

## Treatment Patterns and Cost of Actinic Keratosis During 12 Months – A Swedish Register-based Study

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Actinic keratosis is associated with sun-damaged skin and may progress to squamous cell carcinoma. Information about treatment patterns of actinic keratosis in Sweden is limited. The objective was to analyse costs and treatment patterns in clinical practice. Patients with a new primary diagnosis were identified ( $n=952$ ). Information about visits, treatment procedures and topical treatments were retrieved from registries. The majority of patients (73%) had one registered visit. Most visits were in specialist care (82%). Cryotherapy was most common (61%). Topicals were used by 12% of patients. Each imiquimod prescription generated 1.7 dispatches, indicating insufficient first treatment. The annual cost per patient was SEK 1,661. Specialist care costs were dominating, whereas topicals and primary care constituted a limited part. Although there are direct costs associated with management of actinic keratosis, the burden for patients, health care, and society may be even higher if the disease progresses to squamous cell carcinoma. **Key words:** *actinic keratosis; treatment pattern; cost of illness; squamous cell carcinoma; non-melanoma skin cancer.*

Actinic keratosis (AK) is a skin condition disease associated with cumulative sun exposure. AK is regarded as the initial clinical manifestation of a disease continuum that may result in squamous cell carcinoma *in situ* (SCCIS) and ultimately in squamous cell carcinoma (SCC) (1–6). In addition to sun exposure, known risk factors for AK are advancing age, immunosuppression and fair skin (7, 8). The prevalence of AK has been estimated to between 1.4 and 25% (8–14), with higher prevalence in elderly populations and in areas with high UV exposure such as Australia (14).

In Sweden this corresponds to an annual estimated number of approximately 70,000–100,000 cases (15). Since there is a risk of AK progressing into SCC the current recommendation in Sweden is to treat AK (15).

The choice of AK treatment in Sweden depends mainly on physician experience, availability, and cost of the treatment alternatives and a number of patient factors including number of lesions, their localisation, thickness and size and patient age. Treatment practice for AK is broadly divided into 2 categories; lesion-directed treatment and field-directed treatment. Lesion-directed treatment includes cryotherapy or curettage (16, 17). For patients with multiple lesions topical treatments or photodynamic therapy with methyl aminolevulinate can be used (16, 17). Topicals currently used in Sweden are imiquimod cream 5%, 5-fluorouracil cream 5% (currently only available as licensed product) or diclofenac (15) and recently, ingenol

mebutate gel. Topicals are often associated with local skin responses such as erythema, crusting, scaling and pruritus (18). In a recent study duration of topical therapy was associated with increasing rates of non-adherence (19).

Previous research about treatment patterns and resource use of AK in Sweden is limited. We found no studies analysing treatment patterns in Swedish clinical practice. Two studies have analysed the total cost of skin cancer in Sweden where the cost of AK was included. One study estimated the total societal cost of skin cancer in Sweden 2005 to about 142.2 million EUR, out of which 15 million EUR was related to AK (20). Another study estimated the total annual direct and indirect costs of skin diseases caused by ultraviolet radiation in 1999 in Stockholm to SEK 162 million, out of which SEK 5.4 million was due to AK (21).

The objective of this study was to analyse treatment patterns of AK during 12 months following the first AK diagnosis. An additional objective was to analyse direct costs of AK, during 12 months following the first diagnosis, in terms of direct treatments and health care resource use in primary and specialist care in Swedish everyday practice.

### Methods

Subjects were identified in an administrative health care register in the County of Östergötland, a region of 430,000

inhabitants. The register includes administrative records of all publicly produced health care utilisation in the county including both outpatient and inpatient care. There was only one private dermatologic clinic in the County of Östergötland in 2010–2011, which was not included.

The analyses are based on retrospective data from the regional administrative health care register in Östergötland, registers at the National Board of Health and Welfare (NBHW) and from Statistics Sweden.

Patients with a primary diagnosis of AK in 2010 in primary care, specialist outpatient or inpatient care were identified. Resource utilisation during a 12-month period following the first diagnosis was retrieved from the registers. Only patients with a new primary AK diagnosis were selected in order to analyse treatment patterns and ensure that treatments used were used for the first time. Patients who had previously received an AK diagnosis in 2002–2009 were therefore excluded from the analysis. Accordingly, only observations where AK was registered as the primary diagnosis in 2010 were used in order to reflect treatment patterns of new AK lesions accurately.

Health care visits with AK diagnoses (ICD-10 L57.0) and follow-up control visits (ICD-10 Z09.8) registered as primary diagnoses were retrieved from the regional register for the selected patients. Topical treatments used for AK (diclofenac 3%, imiquimod 5% and 5-fluorouracil 5%) were retrieved from the Prescribed Drugs Register at the NBHW for the selected patients. Ingenol mebutate gel was not available during the study

period. The Prescribed Drugs Register includes all purchases of prescribed pharmaceuticals since 2005. The regional register includes codes for medical interventions performed at health care visits. Relevant treatment codes for procedures used to treat AK were identified by a clinical expert in dermatology. Year of death and county of residence were retrieved from the Total Population Register at Statistics Sweden.

Unit costs of health care resource use were based on the Southern Health Care Region's Pricelist 2011, as the pricelist of the County of Östergötland was not sufficiently detailed. The unit cost for primary care included physician cost and all medical services performed at that occasion. Thus, no additional costs for specific procedures were included. In specialist outpatient care there are specific unit costs for the different procedures. All such procedures, except for biopsies, included the cost of a specialist outpatient care visit.

Unit costs of topical treatments are recorded in the prescribed drugs register, for each individual prescription. Costs for the respective topical treatment were retrieved from the register in 2011. As the price varied somewhat during the year, the most frequently listed price during 2011 was used in the calculations. The total cost of topical treatments, including both costs paid by the patient and by the county council, was included. Unit costs of health care visits, procedures and topical treatments are listed in Table I.

Patient characteristics for the selected population, including age and sex, distributions and the number and percentage of

Table I. Resource use during 12 months following first primary AK diagnosis in 2010. Costs and frequencies of specific health care resources (in SEK 2011 prices)

Health care resource	Frequency <sup>a</sup>	Unit cost	Total cost
Primary care physician visit (including all medical service)	227	1,325.00	300,775
Primary care nurse visit (including all medical service)	1	540.00	540
Specialist care physician visit	375	910.00	341,250
Specialist care nurse visit	12	456.00	5,016
Biopsy (additional to physician cost)	115	809.00	93,035
PDT (including physician cost and cost of topical treatments)	26	3,643.00	94,718
Cryotherapy, single tumour (including physician cost)	597	910.00	543,270
Cryotherapy, multiple tumour <sup>b</sup> (including physician cost)	42	1,367.00	57,414
Excision + clinical assessment (including physician cost)	12	991.00	11,892
Laser (including physician cost)	1	4,833.00	4,833
Diclofenac Solaraze gel 3% 25 gram	9	274.50	2,471
Imiquimod Aldara creme 5%, 12 x 250 mg, Meda <sup>c</sup>	52	694.50	36,114
Aldara creme 5%, 12 x 250 mg, Orifarm	42	692.50	29,085
Aldara creme 5%, 12 x 250 mg, Pharmachim <sup>d</sup>	78	693.50	54,093
5-fluorouracil Efidix creme 50 mg/g 20 gram <sup>e,f</sup>	19	345.00	6,555
Total	1,608		1,581,517

<sup>a</sup>Number of treatment occasions or packages of topicals.

<sup>b</sup>Between 2 and 4 procedures were performed at the same time. There were in total 88 procedures at 42 occasions.

<sup>c</sup>Unit cost in 97% of observations in 2011, 3 % had a unit cost of SEK 629.5.

<sup>d</sup>Unit cost in 81 % of observations in 2011, 19% had a unit cost of SEK 630.5.

<sup>e</sup>Unit cost in 40 % of observations in 2011 (and in 74 % in 2010).

<sup>f</sup>5-fluorouracil is only available for prescription on license in Sweden. Licence fee for 5-fluorouracil at pharmacy level is SEK 220 (information received from The Dental and Pharmaceutical Benefits Agency, TLV, in 2012). The cost of 5-fluorouracil does not include the licence cost in the calculations.

patients registered with SCC or SCCIS as secondary diagnoses and the number and percentage of patients registered in the different health care levels were analysed. In addition, the number of visits and treatments (procedures or topicals) per patient, the total number and percentage of treatment occasions and patients with each type of treatment were analysed. The mean time between the first and second treatment occasion was calculated among patients with at least 2 registered occasions. The use of the most common topical treatment, imiquimod, was analysed in detail.

Frequencies and unit cost for health care visits, procedures and topical treatments were analysed, as well as the total cost for each visit or treatment. The total mean cost and mean cost per patient were calculated for primary care, specialist health care and topical treatments. The total annual cost for all patients identified and the annual mean cost per patient for AK as primary diagnosis, including visits, procedures and topical treatments during the 12-months following the patients' first AK diagnosis were also calculated.

Statistical analyses were performed using Stata Statistical Software: Release 11.1. College Station, Texas, USA. Statistical significance tests were two-sided and conducted using a significance level set at 5% unless otherwise specified. The study was performed with ethical approval from the regional ethics board of the University of Lund; Dnr 2012/30.

## Results

In 2010, 952 patients with a new AK diagnosis were identified in the County of Östergötland and followed for 12 months regarding treatment patterns and resource use. Patient characteristics are listed in Table II. The mean age was 71 years and 61% were women. Most patients, 88%, were treated in specialist outpatient care. Less than one percent of patients had SCCIS and/or SCC registered as a secondary diagnosis during the 12-month follow-up.

All 952 patients were residents in the County of Östergötland by the beginning of 2010. Two percent of patients ( $n=20$ ) died and 5 patients moved from the county during the 12-month follow-up period.

A total of 1,289 health care visits were registered, out of which 98% ( $n=1,268$ ) were AK primary diagnoses and the remaining 2% ( $n=21$ ) were coded as control visits for AK. The majority of visits, 82% ( $n=1,061$ ) were in specialist care and 18% ( $n=228$ ) were in primary care. No inpatient occasions were registered with AK as primary diagnosis.

The majority of patients, 73% ( $n=699$ ), had only one health care visit registered in either primary and/or specialist care,

Table II. Characteristics among patients with a new primary actinic keratosis (AK) diagnosis in 2010

Total number of AK patients <sup>a</sup> , $n$ (%)	952 (100)
Sex, $n$ (%)	
Men	372 (39)
Women	580 (61)
Age, year, mean (SD), min/max	70 (11.8), 26/101
AK as primary diagnosis, $n$ (%)	952 (100)
and SCCIS as secondary diagnosis, $n$ (%)	3 (<1)
and SCC as secondary diagnosis, $n$ (%)	7 (<1)
Health care level <sup>b</sup> , $n$ (%)	
Primary care	218 (23)
Specialist care	831 (88)
Inpatient care	0 (0)

<sup>a</sup>Patients who were diagnosed with a new AK as primary diagnosis in 2010.

<sup>b</sup>Only at occasions where AK was primary diagnosis. Note that some patients were treated at several health care levels.

SCC: squamous cell carcinoma, SCCIS: squamous cell carcinoma *in situ*.

during the 12-month follow-up. Twenty percent ( $n=195$ ) had 2 visits and the remaining 7% ( $n=58$ ) had more than 2 visits. There were 78% ( $n=741$ ) of patients who had their first registered visit in specialist care.

Most patients, 72% ( $n=685$ ), had at least one treatment, i.e. a procedure in specialist care or a prescription, which was registered. Twenty-eight percent of patients had no specific treatment registered, just a health care visit (Table II). Note that several procedures in specialist care could be performed on the same occasion. In total there were 959 treatment occasions. Twenty percent of the treatment occasions were topical use and 80% were procedures. Patients had up to 4 different treatments at the same occasion. Cryotherapy was the most common treatment, used by 61% of patients and in 71% of treatments. There were 13% of patients ( $n=125$ ) who had 2 or more treatment occasions during 12 months. The mean time between the first and the second treatment occasion was 4.2 months.

There were 98 patients who used imiquimod during the 12-month follow-up. About 42% of these patients ( $n=41$ ) had used more than one package of imiquimod during the 12-month period. Among the 98 patients, there were 164 dispatches and based on 112 imiquimod prescriptions, i.e. 1.67 dispatches per patient. Most prescriptions, 66% ( $n=74$ ), were dispatched only once. Twenty-seven percent ( $n=30$ ) of prescriptions were used twice and the remaining 7% ( $n=8$ ) of prescriptions were dispatched for more than 3 times (data not shown).

Table I presents the resource use 12 months following the first AK diagnosis for the respective treatment/visits. Biopsies, only registered in specialist care, were used in total 115 times.

Cryotherapy accounted for the greatest part of total costs of all treatments. Excision and laser were not commonly used, only on 12 and one occasion/s, respectively. Note that cryotherapy may be used multiple times at the same occasion. Therefore, frequencies of cryotherapy in Table III reflect treatment occasions whereas frequencies of cryotherapy in Table I reflect actual number of single versus multiple procedures. Likewise, frequencies of topical treatments in Table III reflect number of purchase occasions, while Table I shows the number of packages purchased.

Total resource use and mean cost per patient during the 12-month follow-up is presented in Table IV. In the county of Östergötland, the total annual cost for AK as a primary diagnosis, including visits, procedures and topical treatments during 12-months following the first AK diagnosis was about SEK 1.6 million in 2011 price level. The annual cost per patient was SEK 1,661.

### Discussion

Registry-based data is a valuable source of information that fills an information gap by providing knowledge about treatment patterns and costs of AK. The strength of this study was the possibility to link individual-level data from different registries. This data reflecting treatment patterns in clinical practice in Sweden shows that cryotherapy is the most common therapy for AK, and that topicals are the second most used therapy among patients who had their first AK diagnosis in 2010. Furthermore, it shows that 73% of patients had only one health care visit during a 12-month follow-up period.

The present study included resource use related to the first primary AK diagnosis in 2010 and the following 12 months. Patients with AK in 2010 who had received a diagnosis in previous years were thus not included. Assuming that the excluded patients had the same resource utilisation, the total annual cost of treating all cases of AK in the County of Östergötland would be approximately SEK 3.1 million.

In the County of Östergötland a referral from primary care is mandatory in order to access specialist outpatient care. There is likely to be a substantial number of missing registrations of

Table III. Registered actinic keratosis treatments among patients with a new diagnosis in 2010

	Treatments <i>n</i> (%)	Patients <i>n</i> (%)
Photodynamic therapy	26 (3)	20 (2)
Excision	12 (1)	12 (1)
Cryotherapy occasions	685 (71)	580 (61)
Other physical removal <sup>a</sup>	47 (5)	38 (4)
Diclofenac dispatches	9 (1)	7 (1)
Imiquimod dispatches	164 (17)	98 (10)
5-fluorouracil dispatches	16 (2)	13 (1)
Registered health care visits without any specific procedure or prescribed topical		267 (28)
Total	959 (100)	952 (100)

<sup>a</sup>One laser, 7 electrodesiccation, 39 other puncture, incision or destruction, none curettage.

Note that each patient may have used several treatments.

AK diagnoses in primary care, partly because the registration of diagnoses is generally less complete than in specialist care, but also because patients first seek health care in primary care but they will not receive a specific diagnosis until they have been referred to specialist care. Thus, for patients who did not have a diagnosis of AK in primary care an additional cost for primary care visit of SEK 1,325 associated with their AK could be assumed. The additional total annual cost for treatment of patients with a first primary AK in the region would then be almost one million SEK higher.

As only individuals who sought public health care for their AK lesions in the County of Östergötland were included, people who did not seek health care for their AK, or who sought healthcare elsewhere, were thus not registered. Based on the number of visits at the only private dermatology clinic in the County of Östergötland in a previous study, the extent of private health care is limited (20).

One limitation of the register data was that information about disease severity was not available. It was therefore not possible to consider this in relation to type of treatment.

Imiquimod was the most commonly used topical treatment in the analysis of a 12-month follow-up after AK diagnosis in 2010. Among patients treated with imiquimod, 34% used their prescription more than once, which may indicate that the first

Table IV. Resource use during 12 months following first primary AK diagnosis in 2010. Mean costs per patient and total cost in primary care, specialist care and topical treatments (in SEK 2011 prices)

Resource use	Patients, <i>n</i>	Occasions, <i>n</i>	Mean cost/patient <sup>a</sup>	Total cost
Primary care	218	228	317	301,315
Specialist care (including procedures)	831	1,061	1,210	1,151,884
Topical treatments	117	189	135	128,318
Total	952	1,478	1,661	1,581,517

<sup>a</sup>The mean cost is based on the total study population of 952 patients with primary AK diagnosis in 2010.

treatment was not sufficient. A mean of 1.67 dispatches were made on each prescription.

In this study patients were assumed to receive the registered treatments for their AK only. Some of the included treatments, however, may be used for other indications too. This is a limitation of the register-based design. To provide more detailed data, a retrospective review of patient records or a prospective study would have been necessary, which would have been both time-consuming and costly.

There is limited information available about treatment patterns and costs of AK in Sweden and elsewhere. Two previous studies have estimated the total cost of non-melanoma skin cancer in Sweden, including the cost of AK. Results from the present analysis are similar to a study from Stockholm, in which 86% were treated in specialist outpatient care and 28% in primary care. In the present study, 88% were treated in specialist care and 23% in primary care. Total cost of AK in Stockholm (approximately 1.8 million inhabitants) were estimated at SEK 5.4 million in 1999 (not adjusted for inflation) (21). That would equal to approximately SEK 1.6 million in the population size of Östergötland in 2011 price level, which is in accordance with the present result.

In another previous study based on data from the County of Östergötland, the total cost of AK in 2005 in Sweden was estimated at 15 million EUR (22), which would equal to approximately SEK 7 million in 2011 price level in a population size of Östergötland. Although the present study only included new cases of AK, the difference in estimated costs was considerable.

One explanation for the cost discrepancies may be that the previous study had a different approach of estimating costs (22). Calculations in outpatient care were based on the Cost-Per-Patient database, which includes all health care costs in the overall budget, divides it between different health care units and finally attributes it to a patient. The advantage of that approach is that there are no costs left out; all costs in the health care sector are attributed to a patient. The disadvantage of such approach is the lack of transparency and the possibility of overestimating costs. In addition, the previous study reported 9 cases of inpatient care episodes for AK patients nationally, with a cost of 4,352 EUR per episode. According to clinical experts inpatient care for AK would be highly unlikely. Unit costs of health care visits used in the present study include overhead costs, such as hospital administration, but they may underestimate such costs. The present study is, nonetheless, more transparent as each health care visit and treatment is associated with a unit cost.

Unit prices differ somewhat between different health care regions in Sweden. The southern regional price list, used in this study, seems to have a lower price level for dermatology clinics compared to other regions. For example, a physician visit at a dermatologic clinic in 2011 varied between SEK 955 and SEK 1,798 compared to SEK 910 in the present analyses. This may also have influenced the total costs to be lower than they would have been if using unit costs from other regions.

This report of treatment patterns in clinical practice suggests that specialist care dominate the costs of AK and that costs of topicals and primary care constitute a limited part of the total cost. The analyses show that the majority of patients with first time diagnoses of AK are not followed-up after an initial visit. Furthermore, about one third of patients had neither a procedure nor a topical treatment, which suggest that some of them did not receive any treatment. These findings are unexpected as AK may progress to SCC. Although there are costs associated with management of AK in health care, the burden for patients, health care, and society may be even higher if the disease progresses to SCC. More future research is needed about the costs and cost savings associated with treating AK and preventing the future burden of SCC.

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## References

1. Glogau RG. The risk of progression to invasive disease. *J Am Acad Dermatol* 2000; 42: 23–24.
2. Berner A. [Actinic keratosis and development of cutaneous squamous cell carcinoma]. *Tidsskr Nor Laegeforen* Jun 16 2005; 125: 1653–1654 (in Norwegian).
3. Criscione V D, Weinstock MA, Naylor MF, Luque C, Eide MJ, Bingham SF. Actinic keratoses: Natural history and risk of malignant transformation in the Veterans Affairs Topical Tretinoin Chemoprevention Trial. *Cancer* 2009; 115: 2523–2530.
4. Feldman SR, Fleischer AB, Jr. Progression of actinic keratosis to squamous cell carcinoma revisited: clinical and treatment implications. *Cutis* 2011; 87: 201–207.
5. Salasche SJ. Epidemiology of actinic keratoses and squamous cell carcinoma. *J Am Acad Dermatol* 2000; 42: 4–7.
6. Werner RN, Sammain A, Erdmann R, Hartmann V, Stockfleth E, Nast A. The natural history of actinic keratosis: A systematic review. *Br J Dermatol* 2013; 169: 502–518.
7. Oppel T, Korting HC. Actinic keratosis: the key event in the evolution from photoaged skin to squamous cell carcinoma. Therapy based on pathogenetic and clinical aspects. *Skin Pharmacol Physiol* 2004; 17: 67–76.
8. Memon AA, Tomenson JA, Bothwell J, Friedmann PS. Prevalence of solar damage and actinic keratosis in a Merseyside population.

- Br J Dermatol 2000; 142: 1154–1159.
9. Harvey I, Frankel S, Marks R, Shalom D, Nolan-Farrell M. Non-melanoma skin cancer and solar keratoses. I. Methods and descriptive results of the South Wales Skin Cancer Study. Br J Cancer 1996; 74: 1302–1307.
  10. Schafer T, Merkl J, Klemm E, Wichmann HE, Ring J. The epidemiology of nevi and signs of skin aging in the adult general population: Results of the KORA-survey 2000. J Invest Dermatol 2006; 126: 1490–1496.
  11. Lichte V, Dennenmoser B, Dietz K, Hafner HM, Schlagenhauß B, Garbe C, et al. Professional risk for skin cancer development in male mountain guides--a cross-sectional study. J Eur Acad Dermatol Venereol 2010; 24: 797–804.
  12. Naldi L, Chatenoud L, Piccitto R, Colombo P, Placchesi EB, La Vecchia C. Prevalence of actinic keratoses and associated factors in a representative sample of the Italian adult population: Results from the Prevalence of Actinic Keratoses Italian Study, 2003–2004. Arch Dermatol 2006; 142: 722–726.
  13. Bernard P, Dupuy A, Sascó A, Brun P, Duru G, Nicoloyannis N, et al. Basal cell carcinomas and actinic keratoses seen in dermatological practice in France: a cross-sectional survey. Dermatology 2008; 216: 194–199.
  14. Frost CA, Green AC. Epidemiology of solar keratoses. Br J Dermatol 1994; 131: 455–464.
  15. Paoli J. Aktinisk keratos. internetmedicin.se. 2011; <http://www.internetmedicin.se>.
  16. Dinehart SM. The treatment of actinic keratoses. J Am Acad Dermatol Jan 2000; 42: 25–28.
  17. Drake LA, Ceilley RI, Cornelison RL, Dobes WL, Dorner W, Goltz RW, et al. Guidelines of care for actinic keratoses. Committee on Guidelines of Care. J Am Acad Dermatol 1995; 32: 95–98.
  18. Ulrich M, Drecoll U, Stockfleth E. Emerging drugs for actinic keratosis. Expert Opin Emerg Drugs 2010; 15: 545–555.
  19. Shergill B, Zokaie S, Carr AJ. Non-adherence to topical treatments for actinic keratosis. Patient Preference and Adherence 2014; 8: 35–41.
  20. Tinghög G, Carlsson P, Synnerstad I, Rosdahl I, eds. Samhällskostnader för hudcancer samt en jämförelse med kostnaderna för vägtrafikolyckor. LiU-Tryck, Linköpings universitet ed: CMT Rapport 2007; 5; 2007.
  21. Nilsson G H, Carlsson L, Dal H, & Ullen H. Skin diseases caused by ultraviolet radiation: the cost of illness. Int J Technol Assess Health Care 2003; 19: 724–730.
  22. Tinghög G, Carlsson P, Synnerstad I, & Rosdahl I. Societal cost of skin cancer in Sweden in 2005. Acta Derm Venereol 2008; 88: 467–473.