

“Pyoderma Gangrenosum”

Alex G Ortega Loayza, M.D., M.C.R, C.W.S.P.

Professor and Chair of Dermatology

Oregon Health & Science University

Conflicts of interest

- Board positions:
 - The CHORD COUSINS Collaboration (C3)
 - Honorary Editorial Board Member: American Journal of Clinical Dermatology
- Associate editor: Dermatology (Karger)
- Advisory Board:
 - Leo pharma, Otsuka
- Consultant:
 - Corvus Pharmaceuticals
- Research Grant:
 - Janssen, Incyte, Boehringer Ingelheim, UCB

Conflicts of interest



Patient Organization-Cofounder, Medical Director



Educational and Advocacy Organization-Cofounder



OBJECTIVES



Characterize the early clinical phase of PG

Describe clinical trajectories over time:
treatment approaches, outcomes, and recurrence.

Discuss emerging opportunities for clinical research in PG.



**Julia
Nunley, M.D.**



**W. Kenneth
Blaylock, M.D.**



**Scott
Walsh, Ph.D.**



**Jerome
Strauss,
M.D. Ph.D.**







2 days





3 days



11 days





8 days



6 days

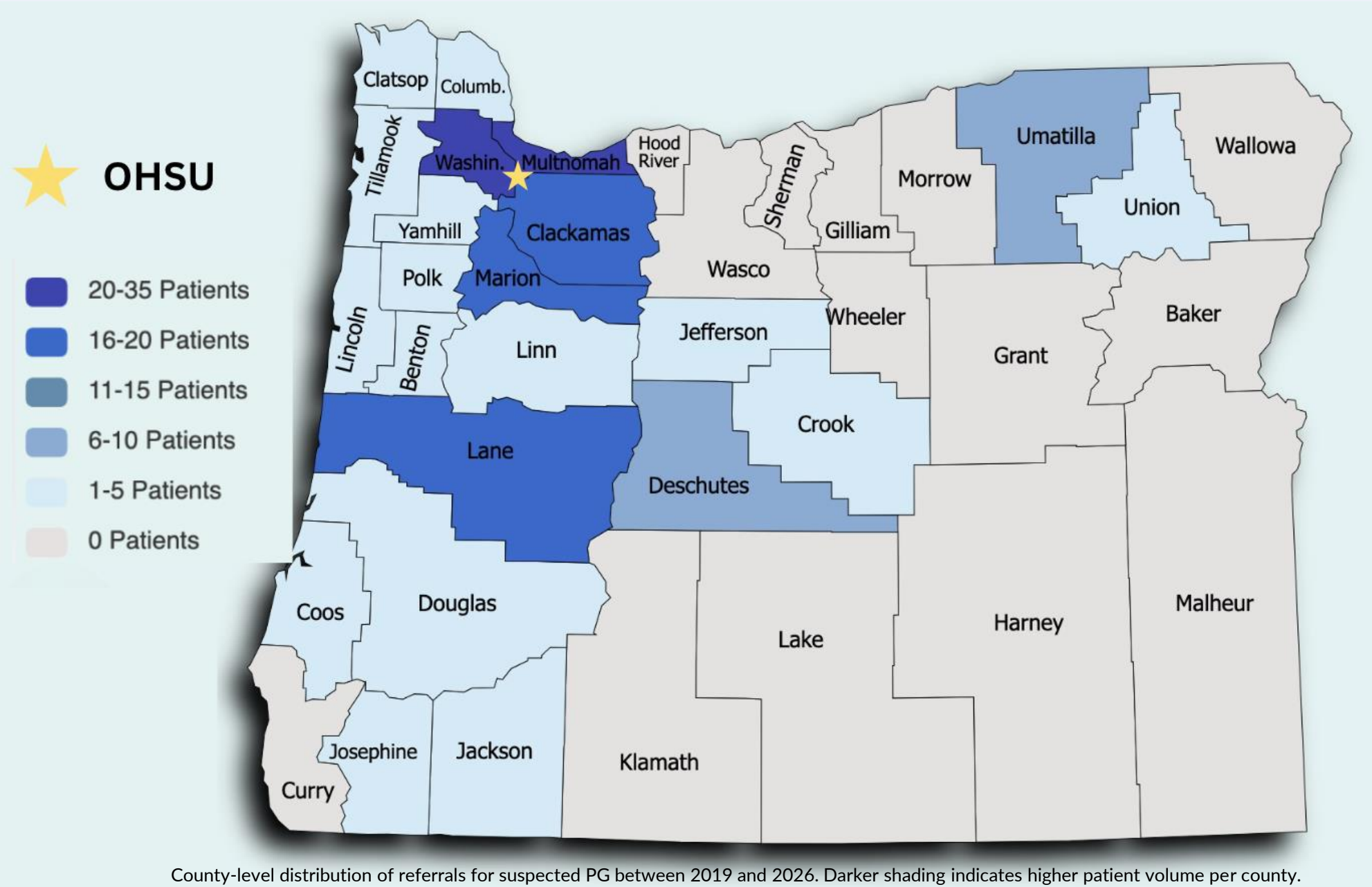




OHSU
Dermatology



Patients with Suspected PG Are Referred from Across Oregon



"Participant" Form

Completed at baseline and updated longitudinally

- Participant management, consent, and attestation
- Demographics and social history
- Medical history (conditions affecting wound healing and diagnostic history)
- Pre-referral PG lesion history survey
- Comorbidities
- Medication history
- Wound care and referral details
- Concurrent medications
- Protocol deviation and unanticipated problem logs

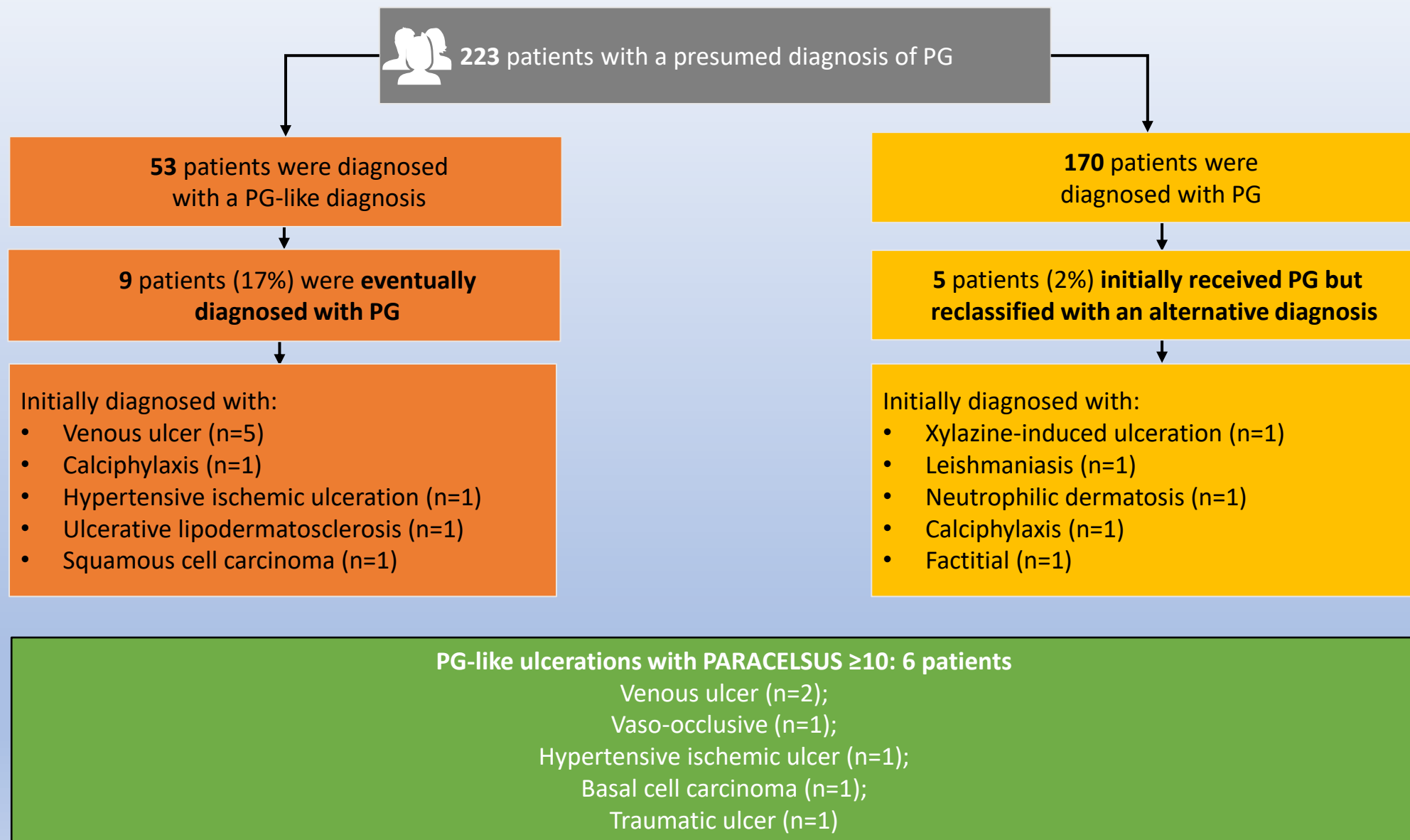
"Lesion" Form

Completed at baseline and clinical follow-up visits

- PARACELSUS diagnostic score
- Target lesion characteristics and photographs
- Location and clinical descriptors of both target and non-target lesions
- Laboratory and imaging data obtained to rule out alternative diagnoses
- Lesion disposition metrics such as Physician Global Assessment (PGA), healing or resolution status



Skin ulcers misdiagnosed as PG: A cohort study





- A)Ulcerative lipodermatosclerosis
B)Hypertensive ischemic ulcer
c)Calciphylaxis
D)Vasoooclusive ulcer

Various laboratory investigations are important for diagnosis

Essential work-up

- Full blood count
- Comprehensive metabolic profile including liver and renal function tests
- Biopsy

Specific work-up

- Autoimmune and inflammatory panels
- Hypercoagulable screen
- Protein electrophoresis
- Hepatitis screen

Additional investigations

- **Fecal calprotectin** – clinical suspicion of inflammatory bowel disease
- **CT scan** – suspicion of underlying malignancy
- **Protein and urine electrophoresis** – suspicion of leukemia
- **Blood cultures** – to rule out infection
- **Joint exploration (ultrasound, X-Ray, CT scan, etc.)** – if clinical suspicion of inflammatory arthritis

PyGaS registry study at OHSU: Demographics



Category	Subcategory	n (%)
Sex	Female	169 (69.0%)
	Male	76 (31.0%)
Race	White	216 (88.2%)
	Black	8 (3.3%)
	American Indian/Alaskan Native	5 (2.0%)
	Asian	1 (0.4%)
	Native Hawaiian or Other Pacific Islander	1 (0.4%)
	Unknown	16 (6.5%)
Age (years)	18-29	10 (4.1%)
	30-49	74 (30.2%)
	50-69	101(41.2%)
	≥70	60 (24.5%)
Subtypes (n = 245)	Classic	197 (80.4%)
	Peristomal	34 (13.9%)
	Vegetative	11 (4.5%)
	Bullous	2 (0.8%)
	Subcutaneous	1 (0.4%)
Residence	Urban	152 (62.0%)
	Rural	93 (38.0%)

Race categories were not mutually exclusive, and percentages may exceed 100%. A total of 29.4% of patients resided outside Oregon, and 0.4% resided outside the United States.

Classic PG n=205



Represents ~85% of the registry. Characterized by lower extremity presentation and higher risk of diagnostic delay.

Peristomal PG n=35

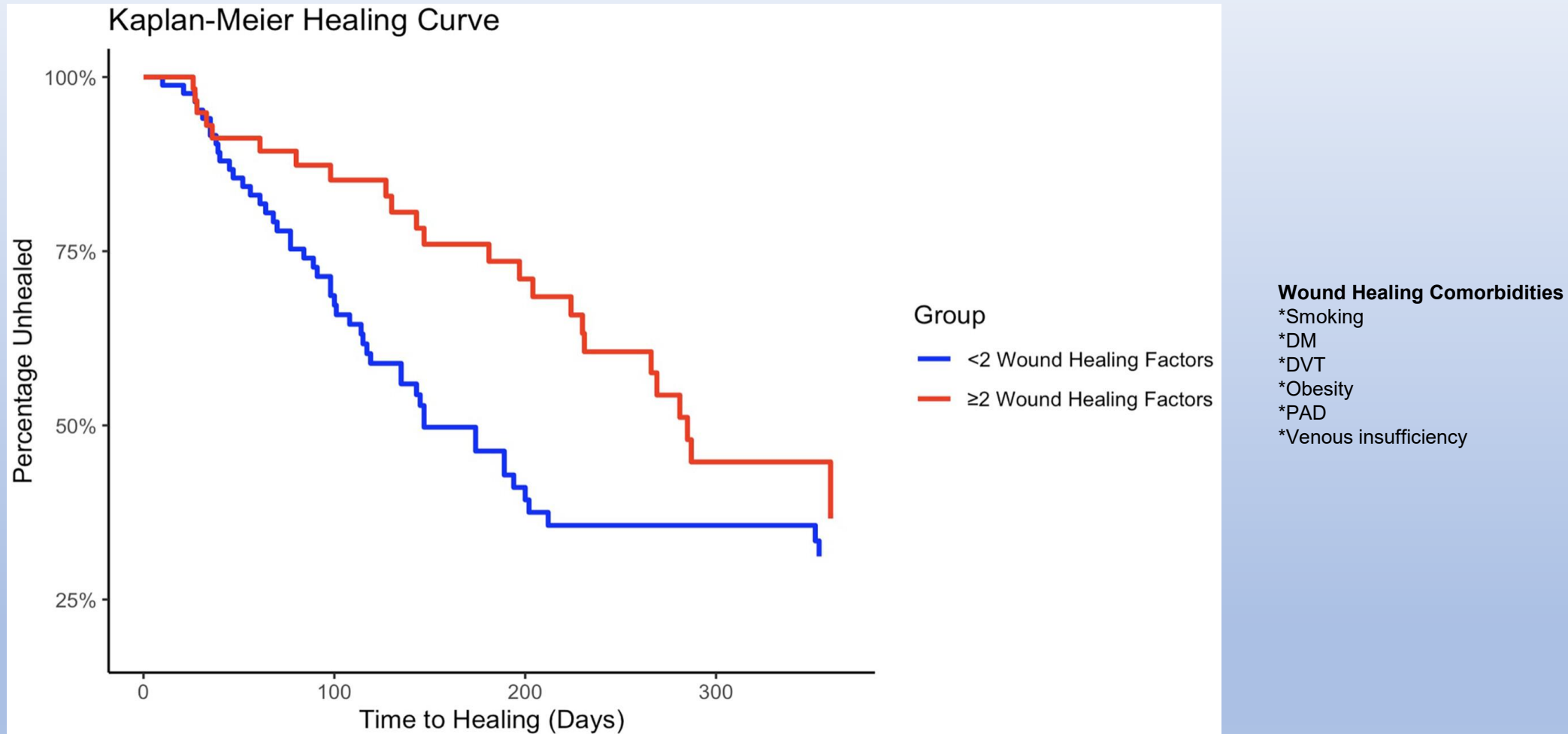


Represents ~15% of the registry. Characterized by trunk presentation and strong ties to underlying gastrointestinal disease.

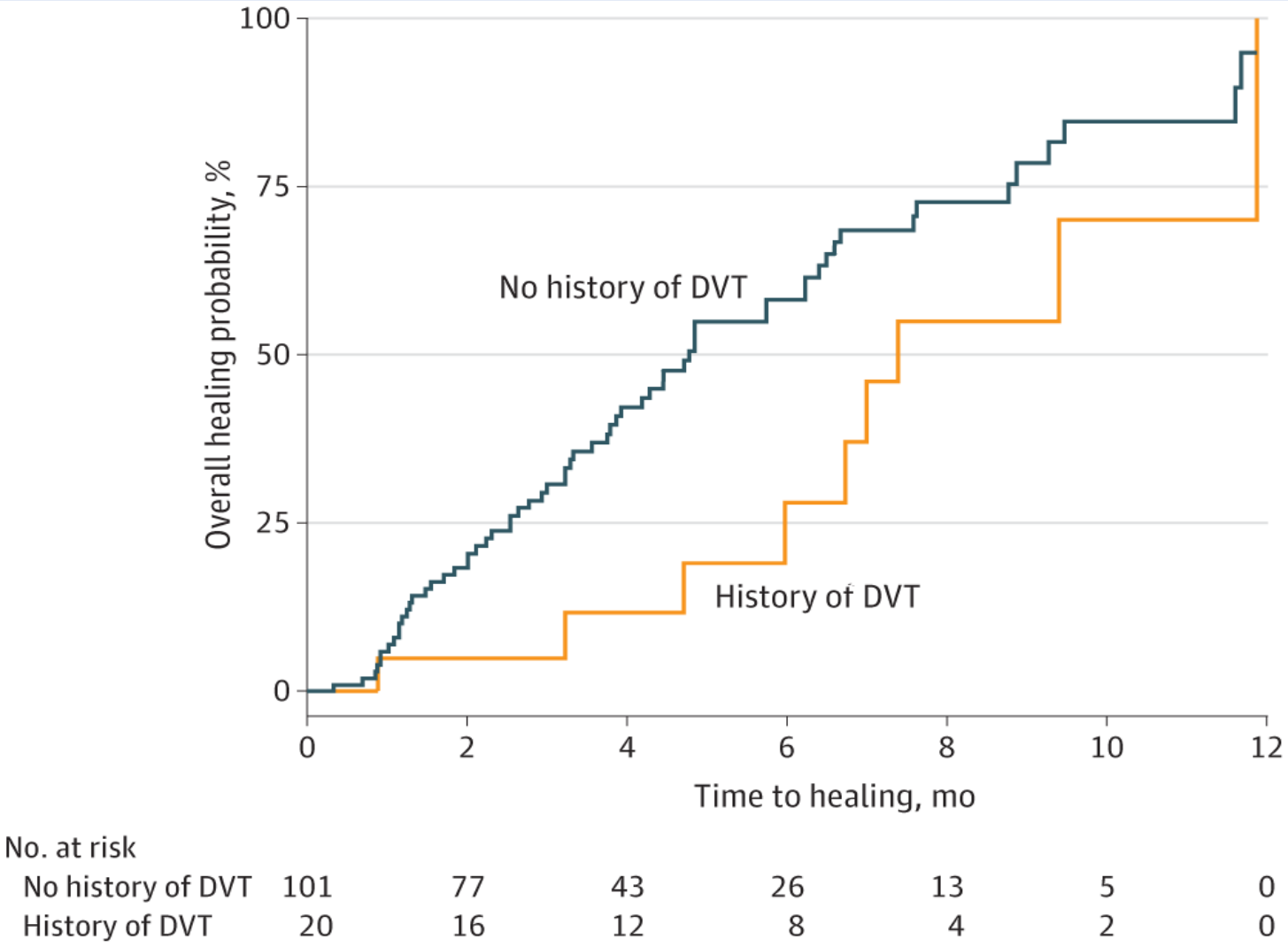
**Classic PG overlaps with chronic medical conditions
which complicates delay diagnosis and treatment outcomes**

Variable	Classic PG	Peristomal PG
Demographics	Median Age 58 71% Female	Mean Age 51.7 71% Female
Primary Comorbidities	Hypertension (55%) Venous Insufficiency (35%) Diabetes (27%)	Inflammatory Bowel Disease (66%) Solid Cancer (31%)
Current Smoker	18.5%	5.7%

Kaplan–Meier curve showing a statistically significant difference in wound healing outcomes at 6 months, 9 months and 1 year in patients with ≥ 2 wound healing comorbidities; $p = 0.02$



Kaplan-Meier curve showing a statistically significant difference between patients with classic PG who have DVT history exhibited a significantly greater median healing time (224 days) than those without DVT history (145 days); $p=.04$



Classic PG ulcers are 5x larger and 3x longer duration at baseline

Classic PG

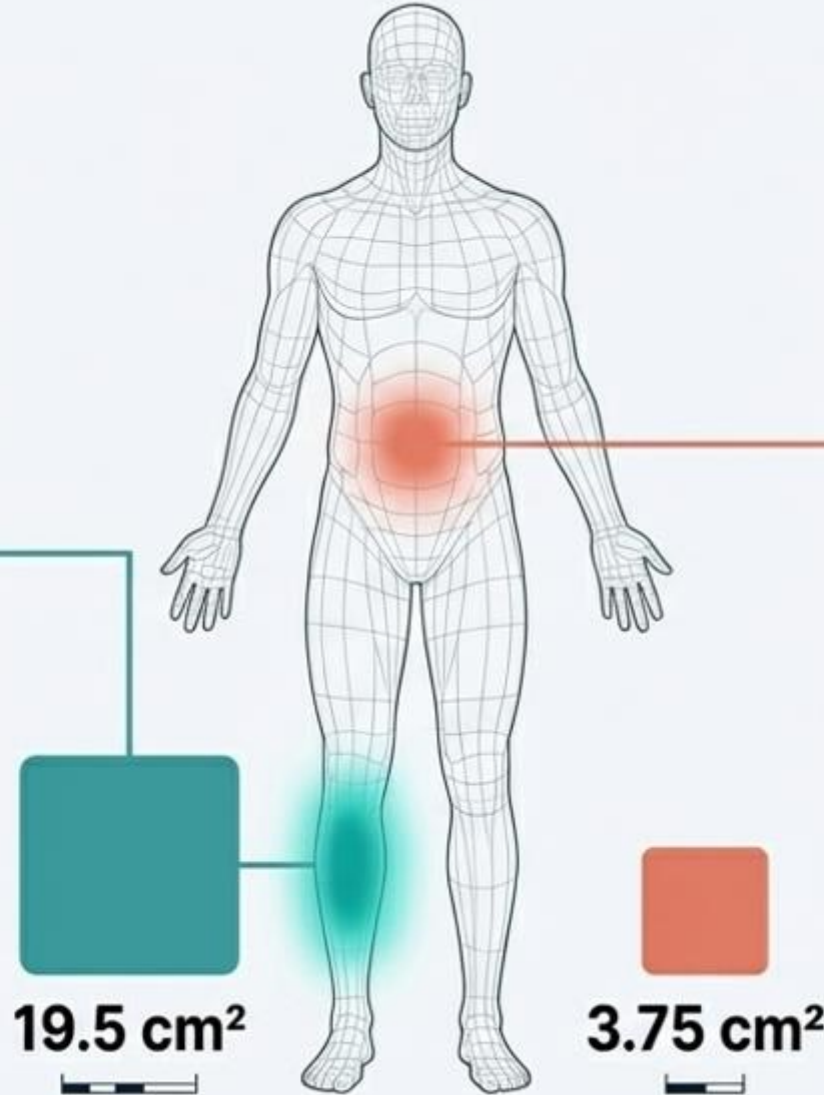
Location:
69.8% Lower Extremity

Median Size:
19.5 cm²

Wound Age at Presentation:
6.0 months

Initial Symptoms:
Trauma (27%), Pain (25%)

History of Prior Ulcers:
38%



Peristomal PG

Location:
Peristomal / Trunk

Median Size:
3.75 cm²

Wound Age at Presentation:
2.0 months

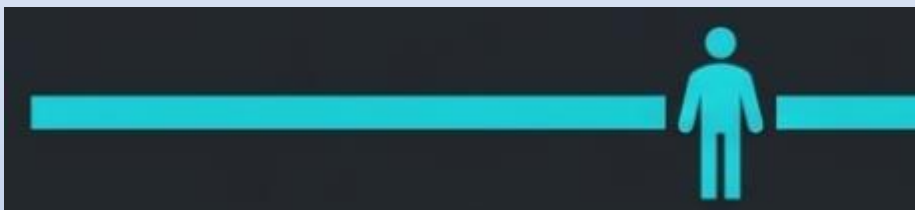
Initial Symptoms:
Pain (40%), Redness (31%)

History of Prior Ulcers:
31%

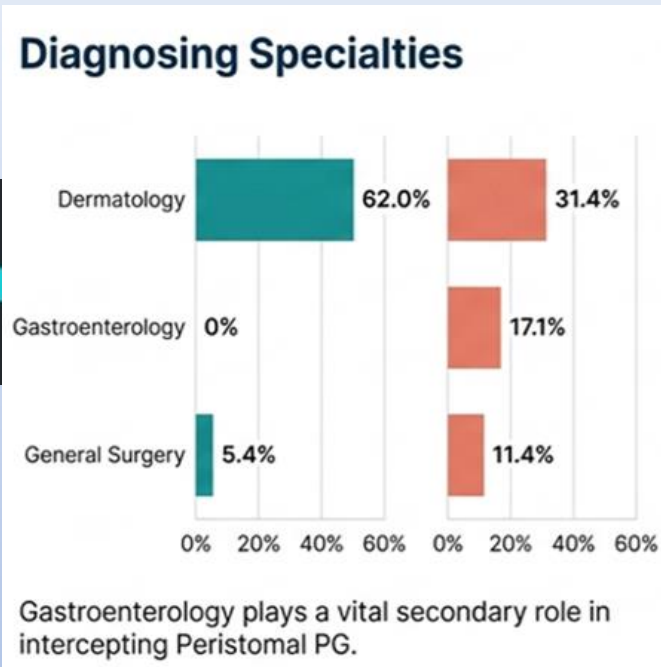


**Median time
to accurate diagnosis:
4 months (IQR 2-11)**

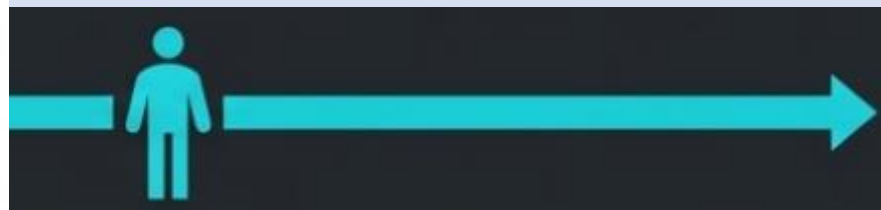
**Median time
to first provider:
0.8 months**



**Median time
to first provider:
0.5 months**



**Median time
to healing:
10.2 months (IQR 5.6-18.9)**



**Median time
to healing:
5.4 months (IQR 3.54-12.57)**

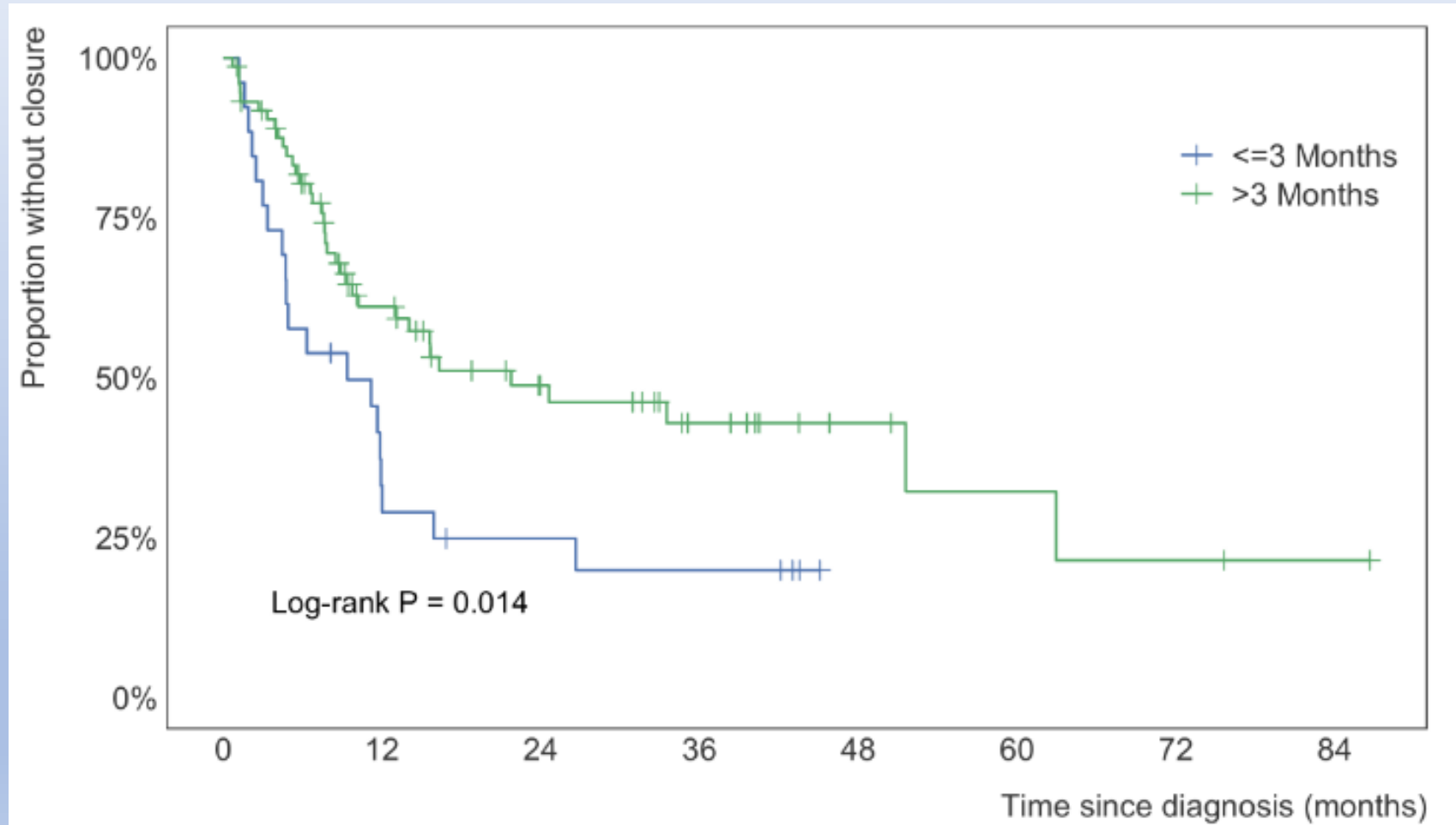


**Median time
to accurate diagnosis:
1.75 months (IQR 1-3.5)**

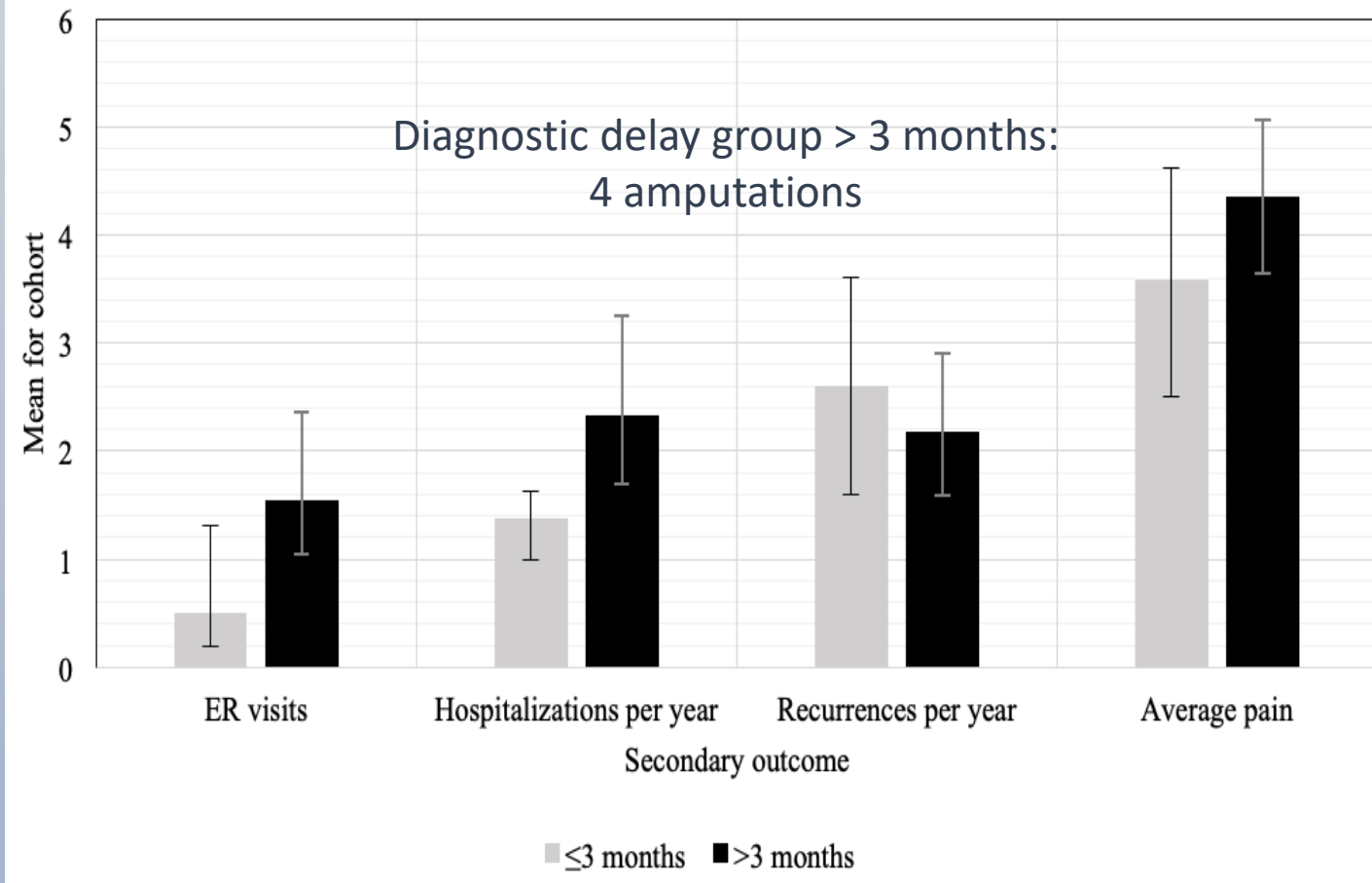
Diagnostic delay in classic PG patients impacts healing time



Median healing time
≤3 mos: 14 mos
>3 mos: 21.7 mos
***P*=.014**



Diagnostic delay in classic PG patients increases healthcare utilization



**# ER visits and yearly hospitalizations
higher for a diagnostic delay of >3 months
(ER visits $p = 0.031$; hospitalizations $p = 0.011$)**

Pyoderma gangrenosum: a report of 44 cases with follow-up

P.VON DEN DRIESCH

Department of Dermatology, Friedrich-Alexander-University of Erlangen-Nuremberg, Hartmannstr. 14, 91052 Erlangen, Germany

Accepted for publication 18 July 1997

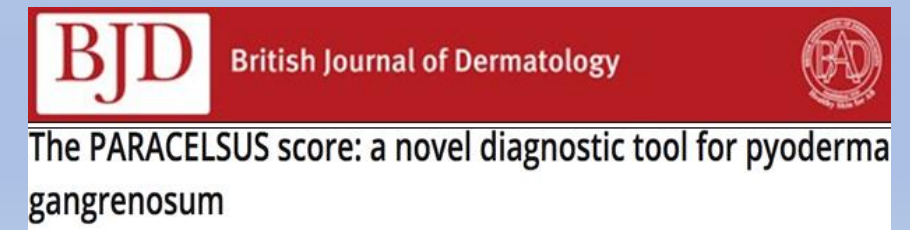
1997



2004



2018



2019

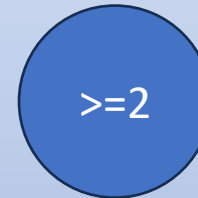
EARLY PG DIAGNOSTIC CRITERIA: EUROPE AND THE UNITED STATES



Major criterion

Rapid progression of a painful, necrolytic cutaneous ulcer with an irregular violaceous and undermined border

Other causes of cutaneous ulcerations have been excluded



Minor criteria

Systemic diseases associated with PG

Histopathological findings sterile (sterile dermal neutrophilia, mixed inflammation, lymphocytic vasculitis)

Rapid treatment response to systemic steroids

History of pathergy phenomenon or cribriform scars

First International Consensus Diagnostic Criteria for Pyoderma Gangrenosum



Major criterion

Biopsy of ulcer edge with neutrophilic infiltrate



Minor criteria

- Exclusion of infection
- Pathergy phenomenon
- History of IBD or inflammatory arthritis
- History of papule, pustule, or vesicle rapidly ulcerating
- Peripheral erythema, undermining border, and tenderness
- Multiple ulcerations, at least one on an anterior lower leg
- Cribriform scars at healed ulcers
- Decrease ulcer size within one month of initiating immunosuppression

A PARACELSUS score of ≥ 10 signifies a high likelihood of PG diagnosis

Major criteria (3 points)

- P**rogression of disease
- A**ssessment of differential diagnoses
- R**eddish violaceous wound border

Minor criteria (2 points)

- A**melioration by immunosuppressive drugs
- C**haracteristically irregular ulcer shape
- E**xtrême pain ($>4/10$ on visual analog scale)
- L**ocalization of lesion at site of trauma

Additional criteria (1 point)

- S**uppurative inflammation on histopathology
- U**ndermined wound border
- S**ystemic disease associated



Performance comparison between PG diagnostic criteria

Study	Patients	Diagnosis		Su	Delphi consensus	PARACELSUS
Single-center retrospective ¹	N=47 (PG) ¹	Agreed upon blind review by two PG experts ¹	Sensitivity ²	74%	74%	89%
Multicenter retrospective ²	N=157 (PG and mimickers) ²	By academician ³	Sensitivity ²		32%	99%
			Specificity ²		57%	60%
MEDLINE cases ⁴	N=162 (PG and mimickers) ⁴	By two independent reviewers ⁴	Sensitivity ²	86%	88%	96%
			Specificity ²	70%	90%	5%
			Mean effectiveness ⁵	48%	50%	58%

Adapted from Shakshouk H, et al. *J Am Acad Dermatol*. 2024; 91:1035–1048. Copyright © 2024 by the American Academy of Dermatology, Inc.

1. Haag C, et al. *J Invest Dermatol*. 2021;141:59–63.

2. Shakshouk H, et al. *J Am Acad Dermatol*. 2024; 91:1035–1048.

3. Min MS, et al. *Br J Dermatol*. 2022;186:1035–1037.

4. Ji-Xu A, et al. *JAMA Dermatol*. 2023;159:337–338.

5. Nusbaum KB, et al. *Int J Dermatol*. 2024;63:e33–e73.

Which diagnostic criteria clinicians are using?



Diagnostic framework	Total
Combination of any	12 (29%)
PARACELSUS (2019)	8 (19%)
Delphi consensus (2018)	8 (19%)
I use my own	7 (17%)
Mayo (2004)	4 (10%)
I was not aware of any diagnostic criteria	2 (5%)
Von den Driesch (1997)	1 (2%)

Which diagnostic criteria clinicians are using?



Diagnostic framework	Total
Combination of any	12 (29%)
PARACELSUS (2019)	8 (19%)
Delphi consensus (2018)	8 (19%)
I use my own	7 (17%)
Mayo (2004)	4 (10%)
I was not aware of any diagnostic criteria	2 (5%)
Von den Driesch (1997)	1 (2%)

Optimizing the PARACELSUS Diagnostic Cutoff

A PARACELSUS score >10 signifies a high likelihood of PG diagnosis. Data from a multicenter study of 1,403 cases.



New Standard Cutoff

Specificity
93.2% → **96.8%**
↑ (+3.6%)

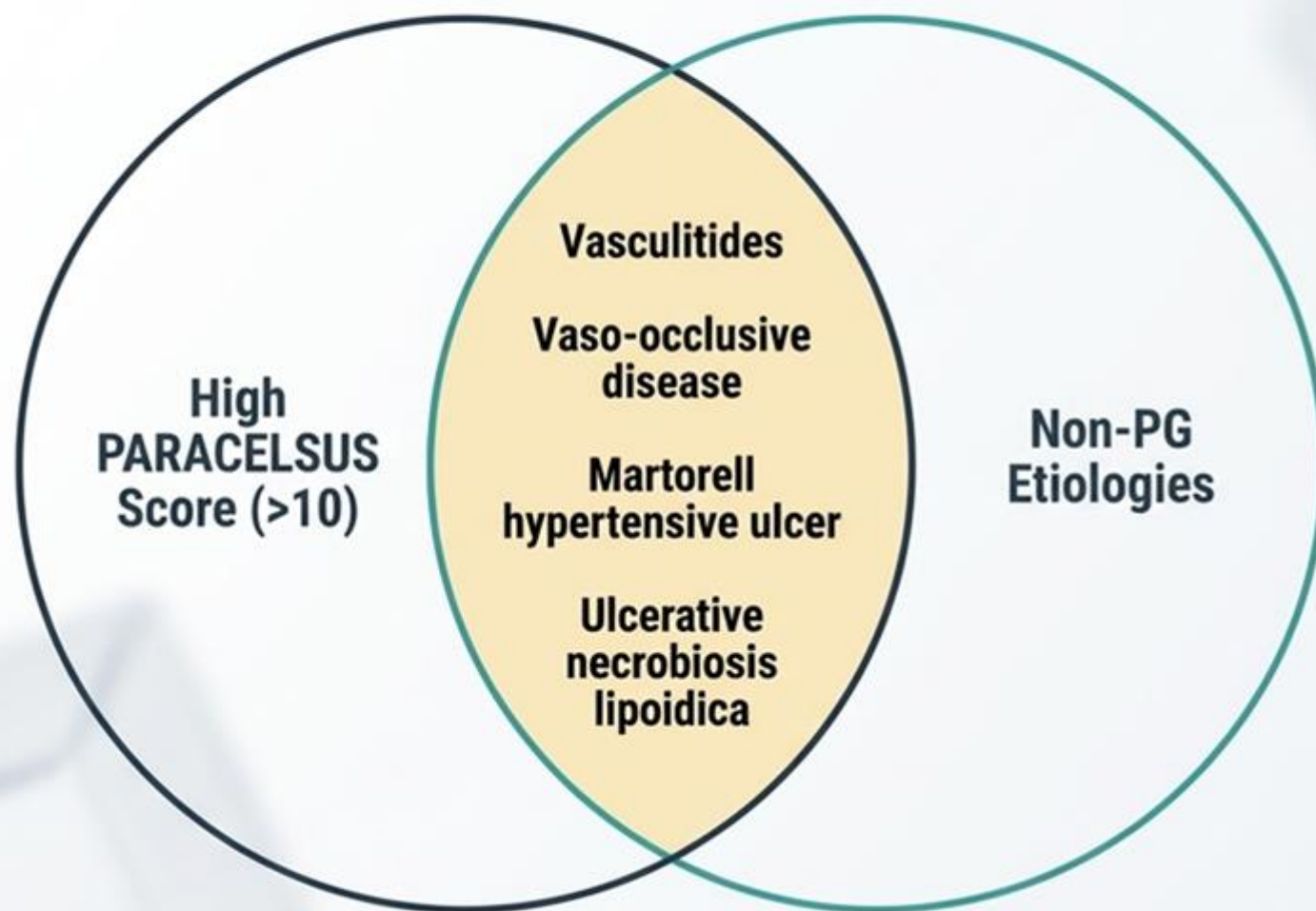
PPV
68.4% → **96.8%**
↑ (+28.4%)

Accuracy
94.1% → **97.0%**
↑ (+2.9%)

Sensitivity
Remained steady
98.3%

The optimized threshold definitively reduces false positives while maintaining near-perfect sensitivity.

The Edge Cases: Etiologies that Achieve High PARACELSUS Scores



Why do these mimics score so highly?

- 1** They present as progressive, highly painful ulcers.
- 2** They exhibit irregular, highly suspicious morphologies.
- 3** They are frequently associated with confounding systemic diseases.

The Vulnerability of Current Diagnostic Frameworks

The Weakness

Heavy reliance on subjective clinical features.

The Biological Reality

Neutrophil-predominant inflammation is surprisingly uncommon.

There is an urgent clinical need for objective and reproducible diagnostic measures.



Omics

Fluorescent
imaging

OBJECTIVE MARKERS

High
frequency
US

Artificial
intelligence





Omics

Fluorescent
imaging

OBJECTIVE MARKERS

High
frequency
US

Artificial
intelligence



Venous ulcer



Calciphylaxis



Factitial ulcer



Polyarteritis nodosa



Squamous cell carcinoma



Livedoid vasculopathy

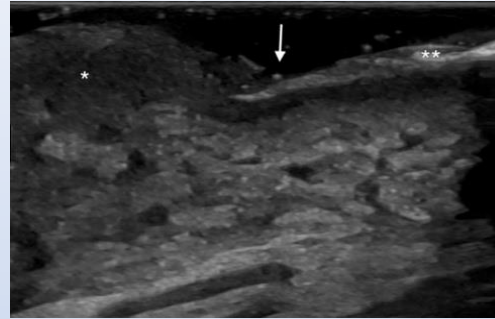
Differentiation of PG and mimickers using HFUS



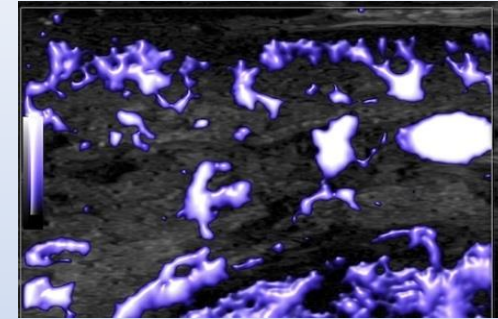
**Active PG
Ulcer**



Clinical Photography



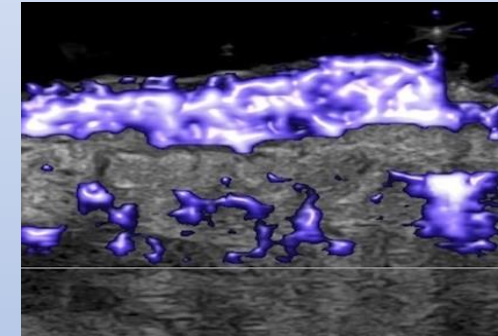
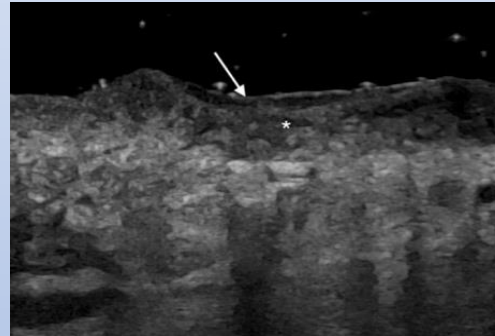
HFUS Grayscale



**HFUS Microvascular Imaging
(Doppler)**

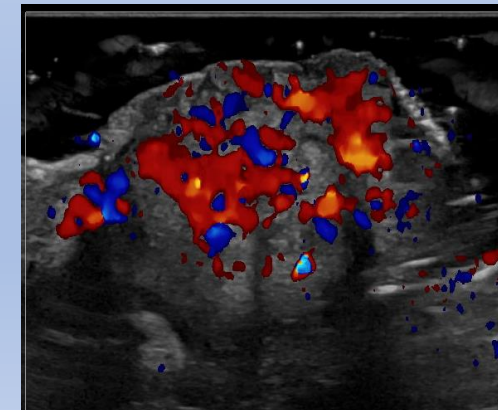
Heterogeneous ulcer bulging up through skin (*); abrupt disruption of tissue layers at the ulcer edge (arrow); interstitial edema in subcutis. Microvascular imaging shows increased vascularity with acute angle vessel branching.

**Basal Cell
Carcinoma**



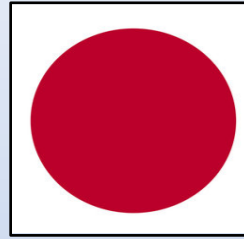
Shallow heterogeneous wound bed (*); hyperechoic layer over entire wound with underlying hypoechoic layer (arrow). Microvascular imaging shows extensive hyperemia in wound bed.

**Epithelioid
Sarcoma**



Heterogeneous mass bulging up through skin with loss of normal tissue organization and internal shadowing; hyperechoic layer covers entire mass. Color Doppler shows increased vascularity throughout.

Approved treatments for PG by regulatory agencies



European Medicines Agency

Pharmaceutical and Devices
Agency

Food Drug and Administration

Prednisolone

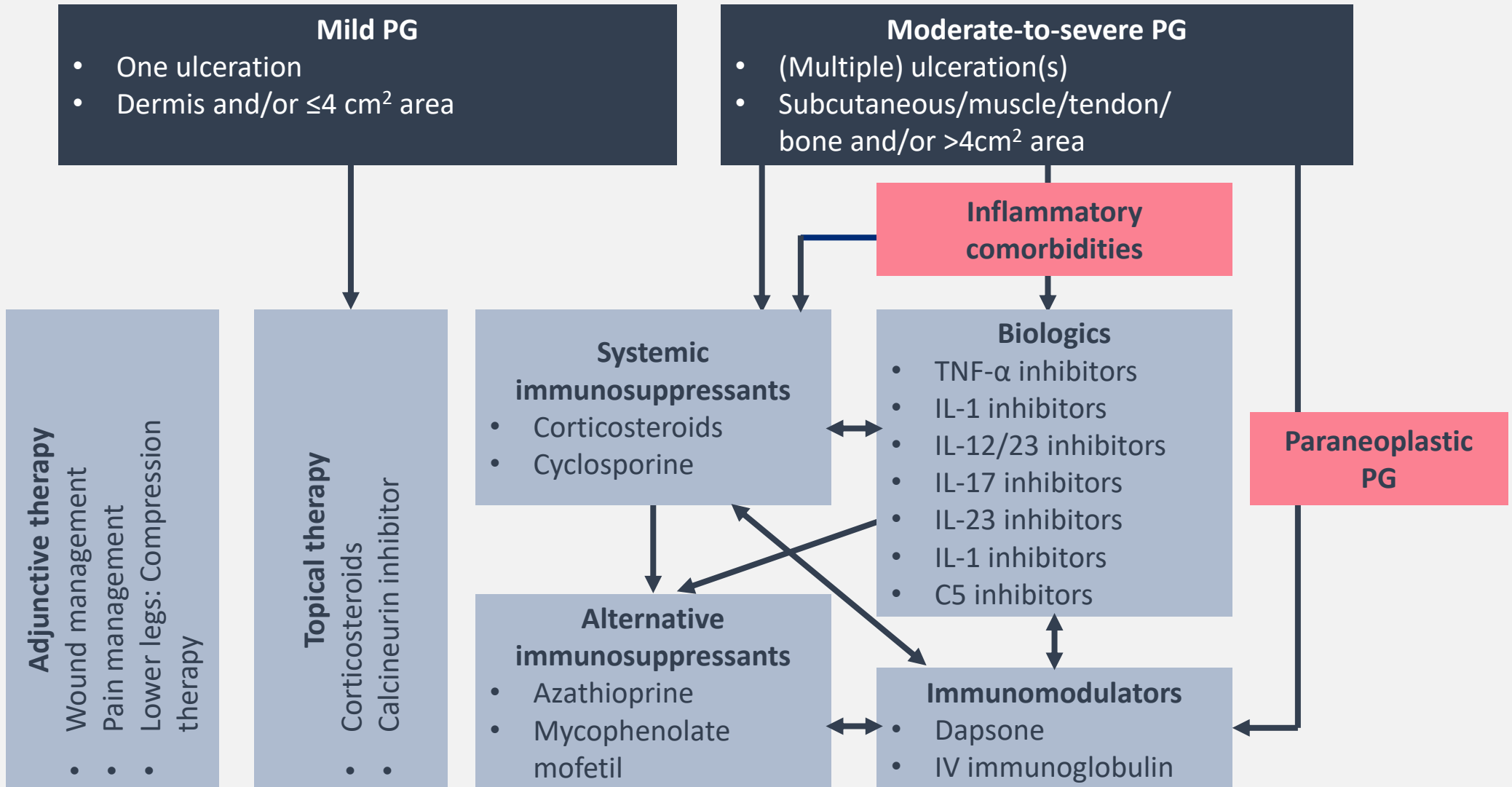
Adalimumab

None

Levels of evidence for systemic treatments

	Administration	Level of Evidence
Classic immunosuppressants		
Prednisolone	PO	1B
Cyclosporine	PO, IV	1B
Biologics		
Infliximab	IV	1B
Adalimumab	SQ	2B
Canakinumab	SQ	2B
Secukinumab	SQ	2B
Vilobelimumab	IV	2B
Tildrakizumab	SQ	2B
Ustekinumab	SQ, IV	3A
Small molecules		
Baricitinib	PO	2B
Other immunosuppressants		
Mycophenolate mofetil	PO	2B
Immunomodulators		
Dapsone	PO	2B
IVIG	IV	3A

Treatment algorithm



Combination of systemic agents



	1	2	3	Total
First line immunosuppressant + Biologic	11(41%)	9 (33%)	7(26%)	27
First line immunosuppressant + First line immunosuppressant	19(73%)	6(23%)	1(4%)	26
First line immunosuppressant + Immunomodulator	7(28%)	11(44%)	7(28%)	25
First line immunosuppressant + Other immunosuppressant	4(27%)	5(33%)	6(40%)	15
Biologic + Immunomodulator	0(0%)	5(33%)	10(67%)	15
Biologic + Other immunosuppressant	1(1%)	3(3%)	5(56%)	9
Immunomodulator + Other immunosuppressant	0(0%)	2(50%)	2(50%)	4

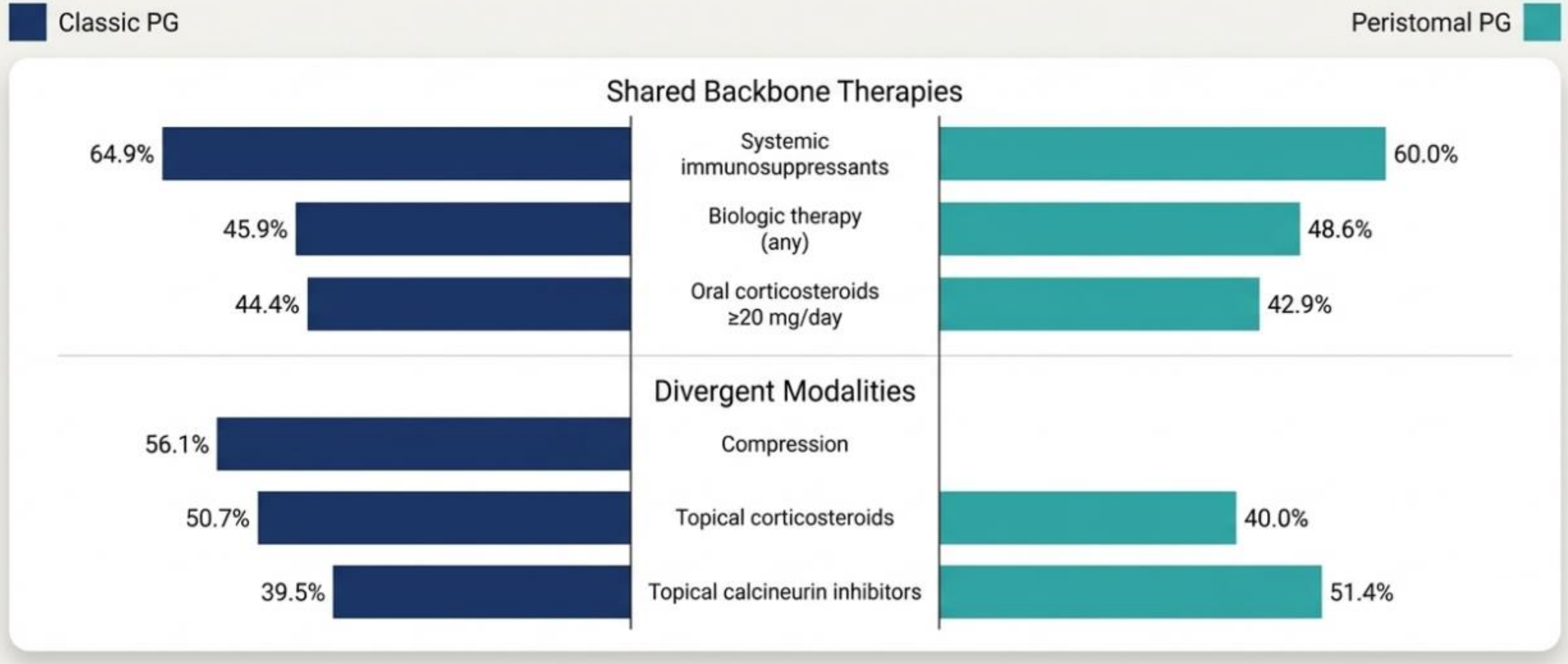
Combination of systemic agents for at least 4 weeks



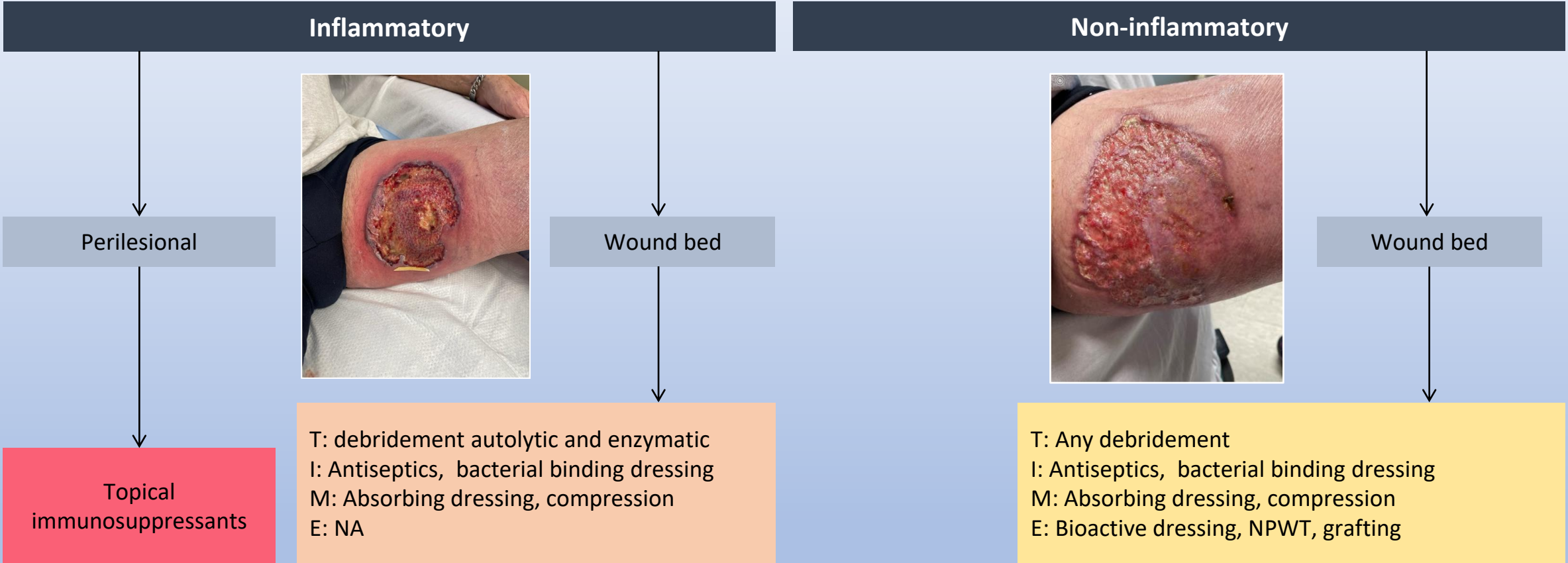
	1	2	3	Total
First line immunosuppressant + Biologic	11(41%)	9 (33%)	7(26%)	27
First line immunosuppressant + First line immunosuppressant	19(73%)	6(23%)	1(4%)	26
First line immunosuppressant + Immunomodulator	7(28%)	11(44%)	7(28%)	25
First line immunosuppressant + Other immunosuppressant	4(27%)	5(33%)	6(40%)	15
Biologic + Immunomodulator	0(0%)	5(33%)	10(67%)	15
Biologic + Other immunosuppressant	1(1%)	3(3%)	5(56%)	9
Immunomodulator + Other immunosuppressant	0(0%)	2(50%)	2(50%)	4

Preferred immunosuppressant: corticosteroid
Preferred biologic: TNF inhibitor

Treatments from PyGaS registry

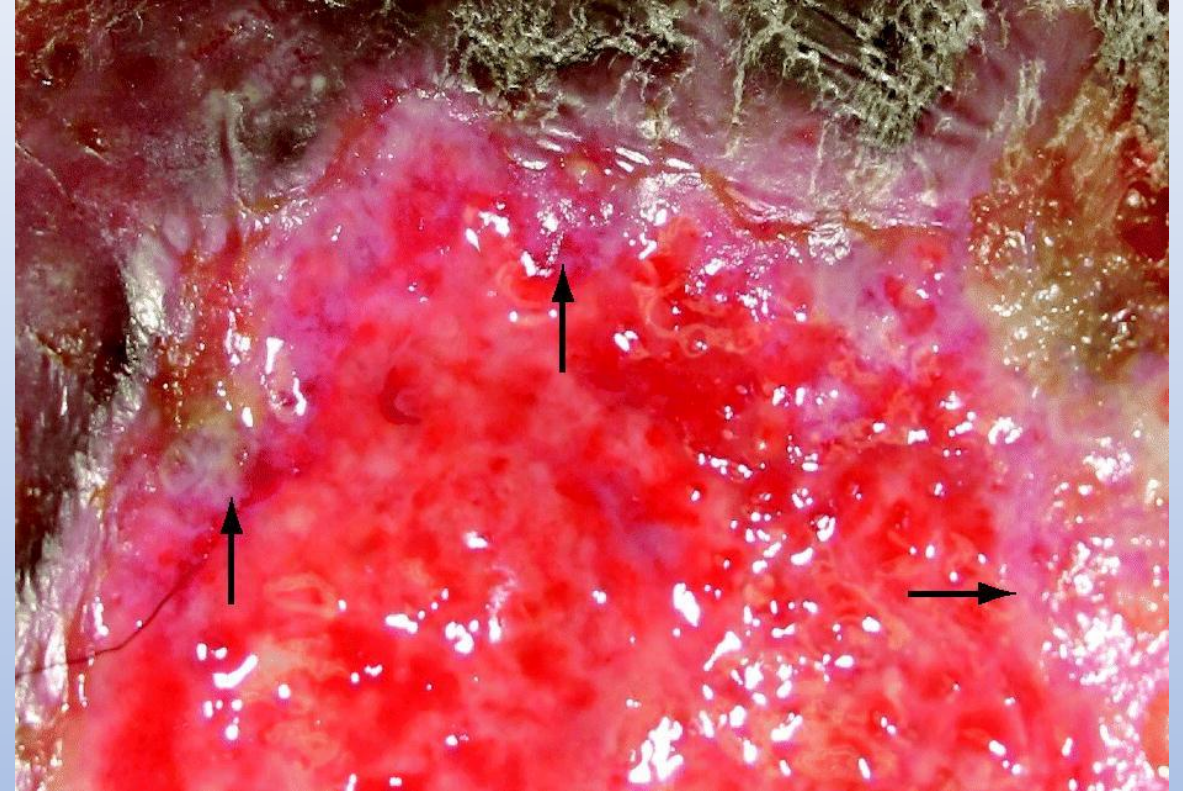
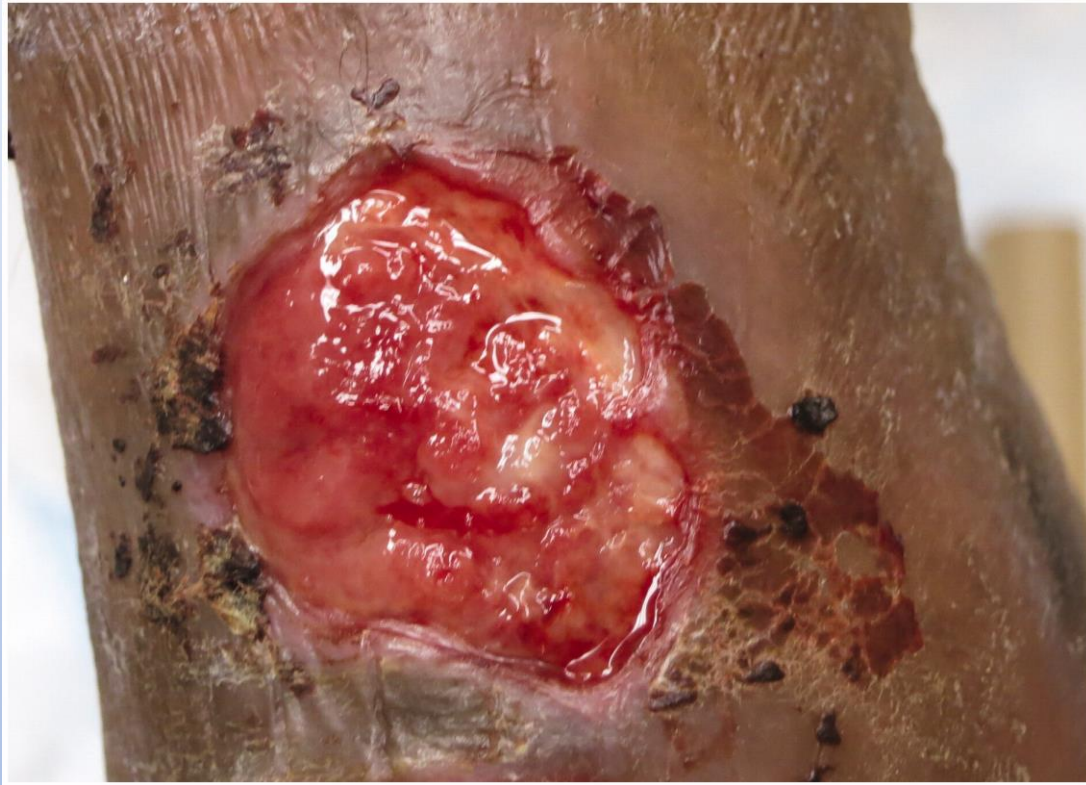


Wound management: debridement and compression are essential



T: Tissue; I: Infection; M: Moisture balance; E: Epithelial advancement edges

Gulliver's sign: transition in PG patients which indicates that inflammation is under control



Note the new epithelial growth (designated by arrows) connecting the ulcer bed to the surrounding normal skin.

WEEK 0



Gulliver's sign



WEEK 11



Treatment:

- Adalimumab
- Prednisone Taper
- Dapsone
- Compression

Smaller baseline ulcers and faster diagnosis drive rapid healing in peristomal PG

Classic PG



44.9% Completely Healed

Peristomal PG



60.0% Completely Healed

Recurrence remains a greater threat in peristomal PG than in classic PG

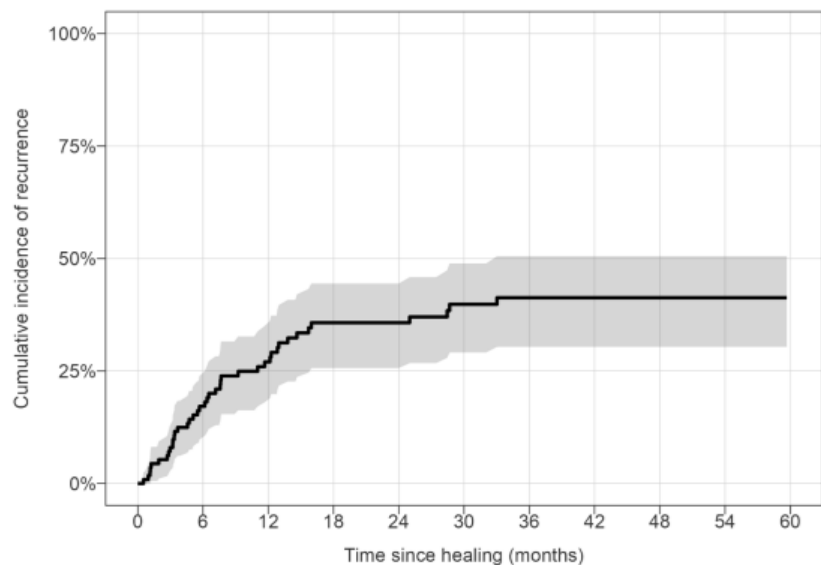


Fig. 1: Cumulative incidence of recurrence. Estimated cumulative incidence of pyoderma gangrenosum recurrence over time following healing estimated from the Kaplan-Meier recurrence-free survival curve following healing of the target ulcer. The shaded region represents the 95% CI.

At 1 year: 27% (95% CI: 18.1-35.0)
At 5 years: 41.3% (95% CI: 30.4-50.5)

Number healed: 116 patients
Number of recurrences: 41 (35%) patients
→ 30 (73%): classic
→ 9 (22%): peristomal
→ 2 (5%): verrucous

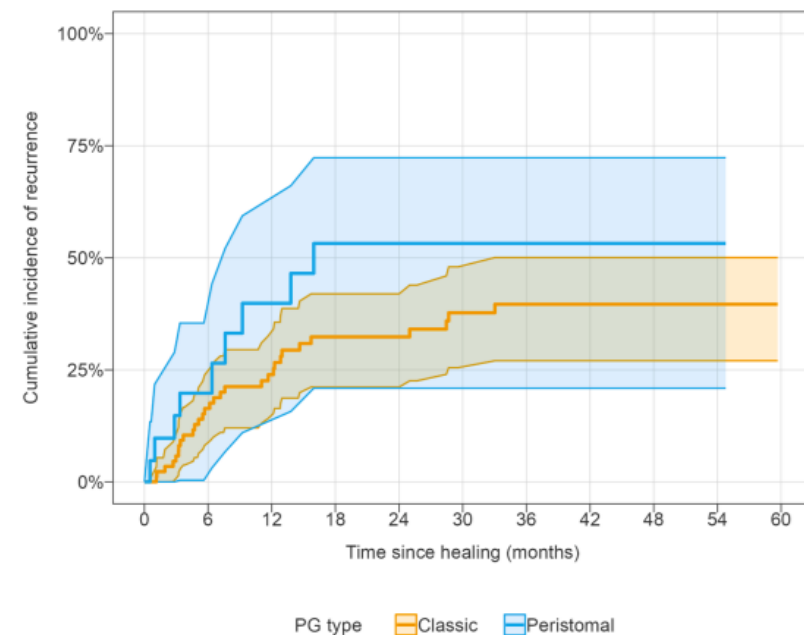


Fig. 3: Cumulative incidence of recurrence by pyoderma gangrenosum subtype. Estimated probability of pyoderma gangrenosum recurrence over time following healing estimated from the Kaplan-Meier recurrence-free survival curve following healing of the index ulcer stratified by pyoderma gangrenosum subtype. Shaded region represents the 95% CI. PG, pyoderma gangrenosum.

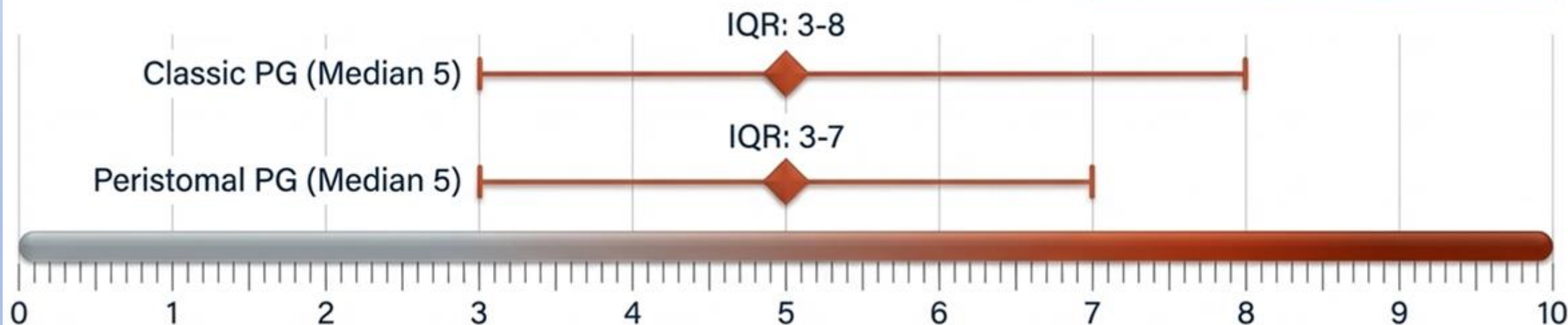
Classic:
At 1 year: 23.9% (95% CI: 14.2-32.6)
At 5 years: 39.6 (95% CI: 27.0-50.1)

Peristomal
At 1 year: 39.8% (95% CI: 11.0-59.4)
At 5 years: 53.2% (95% CI: 20.9-72.3)

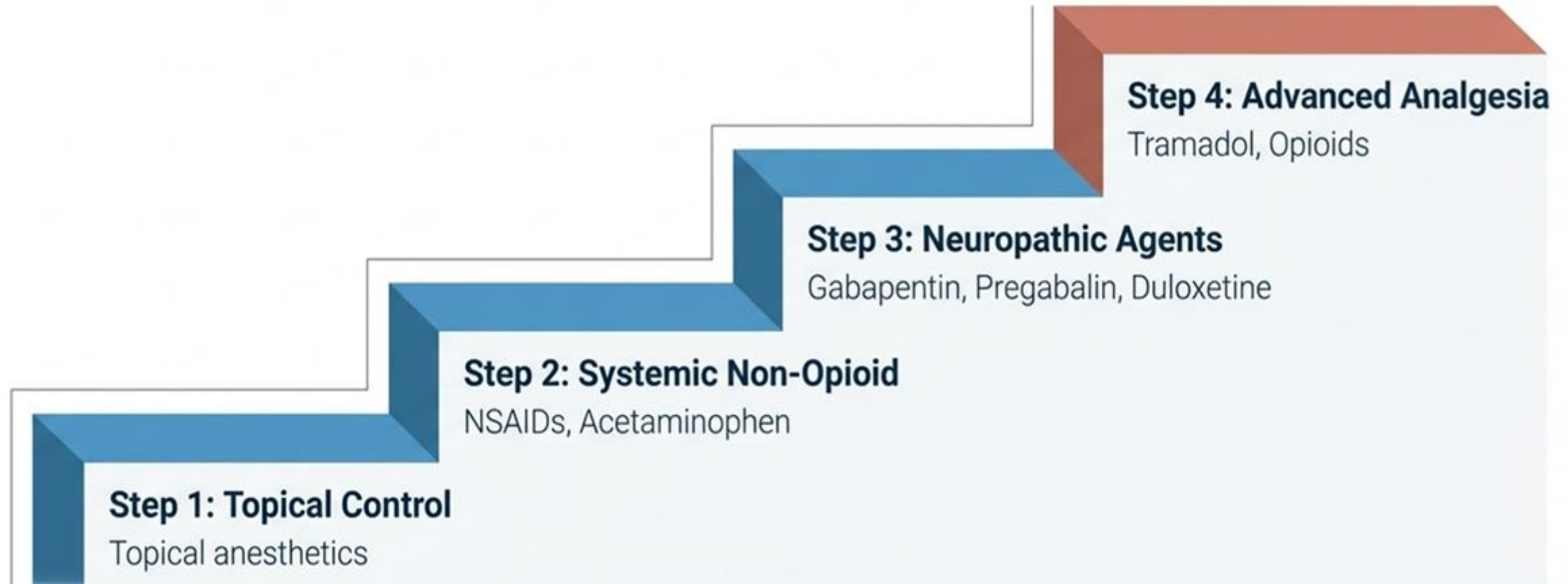
Quantifying the Patient Symptom Burden

85%

Pain is the most bothersome symptom in PG.



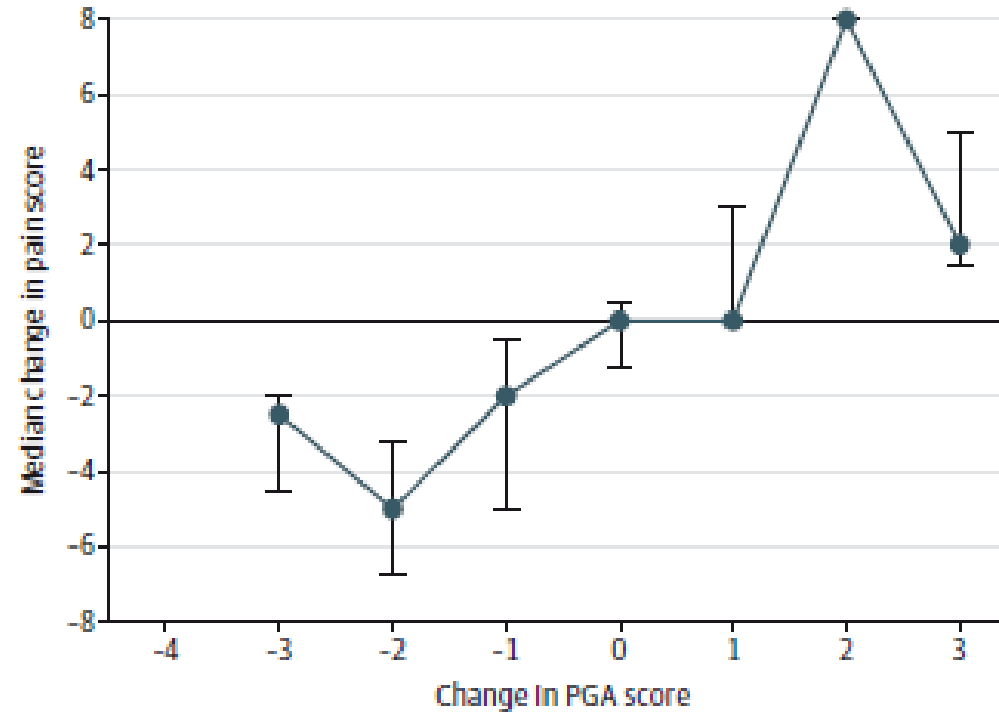
A Stepped Approach to PG Pain Management



NRS improvement of ≥ 2 points in pain *may be an indication* that a patient is responding to treatment



Figure. Change in Pain Associated With Change in Patient Global Assessment (PGA) Score



MID for pain in PG

The Next Frontier in PG Research

Data & Technology

Implementation of **Artificial Intelligence (AI)**

Spatial Transcriptomics mapping



Clinical Infrastructure

Development of **comprehensive Registries**

Large-scale **Prospective Studies**



Standardization & Metrics

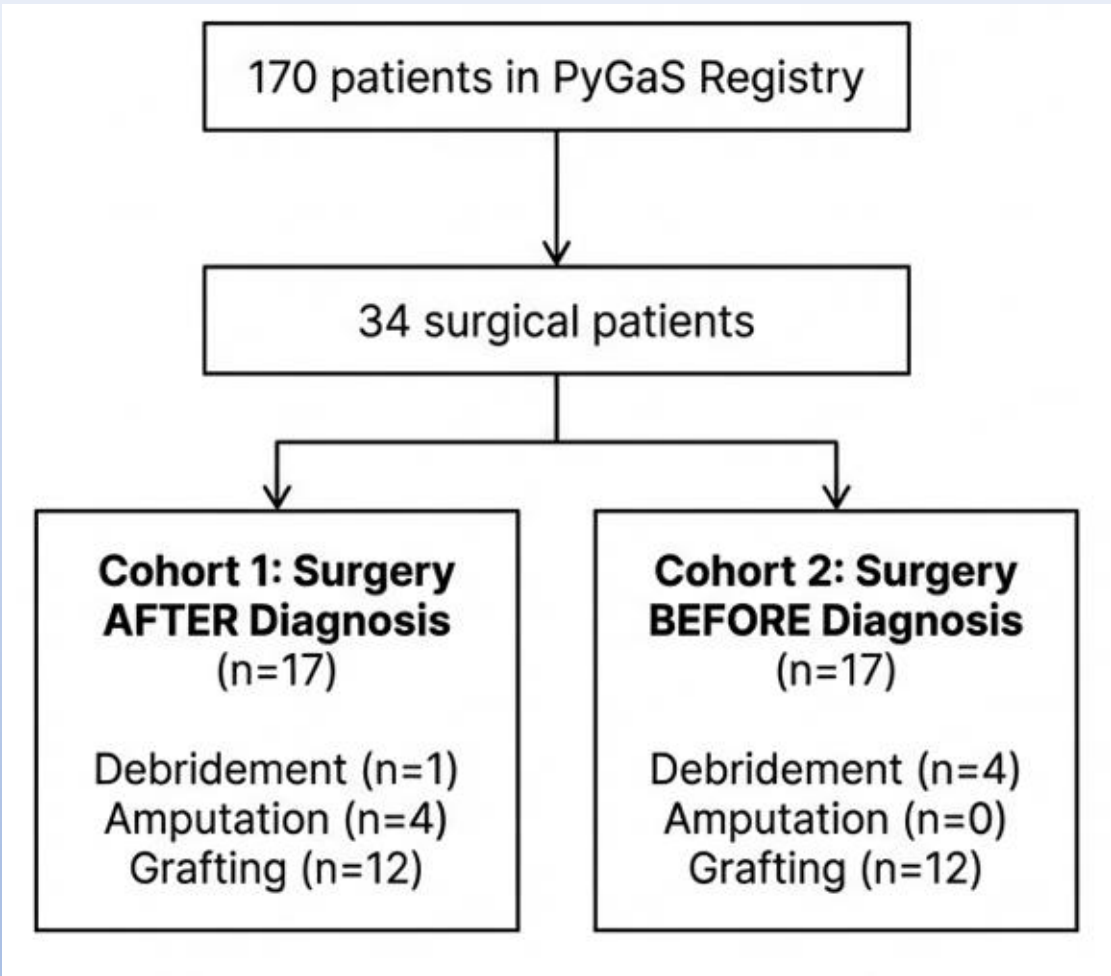
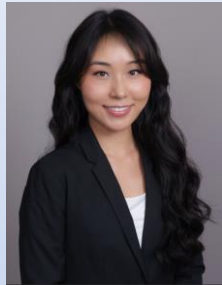
Redefining the **standard of care**

Establishing **universal outcome instruments**

Defining precise clinical **endpoints**



1) Appraise future research in PG: Surgical Management of PG

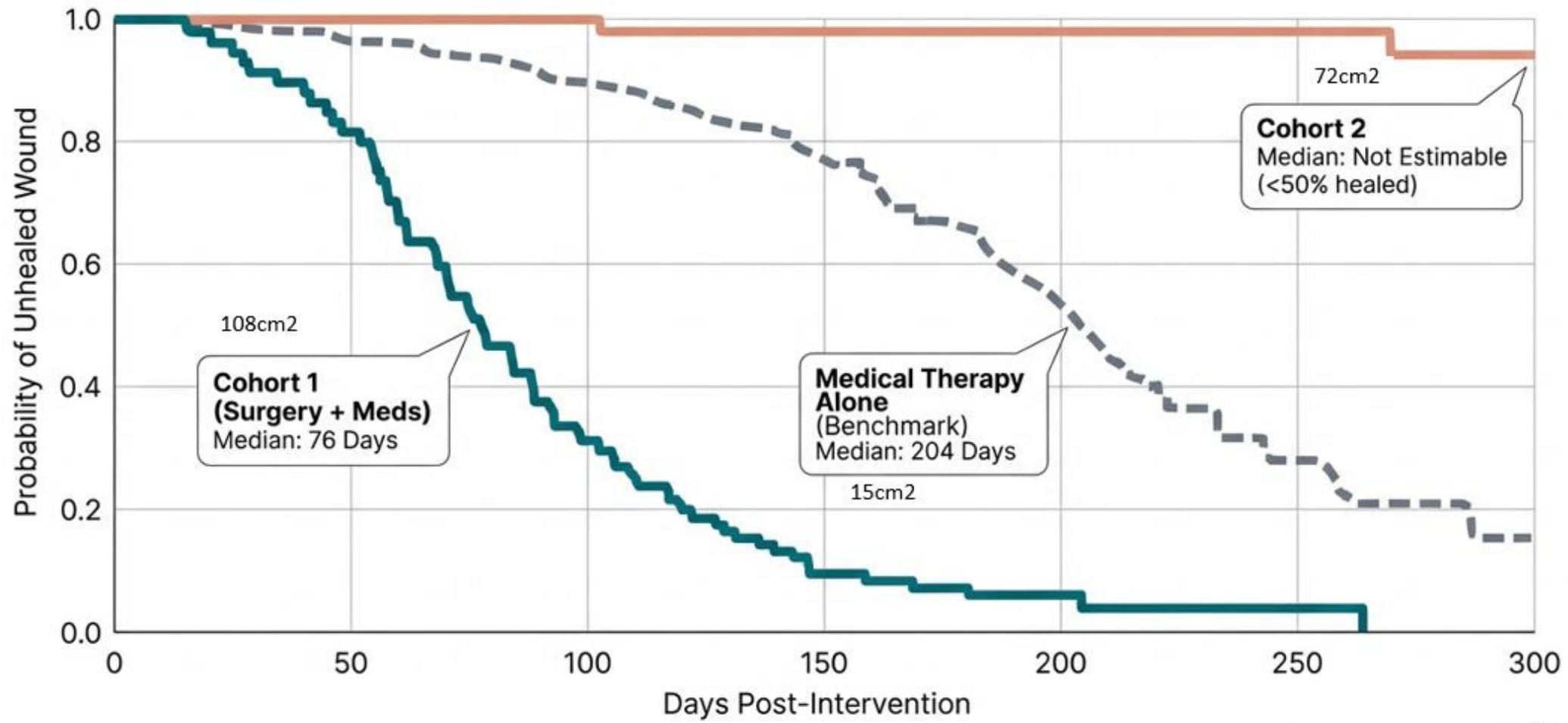


Baseline Characteristics	Cohort 1	Cohort 2
Median age	53	54
Sex (Female)	71%	76%
Comorbidities*	24%	24%
Smoking history	65%	65%
Pathergy history	59%	65%
Median wound duration	6	5

*Comorbidities primarily IBD and RA

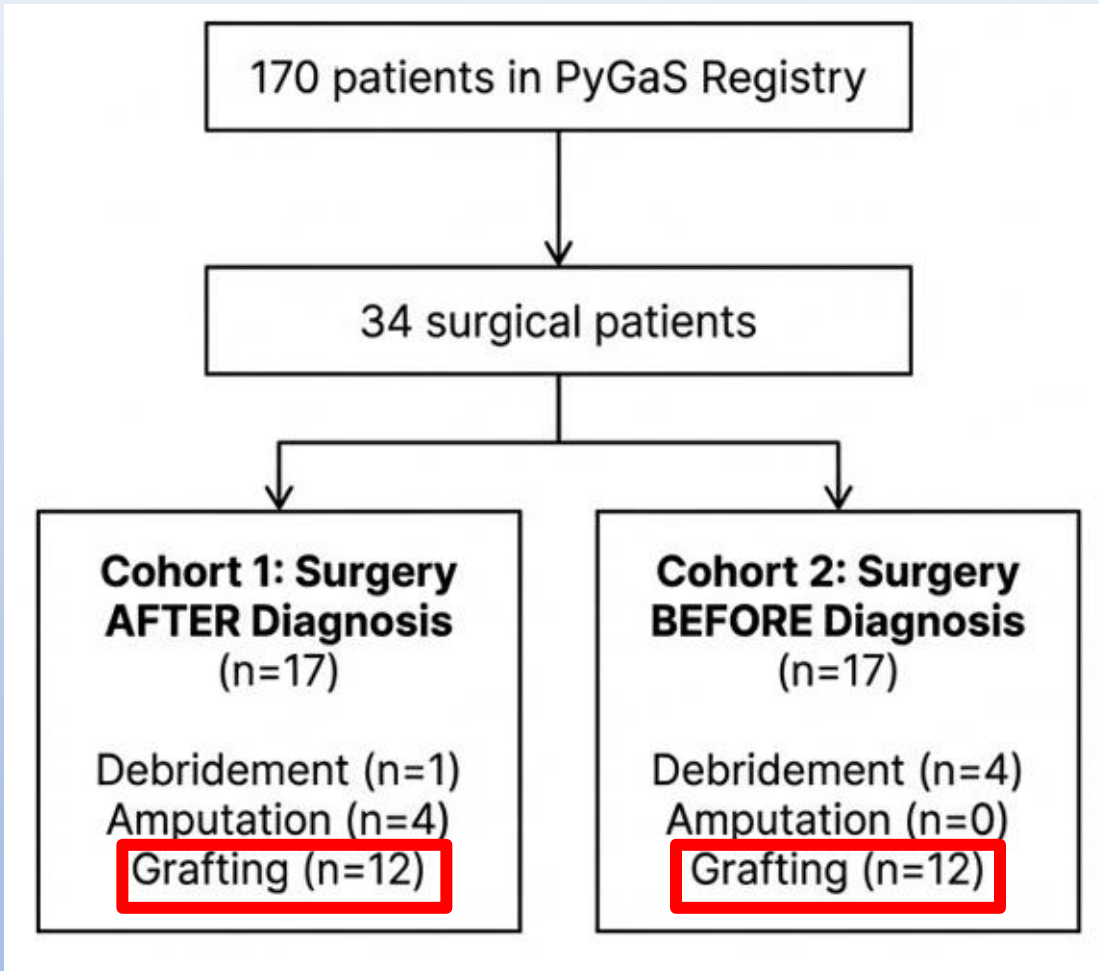
Two Nearly Identical Populations, One Critical Difference

Across All Surgical Procedures



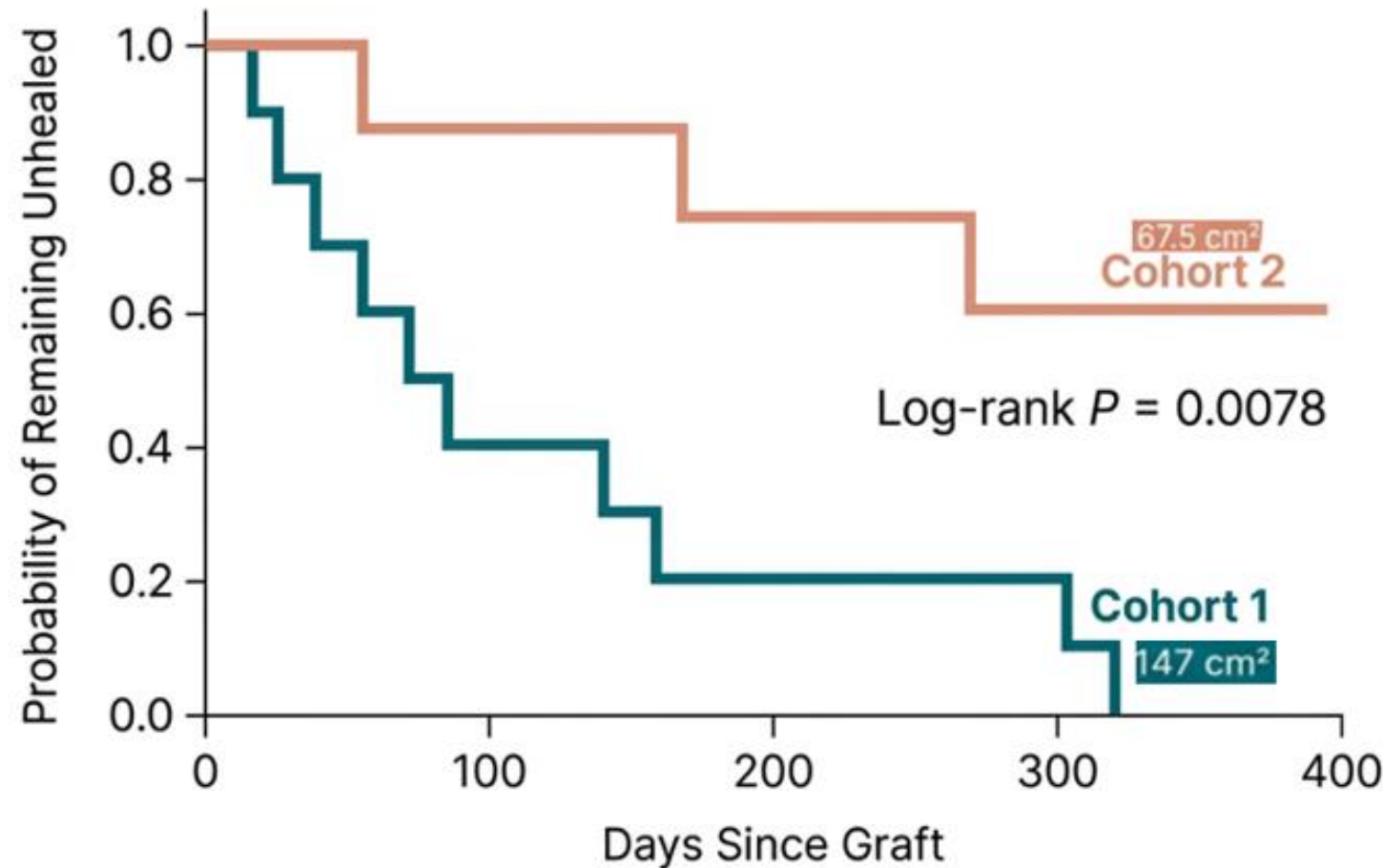
NotebookLM

Grafting Sub Analysis



Baseline Characteristics	Grafting Cohort 1	Grafting Cohort 2
Median age	50	51
Sex (Female)	75%	83%
Comorbidities *	24%	24%
Smoking history	58%	67%
Pathergy history	58%	60%
Median wound duration	6	5

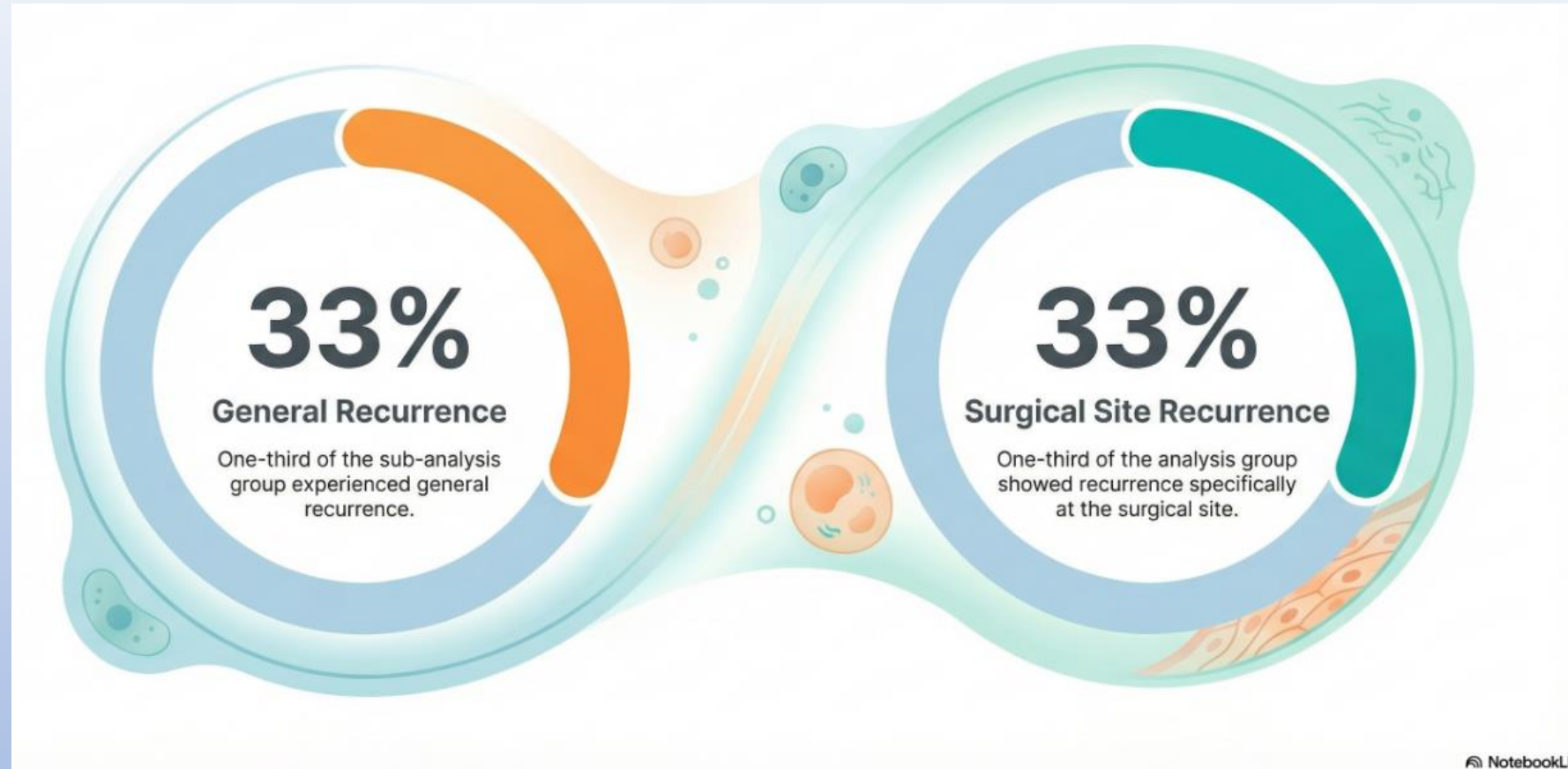
Healing time is shorter in the cohort that received the diagnosis of PG before skin grafting



Median time to healing
(Cohort 1): 64 days

Cohort 2 could not be
estimated (<50% healed)

Recurrence Rates Similar to Clinical Trials



Across all healed grafts
33% surgical site recurrence Cohort 1
33% general recurrence (25% cohort 1, 8% cohort 2)

2) Appraise future research: Novel outcome instrument

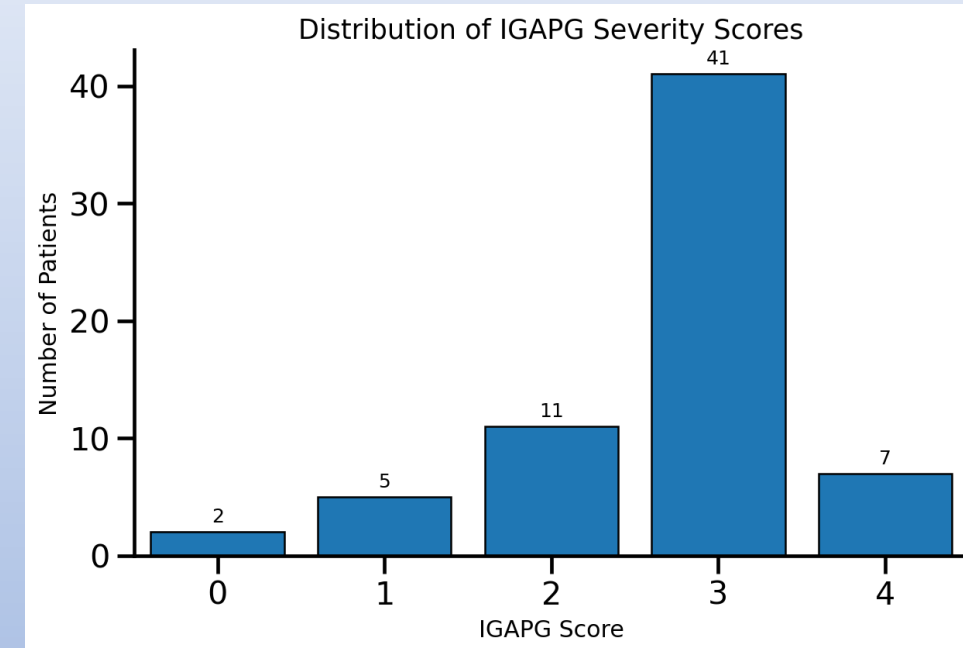
IGAPg

The score is selected using the descriptors below that best describe the overall appearance of the majority of the involved area at a given time point. For a rating of clear, all three morphological descriptions must apply to all of the involved tissue. It is not necessary that all characteristics under *Morphological Description* be present. Please include all affected areas in their totality.

Score	Morphological Description
0-Clear	Complete re-epithelization. No redness. No accumulation of drainage on the surface of the ulcer.
1-Almost Clear	Erosion. Light redness around the ulcer borders. The wound surface is moist.
2-Mild	Ulceration extends to the dermis. Dull redness around the ulcer borders. Presence of pooling regions of exudate on the surface of the ulcer.
3-Moderate	Ulceration extends to the subcutaneous tissue. Bright redness around ulcer borders. Presence of a confluent layer of exudate covering the wound surface. Undermining may be present in <50% of the ulcer borders.
4-Severe	Presence of muscle, bone, or tendon in the ulcer. Violaceous/gunmetal grey discoloration around ulcer borders. Blistering may be present in the periwound area. Evidence of a layer of exudate extending beyond wound borders. Undermining may be present in up to 100% of the wound borders.

In indeterminate cases, please use extent (size and/or quantity of lesions) and/or involvement of special sites (head, neck, and/or genitalia) to differentiate between scores

© 2025, Oregon Health & Science University



TAKE HOME MESSAGE: COMPREHENSIVE MANAGEMENT OF PG



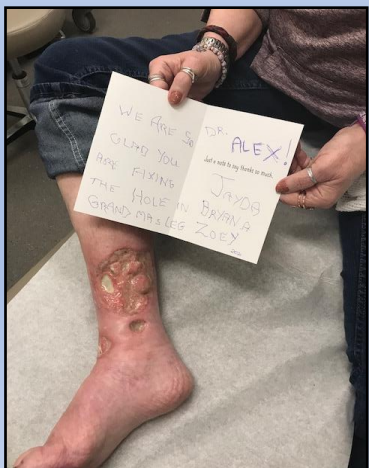
**CONTROL
INFLAMMATION**

**OPTIMIZE
WOUND CARE**

**ADDRESS
PAIN**

message
Tue, Nov 6, 5:15 AM

Dr. Ortega, this is [REDACTED]
[REDACTED] I wanted you to know that Michael, after a 9 month battle with so many different illnesses, spending most of his time at VCU, went to Heaven on Saturday morning. We were going to take a last picture of his PG because it was almost completely healed, even with the low blood counts the last 3 months, but we never got around to doing that. Not only were you Michael's Dr, he considered you friend. In the days to come I will look at his pictures and send the latest ones to you of the PG for your research.



PHYSICIANS TEAMING UP TO ID AND TREAT MAKEBA'S RARE SKIN CONDITION

A dermatologist and a plastic surgeon work together to identify the source of a patient's persistent ulcer— and craft a treatment plan to recovery.

Makeba Garner, Patient

Alex Ortega, MD

EC



Last Saturday was the two year anniversary of my first appointment with you. Jeff and I talked about how it doesn't seem like it has been that long. More like a year ago.

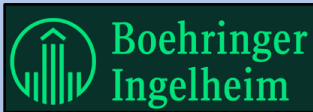
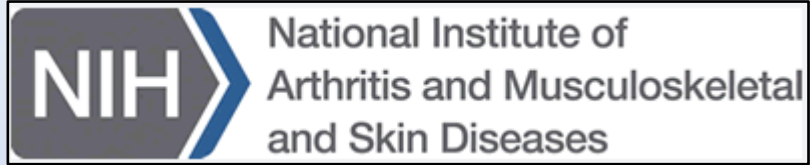
5/19/26 10:49 PM

I remember feeling like I may never get my health back, and that I would have to stop doing many of the things I like to do.

Thank you so much for all of your help and guidance in restoring my health. And in keeping me wound free. I have been able to do all the things I did before-with more joint issues as I age. Never in a million years did I think, back then, that I could handle something like buying and moving to a house I love.

I hope you and your family are doing well.

Acknowledgements



*Ortega's Lab

- Sharon Choe
- Alexandra Phillips
- Emilie Foltz
- Laura Morales

*PYGAS Group

- OHSU medical students and residents

*OHSU Biostatistics

- Emile Latour
- Jeong Youn Lim

*UPGRADE Leadership

- Sanna Prinsen
- Arash Mostaghimi
- Ben Kaffenberger

*OHSU Collaborators

- Eric Simpson
- Jesse Keller
- Nicole Fett
- Olivia Lucero
- Josh Moreau

Email: ortegalo@ohsu.edu

X: @ThePGguy