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Health and economic burden of herpes zoster in adults in Finland: A retrospective nationwide database study

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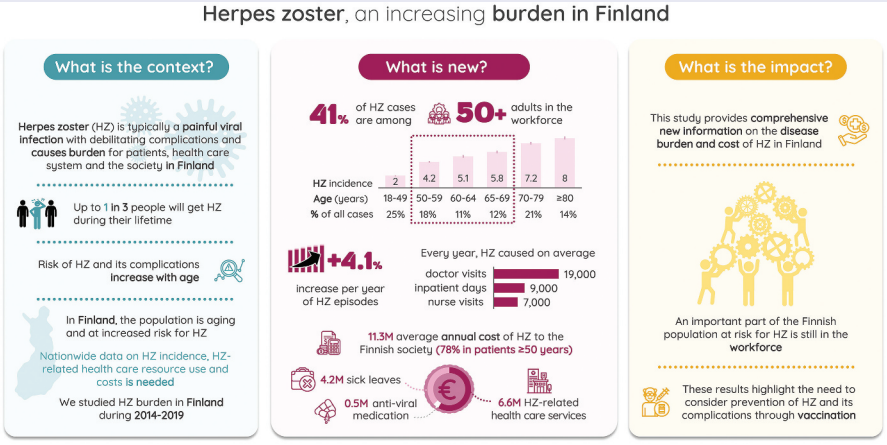
ABSTRACT

The risk of herpes zoster (HZ) and its complications, such as postherpetic neuralgia (PHN), increases with age and burdens patients, the healthcare system, and society. We aimed to estimate the incidence, healthcare resource use (HCRU), and direct and indirect costs due to HZ and HZ-related complications (i.e. PHN) per age group in the adult population in Finland. This retrospective, non-interventional population-based registry study collected data from four different registers over 2014–2019: three with nationwide coverage and one with partial nationwide coverage. International classification codes were used to identify HZ and PHN cases. The incidences of HZ and PHN were stratified annually and per age group (18–49, 50–59, 60–64, 65–69, 70–79, ≥80 years of age [YoA]). The HZ-associated HCRU, and direct and indirect costs were estimated by counting healthcare contact, medications, and their unit costs from national registries. HZ incidence rate increased with age from 1.99/1,000 persons in 18–49 YoA to 8.04/1,000 persons in ≥80 YoA over 2014–2019. PHN incidence also increased with age. The HZ 5-year recurrence rate was 4.5%. Average total annual costs of HZ amounted to €11.3 million; the individual costs of an HZ and a PHN HZ episode were €649 and €1,910, respectively. Estimated total costs were split between sick leave (37%), inpatient days (30%), outpatient visits (29%), and outpatient antiviral drugs (4%). In Finland, HZ poses a significant health and economic burden that increases with population aging, highlighting the need to consider HZ prevention.



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Introduction

Herpes zoster (HZ), or shingles, is a viral infection typically associated with a painful rash. It is caused by the reactivation of the varicella zoster virus (VZV), remaining dormant in the nervous system after the primary

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varicella episode.[1] Postherpetic neuralgia (PHN) is a common complication of HZ, in which pain persists in the rash area for over 90 days after the original HZ episode.[1–3] Other serious complications of HZ include, e.g., blindness due to ophthalmic zoster, central nervous system infections such as meningitis and encephalitis, facial palsy, and bacterial superinfections of skin lesions.[4,5]

Over 95% of immunocompetent individuals over 50 years of age (YoA) are seropositive for VZV and therefore at risk of developing HZ.[6] The lifetime risk of developing HZ is estimated at 30–36%.[1,7] About 20–30% of HZ cases will further develop PHN, and this risk increases with age.[8] A systematic literature review including 27 European countries over 1960–2010 found HZ incidence varied by country from 2.0 to 4.6 per 1,000 person-years.[9]

HZ incidence increases with age, particularly after 50 YoA.[9,10] Individuals who are immunosuppressed due to disease or following treatment with immunosuppressive medication have an increased risk of developing HZ. The risk of HZ is increased in patients with, for example, malignancies, organ transplants, and autoinflammatory diseases such as rheumatoid arthritis, inflammatory bowel disease, systemic lupus erythematosus, and psoriasis, but is also slightly increased in patients with common comorbidities such as diabetes and cardiovascular or renal diseases.[7,11–14]

HZ and its complications, particularly PHN, cause a significant burden for patients, healthcare professionals, healthcare systems, and employers.[5] A study assessing the burden and societal costs of HZ and PHN in Sweden for the year 2011[15] concluded that the societal costs to treat HZ per patient, including HZ cases with PHN, were €870, of which 28% were due to sick leave.

The current data on HZ incidence in Finland are limited to one retrospective public healthcare registry study investigating HZ incidence in relation to coronavirus disease 2019 (COVID-19) infection and COVID-19 vaccinations during 2018–2022.[16] Public healthcare registers cover the entire population with one caveat: in Finland, the primary contact for outpatient visits for the working-age population is usually occupational healthcare, mainly organized by private healthcare providers who have their own registers, although patients may also use public sector services. From late 2020 onwards, their data has been gradually included in the public healthcare register, but the data coverage is not complete and the HZ incidence based on the public registers has been estimated to be about 30% lower than the true incidence.[16] Therefore, to have data representative of the whole adult population, it is important to also consider the private sector data in addition to public registers. Additionally, data on HZ complications and their associated costs along with data on the contribution of sick leave to the indirect costs of HZ are lacking for Finland.

As HZ and its complications – mainly PHN – may impose a significant burden for patients, the healthcare system, and society, a robust analysis of HZ incidence, HZ complications, HZ-related healthcare resource use (HCRU), and costs is needed. The primary study objective was to estimate the incidence of HZ and HZ-related complications per age group in Finland from 2014 to 2019. Secondary objectives included estimating the HCRU and associated direct and indirect costs per HZ episode, stratified by age group.

Methods

Study design and setting

This retrospective, observational, non-interventional database study was based on secondary use of medical records in Finland. The study population consisted of all individuals in Finland with a diagnosis of HZ or associated complications between the years 2014 and 2019 and aged 18 YoA or older at the time of diagnosis.

Data source/data collection

The study was based on anonymized and aggregated data collected from four different registers: the AvoHilmo register of the National Institute for Health and Welfare (Terveyden ja hyvinvoinnin laitos [THL]), THL's Hilmo register, Terveystalo's patient register, and the Social Insurance Institution of Finland (Kela) sick leave allowance register (Supplementary Table S1). The national (THL) registers in Finland cover the whole population regarding public healthcare services. Terveystalo is the largest private healthcare service provider in Finland, with coverage in all

municipalities and an estimated data coverage of 52% for private occupational healthcare. Therefore, it constitutes a representative sample of the working-age population in Finland geographically, and age and industry wise. Kela's sick leave allowance payment register was used only to validate Terveystalo sick leave. The total population numbers and data for the direct costs associated with HCRU were obtained from Statistics Finland (www.stat.fi). The public and private sector data were not linked, which means that duplicate records for the same patient episode may occur.

The collected data included information on patient characteristics, HCRU, and sick leave (Supplementary Table S1).

Outcomes and measurements

Incidence of HZ

The source data for incidence included the public registers and Terveystalo register for occupational and private healthcare, for which the assumed population at risk was adjusted for age and sex and the results extrapolated to represent the whole working-age population of Finland, by dividing the patient numbers by 0.52 to account for the remaining 48% of private occupational care (see above). The total population numbers were obtained for each corresponding year from Statistics Finland (www.stat.fi).

International Classification of Diseases, Tenth Revision (ICD-10) codes and International Classification of Primary Care, Second Edition (ICPC-2) codes were used for the identification of HZ (Supplementary Table S2). An incident case of HZ was defined as an individual with HZ (ICD-10: B02 or ICPC-2: S70) as primary or secondary diagnosis, regardless of care level (specialized or primary) when diagnosed.

The study methodology followed the methods used by Insinga et al.[17] with some variations. HZ episodes were created by identifying the first diagnosis (index event) using ICD-10 codes and a washout period of 365 days, and then including all events related to this first HZ diagnosis for the 365 days from the index episode.[18,19] Thus, all HZ-related events within one year of the initial event were considered part of the same HZ episode. Any new HZ index event would have to be preceded by a period of at least 365 days after the previous HZ-related event, without diagnosis of HZ and without conditions directly related to HZ.

The incidence of HZ was calculated as follows for the total number of inhabitants in Finland and for each corresponding age group (population at risk) per year and expressed per 1,000 persons:

Incidence rate = (adjusted number of incident HZ cases in target population/size of target population in Finland) × 1,000.

The incidence rates were stratified by sex and age at diagnosis in categories (18–49, 50–59, 60–64, 65–69, 70–79, and ≥80 YoA).

Recurrence of HZ

Recurrence was defined as a new HZ diagnosis (ICD-10: B02) occurring at least 365 days after a previous HZ event. As for initial HZ, an episode was composed of the index event and subsequent HZ-related events; the HZ episode could extend beyond 365 days if the time between two subsequent HZ-related events within that episode was <365 days. Time to recurrence was calculated for the cohort with index events in 2014 or 2015 to ensure a sufficient follow-up period until 2019. Only the first recurrence was included in the calculations.

Incidence of HZ complications

Incidence of HZ complications was based on ICD-10 codes (Supplementary Table S2) recorded for patients regardless of care level, similar to the method used to identify HZ cases. HZ episodes were defined as PHN-related episodes if the patient had at least one PHN-related event during the HZ episode (ICD-10 codes: B02.2 or B02 in combination with G53.0). HZ episodes with complications other than PHN were pooled due to low case numbers.

The incidence rate of PHN was calculated similarly to HZ incidence. In addition, the proportion of HZ cases followed by a PHN complication was computed.

HCRU

To analyze HZ-related HCRU, the number of encounters with outpatient and inpatient care in both primary and specialized care with an HZ-related ICD-10 code (B02*) as primary or secondary diagnosis was used. For outpatient care, the visits were categorized as physician visits or nurse visits to estimate associated costs. Unit costs for each HCRU unit were derived from THL, and the same costs were used for Terveystalo visits.[20] The HCRU-related costs were then calculated by multiplying the number of observed HCRU units with associated unit costs. All HCRU costs are reported for the calendar year in which the index event of the HZ episode occurred and were adjusted to the 2019 price level using the public expenses price index of Statistics Finland. The cost of antiviral drug treatment for HZ (acyclovir [J05AB01], valacyclovir [J05AB11], and famciclovir [J05AB09]) was also included. The drug use was based on the prescription data registered in conjunction with each outpatient or inpatient event. Unit costs for antiviral drugs were derived from the open database of the Association of Finnish Pharmacies.[21] All antiviral drug prescriptions within the HZ episode were reported for the calendar year of the index event.

Sick leave

Kela only has data on sick leave lasting over 10 days (i.e., episodes of leave transferred to the social security system), as the first 10 days of sick leave are covered by the employer. Data from Terveystalo include all sick leave days prescribed for the patient, and thus it was used to estimate the length and number of episodes of sick leave for the whole study population of working age. Treatment guidelines were assumed to be similar in private and public sectors, resulting in similar sick leave prescription, i.e., sick leave days per episode were identical between public and private sectors. The average number of sick leave days per episode was calculated from the Terveystalo data for each age group, episode type, and calendar year. This estimate was then applied to the public sector data.

The costs to society incurred as a result of HZ-related sick leave were calculated using the human capital method. According to the Confederation of Finnish Industries (EK),[22] the average cost of one sick leave day for the employer was €350 in 2019. Actual sick leave costs cannot be directly linked to corresponding HZ episodes, and thus the average is used for all episodes.

Statistical analyses

The 95% confidence intervals (CIs) for incidence rates were calculated by assuming a Poisson distribution for the incidence of HZ cases.

The percentage of change from 2014 to 2019 was used for absolute numbers of HZ cases and incidence rates to demonstrate growth rates over time.

Study conduct, management, and ethics

This study was conducted in accordance with ethical principles derived from international guidelines, including the Declaration of Helsinki and the Council for International Organizations of Medical Sciences' *International Ethical Guidelines*; the Food and Drug Administration's *Code of Federal Regulations Title 21*; all other applicable regulations and local laws; and approvals by institutional review boards. The data permit for the conduct of this study and the sharing of aggregated and anonymized patient data was sought from Findata (Finnish Social and Health Data Permit Authority), the regulatory authority in Finland. This study is a retrospective observational study and as such will have no impact on patients. There is no additional risk to participants, as all data were collected from medical records and patients had no direct involvement in the study. No patient consent was needed for this study. Aggregate-level data do not allow the identification of unique patients.

Results

HZ incidence

During 2014–2019, 104,473 HZ cases were identified in total, corresponding to an average of 17,412 HZ cases per year (Table 1). The number of incident HZ cases increased on average by 4.1% annually; in 2019 the number of HZ diagnoses was 22% higher than in 2014 (Figure 1). The majority (75%) of all HZ cases were diagnosed in patients aged 50 YoA or older, and 41% were in patients 50–69 YoA (Table 1).

The mean cumulative incidence per 1,000 persons for all HZ cases in the adult population was 3.92 during 2014–2019 (Table 1). HZ incidence increased in all age groups during the study period (Figure 2). HZ incidence correlated with age: it was 1.99 (95% CI, 1.94–2.04) in 18–49 YoA compared to 5.78 (95% CI, 5.69–5.86) per 1,000 persons in the ≥50 YoA group. HZ incidence was highest in the ≥80 YoA group with an incidence rate of 8.04 (95% CI, 7.77–8.32) per 1,000 persons and second highest in the 70–79 YoA group with an incidence rate of 7.24 (95% CI, 7.04–7.44) per 1,000 persons.

The proportion of female patients (59%) during the study period was larger than that of male patients (41%). The incidence was higher in women in all age groups (Figure 3).

We identified 3,615 HZ cases with an ICD-coded PHN diagnosis, representing 3.5% of all HZ episodes (Table 1). The mean incidence of PHN during the study was 14 (95% CI, 13–15) per 100,000 population. The majority (94%) of all PHN cases were diagnosed in patients ≥50 YoA (Table 1) and the incidence increased with age, being highest in the age group ≥80 YoA, where 8.1% of the HZ cases were accompanied by PHN (Table 1). During the study period, PHN incidence increased annually by 4.8% on average.

Table 1. HZ and PHN: total cases and IR of in Finland in the adult population (2014–2019).

	HZ in total		PHN		
Age groups* (YoA)	N	IR (95% CI) per 1,000 persons	N	IR (95% CI) per 100,000 persons	% (PHN per HZ case)
18–49	25,853	1.99 (1.94–2.04)	211	2 (1–2)	0.8
50–59	18,551	4.20 (4.07–4.32)	240	5 (4–7)	1.3
60–64	11,276	5.11 (4.91–5.30)	247	11 (8–14)	2.2
65–69	12,931	5.82 (5.61–6.03)	463	21 (17–25)	3.6
70–79	21,716	7.24 (7.04–7.44)	1,315	44 (39–49)	6.1
≥80	14,145	8.04 (7.77–8.32)	1,140	65 (57–73)	8.1
Total	104,473	3.92 (3.88–3.97)	3,615	14 (13–15)	3.5
≥50	78,620	5.78 (5.69–5.86)	3,404	25 (23–27)	4.3

CI: confidence interval; HZ: herpes zoster; IR: incidence rate; N: number; PHN: postherpetic neuralgia; YoA: years of age; *stratified by age at diagnosis.

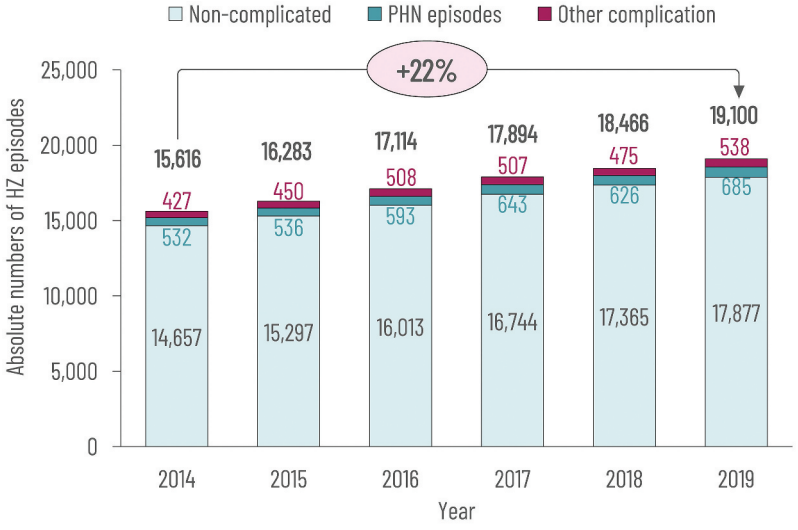

Figure 1. Absolute number of incident HZ episodes in Finland during 2014–2019. HZ: herpes zoster; PHN: postherpetic neuralgia.

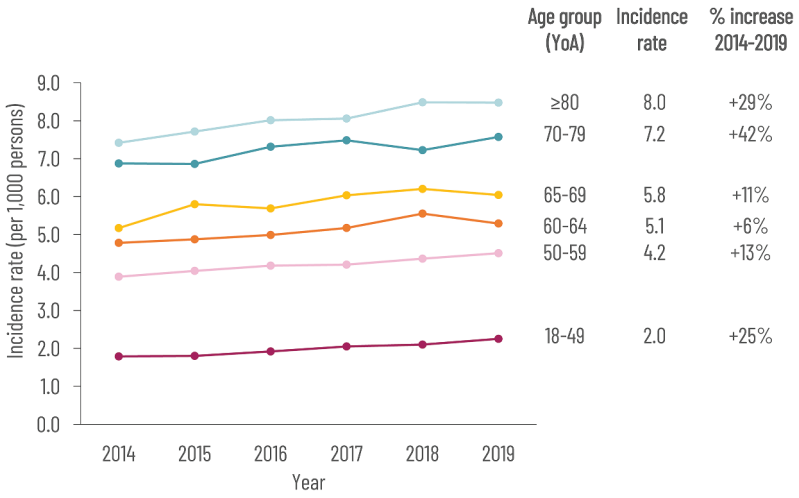

Figure 2. Incidence rate (per 1,000 persons) of HZ episodes during 2014–2019 in Finland. HZ: herpes zoster; YoA: years of age.

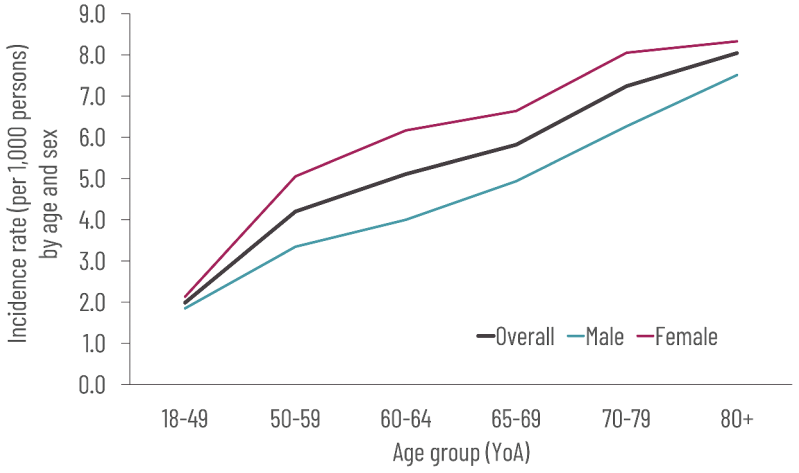

Figure 3. Average HZ incidence (per 1,000 persons) by age and sex in 2014–2019. HZ: herpes zoster; YoA: years of age.

Recurrence of HZ

The 5-year HZ recurrence was investigated in 26,141 patients who experienced an HZ index event in 2014 or 2015 and was followed up until 2019. In this cohort, HZ reoccurred for 1,170 patients, resulting in a 5-year recurrence proportion of 4.5%. Recurrence was the most common in the 65–69 YoA group. The average time to recurrence was approximately 2.6 years when using data from the public sector and 3.4 years when using data from the private sector. There was no major variation in time to recurrence between age groups (Table 2).

HCRU

Annually, HZ caused on average 34,605 HZ-related healthcare encounters (outpatient visits or inpatient days), 81% of which were in patients aged ≥50 YoA and 34% were in patients aged 50–69 YoA.

An HZ episode required 1.5 outpatient visits on average (Table 3). This resulted in an annual average of 18,855 HZ-related doctor visits and 6,692 visits to health professionals other than doctors (e.g., nurses). The majority (84.3%) of all outpatient visits were in primary care.

Table 2. Five-year recurrence rate of HZ in the adult population during 2014–2019.

Age groups (YoA)	Number of unique patients in cohort	Number of patients with recurrent HZ	5-year recurrence rate (%)	Mean time to recurrence (days)	
				Public healthcare	Private healthcare
18–49	5,615	248	4.4	932	1,457
50–59	4,552	217	4.8	992	1,358
60–64	2,871	134	4.7	956	1,276
65–69	3,654	197	5.4	964	1,474
70–79	5,529	273	4.9	963	973
≥80	3,920	101	2.6	952	1,079
All	**26,141**	**1,170**	**4.5**	**960**	**1,270**

HZ: herpes zoster; YoA: years of age.

An average HZ episode required 0.5 inpatient ward days on average (Table 3). Annually, there were 9,058 inpatient days due to HZ on average: 5,693 in primary care and 3,365 in specialized care. Overall, the majority of the inpatient days were in patients ≥50 YoA (99.5% of the inpatient days in primary care and 92.2% of inpatient days in specialized care). For patients below 70 YoA, specialized care was the most frequent inpatient care. After 80 YoA, the number of inpatient days grew significantly and was focused on primary care wards (Table 3).

The direct healthcare resource cost (outpatient visits, inpatient days, and antiviral medication) per any HZ episode was on average €408 (Table 4). The HCRU costs increased with age and were highest in the ≥80 YoA patient population (Table 4).

For HZ episodes with PHN, the direct HCRU was significantly higher, with an average of 2.0 outpatient visits and 3.1 inpatient days (Table 3), resulting in an average HCRU cost per episode of €1,369 (Table 4). Thus, a PHN-related HZ episode accumulated on average €962 more direct HCRU costs compared with an overall HZ episode.

Sick leave

In the Terveystalo database, the mean length of sick leave was 3.7 days in the whole adult population and 4.2 days in the ≥50 YoA population (Table 5). In the case of PHN, sick leave tended to be longer, over 6 days on average.

When the Terveystalo data was extrapolated to the whole adult population, the estimated annual number of episodes of sick leave due to HZ was 4,425, resulting in a total of 16,579 sick leave days per year (Table 5). The loss of human capital due to HZ was estimated to be €4.2 million (M) annually during 2014–2019.

HZ total societal costs

The average total cost per HZ episode, including direct HCRU costs and sick leave, was €649 during the study period (Table 4). Sick leave accounted for 37%, inpatients days for 30%, outpatient visits for 29%, and outpatient antiviral drugs for 4% of the total costs.

For episodes with PHN, the mean total cost per episode was €1,910; the cost for sick leave accounted for around 28% of this total (Table 4).

The average annual costs of HZ in Finland during the years 2014–2019, including inpatient care, outpatient care, antiviral medication, and sick leave costs, amounted to approximately €11.3 M (Table 4). Of the total costs, 78% (€8.8 M) were attributed to HZ in patients ≥50 YoA, and 43% (€4.9 M) to patients 50–69 YoA.

Significant costs originated from sick leave (€4.2 M) (Supplementary Table S3), of which 66% (€2.8 M) was in patients ≥50 YoA and 64% (€2.7 M) in patients 50–69 YoA. On average, €6.6 M was spent on HZ-related healthcare services (outpatient care: €3.2 M (excluding drugs) and inpatient care: €3.4 M; Supplementary Table S3). Of this, 86% (€5.7 M) came from patients ≥50 YoA (76% of the outpatient care costs and 95% of the inpatient care costs). Additionally, costs for antiviral medication accounted for €0.49 M (Supplementary Table S3).

Table 3. Overview of mean annual direct HCRU per HZ episode type during 2014–2019 in Finland.

	Visits												Inpatient days								
	Mean annual number of episodes		Primary healthcare: doctor		Primary healthcare: other than doctor		Specialized care: doctor		Specialized care: other than doctor		Visits per episode		Primary care		Specialized care		Days per episode		Antiviral drugs per episode		Mean annual healthcare episodes of contact
Age groups (YoA)	All HZ	PHN	All HZ	PHN	All HZ	PHN	All HZ	PHN	All HZ	PHN	All HZ	PHN	All HZ	PHN	All HZ	PHN	All HZ	PHN	All HZ	PHN	All HZ
18–49	4,309	35	4,355	36	1,237	3	576	35	145	6	1.5	2.3	26	0	263	17	0.1	0.5	0.52	0.14	6,602
50–59	3,092	40	3,062	34	1,016	6	545	35	165	12	1.5	2.2	58	1	349	13	0.1	0.4	0.46	0.23	5,195
60–64	1,879	41	1,859	40	639	3	297	31	79	10	1.5	2.1	78	11	236	36	0.2	1.1	0.45	0.13	3,187
65–69	2,155	77	1,727	72	776	12	362	45	107	18	1.4	1.9	201	15	352	65	0.3	1.0	0.32	0.26	3,525
70–79	3,619	219	2,921	231	1,391	55	785	117	211	39	1.5	2.0	1,196	171	930	155	0.6	1.5	0.32	0.34	7,434
≥80	2,358	190	1,766	186	778	47	601	99	149	34	1.4	1.9	4,136	1,175	1,234	192	2.3	7.2	0.33	0.35	8,663
≥50	**13,103**	**567**	**11,335**	**564**	**4,600**	**123**	**2,590**	**328**	**710**	**113**	**1.5**	**2.0**	**5,668**	**1,373**	**3,102**	**461**	**0.7**	**3.2**	**0.37**	**0.31**	**28,003**
≥18	**17,412**	**603**	**15,690**	**600**	**5,836**	**126**	**3,166**	**363**	**855**	**119**	**1.5**	**2.0**	**5,693**	**1,373**	**3,365**	**477**	**0.5**	**3.1**	**0.41**	**0.30**	**34,605**

HCRU: healthcare resource use; HZ: herpes zoster; PHN: postherpetic neuralgia; YoA: years of age.

Table 4. Overview of mean total societal costs per HZ episode type during 2014–2019 in Finland.

	Outpatient care (€)		Inpatient care (€)		Antiviral medication (€)		Sick leave (€)		Total cost per episode (€)			
Age groups (YoA)	All HZ	PHN	All HZ	PHN	All HZ	PHN	All HZ	PHN	All HZ	PHN	Mean annual number of HZ episodes	Mean annual societal total cost (€)
18–49	179	472	40	300	36	9	330	2,406	584	3,187	4,309	2,515,904
50–59	195	434	75	214	32	15	501	3,570	803	4,234	3,092	2,482,069
60–64	188	399	88	601	31	9	487	2,100	794	3,109	1,879	1,491,556
65–69	172	337	123	570	22	18	99	–	415	925	2,155	894,377
70–79	191	331	234	615	22	23	22	58	469	1,028	3,619	1,698,161
≥80	195	319	717	2,002	23	24	6	–	940	2,345	2,358	2,216,396
≥50	**189**	**340**	**244**	**1,044**	**26**	**21**	**212**	**426**	**670**	**1,832**	**13,103**	**8,782,558**
≥18	**186**	**348**	**193**	**1,001**	**28**	**20**	**241**	**541**	**649**	**1,910**	**17,412**	**11,298,462**

HZ: herpes zoster; PHN: postherpetic neuralgia; YoA: years of age.

Table 5. Absence from work due to HZ.

Mean annual sick leave		
Number of sick leave episodes	4,425	
Sick leave days	16,579	
Mean length of sick leave (days)		
Age groups (YoA)	**All HZ**	**PHN**
18–49	3.2	7.9
50–59	3.9	5.1
60–64	4.5	3.8
65–69	9.9	N/A
70–79	18.1	N/A
≥80	N/A	N/A
≥50	4.2	4.8
≥18	3.7	6.2
Estimated mean annual loss of capital due to absence from work (€)		
All HZ	4,194,357	
PHN	326,069	

HZ: herpes zoster; PHN: postherpetic neuralgia; YoA: years of age.

In HZ patients under 65 YoA, sick leave represented a major part of the total societal costs of an HZ episode (Figure 4). In older age groups, inpatient care costs became dominant.

Discussion

We described the HZ burden of disease, HCRU, and societal costs in the Finnish setting by including both public and private healthcare registers.

The HZ incidence among adults ≥50 YoA increased by 4.1% annually. Similar observations have been made in several studies on a global level.[7,10] In a systematic literature review over the period 2002–2018, an HZ incidence increase over the years was reported for adults ≥50 YoA in 17 out of 23 studies.[23] This increase in HZ cases could be due to several factors, such as a higher life expectancy and associated population aging, an increase in the use of immunosuppressive treatments, a rise in reporting and awareness, and an improvement in testing systems. In Finland, the proportion of adults ≥65 YoA has increased from 15% in 2000 to 23.6% in 2024.[24] It has been suggested that national varicella immunization programs might indirectly affect HZ incidence by reducing overall circulation of the varicella virus and therefore diminishing the boosting effect of natural virus re-exposure on cell-mediated immunity.[25] However, this is unlikely to affect the observed Finnish HZ incidence, since the program started during the study period, in September 2017, and the trend of increasing HZ incidence was observed already before the varicella vaccination program.[26]

HZ incidence found for Finland in the current study was substantially lower than that seen in other countries.[7,9,10] A recent regional population-based register study in Sweden estimated the burden of HZ increased from 2.5 to 4.2 per 1,000 population between 2005 and 2021[7] and the HZ incidence was higher for

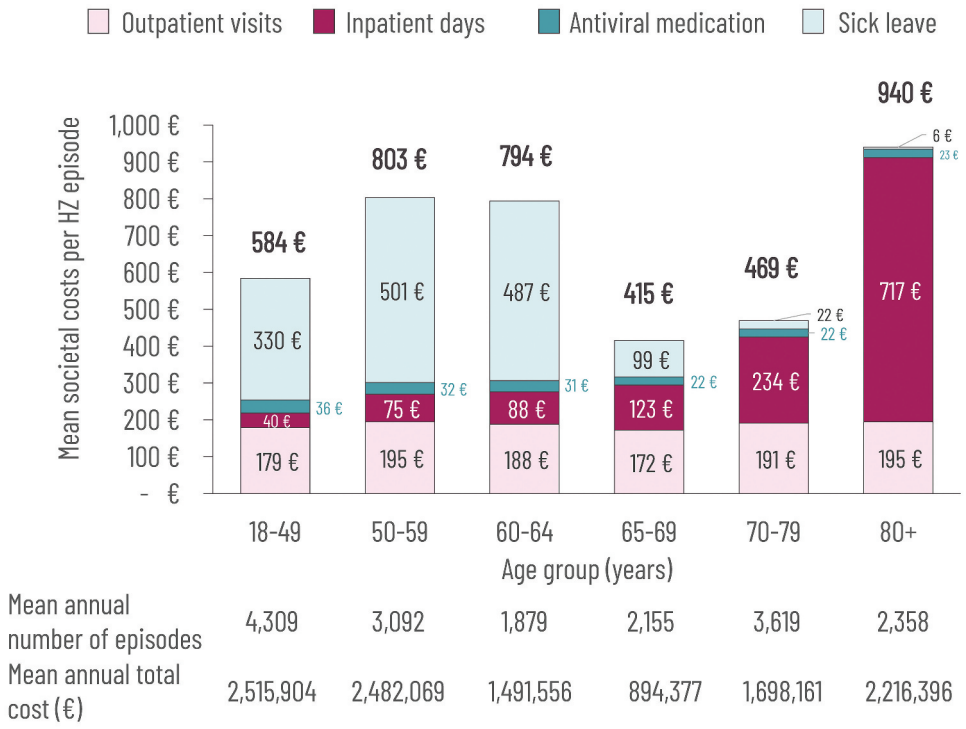

Figure 4. Mean total societal costs per HZ episode in different age groups in 2014–2019. HZ: herpes zoster; YoA: years of age.

age groups above 60 YoA in the Swedish study compared with our results (i.e., 5.25, 6.58, 8.71, and 9.94 HZ cases reported per 1,000 person-years in adults 60–64, 65–69, 70–79, and ≥80 YoA, respectively, versus 5.11, 5.82, 7.24, and 8.04 cases per 1,000 persons in our study). As the methodologies used to capture HZ cases were quite comparable (i.e., HZ identified based on ICD-10 codes), this difference could be partly explained by underreporting – some HZ patients may be assigned nonspecific diagnoses, and most diagnoses for people receiving home care services or living in institutional or residential care are not captured in the registries in the Finnish setting. In a study using linked data from health registers in Norway to identify medically attended HZ cases in 2008–2014, the overall incidence rate of HZ in primary healthcare in adults ≥50 YoA was 4.61 per 1,000 persons,[27] which is in line with our findings of 5.78 per 1,000 persons in this age group. Authors identified several limitations in their study, such as incomplete data capture, potential misclassification, varying coding practices, and coding errors. These limitations are likely applicable to our study as well and may contribute to the incompleteness of the incidence data observed with this methodology.

The recurrence rate for HZ found in our study (4.5%) is comparable to that observed previously in several setups. HZ recurrence rates of 4.7–6.2% were observed in the United Kingdom, the United States, and South Korea, with variable follow-up periods (4.4 to 16 years).[28–30] The observed drop in the recurrence rate among those ≥80 YoA is likely attributable to the shorter period at risk of HZ recurrence due to limited remaining life expectancy. In our study, the mean time to recurrence was higher in the public healthcare sector than in the private healthcare sector. These differences can be partly explained by incomplete national coverage. Individuals who have changed employers over the study period may have other occupational care providers not captured in this study. In addition, public hospitals tend to treat patients that are older and have more comorbidities than patients treated in the private healthcare sector.[31] Thus, patients with immunocompromised conditions, at higher risk for frequent HZ recurrence, may be overrepresented in the public sector.

When comparing PHN incidence, the proportion of HZ cases with PHN in our study was substantially lower as compared to other countries.[7,32,33] This can partly be due to differences in methodologies, as some studies included both ICD-10 codes and medication codes for PHN, whereas the current study only

retrieved data based on ICD-10 codes. For example, in Sweden, the proportion of HZ cases having a PHN complication was 8.4% among adults ≥18 YoA based on ICD-10 codes alone, whereas when considering also analgesics prescriptions that lasted for more than 90 days, the proportion was 13.6% (1.62-fold).[7] Additionally, differences in coding practices could also contribute to explaining this observed gap, and underreporting is likely a common phenomenon in Finland, but this could also apply to other countries.

The average total cost per any HZ episode in this study was €649, which is lower than the societal costs estimated by Nilsson et al. study (€870, in 2013 euros) in Sweden.[15] However, in contrast to our study, the Swedish data also included drugs other than antivirals (e.g., antileptics, opioids, and anti-depressants), and the country-specific healthcare practices might also differ, leading to differences in costs. Another study in Germany estimated HZ costs per patient to €156 from the healthcare system perspective and to €311 from the societal perspective, over 2010–2014.[34] In that study from Germany, patients reported their medical resource use and days of absence from work, and inpatient costs were calculated from a previously published analysis estimating HZ epidemiology and costs from 2004 to 2009. In Italy, between 2009 and 2022, reimbursement costs derived from administrative databases were analyzed. The authors reported mean per-patient HZ costs of €127 for drugs and €91 for hospitalization during the first year after HZ.[35] These cost distributions contrast with our findings, in which hospitalization costs (€193) exceeded drug expenditures (€28). Notably, their analysis also included other medications such as antibacterials or antihypertensives. Both studies also reported costs increasing with age.[34,35]

Sick leaves represented a large proportion (37%) of the total costs and this is in line with the findings by Nilsson et al., who found that sick leaves represented 28% of the total costs for HZ treatment.[15] This stresses the fact that an important part of the Finnish population at risk for HZ and its complications are adults in the workforce. In fact, 41% of all HZ cases observed in our study were in adults 50–69 YoA, who are theoretically still working, whereas HZ cases in the 18–49 YoA group represented only 25% of total cases. In the older age groups, the share of inpatient days in total costs became dominant, reflecting that the risk of severe infection and complications, as well as the impact of infection leading to the need of inpatient care increase with age.

The period covered in this study is limited to the pre-pandemic years when the data in the public healthcare registers and private sector database did not yet overlap. Both the public health registers and the private sector register used in this study are of high quality. However, as in any database study, there are limitations associated with completeness and accuracy of data reporting. Because independent databases were used to calculate incidence, duplicate records of the same HZ episode may have occurred, potentially leading to an overestimation of HZ incidence. Finnish individuals may sometimes choose to use Terveystalo and public services for the same episode, therefore duplicate cases are difficult to ascertain. Further, the Terveystalo register for occupational and private healthcare may not be representative of the general population. PHN diagnosis was based only on ICD-10 codes and not on a prescription database. Antivirals may have been used to treat another or a concomitant infection, such as herpes simplex. Regarding drug costs, only antivirals were taken into account; other drugs (e.g., painkillers) were not included in this study. Other indirect costs, such as caregiver costs and patient transportation costs, were not taken into account in this analysis, as such costs are not readily available in national registers. Another limitation is that incidence and costs cannot be stratified based on whether a person has been vaccinated for HZ since this information is not recorded in the national registers at the patient level in Finland. However, during the study period 2014–2019, only the live zoster vaccine (Zostavax, MSD) was available in Finland, and there was no national immunization program in place. It is likely that shingles vaccination coverage was low during this period, so the potential effect on our study results was most likely marginal.[16]

Conclusion

Despite the likely underreporting of the incidences of HZ and PHN in the Finnish registries, HZ and PHN cause a substantial disease burden in the Finnish adult population for individuals, the healthcare system, and society through direct costs and absence from work. The majority (75%) of the HZ cases occurred among adults ≥50 YoA, with 41% in 50–69 YoA adults still part of the workforce, and the incidence and case numbers increased steadily during the study period in all age groups. These findings make a strong

advocacy from a societal perspective to prevent HZ and PHN, allowing limited healthcare resources to be directed where they are most needed.

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Author contributions

CRediT: **Mari Kanerva:** Conceptualization, Formal analysis, Writing – review & editing; **Suvi E. Heinonen:** Conceptualization, Formal analysis, Writing – review & editing; **Tuukka Hakkarainen:** Conceptualization, Data curation, Formal analysis, Investigation, Writing – review & editing; **Outi Isomeri:** Conceptualization, Data curation, Formal analysis, Investigation, Writing – review & editing; **Marie Nishimwe:** Formal analysis, Writing – review & editing; **Alen Marijam:** Conceptualization; **Riikka-Leena Leskelä:** Conceptualization, Data curation, Formal analysis, Investigation, Writing – review & editing.

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Previous congress activities

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Trademark

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Abbreviations

CI	confidence interval
COVID-19	coronavirus disease 2019
EK	Confederation of Finnish Industries
HCRU	healthcare resource use
HZ	herpes zoster
ICD-10	International Classification of Diseases, Tenth Revision
ICPC-2	International Classification of Primary Care, Second Edition
M	million
N	number
PHN	postherpetic neuralgia
THL	Terveyden ja hyvinvoinnin laitos (National Institute for Health and Welfare)
VZV	varicella zoster virus
YoA	years of age

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