth Eckel, MPH[1]; Jeremy Kuo, MPH[1]; Mary Grace Stobierski, DVM[1]; James Barber, MPH[1]; Meghan Weinberg, PhD[1]; Fatema Mamou, MPH[1]; Sarah Lyon-Callo, PhD[1]; Michigan Local Health Departments; Bureau of Laboratories; Bureau of Infectious Disease Prevention Investigation Team

On March 25, 2024, a Texas dairy farm detected highly pathogenic avian influenza (HPAI) A(H5N1) virus in cows. The outbreak widely spread after interstate cow movement. During March 25–June 17, animals at a total of 102 dairy farms in 12 states, 24 commercial poultry flocks in five states, and multiple backyard flocks tested positive for HPAI A(H5N1) (*1*,*2*). This report describes response activities in Michigan, which led to detection of the second and third human cases related to the 2024 HPAI A(H5N1) outbreak. The activity was reviewed by the Michigan Department of Health and Human Services, deemed not research, and was conducted consistent with applicable federal law, state, and departmental policy.*

Investigation and Outcomes

Infected cows from Texas resulted in introduction of HPAI A(H5N1) virus in a Michigan dairy, detected on March 29. As of May 29, a total of 23 Michigan dairies in 10 counties are known to be affected (*1*). Michigan's first affected commercial poultry facility was confirmed on April 2; currently, seven affected poultry facilities in four counties have been identified (*2*). HPAI A(H5N1) virus has also been detected in a backyard flock, pigeons, foxes, cats, opossums, and a racoon in Michigan. Whole genome sequencing results suggest that, since March 2024, all sequenced isolates have ancestral Texas origins (*3*).

Monitoring of Dairy Workers

Among the 23 affected dairies, 306 persons exposed to affected cows were identified. Lists of exposed persons were obtained by public health officials from 20 (87%) affected dairies. Workers at 12 (60%) of those dairies were enrolled in text-based daily symptom monitoring,† and workers at eight (40%) farms were monitored through a farm point of contact. Because it could be unclear when workers' exposures to cows ended, some workers were monitored for >50 days.

Twenty (6.5%) exposed workers reported symptoms and were tested for influenza A(H5) virus infection. Among persons who received real-time reverse transcription–polymerase chain reaction testing,§ one received a positive test result from a conjunctival swab, similar to the case of HPAI A(H5N1) reported from a dairy worker in Texas (*4*). Before the onset of mild unilateral conjunctivitis, the patient reported direct ocular exposure to raw, unpasteurized milk from an affected cow. A second worker from a different dairy farm experienced respiratory symptoms after close contact with sick cows and received a positive A(H5) virus test result from a nasopharyngeal swab. In both instances, public health officials rapidly collected patient specimens, which tested positive for HPAI A(H5N1). Neither worker was severely ill, neither required hospitalization, and no household or work contacts reported being ill. Both workers wore some personal protective equipment (PPE), but neither wore a mask or respirator.

Monitoring of Poultry Workers

Among seven affected commercial poultry facilities, 857 persons exposed to affected birds were identified. Lists of exposed persons were obtained from all facilities. Workers from four facilities were directly enrolled in text-based daily symptom monitoring, and workers from three facilities were monitored through a farm point of contact who reported results to public health officials. Eighteen (2.1%) symptomatic persons were identified and tested; all test results were negative for influenza A(H5).

Monitoring of Other Exposed Persons

Federal and state employees who responded to affected farms were also observed for symptoms, as were persons with exposure to HPAI A(H5N1) virus–infected animals (domestic or wild) or humans. Overall, 125 such persons were monitored, and 15 (12%) reported symptoms, 14 of whom received negative influenza A(H5) test results.

Preliminary Conclusions and Actions

Among 1,288 Michigan residents who were monitored for signs and symptoms after potential HPAI A(H5N1) virus exposure, 53 (4.1%) reported signs and symptoms, 52 of whom received testing for influenza A(H5). Two dairy workers received positive test results (3.8% of all persons tested, <1% of all monitored dairy workers).

Although the risk for HPAI A(H5N1) virus to the public remains low, novel influenza A viruses such as A(H5N1) have pandemic potential. Therefore, it is critical to notify persons

* 45 CFR part. 46; 5 U.S.C. 301; 42 U.S.C. 289(a); 42 U.S.C. 300v-1(b).
† https://people.health/
§ https://www.cdc.gov/bird-flu/php/severe-potential/?CDC_AAref_Val=https://www.cdc.gov/flu/avianflu/severe-potential.htm

Summary

What is already known about this topic?

Highly pathogenic avian influenza (HPAI) A(H5N1) virus has been detected in wild birds and mammals, poultry, and commercial dairy facilities in the United States. A human case in a Texas dairy worker was reported in April 2024.

What is added by this report?

As of May 23, 2024, Michigan had the largest number of affected dairy and poultry facilities linked to the HPAI A(H5N1) outbreak. Active symptom monitoring and testing of exposed workers led to detection of the second and third known dairy-associated HPAI A(H5N1) cases in 2024.

What are the implications for public health practice?

The current risk to the public from HPAI A(H5N1) viruses is low; however, continued symptom monitoring and testing are critical to characterizing genetic or epidemiological changes that might alter the risk assessment.

with exposure to infected animals, provide education and access to PPE,¶ monitor signs and symptoms, test specimens collected from any exposed person with signs and symptoms, and make antivirals available to symptomatic persons as soon as possible.**

Although the percentage of workers who regularly used PPE is not known, the human cases associated with dairy farms in Texas and Michigan demonstrate the potential value of PPE, including eye and respiratory protection, especially on affected farms (*4*,*5*). The cases identified to date have resulted in mild illness, which might not have been detected without the collaboration of state officials and the engagement of farms and workers. Streamlined, nonintrusive approaches to monitoring, such as the text-message monitoring used in Michigan, might encourage participation and subsequent testing. A One Health†† approach including collaboration with agriculture departments, farms, and workers is crucial to successful public health response.

¶ https://www.cdc.gov/bird-flu/prevention/hpai-interim-recommendations.html

** Antiviral treatment is recommended with oseltamivir as soon as possible for outpatients and hospitalized patients who have suspected, probable, or confirmed cases of human infection with novel influenza A viruses associated with severe human disease. https://www.cdc.gov/bird-flu/hcp/novel-av-treatment-guidance/?CDC_AAref_Val=https://www.cdc.gov/flu/avianflu/novel-av-treatment-guidance.htm

†† One Health is an approach that recognizes the interconnectedness of human, animal, and environmental health. https://www.cdc.gov/one-health/about/index.html

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Michigan Local Health Departments

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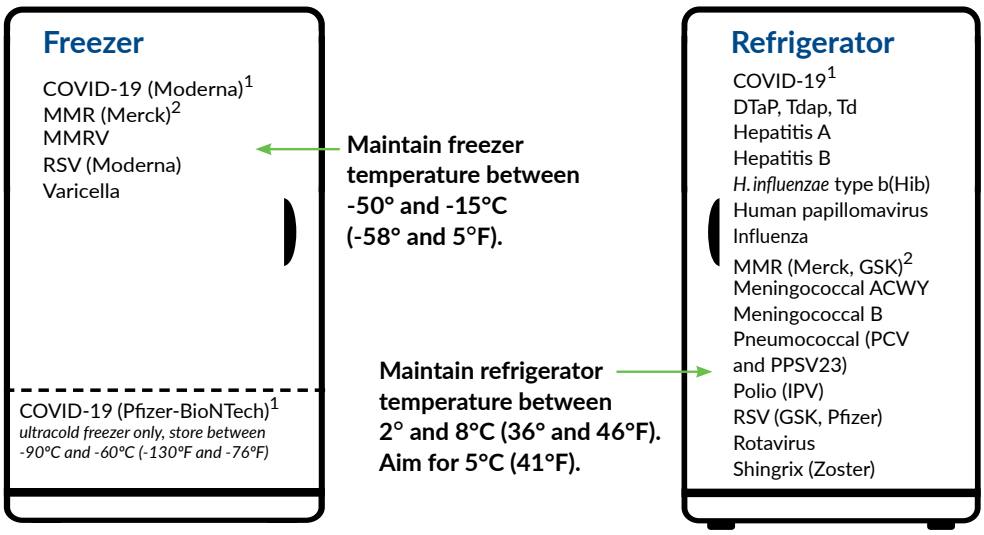
Vaccine Handling Tips

REMEMBER: Improperly stored or outdated vaccines won't protect your patients!



Manage vaccine inventories.

Inventory your vaccine supplies at least monthly and before placing an order. Expired vaccine must never be used, and it becomes "cash in the trash!"

Always use the vaccine with the soonest expiration date first.

Move vaccine with the soonest expiration date to the front of the storage unit and mark it to be used first. These actions help ensure it will be picked up first by someone selecting vaccine from the unit.

Store vaccine appropriately.[3]

Place vaccines in refrigerator or freezer immediately upon receiving shipment. Keep vaccine vials in their original packaging. Place vaccine in clearly labeled[4] baskets or other containers with a 2–3" separation between baskets and from the wall of unit. Separate or clearly mark vaccines to distinguish those that were supplied from your state's Vaccines for Children program (or other state-funded source) from those that were privately purchased. Do not store vaccines in the door or on the floor of the unit.

Stabilize temperatures.

Store ice packs in the freezer and large jugs of water in the refrigerator along with the vaccines. This will help maintain a stable, cold temperature in case of a power failure or if the refrigerator or freezer doors are opened frequently or are accidentally left open. Because frequent opening of either the refrigerator or freezer door can lead to temperature variations that could affect vaccine efficacy, you should not store food or beverages in the refrigerator or freezer.

Safeguard the electrical supply to the storage unit.

Make sure the refrigerator and freezer are plugged into outlets in a protected area where they cannot be disconnected accidentally. Label the refrigerator, freezer, electrical outlets, fuses, and circuit breakers on the power circuit with information that clearly identifies the perishable nature of vaccines and the immediate steps to be taken in case of interruption of power.[5] If your building has auxiliary power, use the outlet supplied by that system.

Notes

1. COVID-19 vaccines requiring storage in an ultracold (Pfizer-BioNTech) or regular freezer (Moderna) may be stored in a refrigerator with a shortened expiration date (see package inserts for details). For links to all current CDC COVID-19 resources, including beyond-use-date (BUD) tracking labels, see Immunize.org's "Checklist of Current Versions of U.S. COVID-19 Vaccination Guidance and Clinic Support Tools" (www.immunize.org/catg.d/p3130.pdf).
2. MMR II (Merck) may be stored in either the freezer or the refrigerator.
3. Refer to package insert for specific instructions on the storage of each vaccine. If you have questions about the condition of the vaccine upon arrival, immediately place the vaccine in recommended storage, mark it "do not use," and then call your state health department or the vaccine manufacturer(s) to determine whether the potency of the vaccine(s) has been affected. For other questions, call the immunization program at your state or local health department.
4. For help with organizing and labeling vaccines, consider using resources developed by and available from CDC at www.cdc.gov/vaccines/hcp/admin/storage/guide/vaccine-storage-labels.pdf and www.cdc.gov/vaccines/hcp/admin/storage/guide/vaccine-storage-labels-flu.pdf.
5. For easy help with labeling units and power supplies, see Immunize.org signs "Do Not Unplug Refrigerator or Freezer" (www.immunize.org/catg.d/p2090.pdf) and "Do Not Turn Off Circuit Breaker" (www.immunize.org/catg.d/p2091.pdf). For guidance on steps to take during a power interruption, see Immunize.org's "Vaccine Storage Emergency Response Worksheet" (www.immunize.org/catg.d/p3051.pdf)

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www.immunize.org/catg.d/p3048.pdf
Item #P3048 (7/31/2024)

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STANDING ORDERS FOR
Administering Pneumococcal Vaccines to Adults

Purpose

To reduce morbidity and mortality from pneumococcal disease by vaccinating all adults who meet the criteria established by the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices.

Policy

Where allowed by state law, standing orders enable eligible nurses, pharmacists, and other healthcare professionals to assess the need for vaccination and to vaccinate adults who meet any of the criteria below.

Procedure

1 **Assess Adults for Need of Vaccination** against *Streptococcus pneumoniae* (pneumococcus) infection according to the following criteria:

Routine Pneumococcal Vaccination

Age 65 years or older

Risk-Based Pneumococcal Vaccination

Age 19 through 64 years with any of the following conditions:

- **Non-immunocompromising chronic health conditions:** Alcoholism, chronic heart disease[1], chronic liver disease, chronic lung disease[2], cigarette smoking, diabetes mellitus, cochlear implant, cerebrospinal fluid (CSF) leak
- **Immunocompromising conditions:** Chronic renal failure, congenital or acquired asplenia, congenital or acquired immunodeficiencies[3], generalized malignancy, HIV infection, Hodgkin disease, iatrogenic immunosuppression[4], leukemia, lymphoma, multiple myeloma, nephrotic syndrome, sickle cell disease and other hemoglobinopathies, solid organ transplant

[1] Chronic heart disease includes congestive heart failure and cardiomyopathies

[2] Chronic lung disease includes chronic obstructive pulmonary disease, emphysema, and asthma

[3] Congenital or acquired immunodeficiency include B- (humoral) or T-lymphocyte deficiency, complement deficiencies (particularly C1, C2, C3, and C4 deficiencies), and phagocytic disorders (excluding chronic granulomatous disease)

[4] Iatrogenic immunosuppression includes diseases requiring treatment with immunosuppressive drugs, including long-term systemic corticosteroids, and radiation therapy

2 **Screen for Contraindications and Precautions**

Contraindications

Do not give pneumococcal conjugate vaccine (PCV15 [Vaxneuvance] or PCV21 [Capvaxive], Merck; PCV20, Prevnar20, Pfizer) or pneumococcal polysaccharide vaccine (PPSV23, Pneumovax 23, Merck) to a person who has experienced a serious systemic or anaphylactic reaction to a prior dose of the vaccine or to any of its components. For a list of vaccine components, refer to the manufacturer's package insert (www.immunize.org/fda) or go to www.fda.gov/vaccines-blood-biologics/vaccines/vaccines-licensed-use-united-states.

Precautions

Moderate or severe acute illness with or without fever

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3 Provide Vaccine Information Statements

Provide all patients with a copy of the most current federal Vaccine Information Statement (VIS). Provide non-English speaking patients with a copy of the VIS in their native language, if one is available and desired. The PCV VIS and its translations can be found at www.immunize.org/vaccines/vis/pcv/ and the PPSV VIS and its translations can be found at www.immunize.org/vaccines/vis/ppsv/. (For information about how to document that the VIS was given, see section 6 titled "Document Vaccination.")

4 Prepare to Administer Vaccine

All PCVs (PCV15, PCV20, PCV21) must be given IM. PPSV23 may be administered either intramuscularly (IM) or subcutaneously (Subcut). For vaccine that is to be administered IM, choose the needle gauge, needle length, and injection site according to the following chart:

BIOLOGICAL SEX AND WEIGHT OF PATIENT	NEEDLE GAUGE	NEEDLE LENGTH	INJECTION SITE
Female or male less than 130 lbs	22–25	⅝"*–1"	Deltoid muscle of arm
Female or male 130–152 lbs	22–25	1"	Deltoid muscle of arm
Female 153–200 lbs	22–25	1–1½"	Deltoid muscle of arm
Male 153–260 lbs	22–25	1–1½"	Deltoid muscle of arm
Female 200+ lbs	22–25	1½"	Deltoid muscle of arm
Male 260+ lbs	22–25	1½"	Deltoid muscle of arm
Female or male, any weight	22–25	1"*–1½"	Anterolateral thigh muscle

* Alternative needle lengths may be used for IM injections if the skin is stretched tightly, the subcutaneous tissues are not bunched, and the injection is made at a 90° angle to the skin as follows: a) a 5/8" needle for adults weighing less than 130 lbs (<60 kg) or b) a 1" needle for administration in the thigh muscle for adults of any weight.

If you prefer Subcut injection of PPSV23, choose a 23–25 gauge, ⅝" needle for injection into the fatty tissue over-lying the triceps muscle.

5 **Administer PCV15, PCV20, PCV21, or PPSV23,** 0.5 mL, by choosing between two options displayed on the following schedules based on the recipient's history of pneumococcal vaccination:

Table 1. Recommendations for adults age 65 years or older

PRIOR VACCINES	OPTION A	OPTION B
None, unknown, or PCV7 only	PCV20 or PCV21	PCV15 followed by PPSV23 in at least 1 year**
PPSV23 only (at any age)	PCV20 or PCV21 at least 1 year after PPSV23	PCV15 at least 1 year after PPSV23
PCV13 only (at any age)	PCV20 or PCV21 at least 1 year after PCV13	PPSV23 at least 1 year** after PCV13
PCV13 (at any age) & PPSV23 before age 65 years	PCV20 or PCV21 at least 5 years after last pneumococcal vaccine dose	PPSV23 #2 at least 5 years after previous PPSV23†
Complete series of PCV13 at any age & PPSV23 at age 65 years or older	May administer PCV20 or PCV21 at least 5 years after most recent pneumococcal vaccination	

**Consider minimum interval (8 weeks) for adults with an immunocompromising condition, cochlear implant, or cerebrospinal fluid leak (CSF).

† For adults with an immunocompromising condition, cochlear implant, or CSF leak, the minimum interval for PPSV23 is at least 8 weeks since last PCV13 dose and at least 5 years since last PPSV23 dose; for others, the minimum interval for PPSV23 is at least 1 year since last PCV13 dose and at least 5 years since last PPSV23 dose.

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Table 2. Recommendations for adults age 19 through 64 years with specified immunocompromising conditions‡

PRIOR VACCINES	OPTION A	OPTION B
None, unknown, or PCV7 only	PCV20 or PCV21	PCV15 followed by PPSV23 in at least 8 weeks
PPSV23 only	PCV20 or PCV21 at least 1 year after PPSV23	PCV15 at least 1 year after PPSV23
PCV13 only	PCV20 or PCV21 at least 1 year after PCV13	PPSV23 #1 at least 8 weeks after PCV13, followed by PPSV23 #2 in at least 5 years§
PCV13 & 1 dose PPSV23	PCV20 or PCV21 at least 5 years after last pneumococcal dose	PPSV23 #2 at least 5 years after PPSV23 #1 and at least 8 weeks after PCV13§
PCV13 & 2 doses PPSV23	May give PCV20 or PCV21 at least 5 years after last pneumococcal dose§	

‡See list of immunocompromising conditions on page 1.
§If PCV20 or PCV21 is not given, CDC recommends that you review pneumococcal vaccine recommendations again when your patient turns 65 years old (see www.cdc.gov/vaccines/vpd/pneumo/downloads/pneumo-vaccine-timing.pdf).

Table 3. Recommendations for adults age 19 through 64 years with a cochlear implant or cerebrospinal leak‖

PRIOR VACCINES	OPTION A	OPTION B
None, unknown, or PCV7 only	PCV20 or PCV21	PCV15 followed by PPSV23 in at least 8 weeks
PPSV23 only	PCV20 or PCV21 at least 1 year after PPSV23	PCV15 at least 1 year after PPSV23
PCV13 only	PCV20 or PCV21 at least 1 year after PCV13	PPSV23 at least 8 weeks after PCV13§
PCV13 & 1 dose PPSV23	May give PCV20 or PCV21 at least 5 years after last pneumococcal dose§	

‖Recommendations for vaccination in the presence of these conditions differ slightly from other non-immunocompromising chronic health conditions.
§If PCV20 or PCV21 is not given, CDC recommends that you review pneumococcal vaccine recommendations again when your patient turns 65 years old (see www.cdc.gov/vaccines/vpd/pneumo/downloads/pneumo-vaccine-timing.pdf).

Table 4. Recommendations for adults age 19 through 64 years with a non-immunocompromising chronic health condition¶

PRIOR VACCINES	OPTION A	OPTION B
None, unknown, or PCV7 only	PCV20 or PCV21	PCV15 followed by PPSV23 in at least 1 year
PPSV23 only	PCV20 or PCV21 at least 1 year after PPSV23	PCV15 at least 1 year after PPSV23
PCV13 only	PCV20 or PCV21 at least 1 year after PCV13	PPSV23 at least 8 weeks after PCV13§§
PCV13 & 1 dose PPSV23	No additional pneumococcal vaccines are recommended at this time.§§	

¶See list of non-immunocompromising chronic health conditions on page 1. Excluding cochlear implant and cerebrospinal fluid leak (see table 3).
§§CDC recommends that you review pneumococcal vaccine recommendations again when your patient turns 65 years old (see www.cdc.gov/vaccines/vpd/pneumo/downloads/pneumo-vaccine-timing.pdf).

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6 Document Vaccination

Document each patient's vaccine administration information and follow up in the following places:

Medical record: Document the date the vaccine was administered, the manufacturer and lot number, the vaccination site and route, and the name and title of the person administering the vaccine. You must also document, in the patient's medical record or office log, the publication date of the VIS and the date it was given to the patient. Note that medical records/charts should be documented and retained in accordance with applicable state laws and regulations. If vaccine was not administered, record the reason(s) for non-receipt of the vaccine (e.g., medical contraindication, patient refusal); discuss the need for vaccine with the patient at the next visit.

Personal immunization record card: Record the date of vaccination and the name/location of the administering clinic.

Immunization Information System (IIS) or "registry": Report the vaccination to the appropriate state/local IIS, if available.

7 Be Prepared to Manage Medical Emergencies

Be prepared for management of a medical emergency related to the administration of vaccine by having a written emergency medical protocol available, as well as equipment and medications. For Immunize.org's "Medical Management of Vaccine Reactions in Adults in a Community Setting," go to www.immunize.org/catg.d/p3082.pdf. To prevent syncope, vaccinate patients while they are seated or lying down and consider observing them for 15 minutes after receipt of the vaccine.

8 Report All Adverse Events to VAERS

Report all adverse events following the administration of pneumococcal vaccine to the federal Vaccine Adverse Event Reporting System (VAERS). To submit a VAERS report online (preferred) or to download a writable PDF form, go to https://vaers.hhs.gov/reportevent.html. Further assistance is available at (800) 822-7967.

Standing Orders Authorization

This policy and procedure shall remain in effect for all patients of the _____ (NAME OF PRACTICE OR CLINIC)

effective _____ (DATE) until rescinded or until _____ (DATE) .

Medical Director _____ (PRINT NAME) / _____ (SIGNATURE) _____ (DATE)

Outbreak of Highly Pathogenic Avian Influenza A(H5N1) Viruses in U.S. Dairy Cattle and Detection of Two Human Cases — United States, 2024

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Abstract

On April 1, 2024, the Texas Department of State Health Services reported that a dairy farm worker had tested positive for highly pathogenic avian influenza A(H5N1) virus after exposure to presumably infected dairy cattle; CDC confirmed these laboratory findings. A(H5N1) viruses were found in high concentrations in unpasteurized (raw) milk from infected cows. CDC is collaborating with the U.S. Department of Agriculture, the Food and Drug Administration, the Administration for Strategic Preparedness and Response, the Health Resources and Services Administration, the National Institute of Allergy and Infectious Diseases, and state and local public health and animal health officials using a coordinated One Health approach to identify and prepare for developments that could increase the risk to human health. Activities include monitoring of exposed persons, conducting syndromic and laboratory surveillance, planning epidemiologic investigations, and evaluating medical countermeasures. As of May 22, 2024, approximately 350 farm workers with exposure to dairy cattle or infected raw cow's milk had been monitored. These monitoring efforts identified a second human A(H5) case with conjunctivitis in Michigan, which was reported on May 22, 2024. CDC considers the current risk to the U.S. public from A(H5N1) viruses to be low; however, persons with exposure to infected animals or contaminated materials, including raw cow's milk, are at higher risk for A(H5N1) virus infection and should take recommended precautions, including using recommended personal protective equipment, self-monitoring for illness symptoms, and, if they are symptomatic, seeking prompt medical evaluation for influenza testing and antiviral treatment if indicated. Pasteurization inactivates A(H5N1) viruses, and the commercial milk supply is safe for consumption; however, all persons should avoid consuming raw milk or products produced from raw milk. Importantly, the risk to the public might change based on whether A(H5N1) viruses acquire genetic changes that increase their transmissibility to and among humans, which could increase the risk of an influenza pandemic.

Investigation and Findings

Identification of Two Human Cases of Influenza A(H5) Virus Infection

On April 1, 2024, the Texas Department of State Health Services reported, after confirmation by CDC, that a commercial dairy farm worker tested positive by real-time reverse transcription–polymerase chain reaction (RT-PCR) for highly pathogenic avian influenza (HPAI) A(H5N1) virus infection after exposure to dairy cattle presumed to be infected with A(H5N1) viruses*,†; CDC confirmed laboratory findings through RT-PCR and sequencing (*1*). The patient only experienced conjunctivitis without other signs or symptoms, was instructed to isolate, was treated with oseltamivir, and recovered. No illness was identified among the patient's household members, all of whom received oseltamivir postexposure prophylaxis. One week earlier, the U.S. Department of Agriculture had reported a multistate outbreak of A(H5N1) viruses in dairy cows.§ A(H5N1) viruses were also detected in barn cats, birds, and other animals (e.g., one raccoon and two opossums) that lived in and around human habitations and that died on affected farms.¶ Genetic sequencing of the A(H5N1) virus from infected cattle and the farm worker** identified clade 2.3.4.4b; this clade has been detected in U.S. wild birds, commercial poultry, backyard flocks, and other animals since January 2022 (*2*). On May 22, 2024, the Michigan Department of Health and Human Services reported an A(H5) case in a dairy farm worker on a farm confirmed to have A(H5N1) virus in cattle; this person was enrolled in an active text-based monitoring program and reported only eye symptoms.†† The investigation into this second case is ongoing. These two cases are the first known instances of presumed cow-to-human spread of an avian influenza A virus.

* https://www.dshs.texas.gov/news-alerts/health-alert-first-case-novel-influenza-h5n1-texas-march-2024#:~:text=Summary,patient%27s%20primary%20symptom%20was%20conjunctivitis
† https://emergency.cdc.gov/han/2024/han00506.asp
§ https://www.aphis.usda.gov/news/agency-announcements/federal-state-veterinary-public-health-agencies-share-update-hpai
¶ https://wahis.woah.org/#/in-review/4451?fromPage=event-dashboard-url
** https://www.cdc.gov/flu/avianflu/spotlights/2023-2024/h5n1-analysis-texas.htm
†† https://www.michigan.gov/mdhhs/inside-mdhhs/newsroom/2024/05/22/influenza-a-detection

Influenza A(H5N1) Viruses in U.S. Dairy Cattle

Although first reported in March 2024, A(H5N1) virus infection of U.S. dairy cows might have been occurring since December 2023, according to preliminary data (*3*). As of May 22, 2024, infected dairy cows had been identified in 52 dairy cattle herds in nine states[§§] (Colorado, Idaho, Kansas, Michigan, New Mexico, North Carolina, Ohio, South Dakota, and Texas). Signs in cattle were nonspecific and included decreased milk production, reduced rumination, and thickened (colostrum-like) milk consistency; some cows also had clear nasal discharge. High A(H5N1) virus levels have also been found in unpasteurized (raw) milk from infected cows(*4*).

Human Cases of Influenza A(H5N1) Worldwide

From 1997 through late April 2024, a total of 909 sporadic human A(H5N1) cases were reported worldwide from 23 countries; 52% of human cases have been fatal (*2*); of the 909 cases, 26 human A(H5N1) cases have been reported from eight countries, including seven deaths, since 2022. Since these numbers were last updated, two additional human A(H5) cases have been detected including the case from Michigan and one case in Australia. Nearly all reported human A(H5N1) cases had reported recent exposure to poultry. In the United States, three human A(H5) cases have been identified to date; all patients had mild illness, were not hospitalized, and fully recovered. The first occurred in April 2022 in a person from Colorado with direct exposure to infected poultry, who only reported fatigue,[¶¶] and the second and third occurred in dairy farm workers with conjunctivitis referenced in this report.

U.S. Outbreak Response Activities

Activities implemented using a One Health[***] approach to respond to this outbreak[†††] include monitoring for infections in exposed persons, conducting syndromic and laboratory surveillance, planning for epidemiologic investigations, and assessing performance of existing medical countermeasures including diagnostic tests, vaccines, and therapeutics. To assess A(H5N1) virus pathogenesis, severity, and transmissibility in an animal model of infection, CDC is also conducting laboratory experiments in ferrets.

This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.[§§§] Ferret studies were approved by the CDC Institutional Animal Care and Use Committee.

[§§] https://www.aphis.usda.gov/livestock-poultry-disease/avian/avian-influenza/hpai-detections/livestock
[¶¶] https://www.cdc.gov/media/releases/2022/s0428-avian-flu.html
[***] https://www.cdc.gov/one-health/about/index.html
[†††] https://www.cdc.gov/flu/avianflu/what-cdc-doing-h5n1.htm
[§§§] 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

Monitoring of Persons Exposed to Influenza A(H5) Viruses

In 2014, CDC began monitoring persons exposed to infected poultry when HPAI A(H5) viruses were first detected in poultry and wild birds in North America (*5*). Recommendations are to monitor persons exposed to infected birds, poultry, or other animals for 10 days after their last exposure and to test symptomatic persons for influenza A viruses by RT-PCR assay using H5-specific primers and probes, in coordination with state or local health departments (*6*).

During February 2022–May 2024, approximately 9,400 persons in 52 jurisdictions have been monitored. As of May 22, 2024, approximately 350 farm workers had been or were currently being monitored for illness after exposure to infected cows or infected raw cow's milk; the number of persons monitored continues to increase; data are updated weekly.[¶¶¶] Monitoring is performed either through direct daily contact by state or local health departments or by providing persons with information on how to self-monitor and where to seek testing and possible treatment should they experience symptoms. The most recent human A(H5) case was identified through active, daily monitoring of exposed farm workers using a text-based illness monitoring program in Michigan (*7*).

National Surveillance Activities

CDC's influenza surveillance systems[****] collect information to track trends in influenza activity and detect changes in circulating influenza viruses, including detection of novel influenza A viruses year-round. Human cases of novel influenza A virus infection have been nationally notifiable since 2007; every identified case is investigated and reported to CDC.

Through approximately 300 clinical laboratories, CDC monitors changes in the percentage of influenza tests with positive results in clinical settings. The National Syndromic Surveillance Program collects data from emergency departments and other health care settings, facilitating the detection of unusual trends in influenza diagnoses, including in jurisdictions where A(H5N1) viruses have been identified in animals.

CDC's National Wastewater Surveillance System[††††] complements other existing human influenza surveillance systems in monitoring influenza trends. These monitoring methods detect influenza A viruses but do not distinguish subtypes of influenza A, meaning that current wastewater testing can detect A(H5N1) viruses but cannot distinguish them from other influenza A viruses or determine the source of the influenza A viruses (e.g., humans versus animals or animal products). Together, these systems provide visibility into U.S. influenza

[¶¶¶] https://www.cdc.gov/flu/avianflu/h5-monitoring.html
[****] https://www.cdc.gov/flu/weekly/index.htm
[††††] https://www.cdc.gov/nwss/wastewater-surveillance/Flu-A-data.html

activity. As of May 18, 2024, no indicators of unusual human influenza activity, including A(H5N1 virus), had been detected in humans through these systems.

CDC's molecular diagnostic assays are used at more than 100 public health laboratories in all 50 states and other U.S. jurisdictions to detect seasonal and novel influenza A viruses; nine centers also perform genetic sequencing for virus characterization. Statistical methods are used to determine the number of specimens needed to have 95% confidence that at least one novel influenza A virus among all influenza positive specimens per week would be detected given varying influenza prevalence; the number varies by timing during the season. Each state's contribution is proportional to its population and has been set as a national weekly goal for public health laboratory testing.[§§§§]

Spring and Summer Activities

Multiple efforts are underway to enhance influenza surveillance activities through the spring and summer as part of this response. CDC is working with commercial laboratories to increase submission of influenza-positive test specimens to public health laboratories to increase the number of specimens available for virus subtyping. Approximately 140,000 of these H5-specific tests are already prepositioned at the state and local level, and another 750,000 tests are available for distribution if needed. CDC also continues to collaborate with manufacturers of commercial diagnostic tests with the goal of having an A(H5N1) test that is widely available if needed. Surveillance for laboratory-confirmed, influenza-associated hospitalizations will also continue during the spring and summer through the Influenza Hospitalization Surveillance Network (FluSurv-NET), which typically conducts surveillance during October 1–April 30 of each influenza season. As well, CDC is working with state and local public health partners, with outreach to providers and clinics, to increase awareness about A(H5N1) so that influenza is considered in patients with conjunctivitis or respiratory illness after exposures, including agricultural fair attendance, that might increase the risk of novel influenza A virus infection.

Medical Countermeasures

As a World Health Organization Collaborating Center, and in partnership with the Administration for Strategic Preparedness and Response (ASPR), CDC regularly develops novel influenza A candidate vaccine viruses (CVVs) for pandemic preparedness. Antigenic characterization of the A(H5N1) virus isolated from the Texas farm worker (A/Texas/37/2024) with ferret antisera produced against existing CVVs confirmed two clade 2.3.4.4b A(H5) CVVs have good cross-reactivity to this virus. Under the National Pre-Pandemic Influenza Vaccine Stockpile (NPIVS) program, ASPR has shared these CVVs with Food and Drug Administration (FDA)–licensed pandemic influenza vaccine manufacturers and has completed initial production of bulk antigen. ASPR is also supporting clinical evaluation of safety and immunogenicity of vaccines using antigen manufactured from one of these CVVs, influenza A/Astrakhan/3212/2020–like virus vaccine, in combination with different adjuvants that are stockpiled under the NPIVS. The clinical study (NCT05874713)[¶¶¶¶] testing cell-based antigen combined with MF59 adjuvant, according to the AUDENZ-licensed manufacturing process, has completed enrollment. The egg-based antigen, produced according to the Q-PAN-licensed process, combined with AS03 adjuvant clinical study (NCT05975840)[*****] is also fully enrolled. ASPR is planning additional clinical studies for combining egg-based antigen with both AS03 and MF59 adjuvants with enrollment expected to start in late summer 2024. If needed, and dependent upon FDA review and regulatory action allowing use, these vaccines could be the first allotment of vaccines used while additional manufacturing, starting with the stockpiled antigens and adjuvants, ramps up for full-scale production.

Four FDA-approved antiviral drugs (baloxavir marboxil, oseltamivir, peramivir, and zanamivir) are recommended for influenza treatment in the United States.[†††††] CDC has conducted phenotypic testing of antiviral susceptibility and found that the A(H5N1) virus isolated from the Texas farm worker is susceptible to baloxavir marboxil (Xofluza, Genentech) and to neuraminidase inhibitors, including oseltamivir (generic or Tamiflu, Genentech). Oral oseltamivir treatment is recommended for persons with confirmed or suspected A(H5N1) virus infection.[§§§§§] Oral oseltamivir is also recommended for postexposure prophylaxis (using twice daily treatment dosing) of close contacts (e.g., household members) of a confirmed A(H5N1) case. Observational studies of patients infected with older and different clades of A(H5N1) viruses, (i.e., not the current clade 2.3.4.4b viruses identified in the United States) have found that starting oseltamivir treatment within 2 days of symptom onset was significantly associated with survival benefit compared with no treatment or later initiation of oseltamivir treatment after symptom onset (*8,9*). All four antivirals are available in the Strategic National Stockpile and in many

§§§§ https://www.aphl.org/aboutAPHL/publications/Documents/ID-Influenza-Right-Size-Roadmap-Edition2.pdf

¶¶¶¶ https://www.clinicaltrials.gov/study/NCT05874713?term=NCT05874713&rank=1

***** https://www.clinicaltrials.gov/study/NCT05975840?term=NCT05975840&rank=1

††††† https://www.cdc.gov/flu/professionals/antivirals/index.htm

§§§§§ https://www.cdc.gov/flu/avianflu/novel-av-treatment-guidance.htm

BOX. Key epidemiologic questions to define the risk of highly pathogenic avian influenza A(H5N1) viruses to humans and to guide evidence-based recommendations — United States, 2024

1. Is there evidence of influenza A(H5N1) virus infections in human populations?
2. If human illness is identified, what is the clinical spectrum of illness?
3. What are the rates of asymptomatic human infection with influenza A(H5N1) virus?
4. What are the routes of exposure to influenza A(H5N1) virus on farms and dairies, and what is the risk for zoonotic transmission?
5. What behaviors, including use of personal protective equipment, are associated with human infection or protection from infection with influenza A(H5N1) virus?

state-managed stockpiles, both of which can be deployed to assist with supply chain constraints should they arise.

The National Institute of Allergy and Infectious Diseases (NIAID) continues to investigate the efficacy of novel direct-acting antiviral medications and host-targeted molecules as well as broadly neutralizing antibodies and more targeted monoclonal antibodies aimed at A(H5N1) viral-specific surface antigens that could protect from death or severe respiratory disease.

Epidemiologic Investigations

To better ascertain and define the risk to humans, CDC is working with states to plan epidemiologic investigations in collaboration with affected farms and health and agricultural partners at local, state, and federal levels. Important public health questions might be addressed through in-depth studies with specimen collection and surveys (Box). CDC conducted a similar study in response to poultry outbreaks of A(H5N1) in 2022 (*10*).

Discussion

CDC is collaborating with the U.S. Department of Agriculture, FDA, ASPR, the Health Resources and Services Administration, NIAID, and state and local public health and animal health officials using a coordinated One Health approach to identify and prepare for developments that could increase the risk to human health. Substantial challenges to identifying and interviewing persons exposed to cattle infected with A(H5N1) viruses for illness monitoring or epidemiologic studies exist. Workers exposed to A(H5N1) viruses might represent socioeconomically vulnerable, or otherwise hard-to-reach populations, including those who live in rural or remote areas; or they might be migrant, transient, or undocumented workers. Further, persons might not be aware of the risks or potential signs and symptoms associated with exposure; dairy farmers and the dairy industry have not previously been major partners in outreach about avian influenza. Recommendations for worker protection have been recently updated[¶¶¶¶¶] and disseminated.

Summary

What is already known about this topic?

Influenza A(H5) virus infection was detected in two U.S. farm workers during a multistate outbreak of A(H5N1) viruses in dairy cows; these are the first known instances of presumed cow-to-human transmission of avian influenza A viruses.

What is added by this report?

Approximately 350 exposed farm workers are being monitored; one of the two cases was identified via daily, active monitoring. Surveillance has identified no unusual influenza activity trends in the United States. A(H5) candidate vaccine viruses are available, and laboratory analyses indicate that A(H5N1) viruses circulating in cows and other animals are susceptible to FDA-approved antivirals.

What are the implications for public health practice?

Current risk to the U.S. public from A(H5N1) viruses is low; however, persons exposed to infected animals or contaminated materials, including raw cow's milk, are at higher risk and should take precautions and self-monitor for illness. A One Health (human, animal, and environmental) approach is critical to preparing for circumstances that could increase risk to human health.

Once exposed persons are identified, defining exposure periods is also difficult. A(H5N1) disease is widespread in poultry, and mortality is high. Rapid depopulation of affected flocks facilitates monitoring of exposed workers because it creates a finite 10-day monitoring window after exposure. In contrast, illness in cows can last for 2–4 weeks, and the duration of infectious virus shedding in cows is unknown. In addition, A(H5N1) virus infection has been identified in some cows without signs of illness; thus, some workers might be unaware of their exposure. Recent testing did not detect live, infectious A(H5N1) viruses in retail dairy samples; however, identification of A(H5N1) viral fragments in approximately one in five retail milk samples from across the country (*4*) suggests that A(H5N1) virus infections of cattle might be widespread. Therefore, monitoring of exposed or potentially exposed persons and animals might be protracted and resource-intensive.

Interpretation of surveillance data can be challenging given that A(H5N1) virus infections might manifest signs and symptoms similar to those associated with infections caused by other pathogens. During periods of low U.S. influenza virus circulation (e.g., spring and summer), syndromic and wastewater surveillance might more readily identify unusual

[¶¶¶¶¶] https://www.cdc.gov/flu/avianflu/h5/worker-protection-ppe.htm

signals in influenza-related symptoms or activity. However, using these systems to detect novel influenza A virus infection trends in the fall and winter, once seasonal influenza A virus circulation increases, will likely be complicated. Interpretation of wastewater data are further limited by the inability to distinguish between human and animal source material.

Currently circulating A(H5N1) viruses do not have the ability to easily bind to receptors that are most prevalent in the human upper respiratory tract and therefore are not easily transmissible to and between humans (*2*). However, because of the widespread global prevalence of A(H5N1) viruses in birds and other animals, continued sporadic human infections are anticipated. Further, if a novel influenza A virus acquires the ability to infect and be transmitted easily between persons in a sustained manner, an influenza pandemic could occur. Thus, investigation of every novel influenza A virus case in humans and comprehensive worldwide surveillance is critical to public health preparedness efforts.

Implications for Public Health Practice

CDC considers the current health risk to the U.S. public from A(H5N1) viruses to be low. However, persons who have job-related or recreational exposure to infected birds, poultry, dairy cattle, or other infected animals or contaminated materials, including raw cow's milk, are at increased risk for infection; these persons should take appropriate precautions, including using recommended personal protective equipment, self-monitoring for illness symptoms (*6*), and seeking prompt medical evaluation if they are symptomatic, including influenza testing and antiviral treatment if indicated. FDA has confirmed that pasteurization inactivates A(H5N1) viruses, and that the commercial milk supply is safe for consumption (*4*); however, all persons should avoid consuming raw milk or products produced from raw milk. A coordinated and comprehensive One Health response to this ongoing outbreak of A(H5N1) virus infections in dairy cows, poultry, and other animals is needed to identify and prepare for any developments that indicate an increase in the risk to public health.

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RESEARCH BRIEF

2024 Public Health Actions to Reduce the Burden of Asthma: Influenza and COVID-19 Vaccination Uptake Among People with Asthma

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PEER REVIEWED

Summary

What is already known on this topic?

Optimal asthma management, including vaccination, can help people with asthma during respiratory virus seasons to protect against infection and severe symptoms.

What is added by this report?

The study highlights significant differences in vaccination rates for people with asthma across demographic categories. Access challenges were not commonly reported as reasons for not getting vaccinated.

What are the implications for public health practice?

Findings identify differences in influenza and COVID-19 vaccination rates based on demographic factors. The results of this study can inform the development and implementation of tailored educational and communication efforts to improve vaccination rates in these populations.

Abstract

This study sought to identify COVID-19 and influenza vaccination rates and barriers among people with asthma. The Asthma and Allergy Foundation of America (AAFA) conducted an online survey from April to May in 2022 among a convenience sample of 350 individuals with asthma. Most survey respondents reported that they had received an influenza vaccine for the 2021–2022 flu season (77%) and at least 1 dose of a COVID-19 vaccine (87%). Age, gender, race and ethnicity, and household income were significantly associated with influenza vaccination. Age and urban–rural classification were associated with COVID-19 vaccination. Access issues were not commonly reported as vaccination barriers, highlighting educational opportunities.

Objective

The onset of the COVID-19 pandemic in March 2020 resulted in major disruption to everyday life. Additionally, the threat of a "tripledemic" — marked by a high number of cases of COVID-19, influenza, and respiratory syncytial virus (RSV) — continued into 2023 (1). Previous literature shows that respiratory infections can be more serious for individuals with asthma, as infection can exacerbate asthma symptoms and lead to poorer health outcomes (2,3). Therefore, practicing optimal asthma management during respiratory virus seasons can be beneficial for people with asthma (4). Vaccines have been shown to help protect people with asthma against respiratory infections and lessen symptom severity if an infection occurs (5). However, previous literature from other countries suggests that influenza and COVID-19 vaccination rates in adults with asthma is suboptimal (6,7). Although national vaccine surveillance data are widely available (8), little is known about influenza and COVID-19 vaccination uptake among people with asthma in the US. We sought to gauge vaccination rates among people with asthma in the US and understand what, if any, demographic differences exist in vaccination rates and barriers in this population.

Methods

The Asthma and Allergy Foundation of America (AAFA), a patient advocacy organization, conducted an online survey from April 6 to May 31, 2022, to assess influenza and COVID-19 vaccination behaviors and barriers among people with asthma and allergies. A convenience sample of people with self-reported diagnoses of asthma and allergies, as well as caregivers (eg, parents, guardians) of people diagnosed with these conditions, was surveyed for participation. Participants were recruited through AAFA's e-newsletters and social media posts. To qualify for the survey, participants needed to live in the US and be a legal adult in

their state of residence. Participants also needed to be a person with, or a caregiver to a person with, a self-reported diagnosis of asthma or allergies. Respondents were screened for eligibility through self-reported responses. The research protocol was reviewed and determined exempt by Advarra Institutional Review Board.

This analysis focused on adults with asthma because of an increased risk of poor asthma outcomes from respiratory infection. Participants responded on their own behalf. Data on adults with asthma were identified for analysis based on self-reported diagnosed conditions. Outcome variables included vaccination status for the 2020–2021 and 2021–2022 influenza seasons, and initial and subsequent COVID-19 vaccinations. To assess vaccination barriers, unvaccinated respondents selected barriers from a list which were then categorized into perceptual (eg, beliefs about vaccine safety or efficacy) and technical (eg, access, scheduling issues) categories. Descriptive statistics on vaccination rates and barriers were analyzed by using SPSS version 29.0 (IBM). Chi-square tests of independence and Fisher exact tests were used to examine relationships between vaccination rates and barriers and self-reported age, gender, race and ethnicity, annual household income, and urban–rural classification. Statistical significance was set at $P \leq .05$ for Pearson χ^2 and Fisher exact tests to identify relationships between vaccination rates and demographic factors.

Results

Of the 1,664 people who began the survey, 537 completed the survey for a completion rate of 32%. Among completed respondents, 350 were adults living with asthma, predominantly identifying as White, women, suburban residents, and having an annual household income exceeding $50,000 (Table 1).

More than three-quarters of respondents with asthma received an influenza vaccine for the 2020–2021 (78%) and the 2021–2022 (77%) influenza seasons. Vaccination rates for the 2020–2021 influenza season were higher among respondents aged 58 to 76 years than among those aged 26 to 57 years ($P < .001$). For the 2021–2022 influenza season, vaccination rates were higher among respondents aged 58 to 76 years than among those aged 26 to 57 years ($P < .001$), among men than among women ($P = .05$), among White respondents than among Hispanic or Latino/a respondents ($P = .04$), and among respondents with an annual household income of $100,000 or more than among those with an annual household income less than $50,000 ($P = .01$) (Table 2).

Most respondents with asthma reported receiving 1 or more doses of a COVID-19 vaccine (87%), completing a primary series for COVID-19 (85%), and completing a primary series for COVID-19 with a booster dose (73%). Initial COVID-19 vaccination rates were higher for respondents aged 58 to 76 years compared with those aged 26 to 57 years ($P < .001$) and for respondents in urban and suburban areas compared with those in rural areas ($P = .003$). The same differences were seen for full COVID-19 vaccination in age ($P < .001$) and urban–rural classification ($P = .01$). COVID-19 booster rates were higher for respondents with an annual household income of $100,000 or more compared with those with an annual household income under $50,000 ($P = .001$) and for respondents in urban and suburban areas compared with those in rural areas ($P = .009$) (Table 2).

Among respondents with asthma who did not receive an influenza or COVID-19 vaccine, no significant demographic differences were found in citing perceptual or technical barriers. Technical barriers were less commonly selected as barriers for influenza vaccines and were not selected by any respondents as barriers for COVID-19 vaccines (Table 3).

Discussion

We investigated influenza and COVID-19 vaccination rates among a subgroup of people with asthma, and although influenza and COVID-19 vaccination rates among this group exceeded national averages (8), we found significant demographic differences. Respondents aged 58 to 76 years were more likely to be vaccinated for influenza and COVID-19 compared with younger respondents, and respondents in urban and suburban areas were more likely to be vaccinated for COVID-19 compared with those in rural areas. These demographic differences mirror national demographic differences in vaccination rates (8). Reasons for variation may include earlier COVID-19 vaccine eligibility for older adults and better access to vaccine resources in urban and suburban communities.

We also examined barriers to vaccination among unvaccinated respondents with asthma. Perceptual barriers (eg, beliefs about vaccine safety or efficacy) outweighed technical barriers (eg, access, scheduling issues), aligning with findings from a previous study among Canadian adults with asthma (9). These results indicate opportunities for education on vaccine safety and efficacy, particularly for people with asthma.

Our study has limitations. We relied on a convenience sample that may be more likely to be vaccinated than the total population of people with asthma. Additionally, most survey respondents were higher-income, White women and therefore not representative of the national population of people with asthma, which is more diverse in income, race and ethnicity, and gender (10). Statistical testing was limited by sample size variations across demographic groups, potentially obscuring significant differences that may be

seen in a more diverse sample. Lastly, the survey relied on self-reported data, which is prone to several biases including social desirability and recall bias.

Despite these limitations, the study contributes valuable insights into vaccination behaviors among people with asthma, a group susceptible to severe illness from respiratory infections. It represents the first attempt, to the authors' knowledge, to analyze influenza and COVID-19 vaccination behaviors in this population in the US. Future research can aim for nationally representative samples to better understand demographic differences in this population, as generational and cultural beliefs can further influence vaccination behavior (11,12). Additionally, future research can examine differences in vaccination rates between people with and without asthma to understand differences in these populations.

Our study offers insights into vaccination behaviors of a subgroup of people with asthma to inform future research. The findings also highlight opportunities for improved vaccine communication strategies to reduce prevalence and severe outcomes of respiratory diseases across demographic groups among people with asthma.

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Tables

Table 1. Demographic Characteristics of Survey Respondents, by Asthma Status, Online Survey of the Asthma and Allergy Foundation of America, April 6 to May 31, 2022

Characteristic	Total (N = 537)	Asthma (n = 350)	No Asthma (n = 187)
	No. (%)		
Age, y			
≤25	11 (2)	7 (2)	4 (2)
26–41	126 (23)	66 (19)	60 (32)
42–57	226 (42)	133 (38)	93 (50)
58–76	162 (30)	135 (39)	27 (14)
≥77	12 (2)	9 (3)	3 (2)
Gender			
Man	47 (9)	39 (11)	8 (4)
Woman	478 (89)	303 (87)	175 (94)
Nonbinary or gender nonconforming	2 (0)	1 (0)	1 (1)
Prefer not to answer	10 (2)	7 (2)	3 (2)
Race and ethnicity			
Indigenous American, American Indian, or Alaska Native	12 (2)	11 (3)	1 (<1)
Asian	14 (3)	7 (2)	7 (4)
Black or African American	28 (5)	21 (6)	7 (4)
Hispanic or Latino/a	37 (7)	23 (7)	14 (7)
Middle Eastern or North African	4 (1)	2 (<1)	2 (1)
Native Hawaiian or Pacific Islander	1 (<1)	1 (<1)	0
White	404 (75)	262 (75)	142 (76)
Other	8 (1)	5 (1)	3 (2)
Prefer not to answer	29 (5)	18 (5)	11 (6)
Annual household income, $			
<50,000	76 (14)	61 (17)	15 (8)
50,000–99,999	152 (28)	113 (32)	39 (21)
≥100,000	194 (36)	101 (29)	93 (50)
Prefer not to answer	115 (21)	75 (21)	40 (21)
Urban–rural classification			
Urban	101 (19)	79 (23)	22 (12)
Rural	117 (22)	70 (20)	47 (25)
Suburban	302 (56)	188 (54)	114 (61)
Prefer not to answer	17 (3)	13 (4)	4 (2)

Table 2. Influenza and COVID-19 Vaccination Rates Among People with Asthma, by Respondent Characteristics, Online Survey of the Asthma and Allergy Foundation of America, April 6 to May 31, 2022[a]

Characteristic	No.	Received an influenza vaccination for the October 2020–May 2021 influenza season, n (%)	Received an influenza vaccination for the October 2021–May 2022 influenza season, n (%)	Received ≥1 dose of a COVID-19 vaccine, n (%)	Fully vaccinated for COVID-19, n (%)[b]	Fully vaccinated and received a booster dose for COVID-19, n (%)
Total[c]	350	272 (78)	269 (77)	304 (87)	299 (85)	257 (73)
Age, y						
≤25	7	6 (86)	7 (100)	7 (100)	7 (100)	7 (100)
26–41	66	40 (61)	40 (61)	51 (77)	48 (73)	40 (61)
42–57	133	96 (72)	94 (71)	108 (81)	107 (80)	87 (65)
58–76	135	121 (90)	119 (88)	130 (96)	129 (96)	115 (85)
≥77	9	9 (100)	9 (100)	8 (89)	8 (89)	8 (89)
P value	—	<.001[d]	<.001[d]	<.001[d]	<.001[d]	.30[d]
Gender						
Man	39	34 (87)	35 (90)	34 (87)	34 (87)	32 (82)
Woman	303	235 (78)	230 (76)	266 (88)	261 (86)	222 (73)
P value	—	.22	.05	>.99[d]	.60	.19[d]
Race and ethnicity						
Indigenous American, American Indian, or Alaska Native	11	9 (82)	7 (64)	10 (91)	10 (91)	8 (73)
Asian	7	4 (57)	4 (57)	5 (71)	5 (71)	5 (71)
Black or African American	21	15 (71)	16 (76)	19 (91)	19 (91)	17 (81)
Hispanic or Latino/a	23	14 (61)	13 (57)	18 (78)	18 (78)	15 (65)
White	262	211 (81)	212 (81)	234 (89)	230 (88)	202 (77)
Other[e]	8	5 (63)	6 (75)	6 (75)	6 (75)	5 (63)
P value	—	.09[d]	.04[d]	.15[d]	.27[d]	.80[d]
Annual household income, $						
<50,000	61	43 (70)	40 (66)	48 (79)	48 (79)	37 (61)
50,000–99,999	113	93 (82)	89 (79)	104 (92)	102 (90)	84 (74)
≥100,000	101	84 (83)	86 (85)	89 (88)	89 (88)	86 (85)
P value	—	.08	.01	.12	.24	.001
Urban–rural classification						
Urban	79	65 (82)	63 (80)	74 (94)	72 (91)	66 (84)
Rural	70	50 (71)	48 (69)	53 (76)	53 (76)	39 (56)
Suburban	188	148 (79)	151 (80)	169 (90)	167 (89)	147 (78)
P value	—	.20	.12	.003	.01	.009

Abbreviation: — , not applicable.
[a] *P* values based on χ^2 test of independence and Fisher exact test; significance set at $P \leq .05$.
[b] "Fully vaccinated" was defined as having completed a primary series of COVID-19 vaccinations.
[c] Respondent characteristics may not add up to total due to exclusion of "prefer not to answer" categories from analysis, as well as categories in which n < 5.
[d] Fisher exact test was used because ≥20% of expected cell values were n < 5.
[e] Includes Middle Eastern or North African, Native Hawaiian or Pacific Islander, and other.

Table 3. Reasons for Not Receiving an Influenza or COVID-19 Vaccination Among Unvaccinated Respondents, Online Survey of the Asthma and Allergy Foundation of America, April 6 to May 31, 2022[a]

Characteristic	Unvaccinated for 2021–2022 Influenza (N = 81)[b]	Reason for Not Receiving an Influenza Vaccine, Perceptual, n (%)[c]	Reason for Not Receiving an Influenza Vaccine, Technical, n (%)[c]	Unvaccinated for COVID-19 (N = 46)[b]	Reason for Not Receiving a COVID-19 Vaccine, Perceptual, n (%)[d]	Reason for Not Receiving a COVID-19 Vaccine, Technical, n (%)[d]
Age, y						
≤25	0	0	0	0	0	0
26–41	26	22 (85)	4 (15)	15	15 (100)	0
42–57	39	31 (79)	8 (21)	24	24 (100)	0
58–76	16	13 (81)	3 (19)	4	4 (100)	0
≥77	0	0	0	1	1 (100)	0
P value	—	<.93[e]		—	—	
Gender						
Man	4	4 (100)	0	4	4 (100)	0
Woman	73	59 (81)	14 (19)	36	36 (100)	0
P value	—	>.99[e]		—	—	
Race and ethnicity						
Indigenous American, American Indian, or Alaska Native	4	4 (100)	0	1	1 (100)	0
Asian	3	3 (100)	0	2	2 (100)	0
Black or African American	5	5 (100)	0	2	2 (100)	0
Hispanic or Latino/a	10	7 (70)	3 (30)	5	5 (100)	0
White	50	42 (84)	8 (16)	216	216 (100)	0
Other[f]	2	1 (50)	1 (50)	2	2 (100)	0
P value	—	.41[e]		—	—	
Annual household income, $						
<50,000	21	18 (86)	3 (14)	11	11 (100)	0
50,000–99,999	24	19 (79)	5 (21)	9	9 (100)	0
≥100,000	15	13 (87)	2 (13)	12	12 (100)	0
P value	—	.83[e]		—	—	
Urban–rural classification						
Urban	16	12 (75)	4 (25)	5	5 (100)	0
Rural	22	21 (95)	1 (5)	16	16 (100)	0
Suburban	37	29 (78)	8 (22)	18	18 (100)	0
P value	—	.17[e]		—	—	

Abbreviation: — , not applicable.
[a] *P* values based on χ^2 test of independence and Fisher exact test; significance set at $P \leq .05$.
[b] Totals for respondent characteristics may not add up to overall total due to exclusion of "prefer not to answer" categories from analysis, as well as categories in which n < 5.
[c] Responses were categorized as technical if respondent selected "I do not have easy access to an influenza shot clinic" or "I haven't found the time to schedule an appointment." All other responses were categorized as perceptual.
[d] Responses were categorized as technical if respondent selected "I have scheduled an appointment for the vaccine for a future date," "I have had trouble finding appointment(s) to get a vaccine," "I have trouble navigating the process to sign up for a vaccine," or "It is difficult for me to travel to a vaccination site." All other responses were categorized as perceptual.
[e] Fisher exact test was used because ≥20% of expected cell values were n < 5.
[f] Includes Middle Eastern or North African, Native Hawaiian or Pacific Islander, and other.

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ORIGINAL RESEARCH

Health Care Use Among Cancer Patients With Diabetes, National Health and Nutrition Examination Survey, 2017–2020

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PEER REVIEWED

Summary

What is already known on this topic?

Cancer patients with multiple chronic diseases have unplanned hospitalizations because of a lack of appropriate care management. Multiple chronic diseases among people with cancer are associated with worse clinical outcomes and survivorship than among people with cancer only.

What is added by this report?

Patients with cancer and prediabetes had higher levels of health care use than patients with cancer only. A diagnosis of type 2 diabetes did not significantly affect health care use among patients with cancer.

What are the implications for public health practice?

Optimal care coordination and early management of prediabetes among patients with cancer via primary care may contribute to improving cancer survivorship.

Abstract

Introduction

Diabetes is a common comorbidity among people with cancer. The objective of our study was to examine patterns of health care use among patients with cancer and either type 2 diabetes or prediabetes.

Methods

We used data from the National Health and Nutrition Examination Survey (NHANES) for 2017–2020. The study population included US adults aged 18 years or older who were diagnosed with any cancer and type 2 diabetes or prediabetes (established by self-report and/or hemoglobin A_{1c} measurement). We used Poisson and multivariate logistic regression models to determine the effect of comorbidity on health care use, defined as health care visits and overnight stays in a hospital.

Results

Of 905 cancer patients representing 27,180,715 people in the US, 24.4% had a type 2 diabetes diagnosis, and 25.8% had a prediabetes diagnosis. Patients with cancer and prediabetes had a significantly higher rate of health care visits (incidence rate ratio = 1.11; 95% CI, 1.01–1.22; $P = .03$) than patients with cancer only. We found no significant association between having cancer and type 2 diabetes and the number of health care visits or overnight hospital stays compared with patients with cancer only.

Conclusion

More emphasis should be placed on optimal care coordination among people with cancer and other conditions, such as diabetes and prediabetes, to reduce the impact of comorbidity on health care use. Interventions integrated with technology to provide timely access to education on preventing or managing diabetes and prediabetes among cancer patients are warranted.

Introduction

Diabetes is a common comorbidity among people with cancer. As patients with cancer live longer due to advances in cancer treatment, rates of chronic conditions, such as diabetes, are expected to rise among people with cancer. People with type 2 diabetes (hereinafter, diabetes) have a substantially higher risk of cancer incidence and death, leading to poorer survivorship compared with people without diabetes (1,2). For example, people with diabetes, compared with people who do not have diabetes, have double the risk for liver and pancreatic cancers and have a higher risk of de-

veloping bladder, colon, and breast cancers (3). In addition, as cancer incidence and death rates have risen consistently over time, the comorbidity of cancer with other chronic diseases has gained attention (4,5). Despite these clinical outcomes, the research is limited on care delivery for people with cancer and other comorbidities.

People with cancer and comorbidities, compared with those who have cancer and no comorbidities, have greater unplanned use of health care services, including higher rates of unplanned hospital readmissions (6,7) and revisits to the emergency department (8). One study showed that among people with cancer and comorbidities, diabetes was the top reason for emergency department revisits (24% of all revisit encounters) (8). Another study found that the average length of hospital stay among people with cancer and diabetes was significantly longer than among patients with no comorbidity (9). In that study, the average length of a hospital stay among patients with colorectal cancer and diabetes who underwent surgery was almost 17 days, which is 3 days longer than among patients with cancer only (9). Furthermore, health care costs are of critical concern. A national study, which used 5 years of data from the Medical Expenditure Panel Survey (2010–2014), found that cancer patients spent on average 4 times more in annual health expenditures than noncancer patients (10). Early initiation of chronic disease prevention and management with a primary care physician can mitigate this financial burden.

Many patients with cancer face the challenges of comanaging cancer and chronic diseases. In a qualitative study conducted in 2021 and 2022 at 3 New York City hospitals among 15 women with breast cancer and either diabetes or prediabetes, participants reported a lack of information and education on managing chronic diseases and the burden of co-management with different providers (11). In addition, patients tended to prioritize cancer treatment over diabetes management with their primary care physician (11). These struggles may be more detrimental for patients who are at a higher-than-average risk of developing diabetes. For example, a national cohort study in Korea found that a diagnosis of cancer increased the risk of subsequent diabetes (12). A case-cohort study in Israel that investigated the association between hormone therapy and diabetes risk among 2,246 female breast cancer survivors found that 48% of diabetes incidence could have been prevented had patients not received hormone therapy (13). Early implementation of a diabetes prevention strategy, particularly for patients with cancer and prediabetes, elevated blood glucose, or active engagement with a primary care physician during cancer treatment, could prevent comorbidity and improve survivorship. Furthermore, cancer treatments such as chemotherapy, radiation, or immunotherapy are associated with a higher prevalence of prediabetes (14).

Comorbidities or complications associated with cancer are linked to increased health care costs and various kinds of health care use, including ambulatory care visits and emergency department visits (15,16). However, evidence that focuses on the effects of specific kinds of comorbidity, such as diabetes, on health care use is limited. One study that used data from a statewide electronic health record database from 2007 to 2017 in the US found a significant association of having both diabetes and colorectal cancer with emergency department visits but did not examine other outcomes, such as hospitalization, which is a major driver of health care costs (17). Furthermore, little is known about how patterns of health care use differ across stages of diabetes. Addressing these gaps may help to improve the delivery of effective clinical care and preventive services for people with cancer and diabetes.

The objective of this study was to examine the association of health care use patterns among patients with cancer, stratified by diagnosis of diabetes or prediabetes. Findings from the current study may guide research to develop an optimal coordinated care model for early detection of prediabetes or diabetes and to enhance cancer survivorship for people with cancer and comorbidities.

Methods

Our study used a cross-sectional design and data from the National Health and Nutrition Examination Survey (NHANES) for the 3-year cycle of 2017–2020, before the pandemic. NHANES has been conducted since 1960 and is designed to assess the health and nutritional status of adults and children in the US. It collects nationally representative data through clinical examinations, selected medical and laboratory tests, and self-reported data. NHANES uses a stratified, multistage probability sample design and recommends using weights, stratification, and cluster variables to account for the complex sample design (18). Thus, we applied these variables to the statistical analyses to generate population estimates.

Study population

Our study population comprised adults aged 18 years or older who were diagnosed with any cancer and had physician-diagnosed diabetes or prediabetes. Those with a cancer history were identified by using the question, "Have you ever been told by a doctor or other health professional that you had cancer or a malignancy of any kind?" Physician-diagnosed diabetes and prediabetes were identified through self-report on the NHANES questionnaire. In addition, to reduce the risk of recall bias, we used NHANES laboratory results of the hemoglobin A_{1c} (HbA_{1c}) test. We excluded data on undiagnosed diabetes because the sample size was too small for generating population estimates. We classified people in-

to 3 categories: 1) those with a cancer history only, 2) those with any cancer history and prediabetes, and 3) those with any cancer history and diabetes. We excluded records that had missing data for these variables.

Outcomes

A primary outcome was the number of visits to a physician's office, a clinic, or "some other place" in the previous 12 months. This visit did not include hospitalizations, emergency department visits, home visits, or telephone calls. A secondary outcome was an overnight stay in a hospital in the previous 12 months. It excluded overnight stays in the emergency department.

Independent variable

A primary independent variable was comorbidity status. We categorized the study population into 3 groups: 1) cancer only, 2) cancer and prediabetes, and 3) cancer and diabetes. Control variables were demographic characteristics (age, sex, and race and ethnicity), education, body mass index (BMI), and having a usual source of care (yes or no). We treated age as a continuous variable. Sex was a dichotomous variable (male or female). We categorized race and ethnicity into 4 categories: 1) Hispanic or Latino, 2) non-Hispanic Black, 3) non-Hispanic White, and 4) Other (American Indian or Alaska Native, Asian, and Native Hawaiian or Pacific Islander) or multiracial. We converted education into a dichotomous variable (less than high school and high school graduate or above). Financial status was measured by the ratio of income to poverty (total family income divided by the poverty threshold) and dichotomized into 2 levels: 1) poor (ratio <1) and 2) rich (ratio ≥1). Health status was measured by self-reported general health condition and grouped into 2 levels: 1) fair or above (excellent, very good, good, or fair) and 2) poor. BMI was categorized into 3 levels: 1) normal (BMI, 18.5–24.9), 2) overweight (25.0–29.9), and 3) obese (≥30.0). Health insurance status was categorized into 2 levels: 1) yes, insured, and 2) no, uninsured. We excluded underweight people due to a high risk of mortality and little relevance to our study. Lastly, we treated usual source of care as a dichotomous variable (has a usual source or does not have a usual source of care). We counted the number of other chronic diseases reported by the survey respondent, such as arthritis, cancer (if the respondent has ≥1 cancers), cardiovascular diseases (eg, congestive heart failure, coronary heart disease, angina, or stroke), chronic kidney disease, depression, hypertension, and pulmonary diseases (eg, emphysema, chronic bronchitis, or asthma). We categorized these data into 4 groups: 1) no other comorbidity, 2) 1 additional comorbidity, 3) 2 additional comorbidities, and 4) ≥3 additional comorbidities.

Statistical analysis

We conducted a descriptive analysis of the baseline characteristics of the 3 groups of NHANES respondents (cancer only, cancer and prediabetes, and cancer and diabetes). We used χ^2 tests and t tests to determine significant differences between groups, with $P < .05$ considered significant. We used a Poisson regression model to determine the effect of comorbidity status (cancer only, cancer and prediabetes, and cancer and diabetes) on the number of health care visits in the previous 12 months. We used a multivariate logistic regression model to examine the risk of an overnight hospital stay associated with comorbidity status. We conducted both unadjusted and adjusted models. The Poisson regression model produced incident rate ratios (IRRs) and 95% CIs, and the multivariate logistic regression model produced odds ratios (ORs) and 95% CIs. The Pearson χ^2 test was used to evaluate the goodness-of-fit for the Poisson regression model, and the Akaike Information Criterion (AIC) was used to evaluate the goodness-of-fit for the multivariate logistic regression model. We used SAS version 9.4 (SAS Institute, Inc) for all analyses. This study was exempted from the University of Florida Institutional Review Board review because of the use of publicly available data. We followed the STROBE statement in conducting methods and reporting results (19).

Results

The unweighted sample size was 905, representing 27,180,715 people in the US. Of these cancer patients, 24.4% (weighted percentage) had a type 2 diabetes diagnosis, and 25.8% (weighted percentage) had a prediabetes diagnosis (Table 1). The mean age of the total study population was 63.9 years. People with cancer and diabetes (mean age, 68.8 y) and people with cancer and prediabetes (mean age, 66.7 y) were older, on average, than people with cancer only (mean, 59.9 y). The percentage of people with less than a high school diploma was significantly larger among people with cancer and diabetes (10.2%) and cancer and prediabetes (9.4%) than people with cancer only (5.2%). The percentage of people who had a BMI in the obese range was significantly larger among people with cancer and diabetes (63.3%) and cancer and prediabetes (43.9%) than people with cancer only (30.7%). The percentage of people with 3 or more additional comorbidities was significantly larger among people with cancer and diabetes (51.0%) and cancer and prediabetes (30.3%) than among people with cancer only (17.1%). Regardless of comorbidity status, more than 95% of people had health insurance. The percentage of people with a usual source of care was significantly larger among people with cancer and diabetes (98.3%) and cancer and prediabetes (97.2%) than among people with cancer only (91.6%).

In the unadjusted Poisson regression model, the IRR for the number of health care visits in the previous 12 months was significantly higher among people with cancer and diabetes (IRR = 1.19; 95% CI, 1.12–1.27; $P < .001$) than among people with cancer only (Table 2). However, after controlling for covariates, the comorbidity of cancer and diabetes was not significantly associated with increases in the number of health care visits (IRR = 1.04; 95% CI, 0.94–1.15; $P = .44$). After controlling for covariates, the comorbidity of cancer and prediabetes was associated with increases in the number of health care visits in the previous 12 months (IRR = 1.11; 95% CI, 1.01–1.22; $P = .03$). The results of the goodness-of-fit test for both unadjusted and adjusted models were not significant, indicating that neither model fit the data well.

In the multivariate logistic regression, the unadjusted model showed that people with diabetes and cancer were 2.5 times more likely than people with cancer only to stay overnight in a hospital (OR = 2.55; 95% CI, 1.54–4.21). However, after controlling for covariates, this association was not significant (OR = 1.57; 95% CI, 0.82–3.02). Moreover, we found no significant association in comorbidity with prediabetes for the risk of an overnight stay in a hospital in either the unadjusted or adjusted model (Table 3). The goodness-of-fit test for the adjusted model had a lower AIC value than the unadjusted model, indicating a better fitting model.

Discussion

The objective of our study was to examine patterns of health care use among people with cancer and either prediabetes or diabetes. In our nationally representative sample, patients with cancer and diabetes had 19% more health care visits than people with cancer only according to the unadjusted regression model, and patients with cancer and prediabetes had 11% more health care visits than people with cancer only according to the adjusted regression model. Future studies may be needed to test strategies to improve care coordination and early initiation of preventive care strategies for people with cancer at risk of developing prediabetes and diabetes.

Having diabetes and cancer increased the risk for an overnight stay in a hospital in the unadjusted regression models, whereas having prediabetes and cancer increased the number of health care visits in the adjusted regression model only. These findings indicate that different stages of diabetes may drive different health care needs. In the qualitative study conducted in 2021 and 2022 at 3 New York City hospitals among 15 women with breast cancer and either diabetes or prediabetes, 7 participants reported glucose levels of more than 200 mg/dL (normal is 70–90 mg/dL) and 9 participants indicated a lack of glucose control during cancer treatment (11). In addition, as cancer treatment tends to be prioritized over other treatment, diabetes prevention and management led by a primary care physician may be paused (20). Medication adherence for chronic diseases may also decline due to the priority of cancer treatment (21,22). In addition, many cancer patients with comorbidities may not receive self-management education or guidelines for preventive care, negatively affecting cancer survivorship (23). Moreover, our study found that patients with cancer and diabetes were 2 times more likely to be hospitalized, whereas patients with cancer and prediabetes did not have significantly higher rates of hospitalization. This finding was supported by literature showing that patients with cancer and at least 1 comorbidity were more likely than patients with no comorbidities to be hospitalized (6,24). Clinical guidelines for managing patients with cancer and prediabetes are lacking, and communication guidelines for coordinated care between oncologists and primary care physicians are limited. Because many patients with cancer tend to prioritize cancer treatment over primary care for prediabetes or diabetes, detrimental clinical outcomes and increased health care use may not be preventable without early prevention or ongoing management. In response to increases in the prevalence of prediabetes and cancer, it is important to develop a systematic preventive care model for early-stage chronic diseases (eg, prediabetes, prehypertension) that includes collaboration between oncologists and primary care physicians. Such a model could be a cost-effective strategy for improving cancer survivorship.

Our study also found that more than 80% of comorbid people were overweight or obese (compared with 67.5% among those with cancer only). It is well established that obesity is significantly associated with cancer incidence and mortality (25) and is a risk factor for cancer and chronic diseases (eg, diabetes, prediabetes) (26,27). Excessive body fat causes chronic inflammation that may be attributed to cancer treatment–associated adverse outcomes (25). Thus, it is important to control overweight and obesity during cancer treatment. A combination of diet and exercise was identified as a more effective intervention for weight loss than a standard of care for patients with cancer (28). Clinicians need to provide self-management guidelines for lifestyle changes when a cancer diagnosis is first made, especially among overweight or obese patients. In the qualitative study among 15 women with breast cancer and either diabetes or prediabetes, participants indicated not receiving guidance on self-management or having a designated clinician who continuously monitored them (11). One in-depth patient interview found that a patient searched for diet or exercise information on Google (11). This research suggests a need for self-management guidelines provided by clinicians for controlling overweight or obesity and monitoring chronic disease progression.

Educational attainment was significantly associated with comorbidity status. Among patients with less than a high school dip-

loma, the percentage of patients with a comorbidity was twice the percentage of patients with no comorbidity (9.4% and 10.2% vs 5.2%). Education may be key to health behaviors and the prevention of adverse outcomes. It is well established that education inequality is associated with cancer survivorship (29,30). For example, a study in The Netherlands showed that among patients with cancer and comorbidity, those with a low level of education (equivalent to primary school) had a 3 times higher risk of death than those with a university degree (29). A study of education differentials in cancer deaths in Lithuania found an inverse educational gradient for selected cancer sites among men and women, noting that substantial shares of cancer deaths (8% to 35%) could have been avoided or postponed (30). Increasing access to resources for patients with low levels of education may help to minimize the number of comorbidities that can arise and ultimately improve their cancer survivorship. Particularly, providing more resources may benefit from developing effective and structured communication strategies with providers.

Optimal coordinated care is crucial to mitigate the burden of comorbidities on health care use and costs among patients with cancer. Despite the growing need for increased care coordination between primary care physicians and oncologists, no standardized care coordination model exists for managing the comorbidity of cancer and chronic diseases such as prediabetes or diabetes (31). Additionally, the involvement of primary care physicians in cancer care is limited, especially during active cancer treatment (32). Previous research identified some barriers to effective cancer care coordination, including inadequate communication between oncologists and primary care providers and between patients and primary care providers; geographic limitations; and limited interoperability of the electronic health record among health care providers (32,33). Fortunately, the recent rapid technological evolution has provided new opportunities to reduce these barriers. Studies conducted at the Johns Hopkins Primary Care for Cancer Survivors clinic in 2015 and the Duke Cancer Institute during 2020–2021 found that comorbid patients were more likely to use telehealth for cancer and primary care, and telehealth improved outcomes such as patient satisfaction and survivorship (34,35). Using artificial intelligence in the care coordination process and communication will become pivotal to improving an efficient and effective care coordination model. An optimal care coordination model integrated with technology can be achieved by using standardized communication channels among health care providers and between health care providers and patients and the interoperability of electronic health records. Moreover, appropriate data privacy and security regulation will be essential to ensure patient trust in the care coordination model. To leverage these benefits, standardized clinical guidelines for managing comorbidities in patients with cancer should be developed. These guidelines would provide clear recommendations on integrating care coordination.

Limitations

Our study has several limitations. First, the diagnosis information obtained from a self-reported survey may be subject to recall bias, and we could not determine the exact timing of the diagnosis of diabetes or prediabetes and cancer. Second, our study used cross-sectional data, which prevented us from following disease progression over time and examining the effects of various treatments. A study that uses longitudinal data is needed to understand the effect of comorbidity on health care use among cancer patients. Third, we could not identify the reasons for health care use because of a lack of data. A study that incorporates electronic health records may identify patient-centered health care needs for those with comorbidities. Lastly, while the study identified patients with cancer who had undiagnosed diabetes, the sample size was too small to generate population estimates. Studies that use larger data sets could examine the role of undiagnosed diabetes on cancer prognosis and outcomes.

Conclusion

Among people with cancer, diabetes was significantly associated with an increased risk of an overnight hospital stay, whereas prediabetes was significantly associated with an increase in the number of health care visits. Our findings suggest that it may be beneficial to prioritize preventive measures (eg, screening) to prevent prediabetes from progressing to diabetes in patients with cancer and develop optimal coordinated care, which could help alleviate the strain on the health care system and improve oncology care.

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Tables

Table 1. Baseline Characteristics of Adults With Cancer, Stratified by Diabetes Status, National Health and Nutrition Examination Survey, 2017–2020[a]

Characteristic	Cancer only	Cancer and prediabetes	Cancer and diabetes	*P* value[b]
Unweighted sample size	403	248	254	—
Weighted sample size, no. (%)	13,532,512 (49.8)	7,024,691 (25.8)	6,623,512 (24.4)	—
Mean age, y	59.9	66.7	68.8	<.001
Sex				
Male	40.8	38.1	46.4	.51
Female	59.2	61.9	53.6	
Race and ethnicity				
Hispanic	6.0	19.4	8.6	.33
Non-Hispanic Black	5.8	32.1	6.3	
Non-Hispanic White	82.2	26.3	79.3	
Other[c]	6.1	19.3	5.8	
Education				
Less than high school	5.2	9.4	10.2	.02
High school graduate or above	94.8	90.6	89.8	
Financial status[d]				
Poor	6.3	5.7	8.9	.33
Rich	93.7	94.3	91.1	
Body mass index, calculated as weight (kg) divided by height in meters squared				
Normal (18.5–24.9)	32.5	16.0	6.5	<.001
Overweight (25.0–29.9)	36.8	40.1	30.2	
Obese (≥30.0)	30.7	43.9	63.3	
Health status				
Fair or above	95.7	95.2	89.1	.02
Poor	4.3	4.8	10.9	
No. of additional comorbidities				
0	30.9	19.2	5.6	<.001
1	30.8	21.1	17.6	
2	21.3	29.4	25.8	
≥3	17.1	30.3	51.0	

[a] All values are weighted percentages, unless otherwise indicated.
[b] Determined by *t* test for continuous variable and χ^2 tests for categorical variables.
[c] Includes American Indian or Alaska Native, Asian, and Native Hawaiian or Pacific Islander, and multiracial.
[d] Measured by the ratio of income to poverty (total family income divided by the poverty threshold) and dichotomized into 2 levels: 1) poor (ratio < 1) and 2) rich (ratio ≥ 1).
[e] Visits to a physician's office, a clinic, or some other place in the previous 12 months, not including hospitalizations, emergency department visits, home visits, or telephone calls.
[f] Excludes overnight stays in the emergency department.

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Table 1. Baseline Characteristics of Adults With Cancer, Stratified by Diabetes Status, National Health and Nutrition Examination Survey, 2017–2020[a]

Characteristic	Cancer only	Cancer and prediabetes	Cancer and diabetes	*P* value[b]
Has a usual source of care				
No	8.4	2.81	1.8	.02
Yes	91.6	97.2	98.2	
Health insurance				
No	3.5	1.4	4.8	.25
Yes	96.5	98.6	95.2	
No. of health care visits in previous 12 months[e]	3.4	3.8	3.8	.13
Had an overnight stay in a hospital in previous 12 months[f]				
No	15.3	15.5	31.6	<.001
Yes	84.7	84.5	68.4	

[a] All values are weighted percentages, unless otherwise indicated.
[b] Determined by *t* test for continuous variable and χ^2 tests for categorical variables.
[c] Includes American Indian or Alaska Native, Asian, and Native Hawaiian or Pacific Islander, and multiracial.
[d] Measured by the ratio of income to poverty (total family income divided by the poverty threshold) and dichotomized into 2 levels: 1) poor (ratio < 1) and 2) rich (ratio ≥ 1).
[e] Visits to a physician's office, a clinic, or some other place in the previous 12 months, not including hospitalizations, emergency department visits, home visits, or telephone calls.
[f] Excludes overnight stays in the emergency department.

Table 2. Results of Poisson Regression for the Number of Health Care Visits[a] in the Previous 12 Months, National Health and Nutrition Examination Survey, 2017–2020

Characteristic	Unadjusted IRR (95% CI) [*P* value]	Adjusted IRR (95% CI)[b] [*P* value]
Cancer only	Reference	Reference
Cancer and prediabetes	1.05 (0.98–1.12) [.14]	1.11 (1.01–1.22) [.03]
Cancer and diabetes	1.19 (1.12–1.27) [<.001]	1.04 (0.94–1.15) [.44]

Abbreviation: IRR, incidence rate ratio.
[a] Visits to a physician's office, a clinic, or some other place in the previous 12 months, not including hospitalizations, emergency department visits, home visits, or telephone calls.
[b] Controlled for age, sex, race and ethnicity, education, poverty-to-income ratio, body mass index, number of additional comorbidities, and health insurance.

Table 3. Results of Multivariate Logistic Regression for Risk of Overnight Stay in a Hospital[a] in the Previous Year, National Health and Nutrition Examination Survey, 2017–2020

Characteristic	Unadjusted odds ratio (95% CI)[b]	Adjusted[c] odds ratio (95% CI)[b]
Cancer only	1 [Reference]	1 [Reference]
Cancer and prediabetes	1.01 (0.63–1.64)	0.84 (0.42–1.65)
Cancer and diabetes	2.55 (1.54–4.21)	1.57 (0.82–3.02)

[a] Excludes overnight stays in the emergency department.
[b] An odds ratio with a 95% CI that includes 1 indicates no significant effect on risk.
[c] Controlled for age, sex, race and ethnicity, education, poverty-to-income ratio, body mass index, number of comorbidities, and health insurance.

Vaccinations for Adults with Diabetes

The table below shows which vaccinations you should have to protect your health if you have diabetes. Make sure you and your healthcare provider keep your vaccinations up to date.

Vaccine	Do you need it?
COVID-19	***Yes!*** All adults need to be up to date on COVID-19 vaccination. Talk to your healthcare provider.
Hepatitis A (HepA)	***Maybe.*** You need this vaccine if you have a specific risk factor for hepatitis A* or simply want to be protected from this disease. The vaccine is usually given in 2 doses, 6–18 months apart.
Hepatitis B (HepB)	***Yes!*** All adults younger than 60 are recommended to complete a 2- or 3-dose series of hepatitis B vaccine, depending on the brand. If you are 60 or older, you or your healthcare provider may decide you should be vaccinated because people with diabetes are at increased risk for hepatitis B. All adults should be screened for hepatitis B infection with a blood test at least one time; talk with your healthcare provider.
Hib (*Haemophilus influenzae* type b)	***Maybe.*** Some adults with certain high-risk conditions,* need vaccination with Hib. Talk to your healthcare provider to find out if you need this vaccine.
Human papillomavirus (HPV)	***Yes!*** You should get this vaccine if you are 26 years or younger. Adults age 27 through 45 may also choose to be vaccinated after a discussion with their healthcare provider. The vaccine is usually given in 2 or 3 doses, depending on the age at which the first dose was given.
Influenza (Flu)	***Yes!*** You need to be vaccinated against influenza every fall or winter for your protection.
Measles, mumps, rubella (MMR)	***Maybe.*** You need at least 1 dose of MMR if you were born in 1957 or later. You may also need a second dose.* Pregnant people and people with a severely weakened immune system should not get MMR.
Meningococcal ACWY (MenACWY, MenABCWY)	***Maybe.*** You may need MenACWY vaccine if you have one of several health conditions,* and also boosters if your risk is ongoing. You need MenACWY if you are a first-year college student living in a residence hall and (1) you have not had a dose since turning 16, or (2) it has been more than 5 years since your last dose. Anyone age 19 through 21 can have a catch-up dose if they have not had one since turning 16. A combination MenABCWY is an option when both MenACWY and MenB are needed.
Meningococcal B (MenB, MenABCWY)	***Maybe.*** You may need MenB if you have one of several health conditions,* and also boosters if your risk is ongoing. You may also consider getting the MenB vaccine if you are age 23 or younger (even if you don't have a high-risk medical condition) after a discussion with your healthcare provider. A combination MenABCWY is an option when both MenACWY and MenB are needed.
Pneumococcal (PCV15; PCV20, PPSV23)	***Yes!*** Adults with diabetes need to get either PCV20 alone, or PCV15 followed 1 year later by PPSV23. If you have previously received either PCV13 and/or PPSV23, your healthcare provider can determine what additional doses you may need.
Respiratory Syncytial Virus (RSV)	***Maybe!*** Adults 60 years and older may choose to be vaccinated after discussing with their healthcare provider. To protect infants from RSV, either the pregnant person should be vaccinated with Abrysvo (Pfizer) RSV vaccine, or the infant should be given RSV preventive antibody (nirsevimab).
Tetanus, diphtheria, pertussis (Tdap, Td)	***Yes!*** If you have never received a dose of Tdap, you need to get a Tdap shot now. After that, you need a Tdap or Td booster dose every 10 years. Consult your healthcare provider if you haven't had at least 3 tetanus- and diphtheria-toxoid containing shots in your life or if you have a deep or dirty wound.
Varicella (Chickenpox)	***Maybe.*** If you have never had chickenpox, never were vaccinated, or were vaccinated but only received 1 dose, talk to your healthcare provider to find out if you need this vaccine.* Pregnant people and those with a severely weakened immune systems should not get varicella vaccine.
Zoster (Shingles)	***Yes!*** If you are 19 or older and have a weakened immune system or are 50 or older, you should get 2 doses of the Shingrix brand of shingles vaccine.

*Consult your healthcare provider to determine your level of risk for infection and your need for this vaccine.

Are you planning to travel outside the United States? Visit the Centers for Disease Control and Prevention's (CDC) website at wwwnc.cdc.gov/travel/destinations/list for travel information, or consult a travel clinic.

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National Institutes of Health
Turning Discovery Into Health

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Accurate blood test for Alzheimer's disease

At a Glance

- A blood test identified Alzheimer's disease correctly in older adults with about 90% accuracy.
- Such tests could help speed the diagnosis of Alzheimer's disease in primary care clinics and help more people access treatments.

Blood tests for Alzheimer's could help speed diagnosis of the disease in primary care clinics and help more people access treatments.*SeventyFour / Shutterstock*

An accurate diagnosis of Alzheimer's disease currently requires either a sample of cerebrospinal fluid or a brain imaging test called a PET scan. Neither of these tests can be done in primary care clinics, where most people with cognitive complaints are first seen.

Such bottlenecks slow or prevent the diagnosis of Alzheimer's disease. Not having an official diagnosis prevents people from receiving drugs that can slow the progression of Alzheimer's. It can also keep them from joining studies of new treatments.

Researchers have been working to develop easier blood tests for Alzheimer's disease. These tests measure proteins related to Alzheimer's disease called amyloid beta and tau. Abnormal buildup of certain forms of amyloid beta and tau can cause them to spill into the bloodstream from the brain. Many blood tests for Alzheimer's disease have shown promising results. However, to date, most studies of these tests have not been done in real-world settings such as community clinics.

In a new study, funded in part by NIH, researchers led by Drs. Sebastian Palmqvist and Oskar Hansson from Lund University in Sweden collected blood samples from people who were being evaluated because of cognitive symptoms. More than 500 older adults were recruited from local primary care clinics and nearly 700 from nearby specialty memory care clinics.

The researchers used a test called PrecivityAD2. This measures the ratio of two types of amyloid beta as well as the proportion of tau made up of a specific type called p-tau217. Both measures were previously shown to predict a diagnosis of Alzheimer's disease. In a previous study, the team defined the levels of these molecules required to confirm a diagnosis of Alzheimer's disease.

In the new study, the researchers compared blood test results with those from either a spinal-fluid test or PET scan. They also compared the performance of the blood test with that of standard clinical evaluations performed by doctors. Such evaluations include a physical examination, cognitive testing, and a CT scan of the brain. Results were published on July 28, 2024, in *JAMA*.

Across all the participants, the blood test predicted a diagnosis of Alzheimer's disease with 88% to 92% accuracy. Further analysis found that measuring the proportion of p-tau217 alone yielded results similar to using both measures.

The blood test performed far better than clinical evaluations done without biomarker-based testing. Such clinical evaluations were 73% accurate at identifying Alzheimer's disease when done in specialty memory clinics, and only 61% accurate when done in primary care settings.

"We see this as a major step towards global clinical implementation of an Alzheimer's blood test," Hansson says. "The next steps include establishing clear guidelines for how an Alzheimer's blood test can be used in clinical practice, preferably by implementing these tests first in specialist care and then in primary care. This work is currently ongoing."

While the test used in the study is sold in the U.S., it is not yet approved by the Food and Drug Administration or covered by most insurance plans. The study also needs to be replicated in more diverse populations than the Swedish one studied.

—by Sharon Reynolds

Related Links

- Quick Test Could Help Reduce Dementia Care Disparities
- Cognitive Impairment Among Older American Indians
- Study Defines Major Genetic Form of Alzheimer's Disease
- Research in Context: Diagnosing Dementia
- Blood Test for Early Alzheimer's Detection
- How Biomarkers Help Diagnose Dementia
- Alzheimer's and Dementia
- Alzheimer's Disease Education and Referral (ADEAR) Center

References: Blood Biomarkers to Detect Alzheimer Disease in Primary Care and Secondary Care. Palmqvist S, Tideman P, Mattsson-Carlgren N, Schindler SE, Smith R, Ossenkoppele R, Calling S, West T, Monane M, Verghese PB, Braunstein JB, Blennow K, Janelidze S, Stomrud E, Salvadó G, Hansson O. *JAMA*. 2024 Jul 28:e2413855. doi: 10.1001/jama.2024.13855. Online ahead of print. PMID: 39068545.

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