



Healthcare costs associated with varicella and herpes zoster in Norway

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ABSTRACT

Background: Norway does not implement routine vaccination against varicella or herpes zoster. Despite substantial health burden associated with both diseases, their economic impact is not well described. The aim of the present study was to document the healthcare costs associated with both conditions in a Norwegian setting.

Methods: We used registry data about patients' contacts with primary and specialized healthcare services from 2008 to 2014 to estimate the costs associated with varicella and herpes zoster in the primary and hospital care sector. We calculated the individual costs by treatment facility (general practitioner and emergency primary care clinic) in primary care and by treatment level (inpatient, outpatient or ambulatory treatment) at hospitals.

Results: We estimate that the annual healthcare cost of patients with varicella and herpes zoster are NOK 85 million (approximately € 9 million). Of the annual costs, 73% are associated with herpes zoster and 27% are due to varicella. The majority (54%) of the total annual cost is represented by patients with herpes zoster treated in hospital.

Conclusion: Varicella and herpes zoster impose a substantial financial burden on the national healthcare services in Norway. Most of the costs are incurred by herpes zoster, which could be prevented by vaccination.

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1. Introduction

The varicella zoster virus (VZV) causes varicella, also known as chickenpox, and herpes zoster (HZ), known as shingles. Almost everyone in Norway will get infected with VZV during their lifetime [1] and will develop varicella translating to the annual incidence being fairly close to the annual number of births which is approximately 60,000 [2,3]. Each year approximately 14,600 varicella-associated visits are registered in the Norwegian healthcare sector [4]. The initial infection is rarely fatal in Norway, with an estimated 0.06 deaths per 100,000 case [4]. Following the initial infection, the virus remains latent in the spinal ganglion and about one in four [5] persons will experience a reactivation of the virus

later in life [6,7]. This corresponds to about 12,000 annual cases of HZ in Norway [2]. Despite the high prevalence and substantial disease burden, the financial burden of varicella and HZ in Norway is not well described. The Norwegian healthcare system is government funded, and the current healthcare expenditure is NOK 62,186 (€ 6840) per capita annually. The total healthcare budget in 2016 was NOK 326 billion (€ 35.9 billion), which corresponds to 10.5% of national gross domestic product (GDP). This percentage is among the highest in the world and has in later years increased by approximately 2% each year [8]. It is therefore important to take measures to reduce and contain healthcare costs where possible.

Effective vaccines against varicella have been available since 1984 [9], but are currently not included in the Norwegian immunisation program. In recent years new vaccines against HZ have been also developed. A live attenuated vaccine (Zostavax[®]) by Merck Sharp & Dohme has been available since 2006, and has been shown to reduce the probability of developing HZ by about 50% [10]. Another new subunit vaccine (Shingrix[®]) by GlaxoSmithKline was approved in the United States in October 2017 [11] and received marketing authorization in the European Union in 2018 [12]. Shingrix[®] is believed to be more effective than Zostavax[®]

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vaccine in preventing HZ, and is now recommended by the US Advisory Committee on Immunisation Practices (ACIP) as the preferred vaccine against HZ [13].

Despite the availability of vaccines against varicella and HZ, few countries use those in routine immunisation, partly due to the concerns related to exogenous boosting hypothesis raised by Hope-Simpson in the 1960s. Hope-Simpson observed that periods with a low incidence of varicella were followed by an increased incidence of HZ [6] and therefore hypothesised that reducing or removing the incidence of varicella from the population through a vaccine will increase the incidence of HZ. It has been estimated previously [2] that universal varicella immunisation in Norway will almost eliminate varicella, but will also increase the occurrence of HZ, with an incidence being 2.6 times higher at the peak compared to the pre-vaccine level. However, given availability of HZ vaccines, reviewing a need for varicella and HZ immunisation is highly relevant. Thus, it is also important to document the costs incurred by the diseases on the healthcare system. The objective of this study was therefore to explore the financial burden of varicella and HZ in the Norwegian healthcare system.

2. Materials and methods

2.1. Study design

This was a retrospective analysis of the costs associated with treating patients with varicella and HZ in the Norwegian healthcare system. We analysed the costs from a healthcare perspective using national registry-based data from the primary healthcare system and hospitals. Our group have previously reported estimates of varicella-related primary care consultations and hospitalisations and mortality based on the same dataset [14].

2.2. Data sources

We used de-identifiable administrative data from the Norwegian Health Economics Administration (HELFO) and the Norwegian Patient Registry (NPR) to estimate costs for primary and hospital care, respectively.

The HELFO database contains the reimbursement claims from both general practitioners (GP) and emergency primary care clinics for each individual patient visit. The claims include information about the out-of-pocket amount paid by the patient, the reimbursement amount, and the amount paid by social security. Norwegian primary healthcare is financed through a combination of patient co-payment, reimbursement, and capitation fees. The HELFO data do not include the latter but capitation fees are derived by multiplying physician reimbursement fees by a factor of two as per the national guidelines for health technology assessment [15,16]. The amount of patient co-payment is set for each primary care visit and for patients who reach the yearly upper limit of co-payment (€ 230 per 2017), the social security covers all co-payments for the remainder of the year.

We used all reimbursement claims containing ICPC (international Classification of Primary Care) codes A72 (varicella) and S70 (HZ) registered during 2008–2014. A unique patient identification number allowed us to identify the number of visits for each individual patient.

From NPR we extracted individual detailed data for all patients who visited a hospital during 2008–2014 with varicella or HZ-related diagnoses as coded by the International Classification of Diseases version 10 (ICD-10): B01.0–B01.9 and P35.8 codes for varicella and B02.0–B02.9 codes for HZ. We included patients having varicella and HZ as their primary or secondary diagnosis and grouped them by treatment level (inpatient, outpatient and ambu-

latory care). The dataset included a unique patient identifier, age, sex, dates of admission and discharge, ICD-10 codes and the associated Diagnosis Related Group (DRG) weights. In Norway, costs per hospital visit is estimated for each of these groups. Since the DRG system is built on classifying groups of patients that are clinically meaningful and intended to be homogenous with regards to resource intensity, these are regarded as good estimates of costs. Hence, the DRG system is used both in financing Norwegian hospitals and recommended for Norwegian health economic evaluations [15]. In practice, average costs per DRG is typically given as a weight, which has to be multiplied by the present monetary value of a DRG-weight to give the average cost of the treatment of a patient within the DRG [15]. Both DRG weights and the corresponding monetary values are updated every year.

2.3. Data analysis

All costs were calculated in 2017 Norwegian kroner (NOK) by adjusting values based on the index for the household real disposable income [17], as recommended by the Norwegian Directorate of Health [16] and converted into 2017 Euros (NOK 1 = € 0.11). Primary care costs were analysed by age and treatment level.

When calculating mean cost of hospital services, we used all individual hospital encounters with complete DRG-weights. For patients with incomplete data, we imputed averages based on age, treatment level, and whether the patient had varicella and/or HZ as the primary or secondary diagnosis. Ambulatory care data from prior to 2013 were incompletely reported, therefore costs of ambulatory care were derived using observations reported during 2013–2014 for both varicella and HZ. In-hospital costs were incompletely reported during the first two years; 2008–2009, we therefore only used data for the period 2010–2014. We calculated costs for different varicella and HZ-specific diagnoses. As patients' diagnoses may change during treatment, all relevant costs for the different diagnoses were included to estimate the total cost. Costs of treatment for patients with HIV/AIDS, malignancies, organ transplants, and immunosuppressive conditions were calculated separately.

3. Results

3.1. Varicella

From 2008 to 2014, there were 100,096 varicella-related visits in primary healthcare in Norway made by 76,168 patients (mean of 1.3 visits per patient). The average total cost of varicella-related visits in primary care was NOK 10.8 million or € 1,188,000 per year, translating to a mean cost per primary healthcare visit of 992 NOK (€ 109). This estimate includes the reimbursement, patient co-payment, a share covered by the social security scheme, and assumed capitation cost. Among all primary care costs, costs of GP visits accounted for 66.3% and costs of visits with emergency primary care clinics for 31.3% (Table 1).

During 2010–2014, a total of 2172 varicella-related visits were registered in Norwegian hospitals giving an average annual cost of NOK 12.4 million (€1,364,000). Hospital costs differed considerably by treatment level, with a wide variation in costs at the inpatient level (Table 2). Average costs per hospital visits for immunocompromised patients were NOK 65,100 (€7200) compared to NOK 26,000 (€2900) for immunocompetent patients (Table A1). Hence, although immunocompromised patients represented only about 7% of all patients with varicella or HZ-related diagnoses, this patients group represented 17% of the costs.

Of the annual costs associated with hospital varicella patients, 65% or NOK 8 million (€ 880,000) represent the cost of patients

Table 1
Costs, in NOK, of varicella-related primary care visits, Norway, 2008–2014. (Euro, €, in parentheses).

Visit type	Varicella as primary diagnosis			Varicella as secondary diagnosis		
	Mean cost (€)	Std. dev. (€)	No. obs.	Mean cost (€)	Std. dev. (€)	No. obs.
GP	337 (37)	206 (23)	74,539	342 (38)	162 (18)	26
Emergency primary care clinic	506 (56)	326 (36)	20,844	457 (50)	217 (24)	2,914
Unknown ^a	318 (35)	136 (15)	820	663 (73)	338 (37)	953
Total	373 (41)	237 (26)	96,203	507 (56)	252 (28)	3,893

GP = General practitioner

^a Data about whether the contact was emergency care or not was not available for 1.8%

Table 2
Costs, in NOK, of varicella-related hospital visits by treatment level, Norway, 2010–2014 (Euro, €, in parentheses).

Varicella	Mean cost (€)	Std. dev. (€)	Obs. ^a	% missing DRG-weight ^b
<i>Primary diagnosis</i>				
Inpatient	58,163 (6,398)	105,510 (11,606)	653	0%
Outpatient	1,834 (202)	453 (60)	850	8%
Ambulatory ^c	4,105 (442)	1447 (159)	20	32%
Estimated mean ^d	24,735 (2,721)	72,624 (7,989)	1,610	
<i>Secondary diagnosis</i>				
Inpatient	66,752 (7,343)	114,328 (12,576)	324	0%
Outpatient	1,512 (166)	615 (68)	188	15%
Ambulatory ^c	4,089 (450)	1,222 (134)	12	11%
Estimated mean ^d	39,196 (4,312)	92,529 (10,178)	562	
Estimated total mean^d	28,477 (3,132)	78,475 (8,632)	2,172	

^a observations represent the number of complete observations with accompanying DRG-weights for the whole period.

^b % missing DRG-weights refers to all observations from 2010 to 2014.

^c ambulatory care costs were calculated using observations made in 2013 and 2014.

^d estimated mean number of observations is based on complete observations, percentage missing and the fact that ambulatory care costs are based on fewer years than inpatients and outpatient costs (see: *, ** and ****)

having varicella as the primary diagnosis. The average annual cost of varicella in primary and hospital care was approximately NOK 23.2 million (€ 2,552,000). The majority of these costs occurred in the age group 0–14 years, with a small increase around the age of 35–39 years, which may be related to increased virus circulation among children and parents (Fig. 1).

Ninety four percent of patients with varicella-related diagnosis had no comorbidities registered. Patients with complications such as encephalitis and pneumonia accounted for a substantial proportion of the costs (28% and 26%, respectively) despite accounting only for 3.5% and 3.0%, respectively, of all varicella cases (appendix Table A2). From 2010 to 2014, eight patients were registered with congenital varicella, which is a very rare

condition that can lead to a continuing need for future healthcare and increased healthcare costs, which were not captured in our data. (Table A2).

3.2. Herpes zoster

During 2008–2014, there were 183,567 visits in the primary healthcare by 78,266 patients with HZ-related diagnoses (mean of 2.4 visits per patient). The total annual cost of these visits amounted to approximately NOK 15.9 million (€ 1,749,000) or on average NOK 1,422 (€ 156) per visit. GP visits accounted for 84% of the total primary care costs, while visits with emergency primary care clinics made up 16% (Table 3). As HZ is not a common

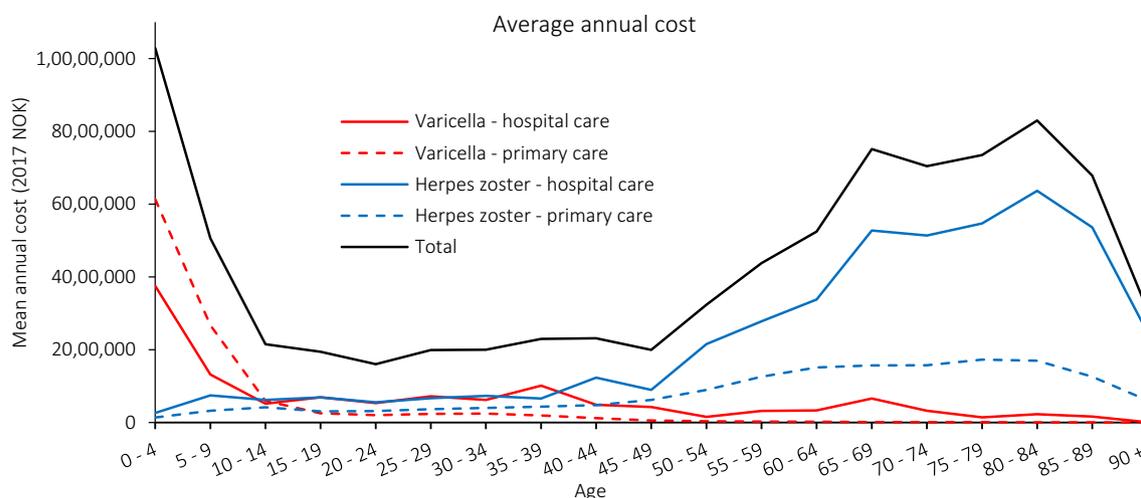


Fig. 1. Average annual cost of varicella and herpes zoster by type of health care.

Table 3
Cost of herpes zoster-related primary care visits by treatment facility, Norway, 2008–2014 (Euro, €, in parentheses).

	Herpes zoster as main diagnosis			Herpes zoster as secondary diagnosis		
	Mean cost (€)	Std. dev. (€)	Obs.	Mean cost (€)	Std. dev. (€)	Obs.
GP	270 (30)	229 (25)	149,166	424 (47)	293 (32)	13,349
Emergency primary care clinics	472 (52)	301 (33)	18,708	605 (67)	387 (43)	904
Unknown ^a	247 (27)	163 (18)	1,382	378 (42)	234 (26)	58
Total	292 (32)	238 (26)	169,256	435 (48)	300 (33)	14,311

GP = General practitioner

^a Data about whether the contact was emergency care or not was not available for 0.8%

disease among the younger age groups, most of the costs were among those aged 50 years and above (Fig. 1)

During 2010–2014, 13,011 hospital encounters with HZ-related diagnoses were registered. The average annual cost was NOK 45.5 million (€ 5 million) (Table 4). Patients with HZ as primary diagnosis represented 76% of all hospital visits related to zoster, which incurred an annual cost of approximately NOK 23.5 million (€ 2,585,000). Ninety one percent of these patients scored zero on the Charlson comorbidity index, suggesting absence of any severe comorbidity. No large differences in costs were observed by diagnosis as compared to hospitalised varicella patients (Table A2).

Although patients with HZ as a secondary diagnosis accounted only for 24% of all zoster-related hospital visits, costs associated with these patients represented almost a half of the total hospital cost (NOK 22 million/€ 2,420,000 annually). The combined healthcare cost of HZ in primary and hospital care was estimated at approximately NOK 61.4 million (€ 6,754,000) per year (Fig. 1), with the majority of costs incurring in hospital care (74%) and in individuals aged above 50 years (82%) corresponding to the increase in the zoster incidence.

3.3. Total cost

We estimate that varicella and HZ-related visits are associated with costs of approximately NOK 85 million (€ 9,350,000) in the healthcare system annually in Norway. The majority of the costs (54%) are associated with hospitalised HZ patients, followed by HZ patients treated by primary care system (19%). Varicella-associated hospital costs account for 14% of the total disease cost, while the remaining 13% occur in the primary healthcare (Fig. 1).

4. Discussion

The aim of this study was to document the economic burden of varicella and HZ in Norway in order to inform a policy decision

about the use of varicella and HZ immunisation in Norway. Both varicella and HZ generate substantial healthcare costs with the majority of the costs being associated with zoster patients. This is important considering that varicella vaccination may increase the incidence of HZ, which will consequently increase the associated costs. However, as estimated by Marchetti et al. [2], it could be possible to contain the negative effects of varicella immunisation by introducing a concomitant HZ vaccination. The impact of HZ immunisation will however depend on several factors such as timing of vaccine introduction, chosen vaccination strategy, achieved coverage and duration of vaccine-induced protection. In addition, introduction of HZ immunisation may be the first public vaccination program for adults in Norway, and development and implementation of such program may incur additional costs that could exceed the benefits.

This is the first cost-of-illness study of varicella and HZ in Norway [18]. It is difficult to compare our findings directly with other industrialised countries due to differences in the cost of labour, medications, and healthcare systems. Other Nordic countries are the most relevant comparators due to similarities in populations and healthcare systems. Nielsen et al. [19] assessed costs of HZ in Sweden by distinguishing between patients with HZ and post-herpetic neuralgia (PHN), which we were unable to calculate. The authors reported an average cost of a hospitalisation at around 32,000 (2013) SEK and around 50,000 (2013) SEK for PHN, which is lower than our estimates for Norway. This difference could be partially explained by a lower average wage rate in Sweden. However, the same study reported an average cost of a GP visit with HZ of 1544 (2013) SEK, which is roughly three times higher than our corresponding estimate. Another study from Denmark [20] reported a cost of a GP visit to be more in line with our findings. Depending on the pain level associated with HZ, the number of visits ranged from 1.5 to 2.7, while cost per visit ranged from DKK 198 (€ 26) to DKK 367 (€ 47) (DKK 1 = € 0.13). This study also reported an average cost of a hospital visit of DKK 8694 (€ 1130), which is close to

Table 4
Costs of herpes zoster-related hospital visits by treatment level, Norway, 2010–2014 (Euro, €, in parentheses).

Herpes Zoster	Mean cost (€)	Std. dev. (€)	Obs. ^a	% missing DRG-weight ^b
<i>Main diagnosis</i>				
Inpatient	63,212 (6,953)	41,267 (4,539)	1,660	0%
Outpatient	1,237 (1 3 6)	533 (59)	4,733	39%
Ambulatory ^c	4,724 (5 2 0)	8,430 (9 2 7)	97	73%
Estimated mean ^d	11,854 (1,304)	28,628 (8,643)	9,892	
<i>Secondary diagnosis</i>				
Inpatient	68,782 (7,566)	96,060 (10,567)	1,549	0%
Outpatient	1,996 (2 2 0)	2,840 (3 1 2)	835	44%
Ambulatory ^c	7,250 (7 9 8)	11,855 (1,304)	28	42%
Estimated mean ^d	35,284 (3,881)	75,452 (8,300)	3,119	
Estimated total mean^d	17,471 (1,992)	45,690 (5,026)	13,011	

^a Number of hospital visits with accompanying DRG-weights for the whole period.

^b % of hospital visits with missing DRG-weights.

^c ambulatory care has been calculated using hospital visits from 2013 to 2014.

^d estimated mean number of observations is based on complete observations, percentage missing and the fact that ambulatory care costs are based on fewer years than inpatients and outpatient costs (see: *, ** and ***)

Table A1

Cost, in NOK, per hospital visit by patient's immunocompetence status, Norway, 2010–2014 (Euro, €, in parentheses).

Varicella		Mean cost (€)	Std. dev. (€)	Obs.
Immunocompromised	Main diagnosis	59,981 (6,598)	166,612 (18,327)	65
	Sec. diagnosis	69,519 (7,647)	127,892 (14,068)	76
Immunocompetent	Main diagnosis	23,322 (2,565)	65,601 (7,216)	1,540
	Sec. diagnosis	34,454 (3,790)	84,895 (9,338)	486

Table A2Mean total cost for patients with varicella and herpes zoster-related diagnoses^a (Euro, €, in parentheses).

	Diagnosis	Mean (€)	Std. dev. (€)	Obs.	
Varicella	B01.0	Varicella meningitis	71,667 (7,883)	53,114 (5,843)	119
	B01.1	Varicella encephalitis, myelitis & encephalomyelitis	140,693 (15,476)	225,740 (24,672)	66
	B01.2	Varicella pneumonia	134,088 (14,750)	272,634 (29,990)	58
	B01.8	Varicella with other complications	41,475 (4,562)	65,620 (7,219)	363
	B01.9	Varicella without complications	17,431 (1,917)	53,764 (5,914)	1,298
	P35.8	Congenital varicella	100,863 (11,095)	101,820 (11,200)	8
Herpes zoster	B02.0	Zoster encephalitis	44,889 (4,938)	88,405 (9,725)	203
	B02.1	Zoster meningitis	49,203 (5,412)	30,861 (3,395)	54
	B02.2	Zoster with other nervous system involvements	52,184 (5,740)	64,495 (7,094)	683
	B02.3	Zoster ocular disease	14,571 (1,603)	44,223 (4,865)	1,799
	B02.7	Disseminated zoster	49,780 (5,476)	58,632 (6,450)	95
	B02.8	Zoster with other complications	50,292 (5,532)	79,992 (8,799)	596
	B02.9	Zoster without complications	35,890 (3,890)	69,237 (7,616)	3,433

^a based on the total cost for all visits the patient made. Patients whose first visit was before 2010 were excluded. Costs for missing DRG-weights are included.

our estimates of hospital visit for patients with HZ as the primary diagnosis (€1304).

In our study we used a retrospective approach, which is limited in its ability to distinguish costs associated with the disease from costs that are not. This is predominantly a problem for estimating costs for hospitalised HZ patients as they often have several comorbidities, which may lead to an overestimation of the true costs directly linked to the disease. Even when using costs associated with patients who had varicella or HZ as the primary diagnoses, we may still have included the costs of any other diagnoses they might have had. If we however excluded patients having either disease as their secondary diagnoses, we risk excluding costs related to the VZV and thus underestimating the true economic burden. Whether varicella or HZ is coded as the primary or secondary diagnosis could be arbitrary, because of accidental coding errors or possibly deliberate miscoding due to the hospitals funding arrangements, thus, it is possible that the costs in our study were underestimated. It is important to note that our estimates represent costs associated with either varicella or HZ assigned diagnosis, hence not all costs included are in fact caused by the VZV. While HZ becomes more severe with age, the increase in the costs seen in older people in our study is also related to a general increase in the morbidity.

We performed our analysis from a healthcare system perspective that does not include costs borne by the patient or society. Although this perspective does not provide a complete picture of all disease costs, it gives a good overview of most important costs, and is also the preferred perspective in the new Norwegian guidelines for pharmacoeconomic analyses [15]. Our approach did not include all costs borne by the healthcare services. For example, we have not included the costs of prescription and non-prescription medications purchased by the patients because we did not have access to these data. Costs of medications administered at hospitals will be however accounted for as these are part of the hospital budget and therefore included in the DRG. Lastly, because we extrapolated costs for hospital visits with missing DRG-weights, our estimates of the total hospital costs may be somewhat imprecise.

5. Conclusion

Our study demonstrates that both varicella and HZ cause a substantial financial burden on the Norwegian healthcare system. The majority of the healthcare costs are associated with HZ, particularly in individuals over 50 years of age, and with varicella in children under age 15 years. These findings contribute to the knowledge base aimed to support the national policy decision about the need for varicella and HZ immunisation, however, a full health economic evaluation is required before an informed decision can be made.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests

Appendix

See [Tables A1 and A2](#).

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