deciphEHR™
connecting the dots of rare disease

SUPPORTING SUSPECT PATIENT RECOGNITION FOR FURTHER CLINICAL EVALUATION

Amyloidosis Program Implementation Guide

deciphEHR™ provides educational resources to help health systems, hospitals, and specialty practices leverage their electronic health record (EHR) systems. Data from the EHR system may help triage suspect patients for further clinician evaluation.

This Implementation Guide will focus on two common forms of amyloidosis, transthyretin-mediated amyloidosis (ATTR) and light-chain (AL) amyloidosis.

AMYLOIDOSIS | ALEXION AstraZeneca

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- Amyloidosis is a group of treatable, rare, heterogeneous, and progressive diseases caused by misfolded proteins that form amyloid fibrils that aggregate in tissues and/or organs, which can lead to organ failure and eventual death[1,2]
- Patients with amyloidosis present with a wide variety of nonspecific symptoms that often mimic more common diseases, which can complicate diagnosis and lead to misdiagnosis and mistreatment[2,3]
- Misdiagnosis and diagnostic delays are associated with a high risk for morbidity and mortality amongst patients[4,5] and a large cost to healthcare organizations (HCOs)[6,7]
- The objective of this guide is to help healthcare providers (HCPs) understand the clinical presentation of amyloidosis and leverage EHR data to triage suspect amyloidosis patients for testing. Specifically, the program will make use of relevant patient history data, disease codes, and test codes to develop suspect patient lists, order sets, and best practice alerts (BPAs)

Key Sections

Clinical Criteria for Amyloidosis

1

Two of the most common forms of amyloidosis are light-chain (AL) amyloidosis, derived from abnormal circulating light chains produced by plasma cell dyscrasia, and transthyretin amyloidosis (ATTR), derived from wild-type (wt) or mutant transthyretin (hereditary).[1-2] Within these subtypes are a variety of phenotypes, including hereditary ATTR polyneuropathy (hATTR-PN), hereditary and wild-type ATTR cardiomyopathy (hATTR-CM, ATTRwt-CM) and mixed phenotype ATTR (patients exhibit polyneuropathy and cardiomyopathy symptoms).[3] Within these phenotypes, presentation can vary widely. Because of the wide array of non-specific symptoms, disease recognition can be challenging.

There is no one single test that can provide all the information needed to diagnose and type amyloidosis.[8,9] The following clinical criteria can aid in the diagnosis of amyloidosis.

When to Suspect AL

Presentation of AL can vary widely based on organ involvement, but AL should be considered if a patient exhibits some of the signs listed below, especially in the presence of heart failure[2,8,10]:

- **AL-specific signs**
  - Macroglossia
  - Periorbital purpura

- **Comorbidities**
  - All monoclonal gammopathy of undetermined significance (MGUS) patients should be routinely screened for AL
  - Multiple myeloma with atypical features, including unexplained weight loss, lower extremity edema, early satiety, and dyspnea on exertion

- **Additional clues from clinical history**
  - Nephrotic range proteinuria
  - Heart failure with preserved ejection fraction
  - Diastolic dysfunction
  - Nondiabetic peripheral neuropathy
  - Unexplained hepatomegaly or diarrhea
  - Chronic gastrointestinal dysmotility
  - Unexplained weight loss
  - Erectile dysfunction

- **Clinical examination and imaging**
  - Amyloid deposits detected by tissue biopsy
  - Monoclonal protein detected
  - Elevated N-terminal pro-B-type natriuretic peptide (NT-proBNP) in the absence of renal failure or atrial fibrillation
  - Left ventricular wall thickness ≥12 mm
  - Biatrial enlargement
  - Discordance between QRS voltage and wall thickness seen on echocardiogram
  - Decreased global longitudinal strain with relative apical sparing
  - Decreased mitral annular systolic velocity
  - Nephrotic syndrome: 24 h protein >500 mg/day, predominantly albumin
  - Elevated concentration of alkaline phosphatase (ALP)

When to Suspect ATTR

ATTR should be considered if a patient exhibits some of the signs listed below[2,3,8,9]:

- **Clues from family history (hATTR)**

- **Clues from clinical history**
  - » Heart failure with preserved ejection fraction
  - » Bilateral carpal tunnel syndrome
  - » Spinal stenosis / lumbar spinal stenosis
  - » Spontaneous biceps tendon rupture

- **Patient demographics**
  - » ATTRwt may be present in up to 25% (n=256) of patients over 80 years of age[12]
  - » Black Americans have a higher prevalence of the most common genetic variant associated with hereditary ATTR in the United States[5]

- **Clinical examination and imaging**
  - » Cardiac uptake on bone scintigraphy performed for extra-cardiac investigations (^{99m}Tc-PYP, -DPD, or -HMDP)
  - » Echocardiographic / cardiovascular magnetic resonance (CMR) findings
  - » Amyloid deposits detected by tissue biopsy
  - » Monoclonal protein NOT detected

ATTR can present as cardiomyopathy (CM), polyneuropathy (PN), or a mixed phenotype.

ATTR-CM should be suspected if patients exhibit some of the following[3,8]:

- **Clues from clinical history**
  - » Hypertrophic cardiomyopathy when > 60 years of age
  - » Low-flow aortic stenosis
  - » Angina without abnormal angiogram
  - » Repeated embolic stroke
  - » Pacemaker implantation (atrioventricular block or symptomatic bradycardia)
  - » Intolerance to standard heart failure-guideline directed medical therapy

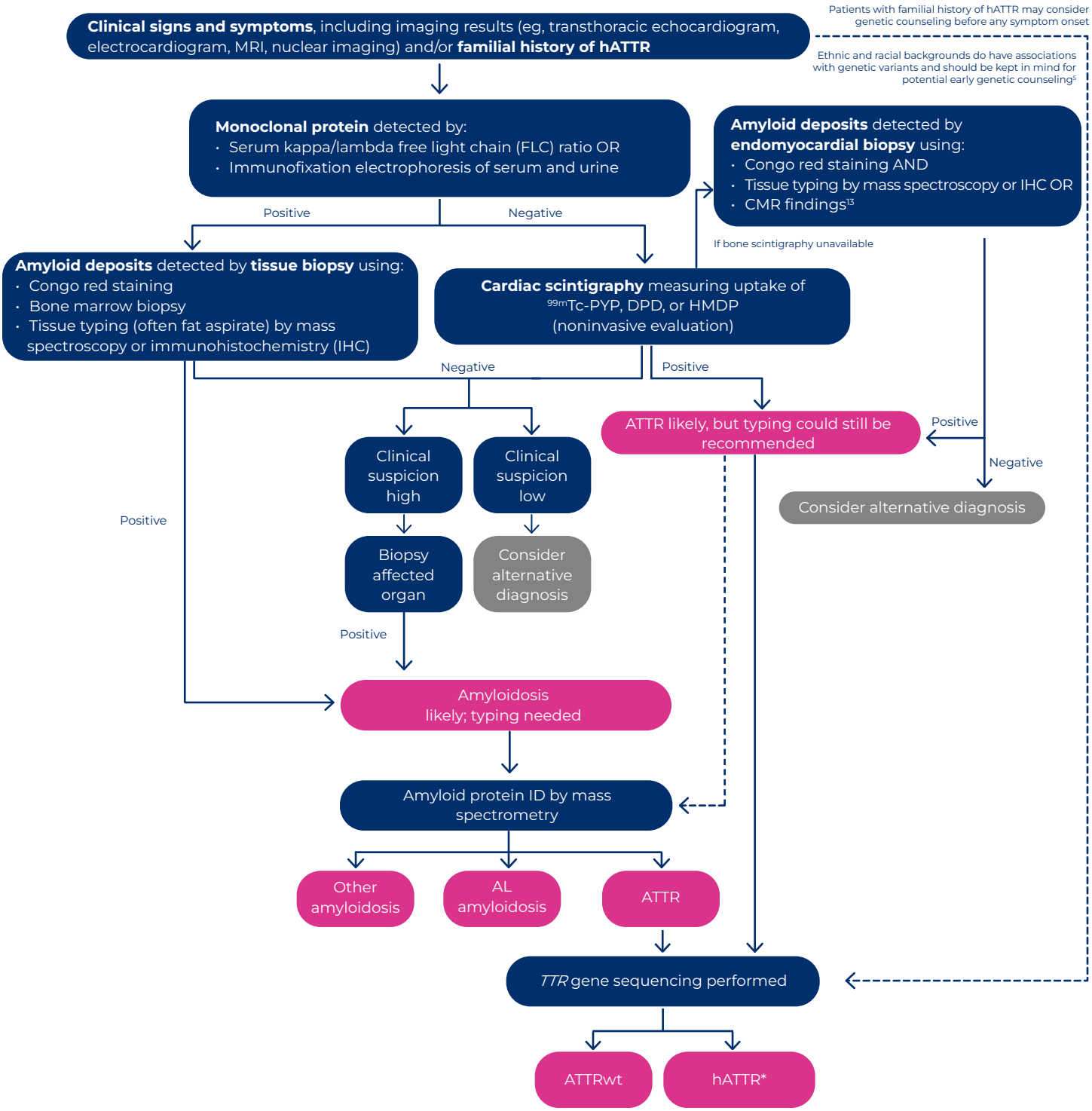
- **Clues from clinical examination and imaging**
  - » Right-sided heart failure
  - » Intractable pleural effusions
  - » Peripheral neuropathy
  - » Orthostatic hypotension
  - » Increased left ventricle wall thickness (≥12 mm) without dilated left ventricle (ECHO / CMR)
  - » Low QRS voltage or pseudo-infarction pattern, heart block, or atrial fibrillation (EKG)
  - » Right ventricle hypertrophy, biatrial enlargement, atrial septal or cardiac valve thickening
  - » Pericardial effusion (ECHO / CMR)
  - » Characteristic distribution of gadolinium within the left ventricle sub-endocardial layer (CMR)

ATTR-PN should be suspected if patients exhibit some of the following[3,9]:

- **Clues from clinical history**
  - » Rapidly progressive sensory-motor axonal neuropathy or atypical chronic inflammatory demyelinating polyneuropathy, plus ≥ 1
    - Autonomic dysfunction
    - Gait disorders
    - Cardiac hypertrophy
    - Heart rhythm disorders
    - Renal abnormalities
    - Unexplained weight loss ≥ 5 kg
    - Vitreous opacities

Diagnostic Criteria for Amyloidosis[8-10]

Once a patient is triaged based on clinical signs and symptoms and/or familial history, they should undergo the following testing to diagnose and type amyloidosis.



*Determine phenotype based on presentation and genetic findings.

Monoclonal Protein Serum Screening:

- **Serum free light chain (sFLC)** assay measures the relative proportion of kappa and lambda light chains (with monoclonality assumed by an abnormal ratio).[8] If a monoclonal protein is present by immunofixation and/or an abnormal sFLC ratio is found, the noninvasive diagnostic pathway is no longer an option and tissue biopsy is needed.[8]
- **Serum immunofixation electrophoresis (SIFE)** and **urine immunofixation electrophoresis (UIFE)** assess for the presence of a monoclonal protein[8]
- Taken together, an abnormal sFLC and monoclonal protein identified by SIFE/UIFE present ~99% sensitivity for the identification of AL amyloidosis,[8] but amyloid typing is still paramount as (1) serum testing alone is not enough information to definitively type amyloidosis and (2) two different types of amyloidosis can occur in individual patients.[14]
- A lack of monoclonal protein does not rule out amyloidosis.[8]

Cardiac Scintigraphy Using Radiotracers

- **^{99m}Tc-PYP, -DPD, and -HMDP** are all radiotracers that can be used in the absence of serum monoclonal protein as a noninvasive way to assess for amyloidosis (commonly ATTR) using cardiac imaging.[8]
- While grade 2 or 3 or H/CL >1.5 uptake is strongly suggestive of ATTR, any degree of ^{99m}Tc-PYP uptake can also be seen in AL,[15] highlighting the need to evaluate monoclonal protein screen for all patients before making a final diagnosis.
- False-negative and false-positives are possible; therefore, biopsy of the affected organs should be considered if clinical suspicion is high.[8]

A qualitative and quantitative scoring system has been developed to make the diagnosis of amyloidosis based on the uptake of these radiotracers (eg, when myocardial uptake of ^{99m}Tc-PYP is visually present on single-photon emission computed tomography (SPECT) images, H/CL ratios of ≥1.5 at one hour are classified as amyloidosis (likely ATTR) positive and ratios of <1.5 as amyloidosis negative). See American Society of Nuclear Cardiology Cardiac Amyloidosis Practice Points for examples of imaging parameters, image interpretation, and reporting best practices.

Confirmation of Amyloid Deposits With Tissue Biopsy

- Systemic amyloidosis can be diagnosed by biopsy of less-invasive sites, such as abdominal fat, skin, or minor salivary gland, but this may lead to false negatives due to patchy distribution of amyloid or amyloidosis being localized to specific organs.[11]
- Biopsy of a less-invasive surrogate site is more likely to correctly detect amyloid in AL rather than ATTR amyloidosis.[16]
- If clinical suspicion is high following a negative biopsy of a less-invasive region, biopsy of the clinically involved organ (eg, heart, kidney) could be completed for the most sensitive method to diagnose amyloidosis.[16]

For Laboratory Scientists: Congo red staining is the most commonly used thioflavin dye used in detecting amyloid deposits that appear dark red under bright-field microscopy and show apple-green birefringence under polarized light. New staining methods using fluorescent oligothiophenes have been recently introduced. Meticulous staining technique is required, as overstaining may lead to false positive results and old stain may give false negative results. Amyloid deposits may be missed in thin tissue samples, so sections at least 5 µm in thickness are recommended.[16]

Amyloid Protein Identification by Mass Spectrometry (MS)

- Once amyloid deposits have been detected, definitive typing is critical in establishing a diagnosis and initiating appropriate therapy to effectively halt disease progression.[17]
- While the type of amyloidosis may be suggested by the clinical presentation or the results of genetic testing, definitive diagnosis requires identification of the amyloid fibril protein.[16]
- Various methods have been used to characterize amyloid deposits in histological sections; immunohistochemistry and immunofluorescence have both been met with variable results, including unacceptably high false positive and negative rates.[16]
- Laser capture microdissection of amyloid deposits followed by tandem mass spectrometry (LCM-MS) has emerged as the gold standard for identification of amyloid fibril proteins.[16]
- **Note:** Although rare, two different types of amyloidosis (ATTR and AL) can co-occur in individual patients.[14]

For Laboratory Scientists: A detailed discussion of LCM-MS as best practices for amyloid typing can be found here.

TTR Gene Sequencing

- Genetic sequencing using blood tests should be used to differentiate between hATTR and ATTRwt.[8]
- In hATTR amyloidosis, there is a correlation between genotype (variant) and phenotype (symptoms).[18]
- **Note:** Patients with familial history of hATTR should consider genetic counseling; there is a 50% chance of an individual transmitting hATTR to their offspring.[19]

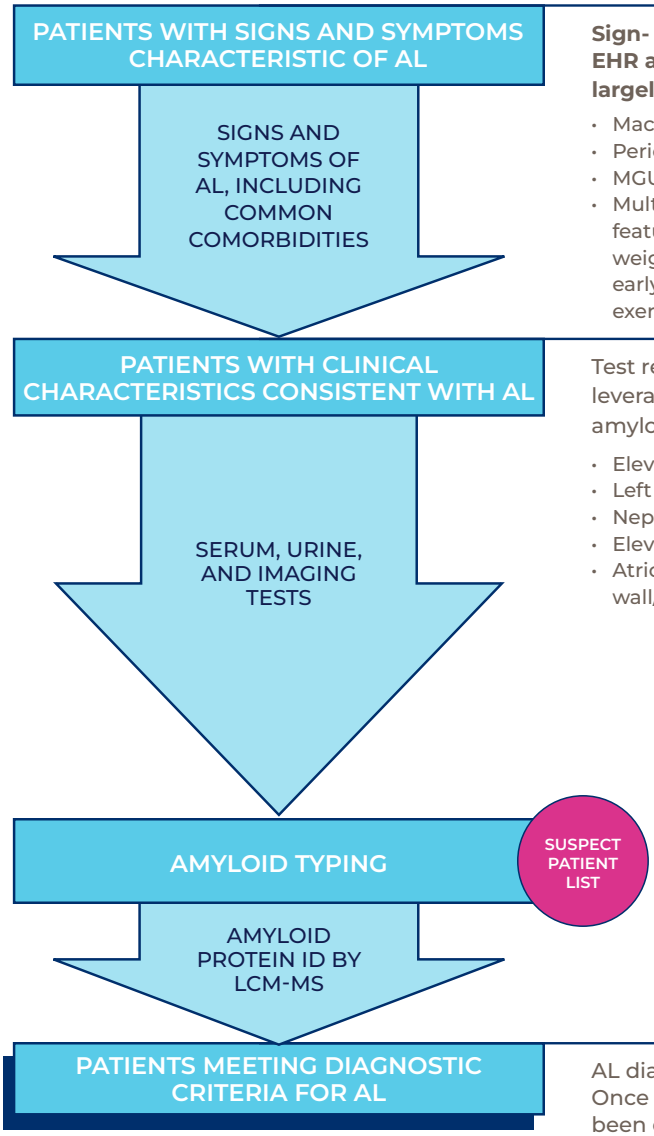
2

A Guide to Generating Suspect Amyloidosis Patient Lists

Amyloidosis that is undiagnosed or misdiagnosed is associated with high risk for morbidity and mortality amongst patients[4,5] and a large cost to the HCOs.[6,7] Utilizing EHR data combined with evidence-based diagnostic criteria to generate suspect patient lists may help to reduce the incidence of undiagnosed and misdiagnosed patients by increasing awareness of suspect patients with amyloidosis for further evaluation by HCPs.

Suggested Clinical Criteria for Suspect Amyloidosis Patient Lists

In an EHR system, a suspect patient list, also referred to as a patient list report, is a list of patients meeting certain clinical criteria. Generating a suspect patient list requires the same clinical criteria used to generate clinical suspicion for and make an amyloidosis diagnosis. In addition to creating a list of suspect amyloidosis patients for further clinical evaluation, a suspect patient list can also be used to flag patient charts with a best practice alert to recommend amyloidosis testing (potentially leveraging order sets) or clinical referral. Please see the charts below for guidance.



Sign- and symptom-specific ICD-10 and SNOMED codes can exist in the EHR and be leveraged to identify patients who have signs and symptoms largely characteristic of AL. Such signs and symptoms include[8,10]:

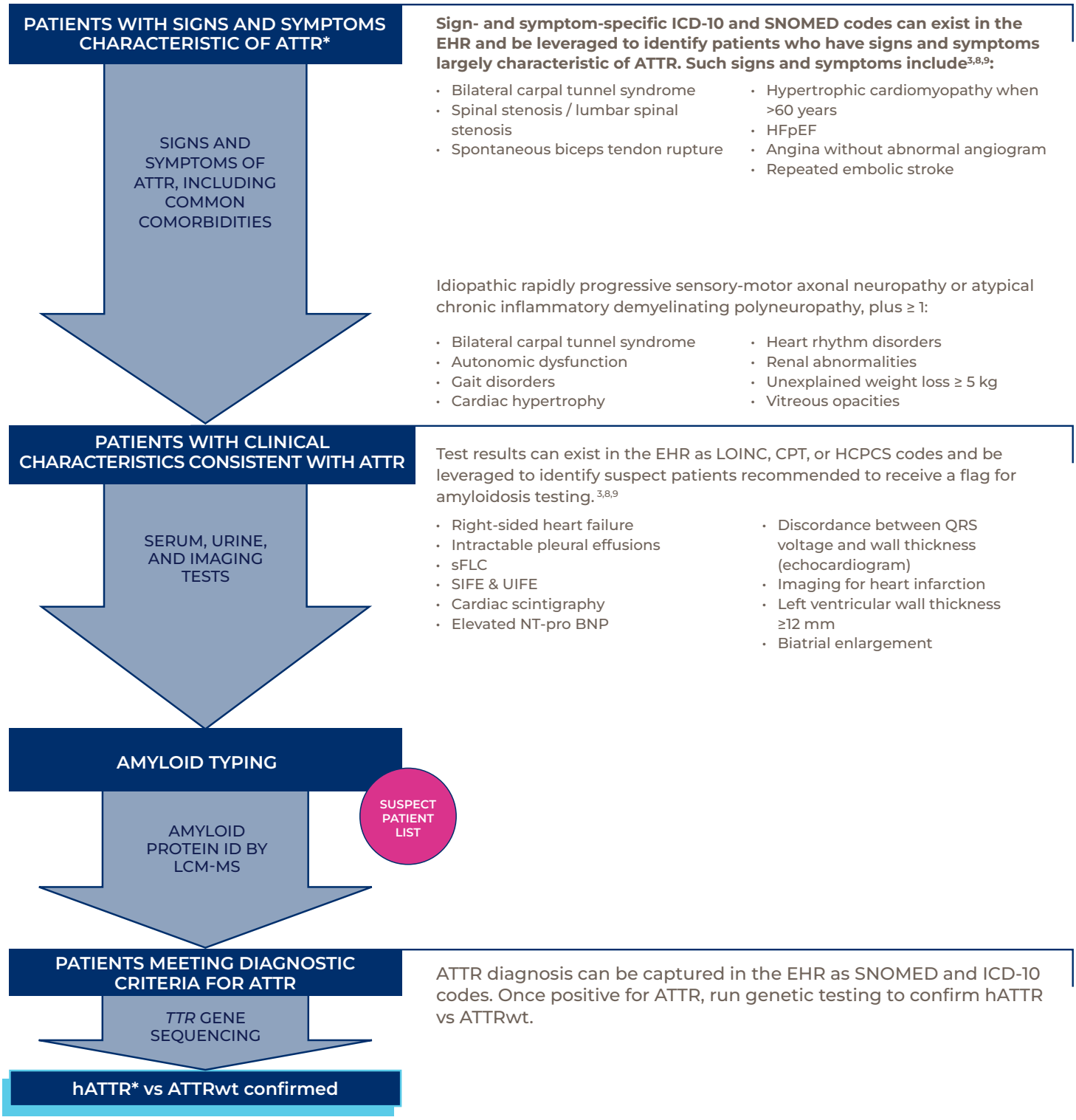
- Macroglossia
- Periorbital purpura
- MGUS diagnosis*
- Multiple myeloma with atypical features, including unexplained weight loss, lower extremity edema, early satiety, and dyspnea on exertion
- Nephrotic range proteinuria
- Heart failure with preserved ejection fraction
- Nondiabetic peripheral or diarrhea
- Chronic gastrointestinal dysmotility
- Unexplained weight loss
- HFpEF

Test results can exist in the EHR as LOINC, CPT, or HCPCS codes and be leveraged to identify suspect patients recommended to receive a flag for amyloidosis testing.[8,10]

- Elevated NT-pro BNP
- Left ventricular wall thickness ≥12 mm
- Nephrotic syndrome
- Elevated ALP
- Atrioventricular valve/right ventricle free wall/interatrial septum thickening
- Diastolic dysfunction
- Biatrial enlargement
- sFLC
- SIFE & UIFE
- Cardiac scintigraphy

AL diagnosis can be captured in the EHR as SNOMED and ICD-10 codes. Once positive for AL, you may want to stage the disease, as staging has been determined to be the most important factor in predicting survival and guiding patient care decisions.[5]

*All monoclonal gammopathy of undetermined significance (MGUS) patients should be routinely screened for AL amyloidosis.



Sign- and symptom-specific ICD-10 and SNOMED codes can exist in the EHR and be leveraged to identify patients who have signs and symptoms largely characteristic of ATTR. Such signs and symptoms include[3,8,9]:

- Bilateral carpal tunnel syndrome
- Spinal stenosis / lumbar spinal stenosis
- Spontaneous biceps tendon rupture
- Hypertrophic cardiomyopathy when >60 years
- HFpEF
- Angina without abnormal angiogram
- Repeated embolic stroke

Idiopathic rapidly progressive sensory-motor axonal neuropathy or atypical chronic inflammatory demyelinating polyneuropathy, plus ≥ 1:

- Bilateral carpal tunnel syndrome
- Autonomic dysfunction
- Gait disorders
- Cardiac hypertrophy
- Heart rhythm disorders
- Renal abnormalities
- Unexplained weight loss ≥ 5 kg
- Vitreous opacities

Test results can exist in the EHR as LOINC, CPT, or HCPCS codes and be leveraged to identify suspect patients recommended to receive a flag for amyloidosis testing.[3,8,9]

- Right-sided heart failure
- Intractable pleural effusions
- sFLC
- SIFE & UIFE
- Cardiac scintigraphy
- Elevated NT-pro BNP
- Discordance between QRS voltage and wall thickness (echocardiogram)
- Imaging for heart infarction
- Left ventricular wall thickness ≥12 mm
- Biatrial enlargement

ATTR diagnosis can be captured in the EHR as SNOMED and ICD-10 codes. Once positive for ATTR, run genetic testing to confirm hATTR vs ATTRwt.

*All patients with familial history of hATTR should consider genetic testing for ATTR as there is a 50% chance of an individual with hATTR transmitting it to their offspring.[19]

IMPORTANT NOTE: While EHR systems may assist providers in generating suspect patient lists, it is the sole responsibility of the HCP to make a diagnosis based on in-person patient evaluation. It is important to indicate that the final suspect list of patients will be sent to the HCP(s) for review. Including criteria for a suspect patient list helps explain to the HCP why the patient is on the report.

For IT Department: High-Level Technical Considerations for Generating Suspect Patient Lists

To leverage EHR codes effectively to build a suspect patient list, you should engage with your healthcare organization's IT department to manage and configure suspect patient lists. See below for an example of processes and considerations for establishing a suspect patient list in Epic EHR. In Epic EHR, a suspect patient list is referred to as a patient list report (a report that identifies all patients meeting certain clinical criteria).

When configuring a suspect patient list, consider addressing the following questions:

- What will the suspect patient list be named?
- Who will own the suspect patient list? (eg, HCP superuser or practice)
- Who will receive the suspect patient list and at what cadence?
- What criteria will be used to determine which patients appear on the suspect patient list based on comorbidities, laboratory results, and signs and symptoms?
- What information will be included on the patient list report? (see clinical criteria above)

Additional considerations for creating an effective suspect patient list:

- The suspect patient list should exclude patients that are deceased or have been ruled out as amyloidosis patients
- Suspect patient lists will be impacted by the data stored in your EHR; for example, any testing that has been conducted and recorded by an outside facility may not be recorded in the EHR, which may lead to a patient being erroneously excluded from the suspect patient list
- Identify and engage with users that have the security privileges and/or technical expertise to configure and monitor suspect patient lists in your EHR
- Consider consulting with epidemiologists to optimize suspect patient list criteria, if available to your institution

Note: The above processes and considerations may not be applicable to all EHR systems. Please consult with your IT department for specific processes and considerations. Additional examples of creating patient lists in other EHR software can be found here: https://support.drchrono.com/hc/en-us/articles/202376054.

Alternatively, your IT department can create patient lists by creating SQL queries allowing near real-time information extraction that can more rapidly account for any changes to suspect patient list criteria. This method may be more efficient and can allow for machine learning and rapid patient list requirement updates, but will only be applicable if all EHR data is mapped to an existing data warehouse.

SQL=structured query language.

3

Order Sets for Amyloidosis

Order sets are a clinical decision support tool in EHR systems consisting of groups of related, evidence-based orders for a particular disease state that physicians can order instantly within their EHR system.[20]

Order sets are available for use and customization in most EHR systems. Order sets allow for efficient and simultaneous ordering of the necessary components associated with effective clinical care, such as lab tests, X-rays, and treatments, etc. Listed below are examples of order sets to test for the presence of amyloidosis. **These lists are not exhaustive and should be modified to meet the clinical needs of your healthcare organization and providers.**

Amyloidosis diagnostic order sets may include[8,16]:

- Serum free light chain (sFLC) assay
- Serum immunofixation electrophoresis (SIFE) and urine immunofixation electrophoresis (UIFE)
- Cardiac scintigraphy using ^{99m}Tc-PYP, -DPD, or -HMDP radiotracers
- Tissue biopsy with staining (eg, Congo red) and light microscopy

Note: Tissue biopsy may be suggested on less-invasive sites, such as abdominal fat, skin, or minor salivary gland, but a negative biopsy test based on a less-invasive site should not rule out amyloidosis if clinical suspicion is high and a biopsy of the affected organ should be taken.[11]

TTR gene sequencing can also be ordered based on clinical suspicion of amyloidosis.

Once there is evidence of amyloidosis, an order set to differentiate amongst subtypes of amyloidosis may include amyloid protein ID by mass spectrometry (eg, LCM-MS).[16,17]

When bringing an order set build request to your IT department or EHR support person, consider including the following information:

- The name of the order set (for example, Amyloidosis Diagnostics and Labs)
- A list of common and medically appropriate labs, diagnostic orders, and clinical tests to include in the order set
- Any subheadings of the order set and more specific tests
- Clinicians who will have access to the order set; for example, cardiologists, neurologists, hematologists, and nephrologists
- Who will be responsible for adding or removing tests based on clinical need

The use of order sets has been found to promote adherence to evidence-based guidelines, enhance workflow with intuitive instructions, reduce potential for medical errors, and ultimately, improve patient outcomes. However, if standard order sets are not carefully designed, reviewed, and maintained to reflect best practices and ensure clear communication, they may actually contribute to errors.

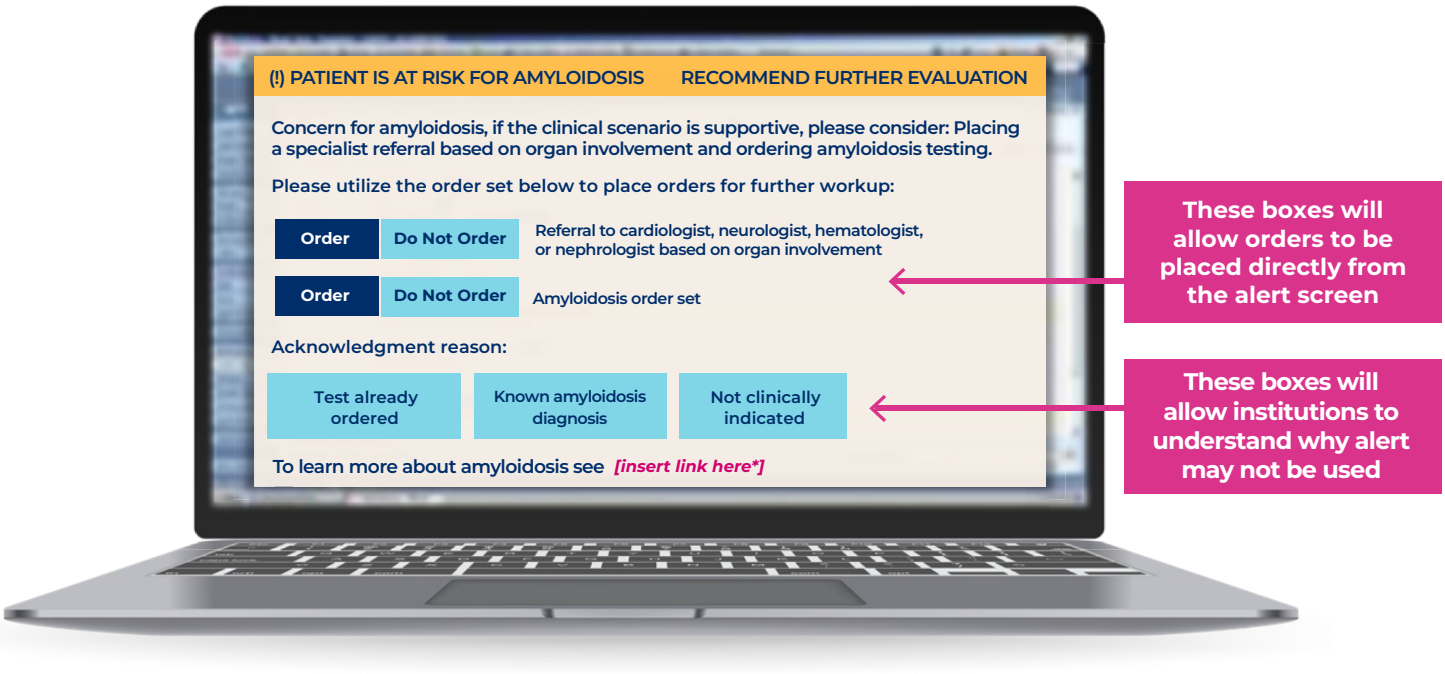
For full Institute for Safe Medication Practices (ISMP) guidelines, see here.

4

Best Practice Alerts to Help HCPs Triage a Suspect Amyloidosis Patient

Use Suspect Patient Criteria and Diagnostic Best Practices to Create Alerts

Using the data in the EHR to surface information in a patient's health record can be the first step in recognizing a suspect amyloidosis patient. Best practice alerts (BPAs) can be created using clinical criteria and the data in the EHR to help alert and guide an HCP in further assessing for amyloidosis. The codes used to triage patients to the suspect patient list may also be used to develop BPAs. An example BPA can be found below.



Illustrative example. BPA should meet institutional guidelines and be specific based on criteria that led to the BPA. Consult with clinical and IT teams for effective implementation.

*Further disease state education may be linked to an amyloidosis page in your institution's EHR system or to an outside resource such as:

- https://www.ncbi.nlm.nih.gov/books/NBK470285/#:~:text=Amyloidosis%20is%20a%20heterogeneous%20acquired,kidney%2C%20blood%20vessels%20and%20nerves
- https://rarediseases.org/rare-diseases/amyloidosis/

High-Level Technical Considerations for Generating BPAs

Automated BPAs can promote quality care by assisting HCPs in providing timely access to diagnostic best practices, reducing misdiagnosis or delays in diagnosis. BPAs can also reduce inefficiency by decreasing the manual effort for HCPs in the diagnostic process.[21] Each EHR system is unique in how to establish automated BPAs, so you should engage with your healthcare organization's IT department. For example, in Epic EHR, a system is in place called "OurPractice Advisory (OPA)" that allows organizations to deliver HCPs with messages through storyboard alerts, interruptive/active alerts, or passive alerts.[21]* These customized, practice-specific alerts can be programmed by the institution's IT team with assistance from clinical leadership to fire according to predetermined triggers, either individual or in combination, using inclusionary or exclusionary logic.[21] IT staff can be provided the suggested BPAs listed above triggered by patients meeting the suggested clinical criteria.

When making an IT request, clinical leaders should be involved in establishing the clinical criteria for BPAs. Consider including the following information to ensure that the suspect patient list is appropriately configured:

- The name for the alert
- The frequency of the alert based on established clinical guidelines
- Indication where the alert should be placed
- Identification of which providers should see the alert

Additional consideration for creating a BPA:

- Privileges on who can configure a BPA may be selective to specific users with security privileges or technical expertise (eg, data scientists in the IT department); therefore, these stakeholders should be identified and engaged with as early as possible

Optimizing BPAs

Improving the visual design of clinical BPAs may help providers recognize medical conditions such as amyloidosis faster. Five presentation elements that have been suggested for EHR alerts include:

1. Physically organizing different information by placing it into bordered blocks
2. Consistency with visual cues (eg, typeface fonts and colors)
3. Using typeface font size and "weight" to help organize and emphasize information
4. Applying color to the boxes used to organize the information
5. Consideration of the use of three-dimensional effects (to accommodate users who are color blind)

*It has been found that there is a **7.7x greater likelihood a BPA will be followed** by an HCP if the alert is active rather than passive.[22]

5

Additional Considerations

There are subtle differences between the various EHR systems. Each has similar functionality, but there may be differences, such as the naming conventions of EHR system features. Additionally, organizations may have established protocols or patient portals for communicating sensitive health information identified by a BPA. The following section highlights some of these considerations.

The toolkit is provided for informational purposes only and does not substitute the internal review of your institution. Please coordinate with your institution's approval process before implementing an EHR build.

Naming Conventions

- Generating and maintaining suspect patient lists empowers organizations to surface patients who meet certain clinical and demographic criteria. These may also be named "worklists" depending on the system.
- BPAs allow organizations to notify providers when certain clinical activities should be prioritized for a particular patient. This functionality can account for a variety of clinical variables throughout the patient journey and may also be named "OurPractice Advisories (OPAs)" or "discern alerts."
- Standardized order sets allow providers to easily understand and order the most relevant tests and management options for patients who meet certain disease criteria or are being seen in a particular department. These may also be known as "power plans" depending on the system.

Each organization may also have its own vocabulary/terms allowed in drop-down lists, formulary, and lab codes. Engage with IT stakeholders at your organization to align on institution-specific variations.

Patient Communication Considerations

HCPs should follow established communication protocols, especially those related to communicating sensitive information to patients.

HCPs may be provided with resources they can give their patient as they begin to understand their diagnosis, such as: https://amyloidosis.org/resources and https://arci.org/patient-resources/.

Note: EHR systems have patient portals that allow patients to stay in touch with their care teams, review their schedules, access personalized patient educational materials, and be more involved in managing their health. These portals may be one way to communicate the need for a follow-up appointment. Some examples of patient portals include:

- Epic MyChart
- Oracle Health Patient Portal
- Meditech Health Portal
- Allscripts® FollowMyHealth®

The patient list and BPA functionality already exist in many EHR systems. AstraZeneca and Alexion did not sponsor, design, create, or otherwise modify this functionality in any manner. The instructions have not been designed to and are not tools and/or solutions for meeting Meaningful Use, Advancing Care information, and/or any other quality/accreditation requirement.

6

Implementing, Monitoring, and Maintaining a Program

The following section provides further guidance on how to implement the deciphEHR™ program in your healthcare organization, as well as how to monitor and maintain the program. To assess the program, including surfaced suspect patients, you will need to monitor it on an ongoing basis. Remember, it will be essential to be clear about what you want to achieve and how you will measure it.

Step 1:

Establish a Clinical Program Lead

- It is important to establish a Clinical Program Lead for the project (a medical specialist with expertise in amyloidosis, most likely a cardiologist) who can answer questions and help direct and oversee successful program implementation
- The Clinical Program Lead can communicate the value of the program to stakeholders throughout the healthcare organization by sharing the deciphEHR™ Amyloidosis Disease Overview and the Rare Disease Overview
- The Clinical Program Lead can provide ongoing support, including monitoring the program and continuing to champion the use of EHR across multiple specialties for rapid triage of suspect amyloidosis patients
- Clinical Program Leads provide support to establish a diagnostic plan based on the clinical criteria for amyloidosis and suggestions for developing suspect patient lists, order sets, and BPAs to help HCPs triage suspected amyloidosis patients

Step 2:

Identify, Engage, and Communicate with Organizational Stakeholders*

- Identify and collaborate with relevant stakeholders within your healthcare organizations who are important in implementing the deciphEHR™ program and encouraging sustainable success
- Stakeholders may vary depending on the organization but may include:

Clinical Leadership

- » Pathology and Specialty Medical Staff
- » Laboratory
- » Pharmacy

Administrative Leadership

- » IT/EHR Resource(s)
- » Data Scientist (if available)
- » Quality Director

- For stakeholder involvement, see here

*You may consider inviting input from representative medical staff during the initiation, implementation, and maintenance of this program.

Step 3:

Establish an Implementation and Support Team

- Consider including the following members on your implementation and support team*:

  - » Clinical Program Lead†
  - » Specialty/Physician Representative(s)‡
  - » Implementation/Project Manager
  - » Super User
  - » EHR Analyst (EHR Builder, Suspect Patient List, BPA Builder)
  - » Workflow Redesign/ Process Engineer
  - » Report Writer/ Measurement and Tracking Lead

Step 4:

Develop and Execute the Implementation Plan

- Engage relevant stakeholders and implementation team to establish the adoption, scope, implementation, and rollout of the program
- Leverage the clinical criteria for amyloidosis (see Section 1) to create suspect patient list for future clinical evaluation by (see Section 2 for technical considerations):
  - » Including recommended medical codes in the Appendix B
  - » Engaging clinical leadership and Super User with IT departments for most effective implementation
- Establish BPAs for HCPs based on clinical criteria (see Section 4 for technical considerations)
  - » Provide amyloidosis education within the clinical alert using web links, such as: https://www.ncbi.nlm.nih.gov/books/NBK470285/#:~:text=Amyloidosis%20is%20a%20heterogeneous%20acquired,kidney%2C%20blood%20vessels%20and%20nerves or https://rarediseases.org/rare-diseases/amyloidosis/

Note: While EHR systems may assist providers in generating suspect lists, it is the sole responsibility of the HCP to make a diagnosis based on in-person patient evaluation.

*Depending on the size and type of your organization, your organization may assign employees to more than one role.
†You may consider an additional stakeholder who has experience leading the implementation of BPAs.
‡For most applicable physicians, see here.

Step 5:

Develop a Monitoring and Evaluation Framework[23,24]

- The Measurement and Tracking Lead may be in charge of continuing to monitor and evaluate suspect amyloidosis patient lists on a routine (eg, monthly, bimonthly) basis to assess the effectiveness of the program (the Super User may be engaged in this process)
- Effectiveness of the program should be measured based on defined metrics for success (for examples, see Step 6)
- The Clinical Program Lead and Super User can monitor and evaluate the BPA program to assess its usefulness and effectiveness in assisting HCPs (eg, through HCP interview)

Step 6:

Measure Success[23,24]

- Metrics for success should be determined at the start of implementation and should be continually measured to assess the success of the program. Metrics for success may include:
  - » Amount of time from suspect patient alert or on a report to the HCP for evaluation to rule in or rule out amyloidosis
  - » Number of times an HCP acts on a BPA
  - » Number of patients for which an alert helps the HCP to confirm an amyloidosis diagnosis

Step 7:

Ongoing Improvement

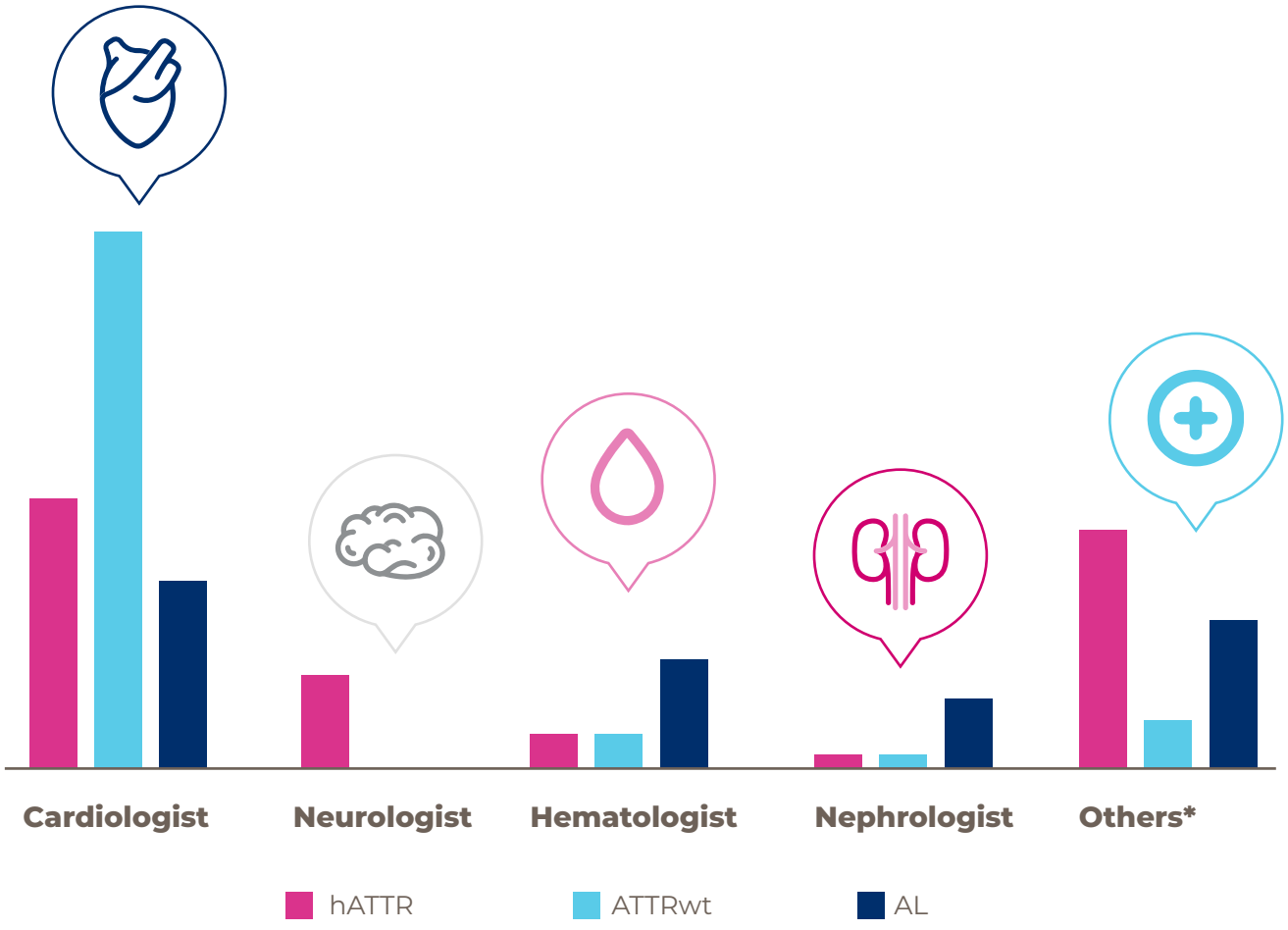
- Engage with Clinical Program Lead to assess amyloidosis diagnostic criteria to ensure they are current
  - » Determine the appropriate timeframe for reassessment based on institutional standards (eg, annually)
  - » Check deciphEHRrare.com for updates
- Evaluate the effectiveness of amyloidosis suspect patient lists and BPAs to triage suspect patients to confirm or rule out amyloidosis
- In case of clinical concerns, reference your implementation and support team
- For EHR implementation troubleshooting and support, consider contacting your EHR provider

7

Appendix A: Medical Staff Considerations

Identify and collaborate with relevant stakeholders within your healthcare organizations (including specialists) who may see undiagnosed amyloidosis patients. See the list of possible specialists below. Learn, understand, and comply with your institution's requirements for implementing.

Patients Presenting Amyloidosis Symptoms Are Most Likely to Visit the Following HCPs on the Path to Diagnosis[25]:



*Other HCPs frequently seeing amyloidosis patients include: internists, oncologists, pathologists, rheumatologists, pulmonologists, gastroenterologists, and hepatologists.

7

Appendix B: Full List of Medical Codes to Support Suspect Patient Lists and BPAs

The clinical criteria for amyloidosis that are required for a patient to appear on the suspect patient list are consistent across all age groups. The medical codes that represent these criteria and suggestions for how to best use these codes are found here in the appendix.

EHR Code Types

The EHR system contains multiple code types, each containing unique information. These codes can be used in combination to triage suspect amyloidosis patients. Below are examples of code types that can be found in the EHR:

- **ICD-10:** International Classification of Diseases, tenth revision, a globally used diagnostic code for epidemiology, health management, and clinical purposes
- **SNOMED:** Systematized Nomenclature of Medicine Clinical Terms, a common language for systems to adopt for indexing, storing, retrieving, and aggregating clinical data
- **LOINC:** Logical Observation Identifiers Names and Codes, a database and universal standard for identifying medical laboratory observations
- **CPT:** Current Procedural Terminology, a uniform language for coding medical services and procedures such as surgeries, diagnostic tests, evaluation, and management services
- **HCPCS:** Healthcare Common Procedure Coding System, a collection of standardized codes that represent basic medical procedures, supplies, products, and services

Suggestions for Leveraging EHR Codes

All codes are listed at the parent level. Determining level of specificity (eg, specific codes within parent trees) is at the discretion of the institution. The institution is responsible for selection of codes based on the specific situation and patient needs.

- Suggested codes for generating suspect patient lists have been divided by:
  1. Patients with suspected AL amyloidosis
  2. Patients with suspected ATTR
- No single code has been found to have high specificity and sensitivity for amyloidosis; therefore, it is suggested that codes be used in combination to develop suspect patient lists
- Codes may change over time; please visit the respective code sites for up-to-date codes
  - » An Excel spreadsheet version is also available on the web page for your convenience
- The codes used to triage patients to the suspect patient list may also be used to develop BPAs

The above codes and suggested use cases for codes are illustrative. Any code implementation should be aligned with Clinical Leadership at your institution.

Suggested Codes for the Suspect Patient Lists Indicated in Section 2

Table 1: Recommended codes for patients with potential AL amyloidosis

These codes are helpful in the triaging process to diagnose AL amyloidosis. The decision on how to implement these codes should be aligned with your institution's Clinical Leadership.

Code Type	Inclusion / Exclusion	Code	Code Description	Suggestions for Implementation
AL-Specific Signs				
ICD-10				
ICD-10	Inclusion	Q38.2	Macroglossia	High-priority code
ICD-10	Inclusion	D69	Purpura and other hemorrhagic conditions	High-priority code
SNOMED				
SNOMED	Inclusion	196592003	Acquired macroglossia	High-priority code
SNOMED	Inclusion	25273001	Enlargement of tongue	High-priority code
Red Flag Comorbidities				
ICD-10				
ICD-10	Inclusion	D47.2	Monoclonal gammopathy	High-priority code; Patients with MGUS should be routinely screened for AL amyloidosis
ICD-10	Inclusion in combination with other codes	C90.01	Multiple myeloma in remission	High-priority code when used in combination with codes for unexplained weight loss, lower extremity edema, early satiety, and dyspnea on exertion
ICD-10	Inclusion in combination with other codes	C90.02	Multiple myeloma in relapse	High-priority code when used in combination with codes for unexplained weight loss, lower extremity edema, early satiety, and dyspnea on exertion
ICD-10	Inclusion in combination with other codes	C90.00	Multiple myeloma not having achieved remission	High-priority code when used in combination with codes for unexplained weight loss, lower extremity edema, early satiety, and dyspnea on exertion
ICD-10	Inclusion in combination with other codes	R63.4	Abnormal weight loss	May be used in combination with codes for multiple myeloma to improve specificity
ICD-10	Inclusion in combination with other codes	R60.0	Localized edema	May be used in combination with codes for multiple myeloma to improve specificity
ICD-10	Inclusion in combination with other codes	R22.43	Localized swelling, mass and lump, lower limb, bilateral	May be used in combination with codes for multiple myeloma to improve specificity
ICD-10	Inclusion in combination with other codes	R68.81	Early satiety	May be used in combination with codes for multiple myeloma to improve specificity
ICD-10	Inclusion in combination with other codes	R06.09	Other forms of dyspnea	May be used in combination with codes for multiple myeloma to improve specificity
ICD-10	Inclusion in combination with other codes	R06.02	Shortness of breath	May be used in combination with codes for multiple myeloma to improve specificity
SNOMED				
SNOMED	Inclusion	35601003	Monoclonal gammopathy of undetermined significance	High-priority code; Patients with MGUS should be routinely screened for AL amyloidosis
SNOMED	Inclusion	277577000	Monoclonal gammopathy of uncertain significance	High-priority code; Patients with MGUS should be routinely screened for AL amyloidosis
SNOMED	Inclusion in combination with other codes	109989006	Multiple myeloma	High-priority code when used in combination with codes for unexplained weight loss, lower extremity edema, early satiety, and dyspnea on exertion

Red Flag Comorbidities (cont.)				
SNOMED	Inclusion in combination with other codes	422868009	Unexplained weight loss	May be used in combination with codes for multiple myeloma to improve specificity
SNOMED	Inclusion in combination with other codes	816190002	Bilateral lower leg edema	May be used in combination with codes for multiple myeloma to improve specificity
SNOMED	Inclusion in combination with other codes	102572006	Edema of lower extremity	May be used in combination with codes for multiple myeloma to improve specificity
SNOMED	Inclusion in combination with other codes	442076002	Early satiety	May be used in combination with codes for multiple myeloma to improve specificity
SNOMED	Inclusion in combination with other codes	60845006	Dyspnea on exertion	May be used in combination with codes for multiple myeloma to improve specificity
Additional Clues From Clinical History				
ICD-10				
ICD-10	Inclusion in combination with other codes	N04	Nephrotic syndrome	High-priority code when used in combination with ≥1 other high-priority code for AL-specific signs or red flag comorbidities
ICD-10	Inclusion	I50.3	Acute on chronic diastolic (congestive) heart failure with preserved ejection fraction	High-priority code
ICD-10	Inclusion in combination with other codes	G62.9	Polyneuropathy, unspecified	High-priority code in the absence of diabetes
ICD-10	Inclusion in combination with other codes	G90.09	Other idiopathic peripheral autonomic neuropathy	High-priority code in the absence of diabetes
ICD-10	Exclusion in combination with other codes	E10	Type 1 diabetes mellitus	May be used in combination with codes for polyneuropathy to improve specificity
ICD-10	Exclusion in combination with other codes	E11	Type 2 diabetes	May be used in combination with codes for polyneuropathy to improve specificity
ICD-10	Inclusion in combination with other codes	R16.0	Hepatomegaly, not elsewhere classified	High-priority code when used in combination with ≥1 other high-priority code for AL-specific signs or red flag comorbidities
ICD-10	Inclusion in combination with other codes	R19.7	Diarrhea, unspecified	High-priority code when used in combination with ≥ 1 other high-priority code for AL-specific signs or red flag comorbidities
SNOMED				
SNOMED	Inclusion in combination with other codes	264867001	Nephrotic range proteinuria	High-priority code when used in combination with ≥1 other high-priority code for AL-specific signs or red flag comorbidities
SNOMED	Inclusion	446221000	Heart failure with normal ejection fraction	High-priority code
SNOMED	Inclusion in combination with other codes	386033004	Neuropathy	High-priority code in the absence of diabetes

Code Type	Inclusion / Exclusion	Code	Code Description	Suggestions for Implementation
Additional Clues From Clinical History (cont.)				
SNOMED	Exclusion in combination with other codes	73211009	Diabetes mellitus	May be used in combination with codes for polyneuropathy to improve specificity
SNOMED	Exclusion in combination with other codes	46635009	Diabetes mellitus type 1	May be used in combination with codes for polyneuropathy to improve specificity
SNOMED	Exclusion in combination with other codes	44054006	Diabetes mellitus type 2	May be used in combination with codes for polyneuropathy to improve specificity
LOINC				
LOINC	Inclusion in combination with other codes	2887-8	Protein [presence] in urine	High-priority code when used in combination with ≥1 other high-priority code for AL-specific signs or red flag comorbidities
Clinical Examination and Imaging				
ICD-10				
ICD-10	Exclusion in combination with other codes	N17.9	Acute kidney failure, unspecified	May be used in combination with codes for NT-pro BNP to improve specificity
ICD-10	Exclusion in combination with other codes	N19	Unspecified kidney failure	May be used in combination with codes for NT-pro BNP to improve specificity
ICD-10	Exclusion in combination with other codes	I48	Atrial fibrillation and flutter	May be used in combination with codes for NT-pro BNP to improve specificity
ICD-10	Exclusion in combination with other codes	I48.91	Unspecified atrial fibrillation	May be used in combination with codes for NT-pro BNP to improve specificity
ICD-10	Inclusion in combination with other codes	N04.9	Nephrotic syndrome with unspecified morphologic changes	High-priority code when used in combination with ≥1 other high-priority code for AL-specific signs or red flag comorbidities
ICD-10	Inclusion in combination with other codes	I50.30	Unspecified diastolic (congestive) heart failure	High-priority code when used in combination with ≥1 other high-priority code for AL-specific signs or red flag comorbidities
ICD-10	Inclusion in combination with other codes	I51.7	Cardiomegaly	High-priority code when used in combination with ≥1 other high-priority code for AL-specific signs or red flag comorbidities
SNOMED				
SNOMED	Exclusion in combination with other codes	236423003	Renal impairment	May be used in combination with codes for NT-pro BNP to improve specificity
SNOMED	Exclusion in combination with other codes	42399005	Renal failure syndrome	May be used in combination with codes for NT-pro BNP to improve specificity
SNOMED	Exclusion in combination with other codes	49436004	Atrial fibrillation	May be used in combination with codes for NT-pro BNP to improve specificity
SNOMED	Inclusion in combination with other codes	55827005	Left ventricular hypertrophy	High-priority code when used in combination with ≥1 other high-priority code for AL-specific signs or red flag comorbidities

Code Type	Inclusion / Exclusion	Code	Code Description	Suggestions for Implementation
Clinical Examination and Imaging (cont.)				
SNOMED	Inclusion in combination with other codes	52254009	Nephrotic syndrome	High-priority code when used in combination with ≥1 other high-priority code for AL-specific signs or red flag comorbidities
SNOMED	Inclusion in combination with other codes	3545003	Diastolic dysfunction	High-priority code when used in combination with ≥1 other high-priority code for AL-specific signs or red flag comorbidities
SNOMED	Inclusion in combination with other codes	395704004	Left ventricular diastolic dysfunction	High-priority code when used in combination with ≥1 other high-priority code for AL-specific signs or red flag comorbidities
SNOMED	Inclusion in combination with other codes	444718001	Bilateral enlargement of atria	High-priority code when used in combination with ≥1 other high-priority code for AL-specific signs or red flag comorbidities
CPT				
CPT	Inclusion in combination with other codes	83880	NT-proBNP	High-priority code when used in combination with ≥1 other high-priority code for AL-specific signs or red flag comorbidities AND in the absence of renal failure or atrial fibrillation
LOINC				
LOINC	Inclusion in combination with other codes	33762-6	Natriuretic peptide.B prohormone N-Terminal [Mass/volume] in Serum or Plasma	High-priority code when used in combination with ≥1 other high-priority code for AL-specific signs or red flag comorbidities AND in the absence of renal failure or atrial fibrillation
LOINC	Inclusion in combination with other codes	33763-4	Natriuretic peptide.B prohormone N-Terminal [Moles/volume] in Serum or Plasma	High-priority code when used in combination with ≥1 other high-priority code for AL-specific signs or red flag comorbidities AND in the absence of renal failure or atrial fibrillation
LOINC	Inclusion in combination with other codes	71425-3	Natriuretic peptide.B prohormone N-Terminal [Mass/volume] in Blood by Immunoassay	High-priority code when used in combination with ≥1 other high-priority code for AL-specific signs or red flag comorbidities AND in the absence of renal failure or atrial fibrillation
Monoclonal Protein Detection				
CPT				
CPT	Inclusion	83521	Immunoglobulin Free Light Chains, Serum	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)
CPT	Inclusion	82784	Immunofixation (IFE), Serum and Protein Electrophoresis, Serum	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)
CPT	Inclusion	86335	Urine Immunofixation by Electrophoresis	High-priority code; EEven in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)
CPT	Inclusion	84156	Immunofixation (IFE) and Protein Electrophoresis, Random Urine	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)
CPT	Inclusion	84166	Immunofixation (IFE) and Protein Electrophoresis, Random Urine	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)
CPT	Inclusion	86335	Immunofixation (IFE) and Protein Electrophoresis, Random Urine	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)

Code Type	Inclusion / Exclusion	Code	Code Description	Suggestions for Implementation
Monoclonal Protein Detection (cont.)				
LOINC				
LOINC	Inclusion	40844-3	Kappa/Lambda Free Light Chain Ratio	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)
LOINC	Inclusion	25700-6	Immunofixation for Serum or Plasma	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)
LOINC	Inclusion	49275-1	Immunofixation for Serum or Plasma Narrative	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)
LOINC	Inclusion	11526-1	EER Immunofix Electrophoresis Serum	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)
LOINC	Inclusion	34550-4	Immunofixation, Serum	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)
LOINC	Inclusion	18301-2	IgG [Presence] in Serum by Immunofixation	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)
Amyloid Deposit				
CPT				
CPT	Inclusion	88313	Demonstration of amyloid in tissues from Congo Red	High-priority code
CPT	Inclusion	83789	Mass spectrometry and tandem mass spectrometry (MS, MS/MS)	High-priority code
LOINC				
LOINC	Inclusion	10782-1	Microscopic observation [identifier] in tissue by Congo red stain	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy of impacted organ) or test rerun due to false negative possibility
LOINC	Inclusion	LP95062-3	LC/MS/MS: liquid chromatography-tandem mass spectrometry	High-priority code
Cardiac Scintigraphy				
LOINC				
LOINC	Inclusion	39891-7	NM Heart Views for infarct and first pass W Tc-99m PYP IV	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy of impacted organ) or test rerun due to false negative possibility
LOINC	Inclusion	39654-9	SPECT Heart for infarct W Tc-99m PYP IV	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy of impacted organ) or test rerun due to false negative possibility
LOINC	Inclusion	82654-5	Cardiac nuclear imaging SPECT panel	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy of impacted organ) or test rerun due to false negative possibility
HCPCS				
HCPCS	Inclusion	A9538	(99m)Tc-pyrophosphate, diagnostic	High-priority code; Even in absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy of impacted organ) or test rerun due to false negative possibility

Table 2: Recommended codes for patients with potential ATTR

These codes are helpful in the triaging process to diagnose ATTR. The decision on how to implement these codes should be aligned with your institution's Clinical Leadership.

Code Type	Inclusion / Exclusion	Code	Code Description	Suggestions for Implementation
Clues From Clinical History				
ICD-10				
ICD-10	Inclusion in combination with other codes	I50.1	Left ventricular failure, unspecified	High-priority code in the absence of hypertension
ICD-10	Inclusion in combination with other codes	I50.3	Acute on chronic diastolic (congestive) heart failure with preserved ejection fraction	High-priority code in the absence of hypertension
ICD-10	Exclusion in combination with other codes	I10	Essential (primary) hypertension	May be used in combination with codes for HFpEF to improve specificity
ICD-10	Exclusion in combination with other codes	I11.9	Hypertensive heart disease without heart failure	May be used in combination with codes for HFpEF to improve specificity
ICD-10	Inclusion	G56.03	Carpal tunnel syndrome, bilateral upper limbs	High-priority code
ICD-10	Inclusion	M48.061	Spinal stenosis, lumbar region without neuogenic claudication	High-priority code
ICD-10	Inclusion	M48.062	Spinal stenosis, lumbar region with neurogenic claudication	High-priority code
ICD-10	Inclusion	M48.07	Spinal stenosis, lumbosacral region	High-priority code
ICD-10	Inclusion	M48.00	Spinal stenosis, site unspecified	High-priority code
ICD-10	Inclusion	M66.829	Spontaneous rupture of other tendons, unspecified upper arm	High-priority code
ICD-10	Inclusion	M66.821	Spontaneous rupture of other tendons, right upper arm	High-priority code
ICD-10	Inclusion in combination with other codes	I42.2	Other hypertrophic cardiomyopathy	High-priority code when occurring in >60 years
ICD-10	Inclusion in combination with other codes	I42.1	Obstructive hypertrophic cardiomyopathy	High-priority code when occurring in >60 years
ICD-10	Inclusion	I35.0	Nonrheumatic aortic (valve) stenosis	High-priority code
ICD-10	Inclusion	I35.2	Nonrheumatic aortic (valve) stenosis with insufficiency	High-priority code
ICD-10	Inclusion	I35.1	Nonrheumatic aortic (valve) insufficiency	High-priority code
ICD-10	Inclusion in combination with other codes	I20.9	Angina pectoris, unspecified	High-priority code without abnormal angiogram
ICD-10	Exclusion in combination with other codes	R93.1	Abnormal findings on diagnostic imaging of heart and coronary circulation	May be used in combination with codes for angina to improve specificity
ICD-10	Exclusion in combination with other codes	R94.39	Abnormal result of other cardiovascular function study	May be used in combination with codes for angina to improve specificity

Code Type	Inclusion / Exclusion	Code	Code Description	Suggestions for Implementation
Clues From Clinical History (cont.)				
ICD-10	Inclusion in combination with other codes	I63.40	Cerebral infarction due to embolism of unspecified cerebral artery	High-priority if the code is repeated in the patient history
ICD-10	Inclusion in combination with other codes	I63.411	Cerebral infarction due to embolism of right middle cerebral artery	High-priority if the code is repeated in the patient history
ICD-10	Inclusion in combination with other codes	I63.412	Cerebral infarction due to embolism of left middle cerebral artery	High-priority if the code is repeated in the patient history
ICD-10	Inclusion in combination with other codes	I63.413	Cerebral infarction due to embolism of bilateral middle cerebral arteries	High-priority if the code is repeated in the patient history
ICD-10	Inclusion in combination with other codes	I63.419	Cerebral infarction due to embolism of unspecified middle cerebral artery	High-priority if the code is repeated in the patient history
ICD-10	Inclusion in combination with other codes	I63.421	Cerebral infarction due to embolism of right anterior cerebral artery	High-priority if the code is repeated in the patient history
ICD-10	Inclusion in combination with other codes	I63.422	Cerebral infarction due to embolism of left anterior cerebral artery	High-priority if the code is repeated in the patient history
ICD-10	Inclusion in combination with other codes	I63.423	Cerebral infarction due to embolism of bilateral anterior cerebral arteries	High-priority if the code is repeated in the patient history
ICD-10	Inclusion in combination with other codes	I63.429	Cerebral infarction due to embolism of unspecified anterior cerebral artery	High-priority if the code is repeated in the patient history
ICD-10	Inclusion in combination with other codes	I63.431	Cerebral infarction due to embolism of right posterior cerebral artery	High-priority if the code is repeated in the patient history
ICD-10	Inclusion in combination with other codes	I63.432	Cerebral infarction due to embolism of left posterior cerebral artery	High-priority if the code is repeated in the patient history
ICD-10	Inclusion in combination with other codes	I63.433	Cerebral infarction due to embolism of bilateral posterior cerebral arteries	High-priority if the code is repeated in the patient history
ICD-10	Inclusion in combination with other codes	I63.439	Cerebral infarction due to embolism of unspecified posterior cerebral artery	High-priority if the code is repeated in the patient history
ICD-10	Inclusion in combination with other codes	I63.441	Cerebral infarction due to embolism of right cerebellar artery	High-priority if the code is repeated in the patient history
ICD-10	Inclusion in combination with other codes	I63.442	Cerebral infarction due to embolism of left cerebellar artery	High-priority if the code is repeated in the patient history
ICD-10	Inclusion in combination with other codes	I63.443	Cerebral infarction due to embolism of bilateral cerebellar arteries	High-priority if the code is repeated in the patient history

Code Type	Inclusion / Exclusion	Code	Code Description	Suggestions for Implementation
Clues From Clinical History (cont.)				
ICD-10	Inclusion in combination with other codes	I63.449	Cerebral infarction due to embolism of unspecified cerebellar artery	High-priority if the code is repeated in the patient history
ICD-10	Inclusion in combination with other codes	I63.49	Cerebral infarction due to embolism of other cerebral artery	High-priority if the code is repeated in the patient history
ICD-10	Inclusion in combination with other codes	Z95.0	Presence of cardiac pacemaker	May be used in combination with codes for atrioventricular block or symptomatic bradycardia to improve specificity
ICD-10	Inclusion in combination with other codes	0JH606Z	Insertion of a pacemaker, dual chamber into chest subcutaneous tissue and fascia, open approach	May be used in combination with codes for atrioventricular block or symptomatic bradycardia to improve specificity
ICD-10	Inclusion in combination with other codes	I44.2	Atrioventricular block, complete	May be used in combination with codes for cardiac pacemaker to improve specificity
ICD-10	Inclusion in combination with other codes	R00.1	Bradycardia, unspecified	May be used in combination with codes for cardiac pacemaker to improve specificity
ICD-10	Inclusion in combination with other codes	T88.7XXA	Unspecified adverse effect of drug or medicament, initial encounter	High-priority code when used in combination with ≥1 other code from clinical history
ICD-10	Inclusion in combination with other codes	G60.3	Idiopathic progressive neuropathy	High-priority code when used in combination with ≥1: -Bilateral carpal tunnel syndrome -Autonomic dysfunction -Gait disorders -Cardiac hypertrophy -Heart rhythm disorder -Renal abnormalities -Unexplained weight loss -Vitreous opacities
ICD-10	Inclusion in combination with other codes	G61.81	Chronic inflammatory demyelinating polyneuritis	High-priority code when used in combination with ≥1: -Bilateral carpal tunnel syndrome -Autonomic dysfunction -Gait disorders -Cardiac hypertrophy -Heart rhythm disorder -Renal abnormalities -Unexplained weight loss -Vitreous opacities
ICD-10	Inclusion in combination with other codes	G90.9	Disorder of the autonomic nervous system, unspecified	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
ICD-10	Inclusion in combination with other codes	G90.8	Other disorders of the autonomic nervous system	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
ICD-10	Inclusion in combination with other codes	R26.9	Unspecified abnormalities of gait and mobility	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
ICD-10	Inclusion in combination with other codes	R26.2	Difficulty in walking, not elsewhere classified	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity

Code Type	Inclusion / Exclusion	Code	Code Description	Suggestions for Implementation
Clues From Clinical History (cont.)				
ICD-10	Inclusion in combination with other codes	I42.2	Other hypertrophic cardiomyopathy	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
ICD-10	Inclusion in combination with other codes	I49.9	Cardiac arrhythmia, unspecified	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
ICD-10	Inclusion in combination with other codes	R00.9	Unspecified abnormalities of heartbeat	Approximate synonyms include abnormal heartbeat and postural pulse change; may be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
ICD-10	Inclusion in combination with other codes	I49.8	Other specified cardiac arrhythmias	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
ICD-10	Inclusion in combination with other codes	R94.4	Abnormal results of kidney function studies	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
ICD-10	Inclusion in combination with other codes	R93.429	Abnormal radiologic findings on diagnostic imaging of unspecified kidney	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
ICD-10	Inclusion in combination with other codes	N28.9	Disorder of kidney and ureter, unspecified	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
ICD-10	Inclusion in combination with other codes	R63.4	Abnormal weight loss	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
ICD-10	Inclusion in combination with other codes	H43.391	Other vitreous opacities, right eye	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
ICD-10	Inclusion in combination with other codes	H43.392	Other vitreous opacities, left eye	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
ICD-10	Inclusion in combination with other codes	H43.393	Other vitreous opacities, bilateral	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
ICD-10	Inclusion in combination with other codes	H43.399	Other vitreous opacities, unspecified eye	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
SNOMED				
SNOMED	Inclusion in combination with other codes	446221000	Heart failure with normal ejection fraction	High-priority code in the absence of hypertension

Code Type	Inclusion / Exclusion	Code	Code Description	Suggestions for Implementation
Clues From Clinical History (cont.)				
SNOMED	Exclusion in combination with other codes	59621000	Essential hypertension	May be used in combination with codes for HFpEF to improve specificity
SNOMED	Exclusion in combination with other codes	38341003	Hypertensive disorder	May be used in combination with codes for HFpEF to improve specificity
SNOMED	Inclusion	12265501000119100	Bilateral carpal tunnel syndrome	High-priority code
SNOMED	Inclusion	18347007	Spinal stenosis of lumbar region	High-priority code
SNOMED	Inclusion	76107001	Spinal stenosis	High-priority code
SNOMED	Inclusion	268002004	Non-traumatic tendon rupture	High-priority code
SNOMED	Inclusion in combination with other codes	233873004	Hypertrophic cardiomyopathy	High-priority code when occurring in >60 years
SNOMED	Inclusion	60573004	Aortic valve stenosis	High-priority code
SNOMED	Inclusion in combination with other codes	194828000	Angina pectoris	High-priority code without abnormal angiogram
SNOMED	Inclusion in combination with other codes	371807002	Atypical angina (Angina pectoris which does not have associated classical symptoms of chest pain. Symptoms may include weakness, nausea, or sweating)	High-priority code without abnormal angiogram
LOINC	Exclusion in combination with other codes	LL3761-5	Other abnormal findings — ocular fundus angiography findings	May be used in combination with codes for angina to improve specificity
SNOMED	Inclusion in combination with other codes	230690007	Cerebrovascular accident	High-priority if code is repeated in patient history
SNOMED	Inclusion in combination with other codes	715770009	Acute motor axonal neuropathy	High-priority code when used in combination with ≥1: -Bilateral carpal tunnel syndrome -Autonomic dysfunction -Gait disorders -Cardiac hypertrophy -Heart rhythm disorder -Renal abnormalities -Unexplained weight loss -Vitreous opacities
SNOMED	Inclusion in combination with other codes	33209009	Idiopathic progressive polyneuropathy	High-priority code when used in combination with ≥1: -Bilateral carpal tunnel syndrome -Autonomic dysfunction -Gait disorders -Cardiac hypertrophy -Heart rhythm disorder -Renal abnormalities -Unexplained weight loss -Vitreous opacities
SNOMED	Inclusion in combination with other codes	444728005	Chronic inflammatory demyelinating polyneuropathy	High-priority code when used in combination with ≥1: -Bilateral carpal tunnel syndrome -Autonomic dysfunction -Gait disorders -Cardiac hypertrophy -Heart rhythm disorder -Renal abnormalities -Unexplained weight loss -Vitreous opacities

Code Type	Inclusion / Exclusion	Code	Code Description	Suggestions for Implementation
Clues From Clinical History (cont.)				
SNOMED	Inclusion in combination with other codes	15241006	Disorder of the autonomic nervous system	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
SNOMED	Inclusion in combination with other codes	230659005	Segmental autonomic dysfunction	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
SNOMED	Inclusion in combination with other codes	22325002	Gait problem	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
SNOMED	Inclusion in combination with other codes	431524008	Abnormal gait due to impairment of balance	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
SNOMED	Inclusion in combination with other codes	266249003	Ventricular hypertrophy	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
SNOMED	Inclusion in combination with other codes	55827005	Left ventricular hypertrophy	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
SNOMED	Inclusion in combination with other codes	698247007	Cardiac arrhythmia	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
SNOMED	Inclusion in combination with other codes	236423003	Renal impairment	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
SNOMED	Inclusion in combination with other codes	39539005	Abnormal renal function	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
SNOMED	Inclusion in combination with other codes	76114004	Decreased renal function	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
SNOMED	Inclusion in combination with other codes	267024001	Abnormal weight loss	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
SNOMED	Inclusion in combination with other codes	699205002	Involuntary weight loss	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
SNOMED	Inclusion in combination with other codes	422061002	Vitreous opacities	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity

Code Type	Inclusion / Exclusion	Code	Code Description	Suggestions for Implementation
Clues From Clinical History (cont.)				
SNOMED	Inclusion in combination with other codes	349061000119107	Vitreous opacity of bilateral eyes	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
SNOMED	Inclusion in combination with other codes	347991000119105	Vitreous opacity of the right eye	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
SNOMED	Inclusion in combination with other codes	348431000119100	Vitreous opacity of the left eye	May be used in combination with codes for idiopathic rapidly progressive sensory-motor axonal neuropathy and/or atypical chronic inflammatory demyelinating polyneuropathy to improve specificity
Clinical Examination and Imaging				
ICD-10				
ICD-10	Inclusion	I50.810	Right heart failure, unspecified	High-priority code
ICD-10	Inclusion	I50.811	Acute right heart failure	High-priority code
ICD-10	Inclusion	J90	Pleural effusion, not elsewhere classified	High-priority code
ICD-10	Inclusion	I95.1	Orthostatic hypotension (excludes neurogenic orthostatic hypotension (G90.3) and orthostatic hypotension due to drugs (I95.2))	High-priority code
ICD-10	Inclusion in combination with other codes	I44.2	Atrioventricular block, complete	High-priority code when used in combination with ≥1 other code from clinical history
ICD-10	Inclusion in combination with other codes	I48.91	Unspecified atrial fibrillation	High-priority code when used in combination with ≥1 other code from clinical history
Monoclonal Protein Detection				
CPT				
CPT	Inclusion	83521	Immunoglobulin Free Light Chains, Serum	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)
CPT	Inclusion	82784	Immunofixation (IFE), Serum and Protein Electrophoresis, Serum	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)
CPT	Inclusion	84156	Immunofixation (IFE) and Protein Electrophoresis, Random Urine	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)
CPT	Inclusion	86335	Urine Immunofixation by Electrophoresis	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)
CPT	Inclusion	84156	Immunofixation (IFE) and Protein Electrophoresis, Random Urine	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)
CPT	Inclusion	84166	Immunofixation (IFE) and Protein Electrophoresis, Random Urine	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)

Code Type	Inclusion / Exclusion	Code	Code Description	Suggestions for Implementation
Monoclonal Protein Detection (cont.)				
LOINC				
LOINC	Inclusion	40844-3	Kappa/Lambda Free Light Chain Ratio	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)
LOINC	Inclusion	25700-6	Immunofixation for Serum or Plasma	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)
LOINC	Inclusion	49275-1	Immunofixation for Serum or Plasma Narrative	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)
LOINC	Inclusion	11526-1	EER Immunofix Electrophoresis Serum	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)
LOINC	Inclusion	34550-4	Immunofixation, Serum	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)
LOINC	Inclusion	18301-2	IgG [Presence] in Serum by Immunofixation	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy)
Amyloid Deposit				
CPT				
CPT	Inclusion	88313	Demonstration of amyloid in tissues from Congo Red	High-priority code
CPT	Inclusion	83789	Mass spectrometry and tandem mass spectrometry (MS, MS/MS)	High-priority code
LOINC				
LOINC	Inclusion	10782-1	Microscopic observation [identifier] in tissue by Congo red stain	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy of impacted organ) or test rerun due to false negative possibility
LOINC	Inclusion	LP95062-3	LC/MS/MS: liquid chromatography-tandem mass spectrometry	High-priority code
Cardiac Scintigraphy				
LOINC				
LOINC	Inclusion	39891-7	NM Heart Views for infarct and first pass W Tc-99m PYP IV	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy of impacted organ) or test rerun due to false negative possibility
LOINC	Inclusion	39654-9	SPECT Heart for infarct W Tc-99m PYP IV	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy of impacted organ) or test rerun due to false negative possibility
LOINC	Inclusion	82654-5	Cardiac nuclear imaging SPECT panel	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy of impacted organ) or test rerun due to false negative possibility
HCPCS				
HCPCS	Inclusion	A9538	(99m)Tc-pyrophosphate, diagnostic	High-priority code; Even in the absence of a positive test, patients with high clinical suspicion should have additional testing ordered (eg, biopsy of impacted organ) or test rerun due to false negative possibility

Table 3: Codes indicating an amyloidosis diagnosis

These codes may indicate an amyloidosis diagnosis and may be considered as exclusionary criteria for the suspect patient list to decrease continued flagging of patients who have already been triaged and assessed.

Code Type	Inclusion / Exclusion	Code	Code Description	Suggestions for Implementation
ICD-10				
ICD-10	Exclusion (with additional considerations)	E85.81	Light chain (AL) amyloidosis	Indicates amyloidosis diagnosis, may consider removing from suspect patient list to decrease continued flagging, but in rare cases patients may have ATTR and AL and need further testing
ICD-10	Exclusion	E85.1	Neuropathic heredofamilial amyloidosis	Indicates amyloidosis diagnosis (hATTR), may consider removing from suspect patient list to decrease continued flagging
ICD-10	Exclusion	E85.2	Heredofamilial amyloidosis, unspecified	Indicates amyloidosis diagnosis (hATTR), may consider removing from suspect patient list to decrease continued flagging
ICD-10	Exclusion (with additional considerations)	E85.4	Organ-limited amyloidosis	Applicable to localized amyloidosis and transthyretin-related (ATTR) familial amyloid cardiomyopathy, may consider removing from suspect patient list to decrease continued flagging, but patients may have a mixed phenotype of ATTR or, under very rare circumstances, ATTR and AL
ICD-10	Exclusion	E85.82	Wild-type transthyretin-related (ATTR) amyloidosis	Indicates amyloidosis diagnosis (ATTRwt), may consider removing from suspect patient list to decrease continued flagging
ICD-10	Exclusion (with additional considerations)	E85.9	Amyloidosis, unspecified	Indicates amyloidosis diagnosis, additional testing likely required to determine subtype to guide treatment decision
SNOMED				
SNOMED	Exclusion (with additional considerations)	17602002	Amyloidosis	Indicates amyloidosis diagnosis, additional testing likely required to determine subtype to guide treatment decision
SNOMED	Exclusion (with additional considerations)	23132008	AL amyloidosis	Indicates amyloidosis diagnosis, may consider removing from suspect patient list to decrease continued flagging, but in rare cases patients may have ATTR and AL and need further testing
SNOMED	Exclusion (with additional considerations)	237868006	Familial non-neuropathic amyloidosis	Indicates amyloidosis diagnosis (potentially hATTR-CM), may consider removing from suspect patient list to decrease continued flagging
SNOMED	Exclusion (with additional considerations)	367601000119103	Hereditary amyloidosis	Indicates amyloidosis diagnosis (hATTR), may consider removing from suspect patient list to decrease continued flagging, but patients may have a mixed phenotype of ATTR or, under very rare circumstances, ATTR and AL
SNOMED	Exclusion (with additional considerations)	56871000	Localized amyloidosis	Indicates amyloidosis diagnosis, further typing likely required
SNOMED	Exclusion (with additional considerations)	89449005	Systemic amyloidosis	Indicates amyloidosis diagnosis (multiple organs involved), further typing is likely required
LOINC				
LOINC	Exclusion	94225-0	TTR gene full mutation analysis in blood or tissue by sequencing	If ATTR has been established, this test can diagnose hATTR amyloidosis; may consider removing from suspect patient list to decrease continued flagging

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Appendix C: Getting Started–Suggested Medical Codes

To begin the implementation of the deciphEHR™ program, your institution may want to use a step approach to implementing the high-priority codes that can be further fine tuned by adding additional diagnostic codes. Below is an illustrative example for which high-priority codes an intuition may want to focus on when starting implementation. The institution and clinical teams at the institution are responsible for the selection of which codes to implement based on specific situations and patient needs.

Table 4: Getting started–codes for potential AL amyloidosis

These codes may be helpful in the initial stepwise approach to implementing the deciphEHR™ program for AL amyloidosis. The decision on how to implement these codes should be aligned with your institution's Clinical Leadership.

Code Type	Inclusion / Exclusion	Code	Code Description	Suggestions for Implementation
Initial Set of Red-Flag Codes				
ICD-10	Inclusion	Q38.2	Macroglossia	High-priority code
ICD-10	Inclusion	D69	Purpura and other hemorrhagic conditions	High-priority code
ICD-10	Inclusion	D47.2	Monoclonal gammopathy	High-priority code; Patients with MGUS should be routinely screened for AL amyloidosis
ICD-10	Inclusion	C90.00	Multiple myeloma not having achieved remission	High-priority code
ICD-10	Inclusion	I50.3	Acute on chronic diastolic (congestive) heart failure with preserved ejection fraction	High-priority code
Codes to Refine the List				
ICD-10	Inclusion in combination with other codes	C90.01	Multiple myeloma in remission	High-priority code when used in combination with codes for unexplained weight loss, lower extremity edema, early satiety, and dyspnea on exertion
ICD-10	Inclusion in combination with other codes	C90.02	Multiple myeloma in relapse	High-priority code when used in combination with codes for unexplained weight loss, lower extremity edema, early satiety, and dyspnea on exertion
ICD-10	Inclusion in combination with other codes	R63.4	Abnormal weight loss	May be used in combination with codes for multiple myeloma to improve specificity
ICD-10	Inclusion in combination with other codes	R60.0	Localized edema	May be used in combination with codes for multiple myeloma to improve specificity
ICD-10	Inclusion in combination with other codes	R22.43	Localized swelling, mass and lump, lower limb, bilateral	May be used in combination with codes for multiple myeloma to improve specificity

The above codes and suggested use cases for codes are illustrative. Any code implementation should be aligned with Clinical Leadership at your institution.

Code Type	Inclusion / Exclusion	Code	Code Description	Suggestions for Implementation
Codes to Refine the List (cont.)				
ICD-10	Inclusion in combination with other codes	R68.81	Early satiety	May be used in combination with codes for multiple myeloma to improve specificity
ICD-10	Inclusion in combination with other codes	R06.09	Other forms of dyspnea	May be used in combination with codes for multiple myeloma to improve specificity
ICD-10	Inclusion in combination with other codes	R06.02	Shortness of breath	May be used in combination with codes for multiple myeloma to improve specificity
ICD-10	Inclusion in combination with other codes	G62.9	Polyneuropathy, unspecified	High-priority code in the absence of diabetes
ICD-10	Inclusion in combination with other codes	G90.09	Other idiopathic peripheral autonomic neuropathy	High-priority code in the absence of diabetes
ICD-10	Exclusion in combination with other codes	E10	Type 1 diabetes mellitus	May be used in combination with codes for polyneuropathy to improve specificity
ICD-10	Exclusion in combination with other codes	E11	Type 2 diabetes	May be used in combination with codes for polyneuropathy to improve specificity

Table 5: Getting started–codes for potential ATTR

These codes may be helpful in the initial stepwise approach to implementing the deciphEHR™ program for ATTR. The decision on how to implement these codes should be aligned with your institution's Clinical Leadership.

Code Type	Inclusion / Exclusion	Code	Code Description	Suggestions for Implementation
Initial Set of Red-Flag Codes				
ICD-10	Inclusion	G56.03	Carpal tunnel syndrome, bilateral upper limbs	High-priority code
ICD-10	Inclusion	M48.061	Spinal stenosis, lumbar region without neurogenic claudication	High-priority code
ICD-10	Inclusion	M48.062	Spinal stenosis, lumbar region with neurogenic claudication	High-priority code
ICD-10	Inclusion	M48.07	Spinal stenosis, lumbosacral region	High-priority code
ICD-10	Inclusion	M48.00	Spinal stenosis, site unspecified	High-priority code
ICD-10	Inclusion	M66.829	Spontaneous rupture of other tendons, unspecified upper arm	High-priority code
ICD-10	Inclusion	I35.0	Nonrheumatic aortic (valve) stenosis	High-priority code
ICD-10	Inclusion	I50.810	Right heart failure, unspecified	High-priority code
ICD-10	Inclusion	I50.811	Acute right heart failure	High-priority code
ICD-10	Inclusion	J90	Pleural effusion, not elsewhere classified	High-priority code
ICD-10	Inclusion	I95.1	Orthostatic hypotension (excludes neurogenic orthostatic hypotension (G90.3) and orthostatic hypotension due to drugs (I95.2))	High-priority code
ICD-10	Inclusion in combination with other codes	G60.3	Idiopathic progressive neuropathy	High-priority code when used in combination with ≥1: -Bilateral carpal tunnel syndrome -Autonomic dysfunction -Gait disorders -Cardiac hypertrophy -Heart rhythm disorder -Renal abnormalities -Unexplained weight loss -Vitreous opacities
ICD-10	Inclusion in combination with other codes	G61.81	Chronic inflammatory demyelinating polyneuritis	High-priority code when used in combination with ≥1: -Bilateral carpal tunnel syndrome -Autonomic dysfunction -Gait disorders -Cardiac hypertrophy -Heart rhythm disorder -Renal abnormalities -Unexplained weight loss -Vitreous opacities
Codes to Refine the List				
ICD-10	Inclusion in combination with other codes	I50.1	Left ventricular failure, unspecified	High-priority code in the absence of hypertension
ICD-10	Inclusion in combination with other codes	I50.3	Acute on chronic diastolic (congestive) heart failure with preserved ejection fraction	High-priority code in the absence of hypertension
ICD-10	Exclusion in combination with other codes	I10	Essential (primary) hypertension	May be used in combination with codes for HFpEF to improve specificity

Code Type	Inclusion / Exclusion	Code	Code Description	Suggestions for Implementation
Codes to Refine the List (cont.)				
ICD-10	Exclusion in combination with other codes	I11.9	Hypertensive heart disease without heart failure	May be used in combination with codes for HFpEF to improve specificity
ICD-10	Inclusion	M66.821	Spontaneous rupture of other tendons, right upper arm	High-priority code
ICD-10	Inclusion	I35.2	Nonrheumatic aortic (valve) stenosis with insufficiency	High-priority code
ICD-10	Inclusion	I35.1	Nonrheumatic aortic (valve) insufficiency	High-priority code

1. Baker KR, Rice L. The amyloidoses: Clinical features, diagnosis and treatment. *Methodist Debakey Cardiovasc J*. 2012;8(3):3-7. **2.** Cuddy SAM, Falk RH. Amyloidosis as a systemic disease in context. *Can J Cardiol*. 2020;36(3):396-407. **3.** Nativi-Nicolau JN, Karam C, Khella S, Maurer MS. Screening for ATTR amyloidosis in the clinic: overlapping disorders, misdiagnosis, and multiorgan awareness. *Heart Fail Rev*. 2022;27(3):785-793. **4.** Gertz MA. Hereditary ATTR amyloidosis: Burden of illness and diagnostic challenges. *Am J Manag Care*. 2017;23(7 Suppl):S107-S112. **5.** Gertz MA, Dispenzieri A. Systemic amyloidosis recognition, prognosis, and therapy: A systematic review. *JAMA*. 2020;324(1):79-89. **6.** Quock TP, D'Souza A, Broder MS, Bognar K, Chang E, Tarbox MH. In-hospital mortality in amyloid light chain amyloidosis: Analysis of the Premier Healthcare Database. *J Comp Eff Res*. 2023;12(2): e220185. **7.** Quock TP, Yan T, Tieu R, D'Souza A, Broder MS. Untangling the clinical and economic burden of hospitalization for cardiac amyloidosis in the United States. *Clinicoecon Outcomes Res*. 2019;11:431-439. **8.** Kittleson MM, Ruberg FL, Ambardekar AV, et al; Writing Committee. 2023 ACC Expert Consensus Decision Pathway on comprehensive multidisciplinary care for the patient with cardiac amyloidosis: A report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol*. 2023;81(11):1076-1126. **9.** Adams D, Ando Y, Beirão JM, et al. Expert consensus recommendations to improve diagnosis of ATTR amyloidosis with polyneuropathy. *J Neurol*. 2021;268(6):2109-2122. **10.** Hasib Sidiqi M, Gertz MA. Immunoglobulin light chain amyloidosis diagnosis and treatment algorithm 2021. *Blood Cancer J*. 2021;11(5):90. **11.** Goldis R, Kaplan B, Kukuy OL, et al. Diagnostic challenges and solutions in systemic amyloidosis. *Int J Mol Sci*. 2023;24(5):4655. **12.** Tanskanen M, Peuralinna T, Polvikoski T, et al. Senile systemic amyloidosis affects 25% of the very aged and associates with genetic variation in alpha2- macroglobulin and tau: A population-based autopsy study. *Ann Med*. 2008;40:232–239. **13.** Maggialetti N, Torrente A, Lorusso G, Villanova I, Ficco M, Gravina M, et al. Role of cardiovascular magnetic resonance in cardiac amyloidosis: A narrative review. *J Pers Med*. 2024;14(4):407. **14.** Sidiqi MH, McPhail ED, Theis JD, et al. Two types of amyloidosis presenting in a single patient: A case series. *Blood Cancer J*. 2019;9(3):30. **15.** ASNC Writing Group, Dorbala S, Bokhari S, et al. ASNC cardiac amyloidosis practice points update ^{99m} TechnetiumPyrophosphate imaging for transthyretin cardiac amyloidosis. *American Society of Nuclear Cardiology*. 2021. **16.** Wisniowski B, Wechalekar A. Confirming the diagnosis of amyloidosis. *Acta Haematologica*. 2020;143(4):312-321. **17.** Leung N, Nasr SH, Sethi S. How I treat amyloidosis: The importance of accurate diagnosis and amyloid typing. *Blood*. 2012;120(16):3206-3213. **18.** Ihne S, Morbach C, Sommer C, Geier A, Knop S, Störk S. Amyloidosis—the diagnosis and treatment of an underdiagnosed disease. *Dtsch Arztebl Int*. 2020;117(10):159-166. **19.** Gopal DM, Ruberg FL, Siddiqi OK. Impact of genetic testing in transthyretin (ATTR) cardiac amyloidosis. *Curr Heart Fail Rep*. 2019;16:180-188. **20.** McGreevey JD 3rd. Order sets in electronic health records: principles of good practice. *Chest*. 2013;143(1):228-235. **21.** Bejjanki H, Mramba LK, Beal SG, et al. The role of a best practice alert in the electronic medical record in reducing repetitive lab tests. *Clinicoecon Outcomes Res*. 2018;10:611-618. **22.** Valvona SN, Rayo MF, Abdel-Rasoul M, et al. Comparative effectiveness of best practice alerts with active and passive presentations: a retrospective study. *In Proceedings of the International Symposium on Human Factors and Ergonomics in Health Care*. 2020;9(1):105-109. **23.** How to...understand and measure impact. The Better Care Fund, National Health Service (NHS) England. Updated May 2015. Accessed October 25, 2024. https://www.england.nhs.uk/wp-content/uploads/2015/06/bcf-user-guide-04.pdf.pdf. **24.** Types of health quality measures. Agency for Healthcare Research and Quality (AHRQ). Updated July 2015. Accessed October 25, 2024. https://www.ahrq.gov/talkingquality/measures/types.html. **25.** Lousada I, Maurer MS, Warner M, et al. Amyloidosis Research Consortium Cardiac Amyloidosis Survey: Results from Patients with AL and ATTR Amyloidosis and Their Caregivers. Amyloidosis Research Consortium; Presented at the XVIth International Symposium on Amyloidosis; March 26-29, 2018; Kumamoto, Japan. https://arci.org/wp-content/uploads/2019/05/ISA-2018-ARC-Cardiac-Amyloid-Poster-V4.pdf.

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