

A systematic review of pneumatic compression for treatment of chronic venous insufficiency and venous ulcers

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Introduction: As part of a reconsideration of coverage policy, the Centers for Medicare and Medicaid Services requested a systematic review of the evidence on the use of pneumatic compression devices in the home environment for treatment of chronic venous insufficiency (CVI) and venous ulcers.

Methods: Articles were found with a systematic literature search of MEDLINE, EMBASE, and AMED (Allied and Complementary Medicine) databases, hand searches of reference lists, and suggestions of experts.

Results: Eight trials that met the inclusion criteria, including several randomized control trials, were found. Most studies were small and may have been underpowered. However, several were well-designed randomized controlled trials. Three studies showed that the devices could alleviate symptoms of CVI. No studies directly measured whether the devices could prevent the occurrence of venous ulcers. Some studies on the treatment of venous ulcers did not show a benefit for pneumatic compression, but other studies showed a benefit for the devices in healing long-standing chronic ulcers that had not healed with other methods. No studies directly compared single-chamber and multiple-chamber devices or studied whether the effectiveness of the pump was dependent on types of treatment used concurrently with the pump. Few adverse events were reported in the trials. Patients generally expressed satisfaction with the pneumatic compression devices, and several studies reported higher compliance than with other compression methods.

Conclusion: The available data cannot be relied on to inform the optimal choice of compression therapy or optimal protocol for patients with CVI or venous ulcers. Methodologically rigorous research designed to answer these questions would be useful for treatment decisions. The Centers for Medicare and Medicaid Services considered the results of this study and issued a decision that pneumatic compression will only be covered for patients with refractory edema with significant ulceration of the lower extremities after a 6-month trial of standard therapies, such as compression stockings, has failed. (*J Vasc Surg* 2003;37:539-44.)

The Centers for Medicare and Medicaid Services (CMS; formerly the Health Care Financing Administration) requested a technology assessment on the use of pneumatic compression devices for the treatment of venous insufficiency and chronic ulcers. This manuscript is based on the technology assessment/systematic review that was submitted to CMS.

At the time of the request, CMS was reconsidering its coverage policy; the policy was to cover pneumatic compression devices for patients with refractory edema with significant ulceration of the lower extremities with failure to heal after 6 months of treatment with other methods, such as compression bandages. CMS requested that the Agency

for Healthcare Research and Quality find and evaluate evidence related to the use of intermittent pneumatic compression devices for the treatment of venous insufficiency and leg ulcers in the home.

BACKGROUND

Chronic venous insufficiency (CVI) of the lower extremities is a condition caused by abnormalities of the venous wall and valves that leads to obstruction or reflux of blood flow in the veins.¹ Symptoms and signs of CVI include hyperpigmentation, stasis dermatitis, chronic edema, and venous ulcers. Severe and persistent edema leads to secondary lymphedema and trapped fluid. The calf becomes permanently enlarged and hard, and ulcers occur more frequently and are more difficult to heal.²

Approximately 3% to 11% of the adult population has skin changes and edema from CVI.¹ Studies of the prevalence of venous leg ulcers found that venous ulcers occur in approximately 0.18% to 1.3% of the adult population, with only 50% with healing by 4 months, 20% with open ulcers at 2 years, and 8% with open ulcers at 5 years.¹

Wide consensus exists in the literature that compression is a necessary part of all treatments for CVI and venous ulcers. A list of reviews and guidelines related to the use of compression is given in Appendix 1 (online only). Compression is commonly provided with stockings; these stockings are not covered by Medicare because they do not fall into any Medicare statutorily defined benefit category.

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APPENDIX 1, ONLINE ONLY

Related reviews and guidelines

The following reviews and guidelines related to the use of compression for the treatment and prevention of venous insufficiency and venous leg ulcers were found through a search of the Cochrane database, the International Network of Agencies of Health Technology Assessment database, and the National Guideline Clearinghouse in March 2001.

Compression for prevention of venous leg ulcers¹: Cochrane review of compression methods (not including pneumatic compression) for the prevention of venous leg ulcers. The reviewers found no trials that compared compression with no compression for the prevention of venous leg ulcers. Studies comparing different types of compression stockings found that noncompliant patients had high rates of recurrence of ulcers, providing circumstantial evidence of the benefit of compression in prevention of the recurrence of ulcers. The review also concluded that recurrence rates might be lower with higher compression stockings (UK class III, 25 to 35 mm Hg at the ankle) compared with moderate compression stockings (UK class II, 18 to 24 mm Hg at the ankle) but that patients were less compliant with the higher compression stockings.

Compression for venous leg ulcers²: Cochrane review of compression methods (not including pneumatic compression) for the treatment of leg ulcers. The reviewers concluded that compression increases ulcer healing rates compared with no compression. High compression was more effective than low compression, but the studies did not measure the amount of pressure applied with the bandages or stockings so that there was no basis for recommending a specific pressure. There were no clear differences in the effectiveness of different methods of high compression.

Care of patients with chronic leg ulcer³: Guideline from the Scottish Intercollegiate Guidelines Network on the treatment of venous leg ulcers. Strong recommendation was given for graduated compression with stockings or bandages, but there was no mention of the use of pneumatic compression devices.

Venous leg ulcer guideline⁴: Guideline from the University of Pennsylvania on the treatment of venous leg ulcers. Authors state that pneumatic compression therapy may be necessary if edema fails to resolve with compression bandages.

REFERENCES

1. Nelson E, Bell-Syer S, Cullum N. Compression for preventing recurrence of venous ulcers (Cochrane Review). Oxford: The Cochrane Library, Update Software; 2001.
2. Cullum N, Nelson E, Fletcher A, Sheldon T. Compression for venous leg ulcers. Oxford: The Cochrane Library, Update Software; 2001.
3. Scottish Intercollegiate Guidelines Network. The care of patients with chronic leg ulcer. Edinburgh, Scotland; 1998.
4. McGuckin M, Stineman MG, Goin JE, Williams SV. Venous Leg Ulcer Guideline. Philadelphia: University of Pennsylvania; 1997.

APPENDIX 2, ONLINE ONLY

Clinical literature search strategy. The medical databases MEDLINE, EMBASE, and AMED (Allied and Complementary Medicine) were searched on March 8, 2001, with the DIALOG system to find relevant clinical trials on the use of pneumatic compression to treat CVI or leg ulcers caused by venous insufficiency. The search included all articles in the databases up to the date of the search. The following search strategy was used.

Table II (online only) was used to find articles related to venous insufficiency or leg ulcers. To find articles related to pneumatic compression, the following searches were used: pneumatic OR pneumocompression OR pump? (3N) compress? OR intermittent (3N) compress? OR wright () linear () pump?. Abbreviations used in the text search were: 3N, requests that terms be adjacent within three words in any order (for example: ulcer? (3N) leg? would find “leg ulcer” or “ulcers on the leg”); and ?, includes any word with the letters before the question mark (for example, extremit? would find extremity or extremities).

Articles were included on the basis of the following criteria: treatment with intermittent pneumatic compression as major therapy (ie, not as adjunct to surgery); medical conditions; venous insufficiency of the lower extremity; leg ulcer; compression pump used in the home setting; and health outcomes, such as reduction of edema or ulcer healing rate measured. Articles were excluded on the basis of the following criteria: use of pneumatic compression to treat lymphedema; venous insufficiency caused by pregnancy; use of pneumatic compression to prevent deep vein thrombosis; studies of fewer than 10 patients; and studies published in a language other than English.

Table I, online only. (continued)

Reference	Study design	Patient population	Protocol	Outcome measures	Results	Comments
		Ulcer duration 18 to 725 d (average, 299 d for Unna's boot group, 316 for HomeRx group) Average ulcer size 9.9 cm ² (standard error, 1.1) No prestudy preparation discussed	Kendall), stocking removed during IPC Control group: Unna's boot, instructed to elevate legs 1 h in early morning and 2 h in evening All patients: COMFEEF hydrocolloid dressing Weekly visits to clinic		respectively); pain scores for Unna's boot versus IPC: 3.1 (standard deviation, 2.3) versus 2.0 (standard deviation, 1.4), not significant	
Smith et al 1990	RCT Intention-to-treat Coin-toss randomization Supported by Kendall Healthcare	45 patients No dropouts mentioned Age range 42 to 78 y Deep venous insufficiency ulcers present 0.5 to 22 y Ulcer size not discussed No prestudy preparation discussed	Sequential gradient compression device (Kendall Healthcare) Test group: 4 h per day; compression device applied over stockings See subsequent "both groups" for other treatment of test group Control group received treatment listed subsequently in "both groups" Both groups ulcers were debrided, cleaned, and dressed; both groups received compression stocking (30 to 40 mm Hg compression at ankle); patients instructed to elevate legs when sitting Patients were reviewed weekly, and wound was measured	No. of patients healed at end of 3-mo study (healed = all ulcers achieved complete healing) Median healing rate: area of ulcer traced and digitized to measure area	One patient of 24 healed in control group compared to with 10 of 21 healed in pump group (<i>P</i> = .009) Median healing rate 2.1% area per week in control group compared with 19.8% area per week in pump group (<i>P</i> = .046)	Some patients were not able to complete 4 h with pump per day because of work or other circumstances Authors mention that higher pressure stockings (40 to 60 mm Hg at ankle) may be more beneficial but many elderly patients have difficulty applying these
Mulder et al 1990	Cohort study (historical control) Not intention-to-treat No support source mentioned	10 patients enrolled Two dropouts (noncompliance, equipment malfunction) Of eight remaining patients average age 68 y (no range provided) Chronic venous ulcers present for at least 1 y Range of ulcer size 3.13 to 10.72 cm ² (average size, 5.70) Before study, patients placed on combined elastic wrap and Unna's boot therapy for 42 d before entry; only patients with no improvement chosen for study	Sequential compression device therapeutic system (Kendall Healthcare products) Use daily for 1 h in the morning and 2 h in evening during duration of 120-day study Wound cleaned and wrapped weekly with compressive dressing consisting of Unna's boot and elastic wrap Wound status, pain assessments, exudate amounts, and segmental leg volume measurements assessed weekly during treatment, at total wound closure, and at 6 wks after closure	Effect of treatment on wound area (measured with digitizing photographs of wounds) over time estimated with linear regression	Significant decrease in wound area over time in patients remaining in study (<i>P</i> < .01) Only one patient was completely healed in 120 d	Patients followed for 1 y after study termination; two patients who discontinued pump use had recurrent wounds that healed after returning to pump use

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Table I, online only. (continued)

Reference	Study design	Patient population	Protocol	Outcome measures	Results	Comments
Hazarika and Wright 1981	Prospective controlled study Not intention-to-treat No indication how patients were chosen for treatment or control Study funded by Department of Health and Social Security, United Kingdom	21 patients No mention of dropouts Age range, 50 to 82 y Chronic ulcers, 19 present for longer than 6 mo Ulcer size measured, but sizes not reported in study Before study, all ulcers had been treated with compression bandaging and topical applications, including antibiotics	Flowtron (single chamber) 2-min inflation, 2-min deflation, 15-changeover, once daily for 2 to 3 h at "comfortable" pressure setting (between 30 and 80 mm Hg) Control group continued compression bandaging and topical applications Follow-up visits at 1 to 3 wk intervals for duration of observation (observation ranged from 5 to 44 wks; average, 26.7 wks)	Size of ulcer (measured at longest and broadest diameters using transparent cm scale) Subjective impression of healing Self-reported compliance	Overall one control patient healed and 11 control patients had nbo change or worsening of ulcers Five IPC patients had improved ulcers and two patients with self-reported low compliance had ulcers that did not change or increased in size (although the latter patient reported subjective improvement)	Results reported as case series (not all patients apparently reported) Some elderly patients had fear of device

Chronic edema/chronic venous insufficiency

Arcerius and Caprini 1996	Cohort study (historic control) Not intention-to-treat No mention of support source	18 patients No dropouts Age range, 23 to 62 y; average age, 45.1 y Before study, patients had been wearing compression stockings	Sequential intermittent pneumatic compression device (SCD, Kendall Healthcare) Compression cycle 35 to 50 mm Hg during 11 s with 60 s between compression cycles, 4 h per day Other treatment: all patients wore knee-length high-pressure graduated elastic compression stockings during study (40 to 50) mm Hg at ankle Patients continued treatment for 6 months, at which point questionnaire was sent to patients to assess outcomes	Clinical improvement based on questionnaire asking about symptoms before and after use of pump, each of the following clinical problems was given score of 1 to 5: swelling, pain/discomfort, discoloration of the skin, cosmetic problems, decreased activity tolerance, depression, sleep problems, and interference with work; Scores reported as median (25% to 75% interquartile range) Patient also rated inconvenience of using device on scale of 1 to 5 and whether standing tolerance and activity tolerance was improved	Total score decreased from 20 (17.2 to 25) before compression to 13 (10 to 16.5) after compression ($P < 0.001$) with significant decreases in all eight individual clinical symptoms Median score for inconvenience of using device: 2.6 (interquartile range, 1 to 4.5), where 1 was no inconvenience and 5 was too inconvenient 14/18 (78%; 95% CI, 59%-97%) patients reported improved standing tolerance	Positive correlation between inconvenience score and age of patient ($r = 0.5$; $P < .027$), suggesting less favorable compliance in older patients Study also measured physiologic measures of response with air plethysmography
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Table I, online only. (continued)

Reference	Study design	Patient population	Protocol	Outcome measures	Results	Comments
					11/18 (61%; 95% CI, 39%-83%) patients reported improved activity tolerance Total reported compliance: devices used an average of 6.5 d every week (range, 1 to 7; 95% CI, 5.7-7.3); mean number of hours of use every day was 2.14 h (range, 0.5 to 4 h, 95% CI, 2.12-3.2)	
Pflug 1975	Cohort study Not intention-to-treat Patients with unilateral or bilateral chronic swelling switched to pneumatic compression No support source mentioned	252 patients with venous edema (188 mild; 64 severe) 56 patients with lymphedema (32 mild; 24 severe) No dropouts No information about patient demographics given No prestudy preparation discussed	Flowtron (single chamber*) Use at least 3 h daily Patients discontinued other forms of therapy Results assessed after 3 wks of treatment	Improvement in "signs" and "symptoms"	185/188 and 171/188 patients with mild venous edema showed improved signs and symptoms 62/64 and 63/64 patients with severe venous insufficiency showed improved signs and symptoms 29/32 and 20/32 patients with mild lymphedema showed improved signs and symptoms 14/24 and 19/24 patients with severe lymphedema showed improved signs and symptoms	Statistical significance not measured Discrepancy in number of patients with mild lymphedema Patients were able to manage use of device at home
Ginberg et al 1999	RCT Not intention-to-treat Supported by grant-in aid from National Health Research and Development program of Health Canada	15 patients No dropouts Mean age, 60 y; age range, 38 to 81 y All patients had failure of condition to improve with use of graduated compression stockings	Jobst extremity pump (multichamber sequential*) Used twice each day (recommended noon and evening) for 20 min each time over 2 mo No mention of other treatment given to patients Patients randomly assigned to use pump at either 50 mm Hg (therapeutic pressure) or 15 mm Hg (placebo pressure) for first mo; After 1 mo, patients asked to switch to use other pressure (those using 50 switched to 15 and vice versa) Patients symptoms were assessed via questionnaire at end of each month	At end of each month, patients given questionnaire to assess symptoms and functional status including: most and least limited activities; degree and duration of pain and swelling; each answer associated with numeric score with minimum score = 10 (most severely affected) and maximum score = 70 (least	Mean symptom score was 14.4 (range, 5 to 24) for period of placebo use and 16.5 (range, 7 to 27) for period of therapeutic use; mean difference (2.1) was found to be statistically significant ($P = .007$); range of difference for improvement between placebo and therapy was -5 to +5	Although patients were not blinded to pump pressure itself, they were told that efficacy and optimum pressure for symptom relief were unknown and that study was to compare effects of different pressure levels

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Table I, online only. (continued)

<i>Reference</i>	<i>Study design</i>	<i>Patient population</i>	<i>Protocol</i>	<i>Outcome measures</i>	<i>Results</i>	<i>Comments</i>
				severely affected); Individual scores summed to obtain overall symptom score At end of second mo, global rating for each patient was obtained via questionnaire; Patients were asked which month they felt better; would they continue using pump; and their perceived rating of differences between pressures; treatment was considered successful if previous factors received positive responses	For 12 patients (80% of sample), treatment was considered successful; of these 12, nine continued to use pumps after study and continued to derive benefits for 6 to 30 mo after enrollment	

* Type of pump was not specified in the study report but was found in "Healthcare product comparison system, hospital edition." Plymouth meeting (PA); 2000.

IPC, Intermittent pneumatic compression.

Table II, online only.

MESH index terms (MEDLINE indexing)	Venous insufficiency—nursing Venous insufficiency—prevention and control Venous insufficiency—rehabilitation Venous insufficiency—therapy Venous insufficiency syndrome Venous leg ulcer
EMTREE index terms (EMBASE indexing)	Vein insufficiency—disease management Vein insufficiency—prevention Vein insufficiency—rehabilitation Vein insufficiency—therapy Vein insufficiency syndrome
Text words	(vein? OR venous?)(3n)insufficien? OR (ulcer?(3N)(leg? OR extremity? OR venous OR vein?)

Many elderly patients have reduced strength and dexterity that makes it difficult to put on the stockings.³⁻⁶ Compression may also be provided with an Unna's boot or with different types of elastic bandages. Some patients have reported difficulty with these methods as well.^{7,8}

Compression to the limb may be provided with pneumatic compression devices. Pneumatic compression devices consist of an inflatable boot and a pneumatic pump that fills the boot with compressed air. The boot is intermittently inflated and deflated, with cycle times and pressures that vary between devices. The boots may have a single chamber that is inflated to a single pressure or multiple chambers that are individually inflated in sequential order, to produce a "milking" effect on the limb. The latter type of device may have preset pressures in each chamber or pressures that are individually set for each chamber. Individually controllable pressures would allow patients to lower the pressure in chambers directly over the site of an ulcer.

EVIDENCE MODEL

Figure 1 outlines an evidence model for the action of pneumatic compression pumps. In this model, pneumatic pumps affect the physiologic processes underlying CVI and venous ulcers, leading to beneficial health outcomes such as reduced edema, prevention of lymphedema, and increased rates of ulcer healing. Pneumatic compression may also lead to adverse events. In this assessment, we searched for data on the use of pneumatic compression in the home environment for patients with venous insufficiency of the lower extremities or leg ulcers from CVI. Studies on patients with lymphedema were excluded because pneumatic compression devices for lymphedema were the subject of a separate Medicare coverage decision.

Many studies investigate the effect of pneumatic compression on intermediate outcomes on the basis of assumptions about the underlying physiology of CVI and venous ulcers. However, these physiologic processes are poorly understood.⁹ One theory of the action of pneumatic compression is that use of the device increases oxygen tension. Studies have shown that venous ulcers, like other wounds, have low oxygen tension and that wounds associated with an oxygen tension of less than 20 mm Hg are unable to heal.^{10,11} Some researchers have found that intermittent pneumatic compression increases oxygen tension in venous ulcers,¹² and others found no difference in oxygen tension with pneumatic compression.¹¹ Another theory is that pneumatic compression increases blood flow (measured with the clearance of small-molecular weight radiolabeled markers or a laser Doppler fluxmeter) and/or lymphatic clearance (measured with the clearance of large-molecular weight radiolabeled markers) at the site of the ulcer. However, different studies found conflicting results on the clearance of large and small molecules with the use of pneumatic compression.¹³⁻¹⁵ Differences between studies may be explained by different protocols of pneumatic compression, different methods of measurement, and different patient populations. More research is needed in this area.

Many studies have measured the effects of different cycle times, pressures, and multichamber versus single-chamber devices on physiologic measurements on healthy volunteers and patients (reviewed by Allsup¹⁶). These studies found that the use of multichamber devices and higher pressures led to greater increases in venous blood flow than single-chamber devices and lower pressures, respectively. However, one study found no additional increases in blood velocity at pressures above 35 mm Hg at the ankle, and another study found that blood velocity continued to increase at pressures above 55 mm Hg at the ankle. Compression with single-chamber devices led to trapping of venous blood in the distal veins, whereas sequential gradient compression results in more complete emptying of the deep veins.¹⁷ Venous system refilling time was approximately 45 seconds in two different studies, which led to a recommendation of a cycle time of approximately 70 seconds to allow the venous system to refill while the devices were deflated.¹⁶ Many of these studies were done on healthy volunteers or a population with the devices to prevent deep vein thrombosis, which led to questions of the applicability of these results to a patient population with CVI. In addition, the poor understanding of the physiologic processes underlying CVI and the mechanism of action of the devices makes interpretation of these studies difficult.

Reporting of adverse events is poor in many areas of medical research,¹⁸ which results in insufficient knowledge about the true spectrum and frequency of adverse events. This is likely to be the case for pneumatic compression devices as well. Peroneal neuropathy and compartment syndrome, where circulation and function of tissues within a closed space are compromised by increased pressure, leaving muscles and nerves susceptible to injury, have been reported with the use of pneumatic compression to prevent deep vein thrombosis.¹⁹ Genital edema has been reported when pneumatic compression devices are used for lower limb lymphedema.²⁰ Pneumatic compression is contraindicated in patients with significant arterial insufficiency, edema from congestive heart failure, active phlebitis, deep vein thrombosis, or the presence of localized wound infection or cellulitis.²¹ These may be relative rather than absolute contraindications. For example, arterial disease may be a relative contraindication; compression with stockings or bandages may be used in these patients at lower pressures.²² Very high compression reduces blood supply to the skin and may lead to pressure damage, and even moderate pressures in patients with impaired blood supply to the legs may result in pressure damage.²³

METHODS

The systematic review was carried out by the Agency for Healthcare Research and Quality (AHRQ) Technology Assessment staff trained in systematic review methodology. The technology assessment was reviewed by four content experts before it was sent to CMS.

The questions and inclusion and exclusion criteria for the systematic review were developed in collaboration with staff from CMS. CMS was given the opportunity to review

and comment on the draft manuscript at the same time the draft was sent to external reviewers. The authors considered the comments of CMS and the external reviewers and modified the manuscript on the basis of the comments. The content of the final report and decisions regarding publication in a peer-reviewed journal rested solely with the authors.

Literature was searched in the medical databases MEDLINE, EMBASE, and AMED (Allied and Complementary Medicine) from the inception of the databases to March 8, 2001, with keywords related to pneumatic compression, venous insufficiency, and venous ulcers. A full description of the literature search is given in Appendix 2 (online only). This search found 91 articles, seven of which contained relevant clinical trials. Reference lists of review articles were hand searched, but no additional articles were found. An expert reviewer suggested an additional study that was included in the review.

Data was extracted from the studies directly into an evidence table (Table I, online only) by one assessor. A second assessor verified the extracted data. The assessors noted key attributes of each study that affect relevance and validity in the comments column of the evidence table.

RESULTS

Results by study

Ginsberg et al²⁴ studied the effect of pneumatic compression in patients with CVI associated with severe post-phlebotic syndrome. All patients were given pneumatic pressure devices, and patients were randomized to either a therapeutic pressure of 50 mm Hg or a placebo pressure of 15 mm Hg for 20-minute sessions twice daily. After 1 month, patients were crossed over to the alternate pressure. Results were measured with a symptom questionnaire; on this questionnaire, higher scores correspond to fewer symptoms, with a score of 70 for the least severely affected patients. The mean symptom score increased from 14.4 with the placebo pressure to 16.5 ($P = .007$) with the therapeutic pressure. The authors state that this difference is clinically significant, but it is very small.

Arcelus and Caprini²⁵ measured clinical improvement in 18 patients aged 23 to 62 years with CVI. Compression was provided with a sequential gradient device, 4 hours per day, 35 to 50 mm Hg for 11 seconds, with 60 seconds between cycles. Clinical improvement was measured with a questionnaire about symptoms before and after the use of the pump. Symptoms included swelling, discomfort, discoloration of the skin, cosmetic problems, decreased activity tolerance, depression, sleep problems, and interference with work. The study measured a significant decrease in the scores, indicating a significant clinical improvement with the use of the pump. Patients rated their pre-pump symptoms retrospectively after using the pump; answers on retrospective questionnaires may be subject to recall bias. Older patients rated the device as more inconvenient, suggesting the potential for lower compliance.

Pflug²⁶ measured the improvement in signs and symptoms of 252 patients with venous edema (188 mild; 64 severe) with the single-chamber device at least 3 hours daily. No demographic information is given about these patients, and no definition of "signs" or "symptoms" is given. More than 90% of the patients had improvements of signs and symptoms. Statistical significance was not measured.

Rowland²⁷ measured the time to ulcer healing, change in ulcer size, and change in lower limb volume. The study was a crossover randomized controlled trial (RCT). Patients were switched to the alternative therapy after 2 to 3 months, depending on the rate of healing. Sixteen patients were originally enrolled, and five patients withdrew from the study after the first or second visit (three from the pump group and two from the bandage group). Patients in the pneumatic compression group received treatment with a single-chamber device, 1 hour each morning and evening. Control patients received high stretch bandaging. There was no difference in intention-to-treat analysis of ulcer healing rate and lower limb volume between the groups. Patients reported that the device was easier to use and more comfortable than the bandaging. Only three patients had complete healing by the end of the study. The authors comment that the power of the study may be too low to detect a real difference.

Schuler et al²⁸ studied the effect of a sequential gradient compression system compared with Unna's boot in a RCT of 54 patients ranging in age from 31 to 85 years. Patients were instructed to use the pneumatic compression devices for 1 hour in the morning and 2 hours in the evening with their legs elevated (12 seconds of compression, 60-second interval, 50 mm Hg at the ankle). Patients wore stockings between pumping sessions. There was no significant difference in fraction of patients who achieved complete healing in 6 months, average healing rates, or pain scores.

Smith et al²⁹ studied the effect of a sequential gradient compression device used 4 hours per day in a RCT of 45 patients ranging in age from 42 to 78 years. Patients in the experimental and control groups received compression stockings (30 to 40 mm Hg compression at the ankle) and were instructed to wear stockings during pumping sessions. One of 24 patients had healing within 3 months in the control group compared with 10 of 22 patients in the pneumatic compression group ($P = .009$). The median healing rate was 2.1% of ulcer area per week in the control group compared with 19.8% of ulcer area per week in the pneumatic compression group ($P = .046$). This was an intention-to-treat analysis.

Mulder and Reis⁸ studied the effect of a sequential gradient compression device in a historic control study on 10 patients with an average age of 68 years. Patients were their own control; they entered the study after 42 days of failed Unna's boot therapy. Patients were instructed to use the sequential compression devices for 1 hour each morning and 2 hours each evening. Two patients dropped out, one for equipment failure and one for lack of compliance. There was a significant decrease in wound area over time in

patients remaining in the study ($P < .01$), with only one patient with complete healing in 120 days. Mulder and Reis⁸ report that patients were followed for 1 year after study termination and that two patients who discontinued pump use had recurrent wounds that healed after a return to pump use.

Hazarika and Wright³⁰ studied the effect of a single-chamber device in a prospective controlled study of 21 patients with an age range from 50 to 82 years. No indication was given on how patients were chosen for treatment or control. Patients used the device once daily for 2 to 3 hours at "comfortable" pressure settings (30 to 80 mm Hg). Most control patients had no change or worsening of ulcers; several pneumatic compression patients had improved ulcers, and a few of those who reported low compliance had ulcers that did not change or increased in size. Statistical significance of the results was not reported.

Results by question

Following is a summary of results in response to specific questions posed by CMS about the effectiveness of pneumatic compression pumps.

At what point in therapy should the pneumatic compression devices be introduced? Three studies^{25,26,31} showed an improvement in signs and symptoms of CVI with the use of pneumatic compression devices. No studies were specifically designed to test whether use of the devices could prevent ulcers. Two patients who discontinued use of the compression device in one study⁸ had recurrence of ulcers that healed when use of the device was reinitiated. This is consistent with circumstantial evidence from studies that compression with stockings and bandaging systems prevents recurrence of venous ulcers.³²

Most patients in the studies of ulcer healing had chronic ulcers that had not healed for several months or more. Therefore, no conclusions can be made about whether pneumatic compression can improve rates of ulcer healing in new ulcers compared with other therapies.

One RCT and two other studies^{8,29,30} found that pneumatic compression devices increased rates of healing in chronic ulcers that had not healed for several months or more with other methods. Two other RCTs^{27,28} found no difference compared with control methods. This may be because of differences in treatment of control patients; however, a previous review had found no difference in ulcer healing rates among high compression methods, such as stockings, bandages, and Unna's boot. This may also be because of differences in protocol (see question 2).

Overall, the results suggest that patients with CVI who have not yet had ulcers develop may have a small benefit from the use of pneumatic compression. No data exist on patients with new ulcers, and data are mixed on whether pneumatic compression pumps aid healing of chronic ulcers that have not responded to other therapies for several months or longer.

What protocol should be used to maximize effectiveness of the pneumatic compression devices? No studies directly compared the effectiveness of single-cham-

ber devices with gradient multichamber devices. Both types of devices had a beneficial effect compared with control methods in some studies and no difference compared with control methods in other studies. Several researchers have made physiologic arguments favoring multichamber gradient devices. Results from different physiologic studies conflict, and more research is needed in this area.

Three of the studies^{8,28,29} on patients with ulcers used sequential gradient multichamber devices; it was not specified whether these were the type with individual pressure control in each chamber. Pressures and cycle times were mostly set as recommended by the manufacturer. Recommendations for these parameters are from physiologic studies. None of the studies directly compared the effects of different pressures or cycle times on health outcomes, such as ulcer healing rates. In most studies, patients were instructed to use the device for several hours each day.

Some studies replace other compression treatments with pneumatic compression, and other studies use the pneumatic compression device in conjunction with other methods of compression. There are many other variables in the studies. For example, one RCT by Schuler et al²⁸ that showed no additional benefit for the devices asked control patients to sit for 3 hours daily with elevated legs. Another RCT by Smith et al²⁹ that showed a benefit of the devices over the control methods only asked the control patients to elevate legs while sitting with no specific time period mentioned. Smith et al²⁹ comment that they cannot rule out that some of the effect may be from pneumatic compression patients sitting with elevated legs for longer periods. Another variable was how the stockings were worn. Patients wore stockings in both studies; however, in the study by Schuler et al,²⁸ patients were asked to remove their stockings during pumping sessions, and in the study by Smith et al,²⁹ patients wore stockings during pumping sessions.

Some studies not reviewed here had patients come to a clinic to receive pneumatic compression sessions. For example, McCulloch et al³³ found that patients who received an hour of pneumatic compression twice weekly had significantly improved rates of ulcer healing compared with control patients.

Overall, there are no data that can be relied on to develop a protocol to maximize the effectiveness of the pneumatic compression pumps.

Are there absolute indications or contraindications to use of pneumatic compression therapy? Indications for the use of pneumatic compression that have been addressed in studies are CVI with edema and CVI with chronic ulceration that had not healed in several months or more with other treatments.

Few adverse events were reported in the clinical trials. However, a few patients dropped out from several trials; this may be because of adverse events. One patient in the study of Schuler et al²⁸ had cellulitis develop with the use of a sequential gradient compression system. One study reported that patients were generally able to use the devices at home,²⁶ but another study reported that some elderly patients had a fear of the devices.³⁰

Pneumatic compression is contraindicated in patients with significant arterial insufficiency, edema from congestive heart failure, active phlebitis, deep vein thrombosis, or the presence of localized wound infection or cellulitis. These may be relative rather than absolute contraindications.

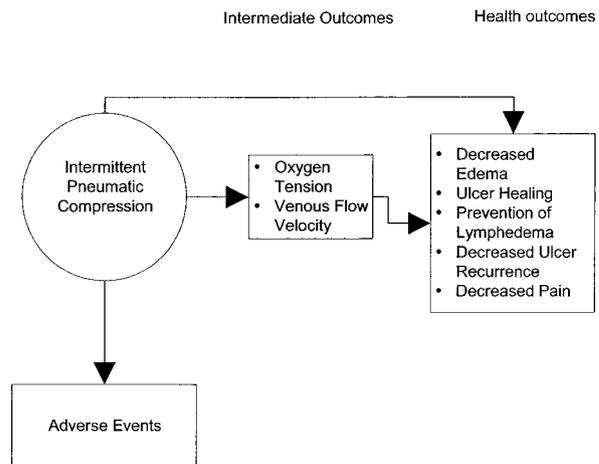
CONCLUSION

Compression therapy is an important part of treatment for CVI and venous leg ulcers. Often patients do not comply with compression therapies, such as stockings, bandages, and Unna's boot, because of difficulty with use of the therapies.

Long-term use of pneumatic compression devices in the home environment may be an alternative to other compression therapies for patients who are unable or refuse to comply with other methods. In addition, pneumatic compression may be effective for patients who have previously failed treatment with other compression devices, either in addition to, or instead of, these other methods. Trials of pneumatic compression devices for the treatment of CVI and venous leg ulcers include few patients and may not have enough power to detect differences. Several studies have randomized designs with well-defined outcome measures and results that reach statistical significance. The results are mixed. There are many protocol differences between studies, including choice of compression system for control patients.

A previous review found no evidence of different effectiveness for different types of compression, such as stockings, bandages, or Unna's boot.²³ However, other variables, such as length of time spent with legs elevated or whether stockings are worn during pumping sessions, might affect results. Several studies did show significant improvement with the use of pneumatic compression devices of long-standing chronic ulcers that had not healed with other methods. Few adverse events were recorded. Some patients expressed fear of using the devices, but patients who agreed to use the devices generally expressed satisfaction and reported higher compliance than with other compression methods.

This systematic review has several potential limitations. The scope of the systematic review was narrowly defined by the policy question asked by CMS. Therefore, the focus of the systematic review was data directly studying the effectiveness of pneumatic compression devices. However, a more broadly defined systematic review that presents an overview of care of patients with venous insufficiency and venous ulcers, including assessment and a full range of treatments, might be useful to clinical decision making. Another potential limitation is the scope of the literature review. We have tried to ensure that the literature search had as little bias as possible by searching three different electronic databases and searching for grey literature through suggestions of experts and hand searches of references in review articles. For practical reasons, we did exclude articles in languages other than English. Ideally, articles in all languages should be included. However,



Evidence model for the action of pneumatic compression pumps.

researchers in other areas have found that 78% of identified meta-analyses have language of publication restrictions and that there is no evidence that language restricted meta-analyses lead to biased estimates of intervention effectiveness.³⁴

CMS considered the results of this technology assessment and decided not to change the coverage policy. Pneumatic compression will only be covered for patients with refractory edema with significant ulceration of the lower extremities after a 6-month treatment with standard methods, such as compression stockings, has failed.³⁵

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REFERENCES

- Nicolaidis AN. Investigation of chronic venous insufficiency: a consensus statement (France, March 5-9, 1997). *Circulation* 2000;102:E126-63.
- Abrams WB, Berkow R, Fletcher AJ. *The Merck manual of geriatrics*. Rahway (NJ): Merck Sharp & Dohme Research Laboratories; 1990.
- Cheatle TR, McMullin GM, Farrah J, Smith PDC, Scurr JH. Three tests of microcirculatory function in the evaluation of treatment for chronic venous insufficiency. *Phlebology* 1990;5:165-72.
- Gutman H, Zelikovski A, Haddad M, Reiss R. Clinical experience treating varicose veins in the aged. *Am Surg* 1989;55:625-8.
- Moody M. Intermittent sequential compression therapy in lower limb disorders. *Prof Nurse* 1997;12:423-5.
- Sarkar PK, Ballantyne S. Management of leg ulcers. *Postgrad Med J* 2000;76:674-82.
- Hofman D. Intermittent compression treatment for venous leg ulcers [published erratum in *J Wound Care* 1995;4:208]. *J Wound Care* 1995;4:163-5.
- Mulder GD, Reis TM. Venous ulcers: pathophysiology and medical therapy. *Am Fam Physician* 1990;42:1323-30.

9. Gloviczki P, Cambria RA, Rhee RY, Canton LG, McKusick MA. Surgical technique and preliminary results of endoscopic subfascial division of perforating veins. *J Vasc Surg* 1996;23:517-23.
10. Vella A, Carlson LA, Blier B, Felty C, Kuiper JD, Rooke TW. Circulator boot therapy alters the natural history of ischemic limb ulceration. *Vasc Med* 2000;5:21-5.
11. Nemeth AJ, Falanga V, Altstadt SP, Eaglstein WH. Ulcerated edematous limbs: effect of edema removal on transcutaneous oxygen measurements [see comments]. *J Am Acad Dermatol* 1989;20(2 Pt 1):191-7.
12. Koları PJ, Pekanmaki K. Effects of intermittent compression treatment on skin perfusion and oxygenation in lower legs with venous ulcers. *Vasa* 1987;16:312-7.
13. Roztocil K, Prerovsky I, Oliva I. The effect of intermittent compression on blood and lymph flow rates in the lower limbs. *Vasa* 1979;8:346-8.
14. Pekanmaki K, Koları PJ, Kiistala U. Laser Doppler vasomotion among patients with post-thrombotic venous insufficiency: effect of intermittent pneumatic compression. *Vasa* 1991;20:394-7.
15. Belcaro GV, Nicolaides AN. Effects of intermittent sequential compression in venous hypertensive microangiopathy. *Phlebology* 1994;9:99-103.
16. Allsup DJ. Use of the intermittent pneumatic compression device in venous ulcer disease. *J Vasc Nurs* 1994;12:106-11.
17. Nicolaides AN, Fernandes e Fernandes J, Pollock AV. Intermittent sequential pneumatic compression of the legs in the prevention of venous stasis and postoperative deep venous thrombosis. *Surgery* 1980;87:69-76.
18. Ioannidis JP, Lau J. Completeness of safety reporting in randomized trials: an evaluation of 7 medical areas. *JAMA* 2001;285:437-43.
19. Lachmann EA, Rook JL, Tunkel R, Nagler W. Complications associated with intermittent pneumatic compression. *Arch Phys Med Rehabil* 1992;73:482-5.
20. Boris M, Weindorf S, Lasinski BB. The risk of genital edema after external pump compression for lower limb lymphedema. *Lymphology* 1998;31:15-20.
21. Kunitomo B, Cooling M, Gulliver W, Houghton P, Orsted H, Sibbald RG. Best practices for the prevention and treatment of venous leg ulcers. *Ostomy Wound Manage* 2001;47:34-50.
22. Angle N, Bergan JJ. Chronic venous ulcer. *Br Med J* 1997;314:1019-23.
23. Cullum N, Nelson E, Fletcher A, Sheldon T. Compression for venous leg ulcers. Oxford: The Cochrane Library, Update Software; 2001.
24. Ginsberg JS, Magier D, Mackinnon B, Gent M, Hirsh J. Intermittent compression units for severe post-phlebotic syndrome: a randomized crossover study. *CMAJ* 1999;160:1303-6.
25. Arcelus JJ, Caprini JA. The home use of external pneumatic compression for the management of chronic venous insufficiency. *Int Angiol* 1996;15(3 Suppl 1):32-6.
26. Pflug JJ. Intermittent compression in the management of swollen legs in general practice. *Practitioner* 1975;215:69-76.
27. Rowland J. Intermittent pump versus compression bandages in the treatment of venous leg ulcers. *Aust N Z J Surg* 2000;70:110-3.
28. Schuler JJ, Maibenco T, Megerman J, Ware M, Montalvo J. Treatment of chronic venous ulcers using sequential gradient intermittent pneumatic compression. *Phlebology* 1996;11:111-6.
29. Smith PC, Sarin S, Hasty J, Scurr JH. Sequential gradient pneumatic compression enhances venous ulcer healing: a randomized trial. *Surgery* 1990;108:871-5.
30. Hazarika EZ, Wright DE. Chronic leg ulcers. The effect of pneumatic intermittent compression. *Practitioner* 1981;225:189-92.
31. Ginsberg JS, Brill-Edwards P, Kowalchuk G, Hirsh J. Intermittent compression units for the postphlebotic syndrome. A pilot study. *Arch Intern Med* 1989;149:1651-2.
32. Nelson E, Bell-Syer S, Cullum N. Compression for preventing recurrence of venous ulcers (Cochrane Review). Oxford: The Cochrane Library, Update Software; 2001.
33. McCulloch JM, Marler KC, Neal MB, Phifer TJ. Intermittent pneumatic compression improves venous ulcer healing. *Adv Wound Care* 1994;7:22-4, 26.
34. Moher D, Pham B, Klassen TP, Schulz KF, Berlin JA, Jadad AR, et al. What contributions do languages other than English make on the results of meta-analyses? *J Clin Epidemiol* 2000;53:964-72.
35. Centers for Medicare and Medicaid Services. CMS decision memorandum. Report No.: CAG-00075. 2001.

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