Herpes Zoster (Shingles) Patient-Centered Wound Outcomes: A Literature Review

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GENERAL PURPOSE: To present a comprehensive review of patient-centered outcomes of topical or systemic interventions applied to those with shingles or postherpetic neuralgia to inform clinical practice and identify related research needs.

TARGET AUDIENCE: This continuing education activity is intended for physicians, physician assistants, nurse practitioners, and nurses with an interest in skin and wound care.

LEARNING OBJECTIVES/OUTCOMES: After participating in this educational activity, the participant will be able to:

1. Explain the importance of early diagnosis and treatment of herpes zoster (HZ).
2. Identify interventions that have resulted in documented improvement of validated patient-centered outcomes in patients with HZ or postherpetic neuralgia.
3. Recognize the average per patient medical costs of HZ in the US.

ABSTRACT

BACKGROUND: One in three people endure herpes zoster (HZ; also known as shingles) during their lifetime, experiencing pain, secondary infections, postherpetic neuralgia, reduced quality of life, and considerable patient costs. These patient burdens remain to be reviewed.

OBJECTIVE: To perform a comprehensive review of patient-centered outcomes of topical or systemic interventions applied to those with shingles or postherpetic neuralgia to inform clinical practice and identify related research needs.

DATA SOURCES: The PubMed database was searched with supplementary Google Scholar searches for Medical Subject Headings "shingles" or "post-herpetic neuralgia" to find clinical studies documenting validated patient-centered outcomes: pain, secondary infection, healing, function, depression, social isolation, treatment costs, or quality of life. Six representative case studies were examined.

DATA SELECTION: Pertinent original and derivative clinical study references were included. Preclinical studies, reviews, or studies of non-HZ conditions were excluded.

DATA EXTRACTION: Two authors tabulated clinical efficacy evidence for interventions affecting patient-centered outcomes.

DATA SYNTHESIS: Evidence supported efficacy for systemic antiviral or topical anesthetic interventions improving pain, healing, sleep, vision, or quality of life for those with HZ or postherpetic neuralgia. Patient cases reported improved pain and/or sleep using occlusive dressings. Treatment costs and secondary infections were reported only in cases or cohort studies.

CONCLUSIONS: Randomized clinical research focused on medications improving patient pain, healing, sleep, or vision outcomes. Research is needed measuring outcomes of adding occlusive dressings to optimal care and effects on secondary infections and treatment costs.

KEYWORDS: herpes zoster, infection, patient-centered outcomes, postherpetic neuralgia, shingles, wound care

ADV SKIN WOUND CARE 2021;34:239–48.
DOI: 10.1097/01.ASW.0000737412.71091.4f

Acknowledgments: The authors gratefully acknowledge the contributions to the understanding of herpes zoster and postherpetic neuralgia made by the patients and professionals whose experience and work is cited here. This work is dedicated to the memory of David T. Rovee, whose pioneering research on moist wound healing illuminated the patient-centered outcomes of wound pain, healing, and infection control.

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INTRODUCTION

Although much is known about the clinical course of herpes zoster (HZ; also called shingles) and its global burdens on healthcare systems and economics[1–4] (Table 1), HZ impact on patients is rarely explored in terms of patient-centered outcomes. Unlike primary varicella-zoster virus (VZV) infection, which is self-limiting, the pain or itch of HZ lesions and associated chronic postherpetic neuralgia (PHN) can be severe, disrupting sleep, vision, or thought processes and causing anxiety and depression so intense that PHN is linked to increased likelihood of suicide among older adults experiencing chronic pain.[5] Often lasting for months to years, PHN follows 9% to 14% of HZ cases, increasing in incidence, severity, and duration with age.[6]

In addition to pain or pruritus during the 2 to 4 weeks before HZ lesions heal, the epithelial barrier remains open to the possibility of secondary infection by microorganisms. After epithelialization, cutaneous discoloration and scarring can be troublesome.[2] Despite high levels of patient distress lasting many weeks or months, significantly compromising patient quality of life,[1,7] HZ's true effect on validated patient-centered outcomes[8] remains to be reviewed.

This comprehensive literature review of clinical trials aimed to describe interventions with documented improvement of validated patient-centered outcomes and/or complications for those with HZ to highlight opportunities for future clinical practice and research. Case studies were also tabulated to illustrate needs for further improvement of these outcomes.

METHODS

One Cochrane-trained author searched the National Institutes of Health, National Library of Medicine PubMed reference database from January 1, 1970 to August 23, 2020 for original and derivative clinical trial references containing the combined Medical Subject Headings (MeSH) terms for "clinical trial" and/or "review" combined with MeSH terms for "Herpes zoster or HZ or shingles or Post-herpetic neuralgia or PHN." Added PubMed searches were conducted for these combined MeSH terms or their synonyms and the general term "Clinical outcome" plus individual searches for these combined MeSH terms and each of the following patient-centered outcomes previously validated[8] as important to patients with wounds: healing, wound infection, pain, odor, analgesic use, amputation, impaired

Table 1. HERPES ZOSTER (HZ) AT A GLANCE

- The disease occurs or recurs when varicella-zoster virus (VZV), the viral cause of chicken pox, is reactivated after remaining in sensory nerve ganglia following an earlier VZV episode or vaccination[1,2] and travels to the affected sensory nerve's endings at the dermoepidermal junction, disrupting the basement membrane of the epidermis.[3]
- Typically, 1 to 21 days before skin lesions erupt, the patient feels acute neuritis causing burning or tingling of the skin, with possible hyperesthesia, numbness, or pruritus. The HZ vesicles usually develop unilaterally on the head, neck, or thorax in affected dermatomes served by the fifth cranial (trigeminal) or fifth or sixth thoracic nerves. These usually resolve in 10 to 15 days,[1–3] but may be followed by months to years of prolonged symptoms associated with postherpetic neuralgia (PHN).
- The VZV can be transmitted from vesicles on a person with active HZ. Those with active infection should avoid contact with pregnant individuals, babies younger than 18 months, or immunosuppressed individuals to limit their increased risk of varicella infection.[1] The risk of VZV spread can be minimized by covering eroded vesicles, avoiding touching the eyes, and hand-washing.[3]
- Special attention is required for HZ vesicles occurring around the eyes or nose. Patients with more than 20 vesicles outside the affected dermatome(s) or lesions crossing the midline may indicate potentially fatal viral dissemination.[3]
- Globally, HZ affects 3 to 12 persons per 1,000 person-years, increasing with age older than 50 years or with compromised immune status.[4] More than one million cases of HZ occur annually in the US, with a 32% lifetime chance of any person experiencing HZ. Risk is higher for women or those of Caucasian descent.[5,6] This may be an underestimate because HZ is not on the CDC National Notifiable Disease Surveillance System list, and mild cases may not be documented.[7]
- The HZ vaccines protect from 54% (single-dose vaccine) to greater than 90% (two-dose recombinant attenuated vaccine) of those older than 60 years from developing HZ and may reduce severity of HZ and subsequent PHN symptoms.
- Ideally, treatment consists of antiviral agents (acyclovir, famciclovir, or valacyclovir) as soon as possible within 72 h after appearance of the rash; analgesics to manage pain or pruritus; and microbial barrier wound dressings to isolate vesicles, optimize healing, and prevent secondary bacterial infection.[8]
- Treatments for subsequent PHN include topical agents such as lidocaine patches or systemic agents such as anticonvulsants (eg, gabapentin).[3]

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sleep, sensory or physical function, quality of life, depression, social isolation, or costs or economics of patient or wound care.[8] The authors also included nonredundant qualifying clinical trials from related reviews. Studies reporting any of these measured outcomes on patients with HZ or PHN qualified for inclusion in this review.

Randomized or convenience-controlled clinical trials; case-controlled registries; or cohort studies, case studies, or derivative references were included if they reported a significant improvement in one or more of these measured patient-centered outcomes for individuals afflicted with HZ or PHN. Preclinical studies, those on conditions other than HZ or PHN, or qualitative studies not measuring one of these outcomes were excluded.

After titles were screened for eligibility, two of the authors reviewed eligible abstracts and/or full-text studies. The last name of the study's first author, publication date, and number of participants studied for each qualifying study were entered into a standardized electronic spreadsheet under columns corresponding to the relevant outcome measure. Each study was categorized by study design: (1) randomized controlled trial (RCT), (2) nonrandomized controlled trial, or (3) case studies/cohorts/registries. Total study frequencies and numbers of patients studied were calculated reporting significant improvements for each patient-centered outcome measured in response to one or more interventions studied for those with either HZ or PHN or both. Study quality and risk of bias were not addressed because this work aimed to describe which patient-centered outcomes were being measured for those with HZ or PHN, not evaluate intervention strength or quality of evidence.

The criterion for statistical significance of any effect reported was $P \leq .05$ of incorrectly rejecting the null hypothesis that the intervention did not affect the related measured patient-centered outcome. Qualitative outcomes were beyond the scope of this study and not analyzed or recorded in the Excel file.

To ensure that qualitative individual patient experiences were represented, clinical data were collected on six patients' sex, age, HZ location(s), healing time, and level of pain or pruritus on a scale of 0 (none) to 10 (unbearable), where an answer of "6" was assigned if the sensation interrupted sleep. Each patient was also asked the open-ended query, "What was your shingles experience like and what PHN symptoms did you experience?" Clinical data and patient answers were tabulated from six HZ patients who granted the authors permission for their deidentified data to be published. Three patients also provided photographs to illustrate their experience and granted permission for them to be published.

RESULTS

Most of the 221 qualifying studies identified in the literature search (Figure 1) focused on immunocompetent individuals at least 50 years of age. Depending on the definition of PHN used by the study authors and the time span measured, 5% to 20% of HZ cases experienced PHN.

Example studies supporting major findings are discussed below for each patient-centered outcome supported by evidence. The studies included in this review provided data relevant to the following patient outcomes: pain, healing, function, secondary infection, patient treatment costs, analgesia, depression, and social isolation. Pain, including pruritus or discomfort, followed by lesion healing and costs of treatment were the most common patient outcomes reported during the first 4 to 12 weeks after HZ onset (Figure 2). During ensuing PHN intervals lasting months to years (Figure 3), pain dominated reported patient-centered outcomes, followed by impaired

Figure 1. PRISMA FLOW DIAGRAM

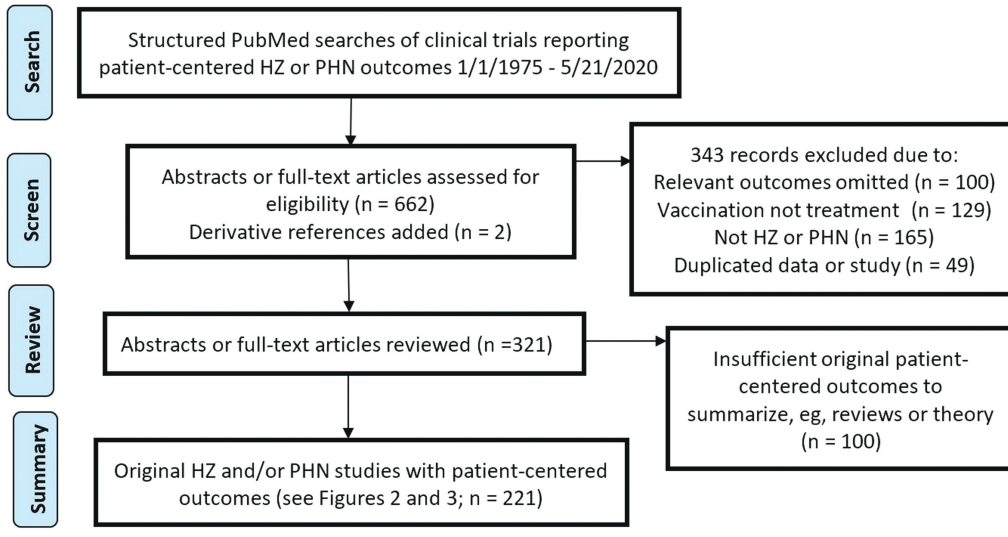
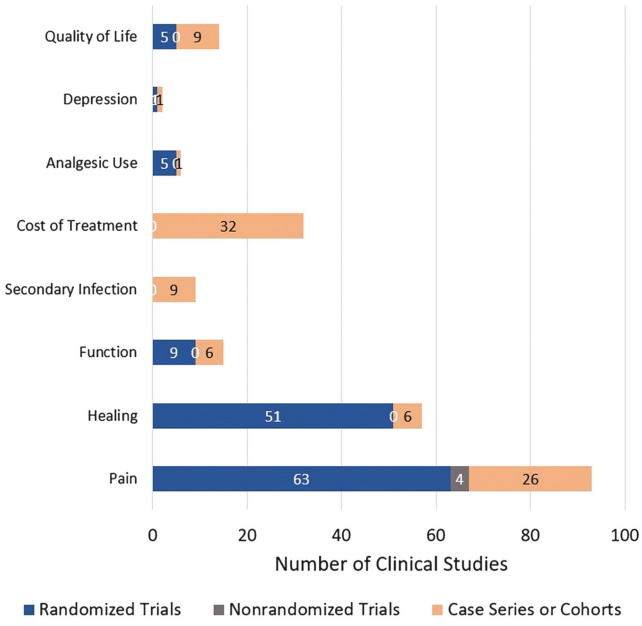


Figure 2. MEASURED PATIENT-CENTERED OUTCOMES FOR HERPES ZOSTER



quality of life, sleep, or visual function and treatment costs to the patient. The literature search returned no clinical studies reporting odor or amputation during either active HZ or PHN (Figures 2 and 3) or social isolation during active HZ episodes (Figure 2).

Note that some studies are represented more than once in Figures 2 and 3. For example, pain was often reported during early active HZ and/or PHN along with healing, quality of life, or analgesic use, so the cumulative studies in the bar graphs sum to more than the 221 studies reviewed.

Pain

Pain was the most commonly measured patient-centered outcome reported, reported by 93 studies of 61,679 patients with HZ and 128 studies of 30,366 patients with PHN. Typically reduced by antiviral agents or anesthetic interventions,[9] HZ or PHN pain was often severe enough to limit sleep and/or activities of daily living, a validated component of quality-of-life measures, with increasing pain severity and duration in older patients.[10,11]

Despite many healthcare professional consults and prescribed medications, most patients with PHN remained dissatisfied with the perceived effectiveness of their pain management interventions, reporting sufficiently severe pain to reduce quality of life (at least 5 on the Zoster Brief Pain Inventory) most or all of the time.[12]

Healing

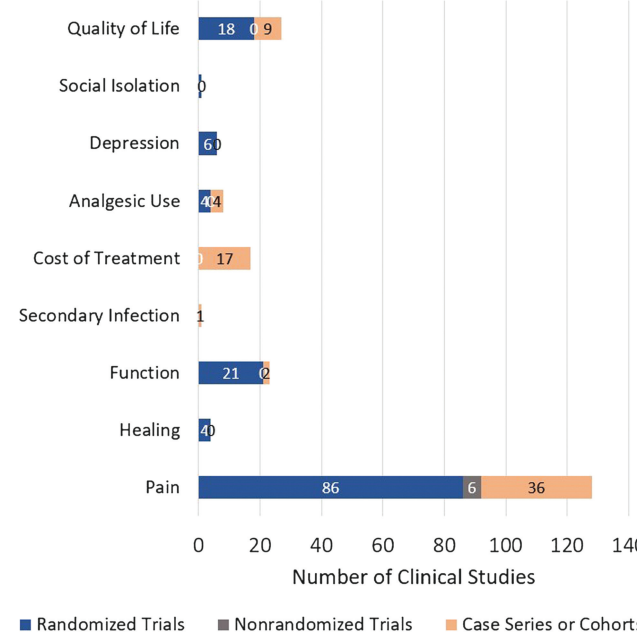
Healing (reported by 57 studies of 13,934 patients with HZ and 4 studies of 531 patients with PHN) was usually measured as a secondary outcome during the acute early weeks after HZ onset. Healing outcomes were quantified as time to crusting of all lesions, complete healing,[13] or percent healed within a specified interval after HZ onset.[14] Administration of effective antiviral agents such as acyclovir, valacyclovir, or famciclovir within 3 to 7 days after HZ onset reduced the time to HZ lesion crusting or healing. Other agents effective in reducing healing time during active HZ included paraspinal nerve block,[15] intracutaneous injection of ropivacaine and methylprednisolone,[15] and IM injections of cyanocobalamin and lidocaine.[16] All four studies documenting healing on the 531 patients experiencing PHN reported pain decreasing as lesions healed[17] with comparable effects of antiviral agents on healing.

Function

The primary patient-centered functions measured were impaired activities of daily living or compromised sleep associated with HZ or PHN pain[17] and/or impaired vision in those affected by ophthalmic HZ (reported by 15 studies of 39,701 patients with HZ and 23 studies on 5,187 patients with PHN). A 22-center study of 38,546 Veterans Affairs Medical Center patients with HZ reported that those who had previously received the HZ vaccine experienced less effect of HZ on activities of daily living.[18]

The only agents effective in improving functional outcomes if administered during HZ were acyclovir with prednisone,[19] acyclovir with "Western medicine"[20] famciclovir, or Chinese traditional medicine.[21] Systemic

Figure 3. MEASURED PATIENT-CENTERED OUTCOMES FOR POSTHERPETIC NEURALGIA



acyclovir was more effective than a topical ophthalmic ointment for improving vision for those with ophthalmic HZ.[22] Standardized Tai Chi exercise improved physical functioning for patients whose HZ affected cell-mediated immunity and physical functioning.[23]

Neuropathic pain, depression, and sleep interference associated with PHN improved in patients randomized to receive 1,800 to 3,600 mg daily of gabapentin as compared with placebo, although the gabapentin was associated with increased incidence of somnolence, dizziness, ataxia, peripheral edema, and infection.[24–28] Pregabalin, an analgesic, anxiolytic, and anticonvulsant agent, in doses of 150 to 600 mg daily offered similar pain and sleep improvement for those with PHN.[29,30]

Secondary Infection

Although listed among key adverse events during the acute phase of HZ (30% of these patients experienced a secondary infection),[31] only 9 case or cohort studies (N = 595) measured this as an important clinical outcome, and only one study (N = 42) pursued this measurement into the PHN phase of clinical experience.[31] No controlled studies attempted to discern comparative treatment effects aimed at reducing the incidence of secondary infections in those with HZ or PHN.

Patient Treatment Costs

In Europe,[32,33] Japan,[34] the US,[35] and Latin America,[2] cohort or registry studies reported substantial costs of HZ (reported by 32 studies of 2,426,647 patients with HZ and 17 studies on 218,462 patients with PHN), increasing with age and complications. Average direct plus indirect total medical costs ranged from US$1,465 in Latin America to US$4,716 in the US.[14,15] Having PHN was associated with the highest incremental cost during the first year after HZ: US$10,918 in the US[24] or US$2,001 in Latin America.[15] The estimated total annual costs of HZ in South Korea were US $143.8 million.[36] A study of the German Statutory Health Insurance system reported that average 2010 costs to the payer during the first year after HZ onset were €210, or €1,123 in the 5% of cases that developed PHN, although costs to society were higher: €376 for HZ or €1,645 for those developing PHN.[37] Total annual healthcare costs of HZ and/or PHN were estimated to be €287 million for Germany and €41.2 million for Italy.[18,38] Annual French costs of managing HZ and PHN were estimated to be €170 million, with approximately only one-third of that covered by national health insurance.[39] A cohort study of 412 Japanese patients older than 60 years with HZ reported total HZ-related costs per patient of ¥57,112, with direct medical costs representing 77%, productivity loss 19%, and transportation costs 4% of the total.[13] The cited costs omit expenses for informal caregivers, formal social care, and other out-of-pocket patient expenses, underestimating patient-centered costs.[13]

Despite abundant evidence supporting the economic burden of HZ and ensuing PHN, this review found no RCTs exploring the effects of HZ or PHN treatments on patient costs of care.

Analgesia

Analgesic use (reported by 6 studies of 726 patients with HZ and 8 studies of 877 patients with PHN) was typically measured as a secondary outcome to the primary outcome of HZ- or PHN-related pain, with effects of treatment paralleling those reported for pain. Intracutaneously injected 15 mL of 37.5 mg ropivacaine plus 40 mg methylprednisolone reduced pain, healing time, and "rescue" use of acetaminophen for patients also receiving acyclovir and pregabalin with acute HZ and reduced the intensity of PHN at 24 months postonset compared with similarly treated patients with HZ receiving placebo saline injection.[40] Patients with acute cervical[41] or thoracic[42] HZ receiving a 7-day course of oral antiviral treatment, pregabalin, and analgesics as needed reported significantly reduced analgesic use and improvement in pain and quality of life after injecting the underlying paravertebral neural root with a liquid anesthetic/anti-inflammatory nerve block as compared with a similar placebo injection. Pregabalin also improved pain and quality of life for patients with PHN, limiting the dosage of oxycodone needed for pain relief.[43]

Depression

Treatments reducing depression were reported by 2 studies of 219 patients with HZ and 6 studies of 1,356 patients with PHN. Hyperbaric oxygen combined with standard-of-care anti-inflammatory and antiviral therapy improved HZ patient depression, pain, and healing time while reducing the likelihood of developing PHN compared with standard of care alone.[44] For those with PHN, the anticonvulsants gabapentin[24,27] or pregabalin[29] improved depression and pain. Chinese traditional medicine (eg, cupping and acupuncture) with local anesthetic injections improved pain, quality of life, and depression, but it was not possible to identify specific effects of the individual components of therapy.[45]

Social Isolation

The only study in the search discussing social isolation was a double-blind RCT (N = 96) reporting that 3 weeks of twice-weekly pulsed radiofrequency stimulation administered through the angula costae of 48 patients with thoracic PHN significantly improved patient-reported social isolation and pain, tramadol analgesic use, and physical function measures compared with 48 similar patients receiving sham treatment.[46] This effect lasted for at least 6 months after treatment ($P < .05$).

Quality of Life

Patient satisfaction measures or global impressions of change were included in quality-of-life studies (including 14 studies of 1,141,078 patients with HZ and 27 studies of 120,733 patients with PHN) because they often reflected improved experiences of daily living. Most quality-of-life studies were conducted on individuals suffering from PHN. Interventions improving quality of life during acute HZ included prior vaccination against HZ,[18] gabapentin,[24,26] cervical nerve root block for cervical HZ,[41] and subcutaneous injection of triamcinolone acetonide and lidocaine in the affected dermatome.[47] These interventions[18,24,26,41,42,47] also improved quality of life for those experiencing PHN as did gastroretentive gabapentin,[48] pregabalin,[29] or pregabalin with oxycodone on demand, reducing oxycodone use compared with oxycodone alone.[43]

Agents received during active HZ also improved subsequent PHN quality-of-life outcomes. Intramuscular methylcobalamin plus lidocaine received during at least 4 of the first 14 days of HZ improved ocular pain and function and quality of life for up to 3 months after treatment for patients with ophthalmic HZ.[16] Oral brivudine taken during HZ reduced the incidence and severity of PHN and improved patient quality of life for up to 17 months after administration, with effects greater than those seen with the standard administration of acyclovir.[49]

Patient Cases

The patient cases in Table 2 revealed clinically important HZ trends that merit further study. First, early diagnosis and antiviral treatment were associated with better patient-centered outcomes. The first four patients who did not receive antiviral treatment took longer to heal than those who did. Second, healing time was 2 to 7 weeks if lesions were dressed with a moisture-retentive dressing versus 9 to 10 weeks if HZ lesions were air-exposed. Finally, two of the six HZ cases occurred in individuals previously vaccinated to prevent HZ. Because the vaccine was presumed to be effective, both patients were diagnosed too late for effective antiviral treatment. See Figures 4–6 for images related to the patient cases.

DISCUSSION

The literature search found evidence supporting positive effects of systemic antiviral agents or vaccines,[13] local nerve blocks,[14] or intracutaneous anesthetics[15] on patient-reported pain, healing, function, quality of life, and costs of care. Having HZ added an estimated $1,079 to $1,673 to direct medical costs for skilled nursing facilities and hospitalizations,[50] but costs to the patient and management of secondary infections were rarely reported separately and remain to be studied in RCTs.

The case studies highlighted further opportunities for research and clinical practice. The two patients who received early diagnosis and antiviral interventions healed within 16 or 17 days after HZ onset as compared with 29 to 63 days for the other four cases. Further research is needed to determine whether early antiviral therapy or some other aspect of early care was associated with faster HZ resolution or if this observation was a coincidence.

One limitation of the case study descriptions was the absence of standardized photographs. Future patient-oriented research should plan to include standardized photographs of HZ lesions coupled with patient reports using validated measures of pain, pruritus, quality of life, functional impairment, and healing.

The importance of topical dressings in improving HZ pain or pruritus and preventing scratching and secondary cutaneous injury or infection as reported in these cases has been recognized for nearly 20 years but neglected by research.[51,52] Hydrocolloid dressings were used in some of the cases because of their viral barrier properties. This does not negate the usefulness of foam or other dressings, such as ibuprofen-impregnated foam, which has been reported to reduce wound-related pain.[53] One author noted:

> *…many years ago we used occlusion for patients with herpes zoster, primarily to decrease pain… however we discovered a number of additional benefits… in the vesicular stage, occlusion with a transparent adhesive dressing not only decreased pain, but averted rupture of the vesicles which decreased the severity of pain and blocked transmission of the virus to nursing staff. Additionally, if the vesicles ruptured, occlusion with a hydrocolloid dressing not only decreased pain but also permitted faster healing with less scarring and provided a viral barrier reducing exposure of staff and other patients to VZV. In our limited experience, likely because of the intracellular nature of the virus, we never saw clinical evidence of increased viral replication beneath these viral barrier dressings.*

Clinical Implications

There is a global need to recognize, diagnose, and treat HZ early to optimize patient pain, healing time, and quality of life and reduce PHN likelihood, severity, and related costs. The case studies support prior RCTs reporting that effective systemic antiviral agents applied during the first week of HZ symptoms reduce lesion healing time and pain.[54,55] Further, providers should not assume that prior HZ vaccination precludes HZ occurrence. An immediate HZ consult is recommended for anyone experiencing localized HZ symptoms regardless of vaccination status.

Table 2. PATIENT-REPORTED EXPERIENCES FROM CASE STUDIES

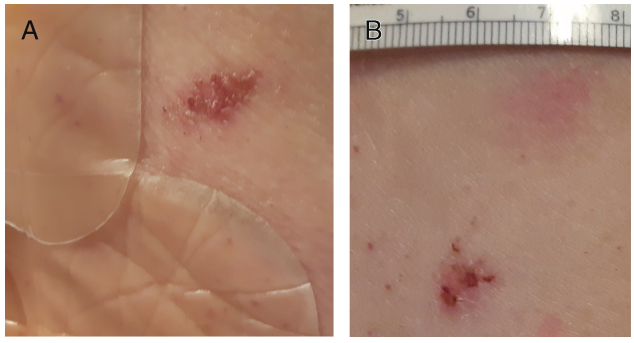
Case No., Sex, Age	Site	Antiviral	Patient-Reported Pain or Pruritus[a]	Healing Time, d	Other Observations and PHN
1, F, 75 y	Right scapula and lower back	None	Day 8, VAS score 6; air-exposed, applied hydrocolloid dressing (Figure 4A); pain dropped to 3 in 2 h, allowed sleep. Itch score 6 replaced the pain by day 18, interrupting sleep days 18–24 until it reduced to score 4 on days 25–40. All HZ sites continued to itch (scores 1–3) for 2 mo after healing.	Dressed lesions healed in 48 d (Figure 4B)	Patient recognized HZ day 7; previously thought it was recurrent hives. Had zoster vaccine 8 y before. Diagnosis on day 8 was too late for antiviral efficacy so none prescribed. Daily hot shower briefly reduced itching as did vigorous activity. Intermittent PHN lasted 6 mo as pruritus (score 1–4) at HZ sites and numb right upper lip, right arm to fingers, and right leg to toes.
2, F, 38 y	Torso, under breast, and on back	None	By day 7, pain (score 9) was too severe for sleep. Decreased to score 4 at 6 h after hydrocolloid dressing application, allowing sleep and remained score 2–4 through day 12. She took 600 mg ibuprofen for score 4 pain. Pain decreased to pruritus before dressings were removed 18 d postonset.	Dressed lesions healed in 29 d; an air-exposed lesion on her back took 14 d longer	No antiviral because HZ was not diagnosed during the first week after onset. No prior vaccination. The HZ was diagnosed on day 10; patient drank ≥2.5 L of water daily. Patient could not sleep until she covered the most severe lesions with thin hydrocolloid dressings. Patient reported no PHN.
3, F, 67 y	Upper back	None	Used moisturizer to control pruritus and stinging (score 6) during the first 42 d after onset until stinging became so severe that she attended urgent care, where HZ was diagnosed.	63 d	Had first recombinant HZ vaccine 8 d before onset. The HZ was diagnosed 42 d after onset. Infectious disease specialist advised to wait 1 y before having her second recombinant HZ vaccine. Patient reported no PHN.
4, F, 39 y	Left side (dermatomes T1-T3)	None	Soreness first week (score 5) increased to score 8 pain as rash emerged at week 2, gradually fading over "many weeks." She stopped nursing her 6-mo-old baby on the left breast and applied a viral barrier hydrocolloid dressing to lesions to prevent virus transmission to her baby, who had his first VZV vaccine shot and was at risk.	Day 39	Diagnosis after day 2 of left arm and shoulder soreness, followed by distinct red rash across left back and chest. Provider did not offer or prescribe antiviral. Took acetaminophen to manage rash pain with minimal benefit. Stronger pain medications were offered but not compatible with nursing. No previous vaccine. There was no PHN and minimal scarring.
5, F, 70 y	Left buttock, medial thigh, lower leg to the left ankle	Acyclovir five times daily	Lesions were dressed with various dressings 48 h after onset of pain (score 8) and 36 h after onset of blisters; all dressings removed 2 wk later. Used panty hose when showering or protective clothing when sleeping. Pain score >6 continued for 2 wk after lesions healed.	16 d	Antiviral received after diagnosis (2 d after first pain). She had received zoster vaccine 7 y prior to onset. Initially, the inflammation was misdiagnosed. Patient received 0.05% hydrocortisone cream. Deep muscle PHN pain score 6 lasted for 2 wk after dressing removal and HZ lesion healing.
6, M, 37 y	Left breast to left scapula	Famciclovir 500 mg twice daily on days 3–9 after first lesion	Score 2 pruritus receded on day 3 when the 10 × 18-cm area HZ lesions were dressed with thin hydrocolloid dressings to protect the lesions.	17 d after first lesion, except for one air-exposed lesion 32 d postonset	The HZ was diagnosed on day 3 of symptoms. Despite patient scratching, HZ lesions under dressings did not deteriorate further and were not infected secondarily. All dressings were removed 17 d after onset of HZ. Patient experienced no PHN.

Abbreviations: F, female; HZ, herpes zoster; M, male; PHN, postherpetic neuralgia; VAS, visual analog scale; VZV, varicella zoster virus.
[a]VAS scored from 0 to 10.

Another important misconception impeding optimal wound care is that HZ vesicles are not wounds. These vesicles, which may coalesce into larger bullae, originate from free nerve endings at the dermoepidermal junction, affecting the epidermis and reticular dermis and generating a dermal wound capable of prolonged inflammation and keloid scarring.[56] There is no reason to deny these wounds the benefits of moist wound healing, which could improve healing and scarring and reduce patient-reported pain and the likelihood of secondary infections.[57–60]

Figure 4. CASE 1

A, Air-exposed herpes-zoster open vesicle near left scapula day 12 after onset, adjacent to day 12 lesions covered with hydrocolloid dressings. B, Same air-exposed lesion on day 48 after onset. Adjacent lesions were healed 2 weeks earlier when dressings were removed.



Implications for Research

The absence of controlled studies exploring the effects of local or systemic treatments on secondary infections of HZ or PHN lesions is surprising given the importance of secondary microbial infection described by the CDC for those with HZ[57] and the abundant literature on interventions to manage or prevent infections of surgical sites, burns, and traumatic or chronic wounds.[58,59]

Further research is needed exploring the effects of moisture-retentive viral barrier dressings such as hydrocolloid or film dressings or those delivering local pain medications to HZ lesions to see if patients experience the reduced pain, healing time, and infection rates reported for other partial-thickness wounds.[58,59] Other dressings, such as foam dressings with or without ibuprofen, also merit research exploring their effects on HZ healing and pain relief.[53]

A rationale for using moisture-retentive dressings has been proposed to reduce pain and healing time for deep partial-thickness herpes simplex wounds.[60] This hypothesis appears not to have been tested in an RCT in the literature reviewed. These authors found no clinical study comparing the effects of adding moisture-retentive dressings to recognized standard-of-care interventions for either herpes simplex virus or HZ lesions.

Focusing on only validated measured patient-centered outcomes may have neglected outcomes such as pruritus, body image, sexuality, or anxiety, which are common issues for patients with HZ and relevant to practice. Although pruritus as noted in pain reports and anxiety measured by standardized depression or quality-of-life measures were included in the analyses, future research is needed to focus on these potentially important patient-reported outcomes individually.

Topical interventions that merit further research include acyclovir, which was reported in a double-blind RCT to have reduced healing time for HZ lesions from 35 to 26 days ($P = .023$).[61] Again, the case studies in Table 1 reported reduced pain and 2-week faster healing for HZ lesions dressed with hydrocolloid dressings compared with air-exposed lesions. Further, the barrier properties of these dressings appear to have prevented viral shedding to a baby nursing near the HZ site. These results merit study in a blinded RCT measuring pain, healing, viral shedding, and incidence of secondary infections. A related hypothesis worthy of further RCT study is that effective doses of topical acyclovir may act in synergy when applied beneath or in the adhesive of occlusive hydrocolloid or film dressings to reduce patient pain, healing time, secondary infection rates, and severity or duration of subsequent PHN.

This review highlights the need for earlier, more definitive HZ diagnosis and more consistent surveillance of HZ and PHN outcomes more fully exploring the incidence, prevalence, and burden that HZ adds to each patient's life and to professional practice. Cross-study comparisons are

Figure 5. CASE 2

A, Day of herpes zoster onset, rash under left breast itched. B, Day 3. Macules, papules, and vesicles developed after onset. Itch and pain were 6/10: "Very bothersome. Sleeping is more difficult. I sometimes forget about my shingles and scratch in my sleep, OUCH!" C, Day 10 after onset, "Today I put on the bandages [pictured in inset at right] around 2 PM. My pain level went from a 9 to a 4 in about 6 hours." D, Day 10 after onset, close-up of dressing in place without ruler. E, Day 18 after onset, when hydrocolloid viral barrier dressings were removed.

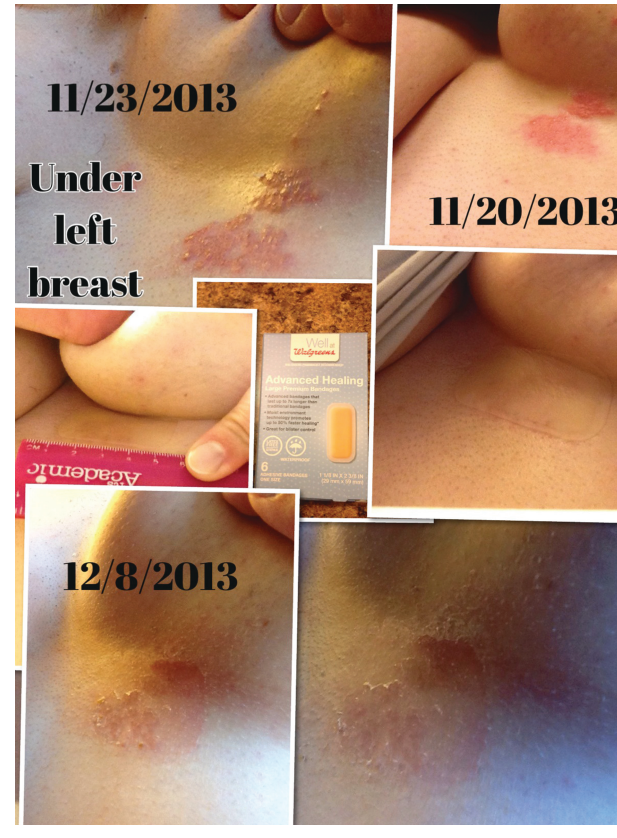
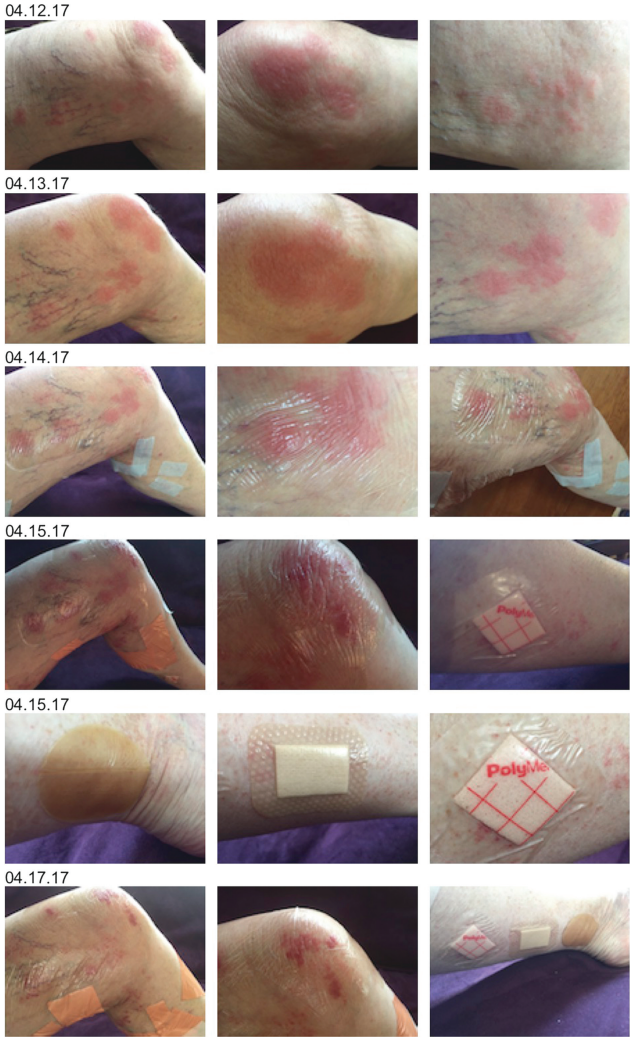


Figure 6. CASE 5
Detail of herpes zoster progression from painful macules at onset to vesicle healing under dressings.



complicated by varied patient-centered outcome measures, treatment techniques, and response measurements. Well-controlled and blind-evaluated studies are needed to determine not only what works to improve patient-centered outcomes of HZ and PHN, but also what does not work.

CONCLUSIONS

Treatments for HZ and PHN have traditionally focused on systemic antiviral interventions. Patient-centered outcomes could benefit from further high-quality RCT research to improve clinical practice including more consistent early diagnosis, care, surveillance, and exploration of the use of topical dressings in synergy with effective systemic and/or topical intervention.

PRACTICE PEARLS

- Both HZ and PHN challenge patients with distressing pain, pruritus, delayed healing, reduced quality of life, loss of sleep or vision, increased treatment costs, and the likelihood of secondary infection.
- Interventions to optimize secondary infection and treatment cost outcomes remain to be studied in RCTs.
- Early diagnosis and antiviral treatment of HZ improve patient-centered outcomes, but HZ or PHN surveillance is not routine practice, and diagnosis is often too late for patient benefit.
- The HZ vesicles are wounds and accordingly require early application of moisture-retentive dressings to prevent damage from scratching; eye contamination; and reduce pain, pruritus, healing time, scarring, and the likelihood of secondary infection.
- Interventions for HZ or PHN that merit further study include topical antiviral and/or anesthetic agents covered with moisture-retentive dressings applied to areas of HZ vesicles. ●

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