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Texas Nursing Jurisprudence and Ethics

This course fulfills the Texas requirement for 2 hours of education on Jurisprudence and Ethics required every third renewal period.

If you have already completed your Texas Nursing Jurisprudence and Ethics requirement, you may skip this course and still receive 20 hours of CE.

Audience
This course is designed for all nurses licensed in Texas.

Course Objective
The purpose of this course is to provide basic knowledge of the laws and rules governing the practice of nursing in Texas in order to increase compliance and improve patient care. Texas nurses are legally obligated to be aware of standards that govern professional accountability. Information contained in this course is not intended to be used in lieu of lawful guidelines, but as a learning tool that increases the understanding of some regulations as they apply to nurses who are licensed within the state of Texas.

Learning Objectives
Upon completion of this course, you should be able to:

1. Outline the pertinent levels of nursing practice in Texas and the general scope of practice of each.
2. Identify specific laws and rules related to the practice of nursing in Texas.
3. Differentiate between ethical and legal practice.
4. Discuss the legal and ethical requirements related to professional boundaries and unprofessional conduct in nursing.

Faculty
Mary Franks, MSN, APRN, FNP-C, is a board-certified Family Nurse Practitioner and NetCE Nurse Planner. She works as a Nurse Division Planner for NetCE and a per diem nurse practitioner in urgent care in Central Illinois. Mary graduated with her Associate's degree in nursing from Carl Sandburg College, her BSN from OSF Saint Francis Medical Center College of Nursing in 2013, and her MSN with a focus on nursing education from Chamberlain University in 2017. She received a second master's degree in nursing as a Family Nurse Practitioner from Chamberlain University in 2019. She is an adjunct faculty member for a local university in Central Illinois in the MSN FNP program. Her previous nursing experience includes emergency/trauma nursing, critical care nursing, surgery, pediatrics, and urgent care. As a nurse practitioner, she has practiced as a primary care provider for long-term care facilities and school-based health services. She enjoys caring for minor illnesses and injuries, prevention of disease processes, health, and wellness. In her spare time, she stays busy with her two children and husband, coaching baseball, staying active with her

own personal fitness journey, and cooking. She is a member of the American Association of Nurse Practitioners and the Illinois Society of Advanced Practice Nursing, for which she is a member of the bylaws committee.

Faculty Disclosure
Contributing faculty, Mary Franks, MSN, APRN, FNP-C, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Division Planner
Sharon Cannon, RN, EdD, ANEF

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Special Approvals
This course fulfills the Texas requirement for 2 hours of education on Jurisprudence and Ethics.

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This course represents an educational model that promotes the importance of learning objectives and individualized learning. Study questions will appear throughout the course to create a link between the learning objectives and the supporting text.

INTRODUCTION

What is the purpose of the Texas Board of Nursing Position Statements?

Nursing practice acts have a long history in the United States, with the first standards being enacted in the early 1900s [1]. In 1907, nineteen nurses from around the state formed the Texas Graduate Nurses' Association in Fort Worth. These women had a collective interest in establishing standards for the delivery of nursing care and creating a nursing board [1]. Using recent Colorado legislation as a model, the Graduate Nurses' Association advocated for nursing legislation in Texas. The Nurses Registration Act of 1909 (an early version of the Nursing Practice Act) passed the Texas Legislature, and thus the Board of Nurse Examiners, which became the Board of Nursing in 2007, was created [1].

The Texas Nursing Practice Act has undergone extensive revision and amendment since 1909 [1; 2]. Legislated to safeguard the public, its purpose is to ensure that minimum safety requirements are met by every nurse practicing in the state. The Nursing Practice Act (i.e., Chapter 301 of the Texas Occupations Code) includes laws and rules regulating nursing education, licensure, and practice [2]. Chapter 301 establishes the Texas Board of Nursing as an authority to adopt rules, develop standards for nursing programs, and discipline nurses who violate regulations [2]. Nurses who fall below the Board's required minimum competency; who present a danger to patients, coworkers, or others; or who fail to comply with all Board of Nursing rules will be prohibited from working in the state.

In addition to Chapter 301 (the Nursing Practice Act), the Board of Nursing stipulates that Texas nurses are required to be familiar with Chapter 303 (Nursing Peer Review) and Chapter 304 (the Nurse Licensure Compact) [2]. Several chapters of the Texas Administrative Code, which is a collection of all state agency rules, also pertain to nursing education, licensure, practice, and discipline. Together, these laws and rules form the basis for the legal practice of nursing and the regulation of nursing by the State of Texas. Although they are not technically laws, the Texas Board of Nursing Position Statements provide guidance regarding patient safety, scope of practice, and other important issues; the Board strongly encourages that nurses read all Position Statements, or at the very least, the Summary of Position Statements [3]. Texas nurses should also be familiar with the principles of nursing ethics and have a firm understanding of professional boundaries [3].

This course fulfills the continuing education requirement on jurisprudence and ethics related to the practice of nursing in Texas for all levels of nursing, including registered nurses (RNs), licensed vocational nurses (LVNs), registered nurse first assistants (RNFAs), and advanced practice registered nurses (APRNs) [3]. While this course will provide an overview of several pertinent sections of the laws and rules, all nurses are required to have up-to-date knowledge of them in their entirety in order to ensure compliance, retain licensure, and practice safely.

STANDARDS OF NURSING PRACTICE

The basic standards of competent practice directly impact how all nurses in Texas provide care. Not only must a nurse possess the knowledge of lawful and current care standards, but the knowledge must be demonstrated through consistent practice and intervention to prevent unauthorized, inappropriate, erroneous, illegal, contraindicated, or intentional nonperformance of care.

The Nursing Practice Act governs the practice of LVNs, RNs, APRNs, and RNFAs. LVNs are those persons licensed to practice vocational nursing, while RNs, APRNs, and RNFAs are all licensed to practice professional nursing, with various levels of specialization [3]. Both professional and vocational nurses are responsible and accountable for making decisions that are based upon their educational preparation and experience in nursing.

LICENSED VOCATIONAL NURSING

According to the Texas Nursing Practice Act, the practice of vocational nursing is defined as a "directed scope of nursing practice, including the performance of an act that requires specialized judgment and skill, the proper performance of which is based on knowledge and application of the principles of biologic, physical, and social science as acquired by a completed course in an approved school of vocational nursing. The term does not include acts of medical diagnosis or the prescription of therapeutic or corrective measures." Vocational nursing involves [2]:

- Collecting data and performing focused nursing assessments of the health status of an individual
- Participating in the planning of the nursing care needs of an individual
- Participating in the development and modification of the nursing care plan
- Participating in health teaching and counseling to promote, attain, and maintain the optimum health level of an individual
- Assisting in the evaluation of an individual's response to a nursing intervention and the identification of an individual's needs
- Engaging in other acts that require education and training, as prescribed by Board rules and policies, commensurate with the nurse's experience, continuing education, and demonstrated competency

Additionally, the Board of Nursing and the Nursing Practice Act state that an LVN requires appropriate supervision of an RN, APRN, physician assistant, physician, dentist, or podiatrist [2]. The LVN is required to function within the parameters of the legal scope of practice and in accordance with the federal, state, and local laws, rules, regulations, and policies, procedures, and guidelines of the employing healthcare institution or practice setting. LVNs are "responsible for providing safe, compassionate, and focused nursing care to assigned patients with predictable healthcare needs" [4].

PROFESSIONAL NURSING

The practice of professional nursing is defined as "the performance of an act that requires substantial specialized judgment and skill, the proper performance of which is based on knowledge and application of the principles of biologic, physical, and social science as acquired by a completed course in an approved school of professional nursing. The term does not include acts of medical diagnosis or the prescription of therapeutic or corrective measures." Professional nursing involves [2]:

- Observation, assessment, intervention, evaluation, rehabilitation, care and counsel, or health teachings of a person who is ill, injured, infirm, or experiencing a change in normal health processes
- Administration of a medication or treatment as ordered by a physician, podiatrist, or dentist
- Maintenance of health or prevention of illness
- Performance of an act delegated by a physician
- The development of the nursing care plan
- Supervision or teaching of nursing
- Administration, supervision, and evaluation of nursing practices, policies, and procedures
- Requesting, receiving, signing for, and distribution of prescription drug samples to patients at practices at which an APRN is authorized to sign prescription drug orders

The Board of Nursing further defines the scope of practice of professional nursing [5]:

> The RN takes responsibility and accepts accountability for practicing within the legal scope of practice and is prepared to work in all healthcare settings, and may engage in independent nursing practice without supervision by another healthcare provider. The RN, with a focus on patient safety, is required to function within the parameters of the legal scope of practice and in accordance with the federal, state, and local laws; rules and regulations; and policies, procedures and guidelines of the employing healthcare institution or practice setting. The RN is responsible for providing safe, compassionate, and comprehensive nursing care to patients and their families with complex healthcare needs.

Advanced Practice Registered Nursing

APRNs are registered nurses who have completed additional accredited advanced-practice education and internship as recognized by the Board of Nursing [6]. The Board of Nursing specifies that APRNs must practice within their individual scope in the advanced role, meaning the particular specialty and population focus that the nurse trained for in an advanced program [7]. The scope of practice may be defined by APRN organizations; however, in many instances, it can be up to the APRN's employer or supervisor to determine what duties he or she can perform and what types of patients can be treated [7]. This decision may be based on the nurse's clinical experience and his/her knowledge, skills, and competencies. APRNs may or may not practice the full scope of the professional role and specialty for which they trained, and an APRN is allowed to perform the full scope of duties of an RN. The Board suggests asking the following questions in order to help decide if an activity is within an individual APRN's scope of practice [7]:

- Is it consistent with the scope of one's recognized title or does it evolve into another advanced practice title recognized by the Board requiring additional formal education and legal recognition?
- Is it consistent with the Standards of Nursing Practice outlined in Board Rule 217.11?
- Are you willing to accept accountability and liability for the activity and outcomes?
- Is it consistent with one's education in the role and specialty?
- Is it consistent with one's professional scope of practice?
- Is it consistent with reasonable and prudent practice?
- Is it consistent with statutory or regulatory laws?
- Is it consistent with evidence-based care?

APRNs may assign tasks to RNs and LVNs, but the task must be within the RN's/LVN's scope of practice [8]. The Texas Board of Nursing states (in Position Statement 15.18) that RNs are expected to carry out orders issued by APRNs if the orders are within the APRN's scope of practice for their specialty [9]. RNs are expected to question an order if it is believed to be non-efficacious or contraindicated.

TEXAS NURSING PRACTICE RULES

In what instances should a nurse be reported to the Board?

In addition to the Nursing Practice Act, there are several chapters of the Texas Administrative Code (i.e., Chapters 211–228) that contain rules pertinent to nursing. Texas Administrative Code Rule 217.11 (Standards of Nursing Practice) contains the minimum acceptable standards for all licensed nurses. It states that the Board of Nursing is responsible for regulating the practice of nursing within the State of Texas for LVNs, RNs, and APRNs, and that action against the nurse's license may result from a failure to meet the minimum acceptable level of

practice, even if no patient injury results from a nurse's actions or inactions [10]. All nurses practicing in Texas must meet the minimum acceptable standards specified in Rule 217.11, which includes requirements to [10]:

- Know and conform to the Texas Nursing Practice Act and the Board's rules and regulations as well as all federal, state, or local laws, rules, or regulations affecting the nurse's current area of nursing practice
- Implement measures to promote a safe environment for clients and others
- Know the rationale for and the effects of medications and treatments and correctly administer the same
- Accurately and completely report and document: the client's status, including signs and symptoms; nursing care rendered; physician, dentist, or podiatrist orders; administration of medications and treatments; client response(s); and contacts with other healthcare team members concerning significant events regarding client's status
- Respect the client's right to privacy by protecting confidential information unless required or allowed by law to disclose the information
- Promote and participate in education and counseling to a client(s) and, where applicable, the family/significant other(s) based on health needs
- Obtain instruction and supervision as necessary when implementing nursing procedures or practices
- Make a reasonable effort to obtain orientation/training for competency when encountering new equipment and technology or unfamiliar care situations
- Notify the appropriate supervisor when leaving a nursing assignment
- Know, recognize, and maintain professional boundaries of the nurse-client relationship
- Comply with mandatory reporting requirements of Texas Occupations Code Chapter 301 (Nursing Practice Act), Subchapter I, which include reporting a nurse: who violates the Nursing Practice Act or a Board rule (except for minor incidents as stated in the Nursing Practice Act and Board rules) and contributed to the death or serious injury of a patient; whose conduct causes a person to suspect that the nurse's practice is impaired by chemical dependency or drug or alcohol abuse; whose actions constitute abuse, exploitation, fraud, or a violation of professional boundaries; or whose actions indicate that the nurse lacks knowledge, skill, judgment, or conscientiousness to such an extent that the nurse's continued practice of nursing could reasonably be expected to pose a risk of harm to a patient or another person, regardless of whether the conduct consists of a single incident or a pattern of behavior
- Provide, without discrimination, nursing services regardless of the age, disability, economic status, gender, national origin, race, religion, health problems, or sexual orientation of the client served
- Institute appropriate nursing interventions that might be required to stabilize a client's condition and/or prevent complications
- Clarify any order or treatment regimen that the nurse has reason to believe is inaccurate, non-efficacious, or contraindicated by consulting with the appropriate licensed practitioner and notifying the ordering practitioner when the decision is made not to administer the medication or treatment
- Implement measures to prevent exposure to infectious pathogens and communicable conditions
- Collaborate with the client, members of the healthcare team and, when appropriate, the client's significant other(s) in the interest of the client's health care
- Consult with, utilize, and make referrals to appropriate community agencies and health care resources to provide continuity of care
- Be responsible for one's own continuing competence in nursing practice and individual professional growth
- Make assignments to others that take into consideration client safety and that are commensurate with the educational preparation, experience, knowledge, and physical and emotional ability of the person to whom the assignments are made
- Accept only those nursing assignments that take into consideration client safety and that are commensurate with the nurse's educational preparation, experience, knowledge, and physical and emotional ability
- Supervise nursing care provided by others for whom the nurse is professionally responsible
- Ensure the verification of current Texas licensure or other compact state licensure privilege and credentials of personnel for whom the nurse is administratively responsible, when acting in the role of nurse administrator.

As noted, nurses are required to be familiar with all Standards of Nursing Practice. Please refer to Chapter 217 of the Texas Administrative Code for Rule 217.11 in its entirety.

ETHICAL AND LEGAL ISSUES IN NURSING PRACTICE

What ethical concepts are central to nursing practice?

In addition to their legal obligations, nurses have ethical obligations to their patients. The practice of nursing is primarily one of caring, and the ethical theories for nursing are often referred to as "the ethics of caring." Nurses are expected to address both ethical and legal issues in their practice, which can be complex. As medical advancements and new technology progress, these must be incorporated into established ethical standards. The American Nurses Association has established the Code of Ethics for Nurses, which is intended to act as "the ethical standard for the profession and provides a guide for nurses to use in ethical analysis and decision-making" [11]. The full text of this Code is available at https://www.nursingworld.org/practice-policy/nursing-excellence/ethics/code-of-ethics-for-nurses.

Major ethical issues that may arise in the practice of nursing are related to the provision of patient-centered care, advocacy, delegation, self-care, and supporting colleagues and the profession [11]. Ethical concepts central to patient-centered care include advocacy, confidentiality, privacy, self-determination, and the dignity and worth of all persons. Ethical concepts central to nursing practice include accountability (i.e., accepting responsibility for one's action or inaction), beneficence (i.e., the duty to do good), competence (i.e., only performing duties within one's scope of practice, acquiring new skills and education), nonmaleficence (i.e., the duty to do no harm), veracity (i.e., truthfulness), and social reform (e.g., advocating for patients and groups). Additionally, as a nurse gains experience in his or her field and specialty, the ethic of teaching comes into play. This can simply involve helping an inexperienced nurse grow by passing along knowledge, or can involve more specific leadership, supervisory, or teaching roles.

Several ethical issues are addressed in the Texas Board of Nursing Position Statements [9]. These include the issue of initiation of cardiopulmonary resuscitation (CPR) in long-term care residents in the absence of a do not resuscitate (DNR) order (e.g., when initiation of CPR would appear futile and inappropriate given the nursing assessment of the resident, despite the premise that a DNR order may only be given by a physician). Other ethical issues discussed in the Position Statements include care of those with whom the nurse has a personal relationship and issues of patient confidentiality and privacy with regard to the use of social media. Reading, thought, and discussion about ethics and potential ethical dilemmas can help nurses respond appropriately and can help prevent unethical behaviors from occurring in the workplace.

There are also a variety of legal issues that affect the provision of nursing care and maintenance of a nursing license. It is important to note that, although possibly related, the laws governing nursing practice are different from the ethical framework(s) that nurses use to guide decision making. Laws pertaining to documentation, licensure, and standards of care have been established to ensure that nurses practice within a defined scope of practice and are aware of the boundaries of independent nursing action and responsibilities. These laws also act to hold nurses accountable for maintaining an acceptable standard of patient care. However, perhaps the greatest legal concern for nurses is the threat of negligence or malpractice claims.

The tort (or medical malpractice) liability system is intended to provide deterrence to clinicians who willful or negligently injure patients; deterrence is theoretically achieved by holding practitioners legally liable for their actions or omissions [12]. According to tort law, four elements must be established for a ruling of malpractice [13]:

- Duty: The nurse owed a duty to meet a particular standard of care.
- Breach of duty: The nurse failed to perform the owed duty.
- Causation: There is a causal connection between the nurse's failure and the patient's injury.
- Damages: An injury occurred for which monetary compensation is adequate relief.

These elements must be shown by a "preponderance of the evidence," defined as more than 50% probability, a lower standard than the "beyond a reasonable doubt" used in criminal law [14; 15]. Malpractice cases are decided on the basis of what a "jury is likely to think is fact" rather than actual fact [16].

PROFESSIONAL BOUNDARIES AND UNPROFESSIONAL CONDUCT

What nursing actions constitute unprofessional conduct?

Another facet of ethical care and practice involves maintaining appropriate limits in the nurse/patient relationship. Based on the idea that there is an imbalance of power and potential for abuse in this relationship (due to the nurse's power and the patient's vulnerability), the State of Texas requires all nurses to be familiar with and abide by the laws and rules regarding the limits of the nurse/patient relationship [3; 17]. Nurses should strive to promote the patient's best interests, dignity, and independence and refrain from inappropriate involvement in the patient's personal relationships and/or the obtainment of personal gain at the patient's expense. Violating professional boundaries of the nurse/patient relationship includes, but is not limited to, emotional, financial, physical, or sexual exploita-

tion of the patient or the patient's family [16]. These violations and other types of unprofessional conduct are grounds for disciplinary action by the Board.

The State of Texas defines unprofessional conduct, in Texas Administrative Code Rule 217.12, as "unprofessional or dishonorable behaviors of a nurse that the Board believes are likely to deceive, defraud, or injure clients or the public" [17]. These behaviors include but are not limited to [17]:

- Unsafe practice, including, but not limited to:
  - Carelessly failing, repeatedly failing, or exhibiting an inability to perform vocational, registered, or advanced practice nursing in conformity with the standards of minimum acceptable level of nursing practice set out in Rule 217.11
  - Carelessly or repeatedly failing to conform to generally accepted nursing standards in applicable practice settings
  - Improper management of client records
  - Delegating or assigning nursing functions or a prescribed health function when the delegation or assignment could reasonably be expected to result in unsafe or ineffective client care
  - Accepting the assignment of nursing functions or a prescribed health function when the acceptance of the assignment could be reasonably expected to result in unsafe or ineffective client care
  - Failing to supervise the performance of tasks by any individual working pursuant to the nurse's delegation or assignment
  - Failure of a clinical nursing instructor to adequately supervise or to assure adequate supervision of student experiences
- Failure of a chief administrative nurse to follow appropriate and recognized standards and guidelines in providing oversight of the nursing organization and nursing services for which the nurse is administratively responsible
- Failure to practice within a modified scope of practice or with the required accommodations, as specified by the Board in granting a coded license or any stipulated agreement with the Board
- Careless or repetitive conduct that may endanger a client's life, health, or safety (whether or not actual injury to a client is established)
- Inability to practice safely, as defined by demonstration of actual or potential inability to practice nursing with reasonable skill and safety to clients by reason of illness; use of alcohol, drugs, chemicals, or any other mood-altering substances; or as a result of any mental or physical condition
- Misconduct, including, but not limited to:
  - Falsifying reports, client documentation, agency records, or other documents
  - Failing to cooperate with a lawful investigation conducted by the Board
  - Causing or permitting physical, emotional, or verbal abuse or injury or neglect to the client or the public, or failing to report same to the employer, appropriate legal authority, and/or licensing board
  - Violating professional boundaries of the nurse/client relationship, including but not limited to physical, sexual, emotional, or financial exploitation of the client or the client's significant other(s)
  - Engaging in sexual conduct with a client, touching a client in a sexual manner, requesting or offering sexual favors, or language or behavior suggestive of the same
  - Threatening or violent behavior in the workplace
  - Misappropriating, in connection with the practice of nursing, anything of value or benefit, including, but not limited to, any property (real or personal) of the client, employer, or any other person or entity; or failing to take precautions to prevent such misappropriation
  - Providing information that was false, deceptive, or misleading in connection with the practice of nursing
  - Failing to answer specific questions or providing false or misleading answers that would have affected the decision to license, employ, certify, or otherwise utilize a nurse
  - Offering, giving, soliciting, or receiving or agreeing to receive (directly or indirectly) any fee or other consideration to or from a third party for the referral of a client in connection with the performance of professional services
- Failure to pay child support payments as required by the Texas Family Code §232.001
- Diversion or attempts to divert drugs or controlled substances
- Dismissal from a Board-approved peer assistance program for noncompliance and referral by that program to the Board
- Other drug-related actions or conduct including, but not limited to:
  - Use of any controlled substance or any drug (prescribed or unprescribed), device, or alcoholic beverages while on duty or on call and to the extent that such use may impair the nurse's ability to safely conduct to the public the practice authorized by the nurse's license

  - Falsification of or making incorrect, inconsistent, or unintelligible entries in any agency, client, or other record pertaining to drugs or controlled substances
  - Failing to follow the policy and procedure in place for the wastage of medications at the facility where the nurse was employed or working at the time of the incident(s)
  - A positive drug screen for which there is no lawful prescription
  - Obtaining or attempting to obtain or deliver medication(s) through means of misrepresentation, fraud, forgery, deception, and/or subterfuge
- Unlawful practice, including, but not limited to:
  - Knowingly aiding, assisting, advising, or allowing an unlicensed person to engage in the unlawful practice of vocational, registered, or advanced practice nursing
  - Violating an order of the Board; carelessly or repetitively violating a state or federal law relating to the practice of vocational, registered, or advanced practice nursing; or violating a state or federal narcotics or controlled substance law
  - Knowingly aiding, assisting, advising, or allowing a nurse under Board order to violate the conditions set forth in the order
  - Failing to report violations of the Nursing Practice Act and/or the Board's rules and regulations
- Leaving a nursing assignment (including a supervisory assignment) without notifying the appropriate personnel

WORKPLACE VIOLENCE

In 2018, the Board issued a new position statement addressing workplace violence [9]. It is important for the interprofessional team to work collaboratively in support of an effective violence prevention program. This includes acknowledging the value of a safe, violence-free workplace; ensuring and exhibiting equal commitment to the safety and health of workers and patients; and maintaining a system of accountability for all involved members of the healthcare team [9].

THE USE OF SOCIAL MEDIA

The issue of exploitive or inappropriate use of patient information or images on social media is becoming increasingly significant. As discussed, the Board of Nursing Position Statement 15.29: Professional Boundaries Including Use of Social Media by Nurses offers clarification on the relevant ethical and legal issues regarding this topic, including the use of social media as a beneficial tool for nurses and patients alike. The statement emphasizes that confidentiality and privacy extend to online posts or conversations and, more specifically, that [9]:

- Patient-related images are not to be transmitted via electronic media, regardless of whether the patient is identified by name; taking photo or video of patients with personal devices, including cell phones, is prohibited. Images taken for legitimate purposes, using employer-provided devices, may be allowed based on employer policy.
- Use caution when having online social contact with patients or former patients. The fact that a patient may initiate contact with the nurse does not permit a personal relationship.
- Nurses should not make disparaging remarks about patients, co-workers, or employers on social media, even if persons are not identified.

For the full text of the Position Statement regarding the use of social media by nurses, and all other Position Statements, please visit https://www.bon.texas.gov/practice_bon_position_statements.asp.html.

CONCLUSION

It is the responsibility of the Texas Board of Nursing to enforce the rules regulating the practice of nursing as the rules are currently stated—not how individuals may wish them to be. As nurses are affected by these rules and regulations, they have the responsibility to keep informed of regulatory changes in order to maintain licensure. It should be remembered that practicing within the minimum standards, though a necessity, is not all that is expected of nurses. Fulfilling ethical obligations to patients, co-workers, employers, and society is also an important part of health care, and it is only when the regulatory and ethical aspects of practice are combined that a nurse can be fully effective.

Customer Information and Evaluation are located on pages 79–80.

Human Trafficking and Exploitation: The Texas Requirement

This course has been approved by the Texas Health and Human Services Commission (HHSC) to meet the requirement for human trafficking training.

Audience
This course is designed for Texas physicians, nurses, social workers, pharmacy professionals, therapists, mental health counselors, and other members of the interdisciplinary team who may intervene in suspected cases of human trafficking Course Objective

As human trafficking becomes an increasingly more common problem in the United States, healthcare and mental health professionals will require knowledge of human trafficking patterns, the health and mental health needs of human trafficking victims, and successful interventions for victims. The purpose of this course is to increase the level of awareness and knowledge about human trafficking and exploitation so health and mental health professionals can identify and intervene in cases of exploitation.

Learning Objectives
Upon completion of this course, you should be able to:

1. Define human trafficking.
2. Identify the forms of human trafficking.
3. Identify individual, family/relationship, community/organizational, and societal/cultural factors that contribute to human trafficking.
4. Analyze the trafficking experience, including how traffickers recruit and the financial implications of trafficking.
5. Explain the psychological, health, and social consequences of human trafficking.
6. Utilize interviewing strategies to assess and identify victims and promote the ethical treatment of trafficking victims.
7. Outline the healthcare professional's responsibilities in identifying and assisting survivors of trafficking, including best practices for referral and collaboration. and/or exploitation.

Faculty
Alice Yick Flanagan, PhD, MSW, received her Master's in Social Work from Columbia University, School of Social Work. She has clinical experience in mental health in correctional settings, psychiatric hospitals, and community health centers. In 1997, she received her PhD from UCLA, School of Public Policy and Social Research. Dr. Yick Flanagan completed a year-long post-doctoral fellowship at Hunter College, School of Social Work in 1999. In that year she taught the course Research Methods and Violence Against Women to Masters degree students, as well as conducting qualitative research studies on death and dying in Chinese American families.

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Faculty Disclosure
Contributing faculty, Alice Yick Flanagan, PhD, MSW, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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INTRODUCTION

Human trafficking is not a new social problem; it has always existed. Trafficking has recently received increased attention as a result of awareness and outreach efforts. It has garnered attention from feminists, religious conservatives, labor activists, immigration specialists, and the mental health professions [1]. This course will provide a basic overview of human trafficking (e.g., the scope, definitions and frameworks, contributing factors, different forms). The course will attempt to provide practitioners a glimpse of the lives of human trafficking victims, including the physical, psychological, social, and sexual abuse that human trafficking victims experience and the types of control tactics that perpetrators use. Specific interventions and responses will be covered, including mental health, social services, educational, prevention, and legal efforts. Finally, for practitioners who work with human trafficking victims, the emotional toil that it takes on practitioners as well as the importance of self-care will be discussed. Practitioners will be encouraged to view films and documentaries about human trafficking, as this is one way to "enter the lives" of human trafficking victims and better understand the dynamics of the complex world of human trafficking.

BACKGROUND

Because human trafficking is a complex issue, it is difficult to determine the scope of the problem. Many scholars and researchers believe that published estimates are just educated guesses. On a global level, the International Labour Organization has estimated that there were 49.6 million people living in modern slavery in 2021, 27.6 million in forced labor, and 22 million in forced marriage [2]. The estimates for the United States are not totally clear, but there were approximately 78,000 human trafficking victims reported to the U.S. State Department in 2016; only an estimated 0.2% are rescued [3]. According to Polaris, which founded and runs the National Human Trafficking Hotline, there have been a total of 40,200 cases of human trafficking reported since 2007 [3]. According to statistics from the U.S. Department of Justice, the number of persons prosecuted for human trafficking increased from 729 in 2011 to 1,343 in 2020, an 84% increase [4].

A wide range of laws have been established to protect human trafficking victims and to prosecute perpetrators. A general knowledge of these laws is helpful when caring for victims and seeking appropriate social services. The Trafficking Victims Protection Act (TVPA) was enacted in 2000 and reauthorized in 2003, 2005, 2008, 2013, 2018, and 2022 by the Trafficking Victims Protection Reauthorization Acts [5]. It emphasizes the three Ps: prevention, protection, and prosecution [5]. The prevention component consists of training and awareness; the protection dimension gives trafficked victims the ability to receive services using federal funds like other refugees; and the prosecution component focuses on laws and policies for the prosecution of traffickers.

Because victims of trafficking are often viewed as criminals, this law states that victims of severe trafficking should not be penalized for any illegal behaviors or acts they engaged in as a result of being trafficked, including entering the United States with false documents or no documentation or working without appropriate paperwork [6]. This law also allows T Nonimmigrant Status (T visas) to be granted to victims of trafficking so they may remain in the United States with the purpose of collaborating with the federal authorities to prosecute the perpetrators. During this time, victims are offered a range of benefits and services, including access to the Witness Protection Program [6]. After three years, victims can apply for permanent resident status [7].

One of the criticisms of the Act is that it places the burden of demonstrating innocence and coercion on the victim [8]. The Act also fails to recognize the complex dynamics of human trafficking. For example, it focuses more on sex trafficking versus other forms [9]. Many victims have been abused and terrorized by the perpetrators, who they must now provide information and evidence against to stay in the country. Victims are continually fearful that they will be deported [8].

Victims who are of minor age are eligible for Unaccompanied Refugee Minors programs, the Children's Health Insurance program, and Temporary Assistance to Needy Families [10]. Furthermore, victims between 16 and 24 years of age are eligible for work permits and can apply for the Job Corps program [10]. It is important to remember that the key to this law is that the victim must have experienced a "severe form" of trafficking and must be willing to assist in the apprehension and prosecution of the perpetrator to receive services [11].

DEFINITIONS OF HUMAN TRAFFICKING

How does the United Nations define human trafficking?

The United Nations defines human trafficking as [12]:

> The recruitment, transportation, transfer, harbouring or receipt of persons, by means of threat or use of force or other forms of coercion, of abduction, of fraud, of deception, of the abuse of power or of a position of vulnerability, or of the giving or receiving of payments or benefits to achieve the consent of a person having control over another person, for the purpose of exploitation. Exploitation shall include, at a minimum, the exploitation or the prostitution or other forms of sexual exploitation, forced labour or services, slavery or practices similar to slavery, servitude, or the removal of organs.

In essence, this definition involves three elements: the transport of the person, the force or coercion of the victim, and the abuse and exploitation [13]. The United Nations Office on Drugs and Crime divides the definition of human trafficking into three sections: the act, means, and purpose [14]. The act, or what is done, generally refers to activities such as recruitment, transportation, transfer, harboring, or receipt of persons. The means of trafficking consists of threats or use of force, coercion, abduction, fraud, deception, abuse of power or vulnerability, or giving payments or benefits to a person in control of the victim. Finally, these acts are carried out for the purpose of exploitation, which includes prostitution, sexual exploitation, forced labor, slavery or forced servitude, and the removal of organs [14].

The TVPA defines human trafficking to include both sex trafficking and labor trafficking [15]:

> Sex trafficking is the recruitment, harboring, transportation, provision, obtaining, patronizing, or soliciting of a person for the purposes of a commercial sex act, in which the commercial sex act is induced by force, fraud, or coercion, or in which the person induced to perform such an act has not attained 18 years of age. Labor trafficking is the recruitment, harboring, transportation, provision, or obtaining of a person for labor or services, through the use of force, fraud, or coercion for the purposes of subjection to involuntary servitude, peonage, debt bondage, or slavery. A victim need not be physically transported from one location to another for the crime to fall within this definition.

In many cases, women and children are considered the typical victims of human trafficking. Hart posits that women are more vulnerable to trafficking due to the lack of social safety nets in many developing countries [16]. Coupled with women's subordinate social status in many cultures, this leads to the "feminization of poverty." Although the social conditions may make women and children more vulnerable to human trafficking, the reality is that men are also victims of human trafficking.

Overall, the definition of human trafficking is ambiguous because of the many intersections with other issues (e.g., sexual abuse, domestic violence, forced marriage, forced labor) [17]. It occurs both domestically and internationally, but is primarily a hidden problem. This makes research efforts, the prosecution of perpetrators, and policy and community efforts to protect victims even more challenging [17]. It is vital to remember that trafficking, as defined by U.S. law, does not require crossing international or even state borders. The transport of victims from one locale to another is not a necessary component of determining whether human trafficking has occurred.

LIMITATIONS OF DATA ON HUMAN TRAFFICKING

Although the United Nations definitions are used in this course, scholars, practitioners, researchers, and policy makers have not come to a consensus definition of human trafficking. Consequently, terms such as sexual slavery, human smuggling, and modern-day slavery have all been used [18]. When the term human trafficking is utilized, it often has connotations of sexual exploitation affecting mainly women and girls, the most visible victims, but this is not accurate [18]. This perspective is partially attributable to the large number of religious and feminist organizations who have worked to eradicate non-consensual sex work [19]. This lack of consensus definition also raises questions about the study population in the research. The involved parties (i.e., the trafficker, those who are trafficked, and the networks) are continually changing in time and space [20].

Defining these terms is essential because it will ultimately influence responses to human trafficking. As stated, all social problems are competing for attention and resources, and the response is influenced by how the social problem is defined and portrayed [21]. Ultimately, the lack of a consensus definition is one of the reasons studying human trafficking has been a challenge and that research yields unreliable prevalence estimates.

Another reason human trafficking has been a difficult topic to research is the hidden and invisible nature of its victims and perpetrators. This makes it difficult for researchers to use traditional sampling methods. Even if trafficked victims are identified, perpetrators can move them to new locations [22]. If and when researchers access this hidden population, victims are often reluctant to talk due to fear, shame, and the stigma associated with their experiences. Consequently, much of what has been studied has relied on interviews with professionals (e.g., lawyers, advocates, police/law enforcement, and other service providers), which has led to recommendations that are not based on firsthand accounts [23].

A host of ethical issues also arise for those conducting research in this area. Protecting study participants' identities is paramount, and consequently, study participants signing informed consent forms, which are often required by institutional review boards, becomes complicated. Understandably, victims and perpetrators often will not want to sign forms using their real names for fear of deportation, arrest, and/or reprisals [22].

FORMS OF TRAFFICKING

The social realities of victims of human trafficking are difficult to comprehend, and some may wonder why victims remain silent and comply with their traffickers. The Silence Compliance Model was created to explore the factors that promote victims' seeming willingness to comply with their traffickers' demands [24]. This model has three categories: coercion, col-

lusion, and contrition. Victims are coerced, brutalized, and threatened, and basic necessities of life are withheld from them. Methods of psychological coercion include isolation, induced exhaustion, threats, degradation, and monopolizing perception [25]. This serves to silence victims and create a sense of helplessness. By isolating and controlling victims' movements and limiting their exposure to the outside world, traffickers have complete monopoly of their attention and perception of reality [25]. Victims are then forced to collude with the traffickers as a result of their relative isolation, fear, false sense of belonging, and complete dependence on the trafficker. Finally, victims feel contrite, ashamed, stigmatized, and remorseful of the things they have been made to do [24].

Another model, the Action-Means-Purpose (AMP) Model, is a device used to illustrate and articulate the federal definition of a "victim of severe forms of trafficking in persons" [26]. The Action category consists of the actions a perpetrator takes to induce, recruit, harbor, transport, provide, or obtain a victim. The Means of force, fraud, or coercion are used for the ultimate Purpose of commercial sex or labor/services trafficking [26].

It is important to remember that human trafficking is not human smuggling. Human smuggling involves an individual being brought into a country through illegal means and is voluntary. The individual has provided some remuneration to another individual or party to accomplish this goal [7].

SEX TRAFFICKING

What is domestic minor sex trafficking?

The TVPA of 2000 is a U.S. federal statute passed by Congress to address the issue of human trafficking and offers protection for human trafficking victims [15]. This statute defines sex trafficking as, "the recruitment, harboring, transportation, provision, or obtaining of a person for the purpose of a commercial sex act" [15]. A commercial sex act is, "any sex act on account of which anything of value is given to or received by any person" [15]. In other words, it usually involves the illegal transport of humans into another country to be exploited in a sexual manner for financial gain [27]. However, it does not always involve the transport of victims from one region to another; such cases are referred to as "internal trafficking" [28]. Victims of sex trafficking could be forced into prostitution, stripping, pornography, escort services, and other sexual services [29]. Victims may be adult women or men or children, although there is a higher prevalence of women and girls. The term "domestic minor sex trafficking" has become a popular term used to connote the buying, selling, and/or trading of children younger than 18 years of age for sexual services within the country, not internationally [29; 30]. An element of force, fraud, or coercion is not necessary, as the victims are children and inherently vulnerable [30]. In the United States, the children most vulnerable to domestic minor sex trafficking are those who are homeless, abused, runaways, and/or in child protective services [29].

Although controversial, it is said that sex trafficking victims differ from consensual sex work in that sex trafficking victims are forced to involuntarily perform sexual services and are often not paid for their "work." Sex trafficking involves the use of force and coercion and can encompass other forms of criminal sexual activities, including forced erotic dancing, "mail-order brides," and pornography [28]. On the other hand, individuals involved in consensual sex work make a decision to provide sex services for a fee. The decision to enter sex work does not eliminate the possibility of being a victim of trafficking if one is held against his/her will through physical and/or psychological abuse [4]. It is also important to remember that this does not necessarily mean sex work is a choice these individuals would have made if other options were available or that they have a choice in selecting their sexual partners and/or sexual activities [31].

BONDED LABOR/FORCED LABOR

The United Nations has defined debt bondage as [32]:

> The status or condition arising from a pledge by a debtor of his personal services or of those of a person under his control as security for a debt, if the value of those services as reasonably assessed is not applied towards the liquidation of the debt or the length and nature of those services are not respectively limited and defined.

Essentially, because the individual does not have money as collateral for the debt owed, the individual pledges his/her labor or, in some cases, the labor of a child or another individual for an unspecified amount of time [33]. These individuals may be transported or trafficked into another country for the purpose of forced labor.

In many cases of bonded labor, the initial loan may be welcomed by the individual. However, the victims do not realize that with the low wages, unspoken high interest rates and other continually accruing fees, and the perpetrator's manipulation of the "accounts," laborers can never repay the loans. Some estimate that half of all persons in forced labor are bonded laborers. The majority of bonded labor cases occur in India, Bangladesh, and Pakistan [34]. Some families find themselves in a cycle of poverty as the debt cannot be paid off and is passed down from generation to generation [33]. Bonded labor can involve laborers in brick kilns, mines, stone quarries, looming factories, agricultural farms, and other manufacturing factories [33]. In the United States, individuals may be trafficked to work long hours in garment factories, restaurants, and other manufacturing sectors. Frequently, the employer/captor will take away victims' identifications, monitor their movements, socially isolate them, and/or threaten deportation if they do not comply [35]. Migrant workers are at high risk of forced labor [4].

In the United States, forced labor is predominantly found in five sectors [35]:

- Prostitution and sex industry (46%)
- Domestic servitude (27%)
- Agriculture (10%)
- Sweatshops and factories (5%)
- Restaurant and hotel work (4%)

It is speculated that most of the forced labor occurs in California, Florida, New York, and Texas, all major routes for international travel [35].

Domestic servitude refers to a category of domestic workers (usually female) who work in forced labor as servants, housekeepers, maids, and/or caregivers, often in private homes. In some cases, young women are lured with the promise of a good education and work, and when they arrive in the United States, they are exploited economically, physically, and/or sexually. Their passports or identification papers are taken away, and they are told they have to pay off the debt incurred for their travel, processing fees, and any other bogus expenses. Because they do not speak English, they find they have no other recourse but to endure exploitative working conditions [36]. Unfortunately, as in many sectors of forced labor, there are no regulations to monitor the conditions under which domestic servants operate [35].

CHILD LABOR

Child labor can be viewed as a specific form of bonded labor or forced labor. However, not all child laborers have been trafficked. Child labor is defined by International Labour Organization (ILO) as economic labor performed by a child younger than 15 years of age or hazardous labor done by a child 18 years of age or younger. Child labor is deeply rooted in poverty and the infrastructure and political stability of the country as well as market forces [37]. The ILO estimates that there were 160 million child laborers in the world in 2020 (63 million girls and 97 million boys) [38]. This accounts for nearly one in ten of all children worldwide [38]. Between 2000 and 2020 there was a nearly 35% decrease in the number of children in child labor. The reduction was greater for girls than for boys . The number of children in child labor has increased from 2008 to 2020 in sub-Saharan Africa (from 65.1 million to 86.6 million), while it has declined in other parts of the world (e.g., Asia/the Pacific, Latin America/the Caribbean) [38].

The definition of child labor is controversial because the definitions for "work" and "childhood" are ambiguous and often culturally defined [39]. On a conceptual level, work may be beneficial for the socialization and educational processes of children [39; 40]. So, it is important to differentiate between child work and child labor. Child work has been defined as activities that are supervised by an adult and that promote the development and growth of the child, while child labor does not benefit the child [37]. Many definitions of child labor create a dichotomy whereby child work is considered not harmful while child labor has negative emotional, intellectual, and social consequences [41]. Work that is exploitative for children has been defined as working long hours at a young age, work that is poorly compensated, and work that produces physical, social, and psychological stress that will hamper development, access to education, and self-esteem [42]. The ILO adds that child labor is work that "interferes with their schooling by: depriving them of the opportunity to attend school; obliging them to leave school prematurely; or requiring them to attempt to combine school attendance with excessively long and heavy work" [40].

It is important to remember that child labor occurs in the United States. Runaway and homeless youths are at greatest risk, often lured by promises of work and housing [43]. The Polaris Project found that the top three forms of child labor trafficking in the United States were begging, peddling, and traveling sales crews [43].

CHILD CONSCRIPTION

In some cases of trafficking, children are kidnapped and trafficked to serve as soldiers. Other times, children are coerced by a narrative indicating they will be serving a higher purpose and avenge the deaths of family and friends; this is known as comradeship [44; 45]. Some children are actively recruited and may be promised a small salary to "voluntarily" join.

It is estimated that at any one time up to 300,000 children younger than 18 years of age are serving as child soldiers [46; 47]. Traffickers prefer to recruit children to serve as soldiers because they are inexpensive and more easily molded and shaped to comply and obey without question [48]. It can be difficult to comprehend the atrocities that these children witness and experience [49; 50].

FACTORS THAT CONTRIBUTE TO VULNERABILITY TO HUMAN TRAFFICKING

INDIVIDUAL

A variety of individual level factors may predispose an individual to human trafficking victimization. A history of physical, sexual, or emotional abuse and/or of witnessing violence in the home has been identified at increased rates among trafficking victims. Other possible risk factors include adherence to rigid gender roles, acceptance of norms supporting sexual exploitation of women and children, overestimation of problem behavior in peers/others, lack of trafficking awareness, and substance abuse [51].

Adverse Childhood Experiences

In more recent years, research has focused on the impact of adverse childhood experiences (ACEs) in general. ACEs are defined as potentially traumatic experiences that affect an individual during childhood (before 18 years of age) and increase the risk for future health and mental health problems (including increased engagement in risky behaviors) as adults [52]. Abuse and neglect during childhood are clear ACEs, but other examples include witnessing family or community violence; experiencing a family member attempting or completing suicide; parental divorce; parental or guardian substance abuse; and parental incarceration [52].

One study found that youths with human trafficking reports were significantly more likely to have experienced ACEs [53]. Specifically, sexual abuse was the strongest predictor of human trafficking. Girls with a history of sexual abuse were 2.52 times more likely to experience human trafficking, and boys who had been victims of sexual abuse were 8.21 times more likely to be trafficked.

Poverty and Economic Disenfranchisement

Poverty and incessant economic stressors caused by civil wars, natural disasters, and collapses of government systems all contribute to human trafficking [16; 30; 54]. In one study, the odds of being trafficked were nine times greater for those who felt extremely hopeless about upward mobility compared with those with lower levels of hopelessness [54].

RELATIONSHIP/FAMILY

Families marked by instability (e.g., domestic violence, child abuse, continual unemployment) are also at higher risk of having a member trafficked [30]. In addition, families entrenched in deep poverty may feel they have no other recourse but to sell a child or may be more easily lured with promises of money and a better future [54; 55; 56].

COMMUNITY/INSTITUTIONAL

How does digital technology play a role in human trafficking?

Community factors (such as high social disorganization characterized by violence, unemployment, and high crime) contribute to higher risk of trafficking [30].

The rampant use of digital technology, such as the Internet, greatly facilitates sex trafficking. The relative anonymity of online contact can empower traffickers to recruit or sell victims. Graphic images of women and children engaged in sexual acts can be easily disseminated over the Internet [57]. Traffickers may employ the Internet for advertising, marketing to those interested in making pornography [57]. In addition, social media sites such as Facebook, Craigslist, and Instagram have been used as a means of facilitating trafficking (e.g., by connecting and grooming potential victims) [58; 59; 60]. Newsgroups offer opportunities for those interested in locating women and children for sexual exploitation.

In a 2013 qualitative study, smartphones were found to be integral in the business of trafficking [58]. Researchers indicated the phones were used "to maintain contact with each other, in order to facilitate the business 'transactions' and stay in touch with transnational 'partners' and other traffickers who remained in the country of origin" [58; 59].

SOCIETAL/CULTURAL

Globalization

Human trafficking has been called one of the "darkest sides of globalization" [61]. Globalization is the term used to describe the interconnectedness of countries and nations, which facilitates easy communication, exchange of ideas, and flow of goods, capital, and services [61]. Crimes such as human trafficking are affected by globalization just as legitimate businesses are [62]. Furthermore, the ideals of Western capitalism may reinforce human trafficking as a business or industry, with its emphasis on the free market and the flow of goods and services across international borders [62].

Globalization has also created the need for cheaper labor [34; 63]. A study involving 160 countries examined the effects of globalization and human trafficking trends [64]. Researchers found a positive relationship between globalization and trafficking for forced labor, sex work, and debt bondage.

Corruption

Human trafficking cannot occur without the existence of corruption within existing infrastructures. Public officials, police officers, and local leaders in many developing countries have been known to take bribes to provide protection to parties involved in various aspects of human trafficking [61; 64; 65].

Racialized Sexual Stereotypes

Race and ethnicity have been inextricably linked to sexual violence and victimization. Myths regarding sexuality in certain cultures or racial fetishization may affect trafficking patterns. For example, there is an over-representation of Asian women on American Internet pornography sites in part due to popular myths sexualizing, eroticizing, and exoticizing Asian women. This has translated into trafficking, as traffickers respond to the demand for young Asian women and girls in part fueled by these stereotypes of exotic, docile, submissive, and eager-to-please Asian women [36]. These stereotypes devalue and dehumanize people, which is the underlying core of human trafficking. This contributes to the acceptability of the exploitation of individuals, particularly members of marginalized groups [66].

These racial stereotypes go beyond simply framing the victims in a particular manner [67]. They raise implicit questions regarding how the powers of state are depicted. In other words, the patriarchal attitudes of certain countries lead to "bad" or "backward" cultural practices or ways of being that then cause trafficking—setting up a dichotomy of the "West" and "others" [67].

Culture

Although many are careful in linking cultural factors to the etiology of human trafficking for fear of imposing judgment on a particular culture, many maintain that cultural ideologies that tolerate sexual trafficking, bonded labor, and child labor may be a stronger factor than poverty in predicting trafficking rates [36; 42]. For example, some cultures emphasize collectivism and prioritizing the needs of the family and group first before the needs of the individual. Some children may feel they have to sacrifice themselves for their family when traffickers promise money [36]. Traffickers also know that they can threaten to hurt victims' families to keep them from escaping [36].

Furthermore, in many cultures, boys are more highly valued than girls, and as a result, girls are considered more dispensable [36]. Sons are considered the family's social security, staying with the family while daughters marry into other families. Therefore, girls may be more likely to be sold into slavery than boys.

Child labor is also inextricably tied to cultural factors. In India, for example, child labor is common because it is believed that children in the lower levels of the caste system (i.e., the "untouchables") should be socialized early to understand their position in society [42]. It has been observed that when traditional cultural and societal norms about women's roles were relaxed in some European countries and more women entered the labor force, child labor decreased [42]. Ultimately, it is difficult to unravel the effects of poverty and culture because the pressures of poverty can lead families to use tradition as a justification to sacrifice young men, women, and children [42].

Ultimately, the conversation about human trafficking is complex, and to attempt to isolate the causes is beyond challenging. Multiple factors have been suggested as possibly predicting human trafficking, including macroeconomic factors (e.g., gross domestic product per capita), unemployment rates, female inequality, cultural oppression, and lack of protection of women's rights [68; 69]. In one study, ease of land access to the destination country appeared to be a powerful predictor in terms of the number of individuals trafficked [68].

TRAFFICKERS: AN OVERVIEW

What are methods of recruitment used by human traffickers?

Much attention has been focused on the victims of trafficking; however, it is important to also understand the perpetrators.

It has been suggested human traffickers employ five general strategies to recruit and traffic victims [6; 70; 71; 72]:

- Kidnapping: Traffickers may kidnap their victims. They may lure them with food or treats or take them by force. Victims with few if any social ties are highly vulnerable, as no one will miss them or report their disappearance.
- Targeting poor families: Traffickers may convince families to sell their children (often daughters). Because many families in developing countries live in abject poverty, traffickers will stress to victims' families how the money will help them to survive. Other traffickers may tell families that selling their daughter will provide her with more promising opportunities.
- Developing a false romantic relationship with victim: A tactic often used with young girls, perpetrators pose as boyfriends by romancing victims, buying gifts, and proclaiming their love. Victims have a difficult time believing that their boyfriends would hurt or deceive them, making them easy targets for trafficking.
- Fake storefronts: Some employment, modeling, or marriage agencies are fronts for illegal trafficking operations. A potential victim might be lured with the promise of employment, a lucrative modeling contract, or an arranged marriage in the United States. After victims have been lured in, traffickers come to assess their "product." Perpetrators may be family members or friends.
- Legal storefronts: Some legal businesses in the tourism, entertainment, and leisure industries integrate trafficking activities into their business structure.
- Recruiting local sex workers: Traffickers might purchase sex workers working in local night clubs from brothel owners or simply lure sex workers by promising them a more affluent future. These trafficked sex workers may later recruit younger victims.

IMPACT ON VICTIMS/SURVIVORS

HEALTH CONSEQUENCES

What are common physical findings in trafficked women?

In studies of trafficked women, headaches, fatigue, dizziness, back pain, pelvic pain, stomach pain, sexually transmitted infections (STIs), unwanted pregnancies, and gynecologic infections were common, generally the result of continual physical, psychological, and sexual abuse [30; 73]. Victims of labor trafficking also experience health issues related to the type of work, workplace conditions, malnutrition, and violence [74]. It is important to remember that some of these somatic complaints, such as headaches, fatigue, and gastrointestinal problems, may be underlying symptoms of anxiety, depression, and stress [73]. Some cultural groups might not use the terms "depression," "sad," or "anxious," but may use metaphors and somatic symptoms to describe their pain, all of which are embedded within cultural ideologies. The most common culture-based idioms of distress are somatic symptoms. Some groups tend not to psychologize emotional problems; instead, they experience psychological conflicts as bodily sensations (e.g., headaches, bodily aches, gastrointestinal problems, and dizziness).

Using an in-depth, direct interview survey designed to explore each stage of the trafficking experience, a multi-country European study identified a range of aversive health, sexual, and reproductive consequences common among women and adolescent victims of human trafficking [75]:

- Pre-departure stage: All victims reported having had limited knowledge of the health implications of having sex with strangers, and only 1 in 25 felt well-informed regarding the risks of acquiring HIV or other STIs.
- Travel and transit stage: Half of those interviewed reported having been confined, beaten, and/or raped during the journey.
- Destination stage: A large majority reported having been "intentionally hurt" (as evidenced by contusions, lacerations, loss of consciousness, and signs of head trauma); subjected to solitary confinement and deprived of human contact and adequate food and nutrition; subject to a variety of physical ailments, including headache, fever, undiagnosed pelvic pain, urinary tract infection, STIs, rash/scabies, and oral/dental health issues. All had experienced repeated sexual abuse or coercion, and 1 in 4 reported at least one unintended pregnancy (often involving negative outcomes of abortions performed in unsafe and unhealthy conditions).

Child and Adolescent Victims

Among child victims of human trafficking, healthy growth and development is especially problematic. Malnourishment and poor hygiene often lead to delayed bone growth, poorly formed teeth, and early dental caries [76]. The intense nature of child labor also has severe negative physical and health consequences.

Under normal circumstances, young children are still developing physically; however, such adverse conditions can halt their development. The lungs of adolescent boys typically experience the most rapid growth around 13 to 17 years of age; working in conditions characterized by excessive toxic dust or unclean air makes them more vulnerable to developing silicosis and fibrosis [77]. In the United States, young children participating in agricultural work are at risk of the major traumas associated with farm work, such as injuries caused by tractors or falling from heights, in addition to those injuries associated with repetitive stress and exposure to toxins. Children have thinner layers of epidermis, which make them more vulnerable to the toxicity of pesticides, and this can ultimately increase their risks for certain cancers [77]. Children working in gold mines do intensive digging, lifting, and transporting and mix mercury with the crushed ore, often with their bare hands. Mercury toxicity can lead to neurologic symptoms such as loss of vision, tremors, and memory loss [78].

DENTAL CONSEQUENCES

Victims may present with dental trauma and loss of teeth from violent acts. Injuries to the face and mouth area are common in abuse cases, and the potential for tooth involvement is high. Other dental problems arise as well, including infectious complications due to HIV, and even oral cancers or gingival disease due to substance use or poor access to dental care [79].

SEXUAL/REPRODUCTIVE HEALTH CONSEQUENCES

In the context of forced sex work among trafficked victims, safeguards against infection (e.g., regular condom use), early diagnosis, and adequate antimicrobial treatment are inconsistently employed or absent entirely [75]. Consequently, in addition to unwanted pregnancy, the risk for pelvic inflammatory disease and subsequent infertility is relatively high. Moreover, the relationship between forced sex work and HIV infection is stronger when sexual violence is involved. Women who are forced into sex work are 11 times more likely to become HIV-infected than women who engage in consensual sex work [80]. Sexual violence may increase the transmission risk as a result of open abrasions and injuries to the vagina. Furthermore, sexual violence can negatively impact self-esteem, which could then deter victims from advocating more strongly for condom use [80].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The British Association for Sexual Health and HIV has identified trafficked women/commercial sex workers as a group vulnerable to sexual violence. Inquiries about such vulnerabilities will help to identify those in need of additional support and help to facilitate appropriate referrals to mental health services, general practitioners, and support agencies. Access to interpreter and advocacy services may be helpful.

(https://www.bashhguidelines.org/media/1079/4450.pdf. Last accessed January 25, 2024.)

Level of Evidence: Expert Opinion/Consensus Statement

PSYCHOLOGICAL AND MENTAL HEALTH CONSEQUENCES

Victims of trafficking experience a host of psychological, mental health, and emotional distress. Depression, suicidal ideation, substance use, and anxiety are typically cited mental health problems [30]. Post-traumatic stress disorder (PTSD) is also common given the trauma many victims experience, including physical and/or sexual violence and abuse; victims forced into sex work experience continual, daily sexual assault [81]. In a study of 192 European women who were trafficked but who managed to escape, the overwhelming majority (95%) disclosed that they experienced physical and sexual violence during the time of their trafficked experience [73]. More than 90% reported sexual abuse, and 76% reported physical abuse.

Trafficked victims experience fear from the start of their capture through the transit phase and after they arrive at their destination. During the transit stage, many victims experience dangerous border crossings, risky types of transports, injury, beatings, and sexual assault [75]. Upon arrival to their destination, many trafficking victims have been socially isolated, held in confinement, and deprived of food [82]. All sense of security is stripped from them—their personal possessions, identity papers, passports, visas, and other documents are taken [75; 82]. The continual fear for their personal safety and their families' safety and the perpetual threats of deportation ultimately breed a sense of loss of control and learned helplessness. It is not surprising that depression, anxiety, and PTSD are common symptoms experienced by trafficked victims.

In a study of 164 survivors of human trafficking who returned to Nepal, the authors examined the extent to which they experienced PTSD, depression, and anxiety [83]. All of the survivors experienced some level of these disorders, but the survivors who were trafficked for sex experienced higher levels of depression and PTSD compared to those who were not trafficked for sex. In a study with Moldovan survivors of human trafficking, researchers found that six months after their return, 54% had a diagnosable mental health issue. Specifically, 35.8% met the diagnostic criteria for PTSD, 12.5% met the criteria for major depression, and 5.8% were diagnosed with an anxiety disorder [84].

There is also some evidence that trafficked victims may experience complex PTSD, a type of PTSD that involves an acute change of the victims' sense of self, their relationship with others, and their relationship with God or a higher being [85]. These persons direct anger inwardly (toward themselves) as well as toward their perpetrators, which results in a loss of faith in themselves and the world [82; 85; 86]. Perhaps due to self-directed anger and shame, some will engage in risky sexual behaviors, self-harm, and substance abuse. Some victims also have difficulty managing and expressing how they are feeling, while others experience dissociation [82].

Substance abuse is also common among victims. In interviews, trafficked women discussed how traffickers forced them to use substances like drugs and/or alcohol so they could work longer hours, take on more clients, and/or perform sexual acts that they could not normally perform [75]. Other victims used substances as a means to cope with their situations. Trafficked individuals who are gender and/or sexual minorities report shame, confusion, and sexual identity issues if forced into heterosexual relationships [86].

Children forced into labor experience grueling hours and are frequently beaten by their captors. Underage victims of domestic sex trafficking fluctuate through a range of emotions, including despair, shame, guilt, hopelessness, anxiety, and fear [87]. Depending upon the level of trauma, some engage in self-destructive behaviors like self-mutilation or suicide attempts. For some, their ambivalence toward the perpetrators may be confusing. On the one hand, they want to escape the abuse, yet simultaneously, they may have a sort of traumatic bond with the perpetrators [87].

Children forced into conscription will also experience a host of psychological symptoms. In a study comparing former Nepalese child soldiers and children who were never conscripted, former child soldiers experienced higher levels of depression, anxiety, PTSD, psychological difficulties, and functional impairments [88]. In another study of former child soldiers from the Congo and Uganda, one-third met the criteria for PTSD [49]. The researchers found there was a relationship between greater levels of PTSD symptoms and higher levels of feelings of revenge and lower levels of openness to reconciliation [49]. In-depth narrative interviews of former child soldiers from northern Uganda found that the children spoke of the violence and atrocities they witnessed without any emotion, as if they had removed themselves from their experiences [89]. This speaks to how the victims have to numb themselves psychologically in order to cope. The researchers also found that the children who lost their mothers were more traumatized by this experience than by the violence they witnessed as soldiers.

Some have argued that the diagnostic criteria of PTSD may not be easily applied to those from different cultures. As a result, it is important to assess for other psychiatric disorders, such as depression. Japan, for example, never used the PTSD diagnosis prior to 1995, despite the fact that they have a large and intricate mental health system [90]. Ultimately, PTSD cannot be universally applied to every culture and for every humanitarian crisis; therefore, if a human trafficking victim does not necessarily fall within the *Diagnostic and Statistical Manual of Mental Disorders* criteria for PTSD, one cannot necessarily conclude that they have not experienced trauma or are not traumatized [90].

SOCIAL CONSEQUENCES AND QUALITY OF LIFE

When rescued and attempting to reintegrate into their communities, victims of human trafficking often experience stigma, ostracism, and marginalization [88; 91]. For example, in Nepal, community members perceived returning child soldiers who had performed acts such as carrying dead bodies or coed sleeping as in violation of Hindu cultural norms [88]. One documentary following former child soldiers living in a refugee camp in northern Uganda found that preconceived notions and myths about children soldiers often led to ridicule and ostracism after they were liberated from the army and returned home.

However, girls who were recruited as soldiers, who were forced to have sex, or who return with children appear to be the most marginalized group [92]. In a qualitative study of former girl soldiers in Sierra Leone, researchers found that, compared to returning boy soldiers, girls were perceived to have violated gender norms and values about sexuality. Although psychologically and developmentally they were still children, the community perceived and treated them as "damaged" or "unclean" women. Their communities were not able to re-integrate them, despite the victimization they experienced. These girls lacked voice and experienced shame, marginalization, poverty, and powerlessness upon their return [92]. In a study of former child soldiers in Uganda, the children reported having difficulty finding jobs or getting married when they returned home. Girls who had been raped were stigmatized and made to feel unwelcome in their communities. Others stated that their community perceived them as murderers [50].

IDENTIFICATION AND ASSESSMENT

INTERACTION WITH VICTIMS

Healthcare providers are often the most likely to encounter a victim of human trafficking under circumstances that provide an opportunity to intervene, and victims may be encountered in most mental health and healthcare venues. One study estimated that 30% to 87.8% of victims accessed medical services at some point during their trafficking [93]. Survivors may seek care in hospital emergency rooms, at local mental health authorities, urgent care facilities, family planning clinics, or outpatient medical settings for a variety of issues, including sexually transmitted infections, pregnancy, depression (including suicidality), injuries resulting from assault, substance abuse-related issues, and PTSD [94]. Because medical and dental appointments may allow for more privacy than a victim's other encounters, they may represent a unique opportunity for healthcare providers to intervene.

Yet, many providers lack the training and confidence to identify and assist victims. In a survey of 110 emergency department physicians, nurses, and physician assistants, the majority (76%) reported having a knowledge of human trafficking, but only 13% felt equipped to identify a trafficking victim and only 22% were confident in their ability to provide satisfactory care for such patients [95]. Less than 3% had ever received any training on this topic. In a separate survey of healthcare and social service providers, only 37% had ever received training on identification of trafficking victims [96]. This lack of healthcare provider knowledge is the root of some victim's reluctance to disclose.

Because human trafficking and exploitation are, by nature, covert processes, the identification and rescue of the victim can be difficult. As stated, traffickers often move victims from one area to another to reduce the risk of identification, and one of the main problems with the assessment of such individuals is that practitioners may only have a one-time encounter with the victim [97]. Other provider challenges include language barriers, the hidden nature of the crime, lack of self-identification as a victim, confusing or contradictory laws/regulations, lack of organizational protocols, and stereotypes/misconceptions [98].

Several barriers exist that prevent survivors from self-disclosing their experiences, including [98]:

- Unable to self-identify
- Lack of knowledge of services
- Fear of retaliation
- Fear of law enforcement/arrest/deportation
- Lack of trust
- Shame/stigma
- Learned helplessness/PTSD
- Cultural/language barriers
- Lack of transportation

TRAUMA-INFORMED CARE

All interactions with patients, regardless of whether or not they are potential victims of trafficking, should be centered on the patient's experiences, needs, and preferences. Providing patient-centered care means that care will be respectful of and responsive to individual patient preferences, needs, and values and will reflect the patient's values. This should be considered at all stages of assessment, intervention, and continued care/follow-up.

It is important to use a trauma-informed approach when assessing and caring for potential victims, which requires that practitioners understand the impact of trauma on all areas of an individual's life [99]. Physical, emotional, and psychological safety is at the heart of trauma-informed care. This approach allows for trust-building and continued communication, two factors that are vital to ensuring that patients receive the care and support they require.

Being trauma-informed is a strengths-based approach that is responsive to the impact of trauma on a person's life. It requires recognizing symptoms of trauma and designing all interactions with victims of human trafficking in such a way that minimizes the potential for re-traumatization. This involves creating a safe physical space in which to interact with survivors as well as assessing all levels of service and policy to create as many opportunities as possible for survivors to rebuild a sense of control. Most importantly, it promotes survivor empowerment and self-sufficiency. Survivors should also have access to services that promote autonomy and are comprehensive, victim-centered, and culturally appropriate. Additionally, trafficking survivors share that one of the most important steps to being trauma-informed is to be survivor-informed [100].

POTENTIAL RED FLAGS

Bruises, scars, and other signs of physical abuse may be missed on examination, as victims are often beaten in areas hidden by clothing (e.g., the lower back) so as not to affect the victim's outer appearance. Physical trauma symptoms may be present, commonly on the torso, breast, and/or genital areas [101]. Burns, broken bones, pelvic pain, and/or STIs (particularly in children) may also be red flags [102]. However, more common physical injuries are also typical with other circumstances, making physical exam of limited value. The entire clinical picture should be considered.

It may also be helpful to assess for tattoos and/or other modifications (e.g., branding, piercings). Some perpetrators use tattoos to identify victims or to signify "ownership" [60].

With regard to episodic clinical encounters, recommendations for providing safe assessments in a culturally sensitive manner are lacking. The Department of Health and Human Services Administration for Children and Families maintains a useful website that addresses practical issues of human trafficking for allied professional groups, known as the Look Beneath the Surface Campaign [76]. Included are diagnostic and interviewing tips to help healthcare providers recognize and refer trafficking victims to appropriate services [76]. Emergency and primary care providers should be cognizant of clues that a patient may be the victim of trafficking and prepared to engage in a greater depth of inquiry with special attention to the following indicators [76; 102; 103; 104]:

- Does someone, other than family, who behaves in a controlling manner, accompany the patient? Traffickers attempt to guard and control most every aspect of the victim's life, while maintaining isolation from family, friends, and other common forms of human interaction.
- Are there inconsistencies in answers to basic questions (e.g., name, age, address)?
- Does the patient speak English? If not, has he or she recently been brought to this country, and from where? Many victims of human trafficking have recently been trafficked from other countries. As discussed, common sending countries/regions include Eastern Europe, Asia, Latin America, Africa, India, and Russia.
- If the patient is accompanied by someone other than a family member, who does the talking, and why? Attempt to interview and examine the patient separately and alone, using an interpreter if necessary. Probe in a sensitive manner for detailed information on the situation and relationship.
- Does the patient show signs of psychosocial stress (e.g., appears withdrawn, submissive, fearful, anxious, depressed)? Can the individual account for this?
- Are there visible signs of physical abuse (e.g., bruises, lacerations, scars)? How does the individual explain these?
- Does the patient lack a passport or other immigration and identification documentation (e.g., driver's license, social security number, visa)? If so, what explanation is given? To control victims' movements, traffickers often take away passports and any legal identification documents.
- What is the patient's home and work situation? Basic questions about what they eat, where they live and sleep, who else lives with them, and what work they do can be revealing. For example, "Can you leave your work or job situation if you wish?" or "When you are not working, can you come and go as you please?"
- Is the explanation given for the clinical visit consistent with the patient's presentation and clinical findings?
- Does the victim appear fearful when asked questions about citizenship, country of origin, immigration status, or residence? This may indicate a fear of deportation.
- If the victim is a minor, is s/he in school? Living with parents or relatives? If not, what reasons are given for these circumstances?

If answers to these questions indicate that an individual may be a victim of human trafficking, one should contact the National Human Trafficking Hotline at 1-888-373-7888. Under the child abuse laws, practitioners who are mandated reporters and who are suspicious that a minor is being abused

should immediately report the abuse. For more information regarding specific states' reporting requirements, please visit https://www.childwelfare.gov/resources/states-territories-tribes/state-statutes.

SCREENING QUESTIONS

Examples of questions to screen for human trafficking include [105; 106; 107]:

- Can you tell me about your living situation?
- Has anyone ever threatened you with violence if you attempted to leave?
- Does anyone force/require you to have sexual intercourse for your work?
- Has anyone ever threatened your family if you attempted to leave?
- Does anyone make you feel scared at work?
- Are you free to come and go as you wish?
- Does your home have bars on windows, blocked windows/doors, or security cameras?
- How many hours do you work?
- Have you ever worked without receiving payment you thought you would get?
- Do you owe your employer money?
- Do you have to ask permission to eat, sleep, use the bathroom, or go to the doctor?

The Polaris Project has developed a flow chart for the assessment of potential trafficking victims, available at https://www.traffickingresourcecenter.org/sites/default/files/Assessment%20Tool%20-%20Medical%20Professionals.pdf. Again, if a person is thought to be a victim, healthcare providers should follow workplace protocols and/or contact the National Human Trafficking Hotline at 1-888-373-7888 for next steps.

INTERVIEWING TRAFFICKED VICTIMS: BEST PRACTICE GUIDELINES

What should a practitioner consider when interviewing a victim of human trafficking?

Service providers should repeatedly weigh the risks and benefits of various actions when interviewing human trafficking victims [70; 108; 109]. Survivor safety is of utmost importance, and a private conversation should be sought, if at all possible. It may be necessary to be discrete or nonchalant when requesting to speak with the victim alone, as angering the trafficker may result in negative consequences for the victim. If the agency has a policy to always speak to patients alone, this may be easier to explain. Other strategies to separate a possible victim from a companion include stating the need for a private exam or testing (e.g., radiology, urine test). A companion's assistance with paperwork may also be requested in an outside office or lobby. If the potential victim does not want to be alone or is reluctant to go to a private location, it is vital to respect her/his wishes.

In addition, the following interviewing recommendations were published by the World Health Organization to encourage service providers to continually and ethically promote human trafficking victims' safety during every phase of the interviewing process [102; 110]:

- Each victim and trafficking situation should be treated as unique; there are no standard templates of experiences. Listen carefully to the victim's story. Each story told is unique, and each patient will voice distinctive concerns. Believe each story, no matter how incredible it may seem. As rapport and trust build (perhaps very slowly), accounts may become more extensive.
- Always be safe and assume the victim is at risk of physical, psychological, social, and legal harm.
- Evaluate the risks and benefits of interviewing before starting the interviewing process. The interviewing process should not invoke more distress. In other words, the interviewing process should not end up re-traumatizing the victim.
- Provide referrals for services where necessary; however, it is necessary to be realistic and not make promises that cannot be kept. Trust is vital because it has been severed on so many levels for trafficking victims.
- Victims' readiness to change will not be based on what society defines as "ready" or on social expectations. Some victims will eagerly grasp new opportunities, while others may be fearful of potential traffickers' threats and be less receptive to help.
- Determine the need for interpreters and if other service providers should be present during the interviewing phase. Ensure that everyone involved is adequately prepared in their knowledge about human trafficking, how perpetrators control their victims, and how to ask questions in a culturally sensitive manner. Keep in mind that often times, traffickers will offer to help with the interpreting. Using interpreters from the same community of the victim should be avoided to prevent breaches in confidentiality.
- All involved should be prepared with an emergency plan. For example, is there a set plan for a victim who indicates he/she is suicidal or in danger of being hurt?
- Always be sure to obtain informed consent. Remember that the informed consent process is going to be unfamiliar to many victims. In addition, self-determination and autonomy have been compromised by continual threats and being forced to commit dehumanizing acts. Avoid using legal and technical jargon.

Providers should assume that human trafficking victims are describing their reality to the best of their ability, given the trauma they have experienced. Responses and behaviors (e.g., being guarded, defensive, belligerent) may be coping mechanisms [99].

SAFETY MEASURES

While it may be necessary to modify the approach depending on the situation, the Advocates for Human Rights recommends that safety plans for trafficking survivors [111]:

- Are personalized, realistic, involve friends and family that the victim trusts, and cover every aspect of the victim's life
- Focus on improving safety in the victims' environment
- Assess the current risk and identify current and potential safety concerns
- Create strategies for avoiding or reducing the threat of harm
- Outline concrete options for responding when safety is threatened or compromised, including:
  - Determining who victims will call in an emergency and memorizing those phone numbers or preparing a small card listing the numbers
  - Identifying where victims will go if there is an emergency
  - Identifying what victims will do if the trafficker contacts them after they leave the trafficking situation (e.g., retain messages, contact the police or a victim advocate)
  - Assessing how to handle safety issues when victims have family or friends, including those in another country, who are at risk of harm from the trafficker
- Are re-evaluated at various stages of the trafficking situation
- Reflect changing circumstances in the victim's life and changes in support or services (e.g., victims may have felt safe with a particular situation at the time of preparing the safety plan, but they may not feel safe in that same situation in the future)
- Address what victims will do in response to flashbacks or triggers, including those in any new workplace
- Strategize how to address and replace technology, such as cell phones, that the trafficker provided or had access to (e.g., leaving phones in places victims are allowed to be or providing phones just for calling 911)

In addition, non-U.S. citizens should have access to an emergency contact in the United States (potentially a legal services provider) and plans for young children (i.e., a decision-making proxy). Youth victims may require housing assistance [111].

DOCUMENTATION

Ideally, the victim of human trafficking should be offered a formal forensic evaluation; this requires written documentation of informed consent. Injuries should be documented in photographs, diagrams, or sketches. A growing number of hospitals now employ dedicated forensic nurses as part of a multispecialty sexual assault team [112]. Often, however, these trained specialists are not the first professionals to interact with the patient. Consequently, all healthcare professionals, particularly those in an emergency care setting, should have an understanding of the principles that govern proper collection and preservation of evidence during the examination of an assault victim.

The initial clinical assessment includes a careful history and physical examination, followed by selected laboratory testing and radiographic studies as indicated by clinical findings. Examination of the forensic patient is conducted in a thorough head-to-toe or toe-to-head manner, with the intent of documenting every indication of injury related to the incident (no matter how insignificant and involving every part of the body) using a body-map or wound chart. The entire body surface should be palpated to identify areas of bruising that may not yet be visible. Documentation and collection of evidence typically occurs at the same time as the physical exam—as evidence is detected it should be collected.

Forensic documentation includes a written component, a diagrammatic component, and a photographic component. Each should accurately inform the other. The written component must be detailed, accurate, and objective; the diagrammatic component must be thorough and legible; and the photographic component must include a measurement scale, be representative of the evidence, and remain objective.

RESPONSE AND FOLLOW-UP

HEALTHCARE PROVIDERS' ROLE

Care and services provided to victims can be organized into three distinct categories: immediate and concrete services at the time of rescue; services related to recovery; and long-term services pertaining to reintegration [113]. When trafficking victims are rescued, a great deal of counseling services and practical, day-to-day assistance will be required. Housing, transportation, food, clothing, medical care, dental care, financial assistance, educational training, reunification (for those who wish to return to their homeland), and legal aid are some of the concrete services needed [24]. Practitioners should connect, coordinate, and case manage these services as much as possible. During this stage, it is also important to understand victims' needs, their strengths, and their risks and vulnerabilities [82].

Safety planning is also crucial in the immediate rescue stage. Traffickers may be continuing to try to locate some victims; placing victims in safe houses may be necessary [86]. The National Human Trafficking Hotline encourages that safety planning be based on the unique needs and circumstances of the individual. One should also take steps to ensure that one's own safety is also protected.

During the recovery and reintegration stages, as discussed, human trafficking victims experience an array of mental health and psychological issues. Mental health counseling is vital, but it is important to remember that the concept of counseling or talk therapy may be foreign to victims from non-Western cultures [70]. The expression of emotions may be in opposition to cultural values of emotional restraint, which can be intensified by feelings of shame and guilt resulting from experiences with sexual and physical assault. Beyond the paramount importance of the practitioner gaining the patient's trust, practitioners may educate patients about the counseling process and explore their patients' expectations about counseling, healing, and recovery [114]. As noted, victims' symptoms may not only be a manifestation of the trauma but also coping mechanisms to cope with self-blame, shame, and trauma [60].

Given differing cultural beliefs about healing, it is crucial that practitioners be open to alternative treatment and explore with patients the use of traditional healing methods [70]. There are many indigenous healing interventions victims may be using, including cultural rituals, faith healing, therapeutic touch, herbal remedies, and spiritual practices [115]. These interventions are multi-layered, taking into account the physical, psychological, communal, and spiritual [115]. These healing methods are historically rooted in specific cultures, and therefore, practitioners should become familiar with traditional healing methods and how they can be integrated with Western counseling techniques [114]. For example, given many cultural groups' beliefs that unmarried girls are defiled if raped, a cultural cleansing ritual may be needed as a first step to help a community accept a returning victim who was sexually assaulted during her trafficking experience [36]. After this ritual is performed, it is possible that both the patient and her family may be more open to counseling and other services.

Other trauma interventions that might be beneficial include cognitive-behavioral therapies, eye movement and desensitization reprocessing therapies, mindfulness techniques, and expressive therapies [60; 86].

Physicians, social workers, nurses, therapists, and counselors must be familiar with legal, case management, educational, job and life skills training, and housing services in the community. Human trafficking victims are not only unfamiliar with navigating the social service system, but many are also not proficient in English. Therefore, practitioners will serve as coordinators and advocates, linking necessary services. In one study, the majority of agencies had to rely on collaboration in order to refer clients [116]. Social workers and practitioners relied on word-of-mouth and community meetings to learn about services in order to better meet the needs of human trafficking victims. Furthermore, because many community organizations and agencies are not familiar with human trafficking, practitioners must take a primary role in educating colleagues about the complex dynamics of human trafficking.

It is important to remember that the evidence supporting interventions and therapies for victims of human trafficking is in its infancy [113]. Most efficacy studies of therapies and interventions do not involve experimental designs, which makes it difficult to draw definitive conclusions regarding efficacy. Future work is needed to develop and evaluate interventions that address the multilayered and complex needs of human trafficking survivors.

REFERRAL

In the initial period, what should referral of trafficking victims focus on?

The needs of human trafficking survivors are diverse, and healthcare professionals should be prepared to refer these individuals to a wide variety of services. In the initial period, acute injuries, mental health crises, and stabilization (e.g., housing, safety) are the greatest concerns. However, many victims experience chronic health and mental health issues related to their traumatization and will also require referral to services that will allow healing throughout their lifetimes.

As such, organizations and healthcare providers should work to build a trusted local network of resources, including substance abuse treatment centers, educational and career advancement services, financial support, PTSD/complex trauma assessment and treatment, and potentially law enforcement representatives with experience providing services to victims of human trafficking. In the state of Texas, statewide and local organizations and government offices are available to assist in building this network. A listing of these resources is available at the end of this course.

The National Human Trafficking Hotline (administered by Polaris) also maintains a National Referral Directory that is searchable by gender, nationality, age, type of trafficking, type of service(s), opportunities/training, and geographic location. The directory is available at https://humantraffickinghotline.org/en/find-local-services.

REPORTING

In addition to addressing crises and stabilization upon identification of a potential trafficking victim, healthcare providers should contact the National Human Trafficking Hotline. This hotline also provides warm transfers of mandatory reporters' intakes to the Texas Department of Family and Protective Services (DFPS), helps build intelligence on human trafficking in Texas, and continuously improves its referral directory of Texas resources for victims seeking assistance for themselves. There are more than 90 Texas service providers listed on the National Referral Directory, with more than 60 of those being listed publicly.

According to Texas Family Code 261.101, any person having cause to believe that a child's physical or mental health or welfare has been adversely affected by abuse or neglect (including human trafficking victimization) by any person is required to immediately make a report to law enforcement or DFPS [117]. Professionals who are licensed or certified by the state or who are employees of a facility licensed, certified, or operated by the state and who, in the normal course of official duties or duties for which a license or certification is required, has direct contact with children are required to make reports within 48 hours; this includes physicians, nurses, social workers, counselors, and pharmacists. Reporting cannot be delegated.

ROLES AND LIMITATIONS OF LAW ENFORCEMENT INVOLVEMENT

Victims of human trafficking should be empowered with choice whenever possible, including the ability to determine whether to participate in the criminal justice process [100]. Cases involving abuse or neglect at the hands of a traditional caregiver may be investigated by the DFPS, but all other cases must be handled by a law enforcement agency [118]. For victims who choose to participate in the criminal justice process, safety and protection considerations apply.

There are limitations to law enforcement involvement, particularly with victims who may be reluctant to trust these figures. It is important that the law enforcement contact be trained and experienced in the intricacies of human trafficking and complex trauma. While building a criminal case and prosecuting perpetrators is important, measures should be taken to avoid re-traumatizing the victim.

ORGANIZATIONAL PROTOCOLS

Whenever possible, facilities should create trauma-informed organizational protocols to ensure that human trafficking survivors receive the best possible care. These protocols should include guidelines for appropriate assessment, documentation, reporting, intervention, and referral and may be incorporated into existing protocols for interacting with potential victims of child abuse, violence, and/or sexual assault.

CONCLUSION

Human trafficking is a severe human rights violation. Because the roots of human trafficking are multifaceted, no one solution exists to eliminate this problem. Unfortunately, as the problem grows, practitioners will be confronted with the issue in their patient populations. Practitioners should be committed to the collaboration amongst disciplines to address poverty, racism, discrimination, and oppression in order to reduce the vulnerable positions of human trafficking victims and their families. Because of the social justice component in the codes of ethics of professionals such as physicians, nurses, social workers, psychologists, and counselors, all practitioners can play a key role in the individual, community, and systemic levels to help address this gross abuse of power. One way to begin is to educate oneself and one's respective disciplines about the global nature of human trafficking and the complex dynamics of the problem.

RESOURCES

NATIONAL

National Human Trafficking Hotline
https://humantraffickinghotline.org
1-888-373-7888
TTY: 711
Text: 233733

U.S. Department of Homeland Security
https://www.dhs.gov/blue-campaign

U.S. Department of State
Office to Monitor and Combat Trafficking in Persons
https://www.state.gov/bureaus-offices/under-secretary-for-civilian-security-democracy-and-human-rights/office-to-monitor-and-combat-trafficking-in-persons

Girls Education and Mentoring Services (GEMS)
https://www.gems-girls.org

Love146
https://love146.org

National Center for Missing and Exploited Children
https://www.missingkids.org

Administration of Children and Families
Office on Trafficking in Persons
https://www.acf.hhs.gov/otip

Polaris Project
https://polarisproject.org

Shared Hope International
https://sharedhope.org

Truckers Against Trafficking
https://truckersagainsttrafficking.org

STATE

Children at Risk
https://childrenatrisk.org/human-trafficking

Children Advocacy Centers of Texas
https://www.cactx.org

Office of the Texas Governor
Child Sex Trafficking Team
https://gov.texas.gov/organization/cjd/childsextrafficking

Attorney General of Texas
https://www.texasattorneygeneral.gov/initiatives/human-trafficking

Texas Health and Human Services
https://hhs.texas.gov/services/safety/texas-human-trafficking-resource-center

Texas Youth Connection
https://www.dfps.state.tx.us/txyouth

LOCAL

To locate your county by DFPS region, please visit https://www.dfps.state.tx.us/contact_us/counties.asp. Organizations marked with an asterisk are faith-based.

DFPS Region 1 (Northwest)

Family Support Services of Amarillo
https://fss-ama.org

No Boundaries International*
https://www.nbint.org

Open Door Survivor Housing Lubbock*
https://opendoorlbk.org

Voice of Hope Lubbock Texas
https://www.voiceofhopelubbock.org/sex-trafficking

DFPS Region 2 (Northwest)

Taylor County Victim's Assistance Division
https://www.taylorcounty.texas.gov/130/Victims-Assistance-Division

Wichita County Victim Assistance
https://wichitacountytx.com/victims-services

DFPS Region 3 (Dallas Fort Worth)

Mosaic
https://mosaicservices.org

Jonathan's Place
https://www.jpkids.org

New Friends New Life, Dallas
https://www.newfriendsnewlife.org

Promise House Dallas*
https://promisehouse.org

Refuge for Women, North Texas*
https://refugeforwomen.org/north-texas

Traffick911
https://www.traffick911.com

Unbound
https://www.unboundnow.org

DFPS Region 4 (East Central)

Texas Legal Services Center
https://www.tlsc.org

DFPS Region 5 (East Central)

Crisis Center of Southeast Texas
https://www.crisiscenterofsoutheasttx.org

Jefferson County Victims' Assistance Center
https://co.jefferson.tx.us/da/VictimsAssist.htm

Children at Risk, Houston
https://childrenatrisk.org/human-trafficking

For the Silent, Tyler, TX
https://www.forthesilent.org

Houston Area Women's Center
https://hawc.org

YMCA of Greater Houston
https://ymcahouston.org

DFPS Region 6 (Houston)

Free the Captives Houston*
http://www.freethecaptiveshouston.com

Houston Area Women's Center
https://hawc.org

The Key2Free
https://www.thekey2free.org

United Against Human Trafficking
https://uaht.org

DFPS Region 7 (East Central)

American Gateways, Austin
https://americangateways.org

Asian Family Support Services of Austin
https://www.afssaustin.org

Central Texas Youth Services Bureau, Belton/Temple
https://www.centraltexasyouthservices.com

The Refuge for DMST, Austin*
https://therefugedmst.org

Unbound
https://www.unboundnow.org

DFPS Region 8 (South)

Alamo Area Coalition Against Trafficking
https://www.facebook.com/alamoacat

Freedom Youth Project Foundation
https://www.freedomyouthproject.org

The Rape Crisis Center, San Antonio
https://rapecrisis.com

DFPS Region 9 (Northwest)

Ector County District Attorney Office
http://www.co.ector.tx.us/page/ector.District.Attorney

Midland County District Attorney Office
https://www.co.midland.tx.us/173/District-Attorney

DFPS Region 10 (Northwest)

Las Americas Immigrant Advocacy Center
https://las-americas.org

El Paso Center for Children
https://epccinc.org

Paso Del Norte Center of Hope
https://www.pdncoh.org

Salvation Army of El Paso*
https://southernusa.salvationarmy.org/elpaso

DFPS Region 11 (South)

Catholic Charities of Corpus Christi Texas*
https://www.catholiccharities-cc.org

Coastal Bend Coalition Against Modern Day Slavery
https://cbcamds.wordpress.com

Mujeres Unidas/Women Together Foundation, Inc.
https://mujeresunidas.org

Customer Information and Evaluation are located on pages 79–80.

Psychiatric Treatment Options in the Older Adult

Includes 1 Pharmacotherapeutic/Pharmacology Hour

This course meets the Texas requirement for Geriatric education.

Audience
This course is designed for all nurses involved in the care of older patients, particularly those with mental health concerns.

Course Objective
The purpose of this course is to review psychiatric treatment options for the older adult and improve outcomes for older adults receiving mental health care.

Learning Objectives
Upon completion of this course, you should be able to:

1. Outline characteristics of the older adult population in the United States.
2. Describe how medical conditions may impact the mental health of the older adult.
3. Review pharmacokinetic considerations when planning psychopharmacotherapeutic approaches for older adults.
4. Identify medications included in the Beers criteria and the potential safety concerns with medications on this list.
5. Discuss nonpharmacologic interventions that can be used for the older adult with mental health conditions.
6. Identify safety needs for the older adult patient and how to implement treatment plan changes while maintaining patient dignity.

Faculty
Megan Hawk, APRN, PMHNP-BC, CNP, has been a psychiatric-mental health nurse practitioner (PMHNP) since 2013 and a nurse since 2007. She obtained her Associate Degree in Nursing from Kent State University in 2007. She went on to obtain her Bachelor's degree from Kent State University in 2011 and her Master's degree from the University of Cincinnati in 2013. As a nurse, she worked in an inpatient psychiatric hospital, and as a nurse practitioner, in an outpatient mental health center. She is currently the program direct of the online psychiatric-mental health nurse practitioner program at Regis College. She has a passion for mental health nursing and teaching the next generation of psychiatric nurse practitioners. She is currently pursuing her doctorate of nursing practice with a focus on nursing education.

Faculty Disclosure
Contributing faculty, Megan Hawk, APRN, PMHNP-BC, CNP, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Division Planner
Mary Franks, MSN, APRN, FNP-C

Senior Director of Development and Academic Affairs
Sarah Campbell

Division Planner/Director Disclosure
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NetCE designates this continuing education activity for 1 pharmacotherapeutic/pharmacology contact hour.

AACN Synergy CERP Category A.

Individual State Nursing Approvals

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This course represents an educational model that promotes the importance of learning objectives and individualized learning. Study questions will appear throughout the course to create a link between the learning objectives and the supporting text.

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the study questions and course material for better application to your daily practice.

INTRODUCTION

What percentage of the U.S. population is currently made up of older adults (65 years and older)?

The oldest person in the United States is 115 years old, and in the 2010 Census, there were 53,364 centenarians (individuals 100 years of age or older) [1]. Older adults, considered to be individuals 65 years of age and older, make up 16% of the U.S. population. Moreover, the number of individuals 85 years of age and older is projected to double by the year 2040, and by 2050, it is projected that one in five people in the United States will be older than 65 years of age [2; 3]. By the year 2060, it is projected that 589,000 people will be 100 years of age or older [4]. These figures alone demonstrate the need for increased familiarity and comfort with the mental health care of the older adult. Aside from age, the older adult presents with other potential complications, such as living in extended care facilities.

The probability of an older adult living in an extended-care facility increases with age, with 1% of individuals 65 to 74 years of age, 2% of those 75 to 84 years of age, and 8% of those 85 years of age and older living in an extended-care facility [2]. As the general population grows older, it is expected that the number of those in extended-care facilities will increase as well.

One in four older adults is impacted by a behavioral health disorder, such as depression, anxiety, dementia, and substance use disorder [5]. However, it is important to note that mental health disorders, including depression and dementia, are not normal parts of aging and can and should be treated. However, it is important to note that some mental health symptoms in older adults may present differently from a younger patient. It can be easy for younger caregivers to lose sight of just how much the older adult has been through; they may have already lost many of the people closest to them. Older adults are often experiencing life-altering changes in physical and cognitive functioning. These challenges can be compounded with new or chronic mental health conditions.

Consider the following case scenario: Patient A presents to the office for an initial psychiatric evaluation. She is 85 years of age. There is an almost palpable sadness that can be felt while in her presence, though she appears to smile through whatever pains her as she answers basic social questions. She denies depressive symptoms and history of trauma and reports only anxiety, with a desire to come off the "nerve pill" that she has been prescribed by her family physician. After a review of her current psychiatric symptoms and a brief break for small talk, talk becomes comfortable enough to disclose that she fled Poland during World War II. It is after a simple, "That had to have been really tough," that she begins to open up, speaking freely to the nurse. Patient A's father died in a concentration camp and she fled Poland with her mother. After coming to the United States, she endured years of physical, emotional, and sexual abuse from a now ex-husband. She cries as she tells her story. It feels like it is her first time feeling comfortable describing these traumatic events. The nurse offers active listening and patience as Patient A works through the topics that have been so difficult to discuss. After she finishes her story, the patient is tearful but looks as though a weight has been lifted off her. With shared decision making, a plan is put in place to taper the previously prescribed benzodiazepine slowly and carefully. She is referred to psychotherapy following a discussion on the benefits.

After this appointment, here are a few points to consider:

- Are healthcare providers doing the very best for older patients?
- Are older patients leaving their appointments feeling heard?
- What are older patients' thoughts and feelings toward receiving mental healthcare?
- Are healthcare providers engaging in shared decision making, taking patients' preferences into account?
- Have healthcare professionals, and nurses in particular, lost touch with older adults' complex needs?

The experiences of the elderly population have helped to form them into the people they are today. They come from a generation that is less likely to reach out for help, especially in terms of mental health care.

Nurses are in a unique position. We can either ignore the stories of older adult patients or hear them, learn from them, and seek out ways to improve their care. It is of utmost importance for nurses to understand how mental health concerns manifest in older adults patients; what pharmacologic interventions are appropriate and inappropriate for the elderly, including what the most up to date Beers criteria state; how medical conditions may play a role in the mental health of the older adult patient; and nonpharmacologic treatment options for the elderly with mental health concerns, recognizing safety concerns in the older adult. A thorough review of these topics is necessary to enhance the care of these patients, thus improving outcomes.

MENTAL HEALTH CONCERNS IN THE ELDERLY

DEMENTIA

What is the most common form of dementia in older adults?

Dementia is a general term for difficulties with cognitive functioning, including impairment in executive functioning (e.g., balancing a checkbook), memory loss, poor judgment, impulsivity, getting lost in familiar places, and taking longer than usual to complete daily tasks. Although the likelihood of developing dementia increases as one ages, it is not considered a normal part of aging. Dementia is further categorized by type and severity. Alzheimer disease is one of the most common forms of dementia, with an estimated 6.5 million individuals 65 years of age and older in the United States affected [6]. Other types of dementia include frontotemporal dementia, vascular dementia, and dementia with Lewy bodies. It has been suggested that the total number of Americans with some form of dementia could rise to 14 million by 2040 [7].

Behavioral and psychological symptoms of dementia (BPSD) can be challenging for patients and caregivers and can include psychosis, anxiety, agitation, depression, wandering, and apathy [8]. Patients with BPSD are more likely to experience delusions than hallucinations, and the more commonly experienced delusions revolve around theft from the home and intruders within the home [8]. The specific symptoms experienced by the patient with BPSD may vary by different types of dementia; for instance, dementia with Lewy bodies has a higher incidence of hallucinations, while vascular depression has a higher incidence of depression and anxiety [9]. The patient with BPSD may try to leave the home, often requiring caregivers to be home with the patient full-time. Caregivers of patients with dementia may experience financial stress associated with decreased employment or leaving their job to provide care. Caregiver financial strain is associated with higher levels of role overload among caregivers in general [10].

DEPRESSION

Much like dementia, older adults are at increased risk for depression, though this should not be considered a normal part of aging. In some cases, depression in older adults is dismissed by providers, brushed off as loneliness or grief—things that cannot be avoided. Risk factors for depression in the older adult include a history of depression, sensory losses, social losses, functional impairment, stressful life events, and increased dependence on others [11]. It is important to note that depression in the older adult can and should be treated. Although the overall symptom profile of depression is the same for older adults as for younger individuals, it is important to point out that older adults are more likely to display physical health-related symptoms when depressed. For example, the older adult is more likely to experience non-specific aches and pains or gastrointestinal distress associated with depression [12]. Furthermore, the older adult may struggle more with loneliness as they grow older. Not being close to family members, friends, or other supports can have a negative impact on the older adult as their functional capacity decreases.

Suicide

Suicide is a public health concern in the United States and worldwide; in 2020, older adults experienced a suicide mortality rate of 16.86 deaths per 100,000 population [13]. Loneliness, dementia, and depression are commonly seen characteristics of the oldest individuals who complete suicide; also, older men had the highest rates of death by suicide in nearly all countries [14]. The older adult is more likely to choose a more violent means of attempting suicide and are more likely to die following an attempt than younger patients [5]. Working with older adults through complex grief, finding meaning in life, relieving psychiatric symptoms, and, above all, establishing a strong therapeutic alliance are crucial to improving quality of life and decreasing suicide risk [12]. Problem solving and problem adaptation therapy are two psychotherapeutic modalities that have shown some promise in decreasing suicide risk in the older adult [12]. Contributing factors should be continually assessed by the nurse caring for the older adult.

ANXIETY

Anxiety disorders are thought to be more common in older adults than depression, with a prevalence rate of 7% to 14.2% for this population [12]. Anxiety can manifest differently in older individuals compared to younger populations due to various factors, including age-related changes, comorbidities, and life circumstances. Furthermore, the older patient may also experience lower self-confidence, reduced activity and movement, loss of friends/social supports, reduced financial and physical independence, and medical comorbidities, all of which can further fuel anxiety symptoms [16]. These factors culminate to the development of anxiety surrounding death among older adults; additionally, generalized anxiety disorder, anxiety related to a general medical condition, and agoraphobia are more likely to occur in late adulthood [12; 17]. As individuals get older, they may experience death anxiety, or a heightened awareness and fear of death, whether conscious or unconscious. The mental health and quality of life of the older adult improves if death anxiety is addressed psychotherapeutically. Lower death anxiety is associated with higher levels of meaning in life [18]. Nurse psychotherapists can be very important in helping the older adult patient find meaning in life to mitigate the risk of depression and anxiety in late life [12].

EVIDENCE-BASED PRACTICE RECOMMENDATION

When assessing an adult with possible social anxiety disorder, the National Collaborating Centre for Mental Health recommends that clinicians be aware of comorbid disorders, including avoidant personality disorder, alcohol and substance misuse, mood disorders, other anxiety disorders, psychosis, and autism.

(https://www.nice.org.uk/guidance/cg159/resources/social-anxiety-disorder-recognition-assessment-and-treatment-pdf-35109639699397. Last accessed January 24, 2025.)

Level of Evidence: Expert Opinion/Consensus Statement

BIPOLAR DISORDER

Bipolar disorder in the older adult population encompasses both those who experience late onset of the disease and those who were diagnosed with bipolar disorder at a younger age (early-onset bipolar disorder). Some epidemiological studies use an age cutoff of 50 years of age to identify older adults with bipolar population, in part due to the shorter life expectancy of individuals with bipolar disorder [19].

As the population grows older, it stands to reason that the number of elderly patients with bipolar disorder will increase. Individuals with late-onset bipolar disorder are more likely to present with bipolar II disorder than bipolar I disorder and are more likely to have co-occurring neurologic disorders or cognitive decline. Most of the literature surrounding bipolar disorder focuses on adolescents and working-age adults rather than older adults, showing a gap in research and knowledge in this area. It is unclear if clinical guidelines focused on younger populations can be safely extrapolated to the older adult population due, in part, to the physical and metabolic changes that occur with age [20]. Due to the lack of available data on treatment recommendations for late- and early-onset bipolar disorder in older adults, experts recommend that treatment should be similar to that of a younger patient, keeping in mind the potential risk factors of common bipolar disorder treatments that may come with advanced age [19]. Safety and tolerability should be taken into account as much as efficacy when choosing a treatment option for the older adult with bipolar disorder [20]. Considerations for psychopharmacology in older adults will be discussed in detail later in this course.

Lithium is considered the criterion standard of bipolar disorder treatment, particularly for the control of mania. Lithium is also known for its narrow therapeutic index for the treatment of mania, with blood levels typically needing to fall between 0.8 mEq/L and 1.2 mEq/L to be effective. In addition to the potential for damage to the thyroid and kidneys with long-term use, lithium can reach toxic levels in the blood. Early signs of lithium toxicity include tremor, sedation, and confusion, all of which can be missed in older adult patients. At higher lithium levels, patients can experience delirium, seizures, and coma [21]. Because of these risks, blood levels of lithium should be monitored periodically. There is some evidence that older patients may respond well to "subtherapeutic" serum levels of lithium, and signs of toxicity may occur at levels less than 1.2 mEq/L in older adults [20; 21].

SCHIZOPHRENIA

People of all age groups can have schizophrenia, with onset most commonly occurring in those around 20 years of age; late-onset schizophrenia develops after 45 years of age. The prevalence of schizophrenia in older adults is projected to double and reach 1.1 million people in the United States by 2025 [22]. It is suggested that healthcare costs will be significantly impacted with the increasing number of older adult patients with schizophrenia [23]. Still, the life expectancy of an individual with schizophrenia is lower than the national average by about 10 years.

Characteristics of schizophrenia in older adults can vary widely from younger individuals diagnosed with the disorder [24]. This may be due to a combination of a different symptom profile among those with late-onset schizophrenia and significant symptom reduction among those with early-onset disease who have reached older adulthood. Older adults with schizophrenia are also more likely to have acquired medical comorbidities that complicate the clinical picture. It has been noted that individuals with late-onset schizophrenia have better premorbid functioning than those who develop the disorder earlier in life [23]. Those who develop schizophrenia later in life tend to have fewer negative symptoms and less severe neurocognitive impairments [23].

There are risks associated with the treatments for schizophrenia that are exclusive to the older adult population, particularly related to drug reactions and interactions.

POST-TRAUMATIC STRESS DISORDER

Older adults experience post-traumatic stress disorder (PTSD) at rates lower than younger populations. It has been suggested that older adults are less likely to be assessed or diagnosed with PTSD due to a lack of research on this demographic. However, this appears to be changing [12]. It has been noted that the prevalence of PTSD in individuals older than 60 years of age ranges from 1.5% to 4.0%; this is lower than the lifetime prevalence of all adults (8.0%) [25]. This raises the question: Do older adults have less trauma, or is this population less treatment-seeking? Experts have suggested that older adults may be less likely to recognize symptoms as trauma-related and may also be less likely to seek care; conversely, clinicians may be less likely to assess for trauma-related disorders in this population [26].

The diagnosis of PTSD was first introduced to the Diagnostic and Statistical Manual of Mental Disorders (DSM) in 1980; individuals who experienced an onset of symptoms before this time may have received a different diagnosis or have not been diagnosed at all, leading to gaps in identification and treatment that persist into older age [26]. It is reasonable to assume that older adults have lived through global and personal events that could create and elicit trauma-related symptoms.

The psychiatric treatment-seeking views of older adults are marked by stigma and a perception of personal responsibility over psychiatric symptoms linked to a lack of psychiatric treatment-seeking [27]. Research indicates that older veterans with PTSD are more likely to endorse somatic complaints (e.g., headache, memory problems, gastrointestinal distress) than PTSD-related symptoms (e.g., hypervigilance, increased startle response) in comparison to their younger counterparts [25].

SUBSTANCE USE DISORDERS

Alcohol use among older adults has increased over time, and an increase in substance use in general has been noted in the "baby boomer" generation (defined as those born between 1946 and 1964) [12]. Age-related changes to pharmacokinetics in older adults, including slowed metabolism of substances, can place this population at greater risk of adverse outcomes related to substance use and misuse.

Alcohol can cause difficulties with cognition, increase the risk of falls, and contribute to potentially dangerous alcohol-drug interactions for the older adult [28]. Careful assessment is required in this group, as changes can be mistakenly attributed to normal age-related changes, other chronic diseases, and/or dementia. When identified, this group requires individualized treatment that considers the impact of advanced age. One study attempted to reduce risky drinking among older male veterans presenting to primary care. It was found that integrated care behavioral health models were more effective at reducing risk drinking than no alcohol-use specific treatment referral at all; there were differences in the changes in risky drinking patterns depending on the treatment facility/location [28]. In one literature review, all studies examined found correlations between alcohol use and cognitive decline and dementia in older adults [29]. Nurses should consider increasing rates of substance use disorder among the older adult population and screen for substance misuse in all patient populations.

PSYCHOPHARMACOTHERAPY IN OLDER ADULTS

When formulating a treatment plan for older adults, nonpharmacologic options should be considered first as a safer alternative. If medication is necessary, adhering to the principle of "start low, go slow, don't stop, be patient" is crucial [30]. "Start low" acknowledges that older adults often require lower initial doses compared to younger patients. In some cases, as little as half or even one-quarter of the recommended starting dose may be appropriate for older adults [21; 30]. "Go slow" advises avoidance of aggressive dose titration commonly used with younger patients. "Don't stop" emphasizes the need to avoid abrupt discontinuation of antipsychotics or any medications in the elderly. "Be patient" suggests allowing older patients sufficient time to adjust to new medications. Demonstrating patience is important when evaluating the effectiveness of psychiatric medication in older adults. Even with a low dose, they may still be sensitive to side effects, so close monitoring is essential to prioritize the safety of the older adult.

PHARMACOKINETICS IN OLDER ADULTS

Older adults account for approximately one-third of all prescription drug use, with a significant amount of over-the-counter usage as well [21]. When considering psychopharmacologic treatment for older adult patients, it is important to consider age-related changes in the absorption, distribution, metabolism, and excretion of medications; medical comorbidities; and drug-drug interactions.

AGE-RELATED CHANGES

What physiological changes in older adults affect drug metabolism?

It is common knowledge that as individuals age, total body water content decreases, muscle mass decreases, body fat increases, and function of several organ systems (e.g., hepatic, renal) decrease. These age-related changes can contribute to differences in drug absorption, distribution, metabolism, and excretion. However, nurses should consider (on an individual basis as much as possible) to what extent these body systems have and will change. For example, glomerular filtration rate (GFR) can decrease with age, and this is considered a normal part of aging [87]. Further, some degree of decreased liver function is expected as hepatic size and blood flow decrease with age. Despite some degree of decreased function, enzyme induction of the CYP450 system can remain relatively unchanged in the older adult; others may experience a decrease of up to 30% of enzyme action [88]. Genetics may play a greater role in

aging and in pharmacokinetics and drug metabolism in older adults than is generally appreciated [89]. Although decreases in hepatic and renal function are highly variable from patient to patient, an overall decrease in both hepatic and renal function is expected and should be part of prescribing decisions and drug monitoring in this group.

MEDICAL COMORBIDITIES

As a patient ages, they are increasingly likely to accrue medical comorbidities. The NCOA has reported that 80% of adults 65 years of age and older have at least one chronic condition, while 68% have two or more [5]. Medical concerns to be particularly watchful of in older adults include dehydration, hyponatremia, and impaired renal function. Some of the most common medical comorbidities in older patients include hypertension, type 2 diabetes, osteoarthritis, coronary artery disease, and hyperlipidemia—all of which often require at least one medication for control [5].

DRUG-DRUG INTERACTIONS

More medical conditions tend to lead to more medications, and older adults are particularly susceptible to polypharmacy. In a scoping review, researchers found that the most current clinical practice guidelines fail to offer guidance on safe prescribing practices for the patient with multimorbidity; most guidelines focus guidance on a single condition only [15]. Safe prescribing practices when caring for older adults with psychiatric disorders rely on knowledge of patient medical comorbidities, accurate medication reconciliation, and knowledge of any over-the-counter, vitamin, supplement, or herbal preparations the patient may be taking. Co-administration of drugs that act on the same or similar receptors are increase the risk of pharmacodynamic drug interactions, including serotonin syndrome, anticholinergic intoxication, seizures, and QTc prolongation.

POLYPHARMACY

At every visit, conducting medication reconciliation and ensuring its accuracy is crucial. Nurses should have a comprehensive understanding of all medications the patient is currently taking, encompassing prescriptions, herbal supplements, vitamins, and over-the-counter medications. It is important to approach medication reconciliation in a manner that encourages the patient to disclose all types of medications, minimizing the risk of unintentional omissions. Caregivers and home health providers can play a valuable role in verifying the patient's medications at their residence and providing updates on functional status. Armed with this information, one can proactively work toward preventing harmful drug-drug interactions and the potential for polypharmacy in older patients.

Polypharmacy is a term used to describe the use of five or more prescription medications at one time. One study found that 16.8% of individuals 65 to 74 years of age have polypharmacy [69]. This number increases to 25.8% for those 75 to 84 years of age and to 34.2% for those 85 to 94 years of age. Polypharmacy and physiologic changes both contribute to the risk and severity of drug-drug interactions in older adults. There are several potential negative outcomes of drug-drug interactions in older patients, including but not limited to shorter life expectancy, decreased overall quality of life, increased hospitalization and rehospitalization, and increased financial burden. It is estimated that one in six older adults is at increased risk for a significant drug-drug interaction [88].

As discussed, it is important for nurses to be well versed in the normal physiologic changes that impact drug absorption, distribution, metabolism and excretion; the risks of polypharmacy; and potential drug-drug interactions. For example, if a patient is prescribed both lithium carbonate and hydrochlorothiazide, this combination carries an increased risk of lithium toxicity and nephrotoxicity; nurses involved in the care of this patient should be vigilant for the signs and symptoms of lithium toxicity and provide patient and/or family/caregiver teaching regarding this potential effect. Medication interaction checkers can provide point-of-care information for provider and patient regarding the potential drug-drug interactions. Nurses should also remember that non-prescription drugs and natural products (e.g., supplements, herbal medications, vitamins) should be included in care planning and monitoring; checkers are also available for natural and over-the-counter products.

BEERS CRITERIA

The Beers criteria were first developed in 1991 by Mark Beers, MD, and colleagues and have since transitioned to the American Geriatric Society (AGS) [31]. The purpose of the Beers criteria is to identify medications that may pose a higher risk to older adults; these risks include drug-drug interactions, increased risk of side effects, increased risk when used with certain medical comorbidities, and dosing adjustments required for the physiological changes that occur with aging [31]. The Beers criteria aim to assist prescribers in making pharmacologic decisions in the best interest of the patient while acknowledging risks and potentially seeking alternatives to the medications on the list. The list serves to identify specific potentially inappropriate medications, with the goal of decreasing exposure to these drugs in older patients. The AGS released the most recent update to the Beers Criteria for Potentially Inappropriate Medication Use in Older Adults in 2023 [31]. The Beers criteria is intended for use by prescribers, though a strong case can be made for its importance to nurses who administer medications and spend more time observing the patient. The list is also not intended to be punitive or as a replacement for clinical judgment by providers.

POTENTIALLY INAPPROPRIATE PSYCHIATRIC MEDICATIONS AND THE ELDERLY

Benzodiazepines

Benzodiazepines are anxiolytic medications known for their calming, sedating effects and have been a topic of discussion, and controversy, for decades among the medical community. In 1955, chemist Leo Sternbach identified the first benzodiazepine, chlordiazepoxide [32]. Variations of chlordiazepoxide emerged, and by the 1970s, benzodiazepines were among the most prescribed medications in the United States. This increase in prescribing coincided with increased issues associated with use of these medications, which are still relevant today: misuse, diversion, and unfavorable side effects. In the 1990s, benzodiazepines began to undergo scrutiny, with additional questions surrounding safety. Although it was initially believed that this class of medications was non-habit-forming, this was discovered to be untrue.

Despite potential drawbacks, benzodiazepine prescribing continues to rise in general, with a 2019 study noting a rise in prescription of this drug class among primary care providers and other specialty providers (except for psychiatrists, whose benzodiazepine prescribing remained stable) [33]. Clinical indications remain for benzodiazepines, though their use should be limited to short-term courses, with caution. Specifically, the 2023 Beers criteria note that benzodiazepines may be appropriate for seizure disorders, REM sleep disorder, benzodiazepine or ethanol withdrawal, severe generalized anxiety disorder, and procedural anesthesia [31]. A short course of a benzodiazepine may also be used for acute agitation.

Special consideration should be given when using these agents in older adult patients, due to the discussed age-related physiologic changes. Slowed metabolism and excretion of medications with increased age results in extended effects of longer-acting benzodiazepines (or those with longer half-lives); these drugs should be assessed closely for appropriateness. Benzodiazepines with longer half-lives include diazepam, clonazepam, and chlordiazepoxide. Examples of shorter-acting benzodiazepines include alprazolam, temazepam, and lorazepam. The benefit-to-risk ratio should be carefully evaluated any time a benzodiazepine is prescribed, due to their potential for drug-drug interactions and psychological and/or physiological dependence. Short-term benefits possible with benzodiazepines may not be worth the risk of prescribing to older adults; other classes of drugs should be considered, when possible [30]. General side effects of benzodiazepines include sedation, dizziness, confusion, and slurred speech. In older adults, benzodiazepines are associated with an increased risk of falls and potential fractures, cognitive impairment, delirium, and motor vehicle crashes [31].

Nurses play a crucial role in patient education, facilitating informed consent and shared decision-making. In cases in which a patient has been on a long-term benzodiazepine prescription, they may not recall the associated risks, benefits, side effects, and alternatives. By providing education, nurses can equip the patient with sufficient information to consider tapering off the benzodiazepine. When assuming the care of a patient on benzodiazepine therapy, nurses can engage in discussions about safe and gradual tapering, while ensuring regular follow-up appointments based on mutual agreement between the patient and provider. While complete discontinuation may not be feasible for some patients, dose reductions can still be beneficial in managing side effects. Additionally, it is important for to be familiar with their state's prescription drug monitoring program, allowing for a thorough review of any controlled substances prescribed to the patient.

Antipsychotics

The term antipsychotic is frequently used to describe medications that target dopamine receptors, serotonin receptors, or both, though use is considered outdated and confusing due to the medication class's utility in the treatment of psychosis, mania, or depression—not just psychosis [34]. Also referred to as neuroleptics, these medications were introduced in the 1950s and were originally developed to treat psychosis. Chlorpromazine was found to improve mania and to have sedating, antihistamine effects; however, it was nearly entirely disregarded [35]. Additional first-generation antipsychotics were developed, including haloperidol, perphenazine, and fluphenazine. These drugs mainly acted by means of dopamine-2 antagonism. Side effects of these first-generation antipsychotic medications include sedation, dry mouth, extrapyramidal symptoms, and neuroleptic malignant syndrome. Extrapyramidal symptoms encompass several different types of movement-related side effects caused by antipsychotics, including akathisia, tardive dyskinesia, neuroleptic-induced parkinsonism, and dystonia. These symptoms can be particularly troublesome for many patients. Initially, it was thought that the more extrapyramidal symptoms the medication caused, the more effective the drug would be in managing psychotic symptoms; this is now known to be untrue.

The very first atypical, or second-generation, antipsychotic was clozapine, developed in 1958. During trials, it was found that clozapine relieved psychotic symptoms without causing as many extrapyramidal symptoms as the first-generation agents. Clozapine prescriptions increased in Europe until the 1970s, when patients started developing agranulocytosis (more commonly referred to as neutropenia) [36]. This caused withdrawal of the drug from the market in the countries in which it was approved and delayed its approval in the United States. In the 1990s,

clozapine was approved for limited use in the United States for treatment-refractory schizophrenia, under strict monitoring and dispensing guidelines [36]. Clozapine's different mechanism of action than the first-generation antipsychotics led to the development of more medications that worked on both the dopamine D2 receptor and the serotonin 2A receptors.

As other second-generation antipsychotic medications entered the market, they were observed to cause fewer extrapyramidal symptoms than the typical antipsychotics. However, the second-generation antipsychotics are associated with a new potential drawback: metabolic side effects. Many of the second-generation antipsychotics are known to cause weight gain, dyslipidemia, elevations in blood pressure, abdominal circumference, and blood glucose levels. Furthermore, both first- and second-generation antipsychotic medications are on the Beers criteria list as a class with the suggestion to avoid use unless being used to treat schizophrenia, bipolar disorder, or for short-term management of chemotherapy-associated nausea and vomiting [31]. Other possible side effects of both first- and second-generation antipsychotics include QTc prolongation, hyperprolactinemia, and orthostatic hypotension.

The entire drug class of antipsychotic medications carries a boxed warning specific to the elderly population related to increased mortality in patients with dementia-related psychosis. The package insert for olanzapine reads, "Cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, were reported in patients in trials of olanzapine in elderly patients with dementia-related psychosis. In placebo-controlled trials, there was a significantly higher incidence of cerebrovascular adverse events in patients treated with olanzapine compared to patients treated with placebo" [37].

Akathisia

Akathisia is the subjective feeling of internal restlessness; this can often be observed as shifting, resituating, crossing and uncrossing legs, rocking, pacing, self-reported anxiety symptoms, and/or a rapid shift from sitting to standing [21]. The underlying mechanisms of akathisia have not been clearly defined, though it is suspected to be related to the dopamine D2 binding affinity of antipsychotic medications [38]. Women are more susceptible to akathisia than men. Akathisia can be quite distressing for the patient and careful assessment should attempt to differentiate other conditions (e.g., anxiety) from akathisia. The Barnes Akathisia Rating Scale (BARS), a four-item scale, is the most-used screening tool for akathisia [21].

Tardive Dyskinesia

Tardive dyskinesia is a delayed effect of antipsychotic medications and includes stereotypical, involuntary, abnormal movements of the muscles of the head, limbs, and trunk [21]. Tardive dyskinesia can more specifically be observed as lip smacking, puffing of the cheeks, or other repetitive perioral movements. It typically presents after six months of treatment but has been observed as early as one month following the initiation of a dopamine D2 receptor antagonist [39]. Women are more susceptible to developing tardive dyskinesia than men. First-generation (typical) antipsychotic medications bind more tightly to the dopamine D2 receptor and therefore are more likely to cause tardive dyskinesia than second-generation (atypical) antipsychotic medications [39].

The DSM-5-TR recognizes tardive dyskinesia and outlines diagnostic criteria for its diagnosis; it is important to note that the symptoms must persist for one month following discontinuation of the offending medication in order to qualify for diagnosis [40]. Tardive dyskinesia symptoms range in severity from mild to debilitating. Patients may be assessed using the Abnormal and Involuntary Movement Scale (AIMS) to evaluate abnormal or involuntary movements that may be associated with tardive dyskinesia.

Neuroleptic-Induced Parkinsonism

Neuroleptic-induced parkinsonism can cause a cluster of symptoms, including muscle stiffness, tremor, drooling, shuffling gait, cogwheel rigidity, shuffling gait, and stooped posture [21]. Like akathisia and tardive dyskinesia, women are more likely than men to develop neuroleptic-induced parkinsonism; however, with this side effect, older adults are also more susceptible than younger patients. Higher potency medications and agents with lower anticholinergic effects (e.g., haloperidol) are more likely to cause this side effect [21]. The efficacy of antipsychotic, or neuroleptic, medications in the elderly is not well-established, though they are used with relatively high frequency. Differentiating neuroleptic-induced parkinsonism from genuine Parkinson disease can be difficult for general practitioners, psychiatric providers, and even neurologists. The recommended tools to assess for parkinsonism and related movement disorder symptoms are the Unified Parkinson's Disease Rating Scale and the Hoehn and Yahr (H&Y) Staging Scale [41].

Dystonia

Dystonia is a movement disorder characterized by intermittent or constant muscle contraction causing slow, twisting movements that may lead to abnormal postures [42]. These sometimes-abrupt muscle movements can be painful and frightening to the patient and can include oculogyric crisis, acute torticollis, abnormal postures of the limbs and trunk, tongue protrusion, and laryngeal-pharyngeal dystonia [21]. Dystonic reactions are more common in young men who have been given doses of high-potency antipsychotic medications [21].

Treatment of Extrapyramidal Symptoms

The treatment of any extrapyramidal symptoms involves administration of anticholinergic medications and/or antihistamines. Certain novel agents that act by reversibly depleting monoamines (e.g., dopamine, serotonin, norepinephrine, histamine) from nerve terminals that are approved for the management of tardive dyskinesia [43]. Improvement in symptoms is also possible via decreasing the dose of or discontinuing the offending agent. It is worth mentioning that antipsychotic medications/neuroleptics are not the only medications that can cause extrapyramidal symptoms, but they are common causes.

Neuroleptic Malignant Syndrome

Aside from extrapyramidal symptoms, antipsychotic medications are known to be associated with the rare but potentially life-threatening complication of neuroleptic malignant syndrome. Neuroleptic malignant syndrome can occur at any time during antipsychotic treatment and has symptoms that initially closely resemble a dystonic reaction. This syndrome can be differentiated from dystonia by its autonomic symptoms of diaphoresis, tachycardia, hypertension, and hyperthermia [21]. Neuroleptic malignant syndrome may also present with abnormal laboratory findings, including elevations in white blood cell counts, creatinine phosphokinase, and liver enzymes [21]. Cases of neuroleptic malignant syndrome in older adults are not well-studied; however, one case report suggested that prescription of antipsychotic medications for older adults at unadjusted dosages (appropriate for younger adults) leads to increased risk.

Despite this extensive side effect profile, first- and second-generation antipsychotics still cautiously have a place in a treatment regimen for older adult patients. A commentary on the *Expert Consensus Guidelines for Using Antipsychotic Agents in Older Patients* suggests that it is inappropriate to use antipsychotic medications in the older adults with generalized anxiety disorder, panic disorder, insomnia, nonpsychotic major depressive disorder, and severe nausea and vomiting [44]. The 2016 APA guidelines recommend that use of non-emergency antipsychotic agents for treatment of dementia-related psychosis should be limited to those patients with severe or dangerous symptoms or symptoms that cause significant distress to the patient (or care partner) after objective discussions about the risks and benefits. Second-generation antipsychotics (e.g., brexpiprazole, pimavanserin) are often considered for short-duration off-label use under close monitoring when absolutely necessary [45]. Antipsychotic medications can be used with caution in the older adult with schizophrenia and bipolar disorder.

Antidepressants

According to the Beers criteria, which antidepressant should be avoided in older adults due to strong anticholinergic effects?

The discovery of the first medication for depression, like the first antipsychotic, happened somewhat by accident. During the period when isoniazid was being used to treat tuberculosis infections, another drug called iproniazid was being developed for the same purpose. Interestingly, it was observed that "side effects" of iproniazid included improvements in sleep, mood, appetite, and psychostimulation, although these effects were not well understood at the time [46]. Subsequently, in 1958, iproniazid became the first antidepressant medication in the class of monoamine oxidase inhibitors (MAOIs). However, as its use increased, adverse reactions (e.g., hypertensive crisis) were noted, often due to MAOIs' interactions with tyramine-rich foods, including aged meats and cheeses [46].

Around the same time, while efforts were underway to develop newer and more effective antipsychotic medications, imipramine was discovered as the first tricyclic antidepressant. Although it did not show improvement in psychotic symptoms, it demonstrated significant efficacy in treating severe depressive symptoms [46]. In the 1960s and 1970s, research began to focus on the role of serotonin in mood and other functions. Subsequently, in the 1980s, fluoxetine emerged as the first selective serotonin reuptake inhibitor (SSRI). Following this, agents targeting norepinephrine and dopamine, such as venlafaxine and duloxetine, were developed.

The Beers criteria identify antidepressants with strong anticholinergic activity, alone or in combination, as drugs to avoid in older adults, as these medications are sedating and may cause orthostatic hypotension. Specifically, antidepressants to avoid include amitriptyline, amoxapine, clomipramine, desipramine, doxepin (>6 mg/day), imipramine, nortriptyline, and paroxetine. The effects of these agents predispose older adults to falls and related injury [31]. Paroxetine affects both anticholinergic and antihistamine receptors, leading to more sedation compared to other SSRIs [47]. It is worth noting that doxepin in doses of 6 mg or less has a safety profile similar to placebo.

In addition to anticholinergic effects and falls risk, certain antidepressants may pose other risks to older adults. SSRIs may cause hyponatremia, a relatively common side effect in older patients [21]. Research has identified frequent coprescription of antidepressant medications with other central nervous system (CNS)-acting agents, which may contribute to increased falls risk in this population [47].

Anticholinergic Medications

Anticholinergic medications block acetylcholine, thus inhibiting the action of the parasympathetic nervous system and can be further differentiated into antimuscarinic blockers and antinicotinic blockers [48]. Common anticholinergic medications include benztropine, trihexyphenidyl, oxybutynin, and scopolamine. Benztropine and trihexyphenidyl are two commonly prescribed medications to treat extrapyramidal symptoms caused by antipsychotic medications. Older adults have decreased acetylcholine-induced transmission within the central nervous system, making them more susceptible to undesirable effects of the medications [48]. Older adults are also more likely to have acquired medical conditions that require treatment with anticholinergic agents, like prostatic hypertrophy, urinary retention, and narrow-angle glaucoma [21].

DE-PRESCRIBING

The treatment plan for the older adult experiencing unacceptable side effects of psychopharmacology should include the practice of deprescribing or tapering and/or discontinuing medications that have been deemed to be more harmful than helpful. Some have proposed a distinction between the terms polypharmacy and medication overload [49]. As noted, polypharmacy is defined as taking five or more medications, which may or may not be associated with adverse effects. Conversely, medication overload describes cases of multiple medications (with no clear quantification as to number of medications) being prescribed to the patient in which the harms outweigh the benefits [49]. Some groups have called for a national strategy to address the issue of medication overload and thus improve the quality of life of older adults. In many cases, older adults can benefit significantly from deprescribing to mitigate problematic and life-altering side effects.

Patients with behavioral and psychological symptoms of dementia are at heightened risk for psychiatric medication-related risks and side effects associated with the antipsychotic medications. The American Psychiatric Association (APA) guidelines suggest deprescribing antipsychotic medications to older patients with dementia after three months [50]. There is a lack of consensus of the dosing recommendations for older adults with dementia, and higher antipsychotic dosages have been associated with worse discontinuation syndromes among these patients [51]. The APA recommend limiting doses to maximums of 50 mg of quetiapine, 1.75 mg of olanzapine, and 0.5 mg of risperidone in those with dementia [51].

Deprescription of antipsychotics in the older adults with behavioral and psychological symptoms of dementia did not experience worsened symptoms following discontinuation of the antipsychotic medication [52; 53].

Nursing and advanced practice nursing care of the older adult extends beyond the patient with psychiatric diagnoses, as potentially inappropriate medications could be prescribed off-label for a variety of reasons. For example, quetiapine may be prescribed in low doses for insomnia in psychiatry and primary care practice. Tricyclic antidepressants (which may prolong the QTc interval) may be used for a combination of insomnia, chronic pain, and nocturia. Anticholinergic medications (e.g., benztropine) may be prescribed alongside antipsychotic medications without evidence of movement-related side effects. A combination of the Screening Tool of Older Person's Potentially inappropriate Prescriptions and the Screening Tool of Alert doctors to the Right Treatment (STOPP/START) can be used to detect prescribing omissions and potentially inappropriate medications in this population [54].

In one qualitative study, most patients did not think they were taking an inappropriate number of medications but were open to the idea of deprescription [55]. A strong therapeutic alliance is necessary in helping the patient to understand the risks associated with medication overload. Factors that contribute to a positive attitude of older adults toward deprescribing include trust in the healthcare provider, adverse effects on quality of life from current medications, prospect of follow-up and monitoring, and alternative treatment options [55].

It is important to remember that polypharmacy may be necessary, particularly for patients with chronic conditions. It is up to the nurse to consider each patient situation on a case-by-case basis.

UNDERSTANDING HOW MEDICAL COMORBIDITIES IMPACT MENTAL HEALTH

As discussed, individuals are more likely to develop medical comorbidities as they age; the most common chronic conditions in older populations include depression, osteoarthritis, dementia, neck and back pain, cataracts, and chronic obstructive pulmonary disease (COPD) [56]. Older adults often have multiple diagnoses simultaneously, which can have varying effects on their mental health and affect treatment options.

FRAILTY

Frailty is a condition commonly observed in older adults, characterized by the cumulative decline in multiple physiological systems over a lifetime [57]. This change disrupts the body's homeostasis and increases vulnerability to minor insults. Frailty in older adults is associated with an elevated risk of falls, delirium, and varying degrees of disability [57]. Medical comorbidities, decreased immune response, and social and psychological vulnerabilities further complicate the healing process for older adults, making it more challenging for them to recover from illnesses [58].

CHRONIC PAIN CONDITIONS

Pain and depression often coexist in older adults, with each condition often exacerbating the other. Research has supported a correlation between depression and chronic pain, as well as between depression and sleep disturbances; sleep and physical activity level are mitigating factors [59]. Chronic pain can have adverse effects on older adults, not only in terms of physical well-being but also socially and emotionally. Another study involving Chinese nursing home residents reported that 46% experienced mild-to-severe pain and 20.7% exhibited symptoms of depression [60]. Monitoring nursing home residents with pain is essential, as they may experience lower levels of social support and self-rated health and are more likely to exhibit higher levels of depression compared with those with stronger perceived social support or better self-rated health [60]. Chronic pain can also contribute to functional impairments in certain patients.

COVID-19

The COVID-19 pandemic was associated with uncertainty and anxiety, particularly for the older population, who were at higher risk due to medical comorbidities and frailty [58]. Older individuals face an increased risk of developing severe COVID-19 or medical complications associated with infection. During the first waves, older adults had a three times higher risk of death from secondary pneumonia compared with the general population [58]. Social distancing measures, implemented to control the spread of the virus, posed additional challenges for older adults, who often already are experiencing loneliness and disconnection [58]. Moreover, those living in long term-care facilities often experienced complete isolation, leading to limited physical interactions with others.

During the early peak of the pandemic, older adults experienced prolonged periods of isolation, which exacerbated existing mental health symptoms or resulted in the development of new mental health disorders in some patients [61]. In one study, increased stress, anxiety, depression, and PTSD symptoms were noted across different age groups during the initial and subsequent waves of COVID-19. Interestingly, older adults demonstrated more adaptive and relaxed coping strategies compared with younger participants [61]. The lower likelihood of developing PTSD-related symptoms in older adults is consistent with their generally lower rates of PTSD [26].

CHRONIC ILLNESS

In addition to physical symptoms, those with chronic conditions may experience psychological and emotional manifestations that may result from the physical symptoms of and treatments for the disease. Because the diagnosis process can be protracted for many chronic illnesses, individuals who receive the diagnosis may be relieved to finally have a name for the condition that afflicts them; the chronic nature of the condition may not be of immediate importance. Initially, the individual may be more focused on treating the symptoms rather than the realization that there is no cure. Individuals with chronic illness often face the uncertainty of the disease process, including the unpredictability of disease flares and remissions. Thus, living with a chronic disease can be overwhelming for patients, marked by uncertainty and the potential loss of function secondary to the disease process.

The psychological impacts of chronic disease can be variable, affecting family life, work, sexual activity, social activities, finances, and day-to-day living [62]. The diagnosis may impact one's current lifestyle and result in a need for changes in that lifestyle pattern. It may affect the ability to maintain employment status, alter financial stability, and create a potential for the loss of a role, status, or independence, all of which can be further affected by advanced age.

NONPHARMACOLOGIC TREATMENT OPTIONS

According to the MacArthur model of healthy aging, maintaining a low risk of disease-related disability and remaining engaged in social activities are key factors in promoting healthy aging [12; 63]. Considering the potential risks associated with certain medications in older adults, there are numerous options available for addressing psychiatric symptoms in this population aside from pharmacotherapy. Nonpharmacological options such as phototherapy, reminiscence therapy, cognitive-behavioral therapy (CBT), creating a familiar environment in long-term care, tai chi, and walking are worth exploring.

For older adults (65 years of age or older) with mild-to-moderate major depressive disorder, the Department of Defense/ Veterans Affairs suggests offering a first-line psychotherapy (e.g., cognitive-behavioral therapy, interpersonal therapy, mindfulness-based cognitive therapy). Patient preference and the additional safety risks of pharmacotherapy should be considered when making this decision.

(https://www.healthquality.va.gov/guidelines/MH/mdd/VADODMDDCPGFinal508.pdf. Last accessed January 24, 2025.)

Strength of Recommendation: Weak for

PSYCHOTHERAPY

Psychotherapy is a noninvasive and evidence-based approach for treating various mental health conditions, often considered a safer alternative to medication for older patients. When providing psychotherapy to older adults, it is important to consider their unique needs. These patients may strive to find a balance between self-acceptance, contentment, engagement, and personal growth in later life [12]. Functional limitations, family stressors, and social support factors should be considered during psychotherapy sessions.

Reminiscence Therapy

Reminiscence therapy is a treatment that places focus on reflections on life and the aging process and makes use of the patient's remote memory [12; 64]. Simple, or unstructured, reminiscence therapy focuses on the telling of life events with focus on the positive to enhance well-being. Unstructured reminiscence therapy can be done in a group format and does not have to be provided by a psychotherapist. Conversely, structured reminiscence therapy involves moving through the life events in an organized way and reframing thoughts about the events in a positive light [12].

In one study, reminiscence therapy was found to be effective at decreasing death anxiety and increasing adaptation to the aging process among older adults [17]. Reminiscence therapy has a growing body of research and may help with improving self-esteem, enhance socialization, and improve symptoms of depression and anxiety in older adults [17; 64].

Cognitive-Behavioral Therapy

CBT is widely used in psychotherapy, including with older adults, for treating various conditions such as depression, anxiety, schizophrenia, insomnia, dementia, and bipolar disorder [12]. This approach aims to identify and challenge faulty or harmful perceptions, enhance understanding of the problem, promote healthier thinking patterns, and improve behavioral outcomes. When working with older adults, adjustments to the treatment plan may be necessary. The therapist can address multiple physical, emotional, social, and cognitive issues brought by the older adult by setting weekly agendas, prioritizing topics, building skills, and focusing on abilities rather than disabilities [12].

CBT for insomnia (CBT-I) is a particularly effective nonpharmacological treatment option for insomnia in older adults. Instead of prescribing potentially inappropriate medications, CBT-I targets the underlying causes of insomnia and has demonstrated efficacy and safety as a first-line treatment for healthy older adults [65]. In general, CBT should be considered as a primary treatment approach for various psychiatric symptoms in older adults.

According to the National Collaborating Centre for Mental Health, the recommended high-intensity psychological intervention for persons with generalized anxiety disorder is cognitive-behavioral therapy (CBT) or applied relaxation.

(https://www.nice.org.uk/guidance/cg113. Last accessed January 24, 2025.)

Level of Evidence: Expert Opinion/Consensus Statement

PHOTOTHERAPY

What is the recommended light intensity for phototherapy treatment?

Phototherapy, also known as bright-light therapy, is a nonpharmacologic intervention most notably used in the treatment of seasonal affective disorder. With this approach, the patient follows the daily habit of sitting in front of a 1,500–10,000 lux lightbox each morning before sunrise [21]. One study explored the use of phototherapy in the treatment of mild-to-severe dementia. The researchers found that the phototherapy was more effective in managing the behaviors associated with severe dementia than mild-to-moderate dementia, but overall, the phototherapy was no more effective than placebo [66]. Another study focused on the treatment of sleep-related problems and the potential role of phototherapy, finding the approach effective for improving the sleep of healthy older people [67]. Another study noted the documented efficacy of phototherapy for seasonal affective disorder and bipolar depression, but studies including and/or focusing on older adults are limited.

COMPLEMENTARY AND ALTERNATIVE THERAPIES

Tai Chi

Tai chi originated as a form of martial art and can also be implemented as a form of Chinese medicine [68]. It is important to note that what is commonly referred to as tai chi in the literature does not represent the ancient, complex traditional practice and is often a modified version [81]. It has been adapted in some places as a low-impact exercise that employs slow, gentle movements with breathing and cognitive techniques to strengthen and relax the body and mind [82]. These modifications, along with video streaming services, have made tai chi a more accessible practice for those who want a gentle, low-impact form of exercise.

One study sought to compare measures related to fall risk (e.g., strength, fear of falls, balance, functional mobility) in a group receiving a tai chi course and a group who did not (i.e., control group) [68]. This study found that the tai chi group improved in all measures, while the control group did not. The improvements in strength and ability to perform functional tasks can serve as a potential fall prevention intervention [68]. This supports the use of community-based tai chi programs in improving fall-risk measures in older adults. There is evidence that tai chi is effective in decreasing symptoms of depression and anxiety, managing stress, and ensuring exercise self-efficacy [10; 70].

In a 2018 study, depressive symptoms improved among older adults who participated in a tai chi program for one hour, three times per week for 24 weeks [10]. Evidence supports tai chi as a reasonable option for older adults. These patients should seek guidance of their primary care provider, physical therapist, and other relevant providers prior to starting a new exercise program.

Chamomile and Lavender

Drinking herbal tea, particularly chamomile-based and lavender-based teas, is a traditional approach to managing symptoms of insomnia. Chamomile is commonly found in commercially available herbal teas and has been promoted for inducing a sense of calm and relaxation. One study involving hospitalized older adults with sleep disorders provided participants with oral preparations of chamomile for four weeks [71]. The intervention significantly improved the sleep quality of the older adults compared with placebo. Similarly, a separate study demonstrated the utility of lavender tea in improving sleep, depression, and anxiety symptoms in the intervention group [72]. In addition, diffusing lavender oil at bedtime for older adults has been found to enhance sleep quality and reduce early morning arousals [73].

Aromatherapy

Aromatherapy is considered a gentle intervention appropriate for all age groups, including older adults [74]. There is, however, very little literature supporting the use of essential oils alone to treat psychiatric symptoms in any population. Limited studies have found that aromatherapy, when paired with massage, can significantly decrease depression- and anxiety-related symptoms in older adults [75; 76]. Most of the literature surrounds the use of diffused lavender oil to support relaxation and sleep. Aromatherapy can also be paired with therapeutic massage as a complementary treatment.

ELDER ABUSE

Which type of elder abuse is most commonly reported in institutional settings?

Elder abuse is a significant issue in the United States, but it is often under-reported; nurses play a crucial role in the identification and reporting of this abuse. An estimated 10% of older adults living at home have experienced elder abuse, including exploitation and neglect [77]. Having knowledge about the different types of elder abuse can assist nurses and other healthcare providers in recognizing signs and symptoms. Their vigilance and action are essential in addressing this problem and ensuring the safety and well-being of older adults.

Elder abuse encompasses physical, sexual, emotional/psychological, neglect, and financial abuse/exploitation. It is often perpetrated by individuals known to the older adult, contributing to significant under-reporting [77]. Victims may be financially dependent on the abuser and lack social support, making help-seeking complicated. They may choose not to question suboptimal care (e.g., missed baths) due to the awareness of caregiver busyness. A qualitative study explored the perceptions and experiences of older adults who had been victims of abuse [78]. One participant described increased vulnerability due to limited mobility and dependence on others for transportation when wheelchair-bound [78]. The study identified four overlapping themes in the participants' reports [78]:

- Vulnerability associated with old age
- Early-life experiences
- Perceptions of abuse
- Consequences and suffering resulting from the abuse

Intimate partner violence (IPV) can manifest in various settings and contexts, often intertwined with other forms of elder abuse, making it challenging to identify specific population needs [79]. In a study involving rural women, many reported experiencing highly controlling behavior as a significant source of stress, although not necessarily identified as IPV [79].

Another study revealed a high prevalence of elder abuse within institutions [80]. The most reported types of institutional elder abuse were psychological/emotional (33%), followed by physical (14.1%), financial (13.8%), neglect (11.6%), and sexual (1.9%) abuse [80].

There is a lack of consensus regarding an appropriate screening tool for assessing elder abuse and the circumstances under which assessment should take place. Nurses, however, hold unique positions that allow them to inquire about abuse during routine visits, potentially recognizing signs of elder abuse and providing necessary interventions.

CULTURAL PERSPECTIVES

International migration, childbearing patterns, and mortality trends have a significant impact on the cultural diversity of the United States [83]. It is the responsibility of all healthcare providers to deliver culturally competent care that takes the patient's own self and culture into consideration; this has been shown to reduce healthcare disparities and improve health outcomes [83]. The U.S. population is becoming increasingly diverse, with notable increases projected in African American, Asian, Pacific Islander, and Native American populations by 2050 [83]. These demographic shifts necessitate an increased ability for nurses and all healthcare providers to provide culturally competent care. It is crucial, however, for nurses to engage in personal reflection and confront their own potential implicit and explicit biases. Implicit bias is defined as attitudes toward a specific social group of which one is not consciously aware and that could negatively influence care. Acknowledging and addressing areas of possible implicit bias are important steps to truly providing culturally competent care.

One key element of culturally competent care includes using professional interpreters instead of relying on family or friends ("ad-hoc" interpreters) for interpretation when caring for a patient with limited English proficiency [84]. When working with an interpreter, it is important for the provider and the interpreter to face the patient directly, with nurse addressing the patient directly rather than focusing on the interpreter.

When treating older adult patients of cultures different from one's own, it is important to ascertain any values or beliefs related to health care or treatment the patient would like to discuss [84]. If in doubt, one may simply ask if there are any aspects of the patient's culture they would like to discuss prior to the appointment. It is important to note older adults who are part of the lesbian, gay, bisexual, transgender, queer/questioning (LGBTQ+) community will encounter similar challenges to their cisgender, heterosexual peers, along with challenges specific to belonging to a minority group, like discrimination and social/structural barriers [85].

Both organizations and individual nurses have a responsibility to provide culturally competent care to a quickly growing older population. At the organizational level, the American Association of Colleges of Nursing has curated a list of cultural competencies for baccalaureate nursing and master's nursing programs to consider when developing programs and courses [86]. Colleges and universities follow these standards to ensure that methods to address social determinants of health and the health needs of minority groups are included in their curricula; the goal is to prepare the future nurse to address these issues in practice. Individual techniques for overcoming bias among healthcare providers include understanding as much as possible as one can about a certain culture and broadening one's understanding of racism, ethnocentrism, and disenfranchisement that affect people of color and other minority groups [83].

CONCLUSION

The older adult population (those 65 years of age and older) of the United States is rapidly growing and is projected to reach 1 in 5 individuals by 2050 [3]. This significant increase necessitates a greater focus on addressing the mental health needs of older adults. Due to medical comorbidities, age-related changes affecting drug metabolism, drug-drug interactions, and potential frailty, older adults are particularly vulnerable when it comes to mental health care. Nurses should possess the ability to explain mental health conditions and understand how these conditions may manifest differently in the older adult. They should also have knowledge of age-related changes that impact medication pharmacokinetics. Familiarity with psychiatric medications, including their mechanisms of action, side effects, effects specific to the elderly, and dosing requirements, is crucial when providing best-quality care to this population. It is worth noting that certain medical comorbidities can complicate the clinical picture. Nurses should also be well-versed in nonpharmacologic treatment options for older adults with mental health concerns. Providing culturally competent care to this growing population while ensuring patient safety and optimal outcomes is of utmost importance.

Customer Information and Evaluation are located on pages 79–80.

Chronic Cough in Adults

Includes 5 Pharmacotherapeutic/Pharmacology Hours

Audience
This course is designed for nurses, physicians, and physician assistants/associates involved in the care of patients with chronic cough.

Course Objective
Chronic cough is difficult to effectively assess and treat, leading to extended periods before diagnosis and significant negative impact on patients' quality of life. The purpose of this course is to provide clinicians with the knowledge and skills necessary to identify and treat patients with chronic cough, regardless of underlying etiology, in accordance with clinical guidelines.

Learning Objectives
Upon completion of this course, you should be able to:

1. Describe the background and terminology related to chronic cough.
2. Compare and contrast available cough severity measures.
3. Outline the epidemiology of chronic cough and underlying etiologies.
4. Evaluate the impact of chronic cough on various dimensions of patients' lives.
5. Discuss the natural history and course of chronic cough.
6. Describe the pathophysiology of chronic cough.
7. Outline components of the initial evaluation of patients with chronic cough.
8. Identify potential underlying etiologies of chronic cough as well as appropriate management approaches for these conditions.
9. Analyze available treatment modalities for chronic cough of various underlying causes, including upper respiratory, lower respiratory, and reflux-associated cough.
10. Identify appropriate modalities for the treatment of refractory chronic cough, including pharmacotherapy, nonpharmacologic approaches, and investigational agents.

Faculty
Mark Rose, BS, MA, LP, is a licensed psychologist in the State of Minnesota with a private consulting practice and a medical research analyst with a biomedical communications firm. Earlier healthcare technology assessment work led to medical device and pharmaceutical sector experience in new product development involving cancer ablative devices and pain therapeutics. Along with substantial experience in addiction research, Mr. Rose has contributed to the authorship of numerous papers on CNS, oncology, and other medical disorders. He is the lead author of papers published in peer-reviewed addiction, psychiatry, and pain medicine journals and has written books on prescription opioids and alcoholism published by the Hazelden Foundation. He also serves as an Expert Advisor and Expert Witness to law firms that represent disability claimants or criminal defendants on cases related to chronic pain, psychiatric/substance use disorders, and acute pharmacologic/toxicologic effects. Mr. Rose is on the Board of Directors of the Minneapolis-based International Institute of Anti-Aging Medicine and is a member of several professional organizations.

Faculty Disclosure
Contributing faculty, Mark Rose, BS, MA, LP, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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INTRODUCTION

Chronic cough, or cough lasting longer than eight weeks, is a debilitating disease that can result in patients coughing hundreds to thousands of times every day. This physically exhausting and socially isolating condition can persist for years or decades, degrade the quality of life in nearly every domain, and result in numerous medical and psychosocial consequences, yet its adverse impact on patients is often overlooked or underappreciated by clinicians. While acute cough is typically transient and self-limited, chronic cough often poses a diagnostic and therapeutic challenge; both non-treatment and over-treatment with ineffective medication are common [1; 2]. Cough that persists despite investigation and treatment is especially vexing for patients and clinicians [3].

BACKGROUND

How are acute, subacute, and chronic cough defined?

The anatomic, diagnostic protocol (ADP) established in the late 1970s that chronic cough in patients with negative chest x-ray findings is a symptom of asthma, postnasal drip, or acid reflux. Later refined to asthma, nonasthmatic eosinophilic bronchitis, upper airway cough syndrome, and GERD, it was believed that treating these underlying etiologies led to a favorable outcome in 90% of patients with chronic cough [4; 5; 6].

However, a large proportion of patients with these conditions do not have chronic cough [7]. Moreover, in many patients, cough persists despite treatment of its presumed cause (referred to as refractory chronic cough) or an underlying cause cannot be identified (referred to as unexplained chronic cough) [8]. This suggested that additional pathophysiological processes were involved [7].

In 2014, the European Respiratory Society (ERS) introduced cough hypersensitivity syndrome, defining chronic cough as a distinct clinical entity [9]. The 2020 ERS clinical practice guideline for chronic cough was pivotal in establishing cough hypersensitivity syndrome, influencing subsequent national and international chronic cough guidelines [10; 11; 12; 13].

In 2016, the "treatable traits approach" was introduced to improve the outcomes of pulmonary patients with complex clinical syndromes (e.g., asthma and COPD) and variable treatment responses by moving beyond practice guidelines directed at diagnostic categories as a single disease entity, to identify and treat relevant phenotypic and endotypic "traits" instead [14; 15; 16]. The treatable traits approach gained rapid acceptance in pulmonary medicine and endorsement in chronic cough guidelines [5; 17; 18].

Cough performs an essential physiological function, mediated by cough reflex pathways in the airways and brain. In some individuals, irritation or inflammation of vagal afferent nerves in the airway leads to cough reflex hypersensitivity, the cardinal feature of cough hypersensitivity syndrome, peripheral and central sensitization, and clinical manifestations of allotussia, hypertussia, and/or laryngeal paresthesia (***Table 1***) [3; 19; 20]. The demographic, pathophysiological, and clinical similarities between cough hypersensitivity syndrome and chronic neuropathic pain are numerous. Chronic pain research has substantially informed how chronic cough and cough hypersensitivity syndrome are understood; both are disorders of sensory processing [4; 21; 22].

Sensitization of cough pathways may persist long after resolution of the inciting acute or subacute event. These chronic coughs will remain unexplained by diagnostic workups that do not consider cough hypersensitivity. Cough hypersensitivity syndrome may improve with the targeted intervention of other treatable traits. If chronic cough persists, the patient has refractory chronic cough [5].

Refractory and unexplained chronic cough are diagnoses of exclusion. A thorough, systematic clinical workup is required so that non-obvious and obvious causes of chronic coughing can be identified. The treatable traits approach may significantly expand clinically important intervention targets. After a diagnosis of refractory/unexplained chronic cough is made, therapeutic attention shifts to downregulating the hypersensitive cough reflex [5].

Maturation in research and practice has led to novel and emerging therapeutic options for patients with refractory chronic cough. Randomized controlled trials of existing centrally acting agents have identified the efficacy of low-dose morphine and gabapentin [10; 23; 24]. The development of P2X3 receptor antagonists, a novel peripherally acting drug class, has led to the approval of gefapixant for the treatment of refractory chronic cough in the European Union, Japan, and Switzerland, with U.S. Food and Drug Administration (FDA) advisory committee review believed imminent as of 2024 [25]. In a given patient, refractory/unexplained chronic cough may primarily involve peripheral mechanisms, central mechanisms, or both, and no tool is available for predicting therapeutic response to peripherally or centrally acting antitussive agents.

As of 2024, there are no FDA-approved treatments for chronic cough or for refractory chronic cough. When chronic cough persists after potential underlying causes are identified and treated according to current practice guidelines (e.g., for chronic cough related to nonasthmatic eosinophilic bronchitis or GERD), all therapeutic options for refractory chronic cough are prescribed off-label.

CHRONIC COUGH TERMINOLOGY	
Term	**Definition**
Acute cough	Cough lasting less than 3 weeks
Subacute cough	Cough lasting 3 to 8 weeks
Chronic cough	Cough lasting more than 8 weeks
Refractory chronic cough	Cough that persists despite guideline-based treatment of the presumed underlying cause(s)
Unexplained chronic cough	No diagnosable cause of cough is found despite extensive investigation for common and uncommon causes
Allotussia	Cough triggered by innocuous stimuli (e.g., laughing, talking, changes in ambient temperature)
Hypertussia	Exaggerated coughing triggered by mildly tussive stimuli (e.g., strong odors, second-hand cigarette smoke)
Urge to cough (laryngeal paresthesia)	A distinct, often debilitating sensation of irritation or "itch" in the throat or chest that precede cough and is not satiated by coughing
Cough reflex hypersensitivity	The cardinal feature of cough hypersensitivity syndrome
Cough hypersensitivity syndrome	Disorder characterized by cough triggered by mildly tussive or innocuous stimuli, with features of allotussia, hypertussia, and/or laryngeal paresthesia
Source: [5; 9; 26]	*Table 1*

Important knowledge advances in this rapidly evolving field are not reaching healthcare professionals in the United States because chronic cough guidelines published for domestic consumption have become outdated. From this course, clinicians will gain current information on chronic cough and refractory/unexplained chronic cough, including the pathophysiology, differential diagnosis, and clinical management, essential for healthcare professionals in primary care, respiratory medicine, and ear/nose/throat (ENT) settings.

COUGH SEVERITY MEASURES

What benefits do patient-reported outcome measures have over objective measures?

Patients with chronic cough experience cough-related physical, psychological, and social burdens, which can result from different aspects of cough severity, including cough frequency, cough intensity, disruption of daily activities due to cough, and cough-specific health-related quality of life. The severity and impact of chronic cough on physical, psychological, and social domains can be quantified through several validated objective and subjective measures [27].

Patient-reported outcome measures obtain a comprehensive understanding of the impact across these domains [27]. Patient-reported outcomes capture many issues that cannot be assessed effectively by objective measures and are also inexpensive, readily available, convenient, and easy to use for the patient [28]. A minimal clinically importance difference, the smallest change in an outcome that patients would perceive as important, is established for both objective and patient-reported outcome tools [29]. Cough measures mentioned throughout this course are summarized in ***Table 2***. Cough frequencies of greater than 700 over an hour have been recorded [28].

EPIDEMIOLOGY

PREVALENCE

What is the estimated prevalence of chronic cough among U.S. adults?

Cough is a frequent reason for seeking outpatient medical attention in the United States, accounting for as many as 30 million clinical visits per year, up to 40% of which result in specialist referral [31].

Chronic cough has a prevalence among U.S. adults of roughly 10%, of whom 92% visited healthcare clinicians in the past six months [32]. Chronic cough is estimated to cost $6.8 billion annually in the United States, and an estimated $3.6 billion is spent annually on over-the-counter therapies [33]. The economic implications of chronic cough include the cost of outpatient visits, plus diagnostic workups, prescription medications to treat cough, and lost work and lost school productivity [1]. While inconsistent definitions prohibit direct comparisons of chronic cough prevalence between different countries or ethnicities, chronic cough appears to be more common in Europe, North America, and Australia than in Asian countries [32; 34].

COUGH MEASURES		
Name	**Domains/Items, Rating and Minimal Clinically Importance Difference (MCID)**	**Comments**
Health-related quality of life patient-reported outcome tools		
Leicester Cough Questionnaire (LCQ)	Seven-point Likert scale (1=all of the time; 7=none of the time); 19 items in 3 domains: physical, psychological, and social. Total score range: 3 (maximal impairment) to 21 (no quality-of-life impairment). MCID: 1.5 to 2.5 increase	The most widely used tool for assessing quality of life impact of chronic cough
Cough Quality of Life Questionnaire (CQLQ)	Four-point Likert scale (1=strongly disagree; 4=strongly agree); 28 items over 6 domains: physical and extreme physical complaints, psychosocial issues, emotional well-being, safety fears, and functional abilities. Total score range: 28 (no adverse effect of cough) to 112 (worst possible impact). MCID: 10.6 to 21.9	Contains more items on physical impact of chronic cough (e.g., fractured ribs, headaches, immune deficiency, tuberculosis)
Hull Airway Reflux Questionnaire (HARQ)	Six-point scale (0=no symptoms; 5=most severe) of 14 items that measure airway hypersensitivity in chronic cough. Total score range: 0 to 70 Normal is <14 MCID: 16	Also used as a diagnostic tool for airway reflux, and to assess unexplained respiratory symptoms
Cough Severity Diary (CSD)	11-point scale (0=never; 10=constantly) of 7 items on frequency; intensity; disruptiveness MCID ≥1.3 total score, −1.4 to −1.1 domain scores	Captures the severity and impact of chronic cough. Developed in response to patient feedback.
Objective assessment tools		
VitaloJAK Cough monitor Leicester Cough Monitor (LCM)	Electronic cough recording monitors worn by patients to measure cough frequency, typically as coughs per hour over 24 hours MCID: ≥20% to 30% decrease	Does not capture the episodic nature of chronic cough, a primary factor in patients' disease burden
Subjective tools		
Visual Analogue Scale (VAS)	Score range 0 (no cough) to 100 mm (worst cough ever) MCID: 30-mm reduction on the 100-mm cough severity VAS	—
Numerical Rating Scale (NRS)	Score range 0 (no cough) to 10 (worst cough ever)	

Source: [28; 29; 30] *Table 2*

In KNHANES, a nationally representative study of the Korean adult population, the point prevalence of acute (<3 weeks), subacute (3 to 8 weeks), and chronic (>8 weeks) cough was 2.5%, 0.8% and 2.6%, respectively. The modal durations of current cough were less than one week (31.1%), and more than one year (27.7%); this bimodal distribution reflects the different pathophysiology of acute and chronic cough [35].

REFRACTORY AND UNEXPLAINED CHRONIC COUGH

Refractory chronic cough is seen in 20% to 59% of patients presenting to specialist cough clinics [36]. At Kaiser Permanente Southern California, 11,290 patients with specialist-diagnosed chronic cough were treated and followed for one year; 40.6% continued coughing despite etiological treatment by specialists (i.e., refractory chronic cough) [37].

Roughly 10% of patients with chronic cough lack an identifiable cause despite thorough evaluation (i.e., unexplained chronic cough), including 17% of patients with chronic cough in the Kaiser Permanente cohort [1; 37]. Of 43,453 patients receiving primary care for chronic cough in the UK, 31% had ongoing chronic cough in the absence of associated comorbidities (i.e., no causal explanation or unexplained chronic cough) [4].

DISEASE BURDEN AND HEALTHCARE UTILIZATION

The Kaiser Permanente study examined the disease burden of chronic cough in comorbidities, medication use, and exacerbations [37]. Diagnoses included GERD (44%), hypertension (42%), allergic rhinitis (33%), chronic rhinitis (31.5%), asthma (31%), chronic sinusitis (24.4%), obesity (24%), upper airway cough syndrome (20.4%), depression (20%), and cough complications (19%). Nearly 40% of patients with unexplained chronic cough consulted at least two different specialist departments. In the previous three years, about half of the patients with emergency department visits (28.5%) or hospitalizations (10%) were for respiratory events [37]. Medications were respiratory: nasal corticosteroids (55%), short-acting b2-agonists (50.5%), inhaled corticosteroids long-acting b2-agonist (27%), inhaled corticosteroid monotherapy (24%), and leukotriene modifiers (18.6%); non-respiratory: antitussive codeine (59%), proton pump inhibitors (PPIs) (45%), antidepressants (26%), anxiolytics (15.5%), and gabapentinoids (14%); and other: systemic antibiotics (72.4%) and oral corticosteroids (47%).

Over one year, patients with emergency department visits (26%) and hospitalizations (12%) remained high; more than 50% were respiratory-related. Antitussive and psychotherapeutic drugs were dispensed at a frequency similar to the baseline year. The clinical and economic burden was especially high in patients with both respiratory disease and GERD, but chronic cough persistence (40.6%) was similar between subgroups [37].

A subsequent Kaiser Permanente study of patient-level burden used patient-related outcomes (average chronic cough 8 years) [38]. Mean scores were 11 on LCQ (maximum: 21), 33 on HARQ (normal: ≤13), and 57 on CQLQ (maximum: 112). Correlations were high between LCQ and HARQ (–0.65), LCQ and CQLQ (–0.80), and HARQ and CQLQ (0.69). Patients with chronic cough-related respiratory and gastrointestinal disorders were generally similar. Treatment responses were suboptimal. Women (compared with men) and non-White individuals (compared with White individuals) reported significantly worse cough severity and poorer LCQ, HARQ, and CQLQ scores.

The patient-reported burden of chronic cough was substantial, with long duration, high severity, poor health status, high degree of cough hypersensitivity, low quality of life, multiple cough triggers, and frequent laboratory testing, specialist care, and medications. The study provides strong evidence that patients with chronic cough exhibit frequent poor responses to medications and overall control [38].

The objective and patient-reported burden of chronic cough is substantial, particularly in women and non-White minorities, which markedly affects daily living with inadequate response to treatments.

RISK FACTORS

Risk factors of chronic cough include smoking, female sex, older age, obesity, asthma, allergic rhinitis, rhinosinusitis, and angiotensin-converting enzyme (ACE) inhibitor use for hypertension treatment [34; 39].

In the United States, 18% of adults who smoke cigarettes have chronic coughs [39]. Cigarette smokers are three times more likely to report chronic cough than never-smokers and ex-smokers, and the cough is usually due to chronic bronchitis. However, most patients in cough specialist clinics are nonsmokers [19]. Among 1,000 patients evaluated at a cough center in the Bronx, 2.7% were active smokers and 27% former smokers [40]. Of 11,290 Kaiser Permanente patients with chronic cough, 65% were never-smokers and 2.3% were current smokers [37].

Age and sex underlie the burden and prevalence of chronic cough; more than 67% of patients presenting with chronic cough to specialist clinics are female, likely due to gender differences in cough reflex sensitivity [1; 19]. Cough reflex sensitivity was assessed in individuals from China, India, and northwest Europe. No differences between ethnic groups were found, suggesting that racial variation in chronic cough prevalence may not reflect differences in cough reflex sensitivity and may be influenced by asthma, allergy, or environmental factors [34; 39; 41]. Women in all three ethnic groups demonstrated lower cough thresholds [41].

While chronic cough can occur at any age, the rate rises substantially in women who are 40 years of age or older and is highest in the 60 to 69 age group. The highest rates in men occur between 50 and 69 years of age [1]. In KNHANES, chronic cough increased significantly with age. The odds ratio of 2.20 suggests a substantial increase in chronic cough likelihood for individuals 65 years of age or older (compared with those 18 to 39 years of age). The associations with older age were independent of current smoking and comorbidities [35].

In separate longitudinal European population studies, chronic cough was associated with low educational level and lower socioeconomic status [34]. A systematic review found a significant association between low education level and risk of chronic cough [42].

In South Korea and China, higher male prevalence of chronic cough was attributed to differences in smoking habits and air pollution exposures, respectively [28]. Occupational irritants, such as fumes, gases, cleaning products or dust, may cause cough by triggering cough reflex or by inducing oxidative stress and eosinophilic inflammation, but the effect of such factors on chronic cough remains elusive. Air pollution is an important risk factor for chronic cough. Levels of fine particulate matter ≤2.5 mcm in diameter (or PM2.5) are higher in East Asian than in European or North American countries but the prevalence of chronic cough is lower, suggesting potential host-environment interactions in developing chronic cough [19].

Persistent cough is a class-wide adverse effect of ACE inhibitors, and the 5% to 35% prevalence is much higher in East Asian than in other populations. In genotype studies, the genetic polymorphisms ACE I/D and SLCO1B1 were related to ACE inhibitor-induced cough and were more common in East Asian populations, which may account for the ethnic differences and possibly predict risk of ACE inhibitor-induced cough [43].

PATIENT IMPACT OF CHRONIC COUGH

Patients report numerous cough-related physical and psychosocial effects, most commonly fatigue, sleep disturbance, exhaustion, breathlessness, headache, dizziness, musculoskeletal pain, wheezing, impairment of speech, vomiting, excessive perspiration, self-consciousness, and interference with daily activities [28; 44]. These effects have a significant impact on patients' quality of life.

PHYSICAL IMPACT

What physical complications are associated with chronic cough?

During vigorous coughing, intrathoracic pressures may reach 300 mm Hg and expiratory velocities approach 500 miles per hour (mph) (85% of the speed of sound). These physical forces cause many of the cardiovascular, gastrointestinal, genitourinary, quality of life, musculoskeletal, neurologic, ophthalmologic, psychosocial, and respiratory complications of chronic cough, ranging from the relatively minor to life-threatening or even fatal. Comorbid illnesses or older age can magnify these effects [44; 45].

Surgical Complications and Hernia

Surgical complications from uncontrolled coughing include extrusion (i.e., expulsion) of ocular contents during eye surgery, and wound dehiscence (i.e., splitting or bursting open) following cardiac or abdominal surgery. Similarly, severe coughing can cause inguinal, femoral, umbilical, lumbar, or abdominal wall hernia [45].

Fracture

Cough-induced rib fractures, another painful and potentially serious complication of chronic cough, often involve multiple ribs, particularly ribs 5 through 7. The number of ribs fractured is associated with higher mortality rates, particularly in older patients who often have decreased bone density due to osteoporosis (also an adverse effect of long-term corticosteroid treatment). However, rib fractures can also occur in patients with normal bone density [44; 46].

Stress Urinary Incontinence

Stress urinary incontinence, defined as the unintentional loss of urine during or following a bout of coughing or other physical activity, significantly contributes to quality-of-life disruption caused by chronic cough in women. Of 210 consecutive adult women evaluated at a cough center for chronic cough, 63.3% reported stress urinary incontinence induced by cough episodes; stress urinary incontinence developed after the onset of chronic cough and solely occurred during or after coughing in 92.5% and at least daily in 47.3%. For context, 3.5% of similarly aged women in the community experience stress urinary incontinence, while only 5% of men with chronic cough report stress urinary incontinence as an issue significantly impacting their quality of life [28; 47].

Surveys have reported lower rates of urinary incontinence in women with chronic cough, but most women will not volunteer a history of cough-induced stress urinary incontinence unless specifically asked. This may explain the higher prevalence in this study, because the establishment of trust between patient and physician may have encouraged sharing such information. After discussion ensues, patients are often relieved to learn this is a common problem faced by women with chronic cough [47].

Cough Syncope

Cough-evoked syncope is a serious and potentially fatal consequence of coughing. Numerous reports of motor vehicle accidents resulting from cough syncope include the deaths of drivers and pedestrians. While the exact mechanism of remains debated, the required generation of very high intrathoracic pressures likely explains the nearly uniform profile of patients with cough syncope as large male subjects with obstructive airway disease [48]. Cough syncope is considered relatively uncommon, although 10% of subjects with chronic cough in a community sample reported experiencing cough syncope [5; 49]. The mandatory loss of driver's license in some countries (e.g., the UK) has a major impact on employment prospects for these patients [28].

PSYCHOSOCIAL AND QUALITY OF LIFE IMPACT

Chronic cough can interfere with all aspects of patients' lives, including daily living activities, social interactions, home management, recreational activities, and employment. Importantly, when triggers of coughing bouts are very difficult to avoid, the psychosocial impact can be substantial. Chronic cough has a negative impact on relationships, with spouses not being able

to tolerate the cough as a key reason for patients' health-related dysfunction [28]. In a multinational European survey of 1,120 persons with chronic cough, most reported that coughing affected their quality of life (96%), disturbed their family and friends (94%), and affected activities they enjoyed (81%) [51].

The psychological effects associated with chronic cough are highly prevalent, with an impact on mental health comparable to that of stroke or Parkinson disease. Studies of patients with chronic cough have reported high rates of anxiety (33% to 52%) and depression (16% to 91%) [28].

Patients may avoid or be uncomfortable in social situations due to the embarrassment of coughing, its effects (e.g., stress urinary incontinence, retching), and/or the perception by others that they have a contagious condition or are a heavy smoker [28]. The COVID-19 pandemic increased the social stigma of persistent coughing due to its association with contagious respiratory diseases [50].

NATURAL HISTORY AND DISEASE COURSE

What FEV1 findings are common in adult patients with chronic cough?

Little is known about the natural history of cough hypersensitivity, but the available evidence suggests that patients often suffer from it for many years [4]. In a longitudinal study of patients with unexplained chronic cough, cough severity worsened (36%) or was unchanged (23%) over 7 to 10 years. Predictors of cough persistence or improvement could not be identified. Unexpectedly, longitudinal spirometry data showed declines in forced expiratory volumes over one second (FEV1) that were well above population norms for similarly aged nonsmokers. The striking magnitude of decline argued against a chance finding. Around 10% of patients developed spirometric features of COPD [52].

The abnormally rapid decline in FEV1 and a significant minority of patients developing COPD raise the possibility that unexplained chronic cough is associated with a persistent damaging airway process and could be a risk factor for COPD [52]. A 2023 study confirmed that chronic cough is highly associated with FEV1 decline, regardless of COPD presence, while chronic cough in patients suffering from COPD is associated with lower FEV1, more dyspnea, worse health status, and is an independent risk factor for exacerbations of COPD possibly linked to altered transient receptor potential (TRP) channel function [53].

Cough is often the most bothersome and intractable symptom reported by patients with asthma, and the significant disease burden of chronic cough was described in a prospective cohort of 323 consecutive adult participants with asthma who received optimized asthma therapy. After 12 months, those with chronic cough had more airflow obstruction; worse asthma control and quality of life; increased airway inflammation; upper respiratory tract infection as a trigger; more psychological, rhinitis, and COPD comorbidities; greater work productivity loss and daily activity impairment; and increased exacerbations. These findings call for more attention to chronic cough in asthma [54].

In summary, chronic cough is related to an accelerated FEV1 decline over time, regardless of smoking history or COPD diagnosis, but the relationship between chronic cough and worse clinical outcomes lacks a clear pathophysiological explanation [55].

PATHOPHYSIOLOGY OF CHRONIC COUGH

NORMAL PHYSIOLOGY

The Cough Reflex

Cough is an innate reflex that protects the airways from foreign objects, clears excess secretions, and preserves airway patency. The cough reflex consists of peripheral airway receptors of afferent nerves, cough control centers in the central nervous system (CNS), and efferent nerves.

Cough occurs in three phases [31; 56]. The first is inspiratory, during which the glottis opens widely followed by rapid inhalation sufficient for generating enough air movement to be productive. The second phase is compression. This phase is characterized by the rapid closure of the glottic apparatus and contraction of abdominal and other respiratory muscles compresses the alveoli and bronchiole, increasing intrathoracic pressure to greater than 300 mm Hg. The final phase is expiration, or the sudden opening of the epiglottis and vocal cords results in rapid, high-volume expiratory airflow that may exceed 500 mph in velocity. The force of this process loosens and expels mucous secretions from the airway wall, while the rapid airflow vibrates the larynx and pharynx, inducing the characteristic sounds of cough.

Vagal Afferents

The cough reflex is activated by vagal afferent A-δ and C fibers, sensory neurons originating from brainstem vagal ganglia that innervate the larynx and proximal airways. A-δ fibers are mechanoreceptors, activated by airway mucus, inhaled foreign bodies, and low pH (i.e., acidity). C-fibers are nociceptive chemoreceptors, activated by signaling molecules and mediators of inflammation or tissue damage within the airway [19; 25; 57; 58].

Neurobiological Processes

Complex neurobiological processes in the peripheral nervous system, brainstem, and higher cerebral cortex mediate coughing [59]. Receptors (e.g., P2X3 purinergic receptors, voltage-gated sodium channels [NaV], bradykinin receptors, and transient receptor potential [TRP] ion channels) and neuropeptides (e.g., substance P, calcitonin gene-related peptide [CGRP]) play important roles [60].

Noxious mechanochemical stimuli in the airways activate ligand-gated ion channels and G protein-coupled receptors on vagal nerve endings; NaV channels depolarize, propagating the signal up the vagus nerve to first-order synapses in brainstem nuclei. From there, the signal is relayed by second-order neurons to brainstem and spinal motor neurons to reflexively modify breathing; to third-order neurons of the primary somatosensory cortex where the unpleasant urge-to-cough sensation is mediated; and to higher-order cortical neurons that mediate conscious perception of cough [23; 60].

These ascending third-order pathways enable perception of airway irritation, and regulatory control of descending motor pathways that terminate in the brainstem and in spinal respiratory circuits [22; 61]. Under physiologic conditions, higher inhibitory brain processes permit the modification of coughing behavior, and the urge to cough may be suppressed [21].

Extrapulmonary airways (i.e., larynx, trachea, and mainstem bronchi) are also reflexogenic sites essential for preventing aspiration, inhalation of noxious chemicals, and accumulation of excessive mucus; all can induce reflex coughing with irritation of vagal afferent nerves [21].

Coughing is a reflex and a voluntary behavior with or without the sensation of an urge to cough. Reflex cough, behavioral cough, and the urge to cough (which precedes the motor act of coughing) are three separate entities, each dependent on their own neural processes [21; 22]. The relevance of these neurophysiological processes is apparent when considering the development of cough hypersensitivity syndrome [21].

PATHOPHYSIOLOGY OF CHRONIC COUGH AND COUGH REFLEX HYPERSENSITIVITY

Chronic cough, unlike protective cough, is a pathologic state that no longer serves a physiologic role [60]. Excessive coughing is a consequence of increased activation of neuronal cough-mediating pathways due to [62; 63]:

- Excessive activation of airway vagal afferent terminals by chemical or mechanical irritants
- Neuroplastic changes in vagal afferent fibers
- Neuroplastic changes in the CNS

Nervous system plasticity, or malleability, dictates that excessive stimulation of peripheral nerve fibers can reshape their excitability through changes in receptor expression; synaptic transmission in the CNS is subsequently altered, further increasing the gain within the system [62].

Chronic cough is most associated with and traditionally considered a symptomatic byproduct of asthma, nonasthmatic eosinophilic bronchitis, upper airway cough syndrome, and/or GERD, but most patients with these chronic inflammatory diseases do not have chronic cough. Further, cough severity correlates poorly with cough-associated disease severity, and chronic cough can occur in the absence of these conditions as unexplained chronic cough or unexplained chronic cough [19; 20; 64]. This implies individual differences in cough reflex sensitivity and that hypersensitivity of airway sensory nerves may underlie chronic cough [65].

Cough hypersensitivity, defined as repeated episodes of coughing often in response to minimal or no discernible triggers, is common to all persons with chronic cough [66]. Extracellular adenosine triphosphate (ATP) may play a prominent role in cough hypersensitivity. During cellular injury or inflammation, cells release ATP to alert neighboring cells to damage. In respiratory conditions associated with chronic cough and airway inflammation, such as COPD and asthma, extracellular ATP may be elevated and sensitivity to ATP is heightened [33]. The NK-1 receptor and its ligand, substance P, may also be involved in inducing and maintaining cough hypersensitivity, both peripherally and centrally, either indirectly through inflammatory mediators or directly by stimulating sensory nerve fibers [33].

Cough Hypersensitivity Syndrome

What is the cardinal feature of cough hypersensitivity syndrome?

Cough hypersensitivity syndrome frames chronic cough as a hypersensitivity disorder, akin to chronic pain. Sensitization of vagal afferents by upper or lower airway inflammation leads to increased cough sensitivity to normally anodyne stimuli, the cardinal feature of cough hypersensitivity syndrome [22; 58].

In chronic cough, as in chronic pain, peripheral sensitization is necessary but probably insufficient without central sensitization, which alters the efficacy of neurotransmission in the brainstem and regulation of cough reflex-mediating brain pathways [21]. Patients with cough hypersensitivity or chronic pain have shown abnormal activity in the same midbrain areas that amplify incoming cough (or pain) signals [58; 67; 68].

Chronic pain research substantially informs the conceptual transformation in how chronic cough and refractory chronic cough are understood. Both disorders involve abnormal sensory processing. Taking inspiration from chronic pain, hypertussia describes abnormal excessive coughing in response to airway irritation. Allotussia describes coughing in response to innocuous stimuli. Laryngeal paresthesia describes noxious sensations in the throat or chest associated with an "urge to cough." Peripheral and central sensitization describe processes that alter cough pathway function [62; 63].

Peripheral Sensitization

Dysregulation of airway innervation contributes to chronic coughing and is considered the main driver of cough in refractory chronic cough [63].

In airway inflammation, vagal neuron sensitization and plasticity is shown by increased production of neuropeptides, upregulation of glutamate receptors and nociceptive ion channels (e.g., TRPV1), and lower thresholds for activating sensory-evoked cough responses. Neuropeptide upregulation occurs in airway sensory neurons where they are not normally expressed. These effects underlie hypertussia by expanding the cough-evoking stimuli field [21].

For example, bronchoscopic biopsies of patients with chronic cough demonstrated increases in airway epithelial nerve length and branching. The remodeling of these vagal C fibers may contribute to airway hypersensitivity through increased density of fiber terminals and enlargement of their receptive fields. The shearing forces of chronically coughing and/or the resultant release of inflammatory mediators (e.g., ATP) may explain the increased density of epithelial innervation [69].

Whether the primary stimulus for peripheral sensitization is cellular damage, mechanical stress, or nociceptor stimulation is unclear, as all three can trigger ATP release, activating P2X3 receptors [59].

Central Mechanisms

While peripheral nervous system dysfunction is the most-described component of cough hypersensitivity, central dysfunction plays a fundamental role [70]. Patients with cough hypersensitivity attempting to voluntarily suppress coughing show reduced activity in dorsomedial prefrontal and anterior mid-cingulate cortices, suggesting diminished ability to inhibit cough reflex activation [66; 67; 71].

Patients with refractory chronic cough demonstrate structural and functional alterations in the left frontal brain regions, including lower gray matter volume and enhanced frontoparietal functional connectivity, which may underlie the higher cough scores, greater psychosocial impact, longer disease duration, and impaired cough inhibition in these patients [72].

Studies of chronic cough in asthma and nonasthmatic eosinophilic bronchitis identified increased neuronal sensitivity and subsequent central sensitization via mechanisms of inflammatory-mediated nociceptor sensitization and altered afferent nerve terminal excitability, phenotypic changes in vagal afferent neurons, and central neuroplasticity resulting from increased synaptic signaling from peripheral afferents [73].

The contribution of CNS mechanisms accounts for the efficacy of centrally acting medications (e.g., gabapentin and low-dose morphine) in patients with refractory chronic cough [58].

Laryngeal Hypersensitivity

A study of refractory/unexplained chronic cough patients with cough hypersensitivity referred to a cough clinic suggests highly prevalent laryngeal dysfunction. The 12-month cohort of all referred patients showed high rates of cough hypersensitivity (100%), multiple cough triggers (75%), laryngeal paresthesias (95%), voice abnormalities (50%), upper airway dyspnea (25%), and laryngeal functional abnormalities on nasoendoscopy (73%). Given the frequent constellation of symptoms typifying laryngeal dysfunction and cough hypersensitivity, the authors suggest designating laryngeal hypersensitivity as a specific cough phenotype [74].

Many refractory chronic cough cases have a sensory neuropathic etiology in the hypopharynx and larynx, with laryngeal hypersensitivity a key mechanism [75]. Pharyngeal/laryngeal sensations (e.g., irritation, tickle, throat-clearing), frequently associated with upper airway cough syndrome and reflux cough, may represent sensory neuron dysfunction of vagal afferents in the upper airways and a phenotype of cough hypersensitivity syndrome. Dysphonia, dysphagia, dyspnea, and abnormalities of vocal fold motion on laryngoscopy may present with chronic cough as part of the pharyngeal/laryngeal nerve dysfunction seen in cough hypersensitivity syndrome [76].

Autonomic Dysregulation

There is also evidence of broader autonomic nervous system dysregulation. Compared with healthy controls, patients with chronic cough report more frequent and severe autonomic symptoms in gastrointestinal, orthostatic intolerance, bladder, and pupillomotor domains, primarily in parasympathetically mediated systems, suggesting this population may suffer from dysautonomia. Whether this results from coughing, or if both the cough and dysfunction are part of wider vagal pathology, is unclear [70].

SUMMARY

Functional changes in TRPV1, TRPA1, and P2X3 nerve channels and the development of peripheral and central sensitization are thought to turn cough from a defensive reflex into a cough hypersensitivity syndrome [77]. Hypersensitivity of the cough reflex and deterioration in central inhibition of the cough explain cough persistence [78].

Cough hypersensitivity syndrome is identified by symptoms of allotussia, hypertussia, and/or laryngeal paresthesia and may improve with the treatment of other treatable traits. If the chronic cough persists, the patient has refractory chronic cough [5].

Owing to nervous system plasticity, sensitization of cough pathways may persist long after resolution of the inciting event, such as acute viral airway infection. These chronic coughs will remain unexplained by diagnostic workups that do not consider cough hypersensitivity [5].

Currently, there are no available methods to identify susceptibility to nervous system plasticity and sensitization, objectively diagnose cough hypersensitivity syndrome, or predict treatable versus refractory chronic cough.

EVIDENCE-BASED PRACTICE RECOMMENDATION

According to the European Respiratory Society, cough hypersensitivity through cell damage and inflammation underlies much of the increased cough seen in other pathologies. The different pathological processes in individual conditions contribute to the disease-specific heterogeneous etiology of cough in other lung disease.

(https://erj.ersjournals.com/content/55/1/1901136. Last accessed August 12, 2024.)

Level of Evidence: Expert Opinion/Consensus Statement

INITIAL EVALUATION OF CHRONIC COUGH

When initially encountering a patient with chronic cough, the primary task is to perform a thorough evaluation that seeks potential underlying treatable causes of chronic cough and to treat the cause(s) according to current clinical practice guidelines [99]. These patients typically undergo extensive medical workup and treatment across multiple subspecialties without improvements in their symptoms, and clinicians should try to break the often-repetitive cycle of investigations, empirical treatment, and worry experienced by these patients [75]. The degree to which patients have been investigated varies, so basic tests may be required. Further investigations depend on the individual's presentation [5]. After a diagnosis of refractory chronic cough is made, the therapeutic focus shifts from identification and treatment of underlying causes to suppression of the hypersensitive cough reflex [99].

The initial evaluation (detailed history and physical examination) accomplishes the key tasks of identifying or ruling out a wide range of diseases underlying the chronic cough and identifying any danger signs that may indicate a diagnosis that needs urgent attention. Any positive findings should guide the initial management [8; 44].

DEFINITIONS OF COUGH

To eliminate confusion on how to define cough, the American College of Chest Physicians (ACCP) and the ERS have standardized the definition of cough according to its duration [10; 100]. Consistently applying these guideline-established definitions is crucial [2].

Thus, the first step in evaluating cough is to determine its duration. This also helps to narrow the differential diagnosis based on the most common underlying causes [10; 100]:

- Acute (<3 weeks) cough:
  - Infectious etiologies, especially with viral causes
  - Exacerbations of chronic diseases (e.g., asthma, COPD)
  - Pneumonia
  - Environmental exposures
- Subacute (3 to 8 weeks) cough:
  - Postinfectious cough
  - Exacerbations of chronic diseases (e.g., asthma, COPD)
  - Upper airway cough syndrome
- Chronic (>8 weeks) cough:
  - Upper airway cough syndrome
  - Asthma
  - Nonasthmatic eosinophilic bronchitis
  - GERD

In chronic cough, allergies are considered secondary to upper airway cough syndrome or asthma.

When cough has lasted three or more weeks and is not postinfectious, some experts recommend not waiting for eight weeks to begin a chronic cough workup [6].

PATIENT HISTORY

A detailed evaluation is performed and should include the following [2; 5; 6; 8; 10; 100]:

- Presenting symptoms or cough characteristics:
  - Duration
  - Productive or nonproductive
  - Associated symptoms (e.g., rhinorrhea, nasal congestion, sneeze, fever, sputum production, hemoptysis, dyspnea, weight loss, dysphonia, dysphagia, peripheral edema)
  - Prior episodes
  - Preceding illnesses (e.g., recent viral infection)
  - Clarify whether the patient is coughing, throat-clearing, or both.
- Medical history, including pulmonary and extrapulmonary (e.g., GERD, hypertension, allergic, immune) conditions
- Surgical history, especially involving cardiac, pulmonary, gastrointestinal, and otolaryngological organ systems
- Family history of atopic disease

- Exposure history
  - Tobacco and cannabis smoking or vaping (e.g., electronic cigarettes)
  - Occupational and environmental exposures
  - Recent travel
  - Country of origin
  - Potential sick contacts
- Review current medications for potential iatrogenic cause. Ask about current use of both prescribed and over-the-counter NSAIDs and aspirin.

It is important to always rule out culprit medications by assessing whether the patient is taking an ACE inhibitor antihypertensive, NSAID, sitagliptin, or any medication that may be suspected of inducing the cough. A dry persistent cough from ACE inhibitor use is caused by bradykinin, substance P, and prostaglandins that accumulate in the upper respiratory tract or lung when ACE is inhibited, enhancing the cough reflex. Stopping the drug typically resolves coughing within four weeks or improves it sufficiently for a diagnosis of iatrogenic cough. Switching to angiotensin II receptor blockers (ARBs) provides antihypertensive control without provoking coughing [6; 101].

PHYSICAL EXAMINATION

The physical examination of a patient presenting with chronic should assess for nasal congestion, pharyngeal erythema, tonsillar swelling, hoarseness, stridor, wheeze (particularly focal wheeze), crackles, and other adventitious sounds.

MANDATORY INITIAL TESTS

Initial diagnostic testing should include chest radiography (usually x-ray). Spirometry testing of pulmonary function is recommended pre- and post-bronchodilator to evaluate possible asthma or COPD.

EVIDENCE-BASED PRACTICE RECOMMENDATION

The European Respiratory Society suggests that clinicians do not routinely perform a chest CT scan in patients with chronic cough who have normal chest radiograph and physical examination.

(https://erj.ersjournals.com/content/55/1/1901136. Last accessed August 12, 2024.)

Strength of Recommendation/Level of Evidence: Conditional recommendation, very low-quality evidence

"RED FLAG" ASSESSMENT OF SERIOUS UNDERLYING CAUSES OF COUGH

What findings on the initial evaluation of chronic cough require further evaluation?

In cough of any duration, the initial evaluation should identify any danger signs that may indicate a diagnosis requiring urgent attention. Important danger signs that will need further evaluation with chest x-ray and possibly laboratory testing and computed tomography (CT) include [44; 100]:

- Systemic symptoms (raises suspicion for chronic infection or rheumatic disease):
  - Fever
  - Night sweats
  - Weight loss
  - Peripheral edema with weight gain
- Hemoptysis, an indicator of infection (e.g., bronchiectasis, lung abscess, tuberculosis), cancer (e.g., lung, bronchus, or larynx), rheumatologic diseases, heart failure, or foreign body inhalation
- Prominent dyspnea, especially at rest or at night, a possible clue to airway obstruction or lung parenchymal disease
- Possible foreign-body inhalation (requires urgent bronchoscopy)
- Smoker older than 45 years of age with a new cough, change in cough, or co-occurring voice disturbance
- Hoarseness
- Trouble swallowing when eating or drinking
- Vomiting
- Recurrent pneumonia
- Abnormal respiratory exam and/or abnormal chest radiograph coinciding with duration of cough

RECORDS REVIEW

If patients have undergone prior evaluations for upper airway cough syndrome, asthma, GERD, or nonasthmatic eosinophilic bronchitis, obtain and review these medical records, including laboratory values, diagnostic reports, and treatments prescribed, to determine if these etiologies have been accurately assessed, diagnosed, and treated. Patients may not have been completely evaluated for these conditions yet diagnosed based on their response (or lack thereof) to empiric trials, which is important to ascertain [2].

THE ANATOMIC DIAGNOSTIC PROTOCOL (ADP)

Even in current international guidelines that emphasize treatable traits, the anatomic diagnostic protocol (ADP) remains useful in the clinical workup of patients with chronic cough for identifying possible treatable conditions, while recognizing that treatment of the presumed cause(s) does not always improve the cough [19]. Consistent with the ADP, this section

EVALUATION OF COMMON CAUSES OF CHRONIC COUGH				
Evaluation	**Common Causes**			
	Asthma	**NAEB**	**UACS**	**GERD**
Spirometry	X			
Bronchodilator reversibility	X			
Bronchoprovocation challenge	X			
Allergy evaluation	X	X	X	
Sputum eosinophilia		X		
Blood eosinophilia		X		
Fractional exhaled nitric oxide (FeNO)		X		
Sinus imaging			X	
Nasopharyngoscopy			X	
Empiric treatment trials[a]	X	X	X	X
[a]Diagnostic-Therapeutic Trials				
UACS	First-generation oral antihistamines Inhaled corticosteroids Inhaled ipratropium			
Asthma or NAEB	Inhaled corticosteroids Systemic (oral) corticosteroids Leukotriene receptor antagonist			
GERD	High-dose proton pump inhibitor (PPI) acid-suppression therapy Anti-reflux lifestyle measures Pro-kinetic agent: metoclopramide			
GERD = gastroesophageal reflux disease; NAEB = nonasthmatic eosinophilic bronchitis; UACS = upper airway cough syndrome.				
Source: [1; 82; 83; 100]				*Table 3*

organizes chronic cough etiologies and management by their lower airway, upper airway, and gastroesophageal origin.

In nonsmoking, immunocompetent patients not taking an ACE inhibitor and with unremarkable chest radiography, cough lasting longer than eight weeks is considered a symptom of asthma, nonasthmatic eosinophilic bronchitis, upper airway cough syndrome, GERD, or any combination [6]. These four common causes to consider should be evaluated (***Table 3***).

The ADP has been modified to simplify the clinical workup by emphasizing empiric treatment trials for suspected, but not fully investigated or confirmed, disease [77]. According to the rationale, objective diagnostic methods for upper airway cough syndrome, asthma, nonasthmatic eosinophilic bronchitis, and GERD are technically demanding, sometimes difficult for patients, and require specialized instruments and personnel. Further, with GERD, discerning causal and temporal relationships between acid reflux and cough is difficult. Thus, sequential empirical therapy is frequently considered and is advised by some before embarking on extensive workup [39; 102]. Because symptom reduction is said to confirm a diagnosis, empiric treatment has been called a diagnostic-therapeutic trial [1].

DIAGNOSTIC TESTS

If airway disease is suspected, the treatable traits approach is advocated to identify and optimize treatment of pulmonary, extrapulmonary, and behavioral traits (***Table 4***). Optimizing airway disease treatment is usually the key to managing cough in these patients. Cough hypersensitivity may be a trait in airway disease and require additional specific treatment [5].

Classic asthma, cough-variant asthma, and nonasthmatic eosinophilic bronchitis are clinical diagnoses with no clear-cut, absolute diagnostic test available to either rule asthma in or out as the cause of a patient's chronic cough [10]. In a stepwise diagnostic approach, initial abnormal lung function testing suggests classic asthma or COPD; normal testing is inclusive of cough-variant asthma, nonasthmatic eosinophilic bronchitis, or chronic bronchitis. Absence of bronchial hyperreactivity to methacholine challenge in patients with normal physical exam and spirometry findings suggests nonasthmatic eosinophilic bronchitis. Negative airway responsiveness can exclude cough-variant asthma. Abnormal spirometry contraindicates bronchial challenge testing [104].

AIRWAY INVESTIGATIONS IN PATIENTS WITH CHRONIC COUGH		
Investigation	**Description**	**Utility**
Lower Airway		
Chest radiograph	Plain radiograph of the chest from anterior or posterior aspect (occasionally lateral view)	**Mandatory**. Abnormal findings should be pursued first as potential cause of chronic cough.
Spirometry	Maximal inhalation and exhalation into a spirometer measures forced expiratory volume in one second (FEV1) and forced vital capacity (FVC)	**Mandatory** test for airflow obstruction. FEV1 ≤80% or FEV1/FVC ratio <70% predicted for age and sex prompts reversibility testing.
Bronchodilator reversibility test	Pre- and post-bronchodilator spirometry in patients with obstructive airflow to measure change 10 to 15 minutes after SABA (e.g., albuterol)	Increase in FEV1 ≥12%, or ≥200 mL, after SABA indicates reversibility. Ideally, perform before starting asthma therapy.
Fractional exhaled nitric oxide (FeNO)	Measurement of nitric oxide levels in exhaled breath to indicate eosinophilic airway inflammation	Increased FeNO levels correlate with type 2 airway inflammation in asthma or nonasthmatic eosinophilic bronchitis. High FeNO (>30 ppb) may predict corticosteroids response.
Induced airway sputum	Patient inhales nebulized hypertonic saline (3% to 5%), inducing sputum expectoration for differential cell count analysis.	The criterion standard assessment of eosinophilic airway, routinely used in cough clinics but not widely adopted
Bronchial challenge/ provocation test	Patient inhales histamine or methacholine; a ≥20% drop in FEV1 confirms bronchial hyperresponsiveness (positive test).	Positive test with isolated cough and normal spirometry indicates an anti-asthma therapy trial. A negative test makes asthma improbable.
Chest computed tomography (CT)	Provides better resolution of lung parenchymal and mediastinal structures than chest x-ray	In productive cough, may identify early lung fibrosis or confirm bronchiectasis. Low utility in chronic cough with normal physical exam and chest x-ray.
Bronchoscopy (fiberoptic)	Allows direct visualization of the upper and lower airways and bronchoalveolar lavage to obtain specimens	**Mandatory** in all patients with suspected inhaled foreign body. Endobronchial appearance typically normal in chronic cough with normal chest x-ray.
Upper Airway		
Laryngoscopy (fiberoptic)	Allows direct inspection of laryngopharyngeal area including epiglottis and vocal cords	Typically unremarkable, but may reveal laryngopharyngeal reflux. Suspected laryngeal dysfunction prompts challenge laryngoscopy.
Sinus CT imaging	Visualizes the frontal, ethmoid, and maxillary sinuses and nasal passages	May provide evidence of sinus opacification or mucosal thickening. Unclear role in patients with chronic cough without nasal symptoms.
Other		
Peripheral blood eosinophil count	Measures absolute number or relative percentage of eosinophils in peripheral blood	May help predict corticosteroid response in respiratory diseases; utility in chronic cough not established.
ppb = parts per billion, SABA = short-acting beta-agonist.		
Source: [10; 19; 103]		*Table 4*

Lung Function Tests

Spirometry can reveal airflow obstruction, variability (>20%) in peak expiratory flow measurements, or an improvement in threshold testing (FEV1 >12%, improvement from baseline of >200 mL) in response to bronchodilators (b-2 agonists). Abnormal spirometry can be seen in patients with classic asthma and COPD, but not cough-variant asthma or nonasthmatic eosinophilic bronchitis [104].

Spirometry

An FEV1/forced vital capacity (FVC) ratio of <70% (or below the lower limit of normal, if available) is a positive test for obstructive airway disease (obstructive spirometry) [103].

Bronchodilator Reversibility Test

Bronchodilator reversibility testing is recommended in patients with obstructive spirometry (FEV1/FVC ratio <70%). Following short-acting beta-agonist bronchodilator administration, improvement in FEV1 of ≥12%, together with an increase in volume of ≥200 mL, is a positive test [103].

Airway Inflammation Measures

Asthma is often, but not always, mediated by eosinophilic inflammation, and measurement of airway inflammation has clinical utility because eosinophilic airway inflammation is associated with favorable inhaled corticosteroid response. Fractional exhaled nitric oxide (FeNO) levels and peripheral blood eosinophil count indirectly estimate airway eosinophilia [5; 10; 84].

Significant (>3%) sputum eosinophilia is the criterion standard for eosinophilic inflammation, but sputum eosinophilia may not be routinely available. Blood eosinophil count is simple and readily available but has diurnal and seasonal variability so multiple assessments should be performed. A blood eosinophil count >0.3 cells/mcL may indicate eosinophilic airway inflammation.

FeNO is a surrogate marker of eosinophilic airway inflammation and inhaled corticosteroid response in classic asthma. FeNO has a relatively high specificity in predicting asthma among patients with chronic cough, but a cut-off level for diagnosis lacks consensus. Elevated FeNO levels (>40 ppb) support a diagnosis of asthma with typical symptoms, but the usefulness in predicting inhaled corticosteroid response in chronic cough is uncertain [5].

A meta-analysis of studies in patients with chronic cough reported significantly higher inhaled corticosteroid response rates in high (>25 ppb) compared with low FeNO (87.4% vs. 46.3%) [105]. After three weeks of high-dose inhaled corticosteroids, the response rate (defined as a ≥1.3-point increase in LCQ) was 68% in patients with high FeNO and no other apparent etiology; LCQ scores and FeNO significantly improved. However, improvements in cough were unrelated to changes in FeNO levels, challenging their direct mechanistic link [106]. Thus, an inhaled corticosteroid trial should be prompted with FeNO >25 ppb but avoided with FeNO <25 ppb unless other factors suggest eosinophilic airway disease [5]. Treatment decisions should not solely hinge on FeNO values [6].

Airway Hyper-Reactivity Measures

In patients with negative physical examination and spirometry findings, bronchial challenge testing (e.g., methacholine) should be performed to confirm airway hyper-reactivity consistent with symptomatic asthma [84]. Bronchial challenge testing is recommended in patients with reactive airway diseases to help diagnosis of asthma and nonasthmatic eosinophilic bronchitis as a cause of chronic cough. A negative bronchial challenge test (defined as an FEV1 decrease of <20% at the highest methacholine challenge dose [10 mg/mL]) has a high negative predictive value of asthma as an etiological diagnosis in chronic cough [104].

Airway eosinophilic inflammation can be present in both asthma and nonasthmatic eosinophilic bronchitis but can be distinguished by a methacholine inhalational challenge (positive in asthma, negative in nonasthmatic eosinophilic bronchitis) because substantially more mast cells localize in the smooth muscle layer in asthma compared with nonasthmatic eosinophilic bronchitis [6].

IDENTIFICATION AND MANAGEMENT OF UNDERLYING ETIOLOGIES

The concept that chronic cough is a disease in its own right has only recently gained acceptance. Different phenotypes of this condition are recognized (e.g., asthmatic cough, reflux cough), but the underlying pathology involves hypersensitivity of the vagus nerve and its central projections. The paradigm of asthma, GERD, and postnasal drip causing the symptom of chronic cough was promulgated from the 1980s onwards. However, after it became apparent that many patients suffering from chronic cough with a particular disease label (e.g., asthma, GERD) failed to respond to treatments for that condition, clinical practice guidance changed [79].

Systematic evaluation and treatment guidelines for chronic cough, based on the anatomic locations of receptors and afferent pathways in the cough reflex, first appeared in 1977 [80]. Using such an approach was estimated to determine the cause of chronic cough in 100% of patients, and the subsequent cause-specific treatment was reportedly almost always successful. Termed the ADP, this stepwise diagnostic approach involves a targeted patient history and physical examination to investigate the possible cause/s of their cough. This information is then used to initiate a stepwise treatment approach until resolution of the cough symptoms [77].

The ACCP recommended the ADP in their comprehensive clinical practice guideline on cough in 1998 and in 2006 [81; 82]. More recent ACCP guidelines evaluate ADP components and provide treatment recommendations on the major causes of cough, including chronic cough due to GERD in 2016, asthma and nonasthmatic eosinophilic bronchitis in 2020, stable chronic bronchitis in 2020, and unexplained/refractory chronic cough in 2016 [77; 83; 84; 85; 86].

However, the understanding of chronic cough has evolved beyond the ADP, especially since 2020 with incorporation of cough hypersensitivity and the treatable traits approach into clinical practice guidelines and endotyping of many cough-associated chronic inflammatory conditions. These knowledge advances are not efficiently reaching U.S. clinicians, because ACCP guidelines on chronic cough have not kept pace. While the ADP remains an important structure of the diagnostic workup for chronic cough patients, its assumptions have been supplanted in recent international chronic cough guidelines.

THE "TREATABLE TRAITS" APPROACH IN CHRONIC AIRWAY DISEASES

In the context of the treatable traits approach, how is a trait defined?

In the late 19th century, Sir William Osler established the modern approach to the diagnosis and treatment of disease, based on the principal organ system where symptoms and signs manifest, with some biological correlates. The Oslerian paradigm of disease classification using diagnostic categories has been in use for more than 100 years, with substantial merit, but limitations of the diagnostic label approach have become evident [16].

As noted, in 2016, the treatable traits approach was introduced to pulmonary medicine to overcome the shortcomings of the diagnostic label approach, which does not consider the biological complexity of airway diseases, the distinct endotypes present in each patient, or common patterns of disease such as chronic cough [14; 17].

The treatable traits approach addresses the complexity of chronic airway diseases as heterogeneous, frequently overlapping, and often comorbid conditions. In clinical trials of patients with asthma and COPD, the treatable traits approach led to significantly greater improvements in health-related quality of life and biological outcomes and reductions in primary care visits (compared with usual care) [16].

A trait is defined as clinically relevant, measurable, and treatable. These traits can be identified by their phenotypes and/or endotypes in pulmonary, extrapulmonary, and behavioral/environmental domains, and can coexist, interact, and change over time in the same patient. The treatable traits approach is agnostic to the traditional diagnostic labels of asthma or COPD and can be used in any patient with airway disease. The treatable traits approach often extends beyond the diagnostic label itself to find more treatment targets, especially in complex patients with suboptimal response to conventional guideline-based treatment [87; 88]. In other words, the treatable traits approach represents a transdiagnostic model.

In asthma, many extrapulmonary traits present as connected comorbidities, meaning they coexist with asthma and may share mechanisms. Extrapulmonary traits (e.g., chronic rhinosinusitis, GERD, anxiety, atopic dermatitis) are clinically relevant as they predict poor outcomes, confound the management of asthma, and are treatable themselves. Through multidimensional assessment of pulmonary, extrapulmonary, and behavioral/environmental domains, the treatable traits approach identifies and targets extrapulmonary traits with effective treatments, improving both asthma and the comorbidity [89].

In the 1970s, the ADP extended the Oslerian classification system to cough, addressing the three common causes (asthma, postnasal drip, reflux) arising from three different anatomical areas. Refined to four causes (asthma, nonasthmatic eosinophilic bronchitis, upper airway cough syndrome, and GERD), this approach benefitted many patients, but in 30% to 40% of these patients, the coughing continues or a presumed cause cannot be identified [16; 90]. In 2023, COPD was added to become a fifth common potential underlying cause of chronic cough [24].

Chronic cough is associated with airway and reflux diseases that are heterogeneous, frequently overlapping, and often comorbid, the same characteristics the treatable traits approach addresses [14; 17]. For instance, asthma is a clinical syndrome with varying phenotypes and endotypes, rather than a single disease entity. COPD is an umbrella term encompassing different respiratory conditions sharing airflow obstruction. Asthma is not always eosinophilic, and GERD is not necessarily acidic [15]. Despite its relatively recent appearance, the treatable traits paradigm is endorsed throughout pulmonary medicine and in post-2019 (international) clinical practice guidelines on chronic cough.

ENDOTYPES OF COUGH-RELATED CHRONIC INFLAMMATORY DISEASES

A phenotype is an observed characteristic resulting from interactions between genotype and environment. An endotype is a specific biological pathway that forms the basis of observable traits in the phenotype [56].

In the 2016 treatable traits paper, the authors broadly call for a shift away from the classical Oslerian top-to-bottom approach (i.e., from symptoms to mechanisms) to reclassifying airway diseases bottom-up, by linking causal molecular pathways (i.e., endotypes) to disease phenotypes (i.e., from molecules to symptoms) [14].

This has been unfolding in allergy and immunology, and these advances are highly relevant to pulmonary medicine and to chronic cough. For instance, the chronic inflammatory diseases of asthma, allergic rhinitis, chronic rhinosinusitis with or without nasal polyposis, eosinophilic esophagitis, and atopic dermatitis, are now defined by a constellation of symptoms that may result from different pathological mechanisms and not as homogeneous diseases [91].

The discovery of new endotypes in allergic and immune diseases has prompted the transition from symptom-focused disease descriptions to biomarkers and pathogenetic pathways—from phenotypes to endotypes [91]. The imperative for transitioning to endotypes is heightened by FDA approval of several biologicals that target specific inflammatory pathways important in disease pathophysiology [92]. These include the most common chronic cough-associated disorders.

Immune dysregulation has been endotyped as type 1, type 2, and type 3 responses. Asthma has been commonly dichotomized as type 2 and non-type 2. Type 2 inflammation is the best-characterized endotype [91; 93; 94; 95].

Type 2 inflammation involves eosinophils as the key players, which contribute to chronic allergic inflammation by producing cytokines, or interleukins (IL), with specific roles in the inflammatory pathway. IL-5 promotes eosinophil recruitment to sites of inflammation. IL-4 and IL-13 promote immunoglobulin E (IgE) production and immune cell trafficking to tissue, driving and sustaining the type 2 response, tissue damage, and chronic inflammation. IL-31 activates binding sites on sensory neurons, which release CGRP and nerve growth factor, causing neurogenic inflammation. In non-type 2 asthma, Th2 cells migrate to asthmatic bronchi and change their phenotype to produce T1 effector cytokines, such as interferon-γ (IFN-γ) and tumor necrosis factor-α (TNF-α), inducing bronchial epithelial apoptosis and remodeling. TNF-α promotes neutrophilic inflammation, which correlates with sputum TNF-α levels in patients with severe asthma. In type 3 inflammation, innate lymphoid cells type 3 (ILC3), T helper lymphocyte type 17 (Th17), and Th22 cells produce cytokines IL-17, IL-22, and IL-23. This mechanism is particularly relevant in the pathogenesis of chronic rhinosinusitis with nasal polyps and neutrophilic asthma [91; 93; 94; 95].

In 2023, the European Academy of Allergy and Clinical Immunology (EAACI) published an updated disease taxonomy with advances in biomarkers, pathogenetic and metabolic pathways, and pathogenic genetic variants. This expanded nomenclature characterizes the following types with relevance to chronic cough [91].

Type V: Epithelial Barrier Defect

The epithelial barrier defect and microbial dysbiosis lead to dysregulation of the immune response, including extensive activation and release of inflammatory cytokines, chemokines and inflammatory mediators (histamine, leukotrienes, reactive oxygen species). The sequence of events eventually leads to tissue damage in asthma, chronic allergic rhinitis, chronic rhinosinusitis, and chronic rhinosinusitis with nasal polyps.

Type VI: Metabolic-Induced Immune Dysregulation

Obesity is a distinguishing variable for clustering and classifying asthma subtypes, and the number of obese patients with asthma has risen dramatically with increasing obesity rates. The obese asthmatic, more likely to be female with adult-onset asthma and to become corticosteroid resistant, has a higher risk of being hospitalized and more frequently presents with severe disease. Higher body mass index (BMI) is associated with increased circulating inflammatory mediators, blood neutrophils, and eosinophils. An additive effect of asthma and obesity further increases inflammatory mediators and airway inflammation.

An asthma endotype introduced in 2020, IL-6-high asthma, is characterized by elevated plasma IL-6 levels, increased markers of systemic inflammation, metabolic dysfunction, and obesity [96].

Type VII: Inflammatory Drug Reactions

These idiosyncratic reactions include hypersensitivity to nonsteroidal anti-inflammatory drugs (NSAIDs) and phenotypes such as NSAIDs-exacerbated respiratory disease in patients with asthma and/or chronic rhinosinusitis ± nasal polyposis. NSAIDs-exacerbated respiratory disease is a chronic inflammatory condition characterized by the triad of asthma, recurrent nasal polyps and hypersensitivity to NSAIDs/aspirin. In the underlying mechanism, cyclooxygenase (COX)-1 inhibition releases eicosanoid mediators, causing bronchoconstriction, increased vascular permeability, mucus production and recruitment of inflammatory cells.

These advances in endotyping chronic inflammatory diseases associated with chronic cough have not yet appeared in practice guidelines on chronic cough, with the exception of eosinophilic airway inflammation, but this science is being translated into practice. For example, cough is the most troublesome symptom for patients with asthma. Older patients with asthma and chronic cough show worse clinical outcomes in asthma control, quality of life, and airway obstruction, and more frequent moderate-to-severe exacerbations, partly explained by the interaction of chronic coughing with aging [97]. Non-type 2 inflammation (e.g., increased neutrophils) is associated with cough in older patients with asthma with chronic cough. Interferon-γ is a non-type 2 biomarker that enhances cough reflex sensitivity by inducing calcium influx in vagal sensory neurons and is associated with increased cough in patients with refractory chronic cough. Older patients with asthma show increased levels of sputum IFN-γ. Non-type 2 inflammation (i.e., neutrophils and IFN-γ) is also associated with reduced inhaled corticosteroid response [54; 97; 98].

TREATMENT

CHRONIC AIRWAY INFLAMMATION

Treatment of chronic airway inflammation includes inhaled corticosteroids, long-acting beta-agonists, long-acting muscarinic antagonists, leukotriene receptor antagonists, systemic corticosteroids, and biologicals. Confirmation that chronic cough is due to asthma (or another chronic cough-associated condition) requires a beneficial response to therapy for asthma, as patients with asthma can also have chronic cough due to non-asthmatic causes [44].

For chronic cough due to cough-variant asthma or nonasthmatic eosinophilic bronchitis, the ACCP recommends inhaled corticosteroids as first-line treatment [84]. With incomplete response, the inhaled corticosteroid dose should be escalated and adding a leukotriene receptor antagonist should be considered. Other causes of cough should be reconsidered as well. For cough-variant asthma, adding beta-agonists should be considered.

In patients with chronic cough in asthma, the first-line treatment is inhaled corticosteroid with or without long-acting beta-agonist [6]. A leukotriene receptor antagonist or long-acting muscarinic antagonist may be added in for those who do not fully respond to initial treatment. Whether biologics can treat chronic cough related to asthma has not been studied.

In adult and adolescent patients with chronic cough due to non-asthmatic eosinophilic bronchitis (NAEB), we suggest inhaled corticosteroids as first-choice treatment.

(https://journal.chestnet.org/article/S0012-3692(20)30045-3/fulltext. Last accessed August 12, 2024.)

Strength of Recommendation/Level of Evidence: 2B (Weak recommendation based on moderate-quality evidence)

When an offending allergen cannot be identified or avoided, chronic cough associated with nonasthmatic eosinophilic bronchitis should be treated with an inhaled corticosteroid. Second-line therapy calls for escalation of the inhaled corticosteroid dose; if response remains incomplete, the patient should be assessed for other causes of cough and a trial of leukotriene receptor antagonist initiated. Occasionally, systemic corticosteroids may be needed.

Tiotropium may be another therapeutic option. In 17 patients with chronic asthmatic cough refractory to inhaled corticosteroid/long-acting beta-agonist, four to eight weeks of tiotropium (5 mcg/day) significantly improved cough reflex sensitivity and cough severity in a subgroup of 11 patients [107]. These results were replicated in a randomized comparison to theophylline 400 mg/day over four weeks. Both drugs improved cough severity and cough-specific quality of life. Tiotropium decreased cough reflex sensitivity, which correlated with changes in cough severity, and higher baseline cough reflex sensitivity predicted greater tiotropium response. The authors conclude that tiotropium may modulate cough reflex sensitivity to alleviate chronic cough in asthma refractory to inhaled corticosteroid/long-acting beta-agonist [108].

EMPIRIC TREATMENT APPROACH

Empiric treatment of chronic cough is systematically directed at the four most common causes of cough, starting with upper airway cough syndrome. In its 2006 guideline, the ACCP states that therapy should be given in sequential and additive steps, because more than one cause of cough may be present [82]. Initial empiric treatment should begin with an oral first-generation antihistamine/decongestant.

If chronic cough persists after treatment for upper airway cough syndrome, asthma as the possible cause should be worked up next. If spirometry does not indicate reversible airflow obstruction, bronchoprovocation testing is performed in the evaluation for asthma.

With the diagnoses of upper airway cough syndrome and asthma ruled out or treated without the elimination of cough, nonasthmatic eosinophilic bronchitis should be considered next, with a properly performed induced sputum test for eosinophils. In most patients with suspected cough due to asthma, a bronchoprovocation challenge should be performed and, if the result is positive, some combination of inhaled corticosteroids, inhaled beta-agonists, and/or oral leukotriene inhibitors should be administered.

In patients whose cough responds only partially or not at all to interventions for upper airway cough syndrome and asthma or nonasthmatic eosinophilic bronchitis, treatment for GERD should be instituted next. In patients with cough whose condition remains undiagnosed after all of these conditions has been worked up, referral to a cough specialist is indicated.

When the cause of chronic cough is identified or suspected, there are two options [26; 44; 57; 109]. The first is to pursue one diagnostic and treatment path at a time; with incomplete response of the cough to one line of therapy, adding therapy for the next most likely diagnosis is reasonable. The second option in patients with more than one suspected cause and a cough that is especially disruptive is to empirically treat or evaluate the likely causes simultaneously. After the cough resolves, treatments can be stopped sequentially, starting with the least likely to have been helpful, observing the patient for any return of cough.

BEHAVIORAL TREATABLE TRAITS

Nonadherence and poor inhalation technique strongly influence outcomes in airway disease. Despite their critical importance, the proportion of patients with poor technique is high, unimproved over the past 40 years, and often unaddressed by

clinicians. These behavioral treatable traits can be improved using strategies such as patient-centered communication, motivational interviewing, shared decision-making, and simplification of drug regimens; and should be assessed in every follow-up visit [110].

Smoking cessation improves cough by resolving chronic bronchitis. Nicotine suppresses the cough reflex, and nicotine withdrawal due to smoking cessation may enhancement cough hypersensitivity; hence, patients may experience more coughing for a period after quitting. This can be attenuated and quit rates improved by using nicotine replacement [5].

LOWER AIRWAY ETIOLOGIES OF CHRONIC COUGH AND MANAGEMENT

Lower airway diseases commonly associated with chronic cough are classic asthma, cough-variant asthma, nonasthmatic eosinophilic bronchitis, and COPD [20].

Chronic cough is a central feature that develops in diverse pulmonary pathologies, such as asthma (an inflammatory airway disease) and idiopathic pulmonary fibrosis (an alveolar fibrosing disease), highlighting the significant role of dysregulated cough pathways in lung disease phenotypes [60]. Chronic cough prevalences have been reported for asthma (8% to 58%), COPD (10% to 74%), bronchiectasis (82% to 98%), interstitial lung disease (50% to 89%) and sarcoidosis (3% to 64%); in all five diseases, patients demonstrate cough reflex hypersensitivity, a cardinal feature of cough hypersensitivity syndrome [111].

Presence of chronic cough generally predicts impaired health status and more severe respiratory disease and is associated with greater symptom burden and disease severity in asthma, COPD, bronchiectasis, and interstitial lung disease. It has also been linked to greater exacerbations in asthma and bronchiectasis and increased mortality and lung transplantation in idiopathic pulmonary fibrosis [111].

Asthma and Nonasthmatic Eosinophilic Bronchitis

Asthma is a complex, chronic airway inflammatory disease of bronchial hyper-responsiveness, intermittent airflow obstruction, and symptoms of wheeze and dyspnea that impacts 26 million people in the United States, results in approximately 10,000 deaths annually, incurs an estimated $56 billion annually in medical care and lost productivity costs, and accounts for cough in 24% to 32% of adult nonsmokers with chronic cough [84; 112; 113]. Asthma prevalence has increased with rising obesity rates. Obesity often precedes an asthma diagnosis, making it an important modifiable risk factor (or treatable trait) [5; 113].

In atopic asthma, the most common type (affecting approximately 50% of adults with asthma), allergens trigger innate and adaptive immune activity, releasing inflammatory mediators such as histamine, prostaglandins, and leukotrienes that promote bronchoconstriction and cough [20; 114]. Classic asthma describes symptoms of wheezing, chest tightness, and dyspnea. In these patients, immune response to allergen exposure results in airway inflammation, airflow obstruction, and characteristic symptoms. Increased mucous secretions in narrowing airways induce cough [31; 112].

Cough-variant asthma, in contrast, presents with persistent cough as the primary or only symptom. Cough receptor density is highest in the proximal airways, decreasing as the airways get smaller. In cough-variant asthma, inflammation is primarily in the proximal airways, where cough is stimulated, and less so distally, where inflammation and narrowing cause wheezing and dyspnea in classic asthma [31; 56]. Some have suggested that asthma-variant cough is a more appropriate term than cough-variant asthma, given that cough hypersensitivity symptoms are the chief complaints, while asthmatic features act as triggers and treatable traits of chronic cough in these patients [115].

Nonasthmatic eosinophilic bronchitis was first described in 1989 as corticosteroid-responsive chronic cough in nonsmokers with airway eosinophilia, but without variable airway obstruction or bronchial hyper-responsiveness [116]. Nonasthmatic eosinophilic bronchitis accounts for 10% to 30% of specialist referrals for chronic cough, but nonasthmatic eosinophilic bronchitis prevalence is uncertain, as its diagnosis requires assessment of eosinophilic airway inflammation [44; 84; 117]. In nonasthmatic eosinophilic bronchitis, patients have chronic cough, no symptoms or evidence of variable airflow obstruction, sputum eosinophilia, and normal bronchial provocation tests [56; 117].

Chronic cough in asthma is mechanistically complex, involving IgE or non-IgE mediated eosinophilic airway (i.e., atopic or nonatopic) inflammation, abnormal neuromechanical properties of the lungs, and presence of cough reflex hypersensitivity independently of airway eosinophilia or bronchial hyper-responsiveness [20].

Nonasthmatic eosinophilic bronchitis and asthma share airway eosinophilia and similar basal membrane thickening, but inflammatory mast cells primarily infiltrate the superficial airway epithelium in nonasthmatic eosinophilic bronchitis versus airway smooth muscle in asthma. Along with lower IL-13 expression in nonasthmatic eosinophilic bronchitis, this partially explains bronchitis and cough with normal airway responsiveness in nonasthmatic eosinophilic bronchitis [116; 118]. Nonasthmatic eosinophilic bronchitis lacks the airway hyper-responsiveness of cough-variant asthma, but both share atopic features of eosinophilia and airway inflammation [109].

Eosinophilic airway inflammation in cough-variant asthma is linked to more severe disease. Cough-variant asthma may be a precursor of classic asthma, and both cough phenotypes can manifest overlapping symptoms, airway inflammation, and bronchial hyper-responsiveness [20]. Chronic dry cough, eosinophilic inflammation, and chronic airflow obstruction can present in both cough-variant asthma and nonasthmatic eosinophilic bronchitis [56].

Chronic Obstructive Pulmonary Disease (COPD)

COPD comprises several lung diseases, including emphysema and chronic bronchitis, with persistent and usually progressive airflow limitation associated with an enhanced chronic inflammatory response in the airways and lungs. Exacerbations and comorbidities contribute to the overall severity, while airway and systemic inflammation in COPD is related to disease progression and mortality [119; 120].

In the United States, 14.2 million adults had diagnosed COPD in 2021, of whom 25% were never-smokers, and COPD accounted for 354,000 deaths in 2020 [121; 122]. Among patients with COPD, 70% experience persistent cough and many consider it extremely severe and impairing [64].

Chronic bronchitis describes productive cough on most days of the week for at least three months total duration in two successive years. Chronic obstructive bronchitis is chronic bronchitis with spirometric evidence of airflow obstruction. Chronic asthmatic bronchitis is a similar condition with chronic productive cough, wheezing, and partially reversible airflow obstruction mostly found in smokers with a history of asthma [123].

Emphysema is defined as the permanent enlargement and damage of the lung air sacs with destruction of the airspace walls, causing symptoms of breathlessness. Emphysema can exist without airflow obstruction but is more common in patients with moderate or severe airflow obstruction [119].

COPD manifests as productive cough with airflow limitation and occasional bronchial hyper-responsiveness [20]. COPD and asthma share symptoms of cough, wheeze, and difficulty breathing. The blurred distinction between chronic obstructive bronchitis and chronic asthmatic bronchitis is termed asthma-COPD overlap [123].

Cigarette smoking is the primary risk factor, but only 15% of smokers develop clinically apparent COPD. Smokers with pre-existing airway reactivity, even in the absence of clinical asthma, have greater risk of developing COPD. Inflammation in the large and small airways can persist after smoking cessation. The genetic disorder alpha-1 antitrypsin deficiency is an important cause of emphysema in nonsmokers and markedly increases susceptibility to COPD in smokers [120; 123].

Idiopathic Pulmonary Fibrosis

Idiopathic pulmonary fibrosis is an interstitial lung disease, a group of pulmonary disorders characterized by inflammation and/or fibrosis of the lung parenchyma associated with progressive dyspnea frequently resulting in end-stage respiratory failure. Interstitial lung disease affects 650,000 people and causes 25,000 to 30,000 deaths per year in the United States [124].

Idiopathic pulmonary fibrosis, the most common interstitial lung disease accounting for 35% to 61% of all patients, is a chronic, progressive, invariably fatal fibrotic lung disease [111; 124]. Despite approvals of two antifibrotic therapies, the five-year survival rate remains 25%, far worse than many common cancers. Pharmacotherapies slow the disease progression, but none address the significant symptoms of chronic cough, fatigue, and dyspnea suffered by 85% to 95% of patients with idiopathic pulmonary fibrosis [125].

Chronic cough in idiopathic pulmonary fibrosis predicts disease progression and mortality, is as distressing as breathlessness for patients, and remains one of the most difficult symptoms to control [64; 125]. Among 1,447 patients with idiopathic pulmonary fibrosis cough, every 1-point decrease in LCQ score increased the risk of respiratory-related hospitalization by 6.5%, death by 7.4%, and lung transplantation by 8.7% over 12 months. Worse cough-specific quality of life independently associated with increased risk of respiratory hospitalization, death, and lung transplantation [126].

Two breakthrough studies demonstrated that low-dose morphine and nalbuphine can safely decrease coughing in idiopathic pulmonary fibrosis patients, as will be described later in this course.

Bronchiectasis

Bronchiectasis is a heterogenous disorder characterized by infection, airway inflammation, failure of mucociliary clearance, and airway structural damage. Absolute suppression of cough is not recommended because bronchiectasis is a suppurative condition with an increased risk of infection. However, much of the cough exceeds what is physiologically needed for sputum clearance and is thus maladaptive or pathological [111]. Cough is a central clinical feature of bronchiectasis that contributes to impaired health status and may be an early indicator of disease exacerbation, but it is almost never evaluated [64].

UPPER AIRWAY ETIOLOGIES OF CHRONIC COUGH AND THEIR MANAGEMENT

In upper airway cough syndrome, diverse chronic infectious, inflammatory, or neurogenic upper airway diseases induce chronic cough [20; 127]. While upper airway cough syndrome lacks a uniform definition, its prevalence in chronic cough patients is probably comparable to other major causes like asthma and GERD; in some studies, it is the first or second leading cause [39; 127].

Rhinitis, comprising most chronic upper airway diseases in upper airway cough syndrome, has a lifetime prevalence up to 33% in the United States [6]. Nasal mucosa inflammation due to allergic or non-allergic cause leads to mucus secretion, sneezing, nasal pruritus, and postnasal drip that irritates the airways and stimulates coughing [31]. In chronic rhinitis, these symptoms persist at least three months, inducing nasal obstruction and increased nasal discharge [119].

DISTINGUISHING CHARACTERISTICS OF RHINITIS PHENOTYPES				
Rhinitis Phenotype	**Primary Symptoms**	**Associated Features**	**More Responsive to**	**Less Responsive to**
Allergic	Sneezing, nasal pruritis, clear rhinitis	Ocular itching, wheezing, atopic dermatitis	INCS, INAH, FGAH, SGAH, SCS, AIT	Decongestants, ABX
Nonallergic noninfectious	Intermittent congestion, clear rhinitis	Physical triggers (temperature changes, food, irritants)	INCA, INAH, INAC	FGAH, SGAH, SCS, AIT, ABX
GERD-associated	Postnasal drip, throat clearing	Epigastric pain, heartburn, dysphagia	GERD diet and lifestyle changes, INAC	FGAH, SGAH, INCS, INAH, SCS, ABX, AIT
Chronic rhinosinusitis with or without nasal polyposis	Anosmia/hyposmia, unremitting congestion, facial pain/pressure	Wheezing, NSAID hypersensitivity	SCS, biologics, intermittent INCS	FGAH, SGAH, INAH
Infectious	Acute onset, sinus pressure, nasal congestion with purulent discharge	Viral prodrome, episodic nature lasting <2 weeks	Saline nasal lavage, INAH, decongestants, INAC	FGAH, SGAH, INCS, SCS, ABX, AIT
ABX = antibiotics; AIT = allergen immunotherapy; FGAH = first-generation oral antihistamines; GERD = gastroesophageal reflux disease; INAC = intranasal anticholinergics; INAH = intranasal antihistamines; INCS = intranasal corticosteroids, SCS = systemic corticosteroids; SGAH = second-generation oral antihistamines.				
Source: [6]				*Table 5*

Rhinitis has numerous phenotypes and the nomenclature is not straightforward (***Table 5***). Allergic rhinitis requires immunoglobulin E (IgE)-mediated sensitization to an allergen exposure [6]. Chronic cough in patients with allergic rhinitis is often related to undiagnosed asthma or nonspecific bronchial hyperreactivity. Bronchial biopsy studies of patients with allergic rhinitis without asthma have shown inflammatory cell infiltration and active structural remodeling of the lower airways similar to that of patients with asthma, thereby potentially contributing to cough in these patients [128].

Chronic nonallergic rhinitis syndromes include chronic nonallergic rhinitis, nonallergic rhinitis with eosinophilia syndrome (NARES), atrophic rhinitis, and drug-induced rhinitis; nonallergic rhinitis accounts for up to 80% of cases [129]. Nonallergic rhinitis phenotypes include [6]:

- Vasomotor
- Irritant
- Infectious
- GERD-associated
- Chronic rhinosinusitis with or without nasal polyposis

Rhinosinusitis is preferred to sinusitis because purulent sinus disease without similar rhinitis is rare [130].

Chronic rhinosinusitis is an inflammatory disease of the sinonasal mucosal lining secondary to infectious and allergic etiology, with symptoms of anosmia, nasal obstruction, thick nasal drainage, and facial pressure [92]. Retention of sinus secretions, the key event in chronic rhinosinusitis development, fosters infection and is caused by obstruction or narrowing of sinus ostia, mucociliary dysfunction, or altered mucus composition; 90% of sinus infections involve the maxillary sinus [119]. Cough, one of the important symptoms of chronic rhinosinusitis, occurs in 1% to 5% of U.S. adults [131].

Chronic rhinosinusitis with nasal polyposis, representing up to 20% of chronic rhinosinusitis cases, is more debilitating than the phenotype without nasal polyposis. Comorbidities in chronic rhinosinusitis with nasal polyps are asthma (55% to 56%), allergy (12% to 77%), and allergic rhinitis (17% to 76%). Asthma with nasal polyps is harder to control and more prone to severe exacerbations [92; 93].

Chronic cough pathogenesis in upper airway cough syndrome was previously tied to postnasal drip, because the nose and sinuses lack vagal sensory innervation. However, only a minority of patients with postnasal drip have chronic cough, some patients with upper airway cough syndrome do not have postnasal drip, and the pathophysiology is more complex [11; 127].

In chronic rhinitis and rhinosinusitis, inflammatory mediators are transmitted via glossopharyngeal and vagal receptors in the pharynx and larynx, and via afferent fibers of the trigeminal nerve, sensitizing the cough reflex centrally [11]. Direct irritation of nasolaryngeal mucosa and stimulation of vagal afferents by postnasal drip lead to hematogenous spread of inflammatory mediators and neurogenic or systemic communication

between upper and lower airways, resulting in airway sensory nerve inflammation, cough reflex hypersensitivity, and chronic cough [10; 39].

Convergence of trigeminal and vagal afferents in central cough pathways provides a mechanistic/neuronal link between upper airway disease and the development of cough hypersensitivity [5]. In general, upper airway diseases lead to chronic cough only if the cough reflex becomes hypersensitive; therefore, they are generally considered a trigger rather than a cause of chronic cough [11].

In 2024, nonallergic rhinopathy was introduced to replace vasomotor rhinitis as the term describing 80% of the larger nonallergic rhinitis category, prompted by evidence that neuro-inflammation and TRPV1 receptor activation play important roles, rather than blood vessels. TRPV1 also contributes to nasal hyper-reactivity in allergic rhinitis, an entity called mixed rhinitis. The management of nonallergic rhinitis requires the correct diagnosis; rhinopathy draws attention to the underlying neuro-immune endotype [129; 132].

Chronic cough is triggered in many patients with chronic upper airway disease (usually allergic rhinitis or chronic rhinosinusitis with or without nasal polyps) with common symptoms and signs of postnasal drip, compulsive throat-clearing, nasal stuffiness, globus feeling, headache/facial pain, loss of smell and taste, recurrent hoarseness, and cobblestone appearance of the pharyngeal mucosa on inspection [11]. The most commonly used tool is the SinoNasal Outcome Test (SNOT) [92].

With numerous symptoms and unclear diagnostic criteria, upper airway cough syndrome diagnosis has been based on first-generation oral antihistamine response, which may have central antitussive effects. Upper airway and other airway disease is frequent in patients with chronic cough, making it unclear whether coughing arises from upper or lower airways [5].

A large case series found allergic rhinitis, classic asthma, chronic rhinosinusitis, and nasal polyposis in 46%, 31%, 12%, and 9% of patients with chronic cough, respectively. The high predictive value for concomitant asthma in upper airway cough syndrome calls for investigating lower airway pathology in chronic cough of upper airway origin [20].

Rhinitis is a principal contributor to upper airway cough syndrome. The lengthy differential diagnosis of rhinitis in upper airway cough syndrome includes both allergic and nonallergic diseases; many patients have a combination of both or mixed rhinitis. Distinguishing these will increase treatment success and decrease the time before symptoms improve [6].

Radiological investigations may be useful and are guided by nasal symptoms. Incidental sinus changes may be present in up to 33% of CT and 67% of MRI scans. PPIs should not be used to treat upper airway symptoms [5].

Laryngeal dysfunction and hypersensitivity are common in chronic cough [5]. Consider treatment of laryngeal hypersensitivity as a symptom of cough hypersensitivity. Laryngitis often leads to chronic cough with voice changes (e.g., hoarseness, aphonia). Chronic cough is frequent in functional voice disorders, (e.g., muscle tension dysphonia) [11].

In vocal cord dysfunction, laryngeal hypersensitivity leads to persistent laryngospasm due to different triggering factors, manifesting as cough, wheeze, breathlessness, and voice disturbance. Coughing can be both a trigger and a symptom. Symptoms may be episodic. Diagnosis is based on findings in history, laryngoscopy, and, if possible, spirometry during an attack [5; 11]. In a refractory chronic cough population, vocal cord dysfunction is a common finding and may be a manifestation of laryngeal hypersensitivity. Treatment is by speech and language therapy intervention [5].

REFLUX DISORDER ETIOLOGIES OF CHRONIC COUGH AND THEIR MANAGEMENT

In GERD, retrograde transit of gastric contents into the esophagus leads to troublesome symptoms of heartburn, esophageal chest pain, and regurgitation (i.e., "typical" esophageal symptoms) [133; 134]. Cough is an extraesophageal symptom of reflux disease [11]. Chronic cough has a low, but potential, pathophysiological relationship to reflux disease [133]. Estimated chronic cough due to GERD vary widely (7% to 85%), with higher prevalence in Western than Asian countries [20]. Chronic cough and GERD are both very common conditions and can therefore co-appear without being causally related [99].

GERD was previously considered a leading chronic cough etiology directly caused by the acidity of proximal esophageal refluxate, but patients with chronic cough and healthy controls show similar proximal reflux events [58; 135]. Many patients with chronic cough report GERD symptoms, but PPI therapy is ineffective in those without acidic reflux and only modestly benefit those with typical esophageal symptoms [109].

Reflux can be acidic or non-acidic, liquid or gaseous, and proximal or distal in location. Reflux can trigger cough, coughing can induce reflux, and chronic cough may also cause GERD or increase reflux episodes [20; 134]. PPIs decrease reflux acidity but not reflux events and work poorly in patients with airway or extraesophageal reflux [136]. PPI failure in chronic cough treatment suggests the acidic component of reflux has little effect on chronic cough or its etiology [58].

In extraesophageal reflux, troublesome symptoms not normally considered esophageal manifest in the lower and upper airways as chronic cough, asthma, laryngitis, dysphonia, pulmonary fibrosis, sinus disease, ear disease, postnasal drip, throat clearing, non-cardiac chest pain, or dental erosion [20; 134].

Laryngopharyngeal reflux is defined as the backflow of weakly or non-acidic "mist" or liquid above the upper esophageal sphincter into the upper airways. Due to weaker mucosal defenses in the upper respiratory tract, inflammation of the mucous membranes and epithelial tissue damage occur with

exposure to fewer, and less acidic, reflux events. A significant negative effect from pepsin, a gastric enzyme, on oropharyngeal and respiratory tract tissues is also demonstrated [58; 137].

Airway reflux is interchangeably used for laryngopharyngeal, non-acid esophageal, extraesophageal, and silent reflux. But it is important to remember that airway reflux is not GERD. Defined by the symptoms of heartburn and dyspepsia, and associated with esophagitis, GERD is a peptic condition predominantly of liquid acidic reflux [59]. The majority of patients with airway reflux/laryngopharyngeal reflux do not have esophagitis or heartburn [137].

Airway reflux shifts the paradigm from traditional GERD to cough hypersensitivity through sensitization of vagal afferents. Evidence that esophageal irritation by acid and non-acid reflux may directly initiate cough led to the concept of an esophagobronchial reflex based on crosstalk at the nucleus tractus solitarius between esophageal and airway sensory neurons converging in this brainstem area [58].

This led to gastroesophageal reflux-associated cough, a cough-predominant phenotype of GERD, as a chronic airway inflammatory disease. Epithelial damage and airway inflammation in gastroesophageal reflux-associated cough patients suggest micro-aspiration, and the esophagobronchial reflex mediated by distal esophageal vagal afferents [136].

Chronic cough may result from GERD/extraesophageal reflux-induced airway inflammation and supra-esophageal pathology. Whether refluxate causes damage leading to extraesophageal reflux, needs to be acidic or merely contain pepsin, or whether neurogenic signaling leads to inflammation and subsequent symptoms remains unclear [134; 136].

In sum, GERD can directly affect the airways when gastric acid backflows into the esophagus, irritating the proximal esophagus and laryngopharyngeal areas, triggering the cough reflex to clear the airways. Gastric content can indirectly cause chronic cough by stimulating the distal esophagus, resulting in vagus nerve irritation and cough reflex sensitization. Airway reflux may comprise most cases of reflux-induced cough, its extraesophageal symptom hampering diagnosis based on symptoms alone [39].

Management

What diet and lifestyle modifications are recommended for all patients with known or suspected reflux-related chronic cough?

As discussed, the role of reflux, esophageal dysmotility, and aspiration in chronic cough is controversial. Studies suggest non-acidic reflux, both liquid and gaseous, may be an etiological factor. However, no tool reliably detects such reflux and diagnosis relies on clinical history supported by validated questionnaires (e.g., the HARQ). Moreover, the high prevalence of esophageal dysmotility in patients with chronic cough suggests esophagopharyngeal reflux rather than GERD may be the problem [10].

Many of the signs and symptoms associated with chronic cough are explicable by reflux and aspiration, including voice change, nasal symptoms, and dysgeusia. Frequent chest infection bronchitis, even frank bronchiectasis, may be the consequence rather than the cause of cough via repeated aspiration. Unsurprisingly, following aspiration of GI contents there is a neutrophilic or eosinophilic inflammatory response that might be giving rise to asthmatic cough and mucus hypersecretion [10].

The 2016 ACCP clinical practice guideline for reflux-associated chronic cough suggests that esophageal manometry and pH-metry be performed in patients with suspected reflux cough refractory to a three-month antireflux trial and being evaluated for surgical management (antireflux or bariatric); or with strong clinical suspicion warranting diagnostic testing for gastroesophageal reflux (***Table 6***). Esophageal manometry assesses for major motility disorder. It involves placing the pH electrode 5 cm above the lower esophageal sphincter in the pH monitoring study after the patient is off PPIs for seven days and histamine H2-receptor antagonists for three days [83].

For overweight and obese patients, treatment of suspected reflux-cough should include diet change to promote weight loss. In all patients, recommended diet and lifestyle modifications include [6]:

- Eliminate coffee, tea, soda, other carbonated beverages, fish oil supplements, chocolate, mints, alcohol, and energy drinks, sports, or other drinks containing citric acid
- Consume no more than 45 grams of fat daily
- Avoid smoking and vaping
- Avoid exercising that markedly increases intra-abdominal pressure
- Elevate the head of the bed and avoid meals within three hours of bedtime

In patients with heartburn and regurgitation, PPIs, histamine H2-receptor antagonists, alginate, or antacid therapy is often sufficient to control these symptoms. Gastrointestinal symptoms respond within 4 to 8 weeks, but cough may take 12 weeks to improve [83]. PPI monotherapy is not recommended for chronic cough with solely extraesophageal symptoms, as it is unlikely to resolve the cough.

The ACCP suggests against antireflux surgery for patients with chronic cough patients with a major motility disorder and/or normal acid exposure time in the distal esophagus, as the procedural risks and lack of supporting evidence make the risk-benefit ratio unacceptable [83]. However, surgery may be considered for presumed reflux-cough in patients with normal peristalsis, abnormal esophageal acid exposure on pH-metry, and refractory to medical therapy.

REFLUX INVESTIGATIONS IN PATIENTS WITH CHRONIC COUGH		
Investigation	**Description**	**Utility**
24-hour esophageal pH testing	A catheter is inserted nasally into the esophagus with two pH sensors for 24-hour measurement of proximal and distal acid reflux	Does not reliably predict response to PPI therapy
Barium meal	Radiographic test that visualizes the movement of barium liquid. Can detect structural and motility abnormalities of the esophagus, stomach, and duodenum.	May demonstrate a hiatal hernia and document the extent of non-acid reflux not identified on 24-hour pH testing
Manometry	A catheter is inserted to assess motility patterns by measuring the amplitude of contractile events in the esophagus and its sphincters	Impaired peristalsis is more prevalent in patients with chronic cough, consistent with symptoms of esophageal dysmotility
Impedance testing	Intraesophageal probes measure impedance and pH to record acid, weakly acidic, and non-acid reflux events	Non-acid refluxate may be important in chronic cough etiology, but impedance testing is not validated to investigate chronic cough
Upper GI endoscopy	Allows direct inspection of the upper GI tract and biopsy of stomach and duodenum	Often unrevealing; endoscopic evidence of GERD less common with atypical (e.g., chronic cough) vs. typical symptoms
Source: [19]		*Table 6*

TREATABLE TRAITS AND THOROUGHNESS

The variable success in managing chronic cough may be due, in part, to guidelines or protocols not being implemented as planned (***Table 7***) [6; 80]. Failure to recognize the complexity of airway diseases can lead to suboptimal outcomes, as diseases with different endotypes can require different therapeutic strategies (precision medicine). Because the treatable traits approach is a label-free approach, it does not start on the assumption that the diagnosis (e.g., asthma, COPD) is well-established and clear, a situation that is not the case in many instances in clinical practice, particularly in primary care. This is a fundamental, but often overlooked, issue in the current guideline-directed management of airway diseases [14; 16].

Pulmonary and Extrapulmonary Traits as "Connected Comorbidities"

As discussed, the treatable traits approach encourages trans-diagnostic thinking about chronic cough and associated diseases to identify distinct endotypes and phenotypes within traditional diagnostic categories, as well as shared mechanisms across diagnostic boundaries. For example, asthma and severe chronic rhinosinusitis with nasal polyposis are frequently associated with other, coexisting type 2 inflammatory diseases, such as NSAID-exacerbated respiratory disease, allergic rhinitis, eosinophilic esophagitis, atopic dermatitis, and type 2 eosinophilic COPD [114]. Chronic rhinosinusitis with nasal polyposis has a 7% prevalence in patients with asthma, increasing to 40% in NSAIDs-exacerbated respiratory disease [138]. In predisposed subjects, a dysregulated type-2 inflammation can develop in epithelial barriers (e.g., airways, intestine, skin) in response to various antigens, such as allergens, micro-organisms, and pollutants. This dysregulated epithelial response leads to diseases such as asthma, rhinitis/rhinosinusitis, eosinophilic gastrointestinal disorders, and atopic dermatitis [95].

Allergens are not the only antigens that trigger inflammation. Rather than allergic disorders, type 2 disorders would be a more appropriate definition, also including non-allergic eosinophilic diseases such as nonasthmatic eosinophilic bronchitis, chronic rhinosinusitis, and eosinophilic disorders of the gastrointestinal tract [95].

Targeted biological therapies can also address conditions with shared type 2 pathophysiology. Biologics with FDA approval targeting type 2 inflammatory disease pathophysiology include dupilumab (anti-IL-4 and IL-13), omalizumab (anti-IgE), mepolizumab (anti-IL-5), and benralizumab (anti-IL-5R) [92]. Mepolizumab has proven effective in chronic rhinosinusitis with nasal polyposis and asthma with high eosinophil levels in sputum. Dual targeting of IL-4 and IL-13 by dupilumab has shown efficacy across chronic rhinosinusitis with nasal polyposis, asthma, eosinophilic esophagitis, and atopic dermatitis, and in uncontrolled COPD with high eosinophil counts [93]. Chronic cough, it should be stressed, has not been examined in any study of biological therapies.

PITFALLS IN THE MANAGEMENT OF CHRONIC COUGH
Upper Airway Cough Syndrome
Failing to recognize that upper airway cough syndrome (also asthma or GERD) can present as a cough-phlegm syndrome, misdiagnosed as chronic bronchitis. Assuming that all histamine H1 receptor antagonists (H1RAs) are the same. H1RAs without anticholinergic activity do not help nonallergic rhinitis conditions. Further, anticholinergic H1RAs may adversely affect memory, glaucoma, and prostate problems. Instead, consider ipratropium bromide nasal therapy. Failing to consider: • "Silent" upper airway cough syndrome when a patient does not sense a postnasal drip or realize their frequent throat clearing • Allergic rhinitis and recommend the avoidance of allergens because symptoms are perennial • Sinusitis because it is nonobvious • NSAID-exacerbated disease • The potentially beneficial role of upper respiratory endoscopy
Asthma
Failing to recognize that: • Asthma can present as cough alone (i.e., cough-variant asthma) • Inhaled medications may exacerbate cough • Positive methacholine challenge alone is not diagnostic of asthma
Nonasthmatic Eosinophilic Bronchitis
Failing to consider the diagnosis, occupational/environmental causes, or order the correct test
GERD
Failing to recognize that: • "Silent" reflux disease can be causal and that it may take two to three months of intensive treatment before cough starts to improve and five to six months to resolve • GERD can be worsened by comorbidities (e.g., obstructive sleep apnea) or their treatment (e.g., nitrates or calcium channel blockers for coronary artery disease, progesterone for hormone replacement) Assuming that: • Cough cannot be due to GERD because cough remains unchanged when gastrointestinal symptoms improve • Vocal cords' appearance can diagnose GERD, when inflammatory changes from coughing can mimic those of reflux Being unaware that acid suppression alone will not improve cough Failing to consider: • Non-acid reflux disease • The role of diet, intense exercise, and prokinetic therapy • Adequately treat co-existing causes of cough that perpetuate the cycle of cough and reflux because cough can provoke reflux
Triad of Upper Airway Cough Syndrome, Asthma, and GERD
Failing to consider that more than one condition may be contributing simultaneously to cough, or failing to consider additional contributing conditions because of another "obvious" cause (e.g., COPD) Failing to appreciate: • These chronic disorders cannot be cured and will periodically flare, especially with viral illness • When cough flares after a period of remission, re-evaluate as if a new problem • Asthma may become a problem when it was not before
Unsuspected Airway Diseases
Failing to perform bronchoscopy when chest x-ray and CT are normal. Transnasal route allows inspection of both upper and lower respiratory tracts. Failing to appreciate that prolonged IV therapy for suppurative airway disease may succeed when the same drug given orally failed
Source: [6; 80] *Table 7*

The Argument for Thoroughness

The optimal clinical approach in chronic cough and refractory chronic cough continues to evolve. The ERS guideline suggests simplifying the diagnostic process to shorten a patient's journey to a diagnosis of refractory/unexplained chronic cough and limiting sequential empiric trials to two to four weeks unless responses are observed [10]. However, the 2023 BTS guideline and others argue for a more assertive approach to identify all treatable traits and maximize therapy response before diagnosing refractory/unexplained chronic cough [5; 78]. This would be the counterargument to the diagnostic-therapeutic empiric trials approach.

In a 2024 study, all 201 patients presenting to a cough center in 2018–2022 were prospectively studied. Refractory chronic cough (defined as persistent cough severity VAS ≥40 with little improvement after at least two treatment attempts) was diagnosed in 30.7% and unexplained chronic cough in 1.5% [78]. The authors suggest a thorough diagnostic algorithm, with frequent second-step investigations, enabled diagnoses of less common cough etiologies and the low (1.5%) unexplained chronic cough rate. As many therapeutic trials as necessary were engaged in order to target all identifiable treatable traits of chronic cough. Treatment followed a stepwise intensification of therapy and introduced add-on treatment of all cough causes, but this was time-consuming and related to difficulties in keeping patients' adherence. In routine practice, the authors usually recommend more than two therapeutic trials before diagnosing refractory chronic cough. When refractory/unexplained chronic cough is diagnosed, additional treatments should be initiated. These patients require nonpharmacologic and/or drug therapies with opioids, neuromodulators, or novel refractory chronic cough agents.

In a separate study conducted at a clinic in China, experts found that among 1,554 patients with chronic cough patients with negative chest x-rays, 58.8% were attributable to common causes, including nonasthmatic eosinophilic bronchitis (18.3%), cough-variant asthma (16.3%), gastroesophageal reflux-associated cough (13.2%), and upper airway cough syndrome (11.1%) [139]. In addition, 18.4% of cases were attributable to other causes: chronic bronchitis (6.1%), bronchiectasis (4.5%), atopic (4.4%), and postinfectious (3.5%) cough; 9.6% had chronic cough of unexplained etiology. Finally, 13.1% of cases were due to rare causes (e.g., bacterial bronchitis, somatic cough syndrome, diffuse panbronchiolitis, obstructive sleep apnea, and interstitial lung disease). These findings suggest that special examinations should be considered after excluding common causes of chronic cough.

It is important to remember that the workup to rule out refractory/unexplained chronic cough is not complete until bronchoscopy has been performed [6]. A study of bronchoscopy involving 54 patients with refractory/unexplained chronic cough with sputum production (more than 1 tbsp/day), atypical urge-to-cough sensations in chest, and unremarkable chest CT revealed bronchoalveolar neutrophilia in 84% and excessive dynamic airway collapse in 31% [140]. Bronchoscopy influenced or changed the management in 89% of patients. Bronchoscopy findings in this specific population have rarely been described, and treatment strategies in these patients differ from typical refractory/unexplained chronic cough. Bronchoscopy provides high diagnostic value in refractory/unexplained chronic cough with mucus production, identifying specific treatable traits of neutrophilic airway inflammation and excessive dynamic airway collapse [140].

Another argument for moving away from the routine use of empiric therapeutic-diagnostic trials is to spare patients with chronic cough from exposure to minimally helpful or unhelpful medications with potentially adverse effects. For example, PPIs are recommended against for chronic cough in patients who lack classic GERD symptoms. Cumulative doses of PPIs dose-dependently increase the risk of developing hypomagnesemia and other side effects. Both hypomagnesemia and its consequent decrease in melatonin production can decrease lower esophageal sphincter tone and trigger a paradoxical iatrogenic cough. Rather than PPI dose escalation for partial responders, magnesium and melatonin supplementation is recommended to curtail side effects of long-term PPIs [104].

Oral corticosteroids, due to their substantial cumulative side effects, are now recommended only as a last resort in the most recent asthma treatment guidelines [141; 142]. Even occasional short courses of oral corticosteroids are associated with significant short-term and cumulative long-term adverse effects, with a pronounced dose-response. Short-term adverse effects of oral corticosteroids include sleep disturbance, increased appetite, reflux, mood changes, sepsis, pneumonia, and thromboembolism. As few as four to five lifetime courses of oral corticosteroids are associated with a significantly increased dose-dependent risk of diabetes, cataracts, heart failure, osteoporosis, and several other conditions [142].

TREATMENT OF REFRACTORY CHRONIC COUGH

What pharmacotherapeutic agents are recommended for the treatment of refractory or unexplained chronic cough?

Refractory and unexplained chronic cough are diagnoses of exclusion. For cases with no clear etiology after an extensive workup, or when guideline-based treatment improves the presumed underlying cause of coughing but not the chronic cough itself, cough hypersensitivity syndrome is the most likely explanation [39].

A variety of organizations have published guideline recommendations for the treatment of refractory and/or unexplained chronic cough (***Table 8***). The British Thoracic Society asserts that cough hypersensitivity is a treatable trait of many conditions and often the foremost problem in patients with chronic dry/unproductive cough [5]. However, there are currently no tools to positively identify cough hypersensitivity. If the con-

GUIDELINE RECOMMENDATIONS FOR NEUROMODULATOR TREATMENT OF REFRACTORY/UNEXPLAINED CHRONIC COUGH						
Drug	**Guideline Organization (Year)**					
	ACCP (2016)	**ERS (2020)**	**GRS (2020)[a]**	**FRS (2023)**	**BTS (2023)**	**NEURO-COUGH (2023)**
Low-dose morphine slow-release	Not reported[b]	Strong recommendation	Strong recommendation	Recommended: Grade B	Recommended	Recommended, very high consensus
Codeine	Not reported	Not recommended	Not reported	Not reported	Recommended against	Not reported
Gabapentin	Recommended	Conditional recommendation	Can be used	Recommended: Grade B	Recommended	Recommended, high consensus
Pregabalin	Not reported	Conditional recommendation	Can be used	Recommended: Grade B	Recommended	Not reported
Amitriptyline	Not reported	Not reported	Can be used	Recommended: Grade C	Not reported	Recommended, high consensus
Baclofen	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported

[a]"Can be used" is a weaker endorsement than "recommendation" (i.e., "should be used").
[b]75% of expert panelists endorsed a recommendation of morphine, falling short of 80% required for inclusion; thus, morphine is neither recommended for nor against.
ACCP = American College of Chest Physicians; BTS = British Thoracic Society; ERS = European Respiratory Society; FRS = French-Speaking Society of Respiratory Diseases; GRS = German Respiratory Society; NEURO-COUGH = New Understanding in the treatment Of COUGH Clinical Research Collaboration; SR = sustained-release.

Source: [5; 10; 11; 12; 18; 86] *Table 8*

dition does not improve with treatment of treatable traits, it is considered refractory chronic cough. In these patients, the most effective treatments are those addressing cough hypersensitivity and include low-dose morphine, gabapentin, and nonpharmacological therapy. In addition, novel therapies are in development, with P2X3 antagonists the most promising [5].

PHARMACOTHERAPY

Neuromodulators are centrally acting agents for refractory chronic cough that can downregulate the hypersensitive cough reflex to decrease coughing. Neuromodulators are first-line options for refractory chronic cough [39; 57]. However, some of the literature on neuromodulator use in patients with refractory chronic cough might seem counterintuitive.

Clinical trials of P2X3 antagonists have shown efficacy in reducing cough frequency in many patients with refractory/unexplained chronic cough, but the exact mechanisms underlying refractory/unexplained chronic cough remain poorly understood. Although data also suggest central mechanisms may be a key component in the pathophysiology of refractory/unexplained chronic cough, antitussive drug development has focused on peripheral targets [143].

Among patients with unexplained chronic cough started on amitriptyline and contacted by mail two to three years later, 64% had stopped the medication due to no improvement (40%) and/or side effects (48%). The most common side effects triggering treatment nonadherence were sedation (18%), dry mouth (18%), anxiety (8%), difficulty sleeping (8%), and dizziness (5%). Combining patients who continued and stopped amitriptyline, 53% reported cough improvement of at least 50%. There is some evidence that as treatment duration increases, amitriptyline efficacy may decrease [144].

Opioid Medications

The concept of chronic cough as a neuropathic condition, treated with neuromodulators, is not new. In 1856, Edward Smith described chronic cough as a "disease in itself" due to "irritability of the nerves" that could be treated with "morphia," 164 years before expert consensus in the European Respiratory Society chronic cough guidelines concluded the same, albeit for refractory chronic cough [10; 111]. Opioids are thought to exert antitussive effects through opioid receptors within inhibitory cortical descending pathways [59].

Codeine

Codeine is a weak opioid that is metabolized to morphine (5% to 10%) by the enzyme cytochrome P450 2D6 (CYP2D6) in the liver to produce its antitussive effects [145]. Codeine has long been used as an antitussive, but a minority of the population possess a genetic variation in CYP2D6 activity, with variable and unpredictable metabolism that increases unpleasant side effects and decreases efficacy. Codeine is now considered an unreliable antitussive and should not be used in chronic cough [5].

Low-Dose Morphine Slow-Release (SR)

Morphine is not affected by interindividual variability in CYP2D6 metabolism; thus, its biological effects are more predictable than codeine [146]. In the first positive results from a double-blind randomized controlled trial for any drug therapy of refractory chronic cough, morphine was selected to minimize the variability of codeine [25; 147]. This study compared twice-daily slow-release morphine 5 mg with placebo for four weeks, followed by four weeks of crossover to the alternate treatment. A three-month open-labeled extension of the randomized controlled trial allowed dose escalation to 10 mg twice per day if patients thought their cough was inadequately controlled [147].

The mean LCQ score significantly improved on morphine but not placebo, with significant improvement in physical, psychological, and social subdomains. A 40% reduction in daily cough scores was noted with morphine; placebo had no discernable effect over baseline. Of patients entering the extension, 67% opted for dose escalation and, after three months, had cough outcome improvements similar to 5-mg full-responder patients. Side-effects of constipation (40%) and drowsiness (25%) were tolerable; no patient dropped out from adverse events. Sedation, previously believed to explain the antitussive action of morphine, was transient, but the antitussive effect continued throughout the core and extension study phases [147].

The authors of this study state that side effects and dependence are obvious concerns with opioid therapy for what is a disabling but non-life-threatening condition. However, they note that the risk-benefit ratio makes low-dose slow-release morphine a credible therapeutic option in patients with refractory chronic cough for whom other treatments have failed. Comparisons of similar therapeutic options were made with patients who require long-term oral corticosteroids for severe nonasthmatic eosinophilic bronchitis or cough-variant asthma with a consequently worse adverse event profile [147].

Another double-blind crossover study randomized previous morphine responders to slow-release morphine 5–10 mg twice daily or placebo. After five days, morphine reduced 24-hour cough frequency by 72% over placebo, including overnight (83%) and daytime (71%) cough frequency [148]. Morphine also significantly reduced noxious somatic sensations driving the urge to cough, suggesting this may be an important component of opioid modality in refractory chronic cough [149].

In a real-world effectiveness and tolerability study of long-term, low-dose opioids, 100 patients were prescribed twice daily slow-release morphine 5–10 mg (72%), oxycodone, or oxycodone/naloxone for a median 52 weeks for refractory/unexplained chronic cough. Median cough severity score (CSS, on a 0–10 scale) decreased from 8 pre-treatment to 4. In all, 60% had good-to-excellent response, while 25% had no response. Side effects (present in 38%) were most commonly constipation (25%), which was managed with dose reduction or constipation therapy; however, 15% stopped treatment due to side effect intolerance. Low-dose opioids improved long-term cough outcomes and were tolerated by most patients with refractory/unexplained chronic cough, but managing constipation allowed more patients to continue therapy [150].

Clinical experience with low-dose, slow-release morphine suggests that up to 50% to 60% of patients with refractory chronic cough obtain benefit [5; 59; 150]. Response dichotomizes into either a large effect on cough symptoms or no effect at all and is usually apparent within five days. The main side effect, constipation, can be managed with laxatives or adding oral low-dose naloxone. Once-daily dosing may be sufficient if cough symptoms are mainly troublesome during waking hours or overnight. Antitussive tolerance does not seem to develop. Unlike in severe chronic pain, there appears to be a dose ceiling for slow-release morphine of twice daily 10 mg, with no further antitussive effect beyond this. Concerns remain about misuse/addiction potential, and patients must be carefully monitored [5; 59]. As noted in a 2024 review, it is unclear why such low doses, compared with those used for analgesia, are effective in some patients with refractory chronic cough [25].

Gabapentinoids

Gabapentin and pregabalin are synthetic analogs of gamma-aminobutyric acid (GABA) that bind the α2δ subunit of voltage-gated calcium channels to block excitatory neurotransmitter release. Both were developed originally for epilepsy treatment and subsequently found to ameliorate chronic neuropathic pain, which is associated with central sensitization. The similar pathophysiologic mechanisms of chronic neuropathic pain and chronic cough suggested that gabapentin and pregabalin may also be beneficial in patients with refractory chronic cough [151].

Gabapentin (1,800 mg/day or the maximum tolerable dose) was compared with placebo for eight weeks in a double-blind randomized controlled trial of 62 patients with refractory chronic cough. Gabapentin significantly improved LCQ score over placebo by 1.8 points, and significantly reduced objective cough frequency and cough severity over placebo. Gabapentin response was greater in patients with symptoms of central sensitization (e.g., laryngeal paresthesia, allotussia, hypertussia). The onset of action of gabapentin took up to four weeks [152]. It was subsequently noted that cough frequency differed between gabapentin and placebo groups at baseline (45.3 vs. 68.8 coughs per hour) and was measured only for one hour at each assessment visit, making interpretation of cough frequency outcomes difficult [25; 146].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The European Respiratory Society suggests a trial of gabapentin or pregabalin in adults with chronic refractory cough.

(https://erj.ersjournals.com/content/55/1/1901136. Last accessed August 12, 2024.)

Strength of Recommendation/Level of Evidence: Conditional recommendation, low-quality evidence

An open-label randomized trial compared gabapentin (300 mg three times per day) to baclofen (20 mg three times per day), an antispasticity drug, in 234 patients with refractory gastroesophageal reflux-associated cough over nine weeks. Compared with baseline, gabapentin and baclofen similarly led to decreased cough symptom scores and patients with success for cough resolution (57.3% vs. 53.0%). Gabapentin led to lower side effect rates than baclofen of somnolence (20% vs. 35%) and dizziness (11% vs. 24%) [151]. In addition to other burdensome side effects, sudden discontinuation of baclofen can result in seizures [5].

In another study, twice daily pregabalin 75 mg was prescribed to 50 consecutive patients with refractory or unexplained chronic cough for three months. Pregabalin response, defined as LCQ total score improvement of ≥1.3, was attained by 56% of patients. Responders were more likely to have refractory (with underlying pulmonary disease) than unexplained chronic cough, and on average were more symptomatic at baseline. There was no information on side effects or dropout [153].

In another study, 40 patients with refractory chronic cough were randomized to speech pathology treatment plus pregabalin 300 mg/day or speech pathology treatment plus placebo for four weeks. Compared with the placebo group, those who received speech pathology treatment/pregabalin experienced a statistically significant improvement [154]. However, CNS adverse effects (e.g., dizziness, disorientation, confusion, fatigue, blurred vision) were common and sometimes intolerable. The effects of pregabalin on 24-hour cough frequency outcome were non-significant [146].

Because gabapentinoids have beneficial effects on anxiety, improvements in mood may contribute to the apparent benefit or changes in symptom perception or cough intensity. Side effects are common, wide ranging, and can be difficult for patients to tolerate. Slow dose escalation may help minimize this, and maximal doses may not be needed to afford some improvement in cough. Gabapentin and pregabalin may have abuse potential in susceptible patients [5].

Gabapentin should be started at a low dose (e.g., 100 mg three times per day) and titrated up to a maximum dose (600 mg three times per day), depending on clinical effects and tolerability. The usual starting dose of pregabalin for chronic cough is 25 mg twice daily, with increases in increments to a maximum 75 mg twice daily. Patients should be reassessed during dose titration and therapy stopped if there are significant side effects or inadequate response to treatment [5].

In clinical experience, the minority of patients who achieve cough suppression often do so at the expense of intolerable adverse effects, usually sedation [57]. Among 38 patients prescribed gabapentin (maximum: 1,800 mg per day) or pregabalin (maximum: 300 mg per day) for refractory chronic cough, 24% developed immediate intolerable side effects and 37% tolerated the drugs but had no response and stopped the medication. Among the 39% with an initial favorable response, 18% eventually developed intolerable side effects and 21% were able to continue with therapy long-term. The most common side effect was drowsiness/sedation. In real-world practice, gabapentinoids are effective in a subgroup of patients with refractory chronic cough, but side effects may outweigh their potential benefits, which were intolerable for 42% of patients [155].

Tricyclic Antidepressants

Amitriptyline and nortriptyline are tricyclic antidepressants with a broad range of pharmacologic actions effecting adrenergic, serotonergic, muscarinic, and histaminergic systems. Amitriptyline is also used in chronic neuropathic pain (e.g., migraine, postherpetic neuralgia, painful diabetic neuropathy) and has been suggested to be effective in the treatment of chronic cough, with anticholinergic properties thought to underlie the antitussive effect [57; 156]. However, clinical experience with amitriptyline in refractory chronic cough suggests more limited value [5].

In a small randomized trial of patients attending an otolaryngology clinic with postviral refractory chronic cough, amitriptyline 10 mg per day was compared with codeine 10 mg/guaifenesin 100 mg combined in a syrup taken every six hours. The majority of patients reported a 75% to 100% improvement in cough with amitriptyline, while most reported no improvement with codeine/guaifenesin. Compared with the control arm, amitriptyline was significantly associated with a response greater than 50% [157]. In a randomized controlled trial of patients with chronic pharyngolaryngeal neuropathy, 67% had subjective improvement with amitriptyline (up to 50 mg/day), compared with 44% with placebo. The mean Voice Handicap Index-10 (VHI-10) score worsened with amitriptyline but was unchanged with placebo. Attrition over the eight-week trial was 40% [158].

Nortriptyline was studied in 42 patients with neurogenic chronic cough, of whom 45% discontinued nortriptyline due to side effect intolerance or lack of response. The average time to clinical response was 5.5 months. The average minimum effective dose was 21 mg per day in responders. Laryngeal asymmetry was present in 85.7% of all patients. Side effects included sedation, xerostomia, and anxiety. The intolerability was surprising, because nortriptyline is both a metabolite of amitriptyline and reported to be better tolerated [159].

Pharmacotherapy for Chronic Cough in Idiopathic Pulmonary Fibrosis

Idiopathic pulmonary fibrosis is a chronic, progressive, and invariably fatal fibrotic lung disease, and 85% of patients with idiopathic pulmonary fibrosis experience cough, a distressing symptom associated with rapid disease progression. Available treatments for idiopathic pulmonary fibrosis slow disease progression but do not improve symptoms or quality of life. Thalidomide benefitted idiopathic pulmonary fibrosis cough in one randomized controlled trial, but its side effect profile renders it practically useless, as only 20% of patients were able to tolerate it [125]. Worse still, the potentially severe adverse effect of peripheral neuropathy suggests it may damage sensory nerves (vagal afferents). Thalidomide should not be considered even as second-line therapy for idiopathic pulmonary fibrosis cough until further evaluation of the benefit/risk ratio has been undertaken [160].

Although studies on refractory chronic cough can help inform the treatment of idiopathic pulmonary fibrosis cough, the biological mechanisms that contribute to cough probably differ in these conditions, as evidenced by the contrasting results with gefapixant, a P2X3 receptor antagonist, in refractory chronic cough (positive findings) and idiopathic pulmonary fibrosis cough (negative findings) [161].

Nalbuphine

Nalbuphine extended-release (ER) is an opioid agonist-antagonist. In a double-blind randomized controlled trial of patients with idiopathic pulmonary fibrosis and chronic cough, nalbuphine ER tablets (titrated up to 162 mg twice daily) led to 75.1% reduction in daytime objective cough frequency, compared with 22.6% with placebo, a 50.8% placebo-adjusted reduction in 24-hour cough frequency, and similar improvements in patient reported outcomes [162]. Nalbuphine ER was the first therapy to show robust effects on chronic cough in idiopathic pulmonary fibrosis [25]. However, nalbuphine side effects of nausea (42.1%), fatigue (31.6%), constipation (28.9%), and dizziness (26.3%) led to a 24% dropout during the drug initiation phase, partially attributed to the inflexible forced-titration study design [162].

Low-Dose Morphine SR

In a multicenter randomized controlled trial of patients with idiopathic pulmonary fibrosis and chronic cough, low-dose, slow-release morphine (5 mg twice daily) reduced objective awake cough frequency by 39.4% over placebo, and all cough-related patient-reported outcomes remained significantly improved when adjusted for placebo. Morphine side effects of nausea (14%) and constipation (21%) resulted in only one participant discontinuing morphine, indicating tolerability for these patients. The authors note that the safety assessments during study visits were reassuring and there appeared to be no changes in mood or excessive fatigue with morphine [161]. The authors advocate for rapid implementation in clinical practice due to the well-established safety profile and worldwide availability [163].

A 2024 study reported variable effectiveness of slow-release morphine (8–32 mg per day) in reducing breathlessness in patients with COPD. But, it provided reassuring safety data by observing no evidence of harm and no worsening of subjective daytime sleepiness, alertness, or sleep quality at one and four weeks in these severely ill patients [164].

INVESTIGATIONAL PHARMACOTHERAPIES

Low-dose, slow-release morphine has the strongest observational and empirical evidence of antitussive benefit in refractory chronic cough of any commercially available (although off-label) medication and may be used safely in this population when patients are carefully screened and monitored. Because as many as 50% of patients with refractory chronic cough have no response to low-dose morphine and with substantial restrictions on opioid prescribing in the United States, effective peripherally acting antitussives are an urgent priority for investigators.

P2X3 Receptor Antagonists

P2X3 receptors form ion channels containing ATP-binding sites. In the lungs and airway, ATP activates P2X3 receptors localized on vagal sensory nerve terminals, resulting in bronchoconstriction, cough, and localized release of inflammatory neuropeptides [165].

A breakthrough occurred when gefapixant, a P2X3 receptor antagonist, demonstrated a dramatic reduction in chronic cough. Other P2X3 antagonists confirmed the efficacy of this drug class in refractory chronic cough. The endogenous ligand for P2X3 is ATP. Epithelial damage is believed to release ATP. Evidence suggests that ATP largely mediates peripheral hypersensitivity; therefore, gefapixant is peripherally acting in refractory chronic cough [166].

P2X3 receptors are ion channels found on sensory afferent nerve fibers, activated by ATP. In preclinical studies, vagal C fibers, including those thought to be important in mediating cough, have been shown to express P2X3 and P2X2. At present, it is unclear whether ATP concentrations are elevated or P2X3 receptor expression increased in the airways of patients with refractory chronic cough, or how antagonism of P2X3 plays a role in reducing coughing to a range of chemical irritants, temperature changes, and mechanical stimuli. Nonetheless, in clinical trials, P2X3 receptor antagonism has provided robust reductions in cough frequency and patient-reported outcomes [25].

Gefapixant

The first novel therapy to have significant effects in patients with refractory chronic cough was gefapixant, a first-in-class P2X3 antagonist that was originally planned to be developed as an analgesic. Gefapixant has become the first therapeutic to undergo systematic development as a treatment for refractory chronic cough following unprecedented reductions in cough frequency.

In a landmark study, twice daily gefapixant 600 mg showed remarkable therapeutic effects in patients with refractory chronic cough [167]. Objective 24-hour cough frequency was reduced 74% compared with placebo, and daytime cough severity VAS score and CQLQ score reduced by −25.6 and −9.2, respectively. However, another important finding was that virtually all treated patients reported ageusia, or loss of taste, and 24% withdrew because of the adverse effect. These taste side effects are likely attributable to the inhibition of P2X2/3 channels on the nerve fibers innervating the taste buds by high-dose gefapixant [146].

Subsequent studies suggest that antitussive effects are retained at much lower doses (30–50 mg twice daily), at which taste was altered rather than lost and hence the therapy was better tolerated. Larger multi-center parallel group studies were performed in the UK and the United States followed by the first-ever global phase 3 trials of an antitussive treatment for refractory chronic cough, which reported positive findings over placebo for a 45-mg twice daily dose [25].

Eliapixant and Filapixant

Following the taste side effects reported for gefapixant, more selective P2X3 antagonists were evaluated for the treatment of refractory chronic cough; however, there was some uncertainty about whether effects at both P2X3 and P2X2/3 channels were both contributing to antitussive efficacy and hence whether more selective agents would have similar efficacy. Eliapixant and filapixant both demonstrated efficacy in dose-ranging studies, but eliapixant appeared to cause less taste disturbance (up to 21% of patients) and was therefore progressed to a phase 2b parallel trial. Although this trial reported positive findings, a small number of cases of liver toxicity prevented further development of this therapy for refractory chronic cough [25].

Sivopixant

Another more selective P2X3 antagonist, sivopixant, exhibited promising findings in a single-dose crossover study, very similar in design to the first gefapixant study. The reduction in daytime cough frequency of 32% over placebo (the primary endpoint) was not quite statistically significant, but taste adverse effects were only reported in 6.4% of patients. In a follow-up, multicenter parallel group study assessing a range of doses for four weeks, no dose of sivopixant could be discriminated from the very large placebo effect—there was 60% placebo reduction in cough frequency from baseline. The largest absolute change in cough frequency was observed for the highest dose (300 mg), but 30% of patients reported taste adverse effects. No further studies of sivopixant in refractory chronic cough have been planned [25].

Camlipixant

Finally, thought to be the most selective P2X3 antagonist, camlipixant is the second compound in this class to be evaluated in phase 3 trials. The first double-blind randomized controlled crossover trial of camlipixant studied escalating doses from 25 mg to 200 mg versus matched placebo. Although the primary endpoint of awake cough frequency did not reach statistical significance, preplanned subgroup analysis in patients with a cough frequency of at least 20 coughs per hour (80% of patients) and those with greater than the median cough frequency (≥32 coughs per hour, 50% of patients) exhibited significant improvements versus placebo for all doses tested. This preplanned analysis was based on observations from several of the gefapixant studies that suggested P2X3 antagonism was most efficacious in patients with the highest baseline cough frequency [25].

In post-hoc analysis of a phase 2a study, among patients who reported cough-related urinary incontinence at baseline, 11%, 15%, and 21% of those treated with 12.5 mg, 50 mg, and 200 mg camlipixant, respectively, reported no cough-related urinary incontinence at day 29 (compared with 3% with placebo) [168]. As of 2024, camlipixant is being evaluated in two large-scale phase 3 studies, again in patients selected for higher cough frequencies [25].

Other Novel Antitussives Under Investigation

The studies completed to date investigating P2X3 antagonists have typically found that between one-quarter and one-third of patients do not experience the 30% reduction in cough frequency thought to be the meaningful clinical threshold, suggesting some heterogeneity in the mechanisms underlying refractory chronic cough. Furthermore, patients with less frequent/severe coughing than those recruited to these trials may not benefit from treatments interrupting the ATP-P2X3 axis. Therefore, treatments with alternative modes of action are required to optimally manage patients with refractory chronic cough [25].

Sodium Channel Blockade

Lidocaine non-selectively blocks voltage-gated sodium channels important in the initiation of action potentials and their conduction and is a local anesthetic agent in routine topical use to reduce coughing during bronchoscopy. Case reports and case series have also described the use of nebulized lidocaine as an antitussive to treat refractory chronic cough [169].

In a three-way crossover study of single-dose lidocaine in refractory chronic cough, lidocaine throat spray reduced coughing by about 50% and was more effective than nebulized lidocaine, probably because nebulization into the lower airways has an irritant effect and evokes coughing initially [169]. The antitussive effects of lidocaine spray are relatively short lived and also associated with numbness in the mouth and lips, preventing patients from safely eating after treatment. Efforts have been made to develop similar therapies with a longer duration of action and without loss of sensation [25].

A novel approach to sodium channel blockade has been developed using a compound that is only active in blocking sodium channels after entering neurons via large-pore ion channels, such as P2X3 channels. As of 2024, a phase 2a clinical trial has been performed but the results are not yet published.

TRPM8 Agonism

Activation of TRPM8 ion channels produces cooling sensations. One new therapy has used an orally dissolving tablet containing a TRPM8 agonist (AX-8) placed on the back of the tongue to act as a counter irritant to the sensations of throat irritation reported by many patients with refractory chronic cough. In a randomized controlled trial, AX-8 reduced cough frequency, but not significantly over eight hours, the duration of action suggested by a previous open-label study. However, the effect was significant over four hours and exaggerated in those patients reporting greater throat discomfort, consistent with the proposed mechanism of action. Further studies in this subgroup of patients are hoped to confirm efficacy [25].

On day 1, AX-8 reduced cough frequency within 15 minutes and more than placebo over two and four hours, but not eight hours. In participants with baseline throat discomfort, reduction in cough frequency was significant over 24 hours, with a maximum reduction compared to placebo of 43% over two hours. Over 14 days, AX-8 significantly improved patient-reported outcomes and the safety profile was good with no serious adverse events. This suggests that TRPM8 agonism has potential for control of refractory/unexplained chronic cough as an alternative or adjunct to other therapies, especially in those patients complaining of cough driven by throat sensations [170].

NK-1 Antagonism

Following a positive study testing aprepitant as a cough treatment in patients with lung cancer, there has been interest in the potential antitussive effects of centrally acting neurokinin-1 (NK-1) antagonists. Following a negative trial in refractory chronic cough, a double-blind randomized controlled trial is in progress testing the effects of orvepitant in patients with cough associated with idiopathic pulmonary fibrosis [25].

NONPHARMACOLOGIC THERAPY

Speech and Language Therapy

Speech and language therapy techniques were first described as improving chronic cough in a randomized controlled trial in 87 patients with refractory chronic cough. The intervention appeared to have positive impact on cough, voice, throat symptoms, and symptom limitation after four therapy sessions over two months. Another study investigated a similar intervention delivered by speech and language therapists and physiotherapists. Compared with sham therapy, LCQ score improved by 1.5 points. Cough frequency improved by 40% more than in the sham-treated arm at four weeks and seemed to be maintained at three months. No larger-scale trials have been completed [25].

Speech and language therapy is a complex intervention, comprising components of education, cough suppression techniques, vocal hygiene, and psychoeducational counseling. Thus, it is difficult to standardize the intervention, and it is not clear whether all or just some of the components are essential for efficacy. In practice, the therapy seems to be most effective when delivered by experienced therapists, who may not be widely available. There is also a question about the durability of the effects over longer timescales when patients may not continue to practice the techniques [25].

The European Respiratory Society suggests a trial of cough control therapy (physiotherapy/speech and language therapy) in adult patients with chronic cough.

(https://erj.ersjournals.com/content/55/1/1901136. Last accessed August 12, 2024.)

Strength of Recommendation/Level of Evidence: Conditional recommendation, moderate-quality evidence

The speech and language therapy approach to the management of chronic cough involves four steps: education, vocal hygiene, cough control/suppression training, and psychoeducational counseling [19].

Education

Patients are provided education on the biology of coughing, chronic cough, and cough hypersensitivity. The negative effects of repeated coughing and throat clearing are explained [19].

Vocal Hygiene

Vocal and laryngeal hygiene and hydration are advised with a reduction in caffeine and alcohol intake. Nasal breathing with nasal douching may be recommended with nasal steam inhalation [19].

Cough Control/Suppression Training

Following identification of patient cough triggers, patients are taught a range of suppression strategies, including forced/dry swallow, sipping water, chewing gum, or sucking non-medicated sweets. Breathing pattern re-education is used to promote relaxed abdominal breathing while inhaling through the nose [19].

Psychoeducational Counseling

Behavior modification is used to reduce over-awareness of the need to cough and facilitate an individual's internalization of control over their cough and to help manage stress and anxiety [19].

Local Injection Therapies

The experience of superior laryngeal nerve block by the injection of local anesthetic agents and corticosteroids has been described retrospectively following implementation in several clinics. In 2024, a small single-blind placebo-controlled study was performed comparing this treatment in 10 patients injected with active treatment and 7 with placebo, finding improvements in cough VAS and LCQ scores. Transient sensations of globus (lump in the throat) and soreness at the site of inject were the main adverse effects. Laryngeal botulinum toxin injections have also been reported to produce improvements in series of patients in clinical care, but no controlled studies have been performed. The broad safety of these interventions and duration of any effect currently remains unclear [25].

CONCLUSION

Chronic cough affects roughly 10% of adults in the United States [32]. These individuals can cough hundreds to thousands of times every day, often with uncontrollable bouts of coughing triggered by laughing, speaking, or changes in ambient temperature. This can continue for many years or decades, leading to substantial physical and emotional symptoms, including fatigue, urinary incontinence, cough syncope, dysphonia, depression, anxiety, embarrassment, social isolation, and severely diminished quality of life [28; 40; 64].

Customer Information and Evaluation are located on pages 79–80.

Course Availability List

These courses may be ordered by mail on the Customer Information form located on page 79.
We encourage you to **GO GREEN**. Access your courses **online** or download as an **eBook** to save paper and **receive a discount** or sign up for **One Year of All Access Online CE starting at only $85!** Additional titles are also available.

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MODERATE SEDATION/ANALGESIA

#30464 • 15 ANCC / 15 Pharm Hours

Book By Mail – $98 • ONLINE – $90

Purpose: The purpose of this course is to provide nurses with the knowledge required for safe drug delivery based on standardized operational guidelines. Preprocedural, intraprocedural, and postprocedural patient care are presented, as well as a thorough review of the drugs used, their advantages and disadvantages, and the safe administration of these agents.
Audience: This course is designed for all nurses, especially those in procedural and diagnostic areas, such as radiology, endoscopy, cardiac cath, outpatient surgery, intensive care, and emergency departments.
Additional Approvals: AACN Synergy CERP Category A, CCMC

TREATMENT OF HEART FAILURE: AN UPDATE

UPDATE

#30934 • 10 ANCC / 3 Pharm Hours

Book By Mail – $68 • ONLINE – $60

Purpose: The purpose of this course is to provide nurses and ancillary nursing personnel with current information about the scientific advances in the treatment of acute heart failure.
Audience: This course is designed for nurses and ancillary nurse personnel involved in the treatment and continued assessment of patients with heart failure.
Additional Approvals: AACN Synergy CERP Category A, CCMC

COMMUNICATION AND SOFT SKILLS IN NURSING PRACTICE

NEW!

#31350 • 3 ANCC Hours

Book By Mail – $26 • ONLINE – $18

Purpose: The purpose of this course is to provide nurses with strategies to support the soft skills needed to provide optimal patient care and enhance professionalism in health care.
Audience: This course is designed for nurses in all practice settings.
Additional Approvals: AACN Synergy CERP Category C

BURNOUT: IMPACT ON NURSING AND QUALITY OF CARE

#31434 • 5 ANCC Hours

Book By Mail – $38 • ONLINE – $30

Purpose: Given the integral relationship between work-related stress, job dissatisfaction, burnout, and patient care, properly addressing nursing burnout is essential. The purpose of this course is to provide nurses with information to identify burnout and with effective strategies to manage work-related stress and prevent burnout.
Audience: This course is designed for nurses and nurse practitioners at all levels and in all settings, especially oncology, palliative care, mental health, and critical care.
Additional Approvals: AACN Synergy CERP Category C, CCMC

WOMEN AND CORONARY HEART DISEASE

UPDATE

#33224 • 15 ANCC / 5 Pharm Hours

Book By Mail – $98 • ONLINE – $90

Purpose: The purpose of this course is to identify the unique challenges that face women with heart disease, including prevention, diagnosis, and treatment.
Audience: This course is designed for all nurses in family practice or medical/surgical areas, especially critical care or cardiac units.
Additional Approvals: AACN Synergy CERP Category A, CCMC

DIABETIC HYPOGLYCEMIA

#34654 • 5 ANCC / 5 Pharm Hours

Book By Mail – $38 • ONLINE – $30

Purpose: The purpose of this course is to provide nurses and healthcare professionals with a foundation of understanding hypoglycemia in order to assure the highest quality of care is provided to patients.
Audience: This course is designed for nurses in any healthcare venue and dietitians with a desire to better understand the causes, recognition, and treatment of hypoglycemia in a variety of settings.
Additional Approvals: AACN Synergy CERP Category A, CCMC

ETHICAL DECISION MAKING

UPDATE

#37074 • 15 ANCC Hours

Book By Mail – $98 • ONLINE – $90

Purpose: The purpose of this course is to assist healthcare professionals to define the predominant ethical theories and principles used in health care, determine any legal and regulatory implications, and in collaboration with their colleagues and patients/clients, make effective decisions that determine the appropriate course of treatment, or refusal of such, for and with those for whom they care.
Audience: This course is designed for all nurses and allied healthcare professionals.
Additional Approvals: AACN Synergy CERP Category B, CCMC

VENOUS DISEASE AND ULCERS

#38632 • 5 ANCC Hours

Book By Mail – $38 • ONLINE – $30

Purpose: The purpose of this course is to enable nurses to accurately assess and treat venous disease and venous ulcers and to provide patient and family education for preventive care and lifestyle changes.
Audience: This course is designed for nurses in all care settings who may care for patients with venous disease or ulcers.
Additional Approvals: AACN Synergy CERP Category A, CCMC

Prices are subject to change. Visit www.NetCE.com for a list of current prices.

Course Availability List *(Cont'd)*

CARING FOR THE GERIATRIC PATIENT
#39101 • 3 ANCC Hours

Book By Mail – $26 • ONLINE – $18

Purpose: The purpose of this course is to provide nurses with an overview of the physical and psychosocial considerations necessary when providing care to geriatric patients.
Audience: This course is designed for nurses in a variety of practice settings who work with older patients.
Additional Approvals: AACN Synergy CERP Category A, CCMC

PULMONARY EMBOLISM
#90120 • 2 ANCC / 1 Pharm Hour

Book By Mail – $23 • ONLINE – $15

Purpose: The purpose of this course is to provide healthcare professionals with the knowledge and clinical strategies necessary to optimally triage and treatment patients with pulmonary embolism.
Audience: This course is designed for physicians, PAs, and nurses involved in assessing, triaging, and managing patients with suspected pulmonary embolism.
Additional Approvals: AACN Synergy CERP Category A

ISCHEMIC STROKE
#90284 • 10 ANCC / 5 Pharm Hours

Book By Mail – $68 • ONLINE – $60

Purpose: The early identification and management of the risk factors for ischemic stroke can lead to substantial health benefits and reductions in cost. However, research has documented gaps between healthcare professionals' knowledge and practice with respect to prevention, demonstrating that adherence to evidence-based or guideline-endorsed recommendations pertaining to all interventions for primary and secondary prevention are underutilized or ineffective. The purpose of this course is to provide needed information about the roles of diagnosis and screening, timely evaluation of individuals with suspected stroke, immediate treatment of stroke, and the elements of effective rehabilitation programs so that healthcare professionals may implement the necessary interventions appropriately.
Audience: This course is designed for physicians, nurses, and physician assistants in the primary care setting. Neurologists and other healthcare practitioners will also benefit from this course.
Additional Approvals: AACN Synergy CERP Category A, CCMC

AUTISM SPECTRUM DISORDER
#92204 • 5 ANCC / 1 Pharm Hour

Book By Mail – $38 • ONLINE – $30

Purpose: The purpose of this course is to educate healthcare professionals about the epidemiology, diagnosis, and management of ASD. Additionally, this course will provide the information necessary to screen children seen in primary care for ASD in order to appropriately refer patients and their families for more expansive assessment and treatment referral as rapidly as possible in order to avoid unnecessary morbidity and mortality.
Audience: This course is designed for healthcare professionals in all practice settings who may be involved in the care of patients with an autism spectrum disorder.
Additional Approvals: AACN Synergy CERP Category A, CCMC

HEALTH ISSUES DISTINCTIVE TO WOMEN
#93314 • 15 ANCC / 2 Pharm Hours

Book By Mail – $98 • ONLINE – $90

Purpose: The purpose of this course is to provide healthcare professionals with updated information related to issues surrounding women across the lifespan to facilitate thorough and appropriate care.
Audience: This course is designed for nurses and other healthcare professionals involved in improving health outcomes for women.
Additional Approvals: AACN Synergy CERP Category A, CCMC

PREDIABETES: AN OPPORTUNITY TO PREVENT DIABETES
#94194 • 15 ANCC / 7 Pharm Hours

Book By Mail – $98 • ONLINE – $90

Purpose: Studies have shown that diabetes can be delayed or prevented in people with prediabetes, but risk reduction relies heavily on lifestyle changes on the part of the patients, making education and counseling of vital importance. The purpose of this course is to provide healthcare professionals with the information and skills necessary to effectively deal with this common condition and learn ways to help patients make healthy lifestyle choices.
Audience: This course is designed for nurses in adult primary care, clinical, and acute care settings, healthcare and behavioral health professionals in public health and preventive medicine settings, and health education specialists.
Additional Approvals: AACN Synergy CERP Category A

HYPERTENSION: STRATEGIES TO IMPROVE OUTCOMES
#94223 • 5 ANCC / 5 Pharm Hours

Book By Mail – $38 • ONLINE – $30

Purpose: The purpose of this course is to provide healthcare professionals with the information necessary to develop treatment regimens associated with optimal adherence and provide adequate patient education, counseling, and support to patients with hypertension.
Audience: This course is designed for all physicians, physician assistants, nurses, and pharmacy professionals involved in the care of patients with hypertension.
Additional Approvals: AACN Synergy CERP Category A, CCMC

INFLUENZA: A COMPREHENSIVE REVIEW
#94424 • 10 ANCC / 5 Pharm Hours

Book By Mail – $68 • ONLINE – $60

Purpose: The purpose of this course is to provide healthcare professionals with an updated review of influenza, including clinical aspects, public health issues, and strategies for prevention. The goals are to minimize the burden of influenza on patients and communities, prevent complications and hospitalizations, and save healthcare dollars.
Audience: This course is designed to help healthcare professionals and allied personnel understand influenza and their role in its prevention.
Additional Approvals: AACN Synergy CERP Category A, CCMC

Prices are subject to change. Visit www.NetCE.com for a list of current prices.

Course Availability List *(Cont'd)*

RESPONSIBLE AND EFFECTIVE OPIOID PRESCRIBING

APRN Mandate

#95152 • 3 ANCC / 3 Pharm Hours

Book By Mail – $26 • ONLINE – $18

Purpose: The purpose of this course is to provide clinicians who prescribe or distribute opioids with an appreciation for the complexities of opioid prescribing and the dual risks of litigation due to inadequate pain control and drug diversion or misuse in order to provide the best possible patient care and to prevent a growing social problem.

Audience: This course is designed for all physicians, osteopaths, physician assistants, pharmacy professionals, and nurses who may alter prescribing practices or intervene to prevent drug diversion and inappropriate opioid use.

Additional Approvals: AACN Synergy CERP Category A, CCMC

Special Approvals: This course meets the Texas APRN requirements for opioid, controlled substances, and pain management education.

SUBSTANCE USE DISORDERS AND PAIN MANAGEMENT: MATE ACT TRAINING

DEA MATE Act

#95300 • 8 ANCC / 8 Pharm Hours

Book By Mail – $56 • ONLINE – $48

Purpose: The purpose of this course is to provide clinicians who prescribe or distribute controlled substances with an appreciation for the complexities of managing patients with substance use disorders and comorbid pain in order to provide the best possible patient care and to prevent a growing social problem.

Audience: This course is designed for all healthcare professionals who may alter prescribing practices or intervene to help meet the needs of patients with substance use disorders.

Additional Approvals: AACN Synergy CERP Category A, CCMC

Special Approvals: This course meets the Texas APRN requirements for opioid, controlled substances, and pain management education. This course meets the DEA requirement for 8 hours of substance abuse education.

SEXUAL ASSAULT

Forensic Nursing

#97023 • 3 ANCC Hours

Book By Mail – $26 • ONLINE – $18

Purpose: The purpose of this course is to address knowledge gaps, enhance clinical and forensic examination skills, highlight management objectives, and improve outcomes for victims of sexual assault.

Audience: This course is intended for physicians, nurses, mental health professionals, and other healthcare professionals who may be called upon to provide care to victims of sexual assault.

Additional Approvals: AACN Synergy CERP Category A, CCMC

Special Approvals: This course meets the Texas requirement for 2 hours of forensic evidence collection education for those who work in an emergency room setting or who treat sexual assault survivors.

MEDICINAL MUSHROOM SUPPLEMENTS

NEW!

#98210 • 3 ANCC / 1 Pharm Hour

Book By Mail – $26 • ONLINE – $18

Purpose: The purpose of this course is to help healthcare professionals in all practice settings increase their knowledge base on medicinal mushrooms.

Audience: This course is designed for healthcare professionals in any practice setting whose patients may be taking mushrooms for potentially medicinal uses.

Additional Approvals: AACN Synergy CERP Category A

DIETS AND DIETARY APPROACHES TO WEIGHT LOSS

NEW!

#98120 • 4 ANCC Hours

Book By Mail – $32 • ONLINE – $24

Purpose: The purpose of this course is to provide healthcare professionals in all practice settings the knowledge necessary to counsel patients regarding diets and dietary approaches to weight management.

Audience: This course is designed for for all physicians, nurses, and allied professionals involved in the care of patients who are interested in exploring dietary options to weight control.

Additional Approvals: AACN Synergy CERP Category A

SUPPLEMENTS FOR AGING

NEW!

#98190 • 5 ANCC / 5 Pharm Hours

Book By Mail – $38 • ONLINE – $30

Purpose: The purpose of this course is to provide healthcare professionals in all practice settings the knowledge necessary to increase their understanding of the supplements that may be used by their older adult patients.

Audience: This course is designed for healthcare professionals whose older patients are taking or are interested in supplements.

Additional Approvals: AACN Synergy CERP Category A

Prices are subject to change. Visit www.NetCE.com for a list of current prices.

ATTENTION TEXAS NURSES,

You may have some questions about your continuing education requirements. We're here to help!

Texas nurses may choose to meet their continuing competency requirement for license renewal by completing 20 contact hours of approved continuing nursing education (CNE). Nurses who choose to complete 20 contact hours must complete courses within their current area of practice. If you do not have a current area of practice, you must refer to your prior area of practice.

HUMAN TRAFFICKING

Any nurse who provides direct patient care must complete a human trafficking prevention course that is approved by the Texas Health and Human Services Commission (HHSC) every renewal period. NetCE's featured course **#97471 Human Trafficking and Exploitation: The Texas Requirement** has been approved by the Texas HHSC to meet this requirement. The course is featured on **page 9**.

GERIATRIC REQUIREMENT

As part of the 20 contact hours, nurses whose practice includes older adult or geriatric populations must complete at least two contact hours of CNE in geriatrics every two-year renewal cycle. Our course **#39040 Psychiatric Treatment Options in the Older Adult** meets this requirement and is featured in this booklet on **page 27**.

NURSING JURISPRUDENCE AND ETHICS

All nurses are required to complete two contact hours in Nursing Jurisprudence and Nursing Ethics every third renewal cycle. These two hours may be included in the 20 hours of required CNE. Our course **#31133 Texas Nursing Jurisprudence and Ethics** meets this requirement and is featured in this booklet on **page 1**.

FORENSIC EVIDENCE COLLECTION

Nurses employed in an emergency room setting or who treat sexual assault survivors must complete a one-time requirement of two hours of CNE relating to forensic evidence collection. Our course **#97023 Sexual Assault** will meet this requirement and is advertised in this booklet on **page 77**.

PAIN MANAGEMENT/OPIOIDS/ CONTROLLED SUBSTANCES

APRNs authorized to receive information from the Prescription Monitoring Program (PMP) licensed prior to September 1, 2020 must complete two (2) contact hours related to approved procedures for prescribing and monitoring controlled substances. APRNs licensed after September 1, 2020 and authorized to receive information from the PMP must fulfill the requirement within one year of initial licensure. Our course **#95152 Responsible and Effective Opioid Prescribing** will fulfill this requirement and is advertised in this booklet on **page 77**.

APRNs who have entered into a prescriptive authority agreement authorizing the prescribing of opioids must complete two (2) contact hours annually (4 contact hours every licensing period) regarding the safe and effective pain management related to the prescription of opioids and other controlled substances. This must include education regarding reasonable standards of care, the identification of drug-seeking behavior in patients, and effectively communicating with patients regarding the prescription of an opioid or other controlled substance. Our courses **#95152 Responsible and Effective Opioid Prescribing** and **#95300 Substance Use Disorders and Pain Management** will fulfill this requirement and are featured in this booklet on **page 77**.

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You may complete ALL four of these courses for a maximum payment of $38.95 (or pay the individual course price).

✓	Course #	Course Title / Contact Hours	Price
	31133	Texas Nursing Jurisprudence and Ethics / 2 Contact Hours	$15
	97471	Human Trafficking and Exploitation: The Texas Requirement / 5 Contact Hours	$30
	39040	Psychiatric Treatment Options in the Older Adult / 5 Contact Hours	$30
	94820	Chronic Cough in Adults / 10 Contact Hours	$60

Additional Courses Available by Mail (ACCESS ONLINE FOR A DISCOUNT!)
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☐	30464	Moderate Sedation/Analgesia / 15	$98
☐	30934	Treatment of Heart Failure: An Update / 10	$68
☐	31350	Communication & Soft Skills in Nursing Practice / 3	$26
☐	31434	Burnout: Impact on Nursing and Quality of Care / 5	$38
☐	33224	Women and Coronary Heart Disease / 15	$98
☐	34654	Diabetic Hypoglycemia / 5	$38
☐	37074	Ethical Decision Making / 15	$98
☐	38632	Venous Disease and Ulcers / 5	$38
☐	39101	Caring for the Geriatric Patient / 3	$26
☐	90120	Pulmonary Embolism / 2	$23
☐	90284	Ischemic Stroke / 10	$68
☐	92204	Autism Spectrum Disorder /5	$38
☐	93314	Health Issues Distinctive to Women / 15	$98
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☐	94424	Influenza: A Comprehensive Review / 10	$68
☐	95152	Responsible and Effective Opioid Prescribing / 3	$26
☐	95300	Substance Use Disorders & Pain Mgmt: MATE Act / 8	$56
☐	97023	Sexual Assault / 3	$26
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☐	98190	Supplements for Aging / 5	$38

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Please read the following questions and choose the most appropriate answer for each course completed.

1. Was the course content new or review?
2. How much time did you spend on this activity?
3. Would you recommend this course to your peers?
4. Did the course content support the stated course objective?
5. Did the course content demonstrate the author's knowledge of the subject?
6. Was the course content free of bias?
7. Before completing the course, did you identify the necessity for education on the topic to improve your nursing practice?
8. Have you achieved all of the stated learning objectives of this course?
9. Has what you think or feel about this topic changed?
10. Did study questions throughout the course promote recall of learning objectives?
11. Did evidence-based practice recommendations assist in determining the validity or relevance of the information?
12. Are you more confident in your ability to provide nursing care after completing this course?
13. Do you plan to make changes in your nursing practice as a result of this course content?

#31133 Texas Nursing Jurisprudence and Ethics	**#97471 Texas Human Trafficking and Exploitation**	**#39040 Psychiatric Treatment Options in the Older Adult**	**#94820 Chronic Cough in Adults**
2 Contact Hours	5 Contact Hours	5 Contact Hours	10 Contact Hours
1. ☐ New ☐ Review	1. ☐ New ☐ Review	1. ☐ New ☐ Review	1. ☐ New ☐ Review
2. ____ Hours	2. ____ Hours	2. ____ Hours	2. ____ Hours
3. ☐ Yes ☐ No	3. ☐ Yes ☐ No	3. ☐ Yes ☐ No	3. ☐ Yes ☐ No
4. ☐ Yes ☐ No	4. ☐ Yes ☐ No	4. ☐ Yes ☐ No	4. ☐ Yes ☐ No
5. ☐ Yes ☐ No	5. ☐ Yes ☐ No	5. ☐ Yes ☐ No	5. ☐ Yes ☐ No
6. ☐ Yes ☐ No	6. ☐ Yes ☐ No	6. ☐ Yes ☐ No	6. ☐ Yes ☐ No
7. ☐ Yes ☐ No	7. ☐ Yes ☐ No	7. ☐ Yes ☐ No	7. ☐ Yes ☐ No
8. ☐ Yes ☐ No	8. ☐ Yes ☐ No	8. ☐ Yes ☐ No	8. ☐ Yes ☐ No
9. ☐ Yes ☐ No	9. ☐ Yes ☐ No	9. ☐ Yes ☐ No	9. ☐ Yes ☐ No
10. ☐ Yes ☐ No	10. ☐ Yes ☐ No	10. ☐ Yes ☐ No	10. ☐ Yes ☐ No
11. ☒ N/A	11. ☐ Yes ☐ No	11. ☐ Yes ☐ No	11. ☐ Yes ☐ No
12. ☐ Yes ☐ No	12. ☐ Yes ☐ No	12. ☐ Yes ☐ No	12. ☐ Yes ☐ No
13. ☐ Yes ☐ No	13. ☐ Yes ☐ No	13. ☐ Yes ☐ No	13. ☐ Yes ☐ No

#31133 Texas Nursing Jurisprudence and Ethics — If you answered yes to question #13, how specifically will this activity enhance your role as a member of the interprofessional team? _____
_____

#97471 Human Trafficking and Exploitation: The Texas Requirement — If you answered yes to question #13, how specifically will this activity enhance your role as a member of the interprofessional team? _____
_____

#39040 Psychiatric Treatment Options in the Older Adult — If you answered yes to question #13, how specifically will this activity enhance your role as a member of the interprofessional team? _____
_____

#94820 Chronic Cough in Adults — If you answered yes to question #13, how specifically will this activity enhance your role as a member of the interprofessional team? _____
_____

May we contact you later regarding your comments about these activities? ☐ Yes ☐ No

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