

Appendix C: Guideline

International Consolidated Venous Ulcer Guideline (ICVUG) 2015 (Update of AAWC Venous Ulcer Guideline, 2005 and 2010)

Scope of Guideline and Definitions

This clinical practice guideline contains systematically developed recommendations intended to optimize patient care and assist physicians and other health care practitioners and patients to make decisions about appropriate health care for venous ulcer (VU) clinical care. The guideline includes the following:

- a. Best available evidence (See Strength of Evidence Ratings)
- b. Expert consensus of opinion (Delphi) with clinical relevance for venous ulcers confirmed by formal content validation by 23 independent multidisciplinary experts in venous ulcer care (See *Content Validity Index* in Legend)
- c. Assessment of the benefits and harms of recommended care (See *Strength of Recommendation* ratings defined in Legend).
- d. Evidence tables (Available at www.aawconline.org)

A venous ulcer (VU) is an open skin lesion of the leg or foot that occurs in an area affected by venous hypertension (O'Donnell 2014). This condition is associated with lower leg swelling (edema) which can progress to dermatitis and VU formation. It may result from incompetent venous valves in the superficial, perforator or deep vein systems and/or inadequate calf muscle pump function (Tang et al. 2012) A VU is considered chronic if it is unresponsive to best-evidence-based management, i.e. reduces in area less than 40% in 3 weeks (Phillips et al., 2000).

The ICVUG Recommendations were derived from systematic literature reviews plus all unique major recommendations contained in Source Documents listed below to serve all wound care disciplines who manage patients with a venous ulcer. As with all evidence based practice recommendations, best available evidence should be considered in conjunction with clinician experience and expertise as well as patient needs, abilities and preferences.

ICVUG Guidelines Were Derived from Systematic Literature Reviews Plus Specialty Sources Below:

1. Alexanderhouse Group. Consensus paper on venous leg ulcers *Phlebology* 1992; 7:48-58.
2. Alguire PC, Mathes BM. Chronic venous insufficiency and venous ulceration. *J Gen Internal Med.* 1997; 12:374-383.
3. Angel D, Sieunarine K, Flexman J, Fraser D, Tibbett, P, Nyal L. Nurse practitioner management of lower leg ulcers in the adult population clinical protocol. Royal Perth Hospital and South Metropolitan Area Health Service, Department of Health, Government of Western Australia. 2007.
4. Black SR Venous stasis ulcers: A review. *Ostomy/Wound Management*, 1995; 41(8):20-29.
5. Burton CS. Venous ulcers. *Amer J Surg* 1994;167(Suppl 1A):37S-39S.
6. Cherry GW, Cameron J, Ryan TJ. Blueprint for the treatment of leg ulcers and the prevention of recurrence. *Wounds* 1993; 3:2-5.
7. ConvaTec. [SOLUTIONS® wound care algorithm](#). 1994 (revised 2013 Sep). NGC:010274 Accessed November 1, 2014 at www.guidelines.gov European Wound Management Association (2003) Position Document: Understanding compression therapy. MEP Ltd, London.
8. Falanga V. Venous ulceration: Assessment, classification and management. Chapter 20 in Krasner D, Kane D. *Chronic Wound Care, Second Edition*. Health Management Publications, Inc. Wayne PA, 1997, pp165-171.
9. Falanga V, Brem H, Ennis WJ, Wolcott R, Gould LJ, Ayello EA. Maintenance debridement in the treatment of difficult-to-heal chronic wounds. Recommendations of an expert panel. *Ostomy/Wound Management*. Suppl:2-13; quiz 14-5, 2008 Jun.

10. Kelechi TJ, Johnson JJ; WOCN Society. Guideline for the management of wounds in patients with lower-extremity venous disease: an executive summary. *J Wound Ostomy Continence Nurs.* 2012;39(6):598-606
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14. Nelson EA, Dale J. The management of leg ulcers. *J Wound Care* 1996; 5(2):73-76.
15. O'Donnell TF Jr, Passman MA, Marston WA, Ennis WJ, Dalsing M, Kistner RL, Lurie F, Henke PK, Gloviczki ML, Eklöf BG, Stoughton J, Raju S, Shortell CK, Raffetto JD, Partsch H, Pounds LC, Cummings ME, Gillespie DL, McLafferty RB, Murad MH, Wakefield TW, Gloviczki P; Society for Vascular Surgery; American Venous Forum. Management of venous leg ulcers: clinical practice guidelines of the Society for Vascular Surgery® and the American Venous Forum. *J Vasc Surg.* 2014 Aug;60(2 Suppl):3S-59S.
16. Phillips T. Successful methods of treating leg ulcers. *Postgraduate Medicine* 1999; 105(5):159-180
17. Registered Nurses Association of Ontario (RNAO). Assessment and management of venous leg ulcers. Toronto (ON): Registered Nurses Association of Ontario (RNAO); 2004 Mar. Accessed October 1, 2010, www.guidelines.gov
18. Royal College of Nursing. The management of patients with venous leg ulcers: Clinical Practice Guideline. 1998; The RCN Institute, Center for Evidence-based Nursing, Univ. of York & School of Nursing, Midwifery and Health Visiting, Univ. of Manchester. Accessed October 1, 2010 at http://www.rcn.org.uk/development/practice/clinicalguidelines/venous_leg_ulcers
19. Rudolph D. Standards of care for venous leg ulcers: Compression therapy and moist wound healing. *J Vasc Nurs* 2001; 19:20-27.
20. Scottish Intercollegiate Guidelines Network (SIGN). Management of chronic venous leg ulcers. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2010 Aug. 44 p. (SIGN publication; no. 120). Accessed October 1, 2010, www.guidelines.gov
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22. Society for Vascular Surgery The care of patients with varicose veins and associated chronic venous diseases: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. 2011 May. NGC:010517
23. Society for Vascular Surgery/American Venous Forum. Management of venous leg ulcers: Clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. *J Vasc Surg* 2014; 60(2) supp, 3S-59S.
24. Tang JC, Marston WA, Kirsner RS. Wound Healing Society (WHS) venous ulcer treatment guidelines: what's new in five years? *Wound Repair Regen.* 2012;20(5):619-37. doi: 10.1111/j.1524-475X.2012.00815.
25. Wound Ostomy Continence Nurses Society. Clinical Practice Guideline #4. Management of Wounds in Patients with Lower-Extremity Venous Disease, 2005. <http://www.guideline.gov>

Legend

1. **Strength of Evidence (SOE) Rating** is the first entry after each recommendation per standardized criteria below:
 - A. Results of a meta-analysis or two or more venous ulcer (VU)-related randomized controlled trials (RCT) on humans provide support. For diagnostics or risk assessment screening: prospective cohort (CO) studies and/or controlled studies reporting recognized diagnostic (e.g. sensitivity or specificity) or screening (e.g. + or - predictive validity) measures.
 - B. Results of one VU-related RCT in humans plus one or more similar Historically Controlled Trials (HCT) or Convenience Controlled Trials (CCT) or one HCT and one CCT provide support or when appropriate, results of two or more RCT in animal model validated as clinically relevant to VU provide indirect support. For diagnostics or risk assessment one VU-related prospective cohort (CO) study and/or a controlled study reporting recognized diagnostic or predictive screening validity measures.
 - C. This rating requires one or more of the following:
 - C1: Results of one controlled VU trial, e.g. RCT, CCT or HCT (or for diagnostics or risk prediction one prospective CO study may be substituted for a controlled trial)
 - C2: Results of at least two clinical VU case series (CS) or descriptive studies or a cohort study in humans
 - C3: Expert opinion (EO)
2. **Best available references** are in parentheses (Last name of first author and publication year of best available supporting evidence). Underscored references support reduced costs of care or improved cost effectiveness.
3. **Content Validity Index (CVI)** is the first Number after the evidence; this is percent of survey respondents rating the recommendation clinically relevant: $CVI = (\text{Number of 3's} + \text{number of 4's}) / (\text{Total N Responding for that recommendation})$. If > 0.75 , it is clinically relevant
4. **Strength of Recommendation (SOR)** is the last entry for each recommendation. Scale 0-2 representing harms and benefits of recommended care.
 - a. 0 = Following the recommendation does more harm than good
 - 1 = Equal benefit and harm
 - 2 = More beneficial than harm
 - b. "High SOR" = 1.5 – 2
 - c. "Moderate SOR" = 1-1.499
 - d. "Low SOR" < 1.0

Major Recommendations

A. Before treatment, a qualified health care professional or multidisciplinary team assesses all aspects of the patient and the wound and documents the ulcer-related diagnosis, patient-centered concerns and risk factors for delayed healing or recurrence of VU to guide management plan, including all risk factors in A.1-3 below.

A (per evidence cited in A.1-3), CVI=1.000, High SOR

A.1. Document patient history in context of physical examination including patient's condition, history of deep vein thrombosis (DVT), pulmonary embolism or malignancy, systemic inflammation, obesity, ulcer treatment history, medical and surgical history and medications (e.g. cancer medications, corticosteroids or blood thinners).

A (Lee et al., 2002; Nelzén & Fransson 2007; Szewczyk et al., 2009), CVI=1.000, High SOR

A.1.a. Document post thrombotic syndrome (PTS) or venous insufficiency in superficial and/or deep vein systems and/or the perforating venous system and if needed, refer for appropriate vascular diagnostics and treatment.

A (Cushman et al, 2010; Kahn et al., 2005; Szewczyk et al., 2009; Volikova et al., 2009),
CVI=0.950, High SOR

A.1.b. Recognize high risk of delayed healing if an individual with a VU experiences the risk factors described as b.i-b.vi with evidence cited for each risk factor:

A.1.b.i. The VU has existed for at least 6 months or failed to contract in area at least 40% during 3 weeks of best evidence-based care.

A (Kulkarni et al. 2007; Margolis et al., 2000; Phillips et al., 2000; van Rijswijk et al., 1993), CVI=0.952, High SOR

A.1.b.ii. History of vascular surgery, trauma, repeated intimal venous damage or varicosities or ankle-to-brachial index < 0.8.

A (Marston et al., 1999; Mudge 1988; Nelzén &Fransson 2007; Nicolaidis et al., 2000),
CVI=0.950, High SOR

A.1.b.iii. Family history of venous ulcer(s).

A (Cushman et al., 2010; Bérard et al., 2002), CVI=0.909, High SOR

A.1.b.iv. Age > 50 years.

A (Cushman 2007; Cushman et al., 2010; Kulkarni et al., 2007), CVI= 0.864, High SOR

A.1.b.v. Male gender.

A (Cushman 2007; Lee et al., 2002; van Rijswijk et al., 1993), CVI= 0.773, High SOR

A.1.b.vi. Documented nutritional deficiency with a body mass index (BMI) >33 kg/m².

A (Cushman et al., 2010; Millic et al., 2009; Prandoni & Kahn, 2009), CVI=0.909, High SOR

A.1.b.vii. Patient-reported ache, heaviness or pain after prolonged leg dependency; itching or tiredness in leg.

C3 (ASPS, 2010; Saedon & Stansby, 2010), CVI= 0.955, High SOR

A.1.b.ix. Multiple pregnancy.

C1 (Bérard et al., 2002), CVI= 0.818, High SOR

A.2. Suitably trained health care professionals, as required by institutional protocols, perform comprehensive physical examination.

A (Carpentier et al., 2003; Eklöf et al., 2004; Nelzén &Fransson 2007; Vasquez et al., 2010; Volikova et al., 2009), CVI= 0.895, High SOR

A.2.a. Document the venous insufficiency using a standardized score, e.g. clinical severity, etiology, anatomy and pathophysiology (CEAP) or VCSS (A.2.a.i and A.2.a.ii) below .

A (Carpentier et al., 2003; Eklöf et al., 2004; Nelzén & Fransson 2007; Vasquez et al., 2010; Volikova et al., 2009) CVI= 0.952, High SOR

A.2.a.i Table 1. CEAP Descriptive Venous Ulcer Scoring System Developed by the American Venous Forum Accepted as Reporting Standards In Venous Disease.

A (Gloviczki et al., 2011; Vasquez et al., 2010) CVI= 0.882, High SOR

<u>Class</u>	<u>Description</u>
C0	No visible or palpable signs of venous disease
C1	Telangiectasies or reticular veins (< 3 mm diameter)
C2	Varicose veins—larger than reticular veins (> 3 mm diameter)
C3	Edema
C4	Skin and subcutaneous tissue changes secondary to cardiovascular disease C4a: Pigmentation or eczema C4b: Lipodermatosclerosis or atrophie blanche,
C5	Healed venous ulcer
C6	Active venous ulcer

A.2.a.ii. Venous clinical severity score (VCSS) uses standardized ratings (Absent = 0; Mild =1; Moderate = 2; Severe = 3) describing clinical severity of conditions related to venous insufficiency (pain, varicose veins, venous edema, skin pigmentation, inflammation, induration, number, size and duration of active VU or adherence to compression therapy (None = 0; Intermittent use of stocking = 1; Wears stocking most days = 2; Fully compliance stockings = 3).

C3 (Marston, et al. 2013; Passman, et al., 2011, Vasquez, M et al, 2010) , CVI= 0.800, High SOR

A.2.b. Physical symptoms associated with VU development or delayed healing include A.2.c.i-vi with corresponding evidence:

A.2.b.i. Lower leg edema.

A (Burton, 1993; Brodovicz et al., 2009; DUBY et al., 1993; Ennis & Meneses, 1995; Kahn et al., 2005; Sampaio et al., 2010), CVI=1.000, High SOR

A.2.b.ii. Increased dermal thickness, e.g. >1.985 mm as measured using high frequency ultrasound or other clinically documented technique.

A (Choh et al., 2010; Vesić et al., 2008; Volikova et al., 2009; Xia et al., 2004), CVI= 0.667, Moderate SOR

A.2.b.iii. Stasis dermatitis including tan or red-brown skin color (hemosiderin deposits) usually at medial ankle, or small erosions that may be open or crusted.

A (Alguire et al., 1997; Burton, 1993; Pappas et al., 1997) CVI= 0.952, High SOR

A.2.b.iv. Lipodermatosclerosis, (fibrosis of dermis resulting in fibrosing panniculitis of leg with severe, chronic venous insufficiency).

A (Geyer et al., 2004; Navarro et al., 2002; Volikova et al., 2009) CVI= 1.000, High SOR

A.2.b.v. Medial lower leg site, with slower healing in ulcers associated with VU location in posterior ankle or back of calf region.

A (McGuckin et al., 2002; Pappas et al., 1997; Szewczyk et al., 2009; Yim et al., 2014), CVI= 0.762, High SOR

A.2b.vi. Growth of hair indicates adequate arterial supply and likely VU healing outcome.

B (Grey et al., 2006; Powell, 2010; Sampaio-Santos et al., 2010) CVI=0.818, High SOR

A.2.b.vii. Varicosities.

C3 (Alguire et al., 1997; Weiss, 1995) CVI= 0.762, High SOR

A.2.b.viii. Atrophie blanche, a dermatologic condition associated with venous insufficiency, appears as atrophic plaques of ivory white skin with telangiectasias.

C2 (Barron GS et al 2007; Maessen-Visch et al 1999; Amato L et al 2006) CVI= 0.773, High SOR

A.3. Perform differential diagnosis to determine cause of ulceration or obtain an appropriate consult to do so. Tests should be performed if the results will influence patient management.

A (Alavi & Kirsner, 2015; Kirsner, 1993; McGuckin et al., 2002; Mustoe 2004), CVI= 0.900, High SOR

A.3.a. Rule out arterial disease in those without palpable pedal pulse by determining ratio of ankle divided by brachial systolic blood pressure index (ABI) by Doppler if feasible. An ABI ratio of < 0.8 or > 1.2 suggests referral to a specialist to assess for arterial disease (See Table 2)

A (Bjellerup, 2003; Forssgren et al., 2008 ; Kjaer et al., 2005; McGuckin et al., 2002; Mustoe 2004) , CVI= 1.000, High SOR

Table 2. Leg Ulcer Causes and Optional Actions to Address Limited Vascular Perfusion or Oxygenation Reflected by ABI Ratios.

A (Bjellerup, 2003; Forssgren et al., 2008 ; Kjaer et al., 2005; McGuckin et al., 2002; Mustoe 2004), CVI= 0.889, High SOR

ABI Observed Condition: Evidence-based Actions Suggested,

> 0.8 Venous insufficiency: compression, reduce edema, VU treatment recommendations

0.6 to 0.8 Peripheral arterial disease (PAD): Consult a vascular specialist to determine severity of arterial occlusion. If edema is present, mild compression may be applied, with caution under close supervision by an appropriately experienced health care professional

0.5 to 0.6 Possible PAD and/or critical ischemia: vascular consult to determine severity of arterial occlusion

< 0.5 Critical ischemia: immediate vascular consult and arterial disease management. Avoid compression.

Over 1.2 Arterial calcification can cause ankle artery to be non-compressible rendering ABI inaccurate: Use alternative testing such as toe / brachial systolic blood pressure (TBI) > 0.6 or trans-cutaneous oxygen partial pressure (TcPO₂) of > 30mmHg near ulcer to assess adequacy of arterial flow

A.3.a.i. Recognize that venous ulcers can exist in the presence of mixed arterial/venous pathology.

C3 (ASPS, 2007; Bonham et al., 2009; Falanga 1997; Kerstein 1996), CVI= 0.952, High SOR

A.3.b. Confirm and localize venous insufficiency using color duplex scanning ultrasound, or other appropriate imaging such as light reflexive rheology, if feasible, in supine and standing positions to measure blood flow, venous refill time (see also A.3.d.) and venous reflux.

A (Kjaer et al., 2005; Lee et al., 2002; Vesic et al., 2008; Yasodhara et al., 2003; Coleridge-Smith P et al,2006) , CVI= 0.864 High SOR,

A.3.c. Use air plethysmography, if feasible, to monitor hemodynamic flow.

A (Cordts et al, 1992; Garcia-Rinaldi et al., 2002; Perrin, et al., 1999), CVI= 0.667, Moderate SOR

A.3.d. Measure venous refill time (VRT) using a below-knee tourniquet and photoplethysmography. VRT less than the normal 20 seconds indicates venous insufficiency and predicts VU non-healing.

A (Heit et al., 2001; Kulkarni et al., 2007; Phillips, 1999) CVI= 0.591, Moderate SOR

A.3.d.i. Increased VRT after vein surgery predicts VU healing and non-recurrence.

A (Gohel et al.,2007; Kulkarni et al., 2007; Phillips, 1999), CVI=0.667, Moderate SOR 1.35

A.3.e. If ABI is unreliable, monitor transcutaneous oxygen tension (TCPO₂) near the VU. TCPO₂ ≥ 30 mmHg rules out arterial disease or predicts VU healing.

A (Alexanderhouse Group, 1992; Belcaro et al., 2003; Lo et al., 2009; Stacey et al., 1990),
CVI=0.727, High SOR

A.3.f. For individuals with a history of deep vein thrombosis, identify and address hypercoagulative conditions such as elevated factor VIII related antigen, lupus anticoagulant and Factor V Leiden.

A (Blomgren et al., 2001; Cushman et al., 2010; Fink et al., 2002), CVI=0.762, High SOR

A.3.g. As feasible, use a peri-ulcer skin perfusion pressure ≥ 30 mmHg to predict VU and other chronic leg ulcer healing.

A (Adera et al., 1995; Lo et al., 2009; Yamada et al., 2008), CVI=0.682, Moderate SOR

A.3.h. If a leg ulcer is refractory (fails to improve within 6 weeks despite consistent evidence-based treatment) it may not be caused by venous insufficiency. Consider biopsy for histological diagnosis, or other procedures to identify suspected malignancy, vasculitis, pyoderma gangrenosum, mycobacterial or fungal infection or other atypical etiologies.

B (Bennett 2000; Chakrabarty 2003; Combemale et al., 2007; Mekkes 2003; Reichrath 2005; Reich-Schupke et al., 2008 and 2015; Senet et al., 2012; Shelling et al., 2010),
CVI=1.000, High SOR

A.3.i. Monitor peri-ulcer skin for elevated temperature. An increase of $>1.1^{\circ}\text{C}$ predicts infection or delayed healing.

A (Fierheller & Sibbald, 2010; Woo & Sibbald, 2009), CVI= 0.636, Moderate SOR

A.3.j. Monitor peri-ulcer skin for erythema or edema and wound margin to inform wound management decisions.

A (McGuckin et al., 2002) CVI=.952, High SOR

A.3.k. If venous ulcer infection (e.g. cellulitis, osteomyelitis or gangrene) is observed or suspected, consult a Microbiology or Infectious Disease specialist using validated quantitative swab technique (Levine or curetted specimen) or biopsy to quantify, identify and address pathogenic microbes.

A (Angel et al. 2011; Davies et al. 2007; Gardner et al., 2006; Reddy et al., 2012), CVI=
0.773, Moderate SOR

B. Document venous ulcer wound characteristics including ulcer-related pain and events that trigger it, location, size, odor, bleeding, base, exudate, condition of the surrounding skin to monitor and plan care to manage ulcer progress.

A (Bolton et al., 2004; Kurd et al., 2009; McGuckin et al., 2002), CVI=1.000, High SOR

B.1. Measure VU area or estimate it from longest length x width to assess healing progress.

A (Kantor & Margolis, 1998; Kantor & Margolis, 2000; Hammond & Nixon, 2011;
McGuckin et al., 2002), CVI=1.000, High SOR

B.1.a. Use validated measures that include wound depth (i.e. Bates-Jensen Wound Assessment Tool® or Wound Bed Score).

A (Bolton et al., 2004; Falanga et al., 2006; Keast et al., 2004; Ratliff & Rodeheaver, 2005), CVI=0.818, High SOR

B.1.b. Document VU progress weekly or as appropriate to patient and setting, or sooner if there is a significant change in ulcer status.

A (Bolton et al., 2004; Kurd et al., 2009; McGuckin et al., 2002), CVI=1.000, High SOR

B.1.c. Inform care-givers if VU area has not decreased by at least 40% after 3 weeks of a treatment regimen and that this indicates that it is likely to experience delayed healing. Re-evaluate diagnosis, factors that delay healing and/or adherence to care plan.

A (Kantor & Margolis, 2000; Kurd et al., 2009; Phillips et al., 2000; van Rijswijk et al., 1993;), CVI= 0.955, High SOR

B.2. As feasible and consistent with setting protocols, plan VU management using a multidisciplinary wound team or clinic to improve healing, pain, and other health-related quality of life outcomes, reducing costs of patient care and hospitalization.

A (Gottrup et al., 2001; Marshall et al 2001; Moffat & Franks, 2004; Van Hecke et al., 2008; Vu et al., 2007), CVI=1.000, High SOR

B.2.a. As feasible, arrange for patients to visit the clinic at least once per week to improve VU healing outcomes more than those with biweekly visits.

A (Edwards et al., 2013; Morrell et al., 1998; Warriner et al 2012), CVI=0.727, Moderate SOR

B.3. Monitor validated quality of care VU outcome indicators including healing, recurrence, health-related quality of life and pain.

A (Persoon et al., 2004, Herber et al., 2007; Edwards et al., 2009; Kjaer et al., 2005) CVI=0.909, High SOR (Valid outcome indicators below were added after validation survey based on evidence cited. CVI and SOR will be determined in next update.)

B.3.a. VU healing indicators capable of consistently measuring healing changes over time or between intervention effects include percent of patients with a completely healed target ulcer or percent of patients achieving 50% area reduction during a pre-specified time interval, time to healing or percent reduction in VU area (determined by standardized planimetry or calculated as longest ulcer dimension as length x longest perpendicular width) from baseline to 2 to 4 weeks.

A (Kantor & Margolis, 2000; Kerstein et al., 2001; Kjaer et al., 2005; Lyon et al., 1998; Phillips et al., 2000; vanRijswijk, 1993). (Valid outcome indicators below were added after validation survey based on evidence cited. CVI and SOR will be determined in next update.)

B.3.b. Measures of VU recurrence capable of consistently measuring change over time or between intervention effects include percent of individuals with a healed VU whose VU recurred after 12 months.

A (Barwell et al., 2004; Kjaer et al., 2005) (Valid outcome indicators below were added after validation survey based on evidence cited. CVI and SOR will be determined in next update.)

B.3.c. Quality of Life. (QOL) tools validated for VU patients include the VEINES-QoL/Sym tool, the Medical Outcomes Survey 12-item Short-Form (SF-12) the Short-Form Health Survey, 36 items (SF-36).

A (Bland et al., 2015, Hopman et al., 2013; Kahn 2004). (Valid outcome indicators below were added after validation survey based on evidence cited. CVI and SOR will be determined in next update.)

B.3.d. Pain measurement tools validated for VU patients include the Medical Outcomes Survey 12-item Short-Form (SF-12), the Visual Analogue Scale, the McGill Pain Questionnaire a subscale of the Nottingham Health Profile.

A (Herber et al., 2007; Persoon et al., 2004; Hopman et al., 2013) (Valid outcome indicators below were added after validation survey based on evidence cited. CVI and SOR will be determined in next update.)

B.3.e. Depression measurement/assessment tools validated for VU patients include the Hospital Anxiety and Depression Scale (HADS), the Euroqol 5 dimensions (EQ-5D), the Nottingham Health Profile.

A (Bland et al., 2015, Jones et al., 2006, Franks et al. 2006) (Valid outcome indicators below were added after validation survey based on evidence cited. CVI and SOR will be determined in next update.)

B.4. If complications, protocol variation or other issues arise, revise care plan or goals of treatment to address wound issues and patient concerns.

C3 (RNAO, 2010; Lorimer et al., 2003), CVI= 0.955, High SOR

C. Engage in patient-centered care to prevent or heal VU and prevent VU recurrence by developing and consistently applying a plan to improve venous return and improve skin and VU condition in accordance with patient goals and capabilities.

A (Lorimer et al 2003; McGuckin et al 2002; Herber et al., 2007, Finlayson 2009 Van Hecke et al 2009), CVI=0.905, High SOR

C.1. Educate patient about relevant VU risk factors, cause(s) of skin breakdown, and how and why to engage in life style changes including smoking cessation, weight management, and protecting affected lower leg skin from accumulating edema and trauma, by consistently using appropriate compression, exercise and leg elevation for life.

A (Lorimer et al 2003; McGuckin et al 2002; Finlayson 2009, Van Hecke et al 2009, Finlayson 2015), CVI=1.000, High SOR

C.2. Appropriately trained health care professional properly fit and apply safe, effective, cost effective compression bandages or stockings to heal venous ulcers, taking precautions to adjust compression as medically needed based on patient preferences, skin or cardiovascular conditions, ulcer location, limb shape, neuropathy, or mixed venous/arterial disease confirmed during diagnostic work-up. Clarity is needed to define compression categories. (includes C.2.a-k below)

A (Brizzio et al.,2010; Flour, 2013; O'Meara, 2012, Mauck, 2014; Mayrovitz et al., 2015; Partsch, 2015; Parker et al., 2015; Szewczyk et al 2009) CVI=0.955, High SOR

C.2.a. Use caution for patients with venous leg ulcer and underlying arterial disease. Use of standard compression has been shown to be safe if ABI ≥ 0.80 . Compression bandages or stockings should not be used if the ankle-brachial index is < 0.5 .

A (Callam et al 1992; Gould 1998; Northeast et al., 1990) CVI=0.762, High SOR

C.2.b. Venous leg ulcers heal more quickly with compression therapy than no compression therapy.

A (Mauck, 2014, O'Meara, 2012; Wong, 2012; Nelson, 2008) CVI=0.955, High SOR

C.2.b.i. Multilayer compression bandages improve VU healing compared to single layer compression.

A (O'Donnell 2014; O'Meara, 2012; Milic 2010) CVI=0.864, High SOR

C.2.b.ii. Elastic compression bandages improve VU healing compared to inelastic compression.

A (O'Meara 2012; Dolibog 2014; Amsler et al 2009; Polignano, Guarnera et al., 2004; Koksai, 2003; Callam, 1992; Northeast, 1990; CVI=0.810, High SOR

C.2.c. According to patient preferences and capabilities, use two-layer stocking compression to achieve similar healing outcomes to 4-layer compression bandages or 2-layer short stretch with the potential to improve comfort, pain or quality of life more than 4-layer or short-stretch compression.

A (Ashby 2014, Finlayson et al., 2014; Jünger, Wollina et al; 2004; Moffat et al 2008), CVI=0.819, High SOR

C.2.d. Compression stockings prevent recurrence in healed VU as compared to no use of compression stockings.

A (Nelson 2012; Nelson & Jones, 2007; Vandongen 2000; Franks 1995) CVI=0.905, High SOR

C.2.e. Gradient compression, descending toward the knee may improve VU healing more than non-gradient compression, but further research is needed to define applicable parameters.

A (McGuckin et al., 2002; Polignano, Guarnera et al., 2004), CVI= 0.857, High SOR

C.2.f. Use intermittent pneumatic compression (IPC) to increase healing compared to no compression. Limited evidence that IPC may improve healing when added to compression bandages. Use with caution if edema occurs centrally.

A (Nelson et al 2014; Comerota 2011; Nikolovska 2005; Coleridge-Smith et al., 1990; Rowland 2000) CVI=0.727, High SOR

C.2.g Use a non-elastic compression strapping device to improve VU healing more than no compression.

A (Blecken et al 2005; DePalma et al 1999; Spence & Cahall, 1996) CVI= 0.818, High SOR

C.2.h. Standardized manual lymphatic massage reduces lower leg edema, a causative factor for VU.

A (Molski et al., 2009; Pereira de Godoy 2008; dos Santos Criso'stomo et al., 2015; Finnane et al., 2015), CVI=0.864, High SOR

C.3. Engage patient in an appropriate program to consistently elevate lower leg to improve VU healing and reduce recurrence.

C2 (Abu-Own et al., 1994; Collins & Seraj, 2010; Finlayson et al., 2015; Shannon et al., 2013; Xia et al 2004; Hegarty, 2010; Finlayson et al., 2009) CVI=0.909, High SOR

C.4. Properly trained health care professionals engage VU patient in a patient-appropriate program of walking, leg elevation and/or appropriate ankle exercise to improve venous hemodynamics or calf muscle pump function.

A (Jull et al., 2009; Meagher et al., 2012; O'Brien et al., 2013; Padberg et al., 2004; Szewczyk et al., 2010; Yim 2015) CVI=0.955, High SOR

C.5. Manage peri-ulcer Skin.

A (Beitz & van Rijswijk 1999; Charles et al., 2002; Finlayson et al., 2010; McGuckin et al., 2002), CVI=1.000, High SOR

C.5.a. Moisturize skin if dry, avoiding skin irritants or allergens to which those with a VU are especially sensitive.

A (Beitz & van Rijswijk 1999; Finlayson et al., 2010; McGuckin et al., 2002) CVI=1.000, High SOR

C.5.a. i. If a sensitization reaction is experienced, confirm source using a patch test, avoid subsequent use of the allergen and, if needed, manage itching and irritation with a patient-appropriate topical steroid formulation applied to the peri-ulcer skin for up to 2 weeks.

C1 (Gallenkemper et al., 1998; Jones et al., 2003) CVI=0.864, High SOR

C.5.b. Use dressings or barriers that manage exudate, minimize pain and protect skin from chemical or physical trauma.

A (Arnold et al. 1994; Bradley et al., 1999; Charles et al., 2002; Sayag et al., 1996),
CVI=0.955, High SOR

C.5.c. Manage peri-ulcer skin infection, inflammation, edema and circulation. Be alert to sensitization reactions.

A (Cameron et al., 2005; Gallenkemper 1998; Mayrovitz & Larsen, 1994; Neander & Hesse, 2003), CVI=1.000, High SOR

C.6. Implement local evidence-based VU wound care, pain and depression management programs and patient education until healed, accompanied by life style changes, exercise and consistent compression adequate to prevent edema.

A (Padberg 2004; Persoon 2004; Harrison et al 2005, Finlayson et al., 2009, Heinen 2011;
Also see evidence cited for B3c, B3d, B3e), CVI=0.941, High SOR

C.6.1. Provide community nursing, coaching and/or peer support to improve healing, functional ability and health-related quality of life.

A (da Silva et al., 2006; Edwards et al., 2005; Edwards et al., 2009; Forssgren et al., 2008, Heinen 2011, Green 2014), CVI=0.864, High SOR

D. Properly trained health care professionals perform local wound care steps D.1-7, avoiding known irritants or allergens.

A (Chaby 2010; Dumville et al. 2009), CVI=0.938, High SOR

D.1. If needed, cleanse VU gently, minimizing chemical or mechanical trauma, at low pressure (4-15 psi) with safe, non-antimicrobial cleanser.

A (Fernandez, 2012; Griffiths et al., 2001; McGuckin et al., 2002; Romanelli et al., 2010),
CVI= 0.857, High SOR

D.2. Debride non-vital tissue to promote chronic VU healing, including options D.2.a-f.

C2 (Doerler et al., 2012; Gethin et al., 2015), CVI=0.941, High SOR

D.2.a. Apply enzymatic debridement to debride venous ulcers.

B (Bergemann et al., 1999; Westerhof et al., 1987), CVI=0.864, High SOR

D.2.b. Use autolytic debridement to debride venous ulcers.

A (Gethin et al., 2015; Alvarez et al., 2012; Dumville et al., 2009; Koksai 2003; Mulder et al., 1993; Romanelli, 1997) , CVI=0.909, High SOR

D.2.c. Larval Therapy (bagged or loose) debrides VU faster, with more pain and similar healing or cost effectiveness to hydrogel.

A (Dumville et al., 2009; Wayman et al., 2000; Davies 2014), CVI=0.727, Moderate SOR

D.2.d. High frequency ultrasound improves healing compared to no ultrasound for 7-8 weeks but not 12 weeks.

A (Cullum et al., 2010), CVI=0.667, Moderate SOR

D.2.e. Low frequency ultrasound (e.g. 25 kHz at a 35-40 W/cm² power intensity) may support healing, reduce pain and improve QOL of non-healing venous or mixed etiology venous ulcers.

A (Gibbons et al., 2015; Herberger et al., 2011) CVI=0.619, Moderate SOR

D.2.f. Sterile sharp debridement with scalpel, curette or scissors is a rapid option of necrotic tissue removal and is more cost or resource efficient than the more invasive surgical debridement performed in the operating room. Use caution to avoid excess tissue damage which may delay healing.

B (Blumberg et al., 2012; Cardinal et al., 2009; Golinko et al., 2009; Williams et al., 2005), CVI=0.864, High SOR

D.2.f.i. Hydrosurgical techniques may shorten the procedural time of debridement or time to debridement.

B (Caputo et al, 2008; Mosti et al., 2005). (Valid outcome indicators below were added after validation survey based on evidence cited. CVI and SOR will be determined in next update.)

D.2.g Mechanical debridement using wet-to-dry gauze can remove VU non-vital tissue and slough, though it may be painful, delay healing and increase likelihood of infection. Improve tolerance with appropriate use of anesthetic formulations and moisture-retentive secondary dressings.

C1 (Donati et al., 1994; Lok et al., 1999), CVI=0.909, High SOR

D.3 Manage wound pain related to VU cleansing, debridement and dressings change.

A (Briggs, 2012; Beitz & van Rijswijk, 1999), CVI=1.000, High SOR

D.3.a. Apply topical anesthetics such as lidocaine-prilocaine cream if needed to reduce debridement pain.

A (Briggs et al., 2012; Lok et al., 1999), CVI=0.864, High SOR

D.4. Select patient-, provider-, and setting-appropriate dressings to support cost effective healing and improve patient quality of life, including D.4.a-d:

A (Franks et al., 2007; Harding et al., 2001; Lyon et al., 1998; Yager et al 1996, Valle 2014 , CVI=1.000, High SOR

D.4.a. Manage excessive exudate to, minimize maceration and odor, improve comfort and reduce dressing change frequency with dressings and supporting evidence listed in D.5.a.i-iv:

D.4.a. i Apply alginate.

A (Bergemann et al., 1999; Lyon et al., 1998; Sayag, et al., 1996), CVI=0.818, High SOR

D.4.a.ii. Apply sodium carboxymethyl cellulose dressings.

A (Armstrong & Ruckley, 1997; Harding et al., 2001; Quintanal, 1999, Meaume et al. 2014), CVI=0.909, High SOR

D.4.a.iii. Apply foam dressings

A (Franks et al., 2007; Gottrup et al., 2008), CVI=0.909, High SOR

D.4.a.iv. Apply composite dressing

A (Daniels et al., 2002; Jones, 2003; Vanscheidt, et al., 2004), CVI=0.864, High SOR

D.4.b. Maintain a moist wound environment, using a moisture-retentive primary or secondary dressing beneath appropriate compression to support cost effective healing and to reduce venous ulcer pain.

A (Chaby et al., 2007; Kerstein et al. 2001; Margolis 1994; Stacey 1997), CVI=0.850, High SOR

D.4.b.i. Use hydrocolloid dressings to improve pain, healing and costs of care compared to gauze dressings, which do not maintain a moist wound environment unless sealed with a secondary moisture-retentive dressing or frequently re-moistened.

A (Arnold 1994; Chaby et al., 2007; Kerstein et al. 2001; Singh et al., 2004; Greguric et al., 1994; Nelson & Jones 2008), CVI=0.818, High SOR

D.4.b.ii. Use hydrogel to improve healing compared to saline gauze or enzymatic debridement.

A (He et al., 2008; Romanelli, 1997, Humbert, 2014), CVI=0.682, High SOR

D.4b.iii. Use moisture-retentive film or foam dressings to maintain moist healing.

A (Charles 2002; Davis et al, 1992; Romanelli, 1997) CVI=0.864, High SOR

D.4.c. Fill deep wounds to avoid dead space.

C2 (Beitz & van Rijswijk, 1999; Bolton et al., 2004), 0.864, High SOR

D.5. Apply additional local anesthetic or analgesic, if needed to manage wound-related pain in patients with a VU.

A (Briggs et al., 2012), CVI=0.941, High SOR1.81

D.5.a. Use ibuprofen-containing foam dressings, available in some countries, to reduce VU pain more than the same non-medicated foam in the first week of use.

A (Briggs et al., 2012; Gottrup et al., 2008; Jørgensen et al., 2006; Romanelli et al., 2009),
CVI=0.619, High SOR

E. Apply adjunctive interventions, e.g. E.1- if best evidence-based wound care does not reduce VU area at least 40% in 3 weeks.

A (Tuttle et al. 2015), CVI=0.882, High SOR

E.1. Apply culture-guided antimicrobial VU topical interventions only in cases of clinical infection, e.g. if increasing pain is observed or if no healing is seen in 4 weeks. Be aware that not all antimicrobial agents are supported by evidence (See E.1.a-e). Well-designed research has not established a causal link between delayed healing and microbial burden or molecular characteristics.

A (O'Meara et al., 2014; Tuttle et al. 2015) , CVI=0.842, High SOR

E.1.a. Cadexomer iodine dressings improve healing of chronic clinically infected VU, with more adverse events compared to standard care. Healing responses are similar to those using a hydrocolloid dressing; paraffin gauze dressing; dextranomer; or silver-impregnated dressings.

A (Hansson, et al., 1998; O'Meara et al., 2014), CVI=0.955, High SOR

E.1.b. Use benzoyl peroxide-based topical treatment to reduce chronic VU area compared to usual care.

A (O'Meara et al., 2014) [Added during review--CVI and SOR to be determined next update]

E.1.c. Apply silver dressings to improve healing and economic outcomes of hard-to-heal or infected VU.

A (Dimakakos et al., 2009; Jemec et al., 2014; Jørgensen et al, 2005; Lazareth et al., 2008; Leaper et al.,2013; Michaels et al., 2009; Senet et al., 2014), CVI=0.909, High SOR

E.1.d. Silver sulphadiazine foam dressings or 1% cream have evidence of safety on VU.

A (Bishop; et al. 1992; Blair et al., 1988; Kotz et al., 2009; Lantis et al., 2011) [Added during review--CVI and SOR to be determined next update]

E.1.e. Apply silver-releasing oxidized regenerated cellulose-collagen dressings to improve VU healing.

C1 (Lanzara, 2008) [Added during review--CVI and SOR to be determined next update]

E.2. Use systemic antibiotics only to address confirmed VU infection. There is insufficient evidence for their healing benefits and their use may foster growth of resistant organisms.

A (O'Meara et al., 2014); Tuttle., 2015) CVI=0.857, High SOR

E.2.a. Use sensitivity-matched systemic antibiotics to treat peri-ulcer cellulitis, e.g. match sensitivity of invading gram positive streptococci or staphylococci or gram negative pseudomonas or other species identified by a validated quantitative swab or biopsy.

C1 (Dall 2005; Edlich 2005; Tuttle, 2015), CVI=0.864, High SOR

E.3. Refer to vascular surgeons to perform corrective vascular surgery to improve vein function.

A (Gloviczki et al., 2011; O'Donnell 2014; Mauck, Asi, et al. 2014), CVI=0.800, High SOR

E.3.a. Minimally invasive subfascial endoscopic perforating vein surgery (SEPS) plus compression can reduce VU recurrence compared to compression alone.

A (Gohel et al., 2007; Van Gent et al., 2006; Wright, 2009, van Gent et al 2015),
CVI=0.667, High SOR

E.3.a.i. SEPS results in lower incidence of wound infections, shorter hospital stays and lower VU recurrence rates than classic open vein surgery.

A (Gloviczki et al., 2009; Luebke et al. 2009,)), CVI=0.619, High SOR

E.3.b. Classic open vein surgery (Linton procedure: high ligation, division, and stripping of the saphenous vein) may be needed for some patients, reducing VU recurrence compared to compression alone.

A (Barwell et al., 2004; O'Donnell, 2010), CVI=0.591, Moderate SOR

E.4. After assuring that the blood supply to the VU is adequate, consider skin replacement or surgical grafting options (e.g. E.4.a-c) to cover a VU as an adjunct to appropriate compression and appropriate treatment of the underlying pathology if less than 40% VU area reduction is seen in 3 weeks.

A (Jones & Nelson, 2013; Kirsner et al 2002; Poskitt 1987; Turczynski 1999, Serena 2014, Gibbons 2015, Valle 2014), CVI=0.765, High SOR

E.4.a. Minimize the tissue level of bacteria, preferably to $\leq 10^5$ CFU/g of tissue, with no beta hemolytic streptococci in the venous ulcer before attempting any of the following options 3c-3g.

C2 (Krizek et al. 1967; Murphy et al. 1986; Raad et al., 2010; Tobin et al. 1984),
CVI=0.818, High SOR

E.4.ab Apply bi-layered bioengineered skin as an adjunct to appropriate compression and appropriate treatment of the underlying pathology if less than 40% VU area reduction is seen in 3 weeks.

A (Atillasoy 2000; Falanga et al., 1999; Jones & Nelson, 2013; Omar 2004), CVI=0.762,
Moderate SOR

E.4.c. If there is the potential to heal the donor site, apply split-thickness autografts to the viable VU surface.

C2 (Puonti & Asko-Seljavara,1998; Turczynski & Tarpila, 1999), CVI=0.762, Moderate SOR

E.4.d. Fresh or frozen allografts.

A (Jones & Nelson, 2013; Goedkoop et al., 2010; Lingren, et al., 1998; Teepe et al., 1993), CVI=0.667, Moderate SOR

E.5. Use a biophysical intervention (e.g. E.5.a-c) as an adjunct to appropriate compression and appropriate treatment of the underlying pathology if less than 40% VU area reduction is seen in 3 weeks.

A (Franek et al., 2000; Houghton et al., 2003; Janković & Binić, 2008) CVI=0.667, Moderate SOR

E.5.a. Electrical stimulation.

A (Franek et al., 2000; Houghton et al., 2003; Janković & Binić, 2008) , CVI= 0.636, Moderate SOR

E.5.b. Use electromagnetic radiofrequency (RF) stimulation to reduce edema if adequate patient-appropriate compression is not effective or feasible.

A (Kenkre et al., 1996; Ieran et al., 1990; Stiller et al., 1992), CVI=0.545, Moderate SOR

E.5.c. Use ultrasound stimulation in combination with adequate patient-appropriate compression and moisture-retentive dressings to add possible VU healing benefit, but be aware that limited evidence supports cost effectiveness, enduring benefit or parameters of application.

A (Al-Kurdi et al, 2008; Chuang et al., 2011; Flemming & Cullum, 2002; Taradaj et al., 2008; Voigt 2011; Johannsen 1998;Watson et al., 2011), CVI=0.727, Moderate SOR

E.5.d Negative Pressure Wound Therapy (NPWT) has mixed evidence to inform clinical decisions about effects on chronic wound healing parameters or on preparing VU for autologous pinch grafting or in VU graft management.

A (Dumville et al., 2015; Joseph et al., 2000; Ubbink et al., 2008; Raad et al., 2010; Vuerstaek et al., 2006), CVI=0.727, Moderate SOR

E.6. For VU showing less than 40% area reduction in 3 weeks, apply systemic nutritional or pharmaceutical agents (e.g. E.6.a-k) as an adjunct to patient-appropriate compression and moisture-retentive dressings to promote VU healing or reduce recurrence, while being aware that all pharmacologic agents may have side effects.

A (Coleridge-Smith, 2005; Jull et al., 2007, Evangelista 2014), CVI=0.786, High SOR

E.6.a. Systemic pentoxifylline improves VU healing compared to placebo when used with appropriate compression.

A (Belcaro 2002; Collins & Seraj 2010; DeSanctis 2002; Falanga et al., 1999; Iglesias & Claxton, 2006; Jull et al., 2007; Nelson et al., 2007), CVI=0.773, High SOR

E.6.b. Patient-appropriate oral zinc supplementation is helpful in healing VU patients only if they are deficient in zinc and it is used as an adjunct to patient-appropriate compression and moisture-retentive dressings.

A (Greaves 1972; Phillips 1977; Myers 1970; Wilkinson 2000), CVI=0.62, High SOR

E.6.c. Oral simvastatin may benefit VU healing.

C1 (Evangelista et al., 2014), [Added by reviewers CVI and SOR to be determined next update.]

E.6.d. Micronized purified flavonoid fraction (Diosminhesperidin) may improve VU healing as an adjunct to appropriate compression and moisture-retentive dressings, but other free-radical scavengers have insufficient evidence.

A (Coleridge-Smith, 2005; Ferrara et al. 2007; Guilhou et al 1997; Glinski 1994), CVI=0.636, Moderate SOR

E.7 Apply topical interventions plus appropriate compression and dressings to heal or prevent recurrence of non-healing VU.

C1 (Gethin et al. 2015), CVI=0.667, 1.73

E.7.a. Use topical Manukah honey to improve healing and pain in larger, longer-duration, sloughy VU compared to hydrogel, with appropriate compression and secondary dressing.

A (Gethin & Cowman, 2008; Gethin et al., 2015; Gulati et al., 2014), CVI=0.591, Moderate SOR

E.8. Consider biologic dressings if no healing is seen in 4 weeks.

C1 (Meaume et al., 2008; Ortonne, 1996; Taddeucci et al., 2004) CVI=0.786, High SOR

E.8.a. Natural tissue constructs such as amniotic membrane or cryopreserved skin, or swine small intestine submucosa support VU healing compared to standardized compression alone, and have insufficient evidence of healing benefits compared to each other.

A (Mostow 2005; Romanelli et al., 2010; Serena et al., 2014), CVI=0.727, Moderate SOR

F. Implement local evidence-based management of healed VU, and documented pain or depression (See Section B.2. for valid assessment tools) programs and patient education, accompanied by life style changes, exercise and consistent compression adequate to prevent edema and VU recurrence for life. See also E3 for Surgical Interventions to prevent recurrence.

A (Padberg 2004; Persoon 2004; Harrison et al 2005, Finlayson 2009, Finlayson 2011;Heinen 2012) Also see evidence cited for specific recommendations below., CVI=0.941, High SOR

F.1. Reduce lower leg edema by applying compression, elevation and engaging patient in a program of calf muscle and ankle exercise.

A (Clark-Maloney, 2014; Van Hecke et al., 2011; McGuckin et al., 2002; Nelson, et al, 2004, Finlayson 2009, Heinen 2012), CVI=0.909, High SOR

F.2. Elastic compression stocking use for 6 months after DVT may prevent PTS skin changes, but effects on VU remain to be clarified.

B (Prandoni & Kahn, 2009; Aschwanden et al., 2008), CVI=1.000, High SOR

G. Perform palliative care in accordance with institutional definitions and protocols to optimize quality of life and patient-centered outcomes for patients with a VU and a life-threatening condition or a condition which may limit capacity to heal the VU.

C3 (Alvarez et al., 2007; Chrisman, 2010; Emmons, et al, 2014, Price et al., 2008; Tippett, 2015; Woo et al., 2015), CVI=0.917, High SOR

G.1. Establish individualized goals of care consistent with patient and family wishes and medical condition. Communicate to interdisciplinary team.

C3 (Alvarez et al., 2007; Chrisman, 2010; Emmons et al., 2014; Maida 2013), CVI=0.955, High SOR

G.2. Continue evidence-based principles of VU care outlined in Sections A-E above to the extent acceptable to the patient and family, including correcting underlying pathology, addressing nutrition and other supportive aspects of care, and sensible, non-harmful local wound management.

C3 (Alvarez et al., 2007; Emmons et al., 2014) CVI=0.909, High SOR

G.3. Attend to patient wound-related quality of life concerns including dressing comfort, wound fluid, odor, and bleeding.

C3 (Alvarez et al., 2007; Chrisman, 2010; Emmons et al., 2014, Price et al., 2008) CVI=0.955, High SOR

G.4. Maintain individual dignity and provide psychosocial support to reduce isolation.

C3 (Chrisman, 2010; Maida, 2013), CVI=0.955, High SOR

G.5. If surgical management is considered, before reaching a decision discuss benefits and risks with patient and family in terms of patient's condition and goals, presence of devitalized tissue, infection potential and underlying pathogenesis.

C3 (Maida, 2013; Lee et al., 2007). CVI=CVI=0.950, High SOR

G.5.a. Healing may not be a realistic goal, but can occur and improve quality of life with use of moisture-retentive dressings.

C3 (Chrisman, 2010; Emmons et al., 2014) , CVI=1.000, High SOR

Recommendations from cited *Source Guidelines* that did not meet either Content Validity Index ≥ 0.75 or A-Level Evidence criteria supporting their use in VU are listed below.

Assessment/Patient History

1. History of vigorous exercise. C1 (Bérard et al., 2002), CVI= 0.636, High SOR
2. Rule out or address other patient conditions associated with delayed healing, such as suspected sickle cell disease, systemic lupus erythematosus or atypical wounds before planning treatment. C1 (Alavi & Kirsner, 2015; Shelling et al., 2010; CVI=0.727, Medium SOR

Surgical Interventions

1. Use a thermal laser to achieve great or small saphenous vein coagulation or ablation. C1 (Gloviczki et al., 2009; Viarengo et al., 2007, Shi et al. 2015), CVI=0.667, High SOR
2. Thermal radiofrequency vein ablation. C2 (Gloviczki et al., 2009; Puggioni et al., 2005) , CVI=0.619, High SOR
3. Sclerotherapy with compression requires more evidence. C1 (Hamel-Desnos et al., 2010; O'Hare et al., 2010), CVI=0.5240, Moderate SOR
4. Valve repair or reconstruction. C2 (Maleti et al., 2006; Perrin et al., 1999) , CVI=0.429, Moderate SOR
5. Transplant or graft valve. C2 (Garcia-Rinaldi et al., 2002), CVI=0.333, Low SOR
6. Stenting of iliac vein for limbs with combined iliac vein obstruction and deep vein reflux. C2 (Raju et al., 2010), CVI=0.571, Moderate
7. Pinch grafts require more evidence. C2 (Christiansen, et al., 1997; Jones et al., 2013; Oein, et al., 1998), CVI=0.682, Moderate SOR
8. Cultured epidermal autografts (autologous keratinocytes) have shown inconsistent VU healing effects. B (Beele et al., 2005; Jones et al., 2013; Vanscheidt et al., 2007; Liu et al., 2004; Mol et al., 1991), CVI=0.636, Moderate SOR
9. Free flap microsurgical reconstruction. C2 (Steffe & Caffee, 1998), CVI=0.545, Moderate SOR

Biophysical Interventions

1. Warming therapy has insufficient evidence of healing efficacy to inform VU management decisions about its use as an adjunct to optimal patient-appropriate compression and moisture-retentive dressings. C1 (Robinson & Santilli, 1998; Santill et al., 1999; Von Felbert et al., 2007), CVI=0.318, Moderate SOR
2. Laser, including infrared (IR) stimulation and monochromatic light stimulation have not been shown to improve VU healing. C1 (Flemming & Cullum, 2002b; Gupta et al., 1998; Kopera 2005; Lagan 2002) , CVI=0.591, Moderate SOR

3. Thirty 90-minute sessions of inspired hyperbaric oxygen at 2.5 ATA during up to 6 weeks reduced chronic VU area compared to sham or usual care controls but there is insufficient evidence of a sustained effect on complete VU healing. B (Hammarlund & Sundberg, 1994; Kaur et al., 2012; Kranke et al., 2015), CVI=0.500, Moderate SOR
4. Avoid using whirlpool therapy for individuals with venous insufficiency as it tends to increase lower leg edema which is associated with VU development. C2 (McCulloch & Boyd, 1992), CVI=0.545, Moderate SOR

Nutritional/Pharmaceutical Interventions

1. Acetylsalicylic acid or aspirin may be used to reduce pain, inflammation and edema associated with a VU. C1 (Layton et al., 1994) CVI=0.429, Moderate SOR
2. Stanozolol may reduce pain, edema or symptoms of venous insufficiency. B (Burnand 1980; Layer 1986; Stacey et al., 1990; Vesić et al., 2008), CVI=0.545, Moderate SOR
3. Solcoseryl (topical or systemic) requires more evidence to inform VU care decisions about its efficacy as an adjunct to patient-appropriate compression and moisture-retentive dressings. C1 (Biland et al., 1985), CVI=0.333, Moderate SOR
4. Defibrotide requires more evidence to inform VU care decisions about its efficacy as an adjunct to patient-appropriate compression and moisture-retentive dressings. C1 (Jull et al., 2006), CVI=0.286, Moderate SOR1.26
5. Iloprost infused intravenously requires more evidence to inform VU care decisions about its efficacy as an adjunct to patient-appropriate compression and moisture-retentive dressings. C1 Ferrara et al., 2007), CVI=0.333, Moderate SOR1.16
6. Use systemic prostaglandins to improve VU healing. C3 (Beitner 1980;; Rudofsky 1989), CVI=0.571, Moderate SOR
7. Use oxerutins to improve VU healing or recurrence. C3 Leach et al., 2006; Wright et al., 1991), CVI=0.545, Moderate SOR

Topical Interventions:

1. Apply Topical cytokine growth factors. C3 (Robson 1995; Robson 2004; Wieman,, 2003) , CVI=0.636, Moderate SOR
2. Use cultured allogeneic keratinocyte lysate effects on VU. C1 (Harding et al., 2005), CVI=0.364, Moderate SOR
3. Apply mimosa extract 5% added to hydrogel to improve healing: compared to hydrogel alone C1 (Rivera-Arce et al., 2007), CVI=0.318, High SOR
- 4.. Use amelogenin extra-cellular matrix protein in addition to high compression therapy to improve healing and reduce pain than compared to compression alone in VU. C1 (Romanelli et al., 2008), CVI=0.318, Moderate SOR
5. Thymosin-beta-4 has not yet significantly affected VU healing. C1 (Guarnera et al., 2010), CVI=0.550, Moderate SOR

6. Platelet-rich plasma has not yet been shown to significantly improve VU healing. C2 (Carter et al., 2011; Stacey 2000; Martinez-Zapata et al., 2012;) CVI=0.524, Moderate SOR
7. Scavengers of oxygen-derived free radicals have not been shown to consistently improve VU healing. C2 (Salim 1991; Salim 1992), CVI=0.500, Moderate SOR
8. Collagen or collagen combinations have insufficient evidence to support improved VU healing. C1 (Lanzara et al., 2008; Vin, et al., 2002[NS], Valle 2014, CVI=0.727, High SOR
9. Hyaluronic acid or other matrix molecular dressings may decrease VU size or fibrin slough but lack sufficient evidence of complete healing. B (Meaume et al., 2008; Ortonne, 1996; Taddeucci et al., 2004), CVI=0.727, High SOR