



Submitted: 1.7.2013

Accepted: 19.9.2013

Conflict of interest

None.

# Quality assurance for care of melanoma patients based on guideline-derived quality indicators and certification

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## Summary

**Background and objectives:** In 2013 the first German S-3 guidelines on the diagnosis, treatment, and follow-up of melanoma were published in the framework of the German Guideline Program on Oncology. Quality indicators were developed at the same time as the guideline development process in order to implement the guideline recommendations.

**Patients and methods:** A multidisciplinary, interprofessional working group developed quality indicators following a standardized process.

**Results:** Twelve quality indicators directly linked to guideline recommendations were generated and agreed on by consensus. They were integrated into the catalogue of requirements for dermato-oncological centers certified by the German Cancer Society.

**Conclusions:** The close cooperation between the guideline group and commission for certification allowed the guideline contents to be implemented in the form of quality indicators in everyday clinical practice. Adherence to the guidelines is required and continuously evaluated as part of certification.

## Background

Malignant melanoma has the highest rate of metastasis of all types of skin cancer. Until just a few decades ago, it was considered to be a rare cancer. Now, according to the Robert Koch Institute in Germany, malignant melanoma is the fifth most common solid tumor in women and the eight most common solid tumor in men [1]. The prognosis is especially poor in patients with advanced or metastatic disease. Reported 5-year survival rates are 78 %, 59 %, and 40 % for tumor stages IIIA, IIIB, and IIIC; in patients with distant metastases, the 1-year survival rates are 62 % in patients with type 1a; 53 % for type M1b; and 33 % for M1c [2]. In recent years, advances have been made in the treatment of metastatic melanoma. All developments which are evidence-based and lead to new guideline recommendations based on interdisciplinary agreement should be included in clinical care.

Guideline-based quality indicators, which are derived from strong recommendations in the current guidelines, may

be used to evaluate the quality of care. They are also important for implementing and subsequently measuring guideline-based processes [3].

There are often hurdles to the implementation of quality indicators [4]. Yet, in the field of oncology, there is a close connection between the oncology guideline program and the certification system for oncological care structures. Quality indicators are adopted in the requirements for certified centers and thus become a part of everyday clinical practice.

Quality assurance by the German Cancer Society for cancer care centers began in 2003 with the certification of the first breast cancer center. The basis for this development were the findings of a European Union working group, which concluded that specialized breast cancer centers were necessary for achieving a significant improvement in survival rates among women with breast cancer [5]. Based on these developments, a three-step cancer care strategy was established, consisting of certified centers; it is now a basic component of the National Cancer Plan of the German Federal government [6].

**Table 1** Status of the certification system (30 June 2013).

	Cancer center (by specialty)						Oncology centers
	Breast	Intestinal	Gyn.	Skin	Lung	Prostate	
Beginning of procedure	2003	2006	2008	2009	2009	2008	2009
Certified centers	216	256	91	39	35	95	46
Certified locations	270	266	93	39	40	96	54
Primary cases: 2011 (total)	50,927	22,224	8,244	9,518	13,449	21,751	–
New reports of cancer <sup>(1)</sup>	69,270	62,956	23,748	18,917 <sup>(2)</sup>	48,986	64,467	–
Total <sup>(1)</sup>	71.7%	35.0%	33.6%	47.9%	27.0%	33.4%	–

<sup>(1)</sup>GEKID data from 2010; <sup>(2)</sup>Only for malignant melanoma

By mid 2013, ten years after the first certification, 840 German centers nationwide that specialize in cancer care had received the a seal of quality from the German Cancer Society (Table 1); 39 of these are certified skin cancer centers in which about 9,500 patients are treated every year after being diagnosed for the first time with melanoma (data from: 31 June 2013).

Certification is based on a questionnaire containing professional requirements as well as a questionnaire on characteristics. The quality indicators and characteristics have clearly defined numerators and denominators which enables analysis and comparable results. Quality indicators and are precisely defined, measurable elements which allow one to assess the quality of care and potential for improvement [7]. The division between quality indicators and characteristics illustrates the difference between how the indices are derived and their different objectives. The characteristics show the goals of a certified network, the interdisciplinary, multi-professional cooperation within the specialty or the expertise of the main treatment partners. Quality indicators are instruments which have been derived from the guideline recommendations using a clearly defined process and added to the questionnaire.

In Germany, the first evidence-based, and consensus-based, guidelines for cutaneous melanoma s were established as part of the guideline program on oncology. This program, produced by the cooperation of the Working Group of Scientific and Medical Societies (*Arbeitsgemeinschaft der wissenschaftlich-medizinischen Fachgesellschaften* [AWMF]), German Cancer Aid (*Deutsche Krebshilfe*), and the German Cancer Society (*Deutsche Krebsgesellschaft*), offers both methodological and financial support for the creation and revision of all evidence-based cancer guidelines (<http://leitlinienprogramm-onkologie.de/Home.2.0.html>). Quality indicators must be derived from the guidelines prior to their final publication; a standardized procedure is used (Figure 1).

## Methodology

In accordance with the methodology in the oncology guideline program, after consensus on the S3 guidelines on melanoma was reached, a multi-professional working group was set up. The group consisted of three guideline committee members from various disciplines, a patient representative, and representatives of the guideline program on oncology and the AWMF. In addition, there was one representative each from different institutions who had already dealt with quality assurance in dermatology: the clinical cancer registry, the certified centers of the German Cancer Society, and the melanoma registry.

The first step consisted of having an external guideline expert on methodology translate the strong guideline recommendations into indicators with defined numerators and denominators. The working group met in person for a preliminary discussion, and strong recommendations were selected. The exclusion criteria were “cannot be operationalized” (in terms of measurability) and “lacking potential improvement in care.” In addition, information from existing indicators – data sets from the melanoma registry and the basic data set of the Working Group German Tumor Centers (*Arbeitsgemeinschaft Deutscher Tumorzentren* [ADT]) – as well as published, international quality indicators (QI) [8, 9], were taken into account. An AWMF-certified guideline moderator was present at the meeting. Consensus was defined as majority agreement (> 75 % of participants).

Similar to the program for the National Health Care Guidelines (*Nationale Versorgungsleitlinien*) [10], the pre-selected set of potential quality indicators (QI) was evaluated by the interdisciplinary committee based on the following criteria: relevance, scientific method, and feasibility of the QUALIFY instrument [11] using a standardized questionnaire (Table 2). Of the 20 QUALIFY criteria, four should be explicitly evaluated, and three may be commented on. The criterion “evidence-based” is implicitly fulfilled by describing

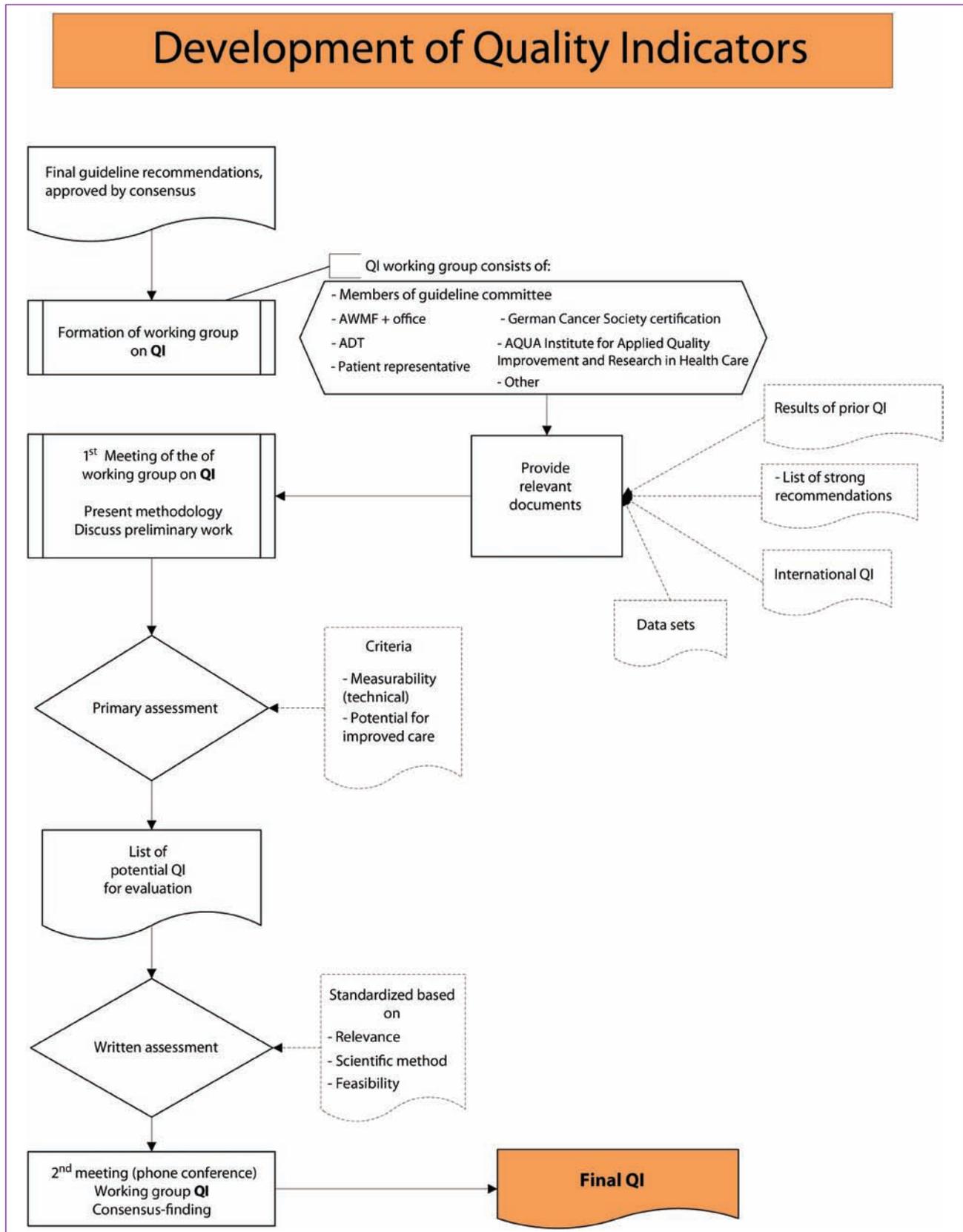


Figure 1 Methodology of guideline based development of quality indicators within the German Guideline program in Oncology.

**Table 2** Assessment sheet for potential quality indicators in accordance with the QUALIFY instrument.

QI No. 1	Possible quality indicator	Guideline recommendation	S3 guidelines on: a) quality goal, b) evidence base			
<b>N:</b>	Patients with radical excision, 1 cm margin of safety	<b>Recommendation No. III.1.a</b> For malignant melanoma, radical excision with curative intent and margin of safety around tumor borders to prevent local recurrence.  <b>LoE 1a, EG A</b> Stage, tumor thickness, margin of safety: pT1, pT2, ≤ 1 mm – 2.0 mm, 1 cm pT3, pT4, 2.01 – ≥ 4.0 mm, 2 cm	a)			
<b>D:</b>	Patients with primary, cutaneous melanoma and curative radical excision, tumor thickness ≤ 2 mm		b) De novo research: Sladden et al. 2010			
<b>Responsible party:</b>	Healthcare providers who can influence the QI.  Healthcare providers who supply the documentation.		1	2	3	4
			Does not apply	Probably does not apply	Probably does apply	Does apply
<b>1. Criterion:</b>						
<i>Importance of QI characteristic for the healthcare system (significance)</i>						
Rate the following statement: “The indicator covers important aspects of quality of life, morbidity, or mortality.”						
<b>2. Criterion:</b>						
<i>Clarity of definitions</i>						
Rate the following statement: “The indicator is clearly and concisely defined.”						
<b>3. Criterion:</b>						
<i>Degree to which the indicator may be influenced</i>						
Rate the following statement: “The quality indicator pertains to an aspect of care that can be influenced by the responsible parties.”						
			<b>Yes</b>		<b>No</b>	
<b>4. Criterion:</b>						
<i>Accounting for potential risks/side effects.</i>						
Answer the following question: “Are there any risks of a controlling error due to the indicator?”						
<b>Comments</b>						
<b>Risk adjustment</b> The following statement is taken into account in the preliminary evaluation: “All known factors that may influence the result of the quality indicator can be accounted for.”						
Are there people to whom the QI does not apply (e.g., age, stage, co-morbidities, etc.)?						
<b>Implementation barriers</b>						
The following statement is evaluated:						
“There are no known barriers to implementation barriers, or, if there are, they may be accounted for with appropriate measures.”						
Are there any notable barriers to implementation?						
<b>Data availability</b>						
The following statement is evaluated:						
“The data are routinely documented by the health services provider, or their documentation involves a reasonable amount of time and effort.”						

**Table 3** Quality indicators of the evidence based guideline “diagnosis, treatment and aftercare of melanoma”.

Characteristic N = numerator D = denominator	Guideline recommendation Level of Evidence (LoE) Source []
<b>QI 1: Margin of safety (1 cm) in radical excision</b>	
<p>N: Patients with radical excision, 1 cm safety margin</p> <p>D: Patients with primary, cutaneous melanoma and curative radical excision, tumor thickness ≤ 2 mm</p>	<p><b>Recommendation</b> For malignant melanoma, radical excision with curative intent and margin of safety around tumor borders to prevent local recurrence.</p> <p><b>LoE 1a [15]</b> Stage, tumor thickness, margin of safety pT1, pT2, ≤ 1 mm–2.0 mm, 1 cm pT3, pT4, 2.01 – &gt; 4 mm, 2 cm</p>
<b>QI 2: Margin of safety (2 cm) in radical excision</b>	
<p>N: Patients with radical excision, 2 cm safety margin</p> <p>D: Patients with primary, cutaneous melanoma and curative radical excision, tumor thickness &gt; 2 mm</p>	<p><b>Recommendation</b> For malignant melanoma, radical excision with curative intent and margin of safety around tumor borders to prevent local recurrence.</p> <p><b>LoE 1a [15]</b> Stage, tumor thickness, margin of safety pT1, pT2, ≤ 1 mm–2.0 mm, 1 cm pT3, pT4, 2.01 – &gt; 4 mm, 2 cm</p>
<b>QI 3: Locoregional lymph node ultrasound</b>	
<p>N: Patients with locoregional lymph node ultrasound</p> <p>D: Patients with malignant melanoma ≥ IB–IIIC</p>	<p><b>Recommendations</b> Locoregional lymph node ultrasound should be performed in patients with a primary diagnosis of malignant melanoma (from tumor stage Ib onward, and in patients with suspected or confirmed locoregional metastasis (stage IIIB/IIIC) of malignant melanoma.</p> <p><b>LoE 1a [16]</b></p>
<b>QI 4: Sentinel node biopsy (SLNB)</b>	
<p>N: Patients in whom SLNB is done</p> <p>D: Patients with primary cutaneous melanoma with a tumor thickness of ≥ 1 mm and without signs of locoregional or distant metastasis</p>	<p><b>Recommendations</b> For staging, SLNB should be done for tumors measuring 1.0 mm or thicker and without evidence of locoregional or distant metastasis.</p> <p><b>LoE 1a [17–23]</b></p>
<b>QI 5: Therapeutic lymphadenectomy (LAD)</b>	
<p>N: Patients with therapeutic LAD in stages IIIB and IIIC</p> <p>D: Patients with malignant melanoma, stages IIIB and IIIC</p>	<p><b>Recommendations</b> Therapeutic LAD should be done if there is detection of lymphogenous metastasis (cytological or histological confirmation, lymph node ultrasound, CT, PET/CT) without detection of distant metastases. (Stages IIIB and IIIC).</p> <p><b>Expert consensus</b></p>

Tabelle 3 Continued.

Characteristic N = numerator D = denominator	Guideline recommendation Level of Evidence (LoE) Source []
<b>QI 6: Postoperative radiation treatment</b>	
N: Patients with radiation treatment with 50–60 Gy in conventional fractionation (5 × 1.8–2.5 Gy/weekly)  D: Patients with malignant melanoma and postoperative radiation of the lymph drainage area	<b>Recommendation</b> If there is an indication for radiotherapy of the lymph drainage area, the dose is 50–60 Gy with conventional fractionation (5 × 1.8–2.5 Gy/weekly).  <b>LoE 2b</b> [24–29]
<b>QI 7: Adjuvant systemic therapy</b>	
N: Patients with adjuvant systemic chemotherapy /dacarbazine  D: Patients with stage I-III malignant melanoma	<b>Recommendation</b> Dacarbazine should not be given as adjuvant therapy for melanoma.  <b>LoE 1a</b> [30, 31]
<b>QI 8: Adjuvant extremity perfusion</b>	
N: Patients with adjuvant extremity perfusion  D: Patients with stage I-III malignant melanoma	<b>Recommendation</b> Adjuvant extremity perfusion with melphalan should not be given as adjuvant therapy for melanoma.  <b>LoE 1b</b> [30]
<b>QI 9: Serum LDH measurements</b>	
N: Patients with LDH measurement  D: Patients with stage IV malignant melanoma	<b>Recommendation</b> As part of the current AJCC classification, serum LDH should be measured in patients with suspected or confirmed distant metastases.  <b>LoE 1b</b> [2, 32, 33]
<b>QI 10: BRAF inhibitor therapy</b>	
N: Patients in whom BRAF-inhibitor therapy has been initiated  D: Patients with stage IV malignant melanoma with a BRAF inhibitor-sensitive mutation	<b>Recommendation</b> Patients with BRAF inhibitor-sensitive mutations should be given treatment with a BRAF inhibitor.  <b>LoE 1b</b> [34].
<b>QI 11: Locoregional lymph node ultrasound during follow-up</b>	
N: Patients with locoregional lymph node ultrasound  D: Tumor-free patients in follow-up of malignant melanoma in stages ≥ IB–IIIC	<b>Recommendation</b> Locoregional lymph node ultrasound should be done in melanoma patients (stage IB onward) as part of follow-up.  <b>LoE 1a</b> [17, 35–37]
<b>QI 12: Skin cancer board</b>	
N: Patients with stage IV disease are discussed by an interdisciplinary skin cancer board  D: Patients with stage VI malignant melanoma	<b>Recommendation</b> Patients with metastatic melanoma (from stage III onward) should be discussed by an interdisciplinary skin cancer board for agreement on further diagnosis and treatment. The possibility of inclusion in a clinical study should be considered.  <b>Expert consensus</b>

the evidence basis of the reference guideline recommendation. In this written assessment, indicators are accepted if they have at least 75 % approval for each criterion.

Finally, there was a moderated phone conference in which the results of the assessment were discussed and the final QI set was defined.

## Results

Based on the above-named methods [12], 12 quality indicators were derived from the 39 strong recommendations contained in the recent S3 guideline (Table 3).

These included the excision margin for the primary tumor, ultrasound diagnosis, surgical removal of lymph nodes with subsequent radiation therapy, measurement of prognostic markers in patients with distant metastases, and follow-up of melanoma patients. Another quality indicator is whether BRAF inhibitor therapy is initiated in patients with the BRAF-V600E mutation. In order to avoid ineffective or unnecessary treatment, certain quality indicators relate to the exclusion of specific treatments. For instance, dacarbazine should no longer be used as an adjuvant systemic treatment for melanoma. Contrary to preliminary studies on historical controls, various prospective randomized studies found no significant benefit among treated patients compared to untreated patients. Nor can adjuvant extremity perfusion with the cytostatic drug melphalan be advised; as there is no evidence that it prolongs metastasis-free survival or overall survival. An essential part of quality treatment is an “interdisciplinary skin tumor conference”, in which all patients with metastatic melanoma should participate to determine further diagnostic procedures and treatment.

## Discussion

With the S3 melanoma guidelines, physicians now have access to current evidence-based recommendations, which have been approved in an interdisciplinary consensus procedure, for the diagnosis, treatment, and follow-up of melanoma patients. A new feature is the methodologically transparent establishment of quality indicators based on strong guideline recommendations. The quality indicators may be used to aid implementation (integrating the strong recommendations into a center’s treatment guidelines) or as an evaluation tool (later evaluation of guideline adherence).

The integration of the majority of indicators by skin cancer treatment centers means that they must show the results for these indicators (and thus the implementation of the guidelines) in their annual audits for certification. The results of the questionnaire on characteristics are analyzed for all centers in an annual assessment. The findings thus provide an

overview of treatment quality at certified centers nationwide [13]. Individual centers can now compare their results with the anonymous results of other centers (benchmarking) and see whether they are near or above average, or where there is a need for optimization. This represents an effective quality assurance (or improvement) instrument, which promotes constructive reflection and discussion by certified centers on the quality of their services based on the guidelines and which may be routinely evaluated in periodic audits.

There are certain limitations to the use of the guideline-based QI presented here. First, only process-related and structural indicators are addressed. Their implementation does not necessarily lead to a desired improvement in patient-relevant outcomes such as quality of life, outcomes, morbidity, or overall survival. Nevertheless, it may be assumed that the recommendations of the guideline group were based on evidence of a positive effect on the endpoints as a result of the advised intervention. Another problem is long-term follow-up of individual patients, given that the centers generally do not provide these data. Connecting the data from the centers with the clinical cancer registries will certainly be useful for depicting the course of disease in patients over time. At present, it is impossible to make any statements about the fulfillment of the QI at centers which are not certified. Yet, once the clinical cancer registries are fully expanded, this information will be available, because the QI from the guidelines will also be included in the data sets of the cancer registries.

The results of the annual assessments will be sent to the guidelines group. The analyses of process and structural indicators will provide the guideline committee with important information on the real situation in cancer care and thus provide the basis for guideline updates. In addition, the results of the indicators form the basis for evaluating quality indicators in an update procedure and help determine whether there is continued need for related improvements in clinical care [14].

The process described here is an example of the quality cycle in cancer care (Figure 2). This provides a solid framework for efficient quality assurance and improvement in the treatment of melanoma patients.

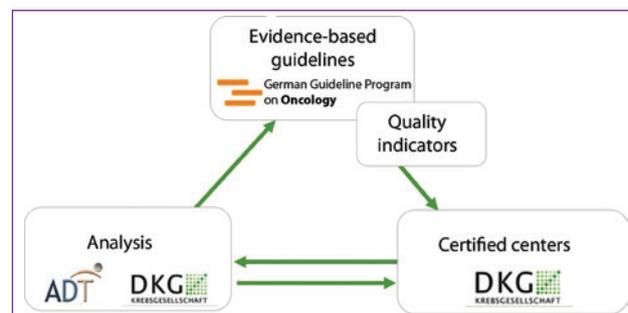


Figure 2 Quality cycle of oncological care.

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