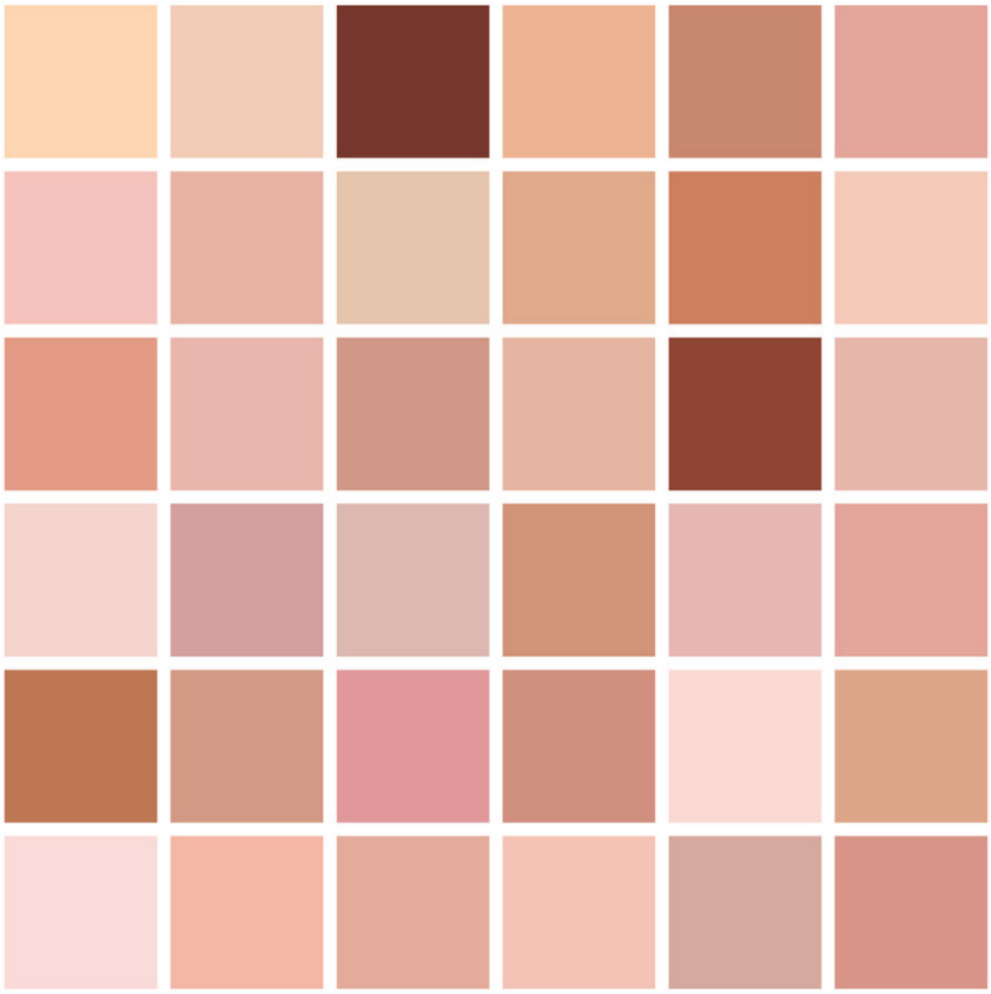
Efficacy, cost-effectiveness, and budget impact of a personalized discharge letter to basal cell carcinoma patients to reduce low-value follow-up care



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Key points

Question What is the efficacy, cost-effectiveness, and budget impact of a personalized discharge letter to first-time basal cell carcinoma patients compared with usual care?

Findings The discharge letter decreased the amount of follow-up visits with 13% during one year, consequently saving €26,04 after five years, and €26,07 after ten years per patient. Overall the budget impact over a period of five years was a cost saving of €2,9 million in the Netherlands.

Meaning The distribution of a personalized discharge letter lowers the volume of follow-up visits and is a cost-effective strategy to reduce unnecessary follow-up visits.

Abstract

Importance The incidence of keratinocyte carcinomas (KC) is high, rapidly growing and shows no signs of stabilizing. Approximately 80% of these diagnoses consist of basal cell carcinomas (BCC). Of these BCCs, 50% is considered to be low risk. The high number of patients makes KCs the fifth most expensive type of cancer in the Netherlands. Currently 83% of the low-risk BCC patients receive more follow-up care than the Dutch BCC guideline recommends, which is limited to one visit post-treatment. More efficient management could reduce unnecessary follow-up care and lower the costs.

Objective To study the efficacy, the cost-effectiveness, and the budget impact of a personalized discharge letter on the number of follow-up visits for patients following a low-risk basal cell carcinoma compared with usual care.

Design Model-based cost-effectiveness analysis using individual patient data gathered via surveys.

Setting Multicenter; one academic hospital, three general hospitals, and two independent sector treatment centers.

Participants The study included 473 first-time BCC patients.

Intervention and control The intervention consisted of a personalized discharge letter on top of one follow-up visit, which is the care as usual in the Netherlands. The control group received only care as usual.

Main outcome measures The outcome measures were number of follow-up visits, costs and quality adjusted life years (QALY) per patient, incremental cost-effectiveness ratio and the budget impact.

Results A personalized discharge letter lowered the number of follow-up visits by 13% in one year. The incremental costs after five years were -€26.04 per patient and -€26.07 after ten years. The QALYs were 4.126 after five years and 7.262 after ten. They were nearly equal in both groups. Using a five-year time horizon, the incremental cost-effectiveness ratio was expected to be -€10,045,-. The budget impact was -€2,9 million after five years.

Conclusion and relevance The distribution of a personalized discharge letter lowers the number of follow-up visits and implementing the intervention in a large eligible population results in large cost savings of €2,9 million and contributes to restrain the growing KC costs.

Introduction

The incidence of keratinocyte cancer (KC) is rapidly growing and it is the most common malignancy in the world (1-3). Of these carcinomas, basal cell carcinomas (BCC) are by far the most common type with a prevalence of 80% (the remaining 20% consist of cutaneous squamous cell carcinomas (cSCC)) (2, 4). It is estimated that 30% of Caucasian individuals will develop a BCC during their lifetime (2). In the Netherlands, the incidence rates of BCCs increase annually by 8% and show no sign of stabilizing (5, 6). In 2017, over 48.000 individuals were diagnosed with a BCC (7). The alarming growth of new cases results in a strain on dermatological care and increases costs (8). KC costs are growing worldwide, and in the Netherlands KC is the 5th most expensive type of cancer with an annual amount of 168.6 million euros. Total KC costs are 1,8 times higher than the costs for melanomas (1, 3, 9). Since the majority of KCs is made up of BCCs, it is crucial to improve the efficiency of BCC care to minimize further increases of health care expenditures.

De-adoption of low-value care is a strategy that can be used to restrain the increasing costs. Low-value care is defined as “care that is unlikely to benefit a patient given the harms, costs, alternatives or preferences” (10). After a low-risk BCC, follow-up visits after the initial check-up can be labeled as low-value (11). In the Netherlands, annual follow-up for BCC is limited to high-risk patients only according to the BCC guideline. Dermatologists are recommended to check the scar of low-risk patients just once within 6-12 months after treatment and are advised to instruct patients in self-examination and provide additional information via brochures (12). About 50% of the BCC patients are considered to be low risk, and therefore are not advised to return annually after the initial check-up (13). However, research has shown that 83% of the low-risk patients received more follow-up than the guidelines recommend during the first five years after treatment (3). There is currently no evidence that shows a health benefit of extra follow-up (14). Therefore, additional follow-up visits for low-risk BCC patients can be considered low-value and require more efficient management.

Research has been conducted to evaluate what the needs and preferences are of patients and dermatologists regarding current BCC management. BCC patients have stated the need for more information that is tailored to their situation and indicated that having this information would lower their need for follow-up visits (15). A discrete-choice experiment revealed that patients preferred a personalized discharge letter (PDL) on paper over other alternatives (e-health, general brochure or website) (manuscript submitted). PDLs can contain relevant information on a patient’s diagnosis, treatment, follow-up, complications, and lifestyle recommendations. These letters improve the amount of received information and the self-management of patients by combining educational with personalized information (16). Providing such a letter could reduce unnecessary follow-up visits among BCC patients and lower the costs of BCC management compared to current practice.

The aim of the study was to explore the efficacy, cost-effectiveness, and budget impact of a personalized discharge letter to first-time basal cell carcinoma patients in comparison with usual care.

Method

The efficacy, cost-effectiveness, and budget impact were determined for the intervention consisting of the distribution of a PDL to first-time BCC patients, compared to usual care (no PDL). The principal outcome of effectiveness was the percentual change in the number of follow-up visits occurring in both strategies. These results were used to conduct a cost-effectiveness analysis (CEA) and a budget impact analysis (BIA). A CEA compares the health outcomes with the costs of the intervention and control strategy per patient (17). However, the decision to implement the intervention on a large scale also depends on the total (budgetary) impact. A CEA, followed by a BIA, allows decision-makers to foresee the entire expected impact of adopting the innovation in their local setting (18, 19). The analyses were performed according to the (inter)national guidelines of CEAs and BIAs as well as the CHEERS checklist for reporting (20-24).

Study population and design

The population for this study consisted of patients with a first BCC who were included after treatment but prior to follow-up. Patients needed to be at least 18 years old and had to be able to speak Dutch. Patients who had any type of skin cancer prior to their first BCC were excluded.
Patients were included in six healthcare centers in the Netherlands. These included one academic hospital, three general hospitals, and two independent sector treatment centers.
All participants were asked to complete a survey at baseline and after three, six, and twelve months. Each survey consisted of general questions regarding demographics, their quality of life (based on the EQ-5D-3L questionnaire), the number of visits to the general practitioner (GP) and specialist related to their BCC, whether they received a new skin cancer diagnosis and the SF-HLQ questionnaire to monitor the effects of a BCC on labor activities (23, 25).
First, the control patients were included in 2014, and their data was collected via the surveys. A discrete choice experiment was conducted in the control group, which led to the development of the intervention (26, 27). In 2016, new patients were included in the study forming the intervention group. The control patients received usual care and no PDL. Intervention patients received usual care and a PDL on paper, which contained information on their diagnosis, treatment, chance of having a subsequent BCC, lifestyle recommendations, information on self-examination and advice for actions when new suspicious lesions appear. The PDL is to be created by the dermatologist or assistant in two minutes, printed and given to the patient. The letter is distributed once post-treatment.

Efficacy

The efficacy of the intervention was expressed as the percentage reduction in BCC-related visits to a specialist during a period of one year.
Due to certain logistic errors in the distribution of the surveys in the intervention group, up to 46.7% and 45.1% of the participants did not respond at t=3 and t=6 months, respectively. This mainly resulted in a data loss on efficacy. The missing data was correlated with age only and therefore considered to be missing at random (MAR). The missing data was imputed with multiple imputation (MI) and pooled using SPSS® 26. With MAR data, MI increases the precision and reduces the level of bias resulting from a complete case analysis (28-30). The number of GP and specialist visits were imputed and used for further modelling.

Cost-effectiveness analysis

The cost-effectiveness was estimated through decision modeling using a patient level health state transition model with a societal perspective. This decision model simulated potential effects on health outcomes and the costs that patients accrued over time to estimate the effect of the intervention (17, 20). The model consisted of several health states between which patients can transition once per cycle. The following health states were included: full recovery from first BCC, new BCC, new cSCC, new melanoma, death due to skin cancer and death due to other causes. Each cycle represented one year and allowed one transition from one state to another.
A schematic overview of the model structure can be found in figure 1.

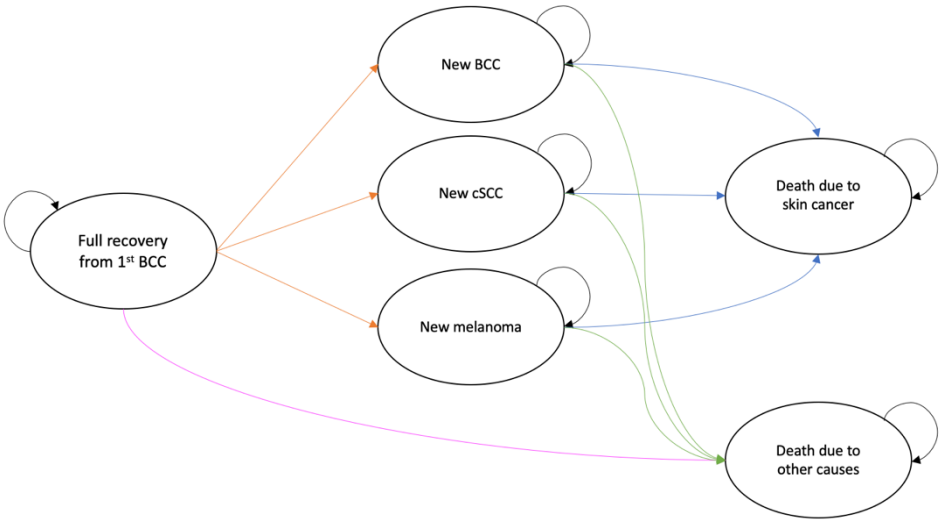

FIGURE 1: SCHEMATIC OVERVIEW OF THE MODEL

The patient characteristics of the survey were used to simulate a cohort of 10,000 hypothetical patients in the model.
BCC is a condition with very low mortality rates; therefore, the incremental effects and incremental costs were expected to stabilize after five years. To assess the stability of these incremental outcomes the model-based analysis was performed for a five- and ten-year time horizon.
Each health state comes with certain costs and health utilities. Costs were accrued in different categories; medical costs, costs for patients and the costs of productivity losses. All costs are presented in Euros (€) and converted to 2019 using the Dutch derived consumer price indices (31). Costs were discounted by 4% and health outcomes by 1.5% according to the Dutch guideline for economic evaluations in health care (23, 32). Disaggregated total deterministic costs were used to express the impact on each cost category. The measured health outcomes are expressed in QALYs and calculated via the scores resulting from the EQ-5D-3L questionnaire. A full description of the included costs, probabilities, utilities and their sources is provided in appendices 1 and 2.
The efficacy results were used to model the number of appointments that were made. For the remaining four years previous trial data from the Erasmus MC was used (33).
The primary outcomes of the model were the total and incremental costs and effects, and the incremental cost-effectiveness ratio (ICER) indicating the cost per QALY gained (17).

To investigate the impact of the joint parameter uncertainty on the results, a probabilistic analysis (PA) was carried out. The PA shows how variation in the input of parameter values affected the outcomes of the model (34). The PA was performed with 5,000 Monte Carlo simulations. The Monte Carlo simulation calculated the outcomes of the model by simultaneously drawing random parameter values from previously determined probability distributions. The health utilities were defined using a beta distribution, whereas the costs were defined using a gamma distribution. Variation in the number of appointments made was simulated using a Dirichlet distribution (35). Some used costs were reference prices, are therefore fixed and did not use a distribution. These costs were nationally set in the Dutch Costing Manual or aggregated from national data and were therefore free of uncertainty (36).
The price of the software was an estimate of €5,000.00 for the first hospital in which the intervention will be implemented and was made by and IT-specialist. To address the uncertainty surrounding this estimate, a scenario analysis was conducted which considered implementation in one hospital and nationally. The model was re-run to monitor its effect on the outcomes.
The parameter inputs are listed in table 1.

TABLE 1: PARAMETER INPUTS

Parameter	Value	Standard error	Distribution	Source
General practitioner appointments				
Intervention				

0	0.986	-	Beta	Trial
1	0.014	-	Beta	Trial
Control				
0	0.978	-	Beta	Trial
1	0.021	-	Beta	Trial
Specialist appointments				
Intervention year 1				
0	0.209	-	Dirichlet	Trial
1	0.380	-	Dirichlet	Trial
2	0.266	-	Dirichlet	Trial
3	0.114	-	Dirichlet	Trial
4	0.023	-	Dirichlet	Trial
5	0.006	-	Dirichlet	Trial
6	0.002	-	Dirichlet	Trial
7-10	0.000	-	Dirichlet	Trial
>10	0.000	-	Dirichlet	Trial
Control year 1				
0	0.138	-	Dirichlet	Trial
1	0.325	-	Dirichlet	Trial
2	0.375	-	Dirichlet	Trial
3	0.136	-	Dirichlet	Trial
4	0.018	-	Dirichlet	Trial
5	0.006	-	Dirichlet	Trial
6	0.002	-	Dirichlet	Trial
7-10	0.000	-	Dirichlet	Trial
>10	0.000	-	Dirichlet	Trial
Control year 2				
0	0.700	-	Dirichlet	Unpublished data
1	0.210	-	Dirichlet	Unpublished data
2	0.040	-	Dirichlet	Unpublished data
3-5	0.040	-	Dirichlet	Unpublished data
6-10	0.010	-	Dirichlet	Unpublished data
>10	0.000	-	Dirichlet	Unpublished data
Control year 3				
0	0.820	-	Dirichlet	Unpublished data
1	0.120	-	Dirichlet	Unpublished data
2	0.050	-	Dirichlet	Unpublished data
3-5	0.010	-	Dirichlet	Unpublished data
6-10	0.000	-	Dirichlet	Unpublished data
>10	0.000	-	Dirichlet	Unpublished data
Control year 4				
0	0.780	-	Dirichlet	Unpublished data
1	0.160	-	Dirichlet	Unpublished data
2	0.050	-	Dirichlet	Unpublished data
3-5	0.000	-	Dirichlet	Unpublished data
6-10	0.000	-	Dirichlet	Unpublished data
>10	0.000	-	Dirichlet	Unpublished data
Control year 5				
0	0.940	-	Dirichlet	Unpublished data
1	0.030	-	Dirichlet	Unpublished data
2	0.030	-	Dirichlet	Unpublished data

3-5	0.000	-	Dirichlet	Unpublished data
6-10	0.000	-	Dirichlet	Unpublished data
>10	0.000	-	Dirichlet	Unpublished data
Quality of life				
No recurrence	0.910	0.010	Beta	Trial
BCC[a] after BCC	0.910	0.025	Beta	Trial
cSCC[b] after BCC	0.910	0.025	Beta	Trial
Melanoma after BCC	0.719	0.011	Beta	(37)
Recurrence after first BCC				
BCC	0.258	0.052[c]	Beta	(38)
cSCC	0.045	0.009[c]	Beta	(38)
Melanoma	0.004	0.001[c]	Beta	(38)
Mortality				
BCC	0.001	0.000 [c]	Beta	(39)
cSCC	0.021	0.004 [c]	Beta	(40)
Melanoma	0.071	0.014 [c]	Beta	(41)
General	Appendix 3	-	Fixed	(42)
Average productivity loss in hours				
Intervention	0.795	0.159 [c]	Gamma	Trial
Control	1.606	0.321 [c]	Gamma	Trial
Costs				
Follow-up at GP[d]	€117.92	-	Fixed	(36)
Follow-up at SP[e]	€34.95	-	Fixed	(43)
Intervention	€1.61	0.322[c]	Gamma	(44)
Software	€5,000.00	-	Fixed	Expert estimate
Travel expenses	€2.78	-	Fixed	(36)
Productivity loss male	€39.56	-	Fixed	(36)
Productivity loss female	€32.98	-	Fixed	(36)

[a] Basal cell carcinoma

[b] Cutaneous squamous cell carcinoma

[c] ±20% of the deterministic value

[d] General practitioner

[e] Specialist

The results of the PA were visualized in the incremental cost-effectiveness plane. Both the model and the PA were performed using Microsoft® Excel 2019 for Mac.

Budget impact analysis

A budget impact analysis was performed to calculate the budgetary impact of implementing the intervention in the Netherlands for a time horizon of five years. The BIA had a societal perspective as the CEA and shows what the impact is for the involved parties (24).

The eligible population for this BIA was low-risk BCC patients who were diagnosed with skin cancer for the first time. About 48,022 individuals were diagnosed with a BCC in the Netherlands in 2017 (7). Half of them are considered to be low risk (13). With a growth of 8% in new cases annually, the eligible population was calculated for five years (5). The intervention uptake was defined as 40% in 2021, 50% in 2022, 60% in 2023, 75% in 2024, and 75% in 2025 based on estimates made by dermatologists, an implementation expert, and on the results of focus group sessions held with dermatologists (11). To address the uncertainty surrounding this estimate, scenario analyses with a lower and higher uptake were conducted. The lower uptake was defined as 20%-30%-40%-50%-50% and the higher uptake was 50%-60%-80%-80%-80%. These scenarios were also run on local (one hospital) and national implementation.

Results

Efficacy

The results of 473 first-time BCC patients were used for this analysis; 278 patients were included as a control and 195 patients received the intervention. Their characteristics are listed in table 2.

TABLE 2: PATIENT CHARACTERISTICS

	Intervention (n = 195)	Control (n = 278)
Sex [n (%)]		
Male	94 (48.2)	145 (52.2)
Female	98 (50.3)	131 (48.2)
Age		
Mean (SD[a])	64.8 (12.7)	66.4 (11.8)
Range	31-94	31-100
Education [n (%)]		
Low	53 (27.1)	90 (32.4)
Medium	84 (43.1)	104 (37.4)
High	62 (26.7)	74 (26.7)
Previous skin cancer diagnosis [n (%)]		
Precursor: Actinic Keratosis	7 (3.6)	4 (1.4)
Precursor: Abnormal birthmark	5 (2.6)	2 (0.7)
Precursor: Unknown	9 (4.6)	15 (5.4)
None	169 (86.7)	250 (89.9)
VAS[b] score at t = 0		
Mean (SD)	81.45 (11.8)	79.65 (14.5)
Range	30-100	19-100

[a]SD = standard deviation

[b]VAS = visual analogue scale

The number of visits to a specialist in the first year in the control group was 1.59 per patient and 1.38 in the intervention group. The distribution of a PDL reduced the number of visits by 13% (95% CI 0.129-0.289; P=<0.001) after imputation. In the complete case set the number of visits was reduced by 32% (95% CI 0.227-0.822; P=0.001).

Cost-effectiveness

The costs per patient after the first five years were €328.89 for the intervention and €354.93 for the control. This resulted in a cost saving of €26.04 per patient. Using a time horizon of ten years resulted in intervention costs of €368.56 and €394.64 for the control group. After ten years the expected cost saving is €26.07 per patient. These results show that effects did stabilize after five years and changes in the outcomes over the next five years were miniscule.

After a period of five years, the QALYs were 4.126 and after ten years 7.262. The QALYs in both groups were very similar with differences smaller than 0.003 for five years and 0.008 for ten years. The ICER was -€10,045 per QALY gained after five years and €3,437.90 after ten years.

The deterministic results of the intervention showed that the cost category medical costs accounted to 66.1% of the price. The costs for patients made up 4.5% and the remaining 29.4% is made up of productivity losses.

The outcomes of the PA showed that 97% of the simulations were in the southern quadrants. This means that the intervention is very likely to be cost saving, already for a five-year time horizon.

Of all the simulations, 37% indicated health loss (left side of the y-axis) and 63% indicated health benefits (right side of y-axis), meaning that improvement of the health outcomes was more likely than deterioration. All outcomes of the simulation are expressed in figure 2.

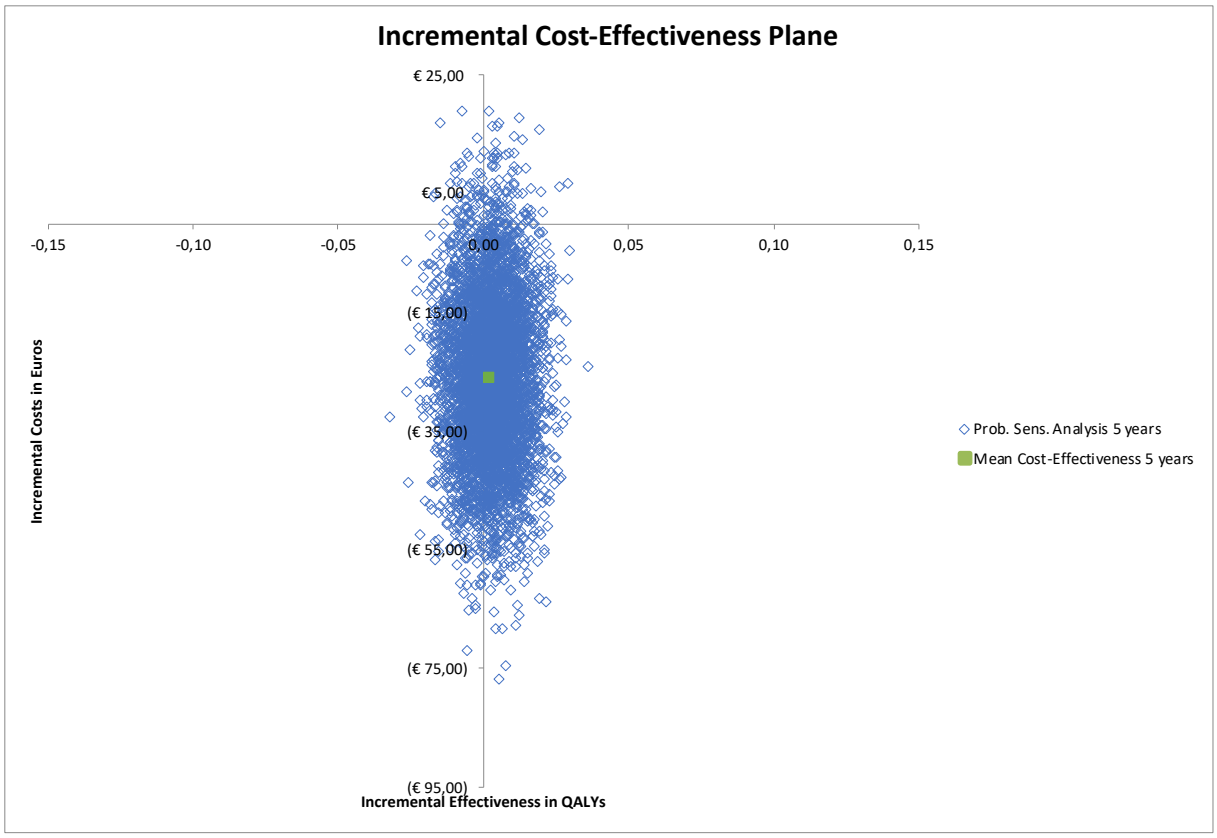

FIGURE 2: INCREMENTAL COST-EFFECTIVENESS PLANE

A scenario analysis was conducted to measure the effect of uncertainty surrounding the costs of the software during implementation. When the software costs were divided over a local setting (one hospital) of 1,000 patients, the cost savings were €26.04 per patient, as mentioned before. If the software costs were divided over the national eligible population of about 31,000, the cost saving was €26.39 per patient (an increase of 1.3%). An overview of the analysis can be found in appendix 3.

Budget impact analysis

The budget impact of implementing the intervention in the Netherlands was -€2,877,749.96 over a five-year period. Implementing the intervention in just one hospital resulted in a budget impact of -€118,279.20. The cost savings for each year and scenario are specified in table 3.

After five years the intervention has nationally resulted in cost savings in the medical category of €1,901,989.02. The costs for patients have dropped with €129,484.88. The productivity loss has lowered with €845,967.89. In the local setting the cost savings for the medical category were €78,182.55, for the patients €5,322.56 and for productivity loss €34,774.09.

A scenario analysis was conducted to discover the impact of a lower and higher uptake. The total national savings on a lower estimate were €1,836,544.43. The total savings on a high estimate were €3,334,590.99. Locally, the lower estimate was -€75,484.33 and the high estimate was -€137,055.96. The full analysis can be found in appendix 4.

TABLE 3: BUDGET IMPACT ANALYSIS

Year	2021	2022	2023	2024	2025	Total
Local implementation						
Eligible population	1,260	1,361	1,470	1,587	1,714	7,392
Expected uptake	40%	50%	60%	75%	75%	75%

Patients receiving the intervention	504	680	882	1,190	1286	4,542
Budget impact	-€13,123.94	-€17,717.32	-€22,961.65	-€30,998.22	-€33,478.08	-€118,279.20
Lower estimate	-€6,561.97	-€10,630.39	-€15,307.76	-€20,665.48	-€22,318.72	-€75,484.33
Higher estimate	-€16,404.92	-€21,260.78	-€30,615.53	-€33,064.77	-€35,709.95	-€137,055.96
National implementation						
Eligible population	30,247	32,667	35,280	38,103	41,151	177,448
Expected uptake	40%	50%	60%	75%	75%	75%
Patients receiving the intervention	12,099	16,333	21,168	28,577	30,863	109,040
Budget impact	-€319,307.34	-€431,064.90	-€558,660.12	-€754,191.16	-€814,526.45	-€2,877,749.96
Lower estimate	-€159,653.67	-€258,638.94	-€372,440.08	-€502,794.10	-€543,017.63	-€1,836,544.43
Higher estimate	-€399,134.17	-€517,277.89	-€744,880.15	-€804,470.57	-€868,828.21	-€3,334,590.99

Discussion

The introduction of a PDL resulted in 13% fewer visits at the dermatologist in one year compared to usual care. The decrease resulted in expected incremental costs of -€26.04 per patient in five years. The expected QALYs remained nearly equal in both groups with 4.126. The budget impact of implementing this innovation nationally was -€2,9 million over a period of five years with an annual saving of approximately €575,500. The cost category that experienced the highest cost saving was the medical costs, followed by productivity losses and finally the costs for patients and family. The cost saving was the highest in the medical category. Insurance companies who pay for these costs will therefore experience the most (financial) benefits from implementation. The employers who will have lower productivity losses are the second largest party who will benefit. Finally, the patients themselves will experience some lowered costs.
To implement this intervention, an investment has to be made to develop the required software. After its development, other hospitals could participate as well. If more hospitals join the number of patients who participate will be higher, which results in lower intervention costs and a greater benefit for all involved parties.

To our knowledge, this is the first study providing evidence on the cost-effectiveness and budget impact of a PDL in dermatology. Research has been conducted on the perceived satisfaction with information. It is rated positively by both patients and professionals and the uptake of the innovation improves when the letter is added to the electronic patient files (16). Personalized information has proven to be cost-effective in the long run (45). Other research has stated the need for more information on the cost-effectiveness of interventions to improve the decision-making process in health care, making this study a valuable resource to the decision-making process for BCC care (46).

One of the limitations of this study was the data collection design. Patients were included in different time periods. Within this period, a new BCC guideline was published for GPs which might have altered the clinical practice and therefore the outcome of the intervention (47). However, the adoption of guidelines among clinicians is often slow and unpredictable, making it hard to investigate its impact on the outcomes (48). The patient characteristics were very similar in both groups, suggesting that the effect of time on the outcomes caused by characteristics will be limited.
Another limitation was that the effect of the PDL has only been monitored for one year. Since patients usually make about one or two follow-up appointments, it is possible that the effect of the letter continued beyond the twelve months of monitoring, which would cause an underestimation of the efficacy. It is also possible that patients who received a PDL still made an appointment after twelve months creating an overestimation. Alterations to the number of follow-up visits could also change the cost-effectiveness both positively and negatively.
The EQ-5D-3L was used for this study and is known for being less responsive to minor changes in the scores than the 5L version (49). However, when this trial started there were no Dutch tariffs known for the 5L version. Hence, the 3L was used instead. The outcomes of the EQ-5D-3L were higher than the Dutch national average (50). Higher scores for KC patients have been registered before and are mainly due to adaption to the new situation which results in a reconsideration of their quality of life (51). These outcomes were therefore in line with expected values from this population.
A strength of the design was the multicenter facet. The trial was conducted at different types of dermatological departments which each have their specific target population creating a representative study population, making the results more generalizable.

There was no data available on the uptake of such an intervention among dermatologists. To improve the chances of success, a well-defined implementation plan could increase the uptake and increase the chances of the PDL becoming a permanent feature in BCC care (52). Making the PDL available in multiple languages or adding more graphical features can help to include harder to reach populations (53, 54). It is also important that the PDL is easy to create. The less hassle it is to create the letter, the more likely that it will be used in practice. This could be achieved through software that automatically creates the letters and does not require manual adaptations (55).

In conclusion, the PDL decreases the amount of low-value follow-up visits among first-time BCC patients. It is a cost-effective strategy and has a positive impact on the health care budget in the Netherlands. The PDL also provides a solution for the patients' need for more and tailored information, which is valuable in itself. Incorporating this intervention in standard BCC care can improve patients' satisfaction with care, helps to decrease the number of unnecessary follow-up visits, and subsequently lowers the costs.

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Appendix

1. Costs used in the CEA

Cost categories

To decide which costs are relevant for a cost-effectiveness analysis, one first has to decide on a perspective. The recommended perspective in the Netherlands is the societal (1). The societal perspective requires information on costs of the following three categories: medical costs, costs for patient and family, and costs for other sectors (2).

Medical costs

Medical costs consist of direct costs related to the condition that is being studied. In this case, these are all the costs that are relevant to BCC follow-up care. It should also include all indirect medical costs that are created due to life years gained (2). However, this intervention does not seek to lengthen the lives of BCC patients. It strives to lower the health care costs while maintaining the same quality of care. Therefore, the indirect medical costs will not be included in this analysis.

Costs can be measured and valued in two varieties: micro costing and gross costing. The choice impacts the accuracy of the cost estimates (3, 4).

To decide which type of costing is preferable, the guideline was used to see what a follow-up session at a specialist for BCC patients should contain. The guideline states that low-risk BCC patients should receive one follow-up visit within 6-12 months after treatment. A follow-up session should contain these two elements: inspection of the scar tissue and a full check of the skin. It is recommended that dermatologists inform their patients on the probability of recurrence and provide a brochure with information. It is also recommended to instruct patients on self-examination. Finally, the dermatologist should send the GP of the patient an update regarding the diagnosis and treatment (5).

A follow-up session at a GP is rather similar. GPs check the scar tissue and the skin of the patient once after treatment. They also advise patients on self-examination (6).

The aim of this intervention is to spread the innovation through the entire country when proven to be cost-effective. The costs used in the analysis should be generalizable for most dermatology departments and GP practices. Therefore, top-down gross costing is the best option for this analysis.

There are also medical costs created when one uses the intervention. Using the personalized discharge letter requires extra effort from a health care worker. On average it took about 2 minutes to develop and print the letter during the study. The letter has a standard format in which small alterations can be made to make it personal. These alterations include the name of the patient, the subtype of BCC, the location of the BCC, the type of treatment that was used, the name of the dermatologist and the prognosis. The price for the development was calculated by taking the average salary of dermatologists (all tiers) and dividing it into 2 minutes.

To make the letter available electronically, some software adjustments have to be made to existing electronic health records. This requires one adjustment for each system. This article targeted the company with the largest market share. An estimate of €5,000.00 was made for the development and access for one hospital. Any extra hospital that wants to participate has to pay an estimated €1,000.00 to get access to the software add-on. The fee for the software only has to be paid once whereas the actual personalization of the letter comes with costs for each letter.

There is no training required for the creation of the letter. The current software systems that are used in the Netherlands are already capable of creating letters. This is adjustment is simply a new template that has to become available for all dermatologists. The actual making of the letter by a dermatologist does not differ from the other letters that can be created with the software program. Hence, there are no costs added for training.

Costs for patient and family

The questionnaires that were filled in by the patients did not contain questions regarding their travel expenses, the type of transport they used or the distance they had to travel. National averages were used to estimate the costs for travel. The follow-up visit is a very general procedure that can be conducted in every healthcare center by a dermatologist. The expected travel costs are therefore low. In the Netherlands, the average distance to a hospital is considered to be 7.0 kilometers (2). The type of transport is unknown. Patients could travel by foot, car, bike, public transport or cab. When the information is unavailable it is recommended to use the standard tariff for car and public transport since most people travel with these. The standard tariff is €0.19

per kilometer (2). The distance of 7.0 km has to be doubled since patients travel this distance twice; from their home to the hospital and back to their home.

Costs for other sectors

When patients have to be present during a follow-up visit, they cannot use that time to work. This is known as productivity loss. There can be productivity loss for both paid and unpaid work.
Loss of productivity was measured during the trial with the SF-HLQ questionnaire. This questionnaire is considered a reliable alternative of general absence registrations (7).
There are average costs for productivity available. The productivity cost for one hour of paid work differs for men and women. On average, the work of men results in €37,90 per hour. The cost for women is €31,60 per hour. There is no sex difference in costs for unpaid work. The price for this type of labor is €14,00 an hour (2).

TABLE 3: THREE COST CATEGORIES (2)

Medical costs
Follow-up session SP
Follow-up session GP
Intervention
Costs for patient and family
Travel expenses
Costs for other sectors
Productivity loss

*SP = specialist, GP = general practitioner

Price index
The used reference prices date from several different years. The prices were indexed to 2019 using the Dutch derived consumer index prices and rounded to two decimals (8).
The current price of older data was calculated by the following formula (2):

$$reference\ price = older\ price * price\ index$$

Discounting
Since the model calculates results for ten years, both costs and health effects have to be discounted to present values. The Dutch guidelines recommend differential discounting with 4% for costs and 1,5% for health effects (1, 9).
The following formula was used to calculate the discounted prices (2):

$$\sum_{t=0}^{n} K_t\ (1+i)^{-t}$$

In which K_t are the costs in year *t* and *i* is the discounting percentage.

Fixed prices
The entire cost-effectiveness analysis incorporates an uncertainty analysis of its outcomes. However, the input data on costs can also contain uncertainty. This study uses reference prices. These are considered to be given, are nationally assigned, and provided via the Dutch costing manual (2). Therefore, they are free of uncertainty
The costs for a follow-up session at a dermatologist were calculated by Vektis (10). Vektis has access to declarations made by Dutch citizens at their health care insurers. This data provides insight in the average cost of a follow-up session for BCC patients after their first treatment. This number was derived from all institutions in the country which performed these follow-up sessions. This leaves no uncertainty regarding the price of a follow-up session.
The software costs were an estimation made by an IT manager. The actual costs for the software could not be obtained as this would be a tailored project. To correct for uncertainty in this estimation, a scenario analysis will be performed. In this analysis the model will be rerun with different implementation scenarios to ascertain its effect on the outcomes. One scenario was a local scenario, which consisted of implementation in one hospital. According to hospital declaration data in 2018, approximately 1000 new low risk BCC patients were

treated at Erasmus MC. Dividing the €5,000 over these patients results in €5.00 software costs. The other scenario is a national implementation where the price of the software was divided over the number of patients who will benefit from the software update. Of the 77 Dutch hospitals, 50 are currently using the HiX system of Chipsoft, which is 65% (11). About 48,000 individuals are diagnosed with a BCC every year. 65% of the incidence results in 31,169 individuals. Of these, 50% is considered to be low risk resulting in 15,585 individuals who can benefit from this software investment. Dividing the investment over the end users results in €3,47 of investment costs per patient.

Calculations

The following calculations show the average costs per patient associated with each visit and the indexed price for 2019.

Medical costs		**Indexed price**	**Calculations**
Follow-up session SP[a] (10) *Check of scar and skin* *Providing information to patient* *Update GP[b]*	€112.69	**€117.92**	€112.69*1.0464
Follow-up session GP[b] (2) *Check of scar and skin* *Providing information to patient*	€33.00	**€34.45**	€33.00*1.0464/1.0025
Intervention *Development of letter (12)*	€1.58	**€1.61**	(((34.03+38.35+42.91+47.49+52.07+56.66+61.24)/7)/30)*1.0464/1.0301
Software adjustment	€5,000.00	**€5,000.00**	
(Additional software access)	(€1,000.00)	**(€1,000.00)**	
Software costs per patient		**€3.47**	(5,000+(49*1,000))/15,585
Total medical costs			€157.45
Costs for patient and family			
Travel expenses (2) *7,0 km from home to hospital*	€2.66	**€2.78**	((€0.19*7.0)*2)*1.0464/1.0025
Total costs for patient and family			€2.78
Costs for other sectors			
Productivity loss paid work (2)			
Man	€37.90	**€39.56**	€37.90*1.0464/1.0025
Woman	€31.60	**€32.98**	€31.60*1.0464/1.0025
Productivity loss unpaid work (2)	€14.00	**€14.61**	€14.00*1.0464/1.0025
Total costs for other sectors			€87.15

[a] Specialist

[b] General practitioner

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2. Probabilities and utilities for the CEA

Probability of getting a new skin cancer diagnosis

The probabilities were derived from literature and are listed in table 1 (1):

TABLE 4: PROBABILITY OF NEW SKIN CANCER DIAGNOSIS

	BCC after BCC[a]	**cSCC[b] after BCC**	**Melanoma after BCC**
First BCC	0.258	0.045	0.004

[a] Basal cell carcinoma

[b] Cutaneous squamous cell carcinoma

These chances of getting a new skin cancer diagnosis are based on the assumption that the intervention (i.e. reducing the number of follow-up visits) has no effect on the chance of developing new tumors or mortality. This effect has recently been studied in melanoma patients where the number of follow-up sessions was lowered which was deemed as safe and cost-effective (2). This model uses the outcomes of the melanoma study since there is no information available on BCC and cSCC patients as of yet.

Probability of making a control appointment

The probability of making a follow-up visit differ with each type of follow-up. The probabilities are divided into the intervention and control group.

Intervention

The behavior of first time BCC patients who received a personalized letter was monitored for 1 year during the trial. Patients recorded the number of visits they made to the GP or the specialist for their BCC in the surveys. The probabilities are presented in table 2.

TABLE 5: OVERVIEW APPOINTMENTS INTERVENTION

Year	**Probability of making an appointment**
First year	
No appointment	0.209
1 appointment	0.380
2 appointments	0.266
3 appointments	0.114
4 appointments	0.023
5 appointments	0.006
6 appointments	0.002
7-10 appointments	0.000
>10 appointments	0.000

Control

The behavior of 88 first time BCC patients was monitored for five years in unpolished data of a prior Erasmus MC study (3). The probabilities in table 3 are of patients who had a low-risk BCC and no recurrence during these five years. They received standard care and were not exposed to any interventions. These results were used to model the appointments from year two onwards. The results from the first year stem from the data of this trial.

The number of appointments stabilizes after five years. Since the time horizon of the model is set to ten years, the assumption was made that the chance of a patient making an appointment does not change after year five.

TABLE 6: OVERVIEW APPOINTMENTS CONTROL

Year	**Probability of making an appointment**
First year	
No appointment	0.138
1 appointment	0.325
2 appointments	0.375
3 appointments	0.136
4 appointments	0.018
5 appointments	0.006

6 appointments	0.002
7-10 appointments	0.000
>10 appointments	0.000
Second year	
No appointment	0.70
1 appointment	0.21
2 appointments	0.04
3-5 appointments	0.04
6-10 appointments	0.01
>10 appointments	0.00
Third year	
No appointment	0.82
1 appointment	0.12
2 appointments	0.05
3-5 appointments	0.01
6-10 appointments	0.00
>10 appointments	0.00
Fourth year	
No appointment	0.78
1 appointment	0.16
2 appointments	0.00
3-5 appointments	0.05
6-10 appointments	0.00
>10 appointments	0.00
Fifth year	
No appointment	0.94
1 appointment	0.03
2 appointments	0.00
3-5 appointments	0.03
6-10 appointments	0.00
>10 appointments	0.00

Utilities

The utilities for no new tumor and a new BCC were calculated from the EQ-5D-3L using the Dutch tariff (4). The calculated utilities are higher than average national scores (5). The EQ-5D-3L is known to be less detailed than the 5L which explains the small impact minor changes have on the overall score (7).

The number of patients who were diagnosed with a melanoma or a cSCC during this study was too low to use the outcomes of the EQ-5D-3L. Two patients were diagnosed with a melanoma and three with a cSCC. Melanoma scores were substituted with results from literature. There is no study that clearly stated the quality of life of cSCC patients alone. Studies frequently combine BCCs and cSCCs when calculating the quality of life for these patients (6, 8, 9). The Global Burden of Disease Study gave both types of keratinocyte cancer the same burden of disease with identical disability weights (10). Therefore, this model assumes that the impact of a cSCC on a patients' quality of life is the same as a BCC. The outcomes of the EQ-5D-3L for BCCs were used for cSCCs as well.

The utilities for every health state overall are expressed in table 4:

TABLE 7: OVERVIEW UTILITIES

Type	Mean utility	SD[c]	SE[d]
Melanoma (11)	0.719	0.211	0.011
BCC[a]	0.910	0.113	0.025
cSCC[b]	0.910	0.113	0.025
None	0.910	0.165	0.010

[a] Basal cell carcinoma

[b] Cutaneous squamous cell carcinoma

[c] Standard deviation

[d] Standard error

Mortality risks

Table 5 specifies the general probabilities of dying per age and gender from the perspective of 2018 in the Netherlands (12).

TABLE 5: OVERVIEW MORTALITY

Gender	Age (on 31st of December)	Probability of dying
Men	18	0.00022
Men	19	0.00032
Men	20	0.00042
Men	21	0.00029
Men	22	0.00045
Men	23	0.00030
Men	24	0.00037
Men	25	0.00046
Men	26	0.00040
Men	27	0.00037
Men	28	0.00057
Men	29	0.00046
Men	30	0.00049
Men	31	0.00065
Men	32	0.00048
Men	33	0.00054
Men	34	0.00050
Men	35	0.00066
Men	36	0.00062
Men	37	0.00082
Men	38	0.00073
Men	39	0.00077
Men	40	0.00074
Men	41	0.00095
Men	42	0.00104
Men	43	0.00116
Men	44	0.00122
Men	45	0.00151
Men	46	0.00132
Men	47	0.00173
Men	48	0.00208
Men	49	0.00202
Men	50	0.00186
Men	51	0.00252
Men	52	0.00292
Men	53	0.00279
Men	54	0.00357

Men	55	0.00378
Men	56	0.00400
Men	57	0.00491
Men	58	0.00538
Men	59	0.00576
Men	60	0.00666
Men	61	0.00715
Men	62	0.00804
Men	63	0.00902
Men	64	0.00985
Men	65	0.01086
Men	66	0.01208
Men	67	0.01315
Men	68	0.01421
Men	69	0.01565
Men	70	0.01724
Men	71	0.01852
Men	72	0.02163
Men	73	0.02399
Men	74	0.02651
Men	75	0.02925
Men	76	0.03180
Men	77	0.03616
Men	78	0.03881
Men	79	0.04482
Men	80	0.05199
Men	81	0.05526
Men	82	0.06791
Men	83	0.07365
Men	84	0.08305
Men	85	0.09376
Men	86	0.11164
Men	87	0.12279
Men	88	0.14195
Men	89	0.15732
Men	90	0.18123
Men	91	0.19571
Men	92	0.21295
Men	93	0.23114
Men	94	0.26255
Men	95	0.28567
Men	96	0.31253

Men	97	0.31726
Men	98	0.33859
Men	99 or older	0.36676
Women	18	0.00022
Women	19	0.00011
Women	20	0.00020
Women	21	0.00020
Women	22	0.00013
Women	23	0.00015
Women	24	0.00018
Women	25	0.00015
Women	26	0.00025
Women	27	0.00022
Women	28	0.00017
Women	29	0.00030
Women	30	0.00027
Women	31	0.00025
Women	32	0.00045
Women	33	0.00030
Women	34	0.00030
Women	35	0.00042
Women	36	0.00038
Women	37	0.00037
Women	38	0.00046
Women	39	0.00056
Women	40	0.00059
Women	41	0.00057
Women	42	0.00089
Women	43	0.00073
Women	44	0.00102
Women	45	0.00095
Women	46	0.00121
Women	47	0.00126
Women	48	0.00126
Women	49	0.00140
Women	50	0.00169
Women	51	0.00191
Women	52	0.00222
Women	53	0.00227
Women	54	0.00254
Women	55	0.00314
Women	56	0.00312

Women	57	0.00387
Women	58	0.00403
Women	59	0.00448
Women	60	0.00506
Women	61	0.00550
Women	62	0.00603
Women	63	0.00660
Women	64	0.00675
Women	65	0.00789
Women	66	0.00841
Women	67	0.00860
Women	68	0.00927
Women	69	0.00988
Women	70	0.01174
Women	71	0.01281
Women	72	0.01403
Women	73	0.01630
Women	74	0.01794
Women	75	0.01864
Women	76	0.02202
Women	77	0.02405
Women	78	0.02777
Women	79	0.02993
Women	80	0.03413
Women	81	0.03873
Women	82	0.04460
Women	83	0.05318
Women	84	0.05872
Women	85	0.06952
Women	86	0.08159
Women	87	0.09371
Women	88	0.10502
Women	89	0.12540
Women	90	0.13453
Women	91	0.15635
Women	92	0.17848
Women	93	0.20248
Women	94	0.22220
Women	95	0.24917
Women	96	0.26724
Women	97	0.30390
Women	98	0.31418

Women	99 or older	0.37089

The table 6 specifies the disease specific mortality probabilities associated with basal cell carcinoma, squamous cell carcinoma and melanoma. These rates are under the assumption that new carcinomas are discovered in a relatively early stage and that there are no competing risks which can increase the mortality risk of skin cancer.

TABLE 6: DISEASE SPECIFIC MORTALITY

Diagnosis	Mortality probabilities
Basal Cell Carcinoma (13)	0.001
Squamous Cell Carcinoma (14)	0.021
Melanoma (15)	0.071

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3. Scenario analysis CEA software

To monitor the effect of different software implementation on the model's outcome, the model has been rerun with software prices per patient of €5.00 and €3.47.

Table 1 shows the results of the original analysis as presented in the article. In figure 1 one can see the incremental cost-effectiveness plane with the outcomes after both five and ten years.

TABLE 1: ORIGINAL ESTIMATE LOCAL IMPLEMENTATION

Probabilistic results for five years		Probabilistic results for ten years	
Expected costs intervention	€328.89	Expected costs intervention	€368.56
Expected costs control	€354.93	Expected costs control	€394.64
Expected QALYs intervention	4.126	Expected QALYs intervention	7.263
Expected QALYs control	4.124	Expected QALYs control	7.255
Expected incremental costs	- €26.04	Expected incremental costs	- €26.07
Expected incremental QALYs	<0.003	Expected incremental QALYs	>0,008
Expected ICER	- €10,044.79	Expected ICER	- €3,437.90

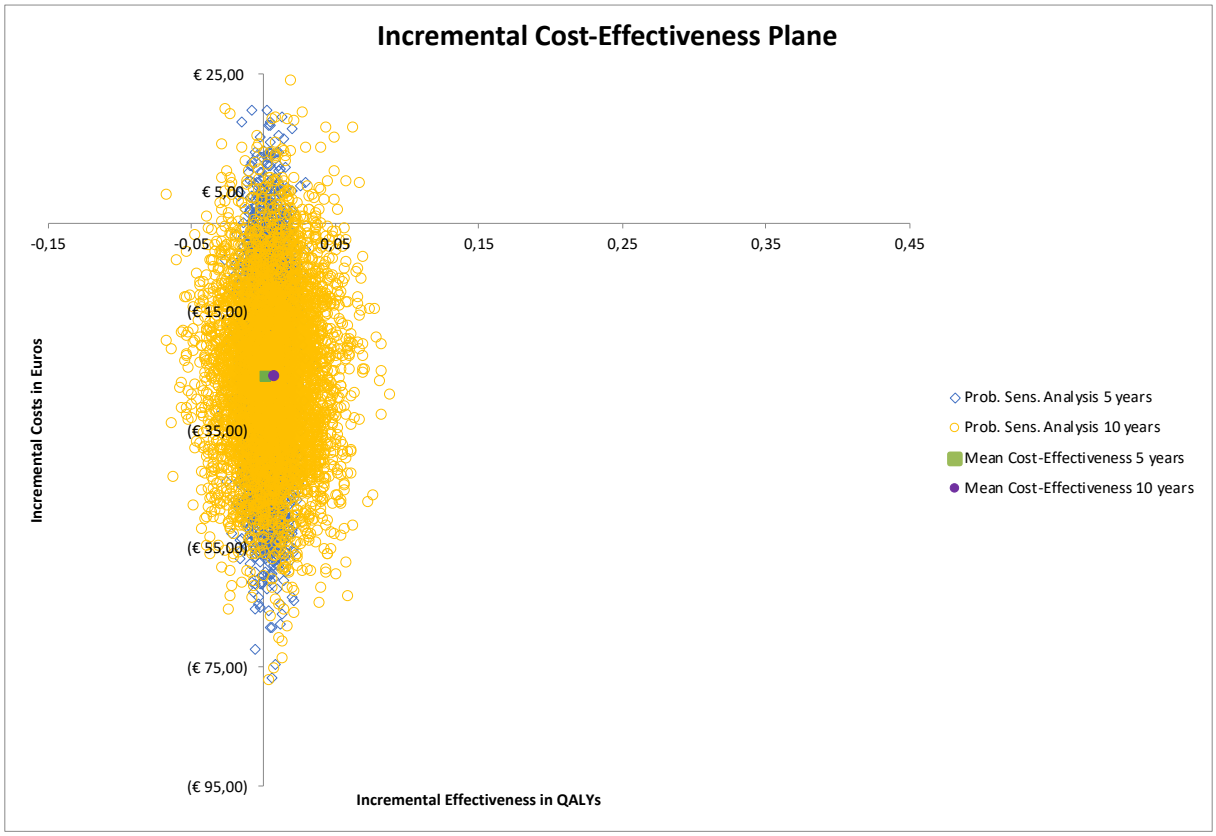

FIGURE 3: INCREMENTAL COST-EFFECTIVENESS PLANE FOR 5 AND 10 YEARS

Table 2 shows the outcomes of the model when the software price can be divided nationally over all eligible patients that are treated in the healthcare centers who use the required electronic patient files. Figure 2 shows the incremental cost-effectiveness plane for both years.

TABLE 2: SCENARIO 2 NATIONAL IMPLEMENTATION

Probabilistic results for five years		Probabilistic results for ten years	
Expected costs intervention	€329.05	Expected costs intervention	€368.54
Expected costs control	€355.44	Expected costs control	€394.92
Expected QALYs intervention	4.126	Expected QALYs intervention	7.261
Expected QALYs control	4.124	Expected QALYs control	7.254
Expected incremental costs	- €26.39	Expected incremental costs	- €26.38

Expected incremental QALYs	<0.003	Expected incremental QALYs	<0.007
Expected ICER	- €12,143.70	Expected ICER	- €3,882.72

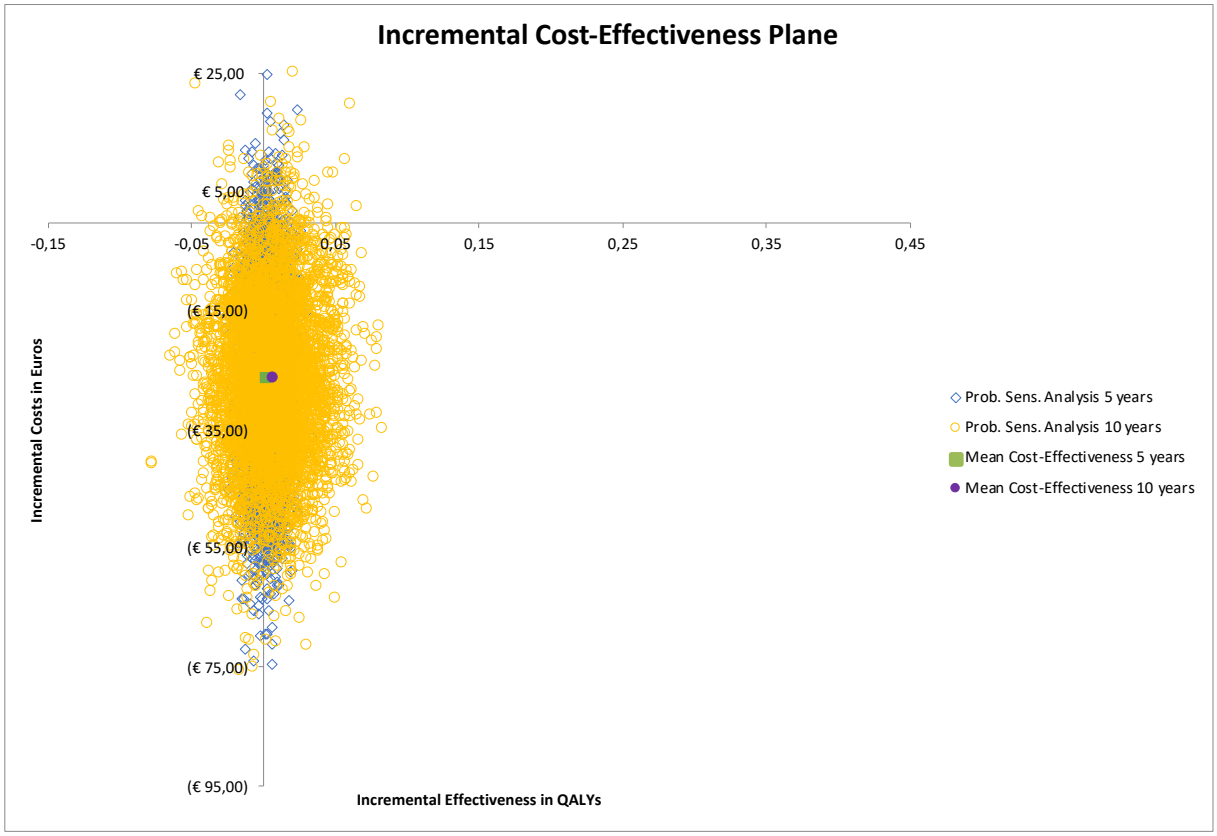

FIGURE 4: INCREMENTAL COST-EFFECTIVENESS PLANE FOR 5 AND 10 YEARS

If the software costs are divided over a national population the five-year cost savings would be €0.35 higher per patient. In ten years, the cost saving would be €0.31 higher. This is a 1.3% and a 1.2% increase in savings. Increasing the number of patients who participate in the intervention affects has very minimal effects on the cost savings per patient. The price of the software has a small effect on the outcome of the model and these scenarios should be recalculated when the definite price is available.

4. Scenario analysis BIA uptake

The uptake of the intervention has an impact on the cost savings that result from it. The more patients participate, the higher the cost savings can become. The budget impact is calculated for different levels of uptake, the cost categories and the implementation setting.

TABLE 1: BIA FOR LOCAL IMPLEMENTATION

Year	2021	2022	2023	2024	2025	Total
Local implementation						
Eligible population	1,260	1,361	1,470	1,587	1,714	7,392
Expected uptake	40%	50%	60%	75%	75%	75%
Patients receiving the intervention	504	680	882	1,190	1286	4,542
Medical costs	-€8,674.92	-€11,711.15	-€15,177.65	-€20,489.82	-€22,129.01	-€78,182.55
Costs for patients	-€590.58	-€797.28	-€1,033.27	-€1,394.92	-€1,506.51	-€5,322.56
Productivity loss	-€3,858.44	-€5,208.98	-€6,750.72	-€9,113.48	-€9,842.56	-€34,774.09
Budget impact	-€13,123.94	-€17,717.32	-€22,961.65	-€30,998.22	-€33,478.08	-€118,279.20
Lower estimate	-€6,561.97	-€10,630.39	-€15,307.76	-€20,665.48	-€22,318.72	-€75,484.33
Higher estimate	-€16,404.92	-€21,260.78	-€30,615.53	-€33,064.77	-€35,709.95	-€137,055.96

The original uptake in the local setting estimates resulted in a cost saving of €118,279.20 after five years. Lowering the uptake, where after five years only 50% of the eligible population receives the interventions created a cost saving of €75,484.33. A high uptake of the intervention saved €137,055.96. Lowering the uptakes drops the cost saving by 36.2%. A higher uptake increases the saving by 15,9%.

TABLE 2: BIA FOR NATIONAL IMPLEMENTATION

Year	2021	2022	2023	2024	2025	Total
National implementation						
Eligible population	30,247	32,667	35,280	38,103	41,151	177,448
Expected uptake	40%	50%	60%	75%	75%	75%
Patients receiving the intervention	12,099	16,333	21,168	28,577	30,863	109,040
Medical costs	-€211,039.55	-€284,903.39	-€369,234.79	-€498,466.97	-€538,344.33	-€1,901,989.02
Costs for patients	-€14,367.29	-€19,395.84	-€25,137.01	-€33,934.97	-€36,649.77	-€129,484.88
Productivity loss	-€93,866.30	-€126,719.51	-€164,228.49	-€221,708.46	-€239,445.13	-€845,967.89
Budget impact	-€319,307.34	-€431,064.90	-€558,660.12	-€754,191.16	-€814,526.45	-€2,877,749.96
Lower estimate	-€159,653.67	-€258,638.94	-€372,440.08	-€502,794.10	-€543,017.63	-€1,836,544.43
Higher estimate	-€399,134.17	-€517,277.89	-€744,880.15	-€804,470.57	-€868,828.21	-€3,334,590.99

In the national implementation the expected budget impact was -€2,877,749.96. With a lower uptake it resulted in €1,836,544.43 cost savings. The higher uptake was €3,334,590.99 of cost savings. A lower uptake reduced the budget impact with 36.2%. A higher uptake increased the budget impact with 15.9%.