

Characteristics of Patients with Herpes Zoster on Presentation to Practitioners in France

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There have been many epidemiological studies of chickenpox but only a few of herpes zoster. We report data from an observational study, conducted in France during a 1-year period, of 9038 patients who presented with acute herpes zoster ($n = 8103$) or postherpetic neuralgia (PHN; $n = 935$) at the office practices of 4635 general practitioners or dermatologists. The incidence of herpes zoster in France was found to be similar to that in the literature: from 1.4 to 4.8 cases per 1000 population per year. The patient profiles and clinical patterns were delineated, as well as the management decisions made according to the type of treating physician. The impact of herpes zoster on quality of life was evaluated on the basis of the Medical Outcome Study Short Form 36 (MOS SF 36) scale, which is widely used for assessing quality of life in the field of health. This study provides reference data on the substantial deterioration in quality of life associated with herpes zoster and PHN.

Varicella (or chickenpox) and herpes zoster (or shingles) are caused by the same virus, herpesvirus varicellae, also known as varicella-zoster virus (VZV). Chickenpox, a highly contagious disease, is the manifestation of primary VZV infection. During this primary infection, the VZV infects the dorsal root ganglia, where it remains latent. Herpes zoster is due to local reactivation of latent VZV resulting from either a modification in the pathogenicity of the virus or a weakening in the host's immune defenses, most notably those mediated by T cells [1, 2]. Whereas chickenpox, a notifiable disease in the United States since 1972, has been the focus of many epidemiological studies, there have been few such studies of herpes zoster, and to our

knowledge there have been no reference studies of the epidemiology of herpes zoster in France.

Herpes zoster, which usually presents clinically as a painful unilateral eruption within a dermatome, raises specific challenges when it involves sites such as the ophthalmic nerve or when it results in ocular or neurological complications. Neurological complications, by far the most common type of complication, are dominated by a persistent pain syndrome known as postherpetic neuralgia (PHN). The immediate clinical manifestations—and even more so, the complications of herpes zoster—can significantly affect quality of life. PHN, which often manifests as excruciatingly severe pain refractory to treatment, is particularly debilitating. PHN can lead to drug dependency, depression, and even suicide.

Numerous research studies on quality-of-life assessment tools have been conducted over the past few years in the field of health, with the goal of improving patients' well-being and satisfaction with treatments and the health care system. These tools rely on judgements made by the patients themselves about their health status. The patients are asked to complete standardized questionnaires aimed at determining the extent to

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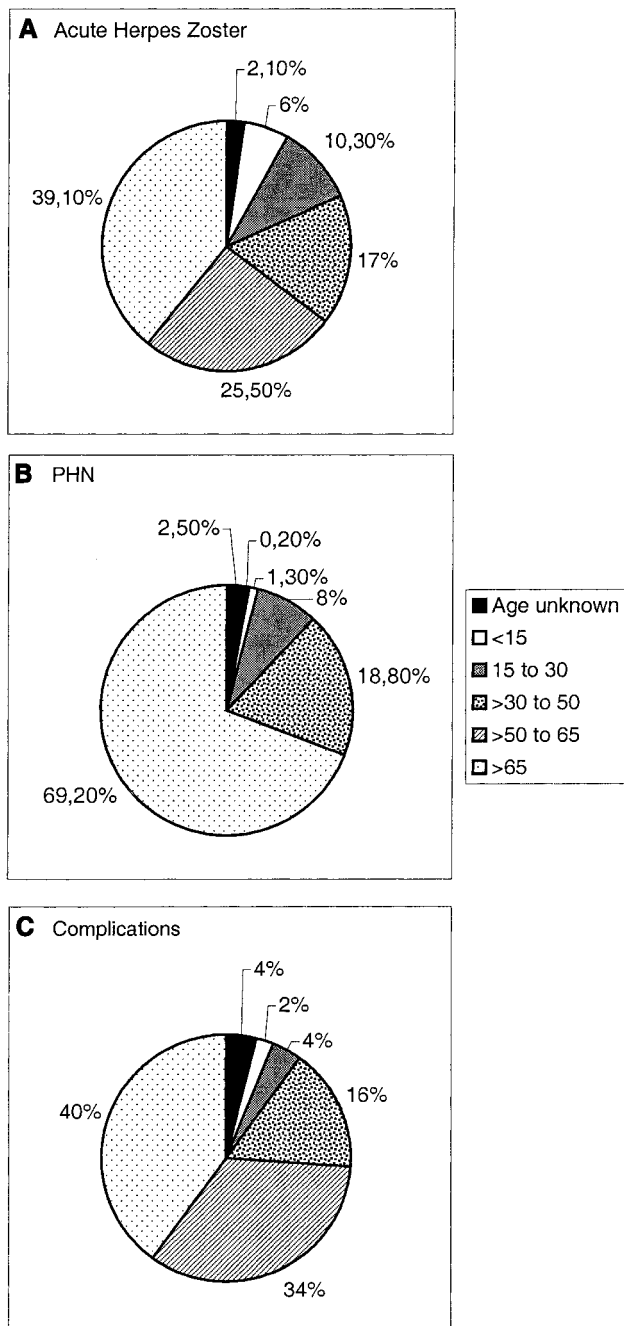


Figure 1. Distribution of ages of patients in relation to the reason for their visit to a dermatologist or general practitioner. PHN, postherpetic neuralgia.

which they are satisfied with their health status or everyday life and the extent to which their life has been modified by the disease and treatments for it.

The objectives of this study were to document the epidemiology of herpes zoster; more specifically, (1) to describe and estimate the annual incidence of herpes zoster and PHN cases seen in office practice by general practitioners (GPs) and dermatologists in France; (2) to identify prophylactic or curative

treatment practices for acute herpes zoster and PHN; (3) to supply an objective measurement of the impact of herpes zoster and PHN on the quality of life of patients; and, as an ancillary objective, (4) to investigate geographic and temporal associations between herpes zoster and chickenpox.

PATIENTS AND METHODS

Recruitment of study physicians. Data were collected during a prospective observational study of patients who made a single visit to a physician for a relevant condition. Each study physician submitted data for eligible patients during a 1-year period. Recruitment of study physicians was by stratified cluster sampling, conducted in a homogeneous manner throughout continental France and Corsica; 90% of the participating physicians were GPs and 10% were dermatologists with office-based practices. The strata reflected the division of France into 130 geographic sectors. Each cluster was composed of 36 GPs and 4 dermatologists selected at random in each geographic sector. The maximum number of patients expected was 25,000.

Patients. The patients were classified into 3 groups on the basis of the reason for the visit that led to their inclusion in the study: (1) acute herpes zoster; (2) PHN, defined as persistence of pain after clearance of skin lesions (i.e., shedding of the scabs covering the initial herpes zoster lesions); and (3) other complications occurring in isolation, whether visceral or neurological (aside from those associated with the eruptive phase and in the absence of PHN). Each patient could be included in the study only once, on the first occasion that any of the 3 reasons listed above was observed.

Study design. Data were collected with both a questionnaire completed by the patient and a questionnaire completed by the physician. Each patient completed a questionnaire at the physician's office, designed to evaluate perceived pain and quality of life with use of the standard Medical Outcome Study Short Form 36 (MOS SF 36) scale. This 36-item questionnaire elicits information for 8 dimensions believed to reflect the perceptions an individual can have of his/her own quality of life [3, 4]: (1) limitations in physical activities because of health problems (physical functioning); (2) limitations in usual role activities because of physical health problems (role physical); (3) bodily pain; (4) general health perceptions; (5) vitality (energy and fatigue); (6) limitations in social activities because of physical or emotional problems (social functioning); (7) limitations in usual role activities because of emotional problems (role emotional); and (8) general mental health (psychological distress and well-being). Each dimension is scored from 0 and 100, from the worst to the best perception.

A questionnaire was completed by the study physician on the day of the visit to collect the following information for the patient: demographic data and medical history; the reason for

Table 1. Reasons for the visits that led patients to be enrolled in the study.

Variable	Physician visited		All visits
	Dermatologist	GP	
Total visits, no. (%)	1260 (100.0)	7828 (100.0)	9088 (100.0)
Reason for visit, no. (%) of patients			
Herpes zoster	1129 (89.6)	6974 (89.1)	8103 (89.1)
PHN	115 (9.1)	820 (10.5)	935 (10.3)
Isolated complications	16 (1.3)	34 (0.4)	50 (0.6)
No. of cases per physician \pm SD			
Herpes zoster	2.2 \pm 2.7	1.5 \pm 2.1	1.6 \pm 2.2
PHN	0.2 \pm 0.6	0.2 \pm 0.5	0.2 \pm 0.5
Isolated complications	0.0 \pm 0.2	0.0 \pm 0.1	0.0 \pm 0.1

NOTE. GP, general practitioner; PHN, postherpetic neuralgia.

the visit; the history of the disease; the distribution of the manifestations; any precipitating factors; the clinical expression of the disease; and the treatments prescribed and laboratory investigations and specialist visits ordered. In addition, the study physicians were asked to record all the cases of chickenpox they saw during the study period.

Statistical methods. The statistical evaluation included a descriptive analysis of the study population. Comparative tests (χ^2 , Student's *t* test) were done between the group of patients enrolled by GPs and the group enrolled by dermatologists. The level for statistical significance was set at .05. The computation of incidence was based on the number of cases reported during the first month of the period of inclusion of each active physician (i.e., physicians who enrolled at least 1 patient during the study period). The incidence of visits by age class (figure 1) was extrapolated by using demographic data for France [5].

In addition, the association between the incidence of chickenpox and the incidence of herpes zoster was evaluated with use of Pearson's empirical correlation coefficient between the number of chickenpox cases and the number of herpes zoster cases in each geographic area.

The impact of herpes zoster on quality of life was compared

with its impact for a French general population after data were matched by sex and age.

RESULTS

Study physicians and patients. A total of 5148 physicians participated in the study, including 4635 GPs and 513 dermatologists distributed throughout France. A total of 9088 patients were enrolled from 1 June 1997 through 31 May 1998; the reasons for inclusion in the study were as follows: acute herpes zoster, 8103 patients; PHN, 935 patients; and another complication, 50 patients. The number of patients enrolled by GPs was 6.2-fold greater than the number enrolled by dermatologists. The mean number of patients enrolled per physician was 2.5 for the dermatologists (median, 2) and 1.7 for the GPs (median, 1). The reason for the visit was acute herpes zoster for 89% of patients, PHN for 10%, and another complication for 1% (table 1).

There was no significant association between sex and the reason for the visit (table 2). The mean age of the study population was 56.2 years and the median was 61 years; the mean age of patients with PHN was about 15 years greater than the

Table 2. Sex and age of patients, as related to the diagnosis and the specialty of the physicians seen.

Patient variable	Condition for which patients were enrolled in the study		
	Acute herpes zoster (<i>n</i> = 8103)	PHN (<i>n</i> = 935)	Other complications (<i>n</i> = 50)
Sex, male/female, %	44/56	41/59	52/48
Age, mean years \pm SD			
Enrolled by a dermatologist	48.8 \pm 23.1	66.0 \pm 15.7	52.1 \pm 24.4
Enrolled by a GP	55.6 \pm 21.3	69.5 \pm 13.7	59.3 \pm 16
Overall	54.7 \pm 21.6	69.1 \pm 14	56.9 \pm 19.3

NOTE. GP, general practitioner; PHN, postherpetic neuralgia.

Table 3. Characteristics and treatment of patients who presented with herpes zoster.

Variable	Patients enrolled, no. (%)			P
	By a dermatologist (n = 1129)	By a GP (n = 6974)	Total (n = 8103)	
Site of symptoms				
Head and neck	563 (50)	2622 (37)	3185 (39)	<.001
Thorax	613 (54)	4361 (63)	4974 (61)	—
Sacrum	117 (10)	876 (13)	993 (12)	—
Low back	120 (11)	716 (10)	836 (10)	—
Total	1129 (100)	6974 (100)	8103 (100)	—
Severity of pain				
Mild	199 (22)	922 (15)	1121 (16)	—
Moderate	388 (43)	2674 (43)	3062 (43)	—
Severe or very severe	312 (35)	2598 (42)	2910 (41)	<.001
Total	899 (100)	6194 (100)	7093 (100)	—
Pattern of pain				
Intermittent	483 (61)	2324 (42)	2807 (45)	—
Permanent	311 (39)	3178 (58)	3489 (55)	<.001
Total	794 (100)	5502 (100)	6296 (100)	—
Medications prescribed				
Valacyclovir	544 (58)	4302 (67)	4846 (67)	<.001
Acyclovir (any form)	158 (17)	1474 (22)	1632 (22)	<.001
Level I and II analgesics	276 (30)	1729 (43)	2005 (42)	<.001
Topical antiseptic dyes or agents that relieve pruritus	229 (25)	899 (14)	1128 (16)	<.001
Any treatment	933 (83)	6463 (93)	7233 (89)	<.001

mean age of patients with acute herpes zoster (table 2). Five percent of the patients had a history of neoplasia or hematological disease, 9.5% had recently experienced an infectious disease, and 4% had recently received immunosuppressive therapy.

Acute herpes zoster: description. The median duration of the acute herpes zoster eruption was 2 days in patients who visited a GP and 4 days in those who visited a dermatologist. Pain was the initial manifestation in 74% of patients, and the median interval between the onset of pain and the onset of skin lesions was 2 days. The eruption was characterized by erythema and vesicles, and 20% of patients also had scabs ($n = 1591$). The most common site of the eruption was the thorax, followed by the head. Involvement of the head and neck was more common in the group seen by dermatologists than in that seen by GPs (table 3). In the majority of the patients, the eruption was accompanied by moderate to severe pain. The proportion of patients with severe or very severe pain and with permanent pain was higher in the group seen by GPs than in the group seen by dermatologists.

Acute herpes zoster: laboratory investigations. Laboratory investigations were ordered for only 9% of patients; patterns were similar for dermatologists and GPs. The investigations

most often ordered were standard blood tests (21% of investigations), including tests for inflammation (erythrocyte sedimentation rate, C-reactive protein level), and HIV serological tests (8% of investigations).

Acute herpes zoster: management. Prescription of pharmacotherapy for the acute herpes zoster was more often reported for the patients enrolled by GPs than for those enrolled by dermatologists (89% vs. 83%; table 3). Antiviral agents, mainly acyclovir and valacyclovir, were prescribed for 89% of patients seen by GPs and for 75% of patients seen by dermatologists. Valacyclovir was prescribed for two-thirds of patients who were given an antiviral agent. The other types of medication prescribed were analgesics (level I and level II) and local adjuvant treatments (antiseptic dyes and/or itch-relieving agents for 16% of treated patients). Analgesics were prescribed more often by GPs (43% of patients) than by dermatologists (30%). In addition, 15% of patients used alternative medical approaches (homeopathy, acupuncture, alternative healer). The proportion of patients referred to another specialist was 16% in the group seen by dermatologists and 7% in the group seen by GPs.

PHN: description. PHN was the reason for inclusion for 9.1% of patients enrolled by dermatologists and 10.5% of those

Table 4. Characteristics and treatment of patients who presented with postherpetic neuralgia (PHN).

Variable	Patients enrolled, no. (%)			P
	By a dermatologist (n = 115)	By a GP (n = 820)	Total (n = 935)	
Site of initial involvement				
Head and neck	61 (54)	439 (54)	500 (54)	NS
Thorax	64 (56)	176 (58)	540 (58)	—
Sacrum	16 (14)	73 (9)	89 (10)	—
Low back	6 (5)	69 (8)	75 (8)	—
Total	114 (100)	814 (100)	928 (100)	—
Severity of pain				
Mild	9 (8)	75 (9)	84 (9)	—
Moderate	25 (22)	334 (41)	359 (39)	—
Severe or very severe	78 (69)	403 (50)	481 (52)	<.001
Total	112 (100)	814 (100)	926 (100)	—
Pattern of pain				
Intermittent	70 (64)	481 (65)	551 (65)	—
Permanent	40 (36)	263 (35)	303 (35)	NS
Total	110 (100)	744 (100)	854 (100)	—
Main medications prescribed				
Valacyclovir	7 (7.4)	52 (7.5)	59 (7)	NS
Acyclovir (any form)	8 (8.5)	56 (8.4)	64 (8)	—
Analgesics				NS
Level I	28 (29)	209 (30)	237 (30)	NS
Level II	37 (39)	295 (42)	332 (42)	NS
Level III	2 (2)	17 (2.4)	19 (2)	—
Total	67 (70)	521 (74)	588 (74)	NS
Antidepressants	18 (19)	131 (19)	149 (19)	NS
Carbamazepine	10 (11)	55 (7.9)	65 (8)	NS
Clonazepam and anticonvulsants	8 (8.4)	98 (14)	106 (3)	NS
Carbamazepine or clonazepam and anticonvulsants	18 (19.4)	153 (22)	171 (11)	NS
Neuroleptics	9 (9.5)	27 (3.9)	36 (5)	.02
Any	95 (83)	697 (85)	792 (85)	NS

NOTE. NS, not significant.

enrolled by GPs. Patients with PHN were more likely to have head or neck involvement (54%) than were those with acute herpes zoster (40%; table 4). In about half the cases, antiviral treatment had been prescribed within 72 h of onset of the eruption. The proportion of patients with severe or very severe pain was 69% in the group seen by dermatologists, vs. 50% in the group seen by GPs (table 4). Ocular, neurological, or visceral complications were present in 10% of the PHN patients. Pain was more often reported as intermittent with PHN than with acute herpes zoster.

PHN: laboratory investigations. Laboratory investigations were ordered for slightly more than 10% of PHN patients, which usually consisted of standard blood tests.

PHN: management. Pharmacotherapy was prescribed for

85% of PHN patients, with no noticeable difference between dermatologists and GPs (table 4). For the PHN patients, analgesics accounted for 74% of prescriptions, of which slightly >2% were level III analgesics. Anticonvulsants were the second most commonly prescribed class of medications. Dermatologists prescribed more neuroleptics than did GPs. Antiviral agents accounted for ~15% of all prescriptions. Among PHN patients, 18% used alternative medical approaches (acupuncture, homeopathy, auriculotherapy, alternative healer) and 20% were referred to a specialist, usually a pain clinic physician (31% of referrals) or a neurologist (28%).

Patients enrolled because of a herpes zoster complication without PHN. Fifty patients (0.6% of the total patient population), sought medical advice for herpes zoster complications

Table 5. Comparison of management for patients with ophthalmic herpes zoster and those with herpes zoster at other sites.

Variable	Site of infection, % of cases		P
	Ophthalmic (n = 1165)	Other (n = 6938)	
Median duration of eruption, days	2	2	NS
Initial pain	74	72	NS
Median duration of pain before eruption, days	2	1	<.001
Presence of scabs	26	20	
Severe or very severe pain	46	40	<.001
Permanent pain	59	54	.002
Pharmacotherapy			
Received prescription	96	92.8	<.001
Valacyclovir	71	65	—
Systemic acyclovir	23	14.8	—
Subtotal	94	79.8	<.001
Topical acyclovir	12.8	6.7	
Laboratory investigations ordered	15	7.9	<.001
Referral to a specialist	40	2.5	<.001
Leading referral specialty	Ophthalmology (86)	Dermatology (47.8)	—

NOTE. NS, not significant.

other than PHN. These complications were articular ($n = 2$), cutaneous ($n = 22$), neurological ($n = 11$), or ocular ($n = 12$).

Ophthalmic herpes zoster. The patients with ophthalmic herpes zoster were compared to those with herpes zoster at other sites. In patients enrolled for acute herpes zoster, duration of eruption, presence of pain, and time from pain onset to eruption onset were not significantly different between the ophthalmic and other-site groups (table 5). In contrast, patients with ophthalmic herpes zoster were more likely to report that their pain was severe and permanent (46% vs. 40%). They were also more likely to receive a prescription for an antiviral drug

(most notably in an ophthalmologic form), a prescription for tests, and/or a recommendation to see a specialist.

Incidence of acute herpes zoster seen by GPs and dermatologists in France. Table 6 summarizes the results of the incidence computation in comparison with the results of other studies [6-13]. Table 7 shows the incidence according to age group and sex. The age group analysis demonstrated 3 marked differences between groups. Among subjects <40 years of age, the incidence of herpes zoster that led to a consultation with a medical practitioner was slightly less than half the incidence in the overall population. The incidence among patients aged 40-60 years was similar to the mean incidence in the overall

Table 6. Annual incidence of herpes zoster among patients seen in community consultation in France, compared to the incidence found by other studies.

Reference	Location of study	Period of study	Recruiting physicians	No. of cases	Annual incidence per 1000 population	Mean age, y
[8]	Rochester, Minnesota	1945-59	GPs	590	1.3	48.5
[7]	Cirencester, England	1947-52	GPs ($n = 1$)	192	3.4	52.9
[9]	Edinburgh, Scotland	1947-48	GPs	184	—	47.8
[10]	Hawick, England	1948-55	GPs	81	4.8	53.8
[11]	Moorfields, Great Britain	1967-82	GPs ($n = 39$) + OD	1200	3.5	—
[12]	Dumfriesshire, Scotland	1969-82	GPs	151	1.7	49.9
[13]	Cheltenham, England	1978-86	GPs (all cases)	1019	1.3-1.6 ^a	58
[14]	Tamworth area, Australia	1982-84	GPs	89	—	52.5
PR	France	1997-98	GPs, Derm	8103	4.8	54.7

NOTE. Derm, dermatologists; OD, ophthalmology department; PR, present report.

^a Range of the annual incidence over a 9-year period.

Table 7. Annual incidence of herpes zoster among patients seen in community consultation in France, by age group and sex of patients.

Age, years	Incidence per year, %		
	Females	Males	Overall
0–19	2.2	2.2	2.2
20–39	2.5	2.3	2.4
40–59	5.8	4.9	5.4
60–74	10.8	8.8	9.9
>74	14.8	8.9	12.8
Total	5.5	4.1	4.8

population. Among subjects >60 years of age, the incidence was one-half that in the overall population and one-third that among women. The relative risk for women was significantly greater than 1 ($P < .05$).

Association between the incidence of chickenpox and the incidence of herpes zoster. There were a total of 7592 cases of herpes zoster and 9926 cases of chickenpox, and the corresponding mean numbers of cases per geographic sector were 79.9 and 104.5. Pearson's empirical correlation coefficient for the number of cases of herpes zoster and chickenpox per sector was 0.72 ($P < .05$). This value denotes a significant positive correlation between the incidence of chickenpox and the incidence of herpes zoster.

Quality of life. The main data from the patient self-questionnaire evaluating the impact of herpes zoster on quality of life are shown in table 8. During the last 3 months prior to the onset of symptoms, 40% of all the patients had experienced an important familial, personal, or professional life event, which was described as negative by 80% of these patients.

Pain-related disruption of life during the last week prior to being seen by the physician was more severe for the patients seen for PHN. Among the patients with ocular involvement, one-fourth reported a troublesome decrease in visual acuity.

Of the 7595 quality-of-life questionnaires completed, only 84% provided evaluable data on all 8 dimensions of the MOS SF 36 scoring. In the overall patient population, all quality-of-life scores were decreased in comparison to those for a French reference population [14]; the lowest value was 41 (for vitality) and the highest was 72 (for social functioning; figure 2). The lowest values for all scores were seen in the PHN group. In particular, scores for the physical functioning and role emotional showed substantially larger decreases in the PHN group than in the other patients.

DISCUSSION

The large number of patients makes this the largest study of herpes zoster in office practice in France and even in the world.

More than 5000 GPs and dermatologists participated in this study, who recruited 8103 patients with acute herpes zoster and 935 with PHN. Mean patient age was 57 years, but most patients were >61 years of age. The annual incidence rate of acute herpes zoster seen by GPs or dermatologists, as estimated from the data collected during this study, was 4.8 per 1000 population.

The rates and mean ages found in this study are consistent with those in the English-language literature. Eight epidemiological studies of herpes zoster were identified. These studies were conducted by GPs in Great Britain and other English-speaking countries. From these studies, it can be concluded that the annual incidence of herpes zoster ranges from 1.3 to 4.8 per 1000 population. The results of descriptive epidemiological studies are closely dependent on the method used to recruit the study patients. In all available studies, patients were recruited by physicians, and consequently results were influenced by the characteristics of the health care system in the country under study and by the extent to which the sample of physicians was representative. The design of this study did not allow inclusion of cases of herpes zoster seen by pediatricians or hospital clinic dermatologists or of cases in patients with immune deficiency [15, 16]. It also did not include patients residing in institutions, which is a potentially important fact, since all available epidemiological data show a marked increase in the incidence of herpes zoster with increasing age.

Although epidemiological data show that VZV infects both males and females, in our study females accounted for a larger proportion of the patients than males. The female-to-male ratio was 1.27:1, which is consistent with that in earlier studies [8]. In most studies, this predominance of females was ascribed to the fact that females account for a larger proportion of the general population aged >50 years. However, our results by age group showed that the incidence of herpes seen in consultation in relation to the type of practitioners in the study was higher among females and that the difference was marked for subjects as young as 40 years of age.

Our study also provided data on the management decisions

Table 8. Main data from the quality-of-life self-questionnaire.

Symptom or complaint	% of patients (n = 7595)
Herpes zoster responsible for pain	89.0
Pain characterized by burning sensations	59.8
Permanent pain	41.9
Severe to very severe pain	44.9
Marked decrease in physical activities	36.0
Marked decrease in walking time	28.6
Marked impact on social life	20.2
Impact on sleep	58.8
Anxiety	30.2

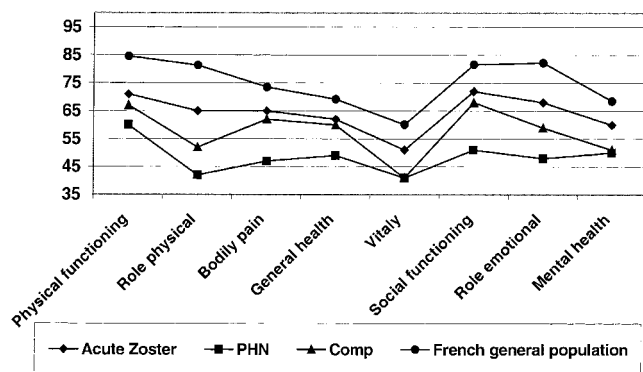


Figure 2. Scores for the Medical Outcome Study Short Form 36 quality-of-life evaluation (MOS SF 36) for the overall patient population. Comp, comparable French reference population; for definitions of the dimensions of health measured by the MOS SF 36, see Methods.

made during the initial visit, according to the profile of the disease. These data were categorized by the type of study physician (GP or dermatologist). One of our findings is that dermatologists saw more younger patients, for whom the unbecoming appearance of the skin lesions is without doubt a major concern. The GPs saw more older patients, who were more likely than their younger counterparts to have PHN and in whom effects on general health were an important aspect of the disease.

Management practices differed between GPs and dermatologists. In particular, for patients with acute herpes zoster, GPs were more likely than dermatologists to prescribe level II analgesics (25% vs. 13%), whereas dermatologists were slightly more likely to prescribe topical antibiotics (8% vs. 2%). Eighty-two percent of patients were given a prescription for an antiviral agent, either acyclovir or valacyclovir, with twice as many prescriptions for the first of these drugs than for the second.

Since 1992, MOS SF-36 questionnaires have been used widely in different studies of a large variety of conditions, such as rheumatism, AIDS, and migraine [17–19]. A recent study in which MOS SF-36 scoring was used to compare several conditions (cancer, chronic obstructive pulmonary disease, AIDS, fibromyalgia, and hyperlipidemia) showed that the quality of life of the patients with those disorders is lower in most domains than in a healthy population [20]. In comparison to findings for a reference French population [14] matched by age and sex, it is shown that herpes zoster has an impact on all MOS SF-36 dimensions.

This objective evidence of quality-of-life alteration should be linked to the high rate of use of alternative medical approaches,

which indicates the significant distress for both patients and physicians brought on by herpes zoster-related pain. This finding strongly suggests that clinicians should manage herpes zoster and PHN more aggressively.

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