

Public Meeting on Patient-Focused Drug Development for Systemic Sclerosis

Tuesday, October 13, 2020

FDA will be streaming a live webcast of the meeting with the presentation slides, which is open to the public at: <http://fda.yorkcast.com/webcast/Play/a992e187a44a4b6eafc1aad859153f4d1d>. The webcast recording and presentation slides, along with a meeting transcript and summary report, will also be made publicly available after the meeting.

 #PFDD



Welcome

Robyn Bent, RN, MS | CAPT, U.S. Public Health Service

Director, Patient-Focused Drug Development Program

Office of Center Director

Center for Drug Evaluation and Research

U.S. Food and Drug Administration



Agenda

- Opening Remarks
- Setting the Context
 - Overview of FDA's Patient-Focused Drug Development Initiative
 - Overview of Systemic Sclerosis
 - Overview of Discussion Format
- Discussion Topic 1: Health Effects and Daily Impacts
- Break
- Discussion Topic 2: Current Approaches to Treatment
- Closing Remarks

Opening Remarks

Nikolay Nikolov, MD

Acting Director

Division of Rheumatology and Transplant Medicine

U.S. Food and Drug Administration

Overview of FDA's Patient-Focused Drug Development Initiative

Theresa Mullin, PhD

Associate Director for Strategic Initiatives

Center for Drug Evaluation and Research

U.S. Food and Drug Administration

FDA's role in medical product development and evaluation

FDA's mission is to **protect and promote public health** by evaluating the **safety and effectiveness of new drugs**.

While FDA plays a critical oversight role in drug development, it is just one part of the process. **FDA does not develop drugs nor conduct clinical trials.**

Review divisions at FDA (e.g., Division of Neurology, Division of Psychiatry, etc.) provide **regulatory oversight** during drug development, make decisions regarding **marketing approval for new drugs, and provide guidance** to regulated industry on clinical, scientific and regulatory matters.

What is Patient-Focused Drug Development (PFDD)?



PFDD is a systematic approach to help ensure that **patients' experiences, perspectives, needs, and priorities** are captured and meaningfully incorporated into drug development and evaluation.¹



Value of FDA's PFDD Meetings

- Patients are uniquely positioned to inform FDA understanding of the clinical context for drug review and regulatory decision making
- Prior to PFDD, available mechanisms for obtaining patient input were limited to discussions related to specific applications under review, such as Advisory Committee meetings and only a few patient representatives
- PFDD meetings provide a more systematic way to obtain patients' perspectives on severity of a condition, and its impact on daily life, and their assessments of available treatment options



PFDD Meetings Provide Key Stakeholders an Opportunity to Hear the Patient's Voice

The PFDD initiative was **established** by FDA.

2013 – 2017

FDA **values gathering patient input** through PFDD meetings. Hosts FDA meetings and attends Externally Led PFDD meetings

2012

FDA conducted **24 disease-specific PFDD meetings**.

FDA established **Externally Led PFDD meeting** option

2017 – Present



PFDD meetings in a wide range of disease areas providing insights

2013	2014	2015	2016	2017
<ul style="list-style-type: none"> Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis HIV Lung Cancer Narcolepsy 	<ul style="list-style-type: none"> Sickle Cell Disease Fibromyalgia Pulmonary Arterial Hypertension Inborn Errors of Metabolism Hemophilia A, B, and other Heritable Bleeding Disorders Idiopathic Pulmonary Fibrosis 	<ul style="list-style-type: none"> Female Sexual Dysfunction Breast Cancer Chagas Disease Functional Gastro-intestinal Disorders Parkinson's Disease and Huntington's Disease Alpha-1 Antitrypsin Deficiency 	<ul style="list-style-type: none"> Non-Tuberculous Mycobacterial Lung infections Psoriasis Neuropathic pain associated with peripheral neuropathy Patients who have received an organ transplant 	<ul style="list-style-type: none"> Sarcopenia Autism Alopecia Areata Hereditary Angioedema <p style="text-align: center;">2018</p> <ul style="list-style-type: none"> Opioid Use Disorder Chronic Severe Pain <p style="text-align: center;">2020</p> <ul style="list-style-type: none"> Stimulant Use Disorder

FDA clinical and statistical review staff have also attended over 28 other *Externally-Led PFDD* meetings 2016-19 conducted by patient advocacy groups

PFDD meetings follow a **town hall style** discussion format



Overview
Clinical Background and Current Available Treatments



Symptoms and Daily Impacts

- Panel of patients and caregivers
- Facilitated group discussion



Current Treatment Options

- Panel of patients and caregivers
- Facilitated group discussion



Each PFDD meeting is tailored to the needs of the specific disease area

- FDA encourages patient advocates, researchers, drug developers, healthcare providers and other government officials to attend PFDD meetings
- However, our focus is on hearing directly from patients and their caregivers, so we ask that others remain silent in listening mode during the discussions since the meetings are a **platform to hear directly from patients, caregivers and patient representatives.**
- After the PFDD meeting, a **Voice of the Patient report** summarizes the input shared by patients and caregivers.



Thank you!

An Overview of Systemic Sclerosis

Dinesh Khanna, MBBS, MSc

Michigan Medicine Rheumatology Clinic | Taubman Center

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Systemic Sclerosis

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Public Meeting on Patient-Focused Drug Development for
Systemic Sclerosis



Disclosures

- Grant support: Bayer, BMS, Pfizer, NIH/NIAID, NIH/NIAMS, Immune Tolerance Network, Horizon
- Consultant for clinical trial design or funding of an investigator-initiated trial:
 - Acceleron
 - Actelion
 - Abbvie
 - Amgen
 - Bayer
 - Boehringer-Ingelheim
 - CSL Behring
 - Corbus
 - Gilead
 - Galapagos
 - Genentech/Roche
 - GSK
 - Horizon
 - Merck
 - Mitsubishi Tanabe Pharma
 - Sanofi-Aventis/Genzyme
 - United Therapeutics
- Stocks
 - Eicos Sciences, Inc.
- No promotional talk

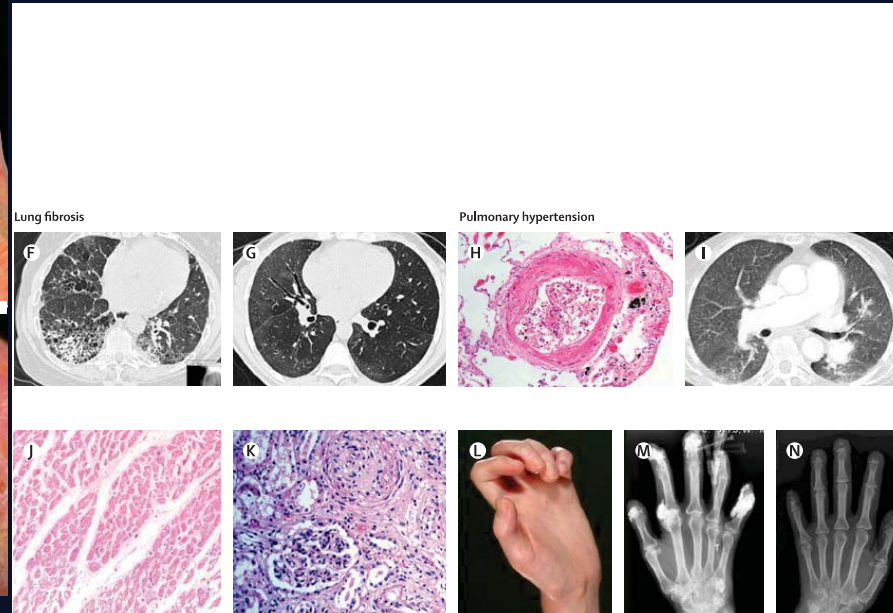
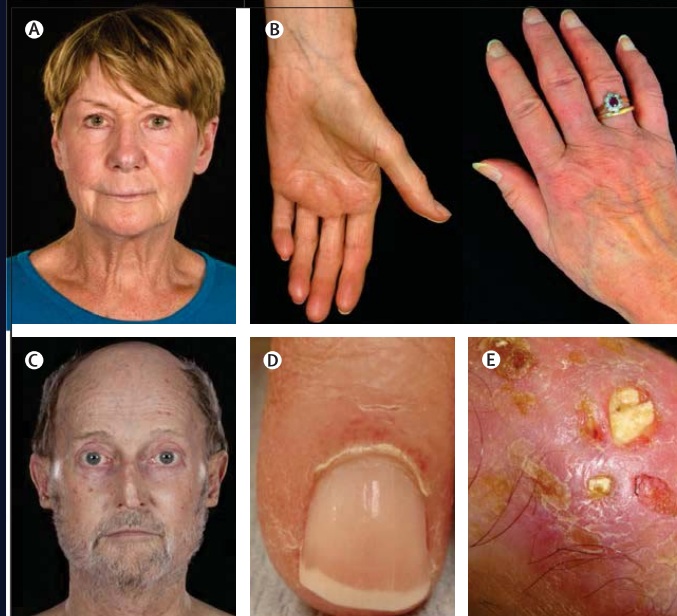


Scleroderma

- ◆ The word “scleroderma” comes from two Greek words: “sclero” meaning hard, and “derma” meaning skin.
- ◆ There are approximately 200,000 patients in US
- ◆ Approximately 75,000-80,000 have systemic sclerosis (SSc)

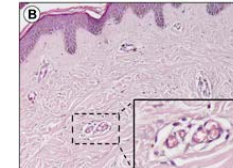
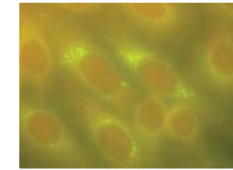
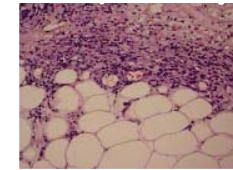
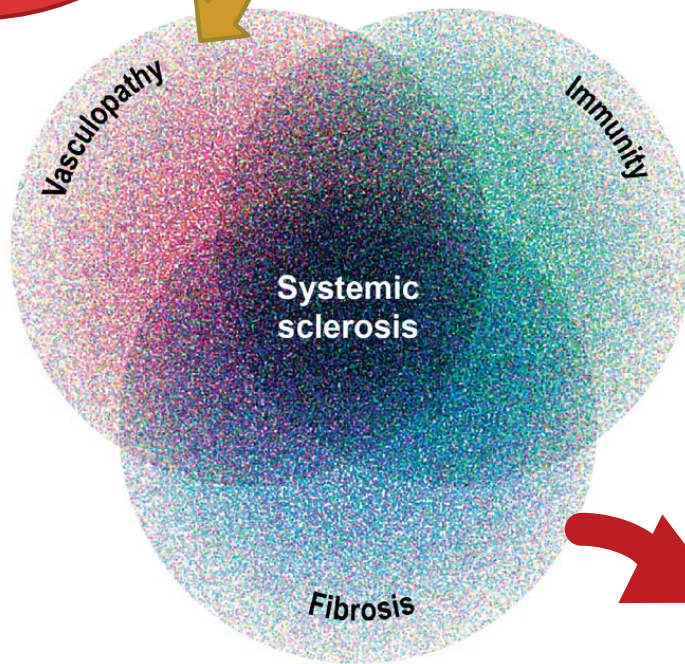
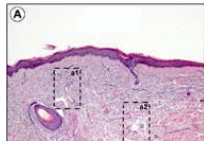
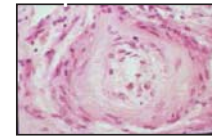


Many faces of SSc

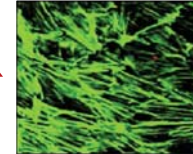


Environmental
trigger,
genetics/epige-
netics

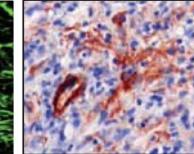
Pathogenesis of SSc



ECM



myofibroblasts





SSc—Epidemiology

- ◆ Peak age 30-50 yrs
- ◆ Female predominance of 3-5:1
- ◆ Rare disease
 - Estimated prevalence¹
 - US 276/10⁶
 - Europe 88-160/10⁶
 - Estimated incidence 18.7 cases/ million/ year².
 - With US population as ~ 328 million people, there are ~ 6,000 new SSc cases diagnosed each year
- ◆ Heterogeneous disease
- ◆ High morbidity and highest mortality among rheumatic diseases

1) Chiffow H Semin Arthritis Rheum 37:223-235²) Mayes et al. Arthritis Rheum 2001
3)Steen V Ann Rheum Dis 2007

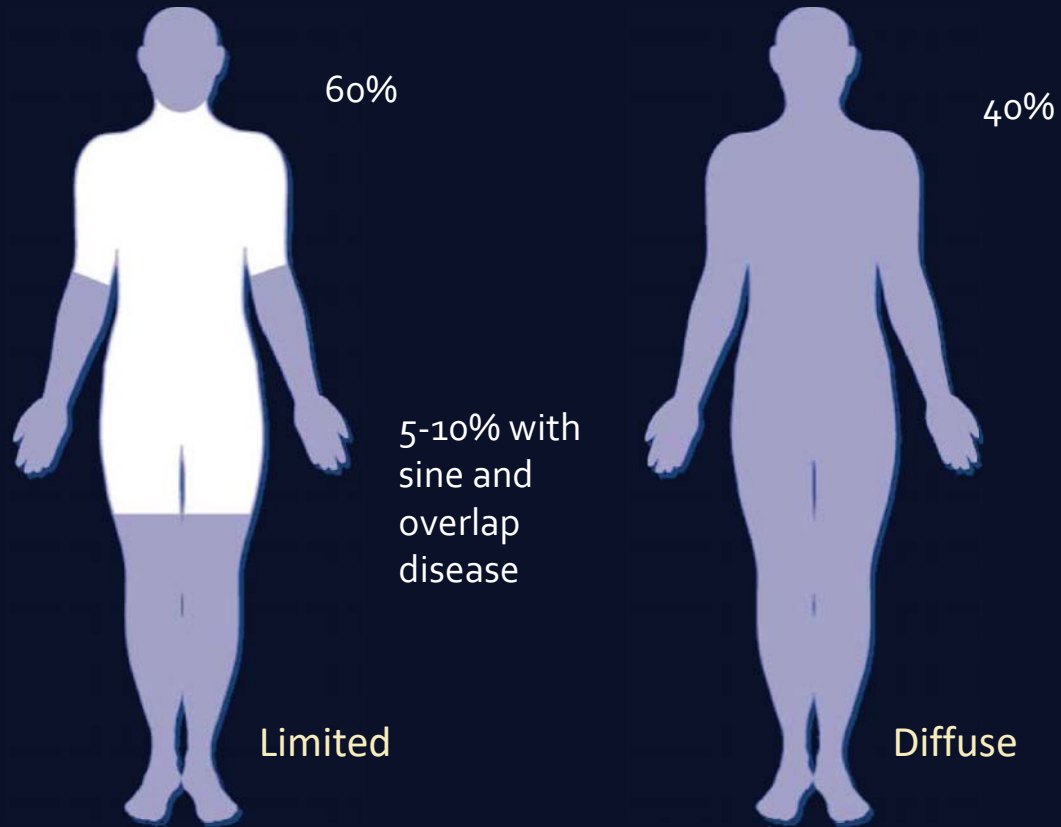


2013 ACR/EULAR Classification Criteria For SSc

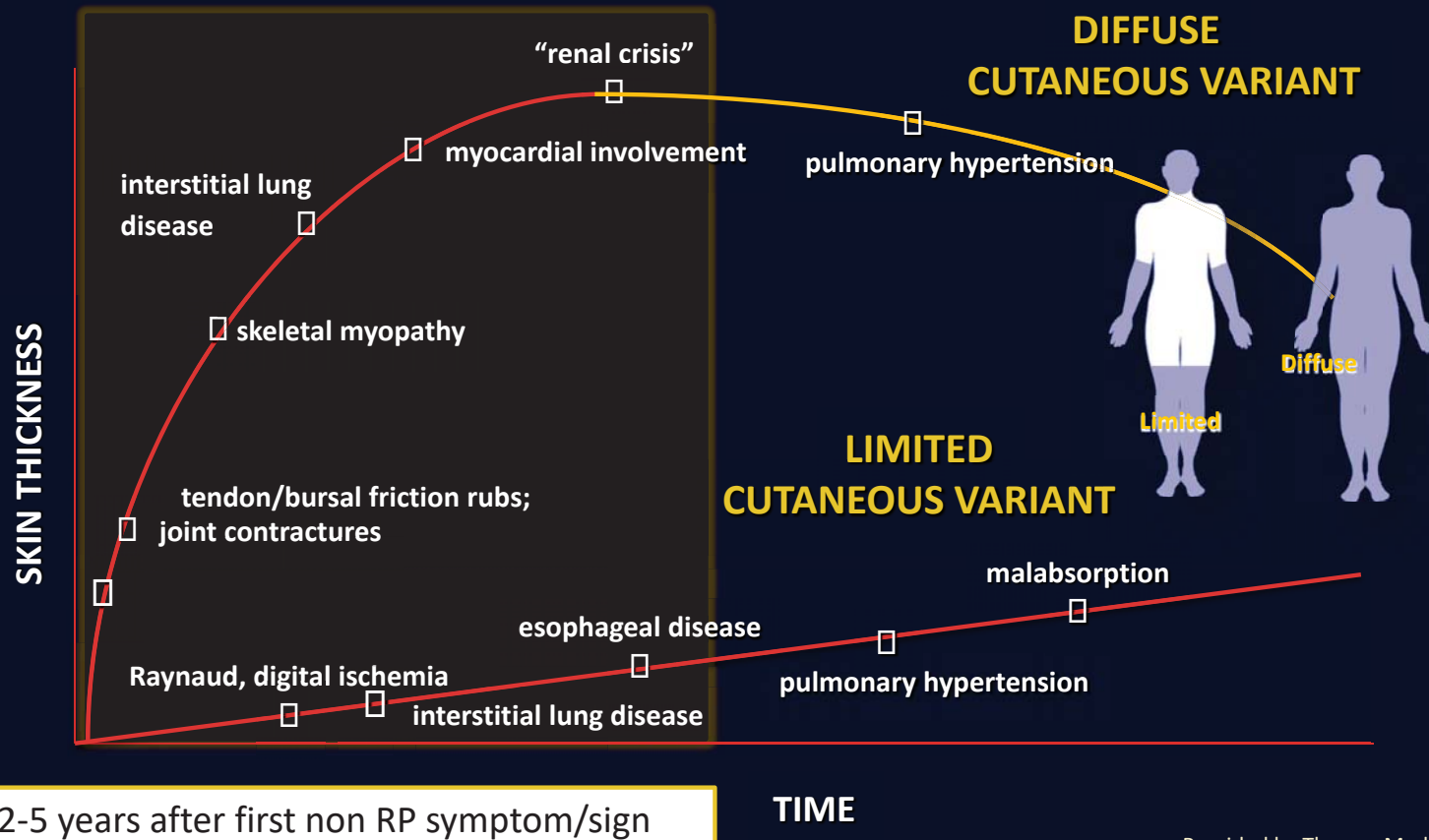
Criteria Domain	Sub-Criteria	Weight
Skin thickening of fingers (count higher of the 2)	Puffy fingers	2
	Whole finger, distal to metacarpophalangeal joint	4
Finger tip lesions (count higher of the 2)	Digital tip ulcers	2
	Pitting ulcers	3
Abnormal nailfold capillaries		2
Telangiectasia		2
Lung involvement	Pulmonary arterial hypertension/ interstitial lung disease	2
Raynaud's phenomenon		3
Scleroderma-associated antibodies	ACA, Anti-SCL-70, Anti-RNA polymerase III	3
TOTAL SCORE of 9 or more as classified as SSc		

Van den Hoogen F, Khanna D. Arth Rheum 2013

Clinical Subsets Limited and Diffuse SSc



Usual Timing of Problems in Systemic Sclerosis





Diffuse vs Limited Scleroderma - Distinguishing Features-

Diffuse


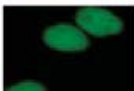
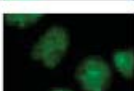


- ◆ Heart (severe in 10%)
- ◆ Kidney (severe in 15-20%)
- ◆ Pulmonary arterial hypertension (5-10%)
- ◆ Large joint contractures
- ◆ Reduced survival due to more severe internal organ involvement

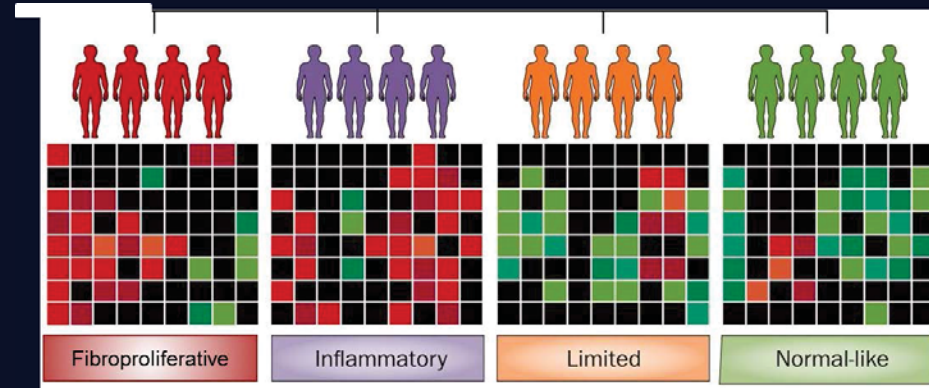
Limited

- ◆ Minimal heart
- ◆ Minimal kidney
- ◆ Pulmonary arterial hypertension (10-15%)
- ◆ Late: Primary biliary cirrhosis (<5%)

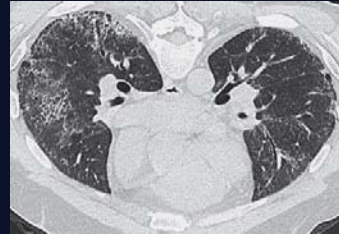
Autoantibody and Molecular Subsets



Target antigen	
	Centromere
	Topoisomerase-1 (Scl70)
	RNA polymerase III
	Fibrillarin (U3RNP)
	Pm-Scl



Clinician Viewpoint



- Vasodilators

Screen and Treat early

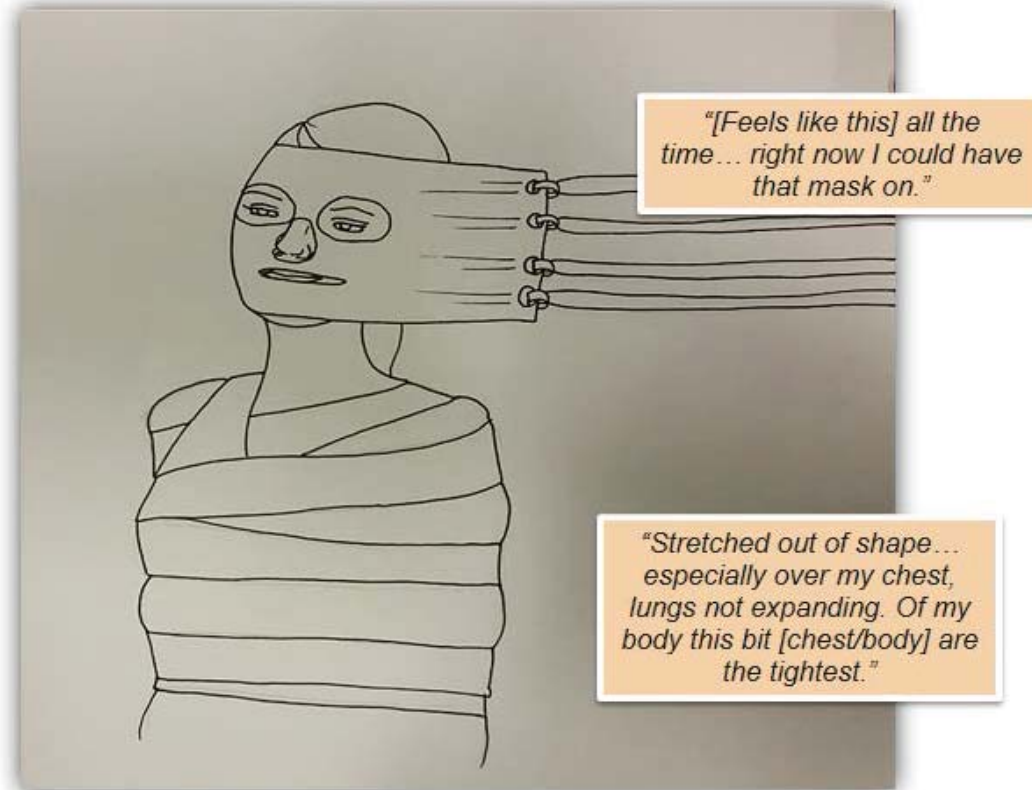
- Screen for early organ involvement
- Prevent internal organ involvement (if possible)
- Reduce disability
- Decrease progressive disease in the heart, lungs, and other organ


- Immunosuppressive medications
- Anti-fibrotic therapies
- Stem cell transplant



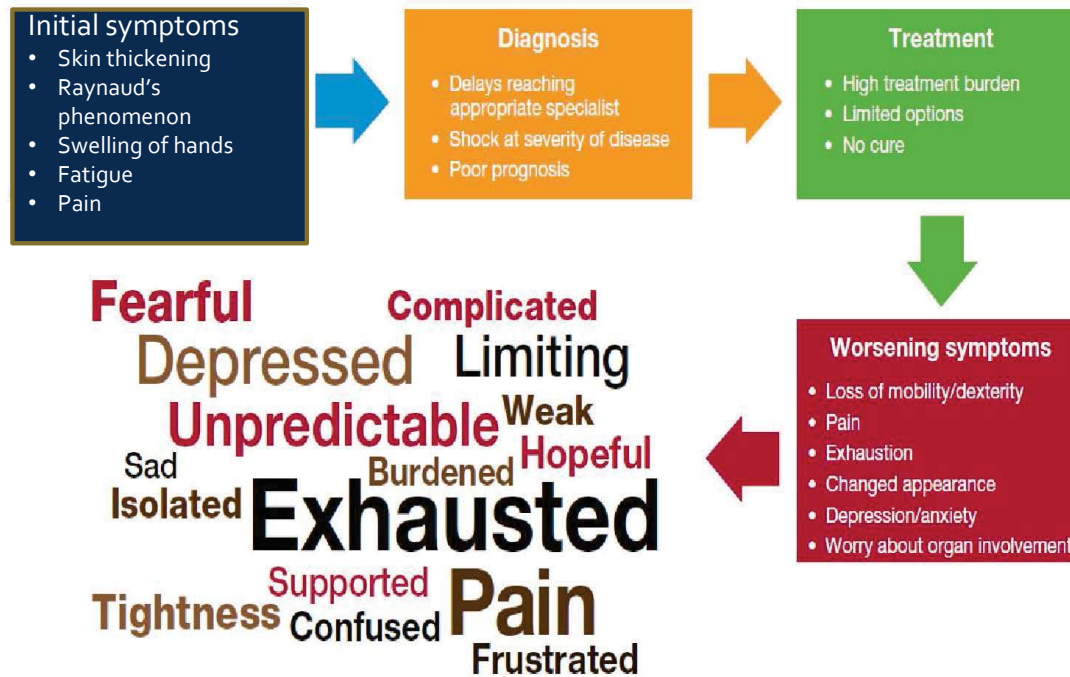
Patient Journey

Patient's own illustration depicting their experience of skin symptoms of SSc



 Patient verbatim from interview

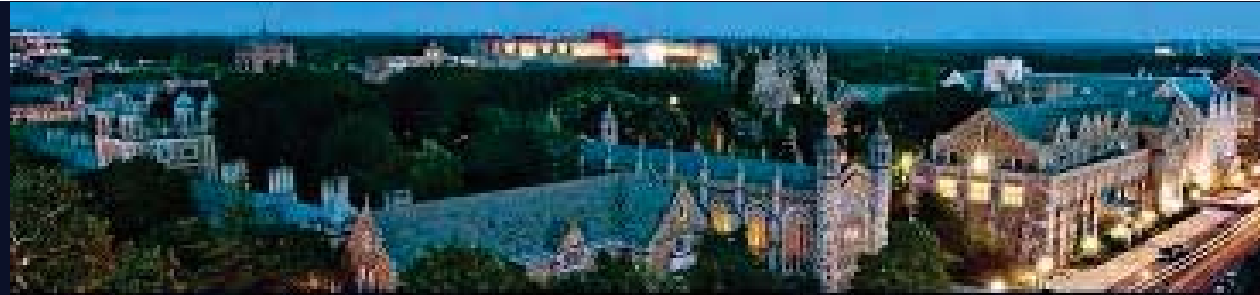
The patient journey with early SSc from initial symptoms to progressive disease





Recent trials-Lessons Learned

- ◆ Finding people with SSc for the trials
 - Difficult in an orphan disease
- ◆ Lack of expertise outside scleroderma community
- ◆ Marked heterogeneity in outcome measures
- ◆ Lack of patients' voice as primary approvable endpoints



M UNIVERSITY OF MICHIGAN



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and Human Services

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National Institute of
Arthritis and Musculoskeletal
and Skin Diseases

Overview of Discussion Format

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Director, Patient-Focused Drug Development Program

Office of Center Director

Center for Drug Evaluation and Research

U.S. Food and Drug Administration



Discussion Overview

Topic 1: Health Effects and Daily Impacts That Matter Most to Patients

- Health effects of systemic sclerosis that have the most significant impact on your daily life
- How your systemic sclerosis has changed over time
- What worries you most about your systemic sclerosis

Topic 2: Current Approaches to Treatment

- Your experience with treating your systemic sclerosis
- What approaches you use to treat your systemic sclerosis
- What you have found to be most effective in helping you treat your systemic sclerosis
- What factors you would consider when considering or seeking treatment



Discussion Format, continued

You will have a chance to answer polling questions

- Their purpose is to aid our discussion
- Participants can use the [mentimeter.com](https://www.mentimeter.com) link to answer polling questions
- Individuals or family members only, please

Participants can add comments through the webcast or by telephone

- Although they may not all be read or summarized today, your comments will be incorporated into our summary report

Send us your comments!

You can send us comments through the “public docket”

- The docket will be open until December 15, 2020
- Comments will be incorporated into our summary report
- Anyone is welcome to comment

Visit:

<https://www.regulations.gov/document?D=FDA-2020-N-1934-0001>

Or Search “patient-focused systemic sclerosis” on www.regulations.gov

And **Click Comment Now!**



The screenshot shows the regulations.gov website interface. At the top, there is a navigation bar with links for Home, Help, Resources, and Contact Us. A search bar contains the text "systemic sclerosis". The main content area is titled "Virtual Public Meeting on Patient-Focused Drug Development for Systemic Sclerosis". Below the title, it states "This Other document was issued by the Food and Drug Administration (FDA)" and provides a link to "Open Docket Folder". The page is divided into sections: "Content" (with a note to see attached files), "Attachments (1)" (listing the virtual public meeting), and a sidebar on the right. The sidebar includes a "Comment Now!" button, social media sharing options (Tweet, Share, Email), and document information such as the ID (FDA-2020-N-1934-0001), date posted (Sep 18, 2020), and submitter information (Federal Government - 00007). A red arrow points from the bottom left towards the "Comment Now!" button.



Discussion Ground Rules

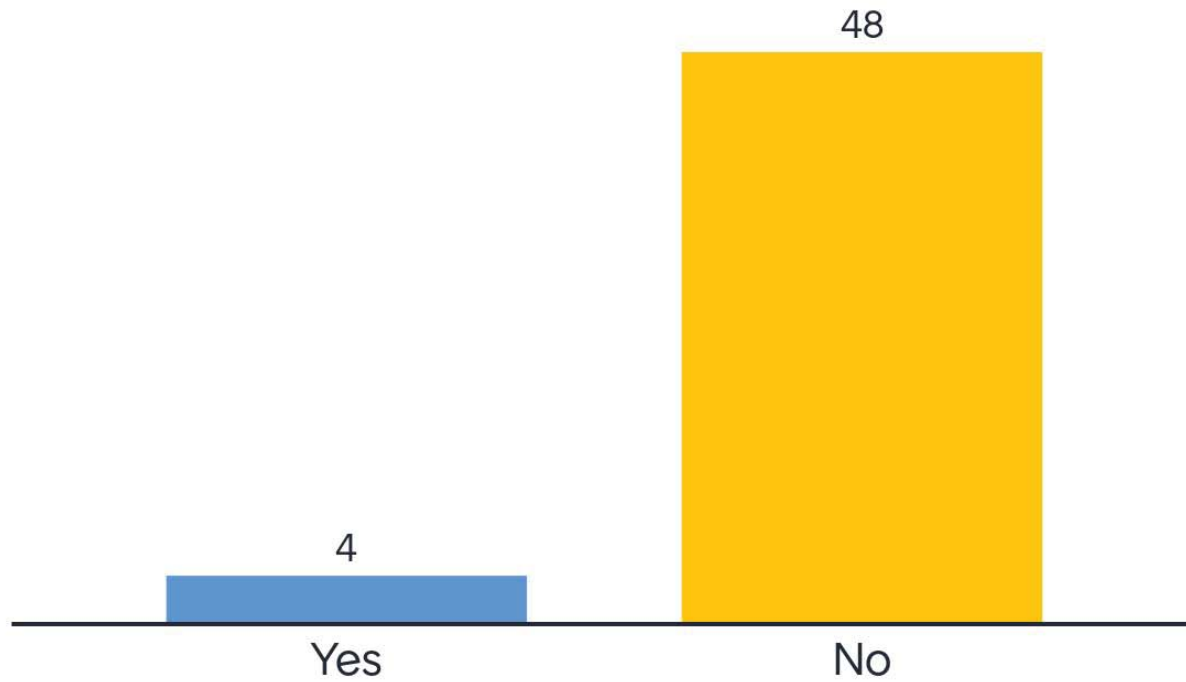
- We encourage all individuals and family members to contribute to the dialogue
- FDA is here to listen
- Discussion will focus on systemic sclerosis health effects and treatment
- The views expressed today are personal opinions
- Respect for one another is paramount

Do you live in the Washington, D.C. metropolitan area (including the Virginia and Maryland suburbs)?

- a. Yes
- b. No

Participation in the polling questions is voluntary. The results are used as a discussion aid only and should not be considered scientific data.

Do you live in the Washington, D.C. metropolitan area (including the Virginia and Maryland suburbs)?



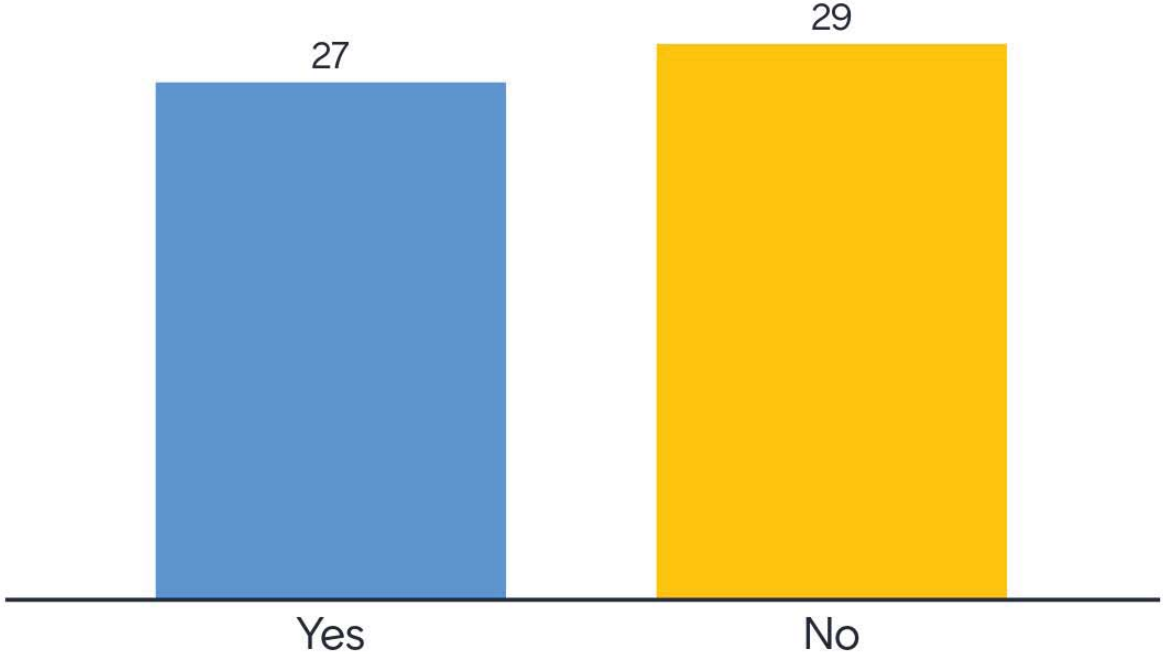


Have you or your loved one ever been diagnosed as having systemic sclerosis?

- a. Yes
- b. No

Participation in the polling questions is voluntary. The results are used as a discussion aid only and should not be considered scientific data.

Have you or your loved one ever been diagnosed as having systemic sclerosis?



We will ask that the remainder of the questions be answered by people who responded “yes” to Question 2. Please answer for the person diagnosed with systemic sclerosis.

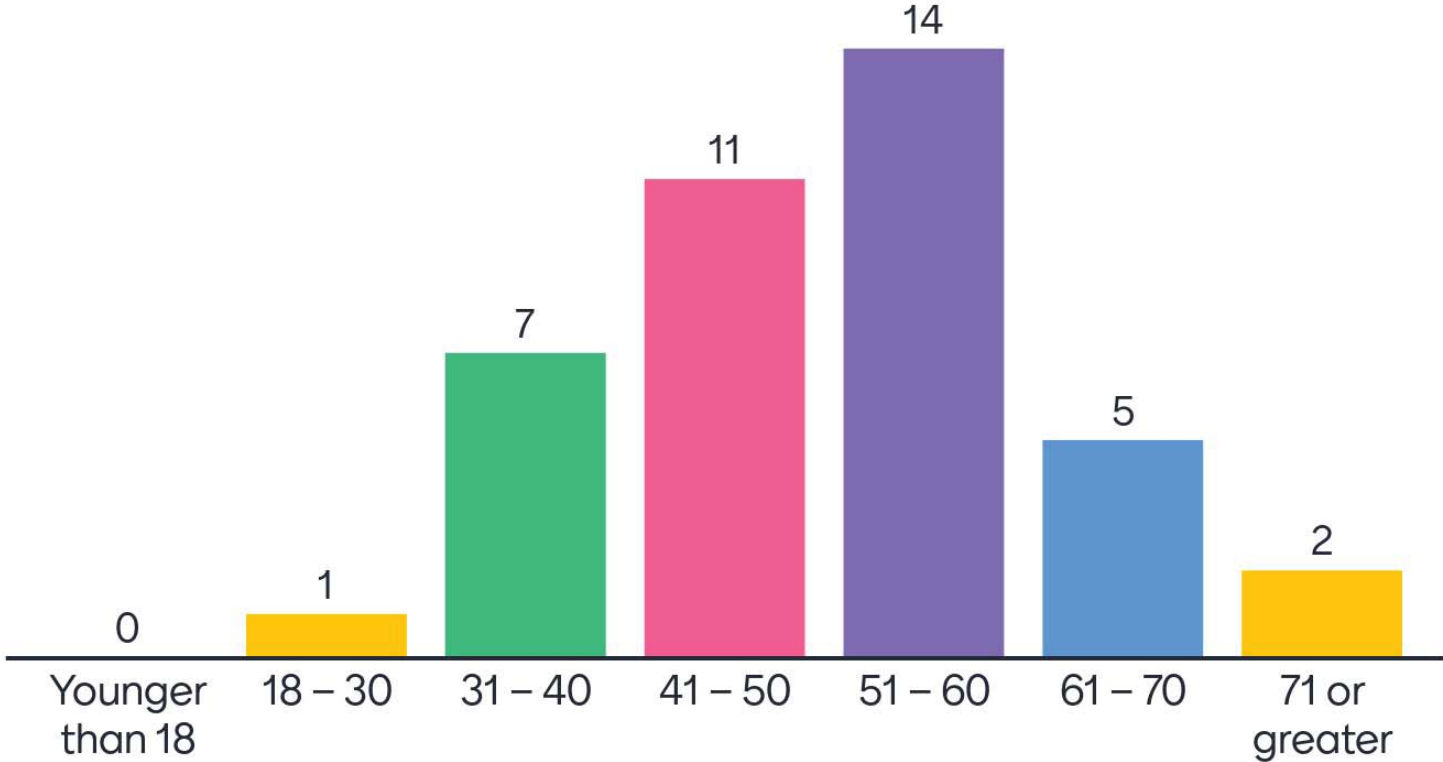


What is you/your loved one's age?

- a. Younger than 18
- b. 18 – 30
- c. 31 – 40
- d. 41 – 50
- e. 51 – 60
- f. 61 – 70
- g. 71 or greater

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What is your age?



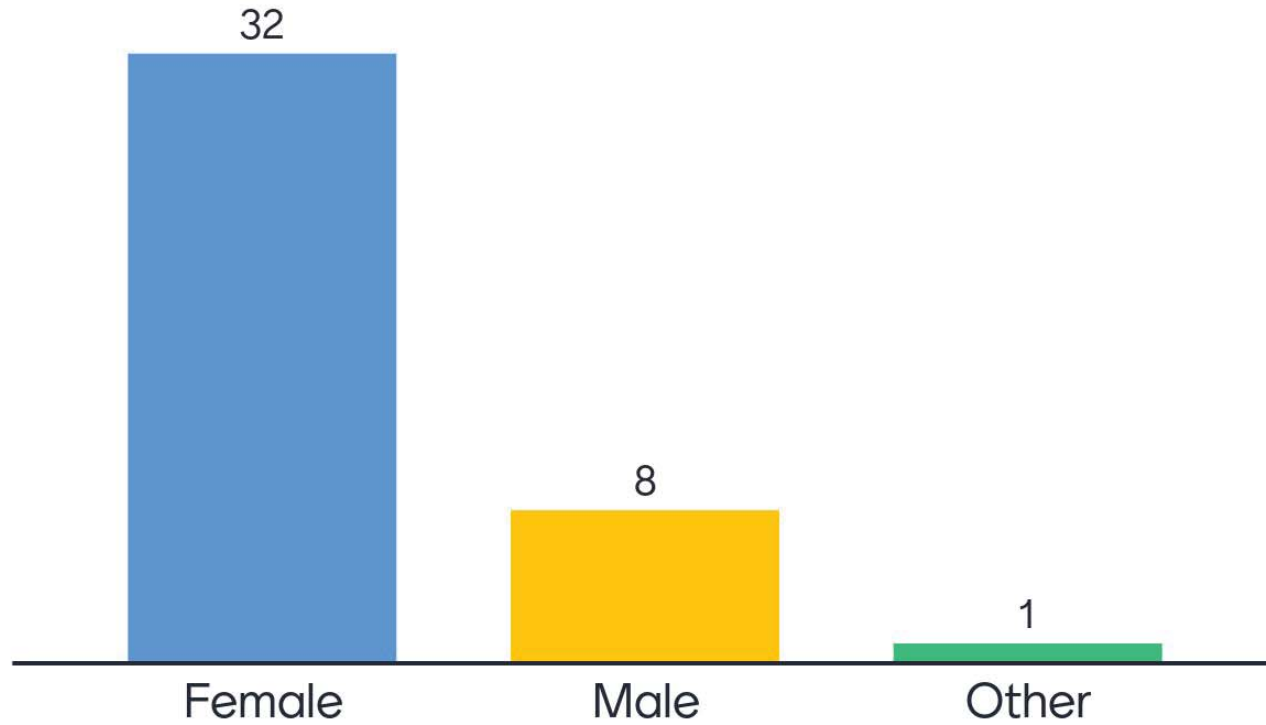


Do you/your loved one identify as:

- a. Female
- b. Male
- c. Other

Participation in the polling questions is voluntary. The results are used as a discussion aid only and should not be considered scientific data.

Do you identify as:



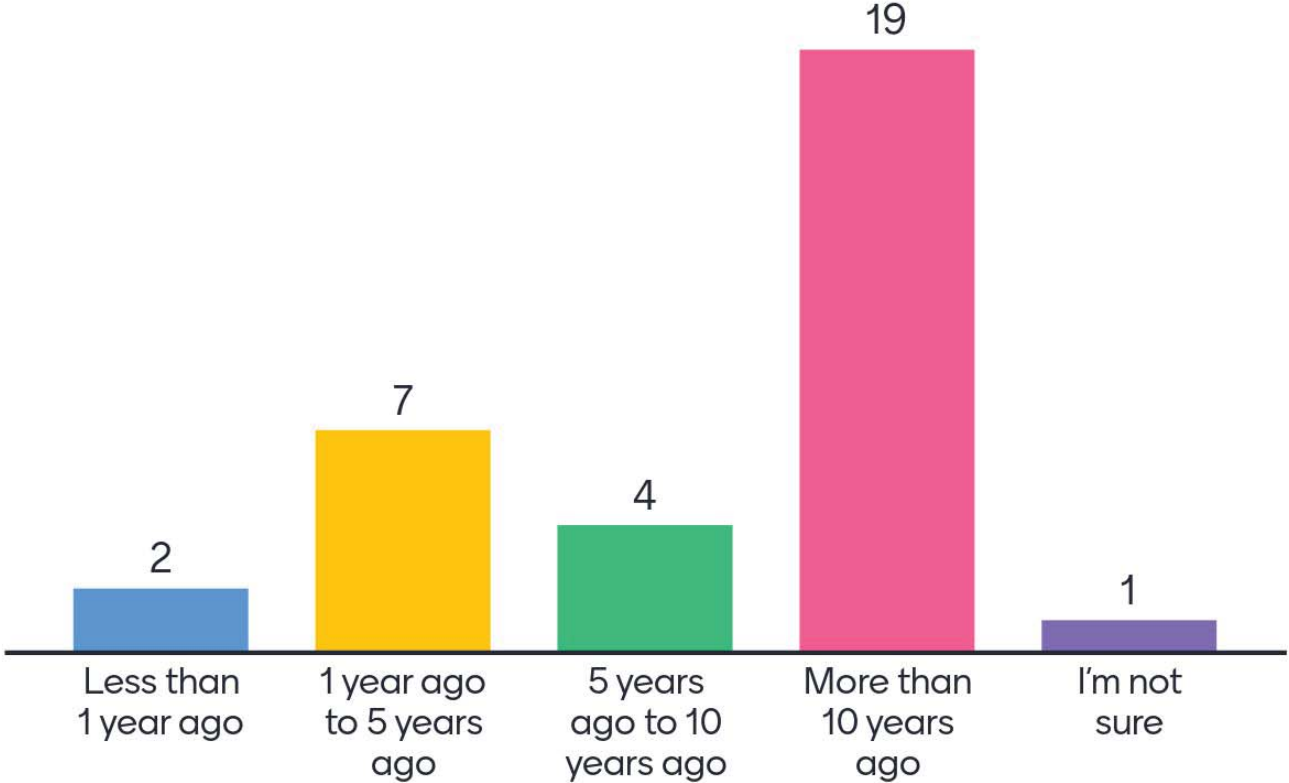


What is the length of time since your diagnosis?

- a. Less than 1 year ago
- b. 1 years ago to 5 years ago
- c. 5 years ago to 10 years ago
- d. More than 10 years ago
- e. I'm not sure

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What is the length of time since your diagnosis?

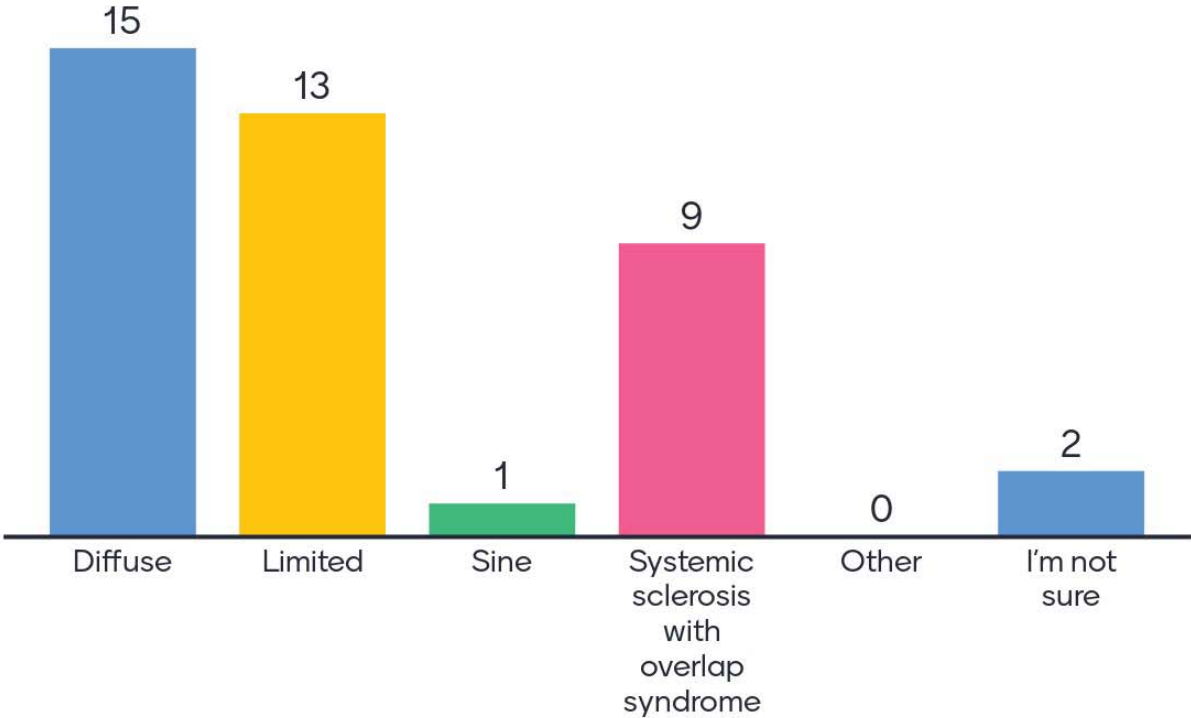


Which subtype of systemic sclerosis have you been diagnosed with? **Select all that apply.**

- a. Diffuse
- b. Limited
- c. Sine
- d. Systemic sclerosis with overlap syndrome
- e. Other
- f. I'm not sure

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Which subtype of systemic sclerosis have you been diagnosed with? Select all that apply.



Discussion Topic 1

**Health Effects and Daily Impacts of
Systemic Sclerosis**



Topic 1 Discussion Questions

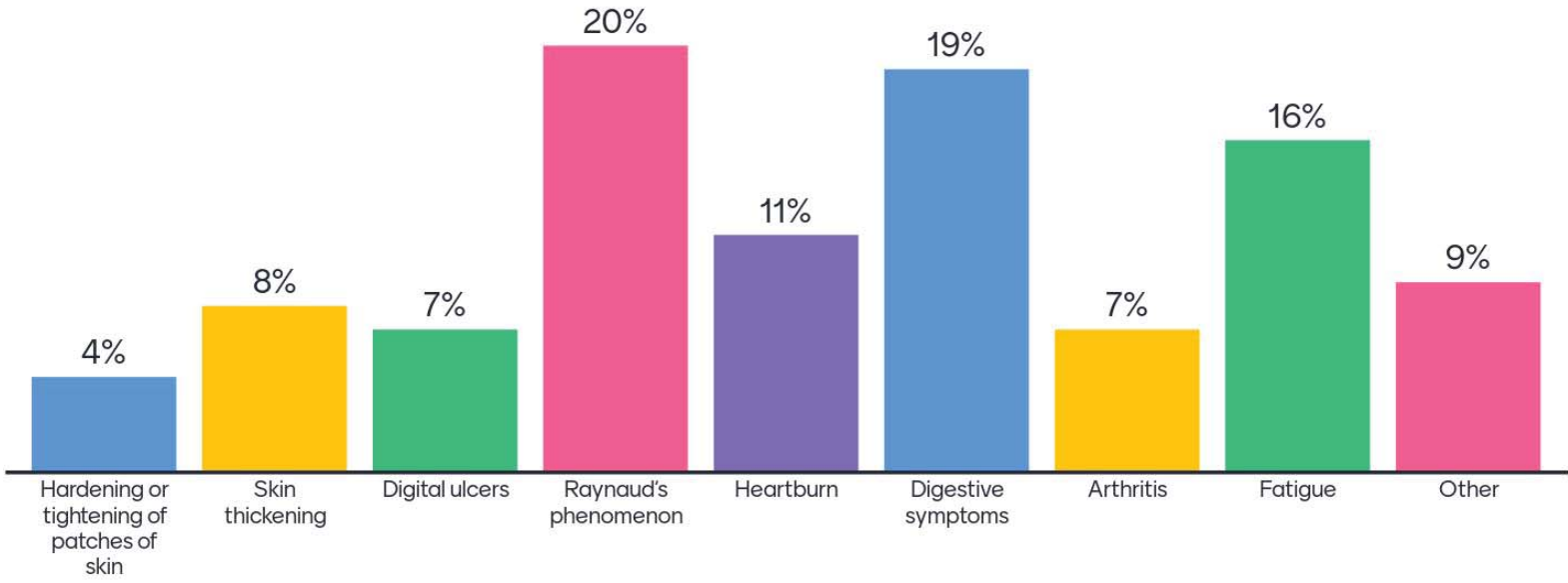
1. Which aspects of systemic sclerosis have the most significant impact on your life?
2. Are there specific activities that are important to you but that you cannot do at all or as fully as you would like because of your systemic sclerosis?
 - a. How does your systemic sclerosis and its impacts affect your daily life on the best days?
 - b. On the worst days?
3. How has your systemic sclerosis changed over time?
 - a. How long have you had symptoms and how long has it been since you were diagnosed with scleroderma?
 - b. Would you define your systemic sclerosis today as being well-managed?
4. What worries you most about your systemic sclerosis?
5. If you could change one thing about your systemic sclerosis, what would it be?

Of all the symptoms you have experienced because of your systemic sclerosis, which do you consider to have the most significant impact on your daily life? **Please choose up to three symptoms.**

- a. Hardening or tightening of patches of skin
- b. Skin thickening
- c. Digital ulcers
- d. Raynaud's phenomenon
- e. Heartburn
- f. Digestive symptoms
- g. Arthritis
- h. Fatigue
- i. Other

Participation in the polling questions is voluntary. The results are used as a discussion aid only and should not be considered scientific data.

Of all the symptoms you experienced because of your systemic sclerosis, which have the most significant impact on your daily life?



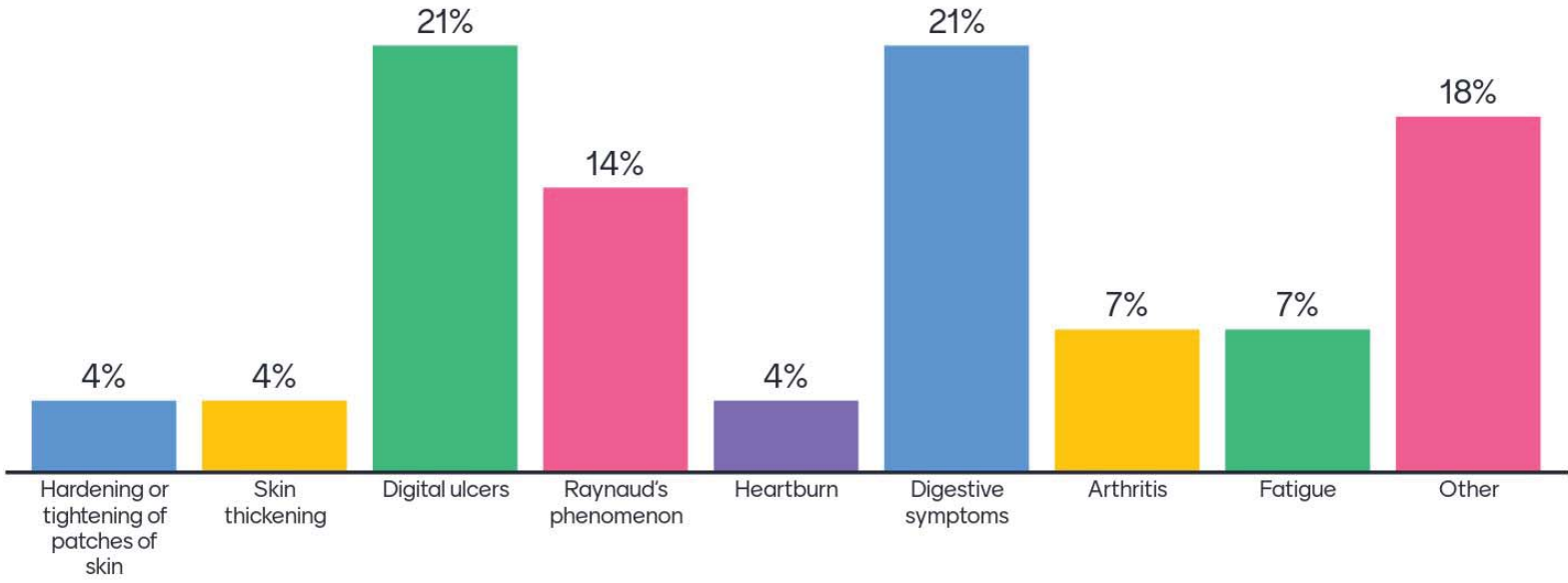


Of all the symptoms you have experienced because of your systemic sclerosis, which **single symptom** do you consider to be most bothersome?

- a. Hardening or tightening of patches of skin
- b. Skin thickening
- c. Digital ulcers
- d. Raynaud's phenomenon
- e. Heartburn
- f. Digestive symptoms
- g. Arthritis
- h. Fatigue
- i. Other

Participation in the polling questions is voluntary. The results are used as a discussion aid only and should not be considered scientific data.

Of all the symptoms you have experienced because of your systemic sclerosis, which single symptom do you consider to be most bothersome?

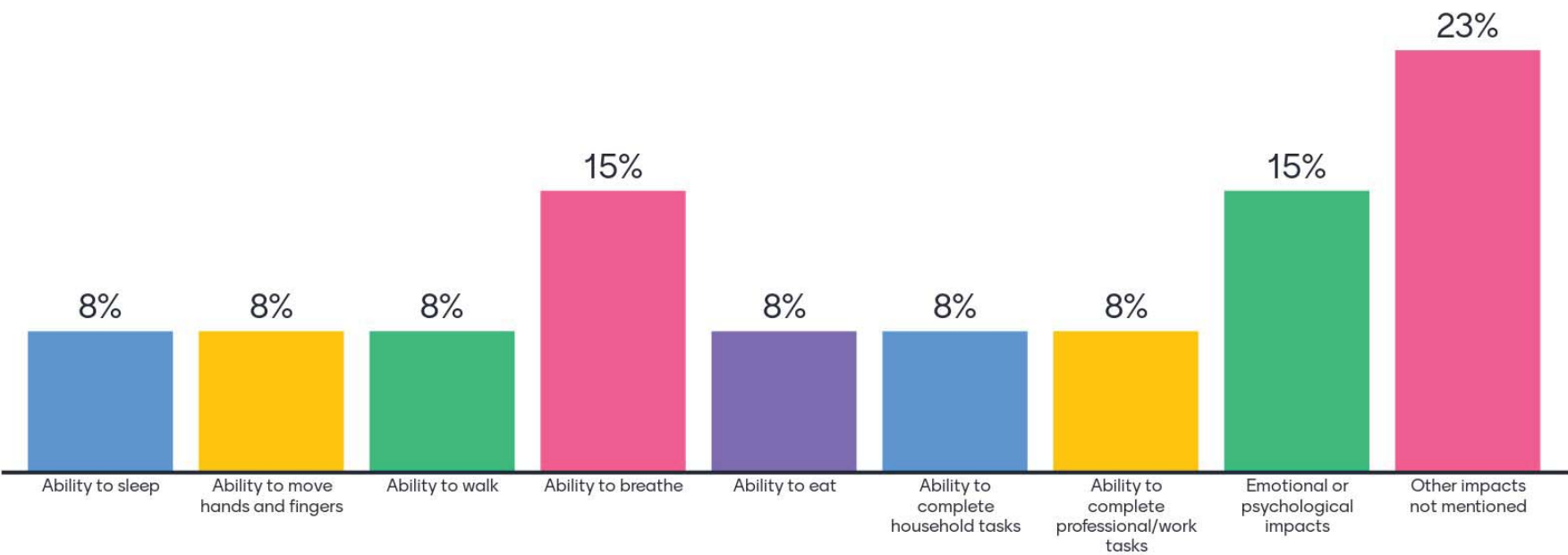


Which aspects of daily functioning or movement are most affected by your systemic sclerosis? **Please choose up to three answers.**

- a. Ability to sleep
- b. Ability to move hands and fingers
- c. Ability to walk
- d. Ability to breathe
- e. Ability to eat
- f. Ability to complete household tasks
- g. Ability to complete professional/work tasks
- h. Emotional or psychological impacts
- i. Other impacts not mentioned

Participation in the polling questions is voluntary. The results are used as a discussion aid only and should not be considered scientific data.

Which aspects of daily functioning or movement are most affected by your systemic sclerosis?



Send us your comments!

You can send us comments through the “public docket”

- The docket will be open until December 15, 2020
- Comments will be incorporated into our summary report
- Anyone is welcome to comment

Visit:

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Or Search “patient-focused systemic sclerosis” on www.regulations.gov

And **Click Comment Now!**



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Discussion Topic 2
Current Approaches to Treatment



Topic 2 Discussion Questions

1. What are you currently doing to help treat your systemic sclerosis?
 - a. How has your treatment regimen changed over time, and why?
 - b. What symptom would you most like to be improved or resolved by treatment?
2. How well does your current treatment regimen treat the most significant aspects of your systemic sclerosis?
3. What are the most significant downsides to your current treatments, and how do they affect your daily life?
4. Aside from a complete cure for your systemic sclerosis, what specific things would you look for in an ideal treatment for your systemic sclerosis?
5. What factors do you consider when making decisions about selecting a course of treatment?
6. Efficacy and safety are important for any treatment. When you think about a treatment for your disease:
 - a. Does it make a difference whether:
 - i. the product might improve your most bothersome symptoms or
 - ii. whether the product might preserve organ function, or
 - iii. would you consider improvement in either of those areas equally worth the same level of risk?
 - b. Does your acceptance of potential safety risks go up with the potential effectiveness of a product?
 - i. What degree of risk are you willing to accept for an effective treatment? Risks associated may range from mild to severe and life-long (such as life-long immunosuppression, risk of potential cancer associated with treatment).
 - ii. If you had to choose between two products, which would you prefer? A very safe product that works somewhat, or a less safe product that works really well?

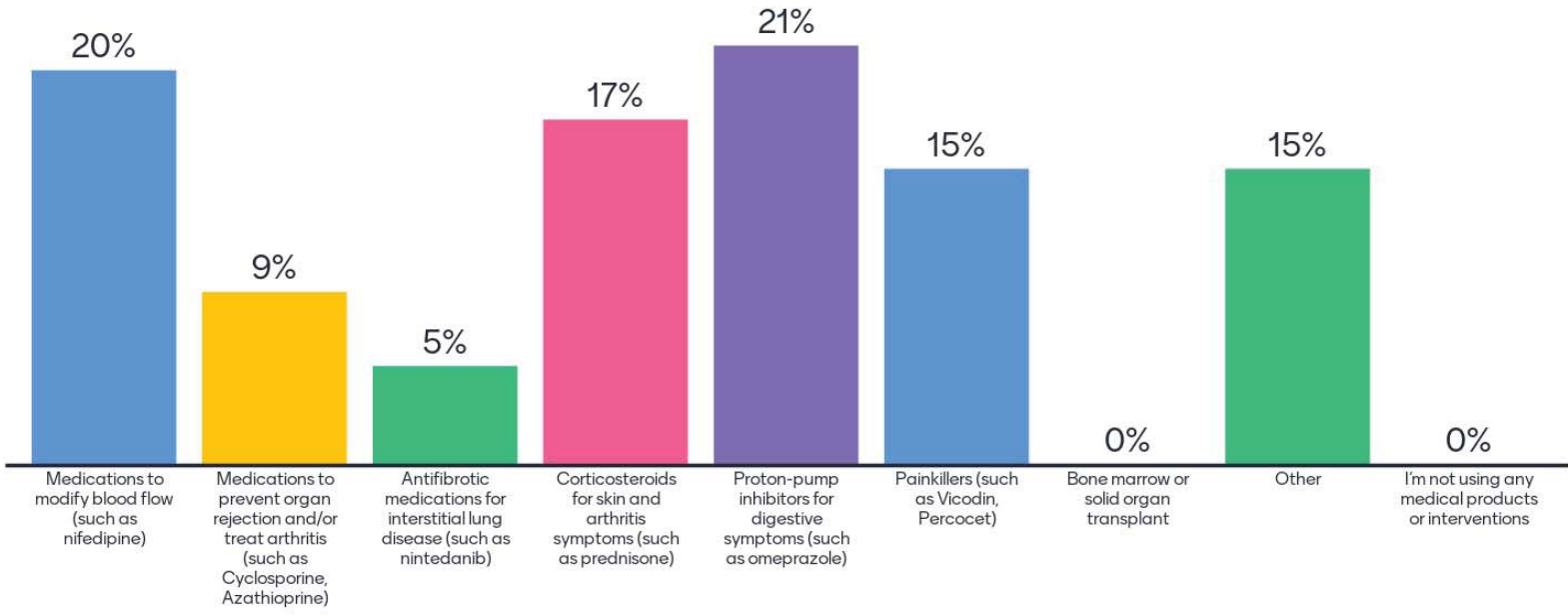


Have you ever used any of the following interventions or medical products (drug therapies or medical devices) to treat your systemic sclerosis? **Check all that apply.**

- a. Medications to modify blood flow (such as nifedipine)
- b. Medications to prevent organ rejection and/or treat arthritis (such as Cyclosporine, Azathioprine)
- c. Antifibrotic medications for interstitial lung disease (such as nintedanib)
- d. Corticosteroids for skin and arthritis symptoms (such as prednisone)
- e. Proton-pump inhibitors for digestive symptoms (such as omeprazole)
- f. Painkillers (such as Vicodin, Percocet, OxyContin)
- g. Bone marrow or solid organ transplant
- h. Other
- i. I'm not using any medical products or interventions

Participation in the polling questions is voluntary. The results are used as a discussion aid only and should not be considered scientific data.

Have you ever used any of the following interventions or medical products (drug therapies or medical devices) to treat your systemic sclerosis?



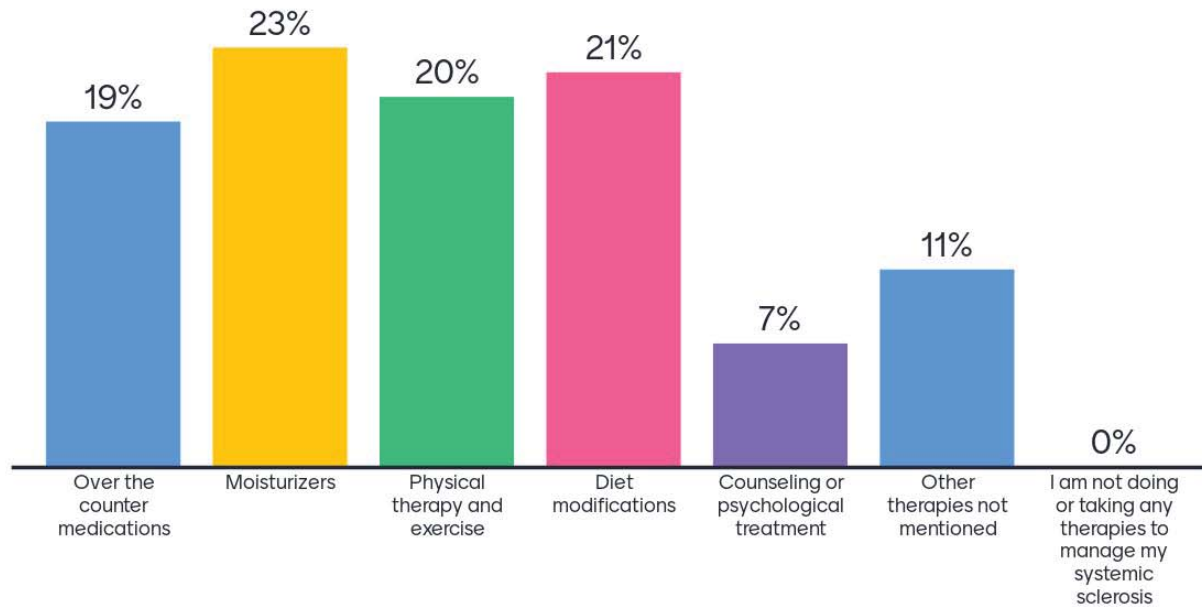


Besides the medical products or interventions mentioned previously, what else are you doing to manage your systemic sclerosis? **Check all that apply.**

- a. Over the counter medications
- b. Moisturizers
- c. Physical therapy and exercise
- d. Diet modifications
- e. Counseling or psychological treatment
- f. Other therapies not mentioned
- g. I am not doing or taking any therapies to manage my systemic sclerosis

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Besides the medical products or interventions mentioned previously, what else are you doing to manage your systemic sclerosis?



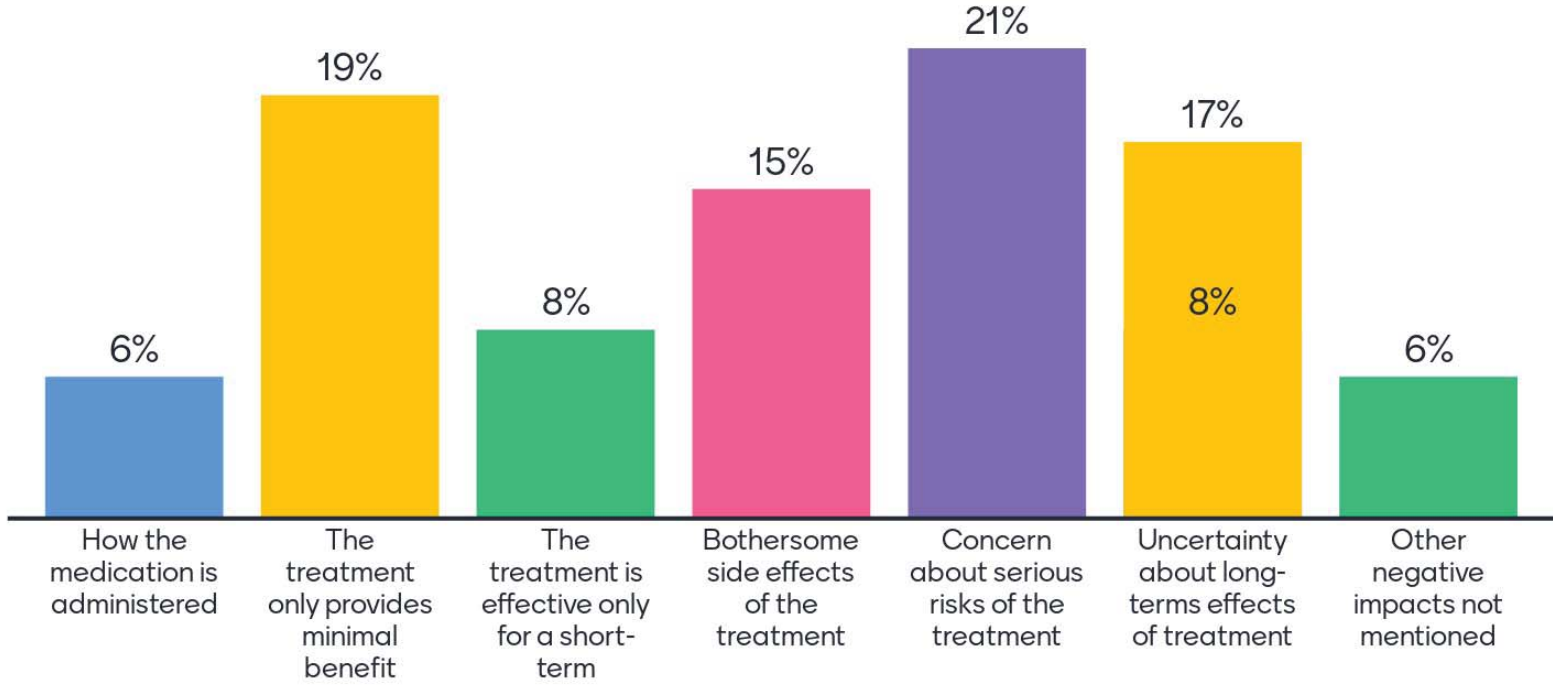


For the medical products or interventions you use, what about the treatment bothers you the most? **Please choose up to three answers.**

- a. How the medication is administered
- b. The treatment only provides minimal benefit
- c. The treatment is effective only for a short-term
- d. Bothersome side effects of the treatment
- e. Concern about serious risks of the treatment
- f. Uncertainty about long-term effects of treatment
- g. Difficulty in accessing treatment
- h. Other negative impacts not mentioned

Participation in the polling questions is voluntary. The results are used as a discussion aid only and should not be considered scientific data.

For the medical products or interventions you use, what about the treatment bothers you the most?



Imagine that a new self-injectable medication indicated to treat systemic sclerosis has recently been approved by FDA. Your doctor believes that you may be a good candidate for this medication.

In the clinical trials that were conducted, the medication was shown to reduce the symptom that most significantly impacts your daily life when injected once weekly.

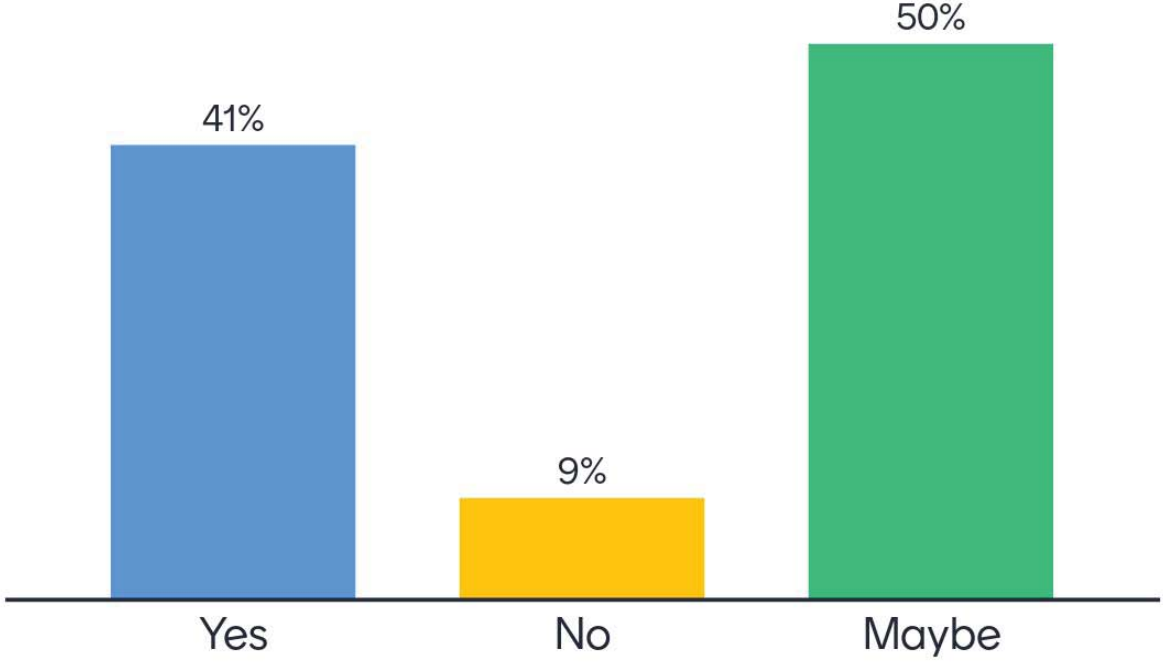
More common side effects of this therapy may include headache, diarrhea, nausea, stomach or abdominal pain, and weight loss. Rarer but more serious side effects may include infection, seizures, trouble breathing, fever, general feeling of discomfort or illness, and risk of bleeding.

Given the risks and benefits, would you take this medication?

- a. Yes
- b. No
- c. Maybe

Participation in the polling questions is voluntary. The results are used as a discussion aid only and should not be considered scientific data.

Given the risks and benefits, would you take this medication?



Send us your comments!

You can send us comments through the “public docket”


- The docket will be open until December 15, 2020
- Comments will be incorporated into our summary report
- Anyone is welcome to comment

Visit:

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The screenshot shows the regulations.gov website interface. The main heading is "Virtual Public Meeting on Patient-Focused Drug Development for Systemic Sclerosis". Below the heading, there is a "Content" section with a link to "See attached file(s)" and an "Attachments (1)" section with a link to "View Attachment". On the right side, there is a "Document Information" section with fields for "Date Posted" (Sep 18, 2020) and "Category" (Federal Government - 00007). A "Comments" section is also visible at the bottom right. A prominent red arrow points from the text "Click Comment Now!" to a "Comment Now!" button located in the top right corner of the document details area.

Closing Remarks

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