Through the patient lens: the diagnostic journey from connective tissue disease to pulmonary arterial hypertension

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Introduction

- Connective tissue diseases (CTDs) such as lupus, systemic sclerosis, and mixed CTD are a diverse group of systemic diseases associated with a risk of developing several cardiopulmonary comorbidities, including pulmonary arterial hypertension (PAH)[1]
- PAH associated with CTD (PAH-CTD) accounts for ~25% of all PAH cases[2]
  - The highest rates of PAH-CTD are seen in individuals with systemic sclerosis (scleroderma, SSc), of whom up to ~15% will develop PAH[1]
  - Guidelines advocate for annual PAH screening among those with SSc;[2] however, there are no formal screening guidelines for other types of CTD
- Since the risk of morbidity and mortality is high with PAH-CTD, early diagnosis and referral to PAH specialists is important to improve survival; yet diagnosis is often delayed[1]
- PAH can be hard to recognize as people may have a more sedentary lifestyle due to their underlying CTD and may not notice shortness of breath. In addition, people with PAH-CTD often have comorbidities such as interstitial lung disease and left-heart disease
- The PAH-CTD patient journey can vary according to the specific type of CTD and there is potential for the diagnosis of two simultaneous rare diseases like SSc and PAH to be missed, since these diagnoses rely on coordination of care across a variety of specialist settings

Objective

- To understand from the patient perspective which providers were involved in each stage of their diagnostic journey, education they received from their provider about PAH risk, and how patients feel about their diagnoses in order to gain insight into what support non-PAH specialist providers may need to successfully identify and manage people with PAH-CTD

Methods

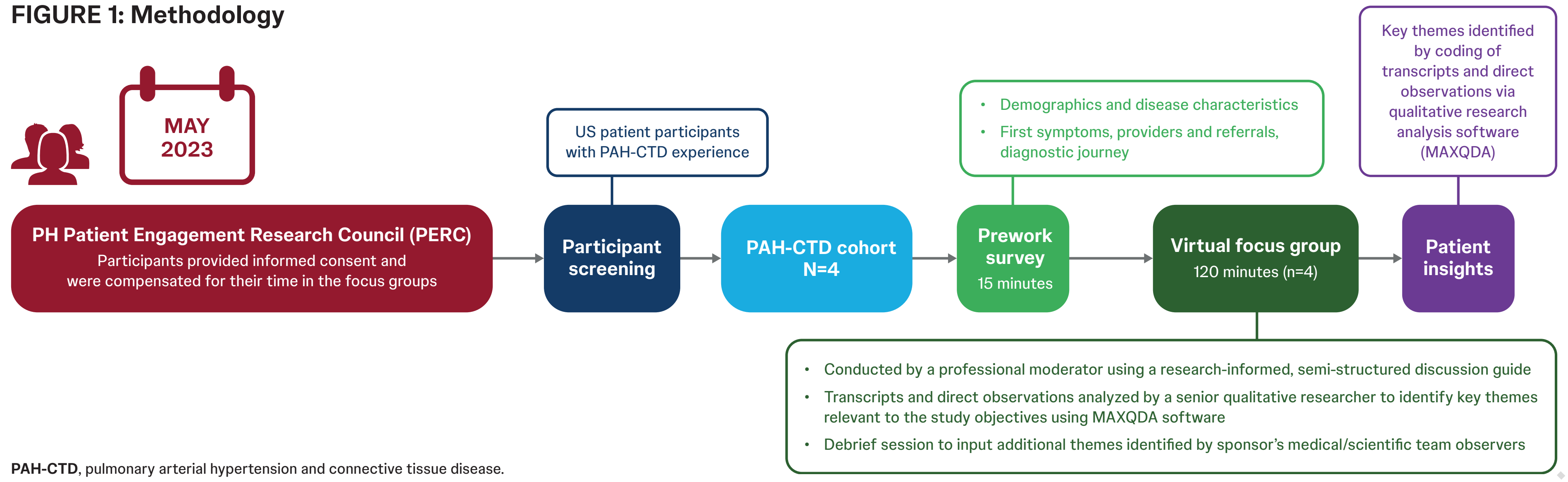
- Individuals were invited to participate via the sponsor's existing pulmonary hypertension (PH) Patient Engagement Research Council (PERC) program
  - The PERC comprises contracted patient advisors residing in the United States with a shared self-reported diagnosis of PH
  - Participants are disease-aware and provide insights into their experiences through specific, structured activities
- In May 2023, 4 individuals with PAH-CTD joined a 2-hour virtual focus group moderated by a patient experience research specialist with live, active input from the sponsor's medical/scientific team (**Figure 1**)
- Eligibility criteria are listed in **Table 1**

TABLE 1: Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
• Diagnosed with PAH-CTD in the past 5 years • PAH functional class I-III	• PAH functional class IV • Diagnosed with sarcoidosis, pulmonary embolism, chronic thromboembolic pulmonary hypertension, interstitial lung disease, idiopathic pulmonary fibrosis, or pulmonary vascular occlusive disease • Diagnosed with PAH-CTD over 5 years previously

PAH-CTD, pulmonary arterial hypertension and connective tissue disease.

FIGURE 1: Methodology



MAY 2023

PH Patient Engagement Research Council (PERC)
Participants provided informed consent and were compensated for their time in the focus groups

US patient participants with PAH-CTD experience

Participant screening

PAH-CTD cohort N=4

- Demographics and disease characteristics
- First symptoms, providers and referrals, diagnostic journey

Prework survey
15 minutes

Virtual focus group
120 minutes (n=4)

- Conducted by a professional moderator using a research-informed, semi-structured discussion guide
- Transcripts and direct observations analyzed by a senior qualitative researcher to identify key themes relevant to the study objectives using MAXQDA software
- Debrief session to input additional themes identified by sponsor's medical/scientific team observers

Key themes identified by coding of transcripts and direct observations via qualitative research analysis software (MAXQDA)

Patient insights

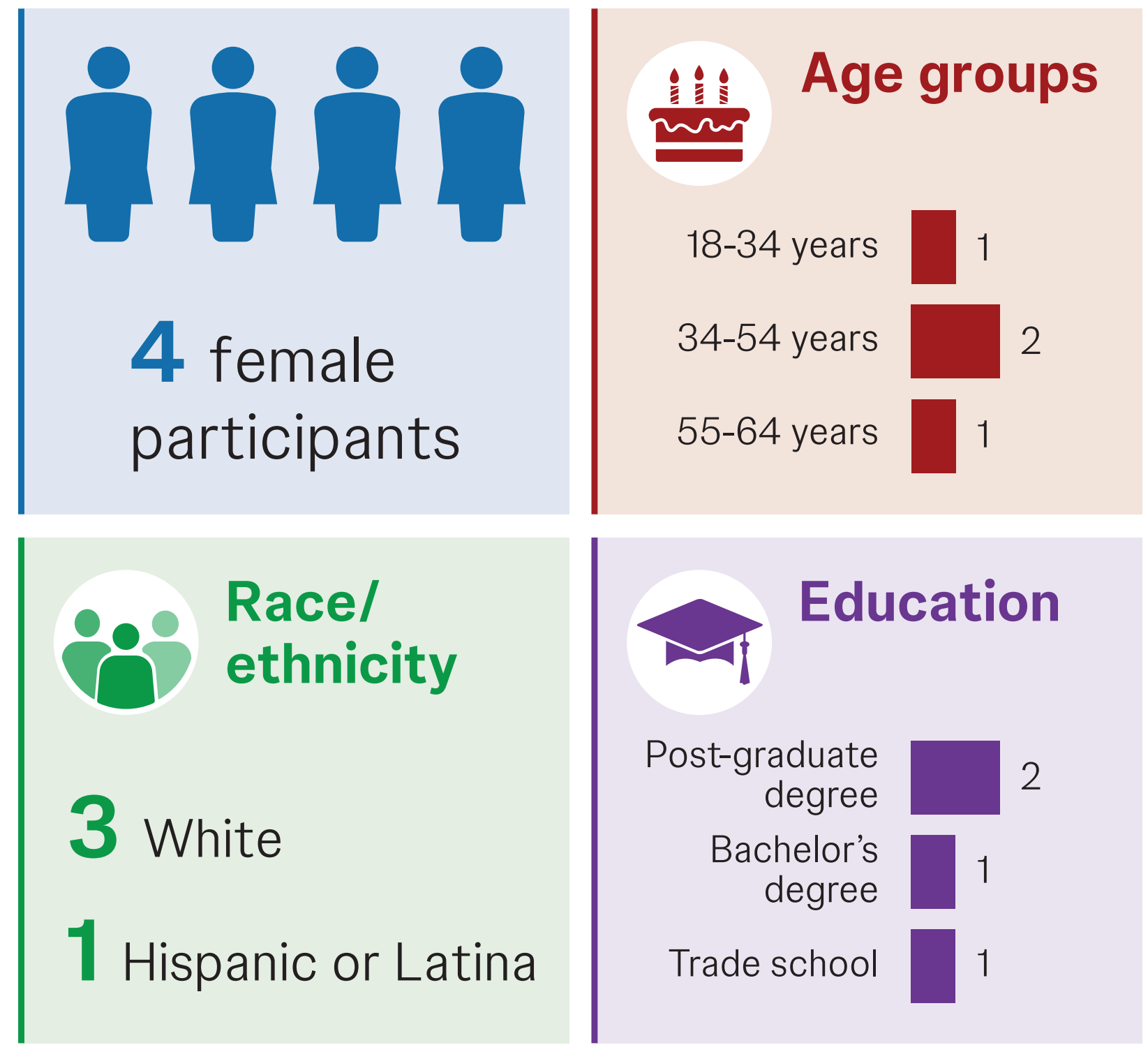
PAH-CTD, pulmonary arterial hypertension and connective tissue disease.

Results

Participant characteristics

- Focus group participants were all female, aged between 29 and 61 years old, and well educated (**Figure 2**)

FIGURE 2: Focus group participant demographics



4 female participants

Age groups

18-34 years	1
34-54 years	2
55-64 years	1

Race/ ethnicity

3 White

1 Hispanic or Latina

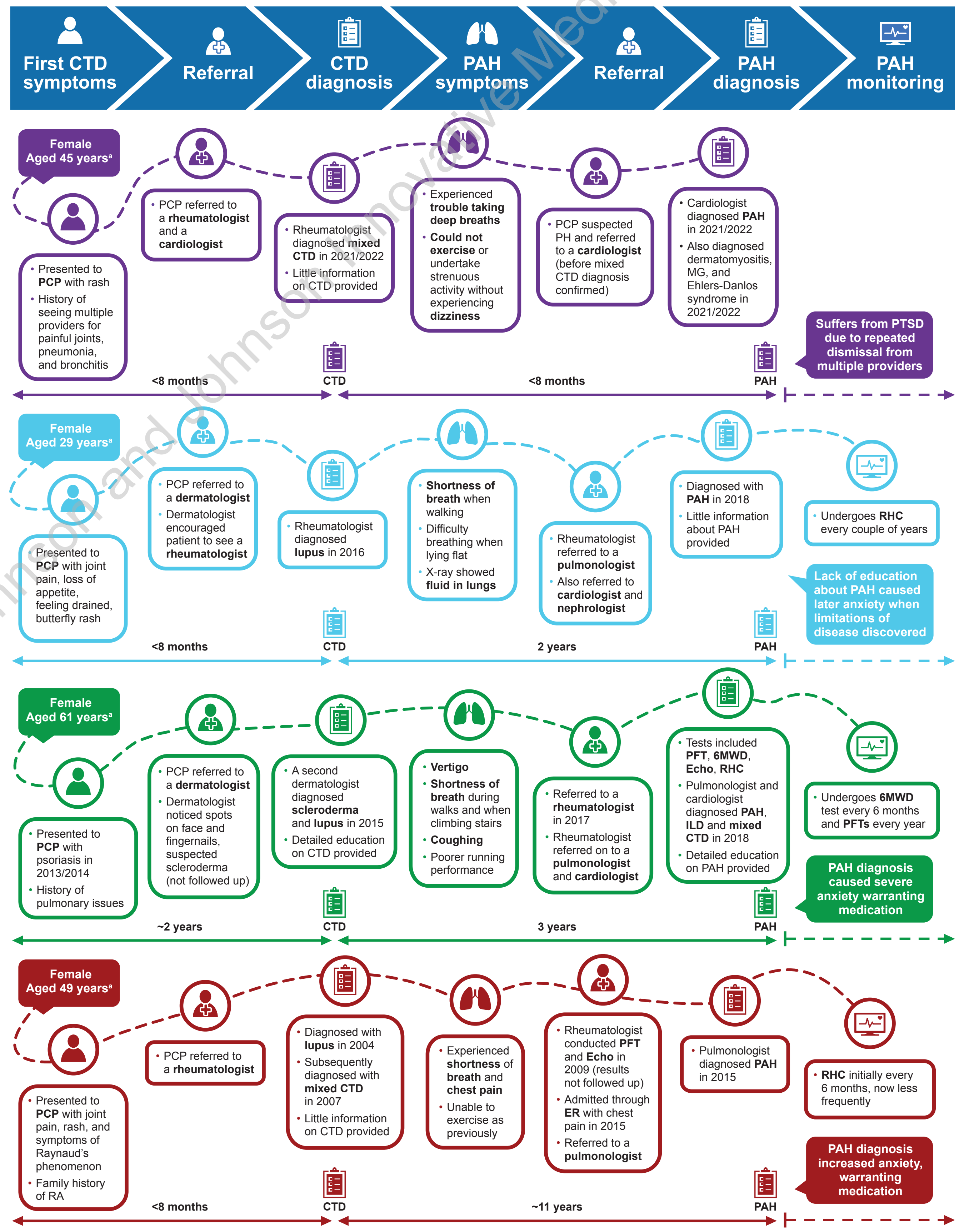
Education

Post-graduate degree	2
Bachelor's degree	1
Trade school	1

Diagnostic journey

- All 4 participants described rash among their first symptoms, alongside joint pain (n=3) and physical fatigue (n=3) (**Figure 3**)
- Worsening symptoms prompted the patients to seek help from their primary care provider (PCP); their satisfaction with this interaction varied, depending on their PCP's willingness to listen (**Figure 4**)
- Within 6 months of experiencing their first symptoms, 3 participants referred to a rheumatologist were diagnosed with CTD (1 with lupus and 2 with mixed CTD); the remaining participant, who had been referred to a dermatologist, took ~2 years to be diagnosed with SSc and lupus
- Some participants received extensive education about CTD, while others reported receiving little to no education and instead relied on their own research to better understand what their diagnosis meant for them
- Only 1 participant was informed about the increased risk of PAH at the time of her CTD diagnosis; the others experienced between 2 to ~11 years between CTD and PAH diagnoses, leaving them at risk for symptom worsening and PAH progression

FIGURE 3: Focus group participant demographics



Female Aged 45 years[a]

- Presented to **PCP** with rash
- History of seeing multiple providers for painful joints, pneumonia, and bronchitis

- PCP referred to a **rheumatologist** and a **cardiologist**

- Rheumatologist diagnosed **mixed CTD** in 2021/2022
- Little information on CTD provided

- Experienced **trouble taking deep breaths**
- **Could not exercise** or undertake strenuous activity without experiencing **dizziness**

- PCP suspected PH and referred to a **cardiologist** (before mixed CTD diagnosis confirmed)

- Cardiologist diagnosed **PAH** in 2021/2022
- Also diagnosed dermatomyositis, MG, and Ehlers-Danlos syndrome in 2021/2022

Suffers from PTSD due to repeated dismissal from multiple providers

Female Aged 29 years[a]

- Presented to **PCP** with joint pain, loss of appetite, feeling drained, butterfly rash

- PCP referred to a **dermatologist**
- Dermatologist encouraged patient to see a **rheumatologist**

- Rheumatologist diagnosed **lupus** in 2016

- **Shortness of breath** when walking
- Difficulty breathing when lying flat
- X-ray showed **fluid in lungs**

- Rheumatologist referred to a **pulmonologist**
- Also referred to **cardiologist** and **nephrologist**

- Diagnosed with **PAH** in 2018
- Little information about PAH provided

- Undergoes **RHC** every couple of years

Lack of education about PAH caused later anxiety when limitations of disease discovered

Female Aged 61 years[a]

- Presented to **PCP** with psoriasis in 2013/2014
- History of pulmonary issues

- PCP referred to a **dermatologist**
- Dermatologist noticed spots on face and fingernails, suspected scleroderma (not followed up)

- A second dermatologist diagnosed **scleroderma** and **lupus** in 2015
- Detailed education on CTD provided

- **Vertigo**
- **Shortness of breath** during walks and when climbing stairs
- **Coughing**
- Poorer running performance

- Referred to a **rheumatologist** in 2017
- Rheumatologist referred on to a **pulmonologist** and **cardiologist**

- Tests included **PFT**, **6MWD**, **Echo**, **RHC**
- Pulmonologist and cardiologist diagnosed **PAH**, **ILD** and **mixed CTD** in 2018
- Detailed education on PAH provided

- Undergoes **6MWD** test every 6 months and **PFTs** every year

PAH diagnosis caused severe anxiety warranting medication

Female Aged 49 years[a]

- Presented to **PCP** with joint pain, rash, and symptoms of Raynaud's phenomenon
- Family history of RA

- PCP referred to a **rheumatologist**

- Diagnosed with **lupus** in 2004
- Subsequently diagnosed with **mixed CTD** in 2007
- Little information on CTD provided

- Experienced **shortness of breath** and **chest pain**
- Unable to exercise as previously

- Rheumatologist conducted **PFT** and **Echo** in 2009 (results not followed up)
- Admitted through **ER** with chest pain in 2015
- Referred to a **pulmonologist**

- Pulmonologist diagnosed **PAH** in 2015

- **RHC** initially every 6 months, now less frequently

PAH diagnosis increased anxiety, warranting medication

[a]Age at time of the PERC engagement.

6MWD, 6-minute walk distance; **CTD**, connective tissue disease; **ER**, emergency room; **ILD**, interstitial lung disease; **MG**, myasthenia gravis; **PAH**, pulmonary arterial hypertension; **PCP**, primary care provider; **PFT**, pulmonary function test; **PH**, pulmonary hypertension; **PTSD**, post-traumatic stress disorder; **RA**, rheumatoid arthritis; **RHC**, right heart catheterization.

FIGURE 4: Participant quotes about their experience with PAH-CTD

Feeling dismissed

> *"My relationship with my PCP was never great but felt I didn't have a choice, and I felt dismissed, and [they] attributed everything to my weight. [It was] narrow-minded. … There was completely a lack of knowledge [about CTD]."*
>
> **– Patient, age 29**

Experiencing delayed diagnosis

> *"I didn't hear anything about [PH risk] until 2009, so five years [after my CTD diagnosis]. … I did the testing and then never heard anything about results. I didn't follow up, and [the topic] didn't come up again until 2015."*
>
> **– Patient, age 49**

Struggling to understand diagnoses

> *"Everything has been a learning process for me because [my pulmonologist] never really described what PH was or what it does. All they told me is, 'Your artery has extra pressure.' No one explained to me what the symptoms are for PH. …"*
>
> **– Patient, age 29**

Feeling validated

> *"[My PCP] listened to me and sent me where I needed to go. Before that, I never went to see a doctor."*
>
> **– Patient, age 49**

Receiving a referral

> *"It was the dermatologist that really noticed the symptoms and wanted me to follow up with a rheumatologist. … [The dermatologist] was very detailed in describing scleroderma, how they monitor it, what test to look for. So, it was very detailed."*
>
> **– Patient, age 61**

Receiving PAH education

> *"And [the cardiologist] sat us down and started drawing pictures of pulmonary arterial hypertension, the difference between that and right heart and versus left heart, and the high blood pressure within your lungs, and he drew the picture and explained it extremely well."*
>
> **– Patient, age 61**

CTD, connective tissue disorder; **PCP**, primary care provider; **PH**, pulmonary hypertension.

- The PERC participants recommended several strategies to help patients receive the appropriate care as quickly as possible (**Figure 5**)

FIGURE 5: Recommendations for providers from people with PAH-CTD

Increase education for providers to improve screening, referrals, and diagnoses of this high-risk population

- **Primary care and advanced practice providers:** improve overall education around CTD and PAH, including signs and first symptoms important in recognizing CTD
- **Rheumatologists:** encourage providers to spend time assessing cardiopulmonary morbidities associated with exercise intolerance in their patients who have CTD and improve education about the risks of developing PAH in CTD
- **Dermatologists:** encourage referral to PAH specialist after diagnosing a patient with a CTD

CTD, connective tissue disorder; **PAH**, pulmonary arterial hypertension.

Conclusions

- ✓ The connection of rare, complicated diseases brings a unique set of diagnostic challenges for physicians
- ✓ Even in this small, exploratory focus group, people with CTD described marked variability in the care they received, provider knowledge, and the time between CTD and PAH diagnosis
- ✓ These findings indicate a need for increased awareness for providers across the diagnostic journey, including primary care and advanced practice providers, rheumatologists, and dermatologists. Having adequate knowledge to recognize CTD, understand the risk of developing PAH in CTD, and confidence in evaluating PAH risk among patients with CTD through targeted questioning, will enable timely referral to PAH specialists

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