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# General discussion and conclusions



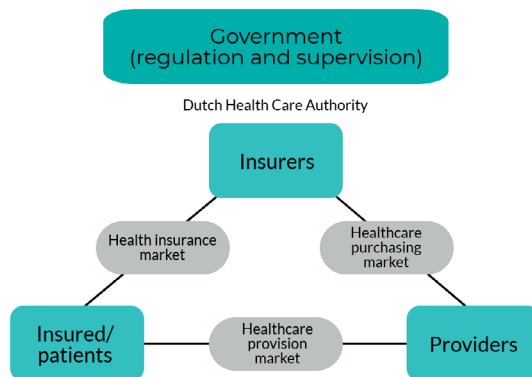
With the ultimate goal of this thesis being to explore and evaluate potentially effective innovations in skin cancer care, we started with exploring the economic burden of skin cancer, followed by an evaluation of healthcare providers' current practices and performances in skin cancer management, to identify existing issues. Next, we explored the views of target groups and identified potential innovations. In the final part of this thesis we tested and evaluated the feasibility of these innovations.

This final chapter summarises and discusses the main outcomes of this thesis, and draws conclusions on the value of the innovations for improving skin cancer management. Finally, this chapter ends with implications for future research and discusses future perspectives.

## ECONOMIC BURDEN OF SKIN CANCER (PART I)

To gain insight in the current situation in terms of costs related to skin cancer care and to identify potential problems or areas for improvement, part I of this thesis was focused on exploring the economic burden of skin cancer care. Although it was already known that skin cancers have the highest incidence rates of all cancers in the Netherlands, and that their incidence rates have been increasing at a higher pace compared to other cancers, a comprehensive overview of the overall costs of skin cancer management was thus far lacking. The study presented in **Chapter 1.1** showed that skin cancer is currently the fourth most costly cancer in the Netherlands, with reimbursed costs being over €465 million in 2017. These costs can be virtually divided into two main groups: (1) expenditures on medical specialist care, and (2) drug expenditures. Within both groups, two separate effects can be distinguished: the price-effect and the volume-effect.

Regarding the first group (i.e. expenditures on medical specialist care), rising expenditures are mainly the result of the volume-effect rather than the price-effect. In other words, the rising expenditures are mainly affected by the rising incidence of skin cancer and therefore increasing patient volume. This conclusion can be drawn from the fact that mean costs of medical specialist skin cancer care decreased, while the total costs increased over the last years. The decreasing mean costs of medical specialist skin cancer care are likely to reflect successful price negotiations between health insurers and providers. In 2006, regulated competition was introduced in the Dutch healthcare system in which three actors (i.e. health insurers, providers and patients) operate in three markets: (1) healthcare purchasing market, (2) healthcare provision market, and (3) health insurance market (Figure 1). In the healthcare purchasing market, health insurers and providers negotiate on price, volume and quality of care, supervised by the Dutch Health Care Authority (Nederlandse Zorgautoriteit).<sup>1</sup> Thus, due to effective price negotiations in the healthcare purchasing market, a price effect regarding expenditures on medical specialist care seems less applicable.



**Figure 1.** Actors and markets in the Dutch healthcare system since 2006, simplified. Adopted from Kroneman et al.<sup>1</sup>

Although health insurers and care providers are increasingly successful in lowering the prices of both medical specialist care and pharmaceuticals<sup>2</sup>, drug expenditures keep on rising due to both a price effects as well as a volume effect. Firstly, the price-effect results from the introduction of new and relatively expensive drugs, driving up the prices. Starting in 2012, many new drugs related to skin cancer care have been introduced into the Dutch healthcare system, including rather expensive targeted and immunotherapies. This price effect is reflected by the increasing mean costs per patient for (both generic and add-on) drugs, from an average €478 per patient in 2012 to an average €2,278 per patient in 2017. Secondly, the volume-effect resulting from the increasing patient volume also applies to drug costs. Whereas the unique number of patients receiving pharmaceutical treatment for skin cancer was 35,601 in 2012, this increased up to 52,910 patients in 2017. Note that this concerns the unique number of patients, meaning that if a patient receives multiple drugs for skin cancer treatment in one year, he/she is only counted once. Therefore, these numbers may be an underestimation of the overall number of patients who receive pharmaceutical treatment related to skin cancer therapy.

With both a price-effect and volume-effect, pharmaceutical treatment seems to have an increasingly important role in skin cancer care. The share of expenditures for skin cancer pharmaceuticals increased from 0.3% in 2007 to 26% (€120/€465 million) in 2017. This is much higher compared to the overall (non-skin cancer specific) ratio, being 8.8% (€2,078 million/€23.498 million) in 2017.<sup>2</sup> Furthermore, with the share of expenditures on expensive new drugs increasing faster relative to expenditures on hospital care, it seems pharmaceutical treatment is suppressing other forms of care, such as surgical care and photodynamic therapy. Though, this not necessarily results in increasing expenditures. For example, since 2013, reimbursement for photodynamic therapy has been restricted in the Netherlands, due to pharmaceutical treatments such as 5-fluoruracil proven to be at least as effective, though less expensive.<sup>3,4</sup>

With skin cancer costs increasing fast, future costs are projected to reach €1.35 billion in 2030, based on an annual increasing skin cancer incidence rate of 5% and inflation rates. Furthermore, additional costs related to the Dutch market entry and broadened indications of several pharmaceuticals were taken into account as well in calculating future projections.<sup>5</sup> However, these additional costs are only known for the 2 years following our dataset (i.e. 2018 and 2019). As the uncertainty is much greater in the further future, it is assumable our future projections are a substantial underestimation of future economic burden. However, it must be noted that the increasingly important role of pharmaceuticals and associated costs is currently receiving a lot of attention. As a result, several initiatives such as EU-wide negotiations on drug prices, no cure no pay models and safe stop study for immunotherapies (EudraCT: 2018-001384-23) are currently launched to counteract the high and increasing drug costs.

Moreover, as evolving demographic and economic trends gain momentum, optimizing the efficient use of resources is increasingly essential and warranted for sustainable healthcare. Previous studies indicated geographical variation in skin cancer care provision, for example concerning referral rates, which could not be fully explained by differences in patient characteristics such as age, sex, comorbidities or socioeconomic variation.<sup>6-8</sup> Therefore, it is suggested there is scope for improving efficiency and decreasing cost of skin cancer care. However, in order to optimize care in terms of efficiency, a thorough study of current healthcare consumption and management was needed to identify areas for improvement.

## CURRENT SKIN CANCER MANAGEMENT (PART II)

In part II of this thesis our aim was to gather knowledge about healthcare providers' current practices and performances regarding AK care, by assessing current patterns of provided care and to explore possible deviations from current guidelines including the reported motives.

In **Chapter 2.1** we explored the healthcare utilization of patients with AK, and the management of AK by healthcare providers in both primary and secondary care. Firstly, our results suggested insufficient awareness of AK exists, with almost 70% of people with AK in a population based cohort not having a AK-related visit in their GP record. Although this number decreased to 50% for those with  $\geq 10$  AKs, thus being extensive, these numbers are still alarming as it implies the potential of under diagnosis and under treatment of AK while having an increased risk of KC. This limited awareness or familiarity in the general population was previously demonstrated in a telephonic interview study, showing whereas 30% of respondents were aware of BCC, only 7% were aware of AK.<sup>9</sup>

Secondly, the management of patients with AK in primary care was found to lack efficiency regarding choice of treatment and referral, due to limited risk stratification by GPs. Similar findings were reported regarding the management of KCs by our colleagues.<sup>10</sup> Furthermore, inappropriate treatments such as antibiotics were chosen in 2% of AK treatments and 6% of KC treatment, although this is likely to be an underestimation since failure to accurately diagnose skin lesions may also result in inappropriate treatment options being chosen. Together with the found underutilization of topical therapies, this may lead to unnecessary costs and suboptimal outcomes.

Thirdly, also the management of patients with AK in secondary care lacked efficiency regarding follow-up regimens. Despite the high and non-stratified referral rate of AKs in primary care, which already overburden secondary care with annually 40,000 new patients with cutaneous premalignancies at the dermatologist, extensive rates of follow-up visits in secondary care were observed. Similar findings applied to BCC, with 83% of patients receiving more follow-up in secondary care than recommended.<sup>10</sup> However, for SCC, the authors of the same study were surprised to find lower follow-up rates than recommended in the Dutch SCC guideline for secondary care. For both AK and BCC, the extensive follow-up rates can be considered a low value service, which is defined as services that are of no or little value to patients and should therefore not be provided.<sup>11</sup> This may lead to longer waiting list and limit access to care for high risk patients, resulting in insufficient use of healthcare resources.<sup>12</sup>

Although the quantitative study signalled the aforementioned AK practices in primary and secondary care, a qualitative study was needed to reveal the underlying motives of healthcare providers. Therefore, an in-depth qualitative interview study was conducted among 40 dermatologists and GPs (**Chapter 2.2**). Qualitative studies, more specifically individual interviews, were considered the most appropriate method to explore current practices and underlying motives, as it encourages participants to propagate their views and opinions freely.<sup>13-18</sup>

Our qualitative study (**Chapter 2.1**) revealed that, for GPs, a lack of knowledge and experience and low perceived value of AK were the main factors contributing to care provision divergent from guidelines for patients with AK in primary care. For dermatologists, it appeared guideline-driven AK care was pursued, although patient preferences and patient-related factors often influenced the choices made.

The provision of care for patients with AK seemed to be vary between GPs. Whereas some reported this to be guideline-conforming, others reported less familiarity with different aspects of AK management. For this latter group, lacking knowledge and experience in AK care, in addition to the absence of a primary care guideline at the time of the interviews, were main contributing factors. Some GPs also indicated that a resulting sense of incompetency of GPs influences the high referral rates to secondary care. Furthermore, the concluded insufficient awareness of AK among the general population in the quan-

titative study (**Chapter 2.1**) may also exist among GPs. In our interview study (**Chapter 2.2**), most GPs indicated to lack a proactive attitude regarding the clinical assessment of cutaneous photodamage, motivated by a perceived lack of value and time. Therefore, AK and skin cancer seem to be underestimated in terms of (rising) number of patients, and undervalued in terms of risk by care providers. Interestingly, in Australia where skin cancer has the highest incidence and profound skin cancer awareness campaigns have been in play since the 1980s<sup>19</sup>, automatic checks by the physician seem to occur more regularly.<sup>20</sup> This same study concluded that in countries with the highest incidence rates of skin cancer, awareness and familiarity are higher, and referral rates are lower. Therefore, this identifies a potential target for improvement.

With extensive (and sometimes even lifelong) follow-up visits for AK observed in secondary care (**Chapter 2.1**), we were also interested in the motives behind this. Dermatologists in the interviews indicated this is mainly influenced by patient preferences and other patient-related factors, such as younger age and patients being less capable of checking themselves. Motives for providing more follow-up care than needed for patients with BCCs appeared to be quite similar to the motives of dermatologists found in our qualitative study regarding AK, involving mainly patient preferences.<sup>10, 21</sup> Though, motives for providing less care than recommended by the secondary care guideline for SCCs remain unidentified.

Although patient-centred care is highly valued and increasingly advocated<sup>22</sup>, inefficiency in care provision and overtreatment should be avoided to optimise the use of healthcare resources, both in terms of costs as well as healthcare personnel. A well-known example of patient-demand leading to overtreatment concerns the overuse of antibiotic treatment.<sup>23</sup> Regarding skin cancer, expectations and preferences of patients may not be feasible with secondary care capacity.<sup>24</sup> This is already seen in AK care with over 40.000 new claims in secondary care annually (**Chapter 2.1**). Therefore, improving clinical outcomes in terms of value should be equally important as patient experience in optimizing care provision. This concept is reflected in multiple international and national initiatives such as 'Choosing wisely', which advocate to provide not more care than needed and not less than necessary.<sup>25-27</sup> As educational interventions (for both patients and provider) have been shown to be effective in reducing overtreatment, for example in lowering prescription rates of antibiotics<sup>23</sup>, an intervention study involving educating patients aiming to reduce follow-up visits is currently being conducted.<sup>28</sup> Hopefully, this may strengthen physicians to curb current overuse of care.

## POTENTIAL INNOVATIONS IN SKIN CANCER CARE (PART III)

For implementing a change in healthcare practice, the primary requisite is urgency.<sup>29</sup> Based on this thesis, showing the rising expenditures (as discussed in **Chapter 1.1**) and care inefficiencies of skin cancer management (as discussed in **Chapter 2.1 and 2.2**), we believe we can say that urgency for change is present, although it may not yet be perceived as such by policymakers and possibly also by care providers. A change is needed to address the increasing pressure on the healthcare system due to the increasing patient volume, with the already overburdened and growing pressure on physicians due to workforce shortages in both primary and secondary care (Figure 2).<sup>30, 31</sup> This increasing pressure will induce time being pressured, which will ultimately affect quality of care.<sup>32, 33</sup> Furthermore, the observed inefficiencies lead to (unnecessary) higher healthcare costs, putting additional strain on the economy.<sup>34</sup> If these issues remain unaddressed and providers carry on with providing care as usual, healthcare spending is expected to continue to increase without enlarging value in return.

Two potential domains to innovate skin cancer, in which we focused on in this thesis, included substitution of care and mHealth. In part III of this thesis, we explored these potential innovations. First, the perceived feasibility to restructure the organisation of skin cancer management by substitution of skin cancer care was assessed, by analysing the views of the target groups. Second, innovating skin cancer care using mHealth was explored by reviewing the development of a smartphone application.



Figure 2. Skin cancer care out of balance. Adapted from KPMG Advisory N.V. 'Healthcare Reimagined' report.

### Substitution of skin cancer care

With healthcare costs growing faster than the economy, one of the frequently mentioned solutions to maintain the sustainability of healthcare is substitution of care.<sup>8, 34-39</sup> Substitution of care implies substituting tasks to primary care, and preventing unnecessary referrals to secondary care. Essential requirements for substitution of hospital care to primary care include (1) the quality of care to be sustained, (2) GPs to have the knowledge and experience to provide the substituted care, and (3) the extent of the disease being sufficient and (4) implementable in primary care (Figure 3).<sup>8</sup> As it is assumed skin cancer care ticks all these boxes, it is viewed as a potential candidate for substitution. By increasing





**Figure 3.** Primary requisites for substitution of care according to NIVEL.<sup>8</sup>

the role of GPs in skin cancer management, the workload and overburdening in secondary care would be decreased and access for high-risk patients improved. Furthermore, it may also benefit patients as care is provided close to home.<sup>40</sup>

Implementation of a change in clinical practice requires a systematic approach.<sup>41</sup> It can be seen as a stepwise process, with the ultimate goal being the desired practice. Whereas several models with different elements on implementing change have been proposed, they all share one essential step: identifying potential barriers to implementing change among the target groups.<sup>41,42</sup> Gaining insight into the target groups views on implementing the change, as well as in their perceived barriers and suggested strategies to improve implementation is of great importance. Furthermore, as different stakeholders may be in a different stage in the implementation process, strategies should be aligned to the different needs in different phases.<sup>41,43</sup>

We first conducted 40 interviews with dermatologists and GPs to explore the general views regarding the concept of substitution of skin cancer hospital care to primary care, and to identify the perceived barriers and potential strategies (**Chapter 3.1**). In addition, focus groups were conducted with GPs with noted willingness to substitute skin cancer care to obtain practical solutions regarding substitution of care.

In **Chapter 3.1**, we found that dermatologists appeared to be more hesitant in their general views regarding substitution, whereas GPs showed more enthusiasm. The concerns among dermatologists seemed to mainly result from the reported barrier of lack of trust in GPs, in addition to patient preferences for dermatologist treatment. Main barriers reported by GPs included lack of confidence in their own skin cancer management skills and perceived lacking trust of patients and dermatologists. In addition, limited time and financial compensation were reported as main barriers for substitution of skin cancer care by GPs.

For substitution of care to succeed, it is essential for dermatologists to trust GPs in providing quality care; especially considering that in the transition phase of implementing substitution, dermatologists are warranted to refer patients back to primary care. If this

trust issue remains unresolved, it is expected that the extensive follow-up rates in secondary care will remain (as discussed in **Chapter 2.1**).<sup>10</sup> This trust issue was affirmed by the GPs in our study; they reported to lack the confidence to perform skin cancer care, which could be traced back to insufficient undergraduate and postgraduate skin cancer training.<sup>40, 44-49</sup> Therefore, sufficient education seems key if substitution of care is to be implemented. If GPs are expected to have a larger role in skin cancer care, while maintaining high quality of care, it is essential to provide GPs with sufficient education, time and resources to manage skin cancer. Examples for this can be drawn from other countries such as Australia, where GPs can specialise in skin cancer (i.e. GPs with special interest or accredited specialisation) and have an essential role in skin cancer management.<sup>50, 51</sup> However, although outcomes in terms of access to care and referrals improve when GPs with special interest services implemented, the cost-effectiveness of such a model remains understudied.<sup>52</sup>

The selected GPs with noted willingness in our study, being a step ahead in the process of substitution, proposed several models as practical solutions to overcome the reported barriers (**Chapter 3.1**). These practical solutions predominantly involved restructuring the current care provision, such as an outreach model of care. An outreach model of care implies a dermatologist to consult in coherence with a GP in a primary care setting. Although it initially seems to address several barriers, such as educating GPs, improving collaboration between GPs and dermatologists, and possibly increasing dermatologists' trust in GPs, the outreach model in itself is not seen as a pure form of substituting care. Several former studies have shown outreach models to be associated with even higher costs, questioning the cost-effectiveness of such models.<sup>53-55</sup> Nevertheless, the model is currently being tested in multiple centres in the Netherlands with a focus on patient outcomes and cost-saving (*Source: <https://www.phizi.nl>*).

### **mHealth in skin cancer care**

All around the globe and in different sectors, there is a rising interest in mHealth. In **Chapter 3.2** we have reviewed the development of the SkinVision smartphone application, which provides a tool for skin lesion risk-assessment. As the domain of e-health and mHealth is a rapidly evolving field, repeated validations are pivotal. Our study (**Chapter 3.2**) revealed that the latest version of the algorithm yielded a 95% sensitivity (78% specificity) to detect skin cancer. It may therefore serve lay persons and/or patients to obtain a more active role in disease screening/management. Therefore, it is believed it has the potential to reduce the burden of skin cancer in several ways. Firstly, easy access to a high quality assessment of skin lesions may reduce the need for doctor visits, thereby lowering the pressure on physicians and prioritize resources for patients with higher risk.<sup>12</sup> Secondly, its use may lead to detection of skin cancers at an earlier stage, when their prognosis and treatment are more favourable. This may lead to lower overall skin cancer management costs, for

example due to decreasing the need for systemic treatment (such as expensive targeted and immunotherapies for late stage melanoma, as discussed in **Chapter 1.1**).<sup>56</sup>

However, over diagnosis and false-positive ratings may increase healthcare utilization and unnecessary diagnostic efforts.<sup>57</sup> In addition, as a previous study showed many patients experience feelings of anxiety by self-measuring and uncertainty about deviating measurements<sup>58</sup>, it questions whether use of such tools may even lead to increased consumption of healthcare resources and doctor visits. Though, current evidence on the benefits and harms of such a tool are currently insufficient to come to a final verdict.

The impact on the healthcare system of implementing this tool may also depend on where it is implemented (i.e. care providers, skin cancer patients, lay population) and the support among stakeholders. Previous studies have assessed the support for such applications among care providers and patients, though quantitatively. These survey studies revealed the support for these tools to vary between and within target groups. Whereas the majority of healthcare providers support the idea of telemedicine in oncological context, and the use of oncological apps by patients<sup>59</sup>, patients themselves appeared to be more hesitant regarding the use of apps for skin cancer and oncology in general.<sup>60, 61</sup> Though, the high rate of unfamiliarity of patients with such tools may have affected this finding. Despite the driving barrier among patients being the wish for personal contact with a physician<sup>60-62</sup>, almost half of patients questioned in a survey confirmed to think that skin cancer apps may supplement or support the care providers' skin examination.<sup>61</sup>

For successful and efficient implementation of mHealth it is needed to assess the views of the target group, and to identify the perceived barriers and facilitators. Therefore, the next essential step is to qualitatively assess the support of each target group regarding implementation of mHealth tools for skin cancer. This study among lay persons, skin cancer patients and care providers is currently being conducted by our research group. Its results will be essential to inform on implementations strategies.

## **EVALUATION OF POTENTIAL INNOVATIONS IN SKIN CANCER CARE (PART IV)**

In Part IV of this thesis we aimed to address the urgency for change by evaluating the feasibility of several potential domains for innovating skin cancer management, in an attempt to improve efficiency and reduce costs. The first domain for innovating skin cancer care concerned revisiting the organizational structure in terms of substitution of care. The second domain for innovating skin cancer care concerned the feasibility of mHealth tools.

## Feasibility of substitution of care

In a (cluster) randomized controlled trial, the SKINCATCH Trial, we evaluated the feasibility of substituting low-risk skin cancer hospital care towards primary care while maintaining quality of care. The primary outcome of the SKINCATCH Trial, i.e. quality of excisions performed in primary care, could not be measured as a result from low inclusion rate of low-risk BCCs. Subsequently, we were not able to assess the effectiveness of substituting low-risk skin cancer care in practice. Although GPs participating in the trial were enthusiastic regarding the concept of substitution of skin cancer care, which was demonstrated in **Chapter 3.1**, effective substitution appeared to be hindered by substantial existing barriers. Therefore, a process evaluation was conducted alongside the trial, in which trial-related barriers to substitution of low-risk BCC care were identified, as well as barriers which were also applicable outside the trial setting (**Chapter 4.1**).

We found that although the highly valued short training course had a 100% exposure, implementation of the trial recommendations (i.e. excision of low-risk BCCs in the primary care setting) was insufficient. Barriers applicable to the trial setting which contributed to this finding mainly involved the administrative challenges. The barriers that also applied outside the trial setting consisted predominantly of low patient volume and patient preferences for dermatologist treatment. As mentioned earlier, sufficient patient volume is one of the essential requirements for substitution of care (Figure 3).<sup>8</sup> While the volume of skin cancer patients is deemed sufficient, only a smaller (and insufficient) proportion appears to be considered low-risk (BCC) when taking into account body site, diameter and histological subtype.<sup>63</sup> However, it must be noted that within the trial setting we opted for more strict criteria for the classification of low-risk BCC; in the trial setting a diameter >1 cm was considered non-low-risk, whereas guidelines hold a margin of >2 cm.<sup>64</sup> The rationale behind this was that excisions of skin lesions >1 cm in diameter are likely to warrant more advanced reconstruction, which we considered not to be feasible in primary care (i.e. the fourth requisite for substitution of care; Figure 3).

The second main barrier to substituting skin cancer care towards primary care concerned patient preferences for dermatologist treatment. It may therefore be concluded that patient preferences not merely seem to have a large role in current inefficiencies in skin cancer care (as discussed in **Chapter 2.2**), but that this also seems to hinder innovative changes (**Chapter 4.1**). Though, these patient preferences for referral to the dermatologist may not be as 'black-and-white' as reported by the dermatologist and some GPs. For example, as discussed in **Chapter 3.1**, there seems to be a substantial group of patients that expressly insists on being treated by the GP. Also, questionnaires among the participating patients in the SKINCATCH Trial revealed that patients referred to a specialist primarily preferred treatment by a specialist, while patients treated by only the GP primarily preferred the GP.

Although substitution of low-risk skin cancer care was not deemed feasible in the current setting, in **Chapter 4.2** we studied the effect of education and training of GPs on the diagnostic accuracy of skin tumours. Previous studies have shown the majority of GP consultations for a suspicious cutaneous lesion end up being benign.<sup>65-67</sup> With increasing incidence and burden of skin cancer, the demand for accurate detection increases as well, highlighting the crucial role of the GP as a gatekeeper.<sup>65, 67</sup> In addition to the increasing demand for high diagnostic accuracy, it has previously been shown that time restrictions in primary care result in less provision of therapeutic services by GPs leading to higher referral rates to secondary care.<sup>32, 49, 65, 66, 68, 69</sup> The increasing burden in primary care therefore ultimately has an impact on the burden in secondary care.<sup>65</sup>

By several research groups, including ours, it has been previously stated that education is key.<sup>40, 44-49</sup> Although previous studies evaluated the effect of training of GPs based on picture assessments, effects based on real-life assessments were lacking. In our study, in which we evaluated real-life assessments, additional education of GPs indeed resulted in significant improvement of the diagnostic accuracy (**Chapter 4.2**). A short training course resulted in the positive predictive value (PPV) of the GPs clinical diagnosis being 56%, compared to 39% for GPs without additional training ( $p < 0.05$ ). However, the significant effect disappeared when the differential diagnosis of the GPs was also considered (PPV 76% for the GPs with additional training versus 69% for GPs without additional training).

As a result of the additional short training course, the use of biopsies increased (76% versus 26%,  $p < 0.05$ ). Furthermore, it significantly affected the number of referrals to secondary care, with 39% direct referrals in the care-as-usual group versus 14% in the intervention group ( $p < 0.05$ ). Even though the overall number of referrals did not significantly differ between both groups, the number of justified (i.e. malignant tumours) referrals did significantly improve (80% in the intervention group versus 55% in the care-as-usual group,  $p < 0.05$ ). With GPs being the gatekeeper in the current setting, this is a highly important finding as additional education and training has the potential to limit or maybe even prevent unnecessary delays in diagnosis and referrals. Ultimately, improving GPs knowledge and skills in skin cancer care will optimize the use of resources, thereby reduce healthcare expenditures.<sup>65</sup>

### Feasibility of mHealth

Although machine learning algorithms have been available for a long time, its embedment in smartphones (i.e. mHealth) is fairly new. Continuing improvements and sophistication of artificial intelligence (AI) technologies result in a rapidly evolving field. Therefore, repeated evaluations are pivotal. In **Chapter 4.3**, we validated the latest version (October 2018) of the SkinVision application risk assessment algorithm. This evaluation showed a substantial improvement over previous versions of the app; its sensitivity increased from 80% (in a prior version) to 95%. Though, the specificity, which is more difficult to validate

due to lacking histopathological confirmation of benign lesions, is somewhat lower at 78%. False-positives feed the discussion on the effect of implementing this tool on healthcare consumption, as previously mentioned. However, especially worrisome is the risk associated with false-negatives if the app is used by lay persons. Though, it must be noted this issue is addressed by the SkinVision service, as every image is verified by an in-house dermatologist to control the quality of the risk rating algorithm. Still, sufficient effort is required to reduce false-negative assessments to a minimum.

Technology in healthcare is widely perceived as an enabler for the urged healthcare transformation. Although these technologies are rapidly evolving and show promising results to improve skin cancer screening (**Chapter 4.3**), some aspects such as delivery of predictions and their definite role in current skin cancer management remain unclear.<sup>12</sup> For optimal and sustainable implementation of mHealth, it is advocated for all parties, including patients, healthcare professionals, entrepreneurs and government, to act together.<sup>70</sup> The government has a pivotal role in enforcing and facilitating mHealth, and their focus should be on new healthcare models stimulating (implementation of) innovations. Furthermore, a crucial element is encouraging digital readiness; we need to move from 'doing digital' to 'being digital'.<sup>71</sup> This includes signalling why the transformation is necessary and demonstrating the beneficial effects of using digital tools, to facilitate engagement by care providers and patients. Since people, and possibly physicians in particular, are naturally reluctant to change<sup>72</sup>, government policy forces may be pivotal in moving to the next step.

## FUTURE PERSPECTIVES

Our exploration of skin cancer care in the Netherlands shows there is room for optimizing the use of resources in both primary and secondary care, for example by improving risk stratification in primary care and reducing follow-up in secondary care. As both annual spending<sup>73</sup> as well as incidence rates<sup>74</sup> of skin cancer have been shown to increase at a faster pace compared to other cancers, this is causing great concern. Therefore, the time has come to transform skin cancer care and to invest in prevention to constrain growth of this heavy burden disease.

### Skin cancer care transformation

Although stakeholders and policy makers are generally positive regarding substitution of skin cancer care towards primary care, the feasibility of its implementation in practice remains questionable. Substantial additional educational efforts are needed, also to address the main perceived barrier of both GPs as well as dermatologists. Even though these efforts showed to significantly improve the diagnostic accuracy of GPs, still 24% of the skin lesions is not reckoned and 44% is inadequately diagnosed. This is likely to lead to the

use of non-indicated treatments, wasting unnecessary time and resources. Furthermore, GPs emphasized the need for compensation in time and means if they are to take over low-risk skin cancer care, as the workload in primary care has already been stated to be unsustainable.<sup>32, 33, 75</sup> As providing education for GPs nationwide also requires a substantial investment, we wonder if this may ultimately lead to skin cancer expenditures to increase rather than to decrease.

As diagnostic and treatment skills of GPs as gatekeepers currently seem insufficient, it may be questioned whether we should invest in improving GPs' education for these purposes, or rather change focus to improving the GPs' approach to skin tumours. In the current setting, with GPs as gatekeepers, additional education showed to significantly improve the appropriateness of referrals. This provides a step towards optimizing the use of resources due to secondary care not being overburdened with benign and premalignant skin lesions. Ultimately, we believe this will also signal dermatologists to refer patients back to primary care earlier on, when they see GPs will adequately refer patients when needed.

Although these efforts reduce the workload in secondary care, it increases the efforts needed in primary care. Furthermore, this does not resolve the issue of the increasing skin cancer patient volume heading towards primary care in the upcoming years. If we want GPs to perform to the best of their ability, we need to address this high and increasing workload as well. One way of doing so is by focussing on self-care at a population level<sup>76</sup>, which is where mHealth comes in. We have already mentioned it a couple times: mHealth has a great potential to optimize the use of resources. As there are not enough dermatologists or skilled GPs to meet the increasing demand of patients with skin lesions, use of risk assessment tools in a patients' own home has the potential to alleviate pressure of the healthcare system. The use of a risk-assessment tool rather than a definite diagnosis makes it also more easy to understand for lay persons. Furthermore, the relative ease and speed of this assessment makes it easily accessible as long as you have a smartphone compatible with the app.

The most obvious place for apps for skin lesion risk assessment is implementation with lay persons, as this is also initially the purpose of the app. Implementation processes are currently being undertaken for example in the NHS in the UK and by one of the largest insurance companies (CZ) in the Netherlands. Though, its' use may also be implemented at other places in the healthcare system. It may be opted to implement these technologies in primary care. For example, the SkinVision application is currently being tested as a tool for triage in several primary care practices in the Netherlands. It may also be implemented in the GPs' consultation room, to support GPs in skin lesion risk assessment and/or diagnosis.

Needless to say, implementation of technologies come with challenges and concerns. As currently the issue of false-negatives withstands, which is of particular concern when the app is implemented with lay persons, clinical validation of should be encouraged continu-

ously as the technology rapidly evolves. Though, as these flaws are frequently pointed out by critics, we must not forget: doctors make these mistakes too. Furthermore, besides the risk of false-negative assessments, lay persons may not have the insight and/or knowledge which skin lesions is worrisome and which is not. This emphasizes the importance of public skin cancer awareness programs discussed later.

Though exhibiting high potential, this does not imply AI is to replace physicians; people ultimately want to see people, especially when it concerns their health. If we want these technologies to be fully adopted by consumers, we need them to associate these technologies with the health system itself, rather than with the technology providers. Therefore, it seems crucial for these technologies to be integrated seamlessly with the physical healthcare provision. One of the suggestions to accomplish this, is to remove or reduce the 'gatekeeper' role of the GP in accessing dermatology care, replacing it with technology. This means that when a patient receives a risk assessment at home, and when the skin lesion is considered to be medium- or high-risk by the algorithm, the patient is given direct access to secondary care.

In the ongoing debate about the implications of gatekeeping, valid arguments have been raised on either side.<sup>77</sup> Examples of arguments for gatekeeping include system efficiency, cost containment, and reduced waiting times in secondary care, whereas examples of arguments against gatekeeping include increased GP workload, increased costs due to delayed diagnosis and suboptimal treatment. Especially with changing patient demographics and increasing demand in primary care, many countries cite workload in general practice as becoming unmanageable. Therefore, questions are raised on whether or not to remove or reduce the gatekeeper role of GPs. Furthermore, with implementation of technologies, many, if not all, of the arguments for gatekeeping may no longer apply. For example, the argument that gatekeeping leads to lower use of health services and prevents flooding of secondary care may not be relevant anymore as the technology may serve as a tool to restrict this. Though, evidence on the health impact of mHealth innovations in skin cancer care is currently lacking. Therefore, we believe future studies need to address this paucity of health impact data, before its widespread adoption may be considered.

With the advancing digitisation of society, the question is how to exploit this to the greatest possible extent rather than if digitisation will change the provision of healthcare. Healthcare is a challenging area when it comes to change, and reimbursement and regulatory issues have been a major factor in holding back the implementation of mHealth. Besides subsidizing implementation strategies, governmental influence and enforcement are needed for transformative changes to happen.

### **Skin cancer prevention programs**

Although skin cancer prevention is not a main topic in this thesis, we cannot neglect this issue: while skin cancer is one of the most occurring and costly cancers, it is also one of the



most preventable.<sup>40, 73, 74, 78-80</sup> In addition to optimizing the use of resources in an attempt to lower healthcare costs, lowering costs over time is also dependent on early intervention and prevention measures. However, it seems health policy makers have limited attention regarding this heavy burden disease, reflected in the relative shortcomings in its prevention. It is likely that the perceived limited value of skin cancer is due to its associated low mortality.<sup>78</sup> Though, with future skin cancer costs projected to reach €1.35 billion in 2030, it seems crucial for policymakers to gain control over this heavy burden disease.

Although the Dutch government adapted more of a supervisor role with the 2006 healthcare reform, it still has an important role in health policy development and implementation, for example regarding disease prevention.<sup>1</sup> Currently, prevention programs in the Netherlands are mainly focused on vaccination programs, screening programs for cervical, breast and colon cancer, and measures to address smoking behaviour, obesity and problem drinking.<sup>81</sup> Despite the high and increasing burden of skin cancer, it had no share in the National Prevention Agreement, which include the ambitions and measures as part of a prevention framework issued by the Dutch government in 2018<sup>81</sup>. This reflects the underappreciation and undervaluation of skin cancer by policy makers.

Skin cancer prevention strategies may be focused on primary or secondary prevention. As UV radiation exposure is the main etiologic factor in all main types of skin cancer, primary prevention focusses on raising awareness and subsequently lowering UV exposure, in an effort to reduce incidence rates. Several studies, and also this thesis, have shown there is a current lack of public understanding and awareness of skin cancer<sup>82, 83</sup>, reflecting the need for public awareness programs on skin cancer. Community-wide and mass-media interventions have internationally been shown to have a positive effect on sun-protection behavior.<sup>84-86</sup> A leading example is Australia, where skin cancer campaigns promote skin cancer awareness among the public (especially regarding preventative behaviour and early detection) since the 1980s, resulting in downturns in skin cancer incidence rates.<sup>19, 87</sup> However, these effective and established skin cancer prevention programs are underused in the Netherlands. Although the Dutch Cancer Society (KWF) started more actively campaigning in recent years on the prevention of skin cancer, for example by educating children in school and commercials, these prevention programs are only minor compared to other countries and other cancers. The government should recognize a substantial and long standing investment is needed to support a multi-faceted skin cancer prevention program in the Netherlands.

Although primary prevention measures are shown to be effective in reducing skin cancer incidence rates, they inherently have a long lag time and require sustained efforts regarding the sun tanning attitude and behaviour of the community. Therefore, in the meantime, it seems just as important to raise awareness among care providers, to facilitate early detection (i.e. secondary prevention). Whereas primary prevention may be effective in reducing incidence rates, secondary prevention has the potential to diagnose skin cancers in

a more early stage when generally less expensive treatments are required, and the chance of treatment being curative is higher. As long as GPs continue to have a gatekeeping role, they (should) have a role in early detection. Although the US Preventative Services Task Force concluded there is insufficient evidence to support a recommendation for skin cancer screening<sup>88</sup>, this was based on evidence on the risk of screening, meaning the number of unnecessary procedures, being less apparent. Therefore, we believe future studies should focus on the health impact of skin cancer screening programs. Furthermore, it would be interesting to assess whether mHealth has a potential role in such screening programs.

We hope that the explorative studies in this thesis will be a good starting point for policy makers in valuing skin cancer and its burden for what it is worth, and recognizing the urgency for change.

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