

The impact of herpes zoster and post-herpetic neuralgia on quality of life: patient-reported outcomes in six European countries

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Abstract

Aim To investigate the impact of an entire episode of herpes zoster (HZ) or post-herpetic neuralgia (PHN) on an individual's quality of life (QoL).

Subjects and methods Individuals aged ≥ 50 years with painful HZ in the previous 5 years were identified across six European countries (Spain, Portugal, The Netherlands, Belgium, Sweden and Switzerland). They participated in a survey comprising bespoke questions to evaluate their previous HZ/PHN episode.

Results A total of 1,005 individuals participated, 874 (87%) having had HZ, and 13% having had PHN. Generally, pain and QoL outcomes were similar irrespective of when HZ was diagnosed (≤ 12 versus 13–60 months) and age (50–59 versus ≥ 60 years). Mean pain scores were significantly higher in those with PHN versus HZ both on average (7.2 versus 6.4) and at worst (8.3 versus 7.4). PHN had a significantly higher impact on patients' perception of their overall QoL, with 37% reporting a high impact (HZ: 19%). Pain

restrictions in the following QoL domains significantly impacted on the respondents' perception of QoL: enjoyment of life (level of impact, 31%), general activity (29%), mood (25%), sleep (8%) and walking ability (8%), and were significantly higher in those with PHN than in those with HZ. Sleep was the area worst affected.

Conclusion HZ, and particularly PHN, is associated with considerable levels of pain that have a significant impact on the QoL of participants across six European countries.

Keywords Europe · Herpes zoster · Pain · Post-herpetic neuralgia · Quality of life

Introduction

Herpes zoster (HZ), also known as shingles, is the clinical manifestation of the reactivation of latent varicella zoster virus (VZV), which as a primary infection causes varicella or chickenpox (Lungu et al. 1995). HZ is a potentially serious and debilitating condition characterised by a unilateral vesicular rash and is usually accompanied by acute pain (Arvin 2005; Hope-Simpson 1965). The most frequent and debilitating complication of HZ is post-herpetic neuralgia (PHN), a persistent neuropathic pain syndrome (Hope-Simpson 1975; Schmader 2001, 2008). Although there is no standard definition of PHN, it is often defined as pain that persists for ≥ 90 days after the onset of HZ rash (Schmader et al. 2008).

The incidence and severity of HZ and PHN increase strikingly with age (Gauthier et al. 2009; Hope-Simpson 1975; Yawn et al. 2007), and are associated with an age-related decline in VZV-specific cell-mediated immunity (Arvin 2005; Levin et al. 2008). Approximately one in four people will develop HZ during their lifetime (Brisson et al. 2001; Yawn et al. 2007), with the risk increasing to one in

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two in those aged ≥ 85 years (Schmader 2001). On average, 10–20% of HZ patients will develop PHN, which can persist for years or even decades after the HZ rash has gone, with rates of 25–50% reported in patients over 50 years old, depending on the definition used (Johnson et al. 2007; Scott et al. 2003). As populations age, the number of cases of HZ and PHN is expected to rise (Dworkin et al. 2008).

Several observational studies have demonstrated that HZ pain/PHN have a significant impact on quality of life (QoL) (Drolet et al. 2010; Katz et al. 2004; Lydick et al. 1995; Schmader et al. 2007; van Seventer et al. 2006). These were prospective studies and, as a result, employed instruments that evaluated the burden of HZ/PHN at specific time points while the patient was suffering from HZ pain/PHN. A retrospective survey was undertaken to assess the impact of the entire HZ/PHN episode on QoL in a German population aged ≥ 50 years that had experienced painful HZ during the past 5 years (Weinke et al. 2010). This was the first study to employ a unique evaluation that provided information regarding the impact of the burden of HZ pain/PHN over the entire HZ/PHN episode rather than at specific time points while the patient had HZ/PHN. This retrospective approach also enabled the inclusion of a statistically sufficient number of 280 individuals, and provided a broader view of the impact of the burden of HZ/PHN on QoL by capturing both pain severity and duration. The results of this German retrospective survey demonstrated that those with HZ and PHN experience high levels of pain affecting many areas of their lives, including daily activities, mobility, work, sleep and mood. Furthermore, those with PHN have consistently worse outcomes in terms of pain and QoL than those with HZ. These results confirmed data reported in observational studies (Drolet et al. 2010; Katz et al. 2004; Lydick et al. 1995; Schmader et al. 2007; van Seventer et al. 2006) and contributed to increased awareness of the significant burden of HZ/PHN.

Our survey was an expansion of the previously reported German survey (Weinke et al. 2010) to assess the impact of HZ and PHN on the QoL of those aged ≥ 50 years who had experienced painful HZ during the past 5 years. Data from six other European countries are reported.

Subjects and methods

Study setting and participants

Between December 2008 and February 2009, a survey was administered by TNS Healthcare (Munich, Germany), to members of the public in Spain, Portugal, The Netherlands, Belgium, Sweden and Switzerland. A representative sample among individuals aged ≥ 50 years in private households was identified by free-random sampling. Press adverts were also published in Portugal. In addition, Omnibus™ (a

quantitative multi-purpose survey) was used as a pre-screening tool to identify individuals aged ≥ 50 years in The Netherlands and Switzerland.

Computer-assisted telephone interviews were conducted in Spain, Portugal, Belgium, Sweden and Switzerland. Online, computer-assisted self-interviews were employed in The Netherlands.

A total of 44,545 individuals identified as aged ≥ 50 years were contacted to determine if they had: (1) been diagnosed with HZ by a physician during the previous 5 years; and (2) experienced HZ-related pain and would therefore be eligible to participate in this survey. Eligible participants were classified, according to the duration of pain, as those with HZ (pain lasting <3 months after HZ rash onset) or those with PHN (pain lasting ≥ 3 months after HZ rash onset).

Survey design

The interview lasted ~20 min and consisted of 22 closed questions (those that can usually be answered by ‘yes’ or ‘no’; providing a specific, simple piece of information; using a numeric scale; or by selecting an answer from a multiple-choice list). The questionnaire comprised bespoke questions of which some were informed from standard QoL questionnaires and further developed to enable the evaluation of the complete course of a previous HZ/PHN episode. QoL domains covered by the questions were interference of pain with usual daily activities (including getting out of the house, going shopping, concentrating on mental tasks, being touched by another person and self-care such as putting on clothes and taking a shower or bath), mobility (walking ability), normal work (including both work outside the home and housework), sleep, mood, anxiety and/or depression, enjoyment of life, enjoying simple leisure activities (such as reading a book, listening to the radio or watching television) and social/family relations.

Participants assessed pain on a scale from 0=‘no pain’ to 10=‘pain as bad as you can imagine’. They assessed the interference of HZ pain/PHN on QoL domains on a scale of 0=‘does not interfere’ to 10=‘completely interferes’ with activity.

All interviews (and the screening process) were carried out in the native language of each country by interviewers who had received comprehensive training regarding the questionnaire. The questionnaire was translated from English into the local language, and was back-translated into English and compared with the original to validate the accuracy of the translation.

Statistical analyses

Significant differences in pain and QoL outcomes were tested using 90% confidence intervals ($p < 0.1$) for proportions and means for the following subgroups: (1) those with HZ

diagnosed during the previous 12 months versus those with HZ diagnosed between 13 months and 60 months ago; (2) those aged 50–59 years versus those aged ≥60 years; (3) those classified as having HZ versus those classified as having PHN. Significant differences in outcomes were also tested for each country versus those across all countries.

Multiple regression analyses were undertaken to determine which areas of pain interference had a significant impact on the respondents’ perception of their QoL. Measurement was by standardised β-coefficients. Normalised values (e.g. areas that have an impact on overall QoL) were set as 100%.

Results are presented for the overall population across the six countries unless specified otherwise.

Results

Patient characteristics

Of 44,545 individuals aged ≥50 years contacted across six European countries, 1,005 individuals who had experienced painful HZ diagnosed by a physician during the previous 5 years were identified. Across all six countries, 874 respondents were classified as having had HZ (87%; pain lasting <3 months after rash onset) and 131 were classified as having had PHN (13%; pain lasting ≥3 months after rash onset). Of these, 323 (32%) were diagnosed with HZ or PHN during the previous 12 months. Similar numbers of respondents were aged 50–59 years (n=454; 45%) and ≥60 years (n=551; 55%). Table 1 shows the distribution of the respondents in the six countries.

The mean age of respondents was 63 years, and most were women (66%; Table 2). One in three of all respondents was employed (full- or part-time), including 59% of those aged 50–59 years and 13% of those aged ≥60 years (Table 2). Many respondents (40%) reported being nervous or stressed and 24% felt sad/depressed or lonely prior to noticing the first symptoms of HZ.

Patient-reported pain

In general, pain and QoL outcomes were similar irrespective of when HZ was diagnosed (≤12 months versus 13–60 months) and age (50–59 years versus ≥60 years). In contrast, every pain and QoL outcome was generally worse in those with PHN compared with those with HZ.

HZ pain/PHN were characterised as ‘burning’ (56% of respondents), ‘itching’ (49%), ‘stabbing’ (40%), ‘shooting’ (21%), ‘throbbing’ (11%), ‘electric shocks’ (10%) and ‘painful cold’ (7%; respondents could use more than one word to describe their pain). Pain was also characterised as ‘continuous, steady and constant’ by 45% of respondents, and ‘rhythmic, periodic and intermittent’ by 34%. More respondents with PHN characterised their pain as ‘continuous, steady and constant’ (52%) compared with those with HZ (45%).

Mean pain scores were 6.5 on average and 7.5 at its worst (Table 3). High pain scores (between 8 and 10) were reported by 33% of respondents when describing their average pain level, and by 56% of respondents describing pain at its worst. As expected, significantly higher mean pain scores, both on average and at its worst, were reported by those with PHN compared with those with HZ, with significantly more of those with PHN reporting high pain scores (8–10) on average and at its worst (Table 3).

Despite 89% of respondents receiving treatment for HZ/PHN, 37% did not receive it within 72 h of rash onset. Only 15% of respondents reported total pain relief, 5% reported no pain relief, with mean levels of pain relief being 64%. Overall, those with PHN received significantly more medications than those with HZ (mean: 2.2 per person versus 1.7, respectively), with significantly more of those with PHN receiving 4 or 5 medications. However, despite receiving significantly more medications, those with PHN experienced significantly less pain relief, compared with those with HZ (mean pain relief: 50% versus 66%, respectively), with significantly more patients not achieving any pain relief (4% versus 12%, respectively).

Table 1 Distribution of participants

	Total (N)	n (%)					
		HZ/PHN ≤12 months	HZ/PHN >12–60 months	Age 50–59 years	Age ≥60years	HZ	PHN
Total	1,005	323 (32)	682 (68)	454 (45)	551 (55)	874 (87)	131 (13)
Spain	253	93 (37)	160 (63)	126 (50)	127 (50)	211 (83)	42 (17)
Portugal	151	50 (33)	101 (67)	57 (38)	94 (62)	133 (88)	18 (12)
The Netherlands	242	69 (29)	173 (71)	102 (42)	140 (58)	208 (86)	34 (14)
Belgium	108	21 (19)	87 (81)	51 (47)	57 (53)	97 (90)	11 (10)
Sweden	101	30 (30)	71 (70)	46 (46)	55 (54)	93 (92)	8 (8)
Switzerland	150	60 (40)	90 (60)	72 (48)	78 (52)	132 (88)	18 (12)

HZ herpes zoster; PHN post-herpetic neuralgia

Table 2 Characteristics of participants

	All	Age (years)		Patient category	
		50–59	≥60	HZ	PHN
All, <i>n</i> (%)	1,005 (100)	454 (45)	551 (55)	874 (87)	131 (13)
Female, <i>n</i> (%)	666 (66)	305 (67)	361 (66)	587 (67)	79 (60)
Age, mean years (SD)	62.8 (9.2)	54.6 (3.1)	69.6 (6.8)	62.5 (9.1)	65.1 (9.9)
Employment status, <i>n</i> (%)					
Full-time	232 (23)	188 (41)	44 (8)	211 (24)	21 (16)
Part-time	107 (11)	78 (17)	29 (5)	92 (11)	15 (11)
Housewife/house-husband	149 (15)	78 (17)	71 (13)	131 (15)	18 (14)
Unemployed ^a	89 (9)	57 (13)	32 (6)	80 (9)	9 (7)
Retired	428 (43)	53 (12)	375 (68)	360 (41)	68 (52)

^a In Switzerland, the term ‘unemployed’ includes ‘unemployed at the moment’, ‘not employed, reason unknown’, ‘other’ and ‘self-employed’.

HZ herpes zoster; *PHN* post-herpetic neuralgia

Side effects related to the medication used to treat HZ were reported by 26% of those who received medication. Most of the side effects reported were somnolence, stomach pain and vertigo.

Impact of HZ and PHN on QoL

Restrictions in the following QoL domains had a significant impact on the respondents’ perception of QoL, as shown by multiple regression analysis (adjusted R^2 : 0.36): enjoyment of life (level of impact: 31%), general activity (29%), mood (25%), sleep (8%) and walking ability (8%). The impact of normal work and relations with others on the perception of QoL were not statistically significant.

Figure 1 and Table 3 illustrate that HZ pain/PHN interfered with every QoL domain. Furthermore, each outcome was generally worse in those with PHN versus those with HZ. Further details on the QoL domains are provided below.

Interference with daily activities

The effect of pain on usual daily life was assessed in depth. Multiple regression analysis demonstrated that restrictions in the following aspects of daily life due to pain had a significant impact on the respondents’ perception of QoL (adjusted R^2 for all: 0.43): going shopping (level of impact: 27%), concentrating on mental tasks (25%), being touched by a person (indicative of cutaneous allodynia – pain resulting from a non-noxious stimulus to normal skin or the scalp: 19%), getting out of the house (19%) and putting on clothes (10%). Interference with ‘getting out of the house’ and ‘going shopping’ had the highest impact on the respondents’ perception of QoL in those with PHN (38% and 40%, respectively) according to multiple regression analysis.

In addition to interfering with all usual daily activities and self-care, many respondents also reported limitations in moderate physical efforts (61%) and climbing a flight of stairs (43%) due to HZ/PHN (Table 3).

Mobility

As well as affecting walking ability, HZ pain/PHN resulted in a significant number of respondents being confined to bed (16% of those with PHN versus 6% of those with HZ).

Work

Of the 52% of respondents aged 50–59 years who were employed while affected by HZ/PHN, 48% reported absence from work as a result of HZ/PHN. The reasons for work absence were mainly healthcare visits (48%), pain (37%), discomfort (38%) and inability to concentrate (28%). Pain (48%) and discomfort (45%) were the most common reasons for work absence in the 25% of those aged ≥60 years who were employed. Those with PHN reported significantly more work absences than those with HZ, with pain being the most common reason for the absences.

Sleep

HZ pain/PHN interfered with sleep to a greater extent than all other areas of QoL tested (Fig. 1). Overall, 55% of respondents reported ‘not getting sufficient sleep’ at least some of the time due to HZ/PHN. Furthermore, sleep was ‘not quiet’ for at least some of the time in 66% of respondents (64% of those with HZ, 78% of those with PHN). Significantly more patients with PHN reported that sleep was ‘not quiet’ all of the time (18% versus 8% of those with HZ).

Table 3 Pain and quality of daily living outcomes

	All	Age (years)		Patient category	
		50–59	≥60	HZ	PHN
Level of pain					
Pain score (0–10), mean					
Average	6.5	6.3	6.6*	6.4	7.2*
At worst	7.5	7.5	7.5	7.4	8.3*
High pain score (8–10), % respondents					
Average	33	30	35*	30	47*
At worst	56	57	55	53	74*
Limitations on daily activities					
Usual daily activities (0–10), mean score					
Taking a shower or bath	3.5	3.3	3.6	3.4	4.2
Being touched by a person	3.8	3.7	3.9	3.6	5.3
Putting on clothes	3.5	3.4	3.6	3.4	4.5
Getting out of the house	3.2	3.0	3.3	3.0	4.3
Concentrating on mental tasks	3.2	3.2	3.2	3.1	4.0
Going shopping	3.5	3.5	3.5	3.4	4.4
Self-care, % respondents					
	27	29	26	26	37
Moderate physical efforts, % respondents ^a					
Limited at least a bit ^b	61	63	60	61	66
Limited a lot	20	20	20	18	36*
Climbing a flight of stairs, % respondents					
Limited at least a bit ^b	43	46	40	41	56
Limited a lot	13	12	14	10	29*
Consequences for family members and social circle, % respondents ^c					
	44	47	40	42	54
Feelings of anxiety/depression and enjoyment of leisure activities, % respondents					
Anxiety/depression					
At least moderate ^d	31	30	32	29	43
Extreme	6	6	6	5	11*
Did not enjoy leisure activities ^e					
	29	30	28	27	41

* $p < 0.1$ versus corresponding group

^a Moderate physical efforts included relocating a table, vacuum cleaning, or playing bowls

^b Limited at least a bit includes ‘limited a bit’ and ‘limited a lot’

^c Consequences for family members and social circle includes ‘few consequences’, ‘moderate consequences’ and ‘severe consequences’

^d At least moderate includes ‘moderate’ and ‘extreme’

^e Did not enjoy leisure activities includes ‘rarely’ and ‘very rarely’

HZ herpes zoster; PHN post-herpetic neuralgia

Mood

In addition to affecting mood and enjoyment of life, HZ pain/PHN was associated with anxiety and/or depression in 31% of respondents, with significantly more respondents with PHN reporting extreme anxiety/depression (11% versus 5% of those with HZ, Table 3).

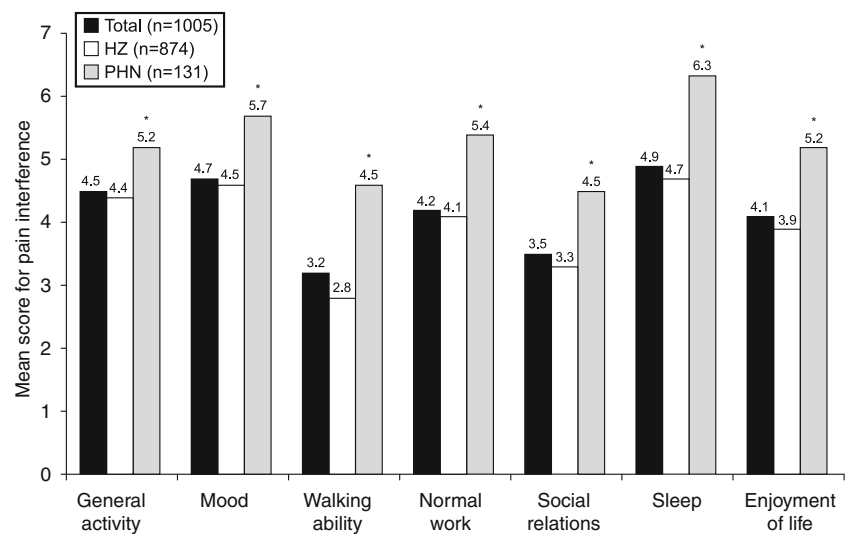
Overall, 29% of respondents reported very rarely/rarely enjoying simple leisure activities such as reading a book, listening to the radio or watching television while suffering from HZ/PHN (Table 3). More respondents with PHN

reported very rarely/rarely enjoying simple leisure activities than those with HZ, with significantly more very rarely enjoying leisure activities (25% versus 14%, respectively).

Social/family relations

More respondents with PHN reported consequences for family members and their social circle, compared with those with HZ (54% versus 42%, respectively; Table 3). Overall, 20% of respondents reported that they specifically felt isolated from their family and friends for at least some of the

Fig. 1 Interference of herpes zoster (*HZ*) pain/post-herpetic neuralgia (*PHN*) on seven aspects of quality of daily life. Pain interference measured on a scale of 0 ('does not interfere') to 10 ('completely interferes') with activity. * $p < 0.1$ for those with PHN versus all respondents and those with HZ



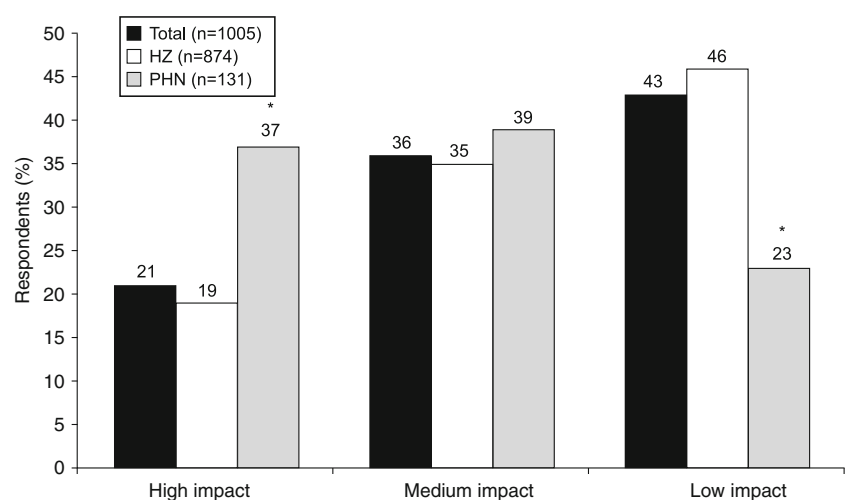
time while suffering from HZ/PHN, resulting in reduced communication (19% and 27% for HZ and PHN, respectively).

Effect of HZ and PHN on overall health status and concomitant conditions

Overall, 31% of respondents perceived HZ/PHN to have had a moderate/severe impact on their overall health status, as measured on a five-point scale from 'no impact' to 'severe impact'. Significantly more respondents with PHN reported this level of impact on their overall health status compared with those with HZ (54% versus 24%, respectively).

In addition, up to 46% of respondents who had comorbid conditions reported some degree of deterioration in those conditions while suffering from HZ/PHN, including osteoarthritis (38% reported deterioration), rheumatoid arthritis (45%), coeliac disease (46%) asthma (42%), heart failure (40%) and diabetes (39%).

Fig. 2 Overall impact of herpes zoster (*HZ*) pain/post-herpetic neuralgia (*PHN*) on quality of daily life. Pain interference with overall quality of life on a scale of 0 ('not affected at all') to 10 ('highly affected'). Proportion of those with high impact (score 8–10), medium impact (score 4–7) and low impact (score 0–3) across six European countries. * $p < 0.1$ for those with PHN versus all respondents and versus those with HZ



Overall impact on QoL

HZ/PHN had a considerable impact on respondents' overall perception of their QoL (Fig. 2). Overall, 21% of respondents perceived the impact of HZ/PHN on their overall QoL to be 8 to 10, on a 10-point scale of 0='not affected' to 10='highly affected'. PHN had a significantly higher impact on the respondents' perception of their overall QoL (Fig. 2).

Country data

Country results that were significantly different from those for all respondents are highlighted.

Patient-reported pain

Significantly more respondents in Portugal and Belgium described their pain as 'continuous, steady and constant'

compared with all respondents (57% and 62%, respectively, versus 45%). In The Netherlands, significantly more respondents described their pain as ‘rhythmic, periodic and intermittent’ (46% versus 34% for all respondents).

As shown in Table 4, Portuguese and Spanish respondents reported significantly higher pain scores at worst, compared with all respondents (7.9 and 8.0, respectively, versus 7.5); significantly more reported a high level of pain at its worst (8–10; 65% and 67%, respectively, versus 56%) with a significantly higher number reporting a pain score of 10 at its worst (41% and 30% versus 19%). In contrast, those in The Netherlands reported the lowest pain score at worst (6.9), with significantly more reporting a medium pain score (4–7; 67% versus 59% for all respondents).

Despite Spanish and Belgian respondents receiving a similar number of medications to treat HZ as all respondents (1.8 and 2.0 versus 1.8, respectively), they achieved significantly higher mean pain relief (70% and 69% versus 64%, respectively). Significantly more Spanish and Belgium respondents received their medication within 3 days of rash onset (73% and 78%, respectively, versus 63% for all respondents). Moreover, significantly more respondents in The Netherlands and Sweden were treated with a single medication (64% and 59% versus 45% for all respondents). In contrast, Portuguese respondents received significantly more medications (2.2 versus 1.8 for all respondents) but achieved only similar mean pain relief as all respondents (61% versus 64%).

Impact on various aspects of QoL

Overall, respondents from The Netherlands reported a significantly higher impact on general activities, compared with all respondents (interference score 5.1 versus 4.5) (Table 4). Although the impact on general activities in Portuguese respondents was not significantly different from all respondents (interference score: 4.9 versus 4.5), significantly more Portuguese respondents reported a high interference score (score 8–10; 30% versus 19%).

The impact of pain on mood was significantly higher in Portuguese and Dutch respondents (interference score: 5.3, 5.2 versus 4.7 for all respondent; Table 4). In addition, significantly more Portuguese respondents reported being anxious and/or depressed while suffering from HZ/PHN (51%) compared with all respondents (31%). Furthermore, significantly more Portuguese respondents also reported feeling sad/depressed or lonely prior to noticing the first symptoms of HZ compared with all respondents (43% versus 24%).

The impact of pain on walking ability was significantly higher in The Netherlands (interference score: 4.5) compared with all respondents (3.2) (Table 4). The Dutch also reported a significantly higher impact of pain on normal work, compared with all respondents (interference score: 5.0 versus 4.2). In addition, the Dutch also reported a significantly higher impact on relations with others compared with all respondents (interference score: 4.6 versus 3.5).

Table 4 Pain and quality of daily living outcomes by country

	All	Spain	Portugal	The Netherlands	Belgium	Sweden	Switzerland
Level of pain							
Pain score (0–10), mean							
Average	6.5	6.7	6.7	6.3	6.5	6.3	6.1
At worst	7.5	8.0	7.9	6.9	7.2	7.2	7.5
High pain score (8–10), % respondents							
Average	33	40	40	25	37	27	27
At worst	56	67	65	42	56	50	55
Interference of HZ pain/PHN on QoL domains, (0–10), mean							
General activity	4.5	4.1	4.9	5.1	4.2	4.0	4.2
Mood	4.7	4.3	5.3	5.2	4.7	4.1	4.6
Walking ability	3.2	2.9	3.2	4.5	3.5	1.8	2.0
Normal work	4.2	3.7	4.3	5.0	4.5	3.4	4.1
Social relations	3.5	2.9	3.5	4.6	2.9	2.6	3.5
Sleep	4.9	4.6	5.0	5.2	5.4	4.4	4.7
Enjoyment of life	4.1	3.4	3.8	5.0	3.8	3.7	4.6
Perception of overall QoL, (0–10)							
Mean	4.4	4.1	4.6	5.3	3.8	2.7	4.6

The Belgians reported a significantly higher impact of pain on sleep compared with all respondents (interference score: 5.4 versus 4.9) (Table 4). The Dutch and Swiss reported a significantly higher impact on enjoyment of life compared with all respondents (interference score: 5.0, 4.6, respectively, versus 4.1).

Overall impact on QoL

The overall impact on the respondents' perception of QoL was significantly higher in Dutch respondents compared with all respondents (impact score: 5.3 versus 4.4), with the Belgians and Swedish perceiving a lower impact (3.8 and 2.7, respectively) (Table 4). Significantly more Portuguese respondents reported a high impact score (8–10; 34%), compared with all respondents (21%).

Discussion

This large, pan-European, retrospective scientific survey of patient-reported outcomes has expanded the findings of the previously reported German survey (Weinke et al. 2010), demonstrating that the burden of HZ, and particularly PHN, are considerable in individuals ≥ 50 years old. The German survey assessed patient-reported pain and QoL outcomes in a sample of 280 affected individuals. The present survey involved 1,005 additional individuals, and indicated that the burden of HZ/PHN is similar across all six European countries surveyed as well as in Germany (Weinke et al. 2010). As noted in the initial survey, pain and QoL outcomes were not generally affected by age (50–59 years old or aged ≥ 60 years). They were also not affected by time since diagnosis (diagnosis ≤ 12 months or 13–60 months), despite patients having to recall information from up to 5 years earlier. This suggests that HZ/PHN is a life event that is not readily forgotten. These data also support the results from earlier, prospective, observational studies (Katz et al. 2004; Schmader et al. 2007; van Seventer et al. 2006). Importantly, this large survey may help to increase the awareness of the burden of HZ/PHN on QoL in different countries, thereby leading to improved strategies for prevention and management.

Prior to noticing the first symptoms of HZ, many of the respondents in our survey reported feeling nervous or stressed or sad/depressed or lonely. Stress and depression are recognised risk factors for HZ and PHN (Irwin et al. 1998; Livengood 2000; Thomas and Hall 2004). Furthermore, one study demonstrated that the VZV-specific cell-mediated immune response in individuals aged < 60 years with major depression was similar to that found in those aged ≥ 60 years without depression, suggesting that major depression reduces cell-

mediated immunity to VZV and is a risk factor for HZ that is independent of age (Irwin et al. 1998).

HZ/PHN was associated with considerable pain. More than half of all respondents reported a high level of pain at its worst (pain score 8–10), including 3 out of 4 of those with PHN. These results are not surprising and are similar to other reports of HZ pain and PHN (Dworkin et al. 2008; Johnson et al. 2010). Indeed, during the acute phase, HZ pain has been described as more intense than post-surgical or labour pain (Katz and Melzack 1999).

The burden of HZ/PHN on QoL was substantial. PHN affected the respondents' perception of QoL to a significantly greater extent than HZ. These results are consistent with previous reports of the interference of PHN with basic activities and daily functioning (Oster et al. 2005; Schmader 2002; Schmader et al. 2007). Sleep was the most affected QoL domain across all countries, with more than half of respondents reporting not getting sufficient sleep due to HZ/PHN. Lack of sleep is important because it has far-reaching consequences. In addition to neurobehavioural deficits such as lapses in attention, depression and cognitive impairment, which can occur when sleep is reduced to < 7 h per night for 14 days, restricted sleep has also been associated with unhealthy physiological changes (Banks and Dinges 2007). Lack of sleep also reduces productivity, performance and safety outcomes, and therefore has cost implications (Rosekind et al. 2010), which could be considerable, as one in three respondents with HZ/PHN in this survey was employed. The loss in productivity and associated cost implications related to lack of sleep are in addition to those associated with absences from work, which in the current survey were mainly due to healthcare visits and pain. The indirect cost of work absence was estimated to be €556 and €795 per case of HZ and PHN, respectively, based on an average daily wage of €80, in one European country, contributing to an annual cost to society of €13 million in a single year (Gialloreti et al. 2010).

A clear correlation between increased intensity of pain and greater interference with QoL has been reported (Lydick et al. 1995). However, the results from the individual countries suggest that QoL can be significantly affected even in those reporting less pain: those in The Netherlands reported the lowest pain score at worst (6.9), with significantly more reporting a medium pain score (4–7; 67%) compared with all respondents (59%), but were the only participants to report a significantly greater impact of HZ pain/PHN on their perception of QoL. Furthermore, the Dutch were the only participants to report a significantly higher impact on general activities, walking ability, normal work and relations with others, compared with all respondents.

Of note is that participants from Spain and Portugal tended to report more intense pain than those in non-Mediterranean countries, particularly those from The

Netherlands. This is consistent with previous studies highlighting that cultural or ethnic factors may play a role in subjects' pain reports (Fillingim 2005). In a US National Comorbidity Survey of subjects with serious health problems, Hispanics reported more pain than Caucasians (Hernandez and Sachs-Ericsson 2006); the authors noted that this may be related to cultural differences in the acceptability and the expression of distress. In a cross-cultural study, women from The Netherlands with rheumatoid arthritis reported lower levels of pain than Egyptian women with comparable rheumatoid arthritis (Vlaar et al. 2007).

Many clinicians incorrectly perceive HZ to be a mild and readily treatable disease (Johnson et al. 2010). In fact, treatment options remain inadequate, particularly for those who develop PHN, with potentially devastating effects on their QoL in the acute and chronic phases (Coplan et al. 2004; Katz et al. 2004; Oster et al. 2005). Disturbingly, despite evidence that antiviral therapy may effectively reduce the severity and duration of HZ if given within 72 h of rash onset (Dworkin 2006), of the 89% of respondents who received medication in the current survey, 37% did not receive it within this 72-h window. Furthermore, despite various treatments, pain relief was not satisfactory; mean pain relief was only 64%, with mean pain relief of only 50% in those with PHN. One in four respondents who received medication reported side effects.

There are several potential limitations associated with the present study. Firstly, the survey was retrospective. However, the design allowed the collection of data once the complete HZ/PHN episode had finished. This provided a broad picture of the patient-reported impact of HZ/PHN on QoL. Furthermore, the retrospective nature of the study had the benefit of a large sample size and provided data more rapidly than prospective studies. Secondly, validated questionnaires could not be used because they prospectively measure the impact of current HZ/PHN on QoL at specific time points. Bespoke questions were prepared, some of which were informed from standard QoL questionnaires and further developed to enable evaluation of the complete previous HZ/PHN episode. In the future, the results of the present study could potentially inform the design of prospective studies to evaluate the impact of HZ and PHN on patients' QoL, and questionnaires that can be used to assess the entire episode of HZ/PHN could be validated. A third potential limitation of this study is that the method used in The Netherlands (online, computer-assisted self-interviews) was different to that used in other countries (computer-assisted telephone interviews). This might have contributed to differences in outcomes between Dutch participants versus all respondents. Fourthly, the survey asked subjects to recall events that occurred up to 5 years previously. However, the pain and QoL results were not affected by age or time since diagnosis, demonstrating that HZ/PHN is a life event that is not readily forgotten.

Until now, HZ and PHN could not be prevented. Furthermore, management modalities for acute HZ pain and PHN remain inadequate. Vaccination is a new option to reduce the burden of HZ/PHN. A live attenuated VZV vaccine (ZOSTAVAX®) is indicated for the prevention of HZ and PHN (ZOSTAVAX® 2006). By boosting VZV-specific cell-mediated immunity (Levin et al. 1998, 1992, 2003; Oxman 1995; Trannoy et al. 2000), which naturally declines with age (Arvin 2005; Levin et al. 2008), the vaccine acts as a 'latent virus blocker' controlling the reactivation and/or subsequent replication of latent VZV and thereby preventing HZ or attenuating its severity (Levin et al. 2008). In the Shingles Prevention Study, a pivotal study involving 38,546 subjects aged ≥ 60 years old, vaccine efficacy was demonstrated by a reduction of 51.3% in the prevalence of HZ ($p < 0.001$ versus unvaccinated individuals) and a 66.5% reduction in the prevalence of PHN ($p < 0.001$ versus unvaccinated individuals; Oxman et al. 2005, 2008). In addition to reducing the HZ/PHN prevalence, the vaccine also reduced the burden of illness due to HZ by 61.1% ($p < 0.001$ versus unvaccinated individuals) – this measure is affected by the incidence, severity and duration of HZ-related pain and discomfort. Importantly, these reductions in HZ/PHN prevalence and burden of illness in vaccinees were associated with improvements in QoL. Interference of HZ on activities of daily living was significantly reduced by 66%, and SF-12 Mental and Physical Component Scores (measures of health-related QoL) were both reduced by 55% (Schmader et al. 2010).

Conclusions

The results of this European survey clearly demonstrate that HZ, and particularly PHN, are associated with considerable levels of pain that have a significant impact on QoL. Indeed, HZ pain/PHN not only has a direct impact on individuals, it also affects their social life, with consequences for family and friends, and it impacts society, in terms of loss of productivity and associated cost implications.

Similar results in terms of pain and QoL outcomes were achieved across seven European countries, including the initial study in Germany (Weinke et al. 2010). Participants across seven European countries were required to recall episodes of HZ/PHN that occurred up to 5 years earlier. Hence, these results, along with those in the initial study (Weinke et al. 2010), indicate that HZ/PHN is a life event that is not readily forgotten.

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Conflict of interest This survey was sponsored by Sanofi Pasteur MSD, the license holder for a vaccine against herpes zoster in the European Union. KL and IB are employees of Sanofi Pasteur MSD. AE was an employee of TNS Healthcare, who conducted the study, at the time the study was undertaken.

Authors' contributions KL conceived of the study, participated in its design and coordination and helped to draft the manuscript. AE participated in the design and co-ordination of the study, undertook the statistical analysis and helped to draft the manuscript. IB participated in the study questionnaires preparation and helped to draft the manuscript. All authors contributed to the content of this manuscript and have approved the final draft.

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