A Collaborative Approach to Amyloidosis and A Multidisciplinary Care Framework –Position Statement from the International Society of Amyloidosis

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Amyloidosis is a complex, multisystem disease. Like many rare and multisystem diseases, the breadth of diagnostic, clinical, and supportive capability required to care for such patients is best met by a multidisciplinary team in a center with dedicated expertise. The establishment of a multidisciplinary and comprehensive amyloidosis center requires adherence to specific criteria to ensure optimal patient care and facilitate advanced research. The International Cardio-Oncology Society emphasizes the importance of centers of excellence in cardiac amyloidosis, highlighting the need for centralized expert providers to manage the complexities of diagnosis and treatment.[1] This position paper from the International Society of Amyloidosis (ISA) outlines optimal requirements for the establishment or recognition of multidisciplinary amyloidosis centers, as well as the different medical disciplines that should be involved.

Essential elements of a multidisciplinary center

A comprehensive amyloidosis center should include the following essential elements (Figure 1). Specialists should have dedicated time for amyloidosis care, research, and education, reflecting a commitment beyond general practice. Given the urgency of diagnosis, an expedited and streamlined workup is essential. Long-term follow-up with structured monitoring is critical to assess treatment response, detect progression, and manage complications. To ensure accountability and improvement across institutions, centers should develop shared quality and outcomes measures such as time to diagnosis, time to treatment, and patient-reported quality of life while recognizing that survival metrics may be misleading due to referral and case mix variability.

1. **Multidisciplinary Team**: The center must have a dedicated team of specialists, including cardiologists, hematologists, nephrologists, neurologists, gastroenterologists, hepatologists, pulmonologists, pathologists, geneticists, nuclear medicine specialists, cardiac imaging experts and radiologists, to address the multisystem nature of amyloidosis. This team should collaborate closely, including via multidisciplinary clinics and team meetings, to provide integrated care.[2, 3]

Another important aspect to consider is the value of regular virtual meetings among amyloidosis centers to facilitate expert consultation and second-opinion discussions, particularly for complex or atypical cases. This approach is especially valuable for centers that may not have in-house expertise in rarer subtypes or in managing unusual disease presentations.

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It would be wise to name who is really essential (shorter list) and then say the core experts seek advice from ...

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2. **Advanced Diagnostic Capabilities**: Access to advanced diagnostic modalities is essential for the evaluation and management of systemic amyloidosis. These include echocardiography, cardiovascular magnetic resonance imaging (CMR), radionuclide imaging, histopathology with typing (e.g., mass spectrometry or immunohistochemistry), genetic testing, and tissue biopsy for screening (e.g. fat aspiration and labial salivay glands) and from involved organs such as the heart, kidney, liver, nerve, and gastrointestinal tract. While some centers may maintain these capabilities on-site, others operate through collaborative networks. Such models highlight the variability in diagnostic infrastructure and emphasize the importance of reliable access, whether direct or through partnerships. Multiple cardiovascular societies recommend multimodality imaging for accurate diagnosis and monitoring.[4]

3. **Expertise in Amyloidosis Subtypes:** The center must demonstrate comprehensive expertise in the diagnosis and management of common amyloidosis subtypes, including immunoglobulin light chain (AL) amyloidosis, hereditary variant transthyretin (ATTRv) amyloidosis, wild-type transthyretin (ATTRwt) and serum amyloid A (AA) amyloidosis. This includes proficiency in

serologic, histologic and genetic testing necessary for accurate subtyping. Localized amyloidosis, while distinct from systemic forms, is not uncommon and should be included among the commonly encountered subtypes. Accurate distinction between localized and systemic disease is critical to avoid misdiagnosis and overtreatment, underscoring the importance of center-level expertise in both forms. The ISA recognizes that expertise in rarer amyloid types may not be available in every center and a model with few centers developing expertise in both diagnosis and management of rarer types of amyloidosis, such as gelsolin (AGel), apolipoprotein A-I (AApoA1), apolipoprotein A-IV (AApoAIV), leukocyte chemotactic factor 2 (ALECT2), fibrinogen A alpha-chain (AFib), beta 2 microglobulin (Aβ2MG) and localized amyloidosis, is crucially important.[2] Establishing referral pathways between centers is important to ensure adequate diagnostic and clinical work up for such patients. Supra-regional or national multidisciplinary teams (MDT) may be necessary for management of rare amyloid types.

4. **Comprehensive Treatment Options**: The center should offer a range of treatment options, including pharmacological therapies, (stem) cell transplantation, and novel therapies like RNA interference, antisense oligonucleotides, gene editing therapies. The European Society of Cardiology outlines the importance of bridging the gap between advances in treatment and clinical practice.[5] Referral pathways for complex novel cellular and other immunotherapies for AL amyloidosis are needed for centers lacking large volume cellular therapy programs. Access to organ transplantation particularly heart and kidney transplantation is also an important component of comprehensive care for selected patients with advanced organ involvement.

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5. **Patient Support Services:** The center should have the capacity to address the holistic needs of patients and their families by providing counseling, psychosocial support, education, nutritional guidance through access to dietitians, and specialty pharmacy services to ensure

unfettered access to disease-modifying therapy. The center should lead and develop patient support groups. The German Cardiac Society highlights the importance of addressing the psychosocial distress associated with amyloidosis.[6]

6. **Research and Education:** The center should engage in ongoing research spanning basic, translational, and clinical studies to advance the understanding and treatment of amyloidosis. It should also provide regular education and training for healthcare professionals to ensure the highest standards of care.[7] Barriers to centralized data and biospecimen sharing remain a challenge; fostering collaborative infrastructures, with the ISA potentially serving a convening role, could help overcome these limitations and advance research and care. In addition, robust clinical research infrastructure, including IRB support and clinical trial programs, is essential to the function of high-performing amyloidosis centers.

7. **Telemedicine Capabilities:** To enhance accessibility and coordination of care, the center should incorporate telemedicine services. This approach can facilitate communication between the amyloidosis center and local healthcare providers, as suggested by the German AMY-NEEDS research and care program.[8]

8. **Collaborative Networks:** The center should be part of a larger network of amyloidosis centers to share knowledge, resources, and best practices. A hub and spoke model of network centers is likely to develop in most settings. Currently, there are three major national networks for amyloidosis. The UK amyloidosis network modeled and nationally funded on this lines, demonstrates the benefits of such collaborative efforts.[9] The French network S, coordinated by the Association Française Contre l'Amylose (AFCA) and the four French National Referral Centres for amyloidosis, has been instrumental in managing systemic amyloidosis. In Italy, the Italian Amyloidosis Study Group and the Italian Cardiac Amyloidosis Network (RIAC) have

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established two interconnected national networks have established All of these networks have facilitated the collection of comprehensive data on amyloidosis prevalence, diagnosis, management, and patient impact, highlighting the need for early and effective treatment to optimize patient outcome. The national networks to increase awareness, achieve early diagnoses, and provide locally qualified care, as well as national guidelines for diagnosis and care. These networks have shown that a multicenter approach can significantly improve patient survival and management outcomes compared to single-center approaches.[11] [12] The Italian Registry for ATTRv amyloidosis, involving 15 referral centers, has provided valuable epidemiological and clinical data, contributing to better planning of diagnostic and therapeutic services.[13] These collaborative efforts in the UK, France, and Italy underscore the importance of national networks in improving the diagnosis, management, and outcomes of amyloidosis patients through shared expertise and resources. Centralizing amyloidosis care within designated referral centers supports the development of specialized expertise and ensures access to comprehensive multidisciplinary services, a strategy that is particularly important in resource-limited regions.

In summary, a multidisciplinary and comprehensive amyloidosis center should integrate specialized expertise, advanced diagnostics, diverse treatment options, patient support services, research initiatives, telemedicine, pharmacy services and collaborative networks to provide the highest quality of care for amyloidosis patients.

Medical disciplines involvement

The primary medical disciplines involved in a multidisciplinary and comprehensive amyloidosis center, considering the need for specialized expertise in managing the multisystem nature of amyloidosis but are also integral to the diagnostic process and frequently serve as the initial referral pathway leading to diagnosis and include:

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1. **Cardiology:** Given the frequent cardiac involvement in amyloidosis, cardiologists are essential for diagnosing and managing cardiac amyloidosis. Their expertise includes functional capacity testing (e.g., six-minute walk test, cardiopulmonary stress testing), the use of advanced imaging techniques such as echocardiography with strain imaging, cardiac MRI, and nuclear scintigraphy. They play a critical role in heart failure drug and device management and arrhythmia monitoring. Close collaboration with interventional cardiology and cardiac surgery program for percutaneous or surgical treatment of valvular disease and with a heart transplant program is essential, along with the ability to refer patients for advanced heart failure therapies, including mechanical circulatory support and transplant evaluation.[1]

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2. **Hematology/Oncology:** Hematologists and oncologists are crucial for diagnosing and treating AL amyloidosis, which involves plasma cell dyscrasias and B cell lymphoproliferative disorders. They manage chemotherapy and other treatments aimed at reducing amyloidogenic light chain production and monitor hematologic response/progression.[3]

3. **Nephrology:** Nephrologists are involved due to the common renal involvement in amyloidosis, managing complications such as nephrotic syndrome, progressive renal dysfunction and renal failure / end stage renal disease.[4] They also play a key role in performing kidney biopsies, which are essential for diagnosis and guiding management. Renal transplantation is a viable option for selected patients who have achieved a hematologic response, with outcomes comparable to the general transplant population. The multidisciplinary approach involving nephrologists is essential for optimizing patient outcomes in renal amyloidosis.

4. **Neurology:** Neurologists address peripheral and autonomic neuropathies that are common in amyloidosis, particularly in ATTRv and AL amyloidosis.

5. **Genetics:** Geneticists play a role in diagnosing hereditary forms of amyloidosis, such as ATTRv amyloidosis, through genetic testing, cascade testing and both family and patient genetic counseling. They also have an important role in recognizing double pathology, such as coexistent ATTRwt amyloidosis and sarcomeric cardiomyopathy.

6. **Gastroenterology:** Gastroenterologists manage gastrointestinal manifestations of amyloidosis, including malabsorption and gastrointestinal bleeding.

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7. **Pathology:** Pathologists are essential for the histological diagnosis of amyloidosis, including the use of Congo red staining and immunohistochemistry/mass spectrometry to identify amyloid deposits.

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8. **Pharmacy:** Pharmacists play a critical role in optimizing medication management for patients with amyloidosis. This includes ensuring safe and effective use of complex therapies, such as transthyretin stabilizers, gene silencers, proteasome inhibitors, monoclonal antibodies, and supportive treatments. Access to a specialty pharmacy is essential to facilitate coordination, patient education, monitoring for drug interactions and adverse effects, and assistance with navigation of drug access and reimbursement.[5]

9. **Palliative Care:** Palliative care specialists provide symptom management and support for patients with advanced disease, addressing quality of life and end-of-life care.[5]

10. **Psychosocial Support:** Psychologists and social workers offer counseling and support services to address the emotional and psychological needs of patients and their families.

11. **Nursing:** Specialized nurses ~~can~~ play a critical role in improving patient care. They enable expanded access to coordinated multidisciplinary care from referral through treatment and

clinical follow-up including effective community outreach. Such involvement can improve quality of life, reduce access barriers and minimize duplication.[14]

These disciplines work collaboratively to provide comprehensive care, ensuring that all aspects of the disease are managed effectively. Each discipline within a comprehensive amyloidosis center plays a critical role in ensuring that patients receive holistic and coordinated care, addressing the complex and multisystem nature of amyloidosis. This multidisciplinary approach is essential for optimizing patient outcomes and advancing research in the field.

Tiered model of multidisciplinary amyloidosis centers

As depicted in **Table 1**, multidisciplinary amyloidosis centers may exhibit different levels of expertise and deliver varying levels of care. For example, centers specializing in cardiac amyloidosis may develop expertise in AL and ATTR amyloid cardiomyopathy but refer to an amyloidosis center of excellence for difficult cases or other rarer types of amyloidosis. A tiered model allows patients, referrers, and institutions to understand the nature of the amyloidosis center. The terms Basic Center, Core Center and Center of Excellence have been suggested but other models such as the hub and spoke model in the UK[9] or the networked Amyloidosis Centers and Affiliate Services in Australia (www.aan.org.au) can successfully be applied.

Discussion and Conclusions

By integrating diverse specialties, ~~including cardiology, haematology, neurology, nephrology, and other relevant sub-specialities,~~ it is possible to build a comprehensive model of care that enhances diagnostic accuracy, strengthens treatment strategies, and ultimately improves patient outcomes and quality of life. Successful amyloidosis services can be built on six key pillars: **a dedicated multidisciplinary team, continuous quality improvement and community**

education, a strong research and innovation framework, access to appropriate therapies, advanced diagnostic capabilities, and active involvement with relevant committees and societies. Addressing regional gaps through **education**, **collaboration with patient support organizations**, and **strategic partnerships** will be essential in ensuring equitable care for amyloidosis patients worldwide. To build on the insights from this position statement, healthcare professionals wishing to establish or improve care of patients with amyloidosis could implement the solutions proposed here.

Additionally, an important consideration for amyloidosis centers of excellence is whether formal recognition by a central authority, such as the ISA, is necessary or whether self-declaration is sufficient. Given the considerable resources and time required for global accreditation, these efforts may be more effectively directed toward advancing patient care, education, and research. Regardless of accreditation status, it is essential that each center provide clear, comprehensive, and transparent documentation—ideally made publicly available on its website—outlining its capabilities. This should include details about the center's clinical and research experts and their specialized expertise in amyloidosis, the diagnostic tests and technologies available for diagnosis and subtyping (whether in-house or through referral networks), the range of treatment options offered and access to clinical trials, the scope of patient support services, protocols for expedited workup and long-term follow-up, and active research and education initiatives. Such transparency enables patients, referring providers, and the broader community to make informed decisions and fosters meaningful collaboration among centers.

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Figure 1: Essential Components of a Multidisciplinary Amyloidosis Center

- **Define a clear mission and vision** for the center with focused program goals and a clear plan to align stakeholders and support long-term institutional buy-in
- **Pursue diverse funding opportunities** to secure sustained financial support
- **Centralized patient triage** to streamline referrals and ensure timely access to subspecialists
- ~~**Integrated subspecialty care** including hematology, cardiology, neurology, nephrology, gastroenterology, and genetics via a multidisciplinary team~~
- ~~**Advanced diagnostic capabilities** such as mass spectrometry, genetic testing, and tissue biopsy interpretation~~
- ~~**Dedicated amyloidosis nursing and care coordination** to support patient navigation, education, and longitudinal care~~
- ~~**Access to clinical trials** and novel therapies, including infrastructure for research coordination and regulatory support~~
- ~~**Robust data systems** for tracking clinical outcomes, monitoring treatment response, and contributing to registries~~
- ~~**Leverage research opportunities** such as clinical trials, biobanking, and retrospective data analysis to support academic growth and encourage institutional engagement~~
- ~~**Patient support services** such as financial counseling, psychological support, and access to patient advocacy groups~~

- **Multidisciplinary Team:** Cardiologists, hematologists, nephrologists, neurologists, gastroenterologists, hepatologists, pulmonologists, pathologists, geneticists, nuclear medicine specialists, cardiac imaging experts, radiologists; multidisciplinary clinics; regular team and virtual meetings
- **Advanced Diagnostics:** Echocardiography, cardiac MRI, radionuclide imaging, histopathology with typing (mass spectrometry, immunohistochemistry, IEM?), genetic testing, tissue biopsy (heart, kidney, liver, nerve, GI tract)
- **Expertise in Subtypes:** Comprehensive knowledge of AL, ATTRv, ATTRwt, AA, and localized amyloidosis; referral pathways for rare types (AGel, AApoA1, AApoAIV, ALECT2, AFib, Aβ2M); supra-regional multidisciplinary teams (MDTs)
- **Treatment Options:** Pharmacologic therapies, (stem) cell transplantation, novel therapies (RNA interference, gene editing); referral for cellular therapies; organ transplantation (heart, kidney)
- **Patient Support Services:** Counseling, psychosocial support, education, nutritional guidance (dietitians), specialty pharmacy, patient support groups
- **Research and Education:** Basic, translational, clinical research; professional education and training; collaborative data/sample sharing infrastructures; IRB and clinical trial support
- **Telemedicine Capabilities:** Virtual consultations and communication with local providers
- **Collaborative Networks:** Participation in hub-and-spoke national/regional networks (e.g., UK, France, Italy)

Table 1: Checklist for Multidisciplinary Amyloidosis Centers: Tiered Model

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Domain	Tier 1 – Basic Center	Tier 2 – Core Center	Tier 3 – Center of Excellence
Multidisciplinary Team	Access to hematology and cardiology	Includes hematology, cardiology, nephrology, neurology, and pathology	Fully integrated team across all relevant specialties; joint case conferences and shared care pathways
Diagnostic Capabilities	Basic tissue biopsy with Congo red staining. Final diagnosis should be completed by experienced lab or center.	Able to obtain confirmatory testing via immunohistochemistry with amyloid-specific in-house antibodies, mass spectrometry, genetic testing for TTR and other mutations	Able to obtain onsite or rapid-access advanced diagnostics CMR, EMB and amyloid typing by immunohistochemistry with amyloid-specific in-house antibodies, mass spectrometry or IG-EM; able to access genetic testing for rarer or new mutations. Access to capability of sequencing large number of genes.
Treatment Infrastructure	Standard therapies for AL and ATTR amyloidosis	Access to investigational therapies and clinical trials	Participation in multicenter trials; onsite clinical trial infrastructure and early-phase study access
Patient Navigation	Basic scheduling support	Dedicated nurse coordinator or patient navigator	Full-time navigation team including nursing, social work, and financial counseling
Education & Training	Ad hoc learning for staff	Regular CME events or internal teaching rounds	Formal training programs, fellowships, or continuing education/observerships for internal and external providers
Data Collection & Research	Case documentation	Contribution to local registries and retrospective studies	Participation in international registries, prospective trials, and publication of original research
Outreach & Referral Network	Receives referrals within institution	Regional referral center with streamlined intake	National/international referral destination with telehealth/remote consultations, outreach, and collaboration agreements
Pharmacy Access	Access to standard therapies via local pharmacy	Support for specialty pharmacy and drug access coordination	Embedded clinical pharmacist; dedicated team for specialty approvals, trial logistics, and patient education

Abbreviations: CMR – Cardiac Magnetic Resonance Imaging, EMB – Endomyocardial Biopsy, CME – Continuing Medical Education