C07 Systemic Sclerosis

This concept set will identify Systemic Sclerosis (SSc; systemic scleroderma)—a systemic, not localized, autoimmune fibrosing vasculopathy. The set must represent current, active systemic disease. This concept set will support an observational study that aims to answer the following research objective:

The study aims to explore treatment utilization among patients newly diagnosed with systemic sclerosis in real-world data.

The concept set will be used to phenotype patients with *systemic sclerosis as the target cohort in this research question.*

Clinical case definition: Systemic Sclerosis (SSc), also known as systemic scleroderma, is a complex, chronic autoimmune disorder characterized by three hallmark features: immune dysregulation (autoimmunity and inflammation), microvasculopathy (vascular injury and remodeling), and progressive fibrosis (excessive collagen deposition) affecting the skin and internal organs (e.g., lungs, gastrointestinal tract, heart, kidneys).

Diagnostic Criteria: Diagnosis is clinical, often informed by the 2013 ACR/EULAR classification criteria (score ≥9). Key elements include skin thickening proximal to the MCP joints (sufficient criterion), Raynaud's phenomenon, digital tip lesions, telangiectasias, abnormal nailfold capillaries, pulmonary arterial hypertension (PAH) and/or interstitial lung disease (ILD), and SSc-specific autoantibodies (Anti-Scl-70/Topoisomerase I, Anti-centromere, Anti-RNA polymerase III).

Presentation and Course: The presentation is heterogeneous and the course is chronic and lifelong. It is categorized based on skin involvement:

- **Diffuse Cutaneous SSc (dcSSc):** Extensive skin thickening, higher risk of early ILD and renal crisis.
- **Limited Cutaneous SSc (lcSSc):** Skin thickening restricted distally. Includes CREST syndrome.
- **SSc sine scleroderma:** Internal organ involvement without skin thickening.

Differential Diagnoses (Conditions to be distinguished and not considered inclusive): Undifferentiated Connective Tissue Disease (UCTD), Mixed Connective Tissue Disease (MCTD), Isolated Raynaud's phenomenon, and various scleroderma mimics (see Exclusions).

Common Treatments/Management: Management is typically overseen by a Rheumatologist. Treatments include immunosuppression (e.g., Mycophenolate Mofetil, Cyclophosphamide) and targeted therapies for ILD (Nintedanib, Tocilizumab, Rituximab).

Clinical Scope

- **Disease entity:** Chronic autoimmune disorder with immune dysregulation, microvasculopathy, and progressive fibrosis affecting skin and internal organs (lungs, GI tract, heart, kidneys). Diagnosis is clinical; 2013 ACR/EULAR elements include proximal skin thickening (sufficient criterion), Raynaud's phenomenon, digital ischemic lesions, telangiectasias, abnormal nailfold capillaries, PAH and/or ILD, and SSc-specific autoantibodies (anti–Scl-70, anticentromere, anti–RNA polymerase III).
- **Subtypes:** Diffuse cutaneous (dcSSc), limited cutaneous (lcSSc, includes CREST), and SSc sine scleroderma (internal organ involvement without skin thickening) all are within scope.
- **Temporality:** capture prevalent established, and active current disease.
- **Severity & acuity:** Include full spectrum from mild to life-threatening, acute manifestations and chronic progression.
- **Manifestations:** Multisystem involvement is in scope **when explicitly linked to SSc** (e.g., SSc-ILD, SSc-PAH).
- **Etiology:** Autoimmune/idiopathic SSc only.
- **Population:** all population

Related, differential conditions or comorbidities that are not sufficient for inclusion

- **Localized scleroderma (critical exclusion):** morphea (generalized/plaque/guttate), linear scleroderma, en coup de sabre.
- **Mimics/fibrosing conditions:** eosinophilic fasciitis, scleredema, scleromyxedema, nephrogenic systemic fibrosis.
- **Induced scleroderma:** drug-induced (e.g., bleomycin, taxanes) or environmental/occupational (silica, vinyl chloride, toxic oil).
- **Other/overlap:** GVHD with sclerodermatous features; MCTD or UCTD unless "systemic sclerosis" is explicitly stated; isolated Raynaud's, acrosclerosis, or sclerodactyly.

Synonyms

- Systemic scleroderma; Progressive systemic sclerosis (PSS); CREST syndrome (limited cutaneous SSc Calcinosis, Raynaud's phenomenon, Esophageal dysmotility, Sclerodactyly, and Telangiectasias).