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A comparison of international breast cancer guidelines – Do the national guidelines differ in treatment recommendations?

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ABSTRACT

Aim of the study: Clinical practice guidelines (CPG) are an appropriate method to optimise routine clinical care. Numerous CPGs for the diagnosis and treatment of breast cancer have been developed by national health institutions or medical societies. While a comparison of methodological criteria has been undertaken before, it is unknown whether these CPGs differ in their actual treatment recommendations.

Methods: We included national breast cancer CPGs from the USA, Canada, Australia, the UK, and Germany that satisfy internationally recognised methodological criteria and are in widespread use in daily clinical care. Treatment recommendations for adjuvant invasive breast cancer including surgery, radiation, endocrine therapy, chemotherapy and anti-HER2-therapy were compared.

Results: Recommendations for endocrine therapy show discordances regarding optimal usage of ovarian function suppression for premenopausal patients and aromatase inhibitors for postmenopausal patients. However, most other treatment recommendations exhibit a large degree of congruency. This reflects the fact that they rest on the same evidence base, and that many national guidelines are adopted from other guidelines so that well accepted guidelines are cited within other guidelines.

Concluding statement: Considering that the development of guidelines is a very expensive and resource-intensive task the question arises whether the development of national guidelines in numerous countries is worth the effort since the recommendations differ only marginally.

1. Introduction

Worldwide clinical practice guidelines (CPG) are being developed in all fields of medicine in order to optimise the quality of patient care.[1,2] CPGs exhibit an increasing level of methodological quality due to advanced achievements in health services research (e.g. AGREE II, Appraisal of Guidelines for Research and Evaluation). High-quality evidence-based guidelines are becoming more and more standard practice.[3] However, it is controversial whether high methodological quality of CPG corresponds with the level of validity of the recommendations.[4] In addition, the effectiveness of guidelines

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Table 1 – List of included guidelines.

Country	Organisation	Included guideline(s)
D	(DKG) German Cancer Society	Interdisciplinary S3 guidelines for the diagnosis, treatment and follow-up care of breast cancer[10]
USA	(NCCN) National Comprehensive Cancer Network	Clinical practice guidelines in oncology: breast cancer[11]
	(ASCO) American Society of Clinical Oncology	Breast cancer: guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer[12] Breast cancer: postmastectomy radiotherapy[13] Breast cancer: update on adjuvant endocrine therapy for women with hormone receptor-positive breast cancer[14]
AU	(NBOCC) National Breast and Ovarian Cancer Center	Clinical practice guidelines for breast cancer[15] Recommendations for use of sentinel node biopsy in early (operable) breast cancer[16] Recommendations for aromatase inhibitors as adjuvant endocrine therapy for post-menopausal women with hormone receptor-positive early breast cancer[17] Recommendations for use of taxane-containing chemotherapy regimens for the treatment of early (operable) breast cancer[18] Recommendations for use of trastuzumab (Herceptin®) for the treatment of HER2-positive breast cancer[19]
CA	(CCO) Cancer Care Ontario Program in Evidence-based Care	Surgical management of early stage invasive breast cancer[20] Breast irradiation in women with early-stage invasive breast cancer following breast conserving surgery[21] Adjuvant systemic therapy for node-negative breast cancer[22] Adjuvant ovarian ablation in the treatment of premenopausal women with early stage invasive breast cancer[23] Adjuvant taxane therapy for women with early-stage invasive breast cancer[24] The role of aromatase inhibitors in adjuvant therapy for postmenopausal women with hormone receptor-positive breast cancer[25]
UK	(NICE) National Institute of Clinical Excellence	Early and locally advanced breast cancer: diagnosis and treatment[26]
	(SIGN) Scottish Intercollegiate Guidelines Network	Management of breast cancer in women[27]

depends not solely on the quality of the guideline but also on dissemination and implementation strategies. The ideal way to enforce the application of CPG is controversial[5] and is highly dependent on the national health care system as well as on the specific content of the CPG.

Recently health services research has focused on the analysis of CPG effects. While improvements in the process of care have been shown in different settings,[2,6] effectiveness in terms of better health outcome for the individual patient has as yet been insufficiently studied.[7,8] For the management of early breast cancer, we have previously shown that adherence to CPG improves the outcome significantly.[9]

As breast cancer is the most common female cancer type and is a primary health care problem in the field of oncology, numerous CPG have been developed. More than 140 evidence-based documents under the keyword of breast cancer are specified at the Guideline International Network, and about 70 of them are CPGs. Nevertheless to date no comparison of the contents of breast cancer guidelines frequently used on an international scale exists. Therefore, we systematically compared the recommendations and statements regarding the treatment modalities of surgery, radiotherapy and systemic therapy in early breast cancer in the following CPGs (Table 1).

Apart from some discordance especially in the recommendations regarding endocrine treatment, we have found large congruency between the analysed CPGs, which reflects the fact that the recommendations are mainly based on the same evidence. This raises the question whether the development of national guidelines in numerous countries and organisations should be encouraged in the future.

2. Methods

The aim of this study was not to analyse comprehensively all existing national breast cancer guidelines but we rather focused on those widely used in the daily care setting of oncology and satisfying internationally recognised methodological criteria (e.g. validity, reproducibility, reliability, representative development, clinical applicability, clinical

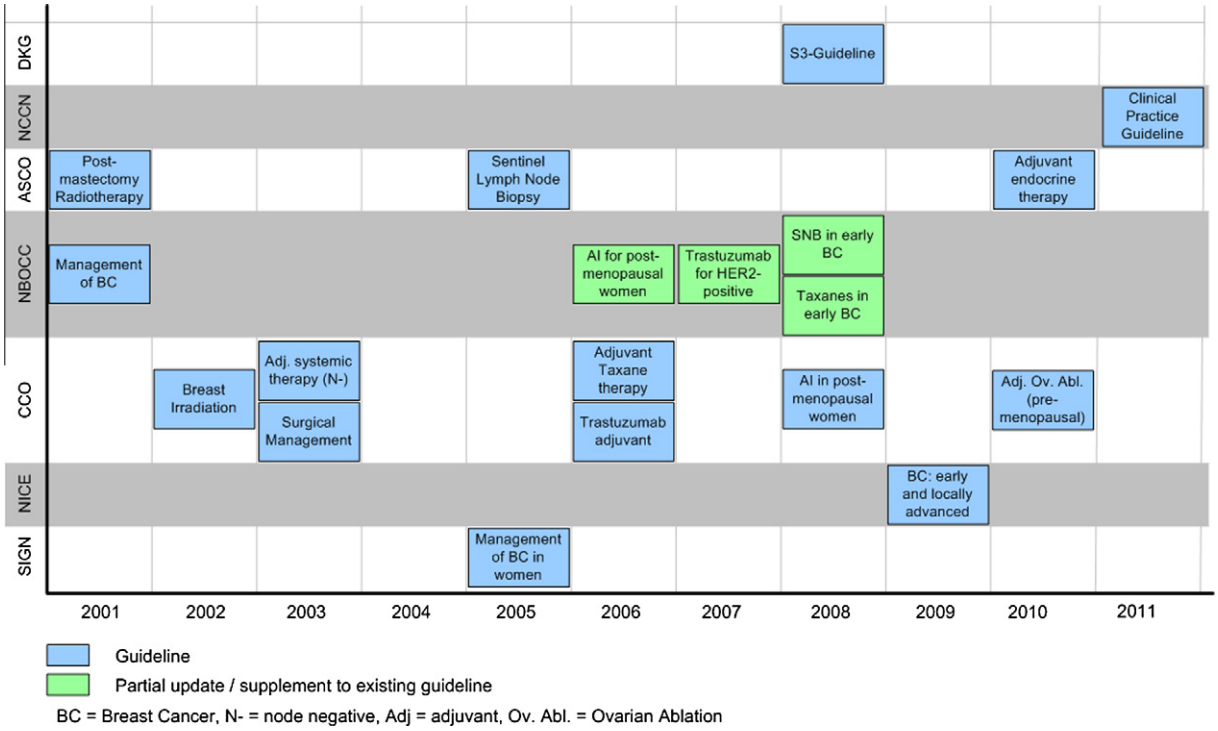

Fig. 1 – Timeline of the development and actualisation of the different guidelines.

flexibility, clarity, meticulous documentation, scheduled review).[28,29] All selected guidelines were published between 2001 and 2011 (Fig. 1). The most relevant therapeutic modalities for adjuvant breast cancer are surgery (breast-conserving therapy, mastectomy, axilla dissection and sentinel-node biopsy), radiation therapy (following breast-conserving therapy and mastectomy), endocrine therapy for pre- and post-menopausal patients, chemotherapy and anti-HER2-therapy. We compared all statements from the CPGs included. In case of a missing recommendation for a specific aspect the explaining texts were reviewed for relevant contents which made them comparable to a recommendation. Only statements regarding invasive breast cancer were considered, since non-invasive breast cancer is not included in this study.

An overview of the subject areas covered by the individual CPG is shown in Table 2. A methodological evaluation of the scientific quality of the guidelines was not provided for this paper but it was found that all of the guidelines use at least consensus and review processes. In addition, CCO guidelines are based on the practice guidelines development cycle,[30] and DKG uses a modification of AGREE.[31,32]

3. Results

The recommendations of all included national CPGs for surgery, radiotherapy and systemic adjuvant therapy were compared and analysed for their congruency.

3.1. *Surgical therapy*

The main issues discussed in the field of surgery are the appropriate surgical procedure (breast-conserving versus mastectomy) and the staging, respectively (resp.), surgery of the axilla (sentinel node biopsy versus axillary dissection) (Table 3). While ASCO and NICE are not covering the area of local surgery, breast conserving surgery (BCS) is recommended by all other guidelines. The indications for BCS are concordant throughout all guidelines: it is indicated for invasive tumours if negative margins can be obtained and if there is a favourable ratio of tumour size to breast volume. For mastectomy resp. as contraindications to BCS the following conditions are stated as indications: extensive malignant microcalcification, multicentricity/multifocality, inflammatory carcinoma, likelihood of an unsatisfactory cosmetic result, contraindication to radiotherapy after BCS, or the patients' preference. They are also concordant – if explicitly given – within the CPGs.

The definition of adequate surgical margins remains controversial. All the guidelines mention the necessity of a negative or clear margin, only the DKG gives an explicit width of 1 mm as minimum on all sides of the tumour.

All CPGs see a clear necessity for the staging of the axilla for invasive tumours. Sentinel node biopsy (SNB) is the preferred method in nearly all guidelines. CCO still recommends axillary dissection as standard care, which is due to the early publishing date (2003).

3.2. *Radiotherapy*

In this section the necessity of radiation after BCS and after mastectomy is analysed (Table 4). Radiotherapy after BCS is recommended by all guidelines (ASCO covers radiation after mastectomy only). Some of the CPGs provide that BCS is contraindicated if radiation therapy cannot be carried out.

Table 2 – Subjects discussed within the different guidelines.

Guideline		Subject											
		Surgery			Radiotherapy		Endocrine therapy		Chemotherapy		Anti-HER2 therapy		
		Mastectomy	BCS	Axilla/SNB	Postmastectomy	After BCS	Premenopausal	Postmenopausal	General	Taxanes for N+		
D	DKG	2008	2008	2008	2008	2008	2008	2008	2008	2008	2008	2008	
USA	NCCN	2011	2011	2011	2011		2011	2011	2011	2011	2011	2011	
	ASCO				2005	2001		2010	2010				
AU	NBOCC	2001	2001	2001	2008	2001	2001	2001	2006	2008	2008	2007	
CA	CCO			2003	2003		2002	2003/10	2003/08	2006	2006	2006	
UK	NICE				2009	2009	2009	2009	2009	2009	2009	2009	
	SIGN			2005	2005	2005	2005	2005	2005	2005	2005	2005	

A necessity for radiation therapy after mastectomy is seen for all cases with a high risk of local relapse, defined by positive margins, more than three positive nodes or tumours with a size of >5 cm. Evidence is unclear for an intermediate local relapse risk and hence the recommendations are phrased less precisely; e.g. for N1–3 DKG states that patients 'can benefit' from radiation, while NCCN recommends to 'strongly consider' radiation for these patients.

3.3. *Endocrine therapy*

Subjects discussed in the area of endocrine therapy are the adequate regimens for premenopausal women (tamoxifen with or without ovarian function suppression) and postmenopausal women (tamoxifen or aromatase inhibitors (AI)) (Table 5).

All guidelines agree that premenopausal women should receive tamoxifen for five years as the treatment of choice. The recommendation for the use of ovarian function suppression is less clear, which reflects the lower level of evidence. While ASCO, CCO and NICE do not recommend ovarian function suppression, DKG, NCCN, NBOCC and SIGN recommend it. This difference can not solely be explained by the differences in publishing dates, but rather reflects on differences in the interpretation of existing evidence.

The statements regarding endocrine treatment of postmenopausal patients are those that differ to the greatest extent of the analysed topics. While DKG, NCCN and ASCO clearly rate AI as superior to tamoxifen, NBOCC, CCO, NICE and SIGN recommend tamoxifen either in general (CCO, SIGN) or for low risk patients (NBOCC, NICE). There is no distinction between the 3rd generation AIs and the different regimens (upfront, switch or extended use).

3.4. *Chemotherapy*

The range of chemotherapy regimens and their combinations is wide and hence the scope of recommendations ranges from general phrases about constellations in which chemotherapy should be performed to explicit recommendations of particular drugs in specific situations (Table 6).

Chemotherapy is indicated in general for all tumours that show a higher risk of recurrence, e.g. tumour size >1 cm or positive lymph nodes. Chemotherapy should be carried out at the recommended dosages of the standardised protocols. Anthracyclin-containing regimens are considered as standard in all guidelines. Taxane-containing regimens are recommended by most guidelines in high risk situations, especially in node positive cases. The slight differences between guidelines are presumably due to the different publication dates.

3.5. *Anti-HER2 therapy*

Anti-HER2 therapy with the monoclonal antibody trastuzumab is indicated for patients with an overexpression of the HER2-neu receptor (Table 7). Guidelines differ in recommending trastuzumab either concurrently or sequentially with chemotherapy.

In most of the CPGs the cardiotoxic effects of trastuzumab are mentioned with clear instructions to the administration

Table 3 – Recommendations for surgery.

	Breast conserving surgery	Mastectomy	SN-biopsy	Axilla dissection	Discordances in recommendations
DKG (2008)	R	R	R[a]	R[b]	[a]SNB is preferred method [b]Axillary dissection must be carried out with removal of at least 10 lymph nodes from levels I and II
NCCN (2011)	R	R	R[a]	R[b]	[a]SNB is preferred method if there is an experienced sentinel node team [b]The axillary dissection should be extended to include level III nodes only if there is gross disease apparent in the level II nodes
ASCO (2005)	0	0	R[a]	0	[a]Data suggest that SNB is associated with less morbidity than ALND, but the comparative effects of these two approaches on tumour recurrence or patient survival are unknown
NBOCC (2001/08)	R	R	R[a]	R	[a]Sentinel node biopsy should be offered as a suitable alternative to axillary dissection for women with unifocal tumours equal to or less than three centimetres in diameter and clinically negative nodes
CCO (2003)	R	R/T	R[a]	R[b]	[a]There is promising but limited evidence that is not as yet sufficient to support recommendations regarding sentinel lymph node biopsy alone [b]Removal and pathological examination of level l and II axillary lymph nodes should be the standard practice in most cases of stage I and II breast carcinoma
NICE (2009)	0	0	R[a]	0	[a]SLNB is the preferred technique
SIGN (2005)	R	R	T[a]	R	[a]Sentinel node biopsy is only recommended as part of a randomised controlled trial or following an evaluated training programme

(R = recommendation, T = textual information, 0 = no recommendation/textual information, SNB = sentinel node biopsy, ALND = axilla lymph node dissection).

and control of cardiotoxic effects. NBOCC only recommends that the combination with anthracyclines is contraindicated due to cardiotoxicity.

3.6. *Level of evidence (LoE) and grade of recommendation (GR)*

Besides the comparison of the therapeutic modalities a methodological aspect deserves attention: every analysed CPG uses a different classification of LoE and GR (Table 8). DKG and SIGN indicate LoE and GR for each recommendation, DKG uses the Oxford classification schemes,[33] SIGN in contrast uses the NICE-classification for LoE and its own classification for GR. ASCO and CCO do not refer to any classification scheme at all. ASCO has preferred not to use classification schemes to assign levels and grades to recommendations; instead evidence summaries, recommendations and the status of evidence are given for each topic.[34] NICE, NCCN and NBOCC use their own categorisations for LoE.

The number of categories for LoE varies in between the guidelines from 4 (NCCN, NBOCC) to 10 (DKG/Oxford). Therefore, a direct mapping of the levels is impossible, but nevertheless the highest level (e.g. meta-analysis) is always indicated by 1 (1a/1++/I).

4. Discussion

More than 70 evidence-based documents specified at the Guidelines International Network under the keyword of breast cancer are CPGs. While a methodological analysis of a number

Table 4 – Recommendations for radiotherapy.

	Radiotherapy after breast conserving therapy	Postmastectomy radiation	Discordances in recommendations
DKG (2008)	R	R[a]	[a]Only for T3/T4, R1/R2 resection, pN+ (>3)
NCCN (2011)	R[a]	R[b]	[a]Consideration of partial breast irradiation if N– [b]No radiation if: N– and $T \leqslant 5$ cm and margins $\geqslant 1$ mm
ASCO (2001)	0	R[a]	[a]N+ (>3), T3, stage III
NBOCC (2001)	R	R[a]	[a]High risk of relapse ($T > 5$ cm, pN > 3, positive margins)
CCO (2002)	R	0	
NICE (2009)	R	R[a]	[a]High risk of relapse (pN > 3, positive margins)
SIGN (2005)	R	R	

(R = recommendation, T = textual information, 0 = no recommendation/textual information).

Table 5 – Recommendations for endocrine therapy.

	Five years tamoxifen	Ovarian ablation	Discordances in recommendations
(A) Premenopausal			
DKG (2008)	R	R[a]	[a]Ovarian function suppression can have a positive impact on the disease; treatment with GnRH-analogue for at least 2 years
NCCN (2011)	R[a]	R[a]	[a]Tam +/– ovarian suppression for 2–3 years, switch to AI if patient is postmenopausal or continue Tam; consider extended ET if patient is postmenopausal after 5 years Tam
ASCO (2010)	R	0[a]	[a]The role of ovarian suppression in addition to tamoxifen for premenopausal patients is not known
NBOCC (2001)	R	R[a]	[a]Ovarian ablation reduces risk of recurrence
CCO (2003/10)	R[a]	0[b]	[a]Patient at moderate risk, for patients at high risk chemotherapy is recommended [b]Ovarian ablation should not be routinely added to systemic therapy with chemotherapy, tamoxifen, or the combination of tamoxifen and chemotherapy
NICE (2009)	R	0[a]	[a]Do not offer adjuvant ovarian ablation to premenopausal women with ER-positive early invasive breast cancer who are being treated with tamoxifen and, if indicated, chemotherapy. Offer adjuvant ovarian ablation/ suppression in addition to tamoxifen to premenopausal women with ER-positive early invasive breast cancer who have been offered chemotherapy but have chosen not to have it
SIGN (2005)	R	R[a]	[a]Combination of tamoxifen plus ovarian ablation should be offered before tamoxifen therapy alone

	Aromatase inhibitor upfront for 5 years	Two to three years of tamoxifen followed by aromatase inhibitors	Five years tamoxifen followed by 5 years of aromatase inhibitor	Five years tamoxifen	Discordances in recommendations
(B) Postmenopausal					
DKG (2008)	R	R	R	0[a]	[a]Third-generation aromatase inhibitors are superior to tamoxifen

Table 5 – (*continued*)

	Aromatase inhibitor upfront for 5 years	Two to three years of tamoxifen followed by aromatase inhibitors	Five years tamoxifen followed by 5 years of aromatase inhibitor	Five years tamoxifen	Discordances in recommendations
NCCN (2011)	R	R	R	0[a]	[a]Women with contra-indication to aromatase inhibitors, who decline aromatase inhibitors or who are intolerant of the aromatase inhibitors, should receive tamoxifen for 5 year
ASCO (2010)	R	R	R	0[a]	[a]Postmenopausal patients intolerant of one AI may be advised to consider tamoxifen or a different AI
NBOCC (2006)	R	R	R	R[a]	[a]For low-risk women
CCO (2003/08)	R	R	R	R[a]	[a]Adjuvant tamoxifen remains an acceptable option for the treatment of women with hormone receptor-positive, early-stage breast cancer
NICE (2009)	R[a]	R	R[b]	R[c]	[a]Postmenopausal women with ER-positive early invasive breast cancer who are not considered to be at low risk should be offered an aromatase inhibitor, either anastrozole or letrozole, as their initial adjuvant therapy. Offer tamoxifen if an aromatase inhibitor is not tolerated or contraindicated [b]Offer additional treatment with the aromatase inhibitor letrozole for 2–3 years to postmenopausal women with lymph node-positive ER-positive early invasive breast cancer who have been treated with tamoxifen for 5 years [c]Offer tamoxifen to low risk patients or if an aromatase inhibitor is not tolerated or contraindicated
SIGN (2005)	R[a]	R[b]	R[b]	R[a]	[a]In postmenopausal women with breast cancer tamoxifen remains the treatment of choice as initial therapy in the adjuvant setting. If there are relative contraindications to its use (high risk of thromboembolism or endometrial abnormalities) or intolerance, an aromatase inhibitor can be used in its place [b]Postmenopausal patients should be considered for a switch to an aromatase inhibitor after either two to three years or after five years of tamoxifen therapy

(R = recommendation, T = textual information, 0 = no recommendation/textual information, ER = oestrogen receptor).

of national breast cancer guidelines was recently undertaken by the German Institute for Quality and Efficiency in Health Care (IQWIG),[28] a direct comparison of the content of treatment related recommendations has not been made so far.

Our analysis of the most relevant therapeutic modalities revealed a large congruency of treatment recommendations. This is not surprising since all guidelines have been developed by using similar high quality methodologies. Nevertheless, we have found some discordance between the analysed guidelines. We have identified three main aspects that we presume to explain these discordances: (1) different dates of publication, which inevitably lead to different evidence bases; (2) evidence remains unclear, which results in less precise recommendations with gradually varying contents; and (3) different interpretation of sufficient evidence.

In the recommendations for surgical therapy there are only minor variations regarding the adequate surgical margin and SNB. The discordant recommendations of SNB are presumably caused by the publishing dates, whereas the varying definitions of an adequate margin reflect on an unclear evidence base. This is also mentioned as a controversy in the latest St. Gallen expert panel publication.[35] According to St. Gallen, the majority of North American radiation oncologists are willing to accept a margin as negative if the tumour does not extend to the inked specimen surface, while surgeons worldwide and European radiation oncologists prefer a clearance of 2–5 mm in addition to this.[35]

Table 6 – Recommendations for chemotherapy.

	General recommendation for chemotherapy	Taxane containing regimen for N+	Discordances in recommendations
DKG (2008)	R[a]	R[b]	[a]For patients with an elevated risk of recurrence, dose-dense treatments should be administered; however, these therapies should be carried out only at experienced centres [b]Patients with axillary lymph-node involvement should receive an adjuvant combination therapy with taxanes
NCCN (2011)	R[a]	R[b]	[a]Chemotherapy should be considered if tumour is pN1 mi or 0.6–1.0 cm [b]Multiple regimens are listed, no clear recommendation for taxane containing regimens
NBOCC (2008)	R	R[a]	[a]A taxane-containing regimen should be considered for women at intermediate-to-high risk of breast cancer recurrence
CCO (2006/03)	R	R[a]	[a]Taxane-containing regimen for T1–3, N+
NICE (2009)	R	R[a,b]	[a]Offer docetaxel to patients with lymph node-positive breast cancer as part of an adjuvant chemotherapy regimen [b]Do not offer paclitaxel as an adjuvant treatment for lymph node-positive breast cancer
SIGN (2005)	R	R[a]	[a]No sufficient data that they offer additional survival benefits over optimal anthracyclines regimens

(R = recommendation, T = textual information, 0 = no recommendation/textual information).

Table 7 – Recommendations for anti-HER2 therapy.

		Discordances in recommendations
DKG (2008)	R	Trastuzumab can be administered concurrently with a taxane or sequential to anthracycline/taxane-containing chemotherapy
NCCN (2011)	R	If tumour is HER2 positive, trastuzumab should be added in general
NBOCC (2007)	R	Adjuvant trastuzumab should be offered with chemotherapy following surgery in patients with node-positive or node-negative tumours larger than 1 cm Trastuzumab concurrently with an anthracycline is not recommended due to risk of cardiotoxicity Trastuzumab can be offered to patients who require radiotherapy, although long-term toxicity is unknown
CCO (2006)	R	Trastuzumab should be offered for one year to all patients with HER2-positive node-positive or node-negative, tumour greater than 1 cm in size, and primary breast cancer and who are receiving or have received (neo)adjuvant chemotherapy. Trastuzumab should be offered after chemotherapy
NICE (2009)	R	Offer trastuzumab, given at 3-week intervals for 1 year or until disease recurrence (whichever is the shorter period), as an adjuvant treatment to women with HER2-positive early invasive breast cancer following surgery, chemotherapy, and radiotherapy when applicable
SIGN (2005)	R	

(R = recommendation, T = textual information, 0 = no recommendation/textual information).

We have found gradual differences in the recommendations for the indication of radiation after mastectomy. These differences are also induced by an unclear evidence base, especially in intermediate risk patients. The differences regarding the optimal usage of adjuvant chemotherapy concern mainly the indication of taxane-containing regimens.

Table 8 – Classification of level of evidence (LoE) and grade of recommendation (GR).

	Classification for LoE	Classification for GR	Annotation to classification scheme
DKG	Oxford[a]	Oxford[b]	[a]Ten categories from 1a to 5 [b]Four categories (A, B, 0, GCP), connected to LoE, up- and downgrading possible
NCCN	NCCN[a]	0	[a]Four categories (1, 2A, 2B,3), evidence and consensus of expert panel are combined
ASCO	0	0	ASCO has chosen not to use classification schemes to assign levels and grades to recommendations. For each topic evidence summary, recommendations and status of evidence is presented
NBOCC	CHOC[a]	0	[a]Four categories (I, II, III, IV)
CCO	0	0	
NICE	NICE[a]	0	[a]Eight categories from 1++ to 4
SIGN	NICE[a]	SIGN[b]	[a]Eight categories from 1++ to 4 [b]Five categories (A, B, C, D) directly connected to LoE

(LoE = level of evidence, GR = grade of recommendation, 0 = no classification).

These slight differences are presumably mostly caused by the differences in publishing dates.

The indication of adjuvant anti-HER2 therapy is mostly congruent. Slight variations are due to insufficient evidence regarding low risk tumours (especially $T < 1$ cm).

The largest discordance was found in recommendations for endocrine therapy. The optimal strategy for pre- and postmenopausal patients remains controversial. In premenopausal patients the evidence for ovarian function suppression is unsatisfactory, thus resulting in conflicting recommendations. The St. Gallen consensus declares that tamoxifen or tamoxifen plus ovarian function suppression, both for a period of 5 years, are acceptable standards for premenopausal women with endocrine-responsive disease.[35] In postmenopausal patients the recommendations for the usage of tamoxifen or AI differ widely. Although the same high quality randomised controlled trials have been used as evidence base, the interpretation of the results vary considerably. While some CPGs rate the consistent benefit in terms of a reduced risk of breast events, albeit unclear overall survival (OS) benefit, as sufficient to recommend AI, others emphasise on an unclear risk–benefit ratio in terms of long-term toxicity and OS and hence do not recommend AI.

A formal comparison of the guidelines is impossible since different systems of LoE and GR classification are used. The employment of one standard classification scheme or at least an indication of how to map the different classification schemes would facilitate considerably the comparison of contents and methodological aspects. Future guideline developments can profit from the GRADE (Grades of Recommendation Assessment, Development and Evaluation) method to evaluate evidence and recommendations. In GRADE evidence is classified into four categories (high, moderate, low and very low) with the possibility to increase or decrease it according to the expert panel's opinion, and recommendations are categorised as beneficent or harmful.[36]

Despite the discordances described above, in our analysis most recommendations exhibit a large degree of congruency. This is due to the fact that they are mainly based on the same evidence and that many national guidelines are adoptions from other guidelines so that well accepted guidelines are cited within the new guideline. As this leads to recommendations with only marginal differences, the question arises whether the development of national guidelines in numerous countries is worth the effort and expenditure, since the development of guidelines is a very expensive and resource intensive task. The German Society of Cardiology, for example, has recently decided to stop the national development of clinical practice guidelines and instead has intensified its commitment to the international guideline development. If needed, comments on the respective European guideline are prepared by the Society.

A discussion is needed whether the current practice of developing guidelines on a national level should be encouraged, or whether international collaboration – for instance the St. Gallen consensus conference – should be emphasised. On the other hand national distinctive features are certainly existent leading to significant variations in breast cancer incidence, biology, and prognosis in a comparison of different countries.[37] These national characteristics are composed of e.g. racial disparities (African American women have a higher mortality albeit a lower incidence than non-Hispanic whites in the USA),[38] socio-economic status,[39] life style factors and different health care systems resp. access to health care. On the other hand, however, the large majority of data that have to be analysed during the process of developing guidelines are not country specific but can be generalised for all breast cancer patients.

The benefit of using CPGs depends also on their actuality. Due to the time consuming process of developing CPGs a certain gap between the CPG and the newest evidence is inevitable (e.g. intraoperative radiotherapy is not recommended by all guidelines). As long as several guidelines exist, a time line for updating them should be explicitly given in all guidelines, as is already recommended for high methodological quality.

The development of guidelines consists of the identification and analysis of the existing evidence, and the formulation of the recommendation text. But also the dissemination and implementation strategies are an integral part of the CPGs and are of no less importance for the aim of improving breast cancer management in general. We suggest that the guideline development process should be optimised by centralisation of the actual evidence based work, which is not specific of any country. On the other hand, the distinctive country-specific features should be analysed and transcribed on a national level. This might lead to a more efficient process and will help to optimise CPGs.

Conflict of interest statement

None declared.

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