Inconvenient Truths about Chronic Wounds from Real World Data

April 17: 10:00 – 10:30

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2019 Analysis of Medicare claims for wound care (complete Medicare dataset)

- Started with the complete list of diagnosis codes seen in ~200 outpatient wound clinics obtained from the US Wound Registry
- 16.4 % of Medicare beneficiaries have a chronic wound
 - ▶ 10.5 million people
 - Prevalence up by 3.4% since 2014 (particularly among patients < 65)
- Most expensive and most common:
 - Surgical complications
 - Pressure ulcers
- The "wounds with no name" still represent a staggering percentage meaning the "chronic ulcer" and the "traumatic wound"
- Cost: Estimates: \$22.5 billion to \$67.1 billion
- Most costs are outpatient
 - Costs have shifted from the HOPD to the physician's office and the home

Chronic wound prevalence and the associated cost of treatment in Medicare Caroline E. Fife¹³

beneficiaries: changes between 2014 and 2019

Taylor & Francis

8 OPEN ACCESS A CHARLES

Marissa J. Carter^a 🚳, Joan Dalfanzo^b, Randall Haught^b, Marcia Nusgart^a, Donna Cartwright^d and

Betherda, MD, USA: "Integra Lifeciences, Princeton, NJ, USA: "Baylor College of Medicine, Houston, TK, USA: "The US Wound Registry.

distribution to determine the cool of second care and presidence of charact seconds for Medican Investigation in the appearance for property by second type, and by certaing between the proc. 2014 and 2019. Methods: This recorporate analysis of Medicans claims dura included beneficiales who experienced six, excluding any kind of deductible), bit mid (primary plus secondary diagnosis with weighted attribution), and (p) high (primary or averaclary diagnosis). The make mixtures, were the presidence of each second laye, Methode expenditure for each second laye, Methode expenditure for each second laye, and approprie, and expenditure for

type of service. Benefits the the X-year pointed the number of Merkicus benefits into white a numeral interaction for XX coulines in 15% reliable. When the Year interacted by 15% from 15.4% in 15.4% for the Year point. As the Armine benefits the wint the largest interaction in others in county developed were those copie of Argonic pointers and the Armine State of decisions in transactive wounds. Lank to Lank, Operational document impaction of the three methods and with a reflection of \$707 fellow in \$725 fellow for the med conversalism medical burget for versus, sizes, in which crob, per Medicare investigation of the two states of \$700 feel per wound document of the states of the s \$2500, and the largest decrease for artest stores (\$900) to \$2500. Regulal entpotient less saw the Largest reduction (\$355 billion to \$25 billion) although home brooks arrange expenditures decreased from 51 a believe to 51.1 billion. Physician offices saw an increase from 51.0 billion to 51.1 billion and deadlife method organization increased from 93.0 billion to 950 billion billion to 51.1 billion and Condensione II approxi. Billion of thems: second one expenditure, have shifted to the physician's efficient

from the hospital-based outpatient department. Given that the prevalence of chronic wounds is increasing, especially among the challed realer 80, 8 will be important to know whether those shifts have profiledly or regulately affected relationers.

• in 2014 cheanic wounds impacted 14.5% of Medicare beneficiaries but this increased to 16.3% by In 2014 channel wounder impaction 1474 of the docume beneficiates but the increased to 14.0% by 2018. The group of Medicare beneficiation most afficient in stems of channel sound generalizate over the 3 years period were those aged 465 years (seeler 12.5% in 16.7%; breaker 15.5% to 1.20%). The largest changes in stems of preventions were increased in anterial ulcors (s.em to 0.0%), doi: disordiest (2.6% to 3.2%), and traumatic wounds (2.2% to 1.4%).

 Over the 5-post period, regardless of the method exed, there was a decrease in chante woun lecrease from 2014 to 2019 of \$6.1 billion to \$6.9 billion, itseed on the most consensative a there was a very large cost reduction observed for outgatesets from \$150 billion to \$2.0 billion, with a correspondingly smaller doctories for impatients of \$3.3 billion to \$4.2 billion, but on increase from \$100 billion to \$4.1 billion for physician offices, in addition, while duable medical equipment.

1980 NCT Joan Dillano 🕮 juan daman perintranda anno com 🕾 Dobron Dallano A Associato II.C. Woma, VA, 1886

Supplemental data for this wride can be account online at terps://doi.org/10.1000/1.000001.00000.2002.2002.56.

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https://www.tandfonline.com/doi/full/ 10.1080/13696998.2023.2232256

RCTs don't study the most common problems

▶ Diabetic foot ulcers: 0.7%

Venous Ulcers: 0.9%

Pressure ulcers: 1.8%

► Surgical wounds: 3.0%

Traumatic wounds: 2.8%

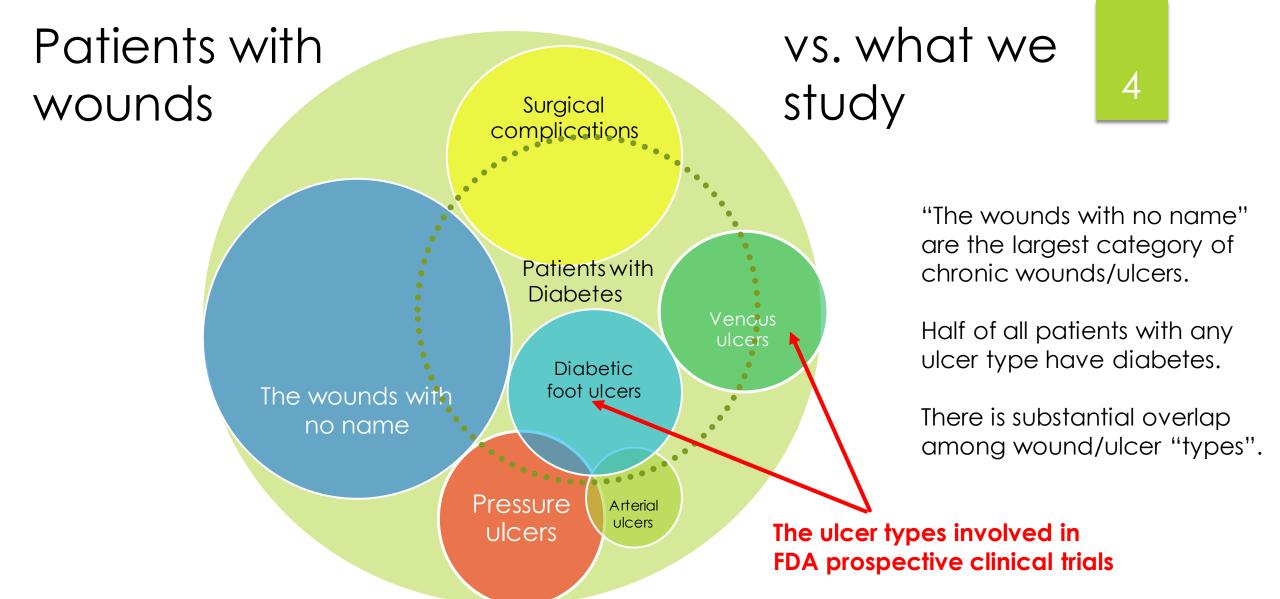
► Chronic ulcers: 2.3%

3.8%

5.1%

The most prevalent wound type are "the wounds with no name" (traumatic wounds that don't heal and chronic ulcers that aren't DFUs, VLUs ore pressure ulcers).

https://www.valueinhealthjournal.com/article/S1098-3015(17)30329-7/fulltext



The design of RCTs has real world implications for Medicare coverage policy

- 1999
- > 72 y.o. female
- Rheumatoid arthritis on prednisone and methotrexate
- Non-insulin dependent diabetes-poorly controlled
 - 5-month history of enlarging leg ulcer due to minor trauma



Healed with NPWT and a cellular product.
Why was this Medicare fraud?

The design of RCTs has real world implications for Medicare coverage policy

Exclusions in the RCTs

- No ulcers that expose muscle, tendon, bone or joint
- Alcohol/drug abuse
- Anticoagulant treatment
- Cellulitis or local wound infection
- Cancer or recent cancer treatment
- Collagen vascular disease/connective tissue disease
- RA/Scleroderma, Lupus any autoimmune disease
- Charcotfootchanges
- Corticosteroid treatment
- Gastrointestinal disease of any type
- Renal disease of any type
- Any organ transplant
- ▶ In diabetics. HbA1c > 8-10
- Nutritional impairment/Albumin < 3.0 mg/dl</p>
- Osteomyelitis
- Peripheral arterial disease

Requirements in the LCD for a "skin substitute"

- "...not involving tendon, muscle, joint capsule, or exhibiting exposed bone or sinus tracts."
- "Elimination of underlying cellulitis, osteomyelitis, or other infection"
- "Appropriate debridement of necrotic tissue
- "Only applied to wounds with adequate circulation/oxygenation"
- "...must not be provided to patients with:
 - uncontrolled diabetes
 - Sascullus
 - rheumatoid arthritis or rheumatoid ulcers
 - radiation and/or chemotherapy within one month immediately preceding application
 - ongoing use of high-dose corticosteroids or immunosuppressants

We don't have the ICD10 codes we need

- Ulcers
 - Pressure ulcers
 - Venous
 - Chronic Non-pressure
- Ulcer types without codes
 - Arienal dicers
 - We can only identify these as "chronic non-pressure ulcers" in patients with atherosclerosis
 - Diabetic feet ulcer
 - We can only identify these as "chronic non-pressure ulcers" of the foot in diabetics



*the International Classification of Diseases 10th Revision (ICD-10) developed by the World Health Organization (WHO)

We can't clearly classify most wounds/ulcers: Can you name this ulcer?



Photo property of C. Fife, MD

A heel ulceration in a diabetic with peripheral arterial disease would be best diagnosed as a:

- A. Pressure Ulcer
- B. Diabetic foot ulcer ("Non-pressure Chronic ulcer")
- c. Arterial ulcer ("Non-pressure Chronic ulcer")

Wound Subjects in RCTs vs. Wound Patients in the Real World

- Among 8,611 wound center out-patients, > 50% would have been excluded from 15/17 major RCTs
 - 88% wound related RCT patients excluded at the "first pass"
- 3 of 4 major trials bringing new products to market enrolled patients healthier than the "girl on the street"



"Show girl" trials

- Average patient age:
 - 60.4 (1 104) years
 - ~2020
 - 24% with CAD
 - <1% current smokers</p>
 - 8.4% on steroids
 - 8% have renal failure or transplant
 - 54% of wounds that were not specifically diabetic foot ulcers were in patients who had diabetes



[&]quot;Estimating the Applicability of Wound-care Randomized Controlled Trials to General Wound Care Populations by Estimating the Percentage of Individuals Excluded from a Typical Wound Care Population in Such Trials:" Marissa J. Carter, Caroline E. Fife, David Walker, Brett Thomson, Advances in Skin and Wound Care, 2009, 22: 316-24.

Table 2. An in-depth comparison of patient demographic and clinical characteristics of a venous leg ulcer randomized controlled trial^{37,43} of a wound case-specific research network vs. the real-world patient dataset in the network's internal consortium of clinics

	VLU RCT dataset			Consortium
Variable	Allograft (n = 53)	SWC (n=31)	Total (n = 84)	dataset (n = 856
Total number of VLUs, n	53	31	84	1,943
Mean age, years	59.0	62.6	NA	70.6
≥65 years, n (%)	21 (39.6%)	11 (35.5%)	33 (39.3%)	586 (68.5%)
Race/ethnicity, n (%)				
White	NA	NA	39 (88.6%) ^a	705 (82.4%)
Black/African American	NA	NA	NA	34 (4.0%)
Hispanic ethnicity	NA	NA	NA	2 (0.2%)
(PAD or atherosclerosis, b n (%)	Excluded	Excluded	Excluded	121 (<mark>14.1</mark> %)
Congestive heart failure, n (%)	Excluded	Excluded	Excluded	133 (<mark>15.5%)</mark>
Mean no. of wounds per patient, n	Unknown	Unknown	Unknown	5.3°
Mean wound duration, weeks	58.4	56	NA	8.6
Mean initial wound area, cm²	6.0	6.3	NA	31.3
Initial wound area ≥20 cm ² , n (%)	Excluded			
No. of patients with VLUs ≥20 cm ² No. of VLUs ≥20 cm ²		Excluded	Excluded	308 (35.9%) 509 (26.2%)
No. of VLUs with reduction in wound size by ≥40% at 4 weeks, n, %	33 (62.3%)	10 (32.3%)	43 (51.2%)	1,613 (83.4%) ^d
Mean reduction in wound size at 4 weeks, %	48.1%	19%	NA	-46.3% ^e
No. outcomed as healed at 24 weeks, fn (%)				
No. of patients outcomed as healed	NA	NA	24 (54.5%) ^a	605 (70.7%)
No. of VLUs outcomed as healed	NA	NA	24 (54.5%) ^a	1,427 (73.4%)
Mean time to heal, weeks	NA	NA	NA	18.6
Mean weeks in service ^g	4	4	4	20.4
Mean Wound Healing Index score	75.9 ^h	75.9 ^h	75.9 ^h	69.3

NA, not available; PAD, peripheral arterial disease; RCT, randomized controlled trial; SWC, standard wound care; VLU, venous leg ulcer.

Serena TE, Fife CE, Eckert KA, Yaakov RA, Carter MJ. A New Approach to Clinical Research: Integrating Clinical Care, Quality Reporting, and Research Using a Wound Care Network-based Learning Healthcare System.

Wound Repair Regen. 25(3): 354-365,

Wound Repair Regen. 25(3): 354-365, 2017.

^aData from 44 participants of original RCT who participated in a follow-up study⁴³; ^bbased on an ankle brachial index >0.75; ^cincludes all wound types; ^ddata available for 1,933 VLUs; ^e18 VLUs increased in size over 10-fold; ^fdefined as complete epithelialization; ^gfor RCT only, follow-up retrospective study looked at 24 weeks for 44 patients from the RCT; ⁴³ ^hestimated.

Chronic wounds are a SYMPTOM, not a disease

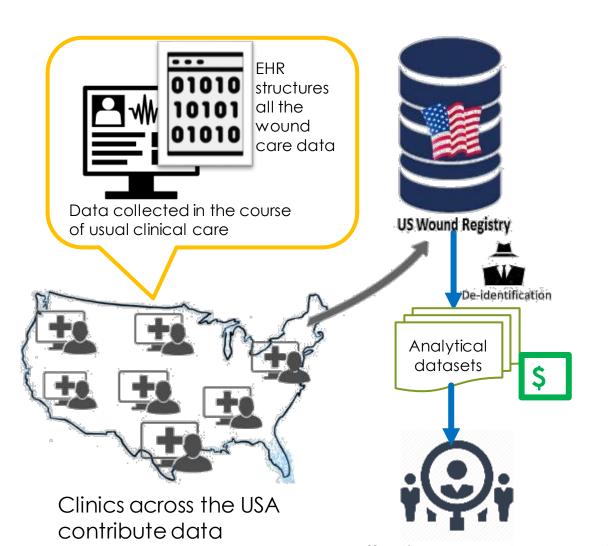
- The mean number of serious conditions per patient is 8
 - ▶ 59.9% had utility values for comorbidities/conditions, which were worse/lower than their wounds' values.
 - ▶ The mean minimum utility value was 0.5
- Nutritional deficits are rampant but underdiagnosed
 - Malnutrition and nutrient deficiencies (both diagnosed and undiagnosed) are rampant
 - ▶ 68% of chronic wound patients score at risk or malnourished on the Mininutritional assessment
- ▶ The average patient with a non-healing wound takes 12 medications
 - Many drugs significantly impact healing

The Impact of Underlying Conditions on Quality-of-Life Measurement Among Patients with Chronic Wounds, as Measured by Utility Values: A Review with an Additional Study. Adv Wound Care (New Rochelle). 12(12): 680-695, 2023.



Meds taken by a patient with a chronic "venous ulcer"

Registries directly from an EHR (e.g., USWR)

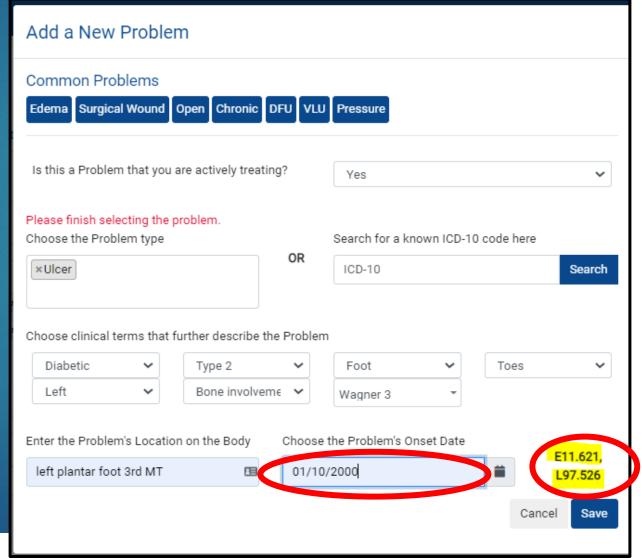


- Clinical data are entered at the point of care in real time
- The electronic medical record (EHR) collects the data in a format for research or "research ready" data
- The entire EHR is structured (all medications, conditions, treatments, etc.)
- There is no secondary data entry by anyone no extra work
- Patients/wounds are followed until outcome
- Data are aggregated inside the US Wound Registry (USWR) which is a Medicare recognized "Qualified Clinical Data Registry" (QCDR)
- No patient consent is needed
- The entire treatment course of each wound is known
- The Wound Healing Index (WHI) is available to create matched cohorts
- Data are collected on all products making CER possible.
- Data continue to accrue due to normal product usage
- All costs are associated with data use and analysis
- There is no selection bias because data are collected on all patients and all wounds

Effectiveness and comparative effectiveness research (CER)

To obtain real world data, we first need to know the correct diagnosis.

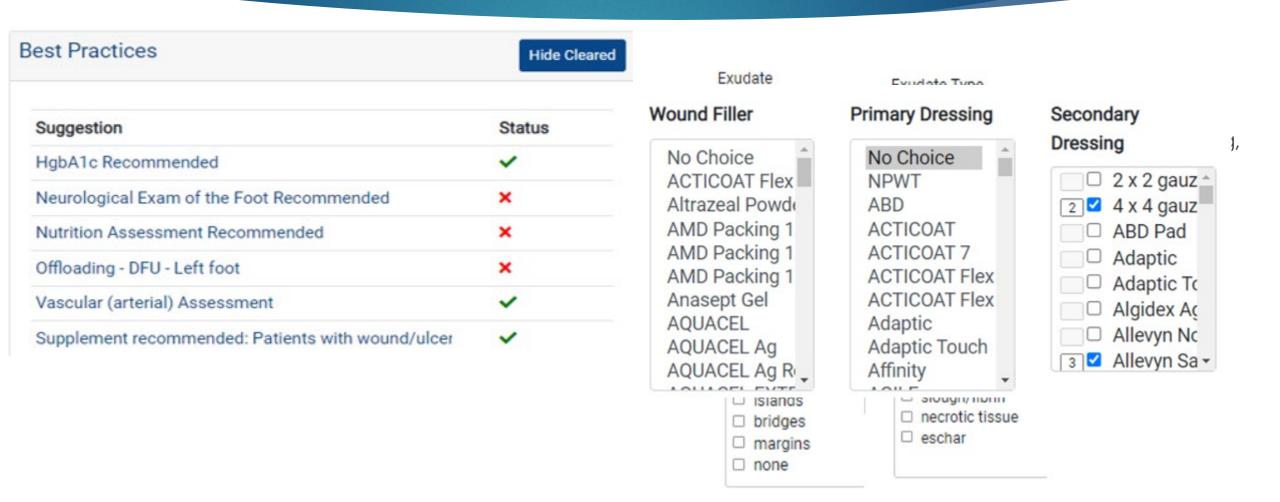
Without specific ICD10-CM codes for DFUs and arterial ulcers, "linked codes" must be created.



A DFU is identified with a combination of the code for diabetes and a chronic ulcer.

This means that research can be done knowing the clinician identified the problem as a "DFU."

RWD requires collecting structured observational data and knowing whether SOC was provided



Real world wound observations

Exudate Amount – in wound-visits

None: 18%

Minimum: 28.8%

Moderate: 46%

▶ Large: 7.1%

Exudate characteristics:

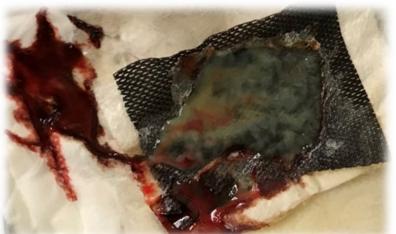
► Malodorous: 35%

Frankly bloody drainage since the advent of new oral anticoagulants

-46.8% none to minimum

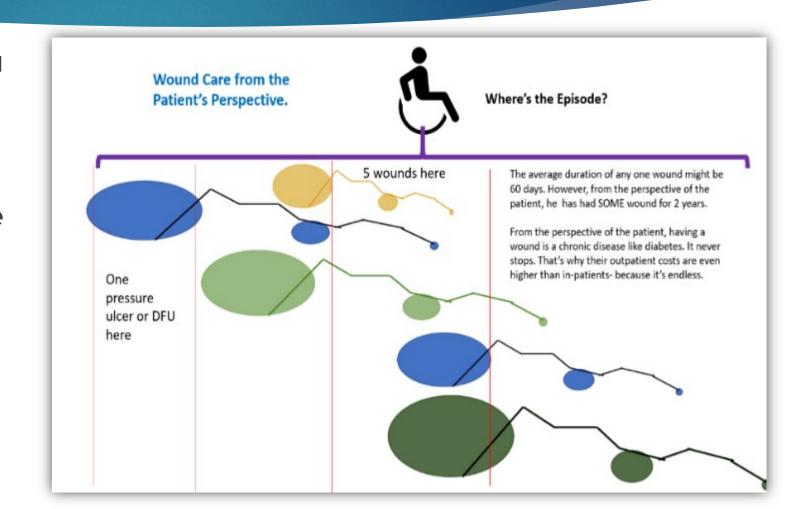
53.1% moderate to large





We need the perspective of the patient and not the ulcer

- About 40% of patients get a new wound while still in service for the original one
- Healing likelihood is inversely proportional to the total number of wounds present on the body
- Wounds are rarely of the same type



Reported "Healing Rates" are a fantasy

- ► A systematic analysis of 48 RCTs:
 - > 2,620 control subjects; 2,624 wounds
 - Overall healing rate for controls: 40%

In a systematic survey of wound center websites from all US States, 85% reported a **mean healing** rate of 92%, usually within 4.3 weeks.

Inflated healing rates may represent the biggest threat to innovation.

Controls in RCTs

- PUs: 40.0% (2 trials)

VLUs: 42.7% (20 trials)

DFUs: 37.9% (26 trials)

USWR at 12 weeks ~35%

PUs: 29.6%

VLUs: 44.1%

DFUs: • 30.5%

USWR ~ 48% (no time limit)

56.9%

43%

45.1%

https://www.liebertpub.com/doi/10.1089/wound.2017.0743

Risk stratification is mandatory (It's the comorbid conditions that determine healing...)

- The DFU WHI score has a value of 0-100 and incorporates the following parameters:
 - Patient age
 - Patient ambulation score
 - ☐ Patient disposition at end\of evaluation visit
 - Concurrent number of wounds
 - Patient on dialysis or is post-renal transplant
 - Patient has PVD
 - Wound area
 - Wound age
 - Wagner grade
 - DFU infection/bioburden status

Fife CE, Horn SD, Smout RJ, et al. Adv Wound Care 2016.

Patient

Parameters

Parameters 4 8 1

Wound

Development of a wound healing index for patients with

Susan D. Horn, PhD'; Caroline E. Rife, MD'; Randall J. Smout, MS'; Ryan S. Barrett, BS';

I restrate for Clinical Companies Senantin Soft Lake Clin Linth and

Sergile, Suits 200, Sull Luky City, 63-

Manuscriet received: May 25, 2012 Accepted in final form: degree 17, 2013

Endonized correlled trids is would one ground to peerly because they endule nations with significant compated conditions. Research using real-world wound care patients is hindered by lack of radialated methods to shallby patients according to according to according filterases. We developed a comprehensive stratification coston for patients with wounds that predicts healing likelihood. Complete medical accord data on 50,967 sounds from the United States Wound Registry were assigned a clear outcome (healed, amputated, etc.). Factors known to be associated with healing were evaluated using legistic organism moticle. Significant variables (p.< 0.05) were determined and subsequently intent on a holidour sample of data. A different modell produced leading for each second eye, Some variables produced participation significantly in mostly all modelic wound now, wound use, member of wounds, evidence of histories, trease type exposed (Wagner grade or stoge), being nonambulatory, and requiring hospitalization during the course of care. Variables significant in some models included retail failure, sensi transplant, malmortton, autoimmune disease. and conferenceing thouse. All tracks validated well when applied to the heldout more and would periods and our facilities comparative effectiveness session to

Randomized controlled trials (BCTic) are the gold statulard to determine clinical efficacy, defined as whether an intervention can be succeeded when properly implemented under contolled-conditions. Patients with chorac wonds suffer from believes and blace who assistant beforest to shortless then from nearly every BCT performed in the past 10 years.²
A recent Journal of the American Medical Americans article emphasized that future studies trust include analyses of patients with consorbid conditions. In authors state that analtronus, rid-sential analysis based on early obtainable classed variables are "frequently feasible, but surely persuch studies has been the lack of a validated method to often risk stratification.
The Centers for Medicate and Medicaid Services has

advanted and that there is beauty to analysing real-world. data to facilitate wound care research. A byproduct of door nothing care within electronic health records (EEELs) is the shifty to nine these fate for clinical research enterties, a concept promoted by The hottude of Medicine," Longitudnelly ledged tillle deatheast are a source of data for com-parative effectiveness research strongly supported by The Federal Coordinating Council for Comparative Hillectiveness

wound centers may not leaf their wounds even though they are eased for over a long period of time (outcomes include over the past two decades have identified specific wound and

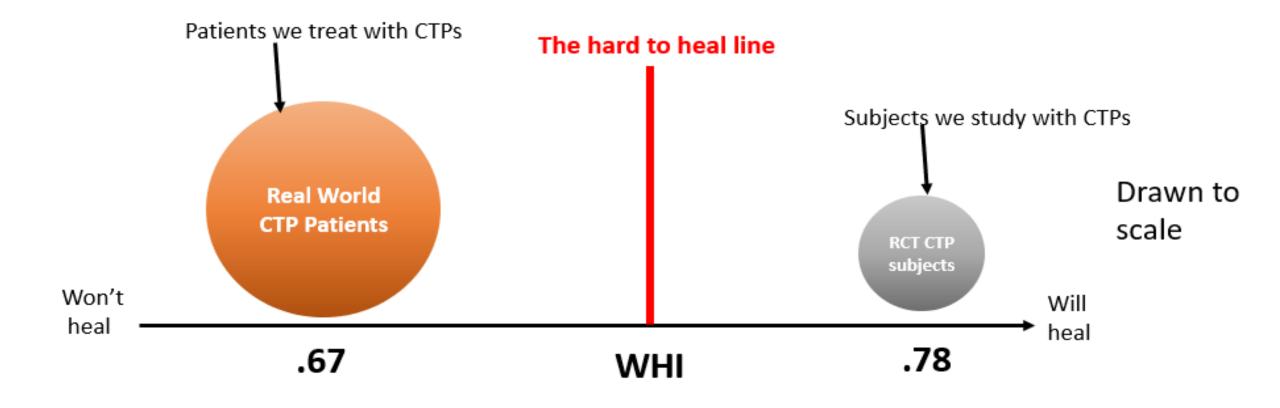
Prefictive factors of failure to heal specific to the wound itself include nior Gloph, was, and dismoted known to negatively affect wound healing include send fallace, the age, and periphent arterial discus-Faroquet conten considered IMD, when cornerhal with disbetic first alons (DFUs), to be a separate disease state comtronleading in patients with both DFUs and PAD." In addia predictive effect on healing, including negative pressure wound therees, beneforie experie therees recorners namelies

patient factors known to have a negative intract on healing

Contrahenalys Severtly Index Decironic health record Clinical Health Intelligent Resource Companyon

Periphose arterial disease Persoun Quality Reporting Section Would Healing Index

The WHI suggests that most subjects enrolled in CTP RCTs would get well on their own



USWR Data on the use of CTPs

- Date range: 2/1/2021 1/23/2024 (~33 months or 2.75 years)
- Clinics/practices/SNFs: 484 (majority HOPD)
- Practitioners: 879
- Patients: 116,926 patients 3.6 wounds/patient
- Wounds/ulcers: 418,770 wounds
 - ▶ There were only ~2 concomitant wounds per patient on the date of CTP application
- ► CTP treated wounds: 5,544 (1.3% of all wounds/ulcers)
- CTP brands: 115 (analysis was brand agnostic)

Inconvenient truths about Real-world CTP applications regardless of wound type

- Tissue type exposed on the date of application
 - ▶ Sub Q: 53% (compared to 34% of all wounds)
 - ► Muscle: 7.1% (2.1% overall)
 - ► **Tendon: 5.2%** (0.8% overall)
 - **▶ Bone:** 10.4% (2% overall)
 - Others (unknown, epithelium, fascia, intact skin, adipose)
- ▶ Green/malodorous drainage
 - ▶ 3.1% (vs. 1.7% overall)

22.7% of applications (in which the procedure is properly documented) are over deep structures

Inconvenient truths about Real-world CTP applications regardless of wound type

Non-viable tissue

Not recorded: 10.7%

None: 3% (vs.7.5% overall)

►0 - 25%: 8.9% (vs. 7.1% overall)

25-50%: 12.6% (vs. 7.4% overall)

Over 50%: 64.7% (vs. 25% overall)

77.3% of CTP applications (in which the procedure is properly documented) are in wounds with $\geq 25\%$ necrotic tissue.

CTP use by wound type

Wound/Ulcer type		CTP Rx % of that ulcer type
Chronic ulcer	51,508 (12.3)	1,070 (19.3)

Overall, there are far more chronic ulcers than DFUs, but DFUs represent the wound type most commonly treated with CTPs, followed by VLUs (due to payer coverage).

Ugly truths about Real World CTP use

- Wound Type (it's not DFUs and VLUs)
 - ▶ We most need treatments for the "nameless wounds/ulcers"
- Wound severity
 - ► They are routinely applied over deep structures
- Wound bed prep:
 - ► They are routinely used over wounds with non-viable or necrotic tissue
- Quality of Care:
 - ▶ DFU off-loading on application visit: 44.4% (2,987/6,724)
 - ▶ VLU compression on application visit: 66.3% (2,878/4,342)
 - (I am not presenting data on lack of arterial screening, lack of nutritional screening or other ways that LCDs are breached)



Ugly truths about Real World CTP use

- Patients have more than one wound at a time
 - ► Overall: Median 2 (1-13; SD 1.4)
- ► Each wound is bigger than most of the available products affordable in the HOPD
 - ► Overall max per wound: Median 9.4 cm2
 - ► At application: Median 3.7 cm2

Regardless of contributing factors, all wounds heal via an identical process



Photos property of C. Fife, MD

Ulcerated hematomas, dehisced surgical wounds, pressure ulcers, and neuropathic DFUs all heal the same way – granulation and then epithelialization.

Diabetes does not a "diabetic ulcer" make

Many patients with VLUs and pressure ulcers have diabetes.





Photos property of C. Fife, MD Do not reproduce without permission

Both these patients have diabetes. That does not make these diabetic ulcers.

All of these diverse problems are "DFUs" – Most in the real world are Wagner 3 – not Wagner 1!









Venous reflux does not a VLU make







All 3 of these were originally coded as venous leg ulcers because the patients have venous reflux.

Between 25% and 50% of problems called "VLUs" in the real world are NOT venous ulcers.

We ignore a lot of VLUs in research

>30 % of ulcers classified as venous can't be measured as discrete lesions









By the way, these are all of the same patient over a 2-year period.

These acute wounds/blisters from edema will be coded as VLUs







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Blisters are due to profound edema, usually acute on chronic heart failure, with or without sleep apnea. They will be coded as "venous leg ulcers" so that needed compression bandaging is covered by payers.

All non-healing traumatic wounds are really chronic ulcers





A traumatic wound that has not healed in 30 days is supposed to be re-coded as a "chronic ulcer" but often continues to be called/coded as a traumatic wound.

The future of innovation depends on risk stratification and honest outcomes reporting

This practitioner heals 70% of the ulcers that had a 25-50% chance of healing.

In this case, a 70% healing rate is a HUGE success.

The target for advanced therapeutics are not the wounds that are expected to heal or those that can't be healed, but the wounds that can be healed with intervention.

