Herpes zoster epidemiology, management, and disease and economic burden in Europe: a multidisciplinary perspective

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***Abstract*:** Herpes zoster (HZ) is primarily a disease of nerve tissue but the acute and longer-term manifestations require multidisciplinary knowledge and involvement in their management. Complications may be dermatological (e.g. secondary bacterial infection), neurological (e.g. long-term pain, segmental paresis, stroke), ophthalmological (e.g. keratitis, iridocyclitis, secondary glaucoma) or visceral (e.g. pneumonia, hepatitis). The age-related increased incidence of HZ and its complications is thought to be a result of the decline in cell-mediated immunity (immunosenescence), higher incidence of comorbidities with age and social-environmental changes. Individuals who are immunocompromised as a result of disease or therapy are also at increased risk, independent of age. HZ and its complications (particularly postherpetic neuralgia) create a significant burden for the patient, carers, healthcare systems and employers. Prevention and treatment of HZ complications remain a therapeutic challenge despite recent advances. This is an overview of the multidisciplinary implications and management of HZ in which the potential contribution of vaccination to reducing the incidence HZ and its complications are also discussed.

Keywords: herpes zoster, herpes zoster diagnosis, herpes zoster treatment, herpes zoster vaccination, multidisciplinary management, postherpetic neuralgia

Epidemiology of herpes zoster and its complications

Varicella zoster virus (VZV) causes a primary infection known as varicella (chicken pox). The virus then migrates from the skin lesions *via* nerve axons and, probably also by viremic spread, to spinal and cranial sensory ganglia where it becomes dormant. Later in life, in some individuals the virus is reactivated (usually within a single ganglion) to cause a secondary infection known as herpes zoster (HZ; shingles). Individuals with HZ can transmit VZV to their seronegative contacts, who may develop varicella, but not HZ [Bloch and Johnson, 2012; Viner *et al.* 2012]. The household transmission rate of HZ (to cause varicella) is 15%, making it significantly less contagious than varicella but nevertheless of relevance to at-risk contacts [Schmid and Juuman, 2010].

Over 95% of immunocompetent individuals aged at least 50 years are seropositive for VZV and are, therefore, at risk of developing HZ. VZV-specific cell-mediated immunity declines with age concomitantly with the rise in the incidence of HZ and its complications that occurs at about 50 years of age (Figure 1) [Burke *et al.* 1982; Helgason *et al.* 2000; Tanuseputro *et al.* 2011; Pinchinat *et al.* 2013; Yawn and Gilden, 2013]. The lifetime risk of developing HZ is between 25% and 30%, rising to 50% in those aged at least 80 years [Studahl *et al.* 2013; Yawn and Gilden, 2013; Chen *et al.* 2014a]. The estimated average overall incidence of HZ is about 3.4–4.82 per 1000 person years which increases to more than 11 per 1000 person years in those aged at least 80 years (Figure 1). In Canada, the overall incidences of medically attended HZ and HZ-related outpatient visits and hospitalizations were reported to increase with age

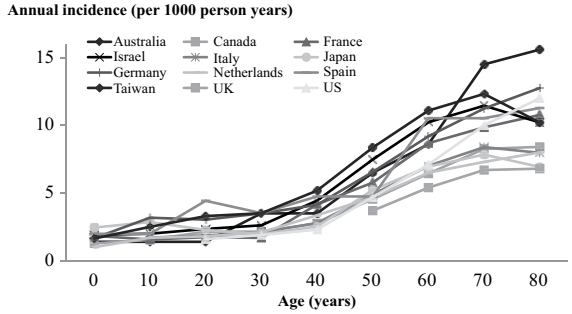

Figure 1. Results from 12 countries showing the risk of developing HZ increases with age, starting at about 50 years old [de Melker *et al.* 2006; Gauthier *et al.* 2009; Stein *et al.* 2009; Toyama and Shiraki, 2009; Gialloreti *et al.* 2010; Gonzalez Chiappe *et al.* 2010; Lin *et al.* 2010; Tanuseputro *et al.* 2011; Ultsch *et al.* 2013a; Weitzman *et al.* 2013; Yawn and Gilden, 2013; Esteban-Vasallo *et al.* 2014].

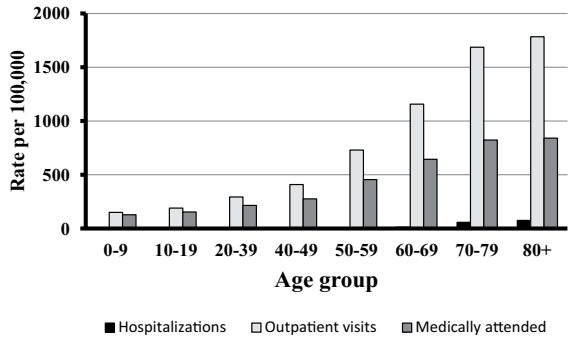

Figure 2. Overall incidence of herpes zoster (HZ)-related hospitalizations and outpatient visits and medically attended HZ as a function of age in Canada [Tanuseputro *et al.* 2011].

(Figure 2) [Tanuseputro *et al.* 2011]. Data from a general practitioner (GP) network in France showed that 1% of patients with HZ were hospitalized and the death rate was 0.2/100,000 [Gonzalez Chiappe *et al.* 2010]. HZ-associated mortality is rare, with reported incidence ranging from 0 to 0.47 per 100,000 person year, and the majority of deaths occur in those aged at least 60 years [Kawai *et al.* 2014; Bricout *et al.* 2015]. However, many studies use electronic or paper death certificates which can lead to underestimations or overestimates of the true mortality rate due to infections other than HZ and noninfectious diseases, particularly in older people.

When reactivated, the virus travels along the affected sensory nerve, causing neuronal damage, to reach the corresponding dermatome in the skin where a vesicular rash develops. Prior to rash appearance, the frequent prodromal itching or pain can lead to erroneous and delayed diagnosis. The vesicles pustulate and then scab, usually within 2–4 weeks, but residual scarring is common. There are three phases of HZ pain: acute pain phase (up to a month), subacute pain phase (any pain 30–90 days after rash healing) and post herpetic neuralgia (PHN) phase (pain for more than 90 days after the onset of rash). Acute pain, largely inflammatory, may progress to persistent neuropathic pain resulting from peripheral and central nerve damage and secondary sensitization.

Postherpetic neuralgia

Pain present for 90 days or more after HZ rash onset is known as PHN [Sampathkumar *et al.* 2009]. PHN is the most common complication of HZ. Although the pain often resolves within a few weeks, it can last for several months or even years. It is a debilitating complication that is challenging to treat and is responsible for most of the HZ-related burden of disease [Johnson and Rice, 2014].

Factors associated with the development of PHN include greater severity of acute pain, older age, greater rash severity, immuno compromised patients and restricted activities of daily living prior to HZ [Opstelten *et al.* 2002; Johnson, 2007; Drolet *et al.* 2010; O'Connor and Paauw, 2013; Johnson and Rice, 2014]. Prodromal pain, female sex, diabetes and presence of herpes zoster ophthalmicus (HZO) have also been reported to play a role [Gnann and Whitley, 2002; Johnson and Rice, 2014].

Other complications

Other complications, both in the primarily affected dermatome and elsewhere, may occur, although these are less common [Oxman, 2000; Harpaz *et al.* 2008; Drolet *et al.* 2013; Kawai *et al.* 2014]. Dermatomal complications include secondary bacterial infections, ophthalmic complications and various degrees of segmental paresis, which can affect extraocular muscles, limbs, abdominal wall or diaphragm, depending on the dermatome involved.

Viral reactivation in the first branch of the trigeminal nerve (i.e. the ophthalmic or V1 division) results in HZO [Ragozzino *et al.* 1982; Arvin, 1996; Gnann and Whitley, 2002; Wang *et al.*

2005]. HZO accounts for about 10–20% of cases of HZ. The lifetime risk of developing HZO is approximately 1% [Liesegang, 2008]. Ocular complications typical of HZO can occur even when there is no visible rash (i.e. zoster sine herpete) [Liesegang, 2008]. Polymerase chain reaction (PCR) analysis has shown that VZV may be present in the cornea and tears, even in the absence of ocular symptoms or skin rash [Pitkaranta *et al.* 2000; van Gelderen *et al.* 2000]. Hence VZV reactivation in the ocular neuronal pathways is frequently misdiagnosed and, therefore, its incidence underestimated. Between 20% and 70% of patients with HZO develop complications that can include blepharitis, keratoconjunctivitis, iritis, scleritis and acute retinal necrosis. Neurological complications are less frequent than ocular complications and may include ophthalmoplegia, optic neuritis and ptosis. Patients presenting with HZO should be treated with oral antiviral drugs, preferably within 72 h after rash onset; however, if new lesions are present, treatment may still be useful after this time [Cobo *et al.* 1986; Hoang-Xuan *et al.* 1992; Severson *et al.* 2003; Liesegang, 2004]. Treatment is usually for 7 days; there is no evidence that longer treatment is beneficial, except in older or immunocompromised patients in whom viral activity has been shown to be ongoing for up to 34 days [Harding, 1993; Wenkel *et al.* 1998; Zaal *et al.* 2001; Liesegang, 2008; Hu *et al.* 2010]. Despite antiviral treatment, chronic disease can persist in 30% of patients with HZO, increasing to 70% in patients over 80 years old. A prominent cause of persistent or chronic disease is vasculitis, perivasculitis, neuritis and perineuritis; the neuronal damage begins before the characteristic dermatomal rash appears and therefore before antiviral treatment is initiated [Liesegang, 2008].

Disseminated zoster occurs mainly in immunocompromised patients and, in the case of visceral location, can lead to pneumonia, encephalitis (with associated cognitive impairment and sensory or motor deficits) and hepatitis with a 5–10% fatality rate, despite antiviral drug treatment [De Broucker *et al.* 2012]. Primary VZV encephalitis is not necessarily associated with immunodeficiency. In a French study, HZ encephalitis was identified as the second most frequent cause of death (15%) after herpes simplex virus (HSV) [Mailles and Stahl, 2009].

Dermatological complications that occur include disseminated HZ usually associated with immune suppression and characterized by vesicles spreading beyond the distribution of the affected dermatome, with the potential to affect other organs (e.g. encephalitis) making the condition potentially lethal [Rommelaere *et al.* 2012]. Others include hemorrhagic HZ, a rare condition also correlated with immune suppression, coagulopathy, thrombocytopenia and Ramsay Hunt syndrome, defined as peripheral facial nerve palsy accompanied by an erythematous vesicular rash in the ear (zoster oticus), resulting from involvement of the geniculate ganglion by HZ reactivation. Chronic varicella zoster is defined as an atypical mucocutaneous wart-like or ulcerative VZV infection, persisting for at least 1 month, mainly occurring in patients who are HIV positive [Wauters *et al.* 2012].

Patients with cancers and other diseases that alter immune function, such as autoimmune inflammatory rheumatic disease (AIRD: rheumatoid arthritis, systemic lupus erythematosus, granulomatosis with polyangiitis) and patients taking immunosuppressants or chemotherapy have a higher risk of HZ [Smitten *et al.* 2007; Hata *et al.* 2011; Yawn *et al.* 2011; Blank *et al.* 2012; Habel *et al.* 2013; Long *et al.* 2013; Chen *et al.* 2014b; Forbes *et al.* 2014]. It has been suggested that in patients with AIRD the drugs used for treatment (e.g. steroids, antitumor necrosis factor α agents and some disease-modifying drugs) add to the risk [Winthrop *et al.* 2013; Che *et al.* 2014]. When HZ is diagnosed, the possibility of stopping immunosuppressive drugs should be considered. Patients who are HIV positive with low CD4 counts also have a higher risk than the general population; the lower the count, the greater the risk [Blank *et al.* 2012; Shearer *et al.* 2014]. In addition, in the first 3 months of HIV treatment there is a higher incidence of HZ, probably as a consequence of immune activation by antiretroviral drug treatment. HZ incidence is lower in patients receiving Highly-active antiretroviral treatment (HAART) but it remains higher than the general population [Blank *et al.* 2012; Shearer *et al.* 2014].

HZ and its complications have been shown to have an adverse impact on quality of life (QoL) and activities of daily living. Some patients, particularly older patients, lose their independence and many patients require help from their families or paid caregivers [Weinke *et al.* 2010, 2014; Bouhassira *et al.* 2012; Gater *et al.* 2014]. In particular, sleep and social activities are most severely affected. Although individuals can recover some

of their loss of independence, they rarely recover to the same level as they had before the HZ episode [McElhaney, 2010]. People who have had HZ or know people who have had HZ are more aware of the risks, associated pain, consequences and impact on QoL of the disease [Álvarez-Pasquín *et al.* 2011; Mortensen, 2011]. An individual's attitude towards HZ prevention is related to their knowledge of HZ and views on vaccination in general.

Impact of varicella vaccination on HZ epidemiology

Hope-Simpson was the first to postulate that re-exposure to circulating VZV, a phenomenon known as exogenous boosting, could prevent reactivation of VZV [Hope-Simpson, 1965; Arvin, 1996; Brisson *et al.* 2002]. Vaccination of children against varicella, which is established in some countries, could have two effects on the epidemiology of HZ. The first is that there will be fewer adults carrying dormant wild type VZV as vaccinated children grow older, thus reducing the incidence of HZ. The second is that, in the shorter term, adults with dormant VZV will have less contact with children with varicella and therefore less opportunity for exogenous boosting [Ogunjimi *et al.* 2013]. Since exogenous boosting is thought to inhibit VZV reactivation, this could result in a temporary increased incidence of HZ and could reduce the age of HZ onset. Mathematical models predict that this increased incidence could last for more than 30 years [Schuette and Hethcote, 1999].

Since the introduction of widespread childhood varicella vaccination, no impact has been observed on the incidence or age distribution of HZ [Tanuseputro *et al.* 2011]. Other studies have reported an increasing trend in the general population as well as in immunocompromised populations, but this trend preceded the implementation of childhood varicella vaccination [Leung *et al.* 2011; Hales *et al.* 2013]. Long-term surveillance will be necessary to establish if there will be an increased incidence of HZ [Leung *et al.* 2011].

Diagnosis

HZ is generally diagnosed clinically, once the rash has appeared. However, prior to the rash occurring and for atypical cases, diagnosis can require laboratory confirmation, using PCR analysis which can detect VZV DNA rapidly and accurately [Schmader, 2006; Cohen, 2013]. HZ can sometimes be confused with HSV or a number of other conditions.

Treatment options

The management of HZ with antiviral drugs and analgesics frequently reduces acute rash and pain and may prevent some complications [Johnson *et al.* 2010; Cohen, 2013]. Antiviral drugs have been shown to reduce acute pain and rash severity, accelerate rash resolution and reduce duration of pain. However, many patients suffer from PHN despite antiviral drug use [Rabaud *et al.* 2013; Li *et al.* 2014]. The prodrugs valacilovir and famciclovir have a more convenient dosing schedule and more constant blood concentrations than acyclovir. Paracetamol alone or in combination with a weak opioid (e.g. codeine) is frequently used as analgesia. Addition of drugs active against neuropathic pain (e.g. tricyclic antidepressants such as amitryptyline, α-2-δ ligands such as gabapentin or pregabalin, strong opioids such as oxycodone) are used for resistant pain but older adults often suffer from adverse effects. Successful PHN treatment needs to not only be effective but to have an acceptable side-effect profile. Generally, systemic drugs are poorly effective for the treatment of PHN (pain reduced by 50% in 50% of patients at best) and they have significant side effects. Topical application of lidocaine patches and treatment with 8% capsaicin patches may provide relief for some patients and avoids systemic side effects [Johnson and Rice, 2014; Finnerup *et al.* 2015].

Multidisciplinary perspectives of clinical manifestations and management of HZ

Patients who develop HZ can be seen by a variety of medical specialists depending on healthcare organization where they live and the evolution of their HZ episode, particularly the occurrence of complications. For example, in Italy a survey reported that HZ was managed by GPs in the majority of cases, with only 18% of cases being referred to specialists, mainly pain specialists, ophthalmologists or dermatologists (mean: 0.2 visits/patient); the number of specialist referrals increased with age [Gialloreti *et al.* 2010]. Only 1.3% were hospitalized; 92% of those hospitalized for HZ or PHN were over 50 years old [Gialloreti *et al.* 2010]. Among the 7.4% patients who developed PHN, 74% were referred to a specialist (mean: 3.5 visits/patient) and 2% were hospitalized. Costs for outpatient care from GPs and

specialists and for hospitalization for HZ-related complications are high [Kawai *et al.* 2014].

Although individual GPs do not generally see many patients with HZ, it often affects their most vulnerable patients who are at risk of severe complications. These patients have an increased iatrogenic risk as they often take several drugs for chronic diseases and are at high risk of decompensation and functional decline [Bruckenthal and Barkin, 2013; Sacks, 2013]. Recommendations are important to provide guidance to GPs as they may have little personal experience due to the low incidence among their patients. Current guidelines recommend that antiviral drugs should not be administered beyond a 72 h window, although most state that this window can be extended when disease is severe or if there is evidence of ongoing viral activity (e.g. new lesions) and for HZO. GPs may refer patients with complications, such as HZO or PHN, to specialists.

The type of patients with HZ seen by geriatricians varies between healthcare systems. In some systems, where older people are regularly seen by geriatricians, they will see most cases, while in others, only 'complicated' cases will be referred to geriatricians or will be hospitalized under their care. Geriatricians are often faced with older patients who have longer and more severe HZ-associated pain and who, on average, can have about five comorbidities at 65 years increasing to almost seven at 85 years [Lopes *et al.* 2013; Miranda *et al.* 2013]. PHN and its treatment can affect the cardiovascular system (increased heart rate and blood pressure, hypercoagulation leading to an increased risk of deep vein thrombosis and pulmonary embolism), the gastrointestinal system (delayed gastric emptying and reduced bowel motility), respiratory dysfunction (leading to hypoxia and cardiac complications), retention of sodium and water (resulting in urine retention, increased cardiac workload and hypertension) [Bruckenthal *et al.* 2013; Lopes *et al.* 2013; Miranda *et al.* 2013; Sacks, 2013]. The immune system can also be depressed, thus predisposing patients to wound and respiratory infections. Poorly treated pain can affect QoL, interfering with sleep, diet and exercise, increase anxiety and give rise to cognitive impairment (disorientation, confusion, concentration difficulties) [Johnson *et al.* 2010; Pickering and Leplege 2011; Pickering *et al.* 2014a, 2014b].

Infectious disease specialists can advise GPs, treat severe cases (e.g. neurological manifestations), complications and recurrences. They are also involved in prevention (prophylaxis, preorgan transplantation consultation, risk of transmission). They are solicited for preventive measures for immunocompromised patients, usually on a case-by-case basis. They generally see 'complicated' HZ as only severe acute cases, complicated cases and patients with debilitating PHN are hospitalized in infectious disease units. Rheumatologists should be aware that their patients with AIRD have a higher risk of HZ and complications, and should interrupt immunosuppressive drugs when HZ is diagnosed.

Patients can be referred to pain specialists and dermatologists to seek advice on the most effective management of pain and dermatologic complications when they occur. An ophthalmic examination should be offered to patients who present with at least one obvious ocular symptom (ocular redness or pain, blurred vision), even if HZO occurred several weeks previously, since inflammatory complications are frequently delayed [Harding *et al.* 1987]. Patients with Hutchinson's sign, defined as skin lesions at the tip or side of the nose (nasociliary skin lesions) should also be checked for intraocular lesions (incidence rate of 80% *versus* 50% in the absence of Hutchinson's sign) [Ragozzino *et al.* 1982; Yamada *et al.* 1990; Zaal *et al.* 2003; Opstelten and Zaal, 2005]. The risk of necrotizing retinitis, a sight-threatening complication, is common in immunocompromised patients with HZO [Batisse *et al.* 1996; Vafai and Berger, 2001].

Prevention of HZ

Prevention of HZ and its complications by vaccination would improve the life of older people and also reduce the societal impact of HZ [Gater *et al.* 2014]. A live-attenuated VZV vaccine against HZ (Zostavax (manufactured by Merck & Co., Inc, NJ, USA and commercialized in Europe by Sanofi Pasteur MSD, Lyon, France)), which has been licensed in a number of countries worldwide for administration to adults aged over 50 years, has been shown to reduce the incidence of HZ, PHN and other complications in immunocompetent adults (Table 1) [Oxman *et al.* 2005; Schmader *et al.* 2012]. Although live-attenuated vaccines are not generally recommended for immunocompromised individuals, in 2012 the Canadian National Advisory Committee on Immunization stated that individuals on low-dose immunosuppressive therapy, including anti-TNF biologics, could receive the HZ vaccine, after review with an expert in immunodeficiency, on a case by case basis [Public Health Agency of Canada, 2014].

Table 1. Summary of vaccine efficacy and 95% confidence intervals from two pivotal efficacy studies by age: Zostavax Efficacy and Safety Trial (ZEST) in individuals aged 50–59 years and Shingles Prevention Study (SPS) in individuals aged ⩾60 years.

	ZEST	SPS				
	50–59 years	⩾60 years	60–69 years	⩾70 years	70–79 years	⩾80 years
Vaccinated/ placebo *N*	11,211/11,228	19,254/19,247	10,370/10,356	8884/8891	7621/7759	1263/1332
HZ incidence	70% (54%; 81%)	51% (44%; 58%)	64% (56%; 71%)	38% (25%; 48%)	41% (28%; 52%)	18% (<0%; 48%)
PHN incidence	Not evaluated	67% (48%; 79%)	66% (20%; 37%)	67% (43%; 81%)	74% (49%; 87%)	40% (<0%; 67%)
% PHN among HZ	Not evaluated	39% (7%; 59%)	5% (<0%; 56%)	47% (13%; 67%)	55% (18%; 52%)	26% (<0%; 68%)
BOI*	73% (53%; 85%)	61% (51%; 69%)	66% (52%; 76%)	55% (40%; 67%)	59% (43%; 71%)	38% (<0%; 67%)

*BOI: burden of illness; incidence, severity and duration of acute and chronic HZ-associated pain. In ZEST D0-D21, in SPS D0-D182.
HZ, herpes zoster; PHN, postherpetic neuralgia.

Vaccination recommendations should target at-risk groups, including older individuals, since age is a known risk factor. In addition, there is no way to predict which patients will develop HZ, when and how severe the disease will be [Harpaz *et al.* 2008; Oxman, 2009; Weaver, 2009]. However, individuals need to be adequately informed about the disease and its complications to enable them to make a personal risk assessment, in consultation with their GP, before deciding to accept HZ vaccination.

HZ vaccination reduces the burden of HZ-related interference with daily life activities in vaccinated subjects, particularly older people, who develop HZ. The vaccine attenuates the severity of HZ and PHN when they occur in individuals of all ages, and thus contributes to a reduction of disease burden. The vaccine has been shown to be effective for reducing the risk of HZO and other complications in those aged over 60 and if HZO occurs, despite vaccination, the risk of PHN is significantly lower [Oxman *et al.* 2005; Gelb, 2008; Tseng *et al.* 2011].

HZ vaccination does not induce herd protection (as HZ is not transmitted between individuals) and protection may persist for up to 10 years, although efficacy decreases with the recipients' age. After its introduction in the US, HZ vaccination has been reported to be associated with lower HZ incidence in vaccinated individuals [Tseng *et al.* 2011; Zhang *et al.* 2012; Langan *et al.* 2013].

Age at vaccination, duration of vaccine protection and vaccine efficacy against PHN are all important variables for determining vaccine cost effectiveness. The results from modeling studies performed with European data suggest that the optimal age for HZ vaccination is 65 or 70 years (Table 2) [van Hoek *et al.* 2009; Annemans *et al.* 2010; Moore *et al.* 2010; van Lier *et al.* 2010; Szucs *et al.* 2011; Bresse *et al.* 2013; de Boer *et al.* 2013; Ultsch *et al.* 2013b]. Cost effectiveness decreases after this age because vaccine efficacy declines with age and life expectancy is shorter. Cost effectiveness is also reduced for vaccination before this age due to uncertainties about the duration of vaccine protection. Therefore, in the light of current evidence, HZ vaccination offers significant clinical benefit to older adults and economic benefit to healthcare systems.

Attitudes and knowledge about HZ disease and vaccination

The results from a survey carried out on the general public in Spain showed that 75% of those questioned knew what shingles was but only 10% knew that a vaccine exists [Álvarez-Pasquín *et al.* 2011]. Other surveys have shown knowledge that long-term pain may follow HZ is low, although those who had a close friend or relative who had suffered from HZ were more aware [Paek and Johnson, 2010].

Two-thirds of healthcare workers considered HZ vaccination to be an important clinical priority but half reported that the vast majority remained unvaccinated [Paek and Johnson, 2010]. Half of patients questioned stated that they would have the HZ vaccine if it was recommended by their

Table 2. Summary of results from cost-effectiveness studies of herpes zoster vaccination in Europe.

Study reference	Year of publication	Country	Perspective	Age of vaccination	Incremental cost effectiveness/QALY
Van Hoek *et al.* [2009]	2006	England and Wales	Provider	65 years	£20,412
Moore *et al.* [2010]	2006	United Kingdom	Society	⩾50 years	£11,417
				⩾65–69 years	£10,033
			Provider	⩾50 years	£13,077
				⩾65–69 years	£10,275
Annemans *et al.* [2010]	2007	Belgium	Society	⩾50 years	€7137
			Provider	⩾60 years	€6799
Van Lier *et al.* [2010]	2008	The Netherlands	Society	60 years	€38,519
			Provider	70 years	€21,716
Szucs *et al.* [2011]	2011	Switzerland	Society	70–79 years	CHF28,544
			Provider	70–79 years	CHF25,528
De Boer *et al.* [2013]	2013	The Netherlands	Society	60 years	€35,555
				70 years	€29,664
Ultsch *et al.* [2013b]	2013	Germany	Society	60 years	€30,212
			Provider	60 years	€28,146
Bresse *et al.* [2013]	2013	France	Provider	70–79 years	€14,198

QALY, quality-adjusted life year.

GP and a third would if it was recommended in the media. The main reasons for not getting vaccinated were that patients did not know that the vaccine existed, did not consider themselves to be at risk and did not know the cost of vaccination [Paek and Johnson, 2010]. HZ vaccine is mainly prescribed by GPs but when prescribed by a specialist, the patients generally said that they wanted to discuss it with their GP first. Therefore, GPs need to be informed about HZ and the efficacy and safety of the vaccine so that they can effectively recommend it and be able to help the patient to evaluate the risks and benefits.

Remaining challenges

The remaining challenges for HZ management include improving knowledge and awareness of physicians and the general public about HZ, establishing programs for HZ prevention and attenuation by vaccination, and improving treatments for HZ and its complications. In particular, prompt consultation and diagnosis would allow treatment to be initiated earlier with improved antiviral drugs to limit neuronal damage. Additionally, more effective treatments for PHN with fewer adverse effects are needed, particularly for older people. Moreover, there is a need for evidence identifying which categories of immunocompromised patients can safely and effectively receive the currently available live-attenuated HZ vaccine and for development of other vaccines to address the needs of this population. The duration of protection afforded by HZ vaccine needs to be established and vaccination programs should take this into account.

Conclusion

HZ is a common disease with the highest burden in older adults who frequently have at least one chronic disease. The risk of drug–drug interactions is higher in this population when treatment for HZ and PHN is required, making management challenging, with the risk of unsatisfactory pain relief, adverse events, decompensation of comorbidities and functional decline. HZ and its complications represent a significant burden on the patients, caregivers, the healthcare economy and employers. Acute disease treatment does not significantly prevent the most common long-term complication, PHN. Treatments for PHN that provide higher levels of pain relief with fewer adverse effects are needed. Less common, but often serious, ophthalmic locations (HZO) and related complications can have permanent detrimental effects.

Future goals include developing new vaccines for specific groups, such as immunocompromised

individuals, and developing an evidence base on which type of immunocompromised individuals can be safely and effectively vaccinated with a live-attenuated vaccine. Prevention and attenuation of HZ and its complications are now feasible for most patients and a rational and economically acceptable integrated vaccination policy is a desirable goal. Improved knowledge about HZ and its complications for the public and physicians is needed so that individuals can make informed decisions about HZ vaccination.

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