Consensus on Postoperative Recommendations After Transsphenoidal Surgery

A Study Among Pituitary Surgeons in Germany and Review of Literature

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Key words

pituitary tumor, transsphenoidal surgery, postoperative recommendations

received 16.05.2018

revised 15.07.2018

accepted 26.07.2018

Bibliography

DOI <https://doi.org/10.1055/a-0664-7710>

Published online: 21.8.2018

Exp Clin Endocrinol Diabetes 2019; 127: 29–36

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ISSN 0947-7349

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AGREE Reporting Checklist 2016 Online content viewable at <https://doi.org/10.1055/a-0664-7710>

ABSTRACT

Background Guidelines for patient behavior following transsphenoidal surgery do not exist. To gain generally recommendations, the German pituitary working group conducted a study among pituitary surgeons to elucidate their opinions and customs of patients' counselling.

Methods Questions concerning daily activities, exertion of sports and work life were addressed. It was asked to provide the postoperative time interval after which specific activities can be resumed both after a routine or an extended approach.

Results Fourteen pituitary surgeons returned the completed questionnaire. Following routine operations, washing the hair was allowed within one week, blowing the nose after 3, flying on an airplane and driving a car after one, lifting heavy weights after 4, playing wind instruments after 6, use of CPAP (continuous positive airway pressure) device after 3, permit leisure sports after 2 to 4 weeks (except for scuba diving). Competitive sports can be resumed after 6 weeks. Occupation with mental demands was considered feasible after 2 weeks, with physical labor after 4 weeks. After extended transsphenoidal surgery, the recommended time interval was roughly twice as long compared to the routine approach. Driving a car was allowed within the first 4 weeks after surgery by some pituitary surgeons, while others allow driving only after 3 months analogous to the regulations after craniotomy. The risk of scuba diving was considered high.

Conclusions The data of our study and the literature, and expert opinions from related scientific fields resulted in a consensus on recommendations for patients' conduct to minimize risks after transsphenoidal surgery.

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Introduction

For more than 40 years, transsphenoidal surgery (TSS) is the standard approach to treat pituitary adenomas, most craniopharyngiomas, Rathke's cleft cysts and other, less frequent pathologies of the sellar and perisellar region [1]. Nowadays microsurgery as well as endoscopy is used with very good results in experienced hands [2–4]. Although different complications of TSS have been reported, it is considered to be a safe procedure, with the complication rate depending on the surgeons experience [5, 6] (6,9 % major complication, 0,7 % death). However, guidelines for patients' level of activity following TSS do not exist. Therefore, the neurosurgeons of the pituitary study group of the German Society of Endocrinology (DGE) started a nationwide survey of the current practice in counselling their patients postoperatively. Stepwise they came to a consensus statement. The focus of this report is on the advice related to the surgical approach only. The recommendations, however, may differ considerably in individual cases depending on the endocrinological, neurological, and ophthalmological state given.

Subjects and Methods

The study was initiated by the speaker of the Pituitary Study Group of the German Society of Endocrinology (DGE). A digital questionnaire was sent to 22 German neurosurgeons who are known to be actively involved in pituitary surgery. Fourteen of 22 pituitary surgeons returned the completed questionnaire (64 %), 9 with microsurgical and 5 with endoscopic focus.

The surgeons were asked about their personal experience with rules of conduct for patients following TSS, namely how many transsphenoidal procedures they had performed or supervised in the preceding year (2016), and how many such operations had been performed in their institution in that period. Moreover, the participants were asked to state whether they mainly use the microscope or the endoscope during TSS. Endoscopically assisted microsurgical technique was assumed microscopic.

The queries addressed both a routine transsphenoidal approach and an extended transsphenoidal approach (e. g. transtuberulum-sellae or transclival approach). The participants were asked to provide the postoperative time interval after which specific activities could be resumed by their patients. The questions addressed 3 topics: daily activities, exertion of sports and work life.

Daily activities

washing the hair, nose blowing, sauna, playing wind instruments, flying on an airplane, lifting heavy weights (about 12 kg, assumed equivalent to a crate of mineral water), driving a car, using a CPAP (continuous positive airway pressure) -device, and having sexual intercourse.

Recreation sports

Nordic walking, jogging, swimming (breaststroke – head above water, and crawl – head under water), scuba diving (snorkeling at the surface assumed to be equivalent to crawling), playing tennis, and playing soccer.

Performing competitive sports.

Work life

Occupation (for 8 h per day) with mental demands or physical labor.

Process of study

Initially, the project was presented and discussed at the meeting of the German pituitary working group. The questionnaire was designed by JBH and UJK and sent to the German pituitary surgeons. The results were graphically presented and discussed at a following meeting of the pituitary working group and a core group of pituitary surgeons (authors) was constituted to screen the relevant literature (via PUBMED), and to elucidate related scientific issues of the items. During 3 telephone conferences, joint recommendations were elaborated. The results were brought together in a manuscript which was then presented to all participating neurosurgeons and consultants, asking for approval, to reach the highest possible grade of agreement. All participants and consultants approved the recommendations as described in this manuscript. The manuscript was checked following the AGREE reporting checklist [7] as far as applicable.

Results

Participants

Fourteen pituitary surgeons returned the completed questionnaire, 9 of them with microsurgical focus and 5 of them with endoscopic focus. During one year (2016) these surgeons were responsible for 1004 (range 8 to 270, mean 72, median 50) transsphenoidal procedures. Of these, 846 operations have been performed using microscopic technique (range 38 to 270, mean 94, median 59), 158 using the endoscope (range 8 to 41, mean 32, median 40). In the institutions of the participants 1060 transsphenoidal operations had been performed in 2016 (range 8 to 286), indicating that most procedures had been performed/supervised by the participating individuals. Consequently, this report reflects the experience with about 1000 transsphenoidal procedures per year.

There was no significant difference of times after which activities could be resumed between surgeons with endoscopic or microsurgical focus (exemplary illustrated in ► Fig. 1), however, independent from surgical technique used, some surgeons tended generally to be more offensive, others more cautious.

Recommendations after routine operations

Daily activities (see Fig. 1)

For nose blowing the answers varied between few days and 8 weeks (median 3 weeks). The authors agreed to use the median of 3 weeks as a common recommendation (► Table 1). In case of intraoperative CSF-leak, blowing the nose is allowed after 4 weeks.

Washing the hair was unanimously allowed in the first week after surgery. Discussion between the authors revealed, that in case of intraoperative CSF-leak the patients should refrain from bending the head downward during washing the hair for 3 weeks.

Having a sauna was permitted after 1 to 12 weeks (median 4 weeks). Recommendation after discussion: 4 weeks (► Table 1).

Playing wind instruments was permitted between 3 and 12 weeks postoperatively (median 6 weeks). After discussion with a consultant for music physiology and musician's medicine (EA),

► **Fig. 1** The expert opinions of 14 German pituitary surgeons about postoperative daily activities following a routine transsphenoidal procedure are shown. The postoperative time interval after which various daily activities can be resumed is depicted (• or ○ individual answer, — final consensus recommendation). There is no significant difference between recommendations after microsurgical (N=9, •) or endoscopic (N=5, ○) procedures.

6 weeks could be the starting point of gradual increase in activity (see below).

For flying on an airplane the primary statements varied between a few days and 8 weeks (median 1.5 weeks after surgery). The recommendation of 1 week would allow patient's transfer to motherland after discharge by airplane. Discussion pointed out, that in case of intraoperative CSF-leak absence of free intracranial air is obligatory (e. g. proven by CT-scan).

Lifting a weight was defined as the equivalent to raise a crate of mineral water, which would be at least 12 kg in Germany. The primary statements varied between a few days and 8 weeks (median 4 weeks), a consensus of 4 weeks was found by the authors.

The majority of pituitary surgeons allowed driving a car early after operation (range a few days to 12 weeks, median 1 week), after discussion between the authors the recommendation was 5 days after surgery. This would allow the patient to drive home by car on discharge. However, two surgeons opted for 12 weeks, following general guidelines of intracranial surgery. For safety reasons, in routine cases also electrolyte imbalance (e. g. hyponatremia) has to be ruled out prior to driving a car.

The results varied considerably concerning the use of a CPAP device (range immediately to 12 weeks, median 3.5 weeks). The

► **Table 1** Instructions for patients' behavior after routine transsphenoidal pituitary surgery or extended transsphenoidal approach for perisellar lesions created from statement of 14 pituitary surgeons, who stand for about 1000 transsphenoidal operations per year.

Activity	routine transsphenoidal operation [weeks]			extended transsphenoidal approach		
	range	median	recommendation	range	median	recommendation
daily activity						
blow the nose	<1 – 8	3	3 ^A	1 – 12	4	4 ^A
wash hair	<1 – 1	<1	<1	<1 – 2	<1	<1
have a sauna	1 – 4	4	4	2 – 12	4	4
wind instrument	3 – 12	6	6 ^B	3 – 26	8	6 ^B
fly on airplane	<1 – 8	1.5	1 ^C	<1 – 8	2.5	2 ^C
lift heavy weight	<1 – 8	4	4	1 – 26	6	6
drive car	<1 – 12	1	<1 ^D	<1 – 12	4	2 ^G
use CPAP	<1 – 12	3.5	3 ^A	<1 – 12	4	4 ^A
have sex	<1 – 4	1	1	<1 – 8	3.5	2
sports						
walking	<1 – 4	2	2	<1 – 6	3	3
jogging	<1 – 6	4	3	<1 – 12	5	4
breaststroke	1 – 8	4	4	2 – 12	6	6
crawl	1 – 8	4	4	2 – 12	6	6
dive	4 – 26	8	12 ^E	6 – 0	12	12 ^E
tennis	<1 – 8	4	4	4 – 12	7	6
soccer	<1 – 8	4	4 ^F	4 – 12	8	8 ^F
competitive sp	4 – 12	6	6	6 – 12	12	10
occupation (8 h/d)						
mental demands	<1 – 3	1.5	2	<1 – 4	2	3
physical work	<1 – 6	3.5	4 ^A	2 – 12	6	6 ^A

^Alonger in case of intraoperative CSF leak (see text). ^Bstarting point for gradual increase in activity (see text). ^Cexclusion of intracranial air provided, e. g. by CT. ^Dprovided hyponatremia is ruled out and patient feels well (see text). ^Estatement of responsible surgeon mandatory. ^Fno headers. ^Gprovided brain surface not involved by tumor or resection. 0 = never; The recommendations indicate the minimum time interval [weeks] after surgery, when a specific activity may be resumed. The authors emphasize that the ability to resume such activities is also dependent on endocrinological, neurological, ophthalmological, and mental state postoperatively. For details see text.

crucial point for this recommendation is whether an intraoperative CSF-leak was evident or not (see discussion).

Having sexual intercourse was considered by the pituitary surgeons to be permissible after a few days to 4 weeks postoperatively (median 1 week).

Sports (see ► Fig. 2)

Most pituitary surgeons allow leisure sports approximately 4 weeks after surgery: Nordic walking after a few days to 4 weeks (median 2 weeks). Jogging after a few days to 6 weeks (median 4 weeks). Swimming (breaststroke) after 1 to 8 weeks (median 4 weeks). Crawling after 1 to 8 weeks (median 4 weeks). Playing tennis after a few days to 8 weeks (median 4 weeks). Playing soccer after 1 to 8 weeks (median 4 weeks). This median values were confirmed as recommendations during discussion, except for jogging (recommendation 3 weeks). However, during soccer headers should be omitted for 12 weeks.

Heterogeneous opinions existed for scuba diving. Primary recommendations varied between 4 and 26 weeks (median 8 weeks). After interviews with experts for diving medicine, evaluation of relevant literature, and discussion between the authors, it is recommended not to dive earlier than 12 weeks after surgery (see discussion below).

According to the surgeons, competitive sports are allowed between 4 and 12 weeks after surgery (median 6 weeks). The final consent is to resume competitive sports not earlier than 6 weeks after surgery.

Working life (see ► Fig. 3)

Occupation (8 h per day) with mental demands was considered feasible immediately after surgery to 3 weeks postoperatively (median 1.5 weeks). A consensus of 2 weeks was worked out.

The postoperative time interval for continuation of an occupation with physical labor varied between a few days and 6 weeks (me-

► **Fig. 3** The expert opinions of 14 German pituitary surgeons about work life following a routine or extended transsphenoidal procedure are shown. The postoperative time interval after which full-time work life can be resumed is depicted (• individual answer, — final consensus recommendation).

► **Fig. 4** The expert opinions of 14 German pituitary surgeons about postoperative sports activities following an extended transsphenoidal procedure are shown. The postoperative time interval after which various daily activities can be resumed is depicted (• individual answer, — final consensus recommendation).

dian 3.5 weeks), recommendation is 4 weeks. The authors want to emphasize that these recommendations consider the operative approach only. Fitness for work is also dependent on endocrinological, neurological, ophthalmological, and mental state postoperatively.

could be forced through the operative defect and cause tension pneumocephalus [18, 19], for which untreated obstructive sleep apnea, cerebrospinal fluid leaks, postoperative positive-pressure mask ventilation, large pituitary tumors, and intraoperative lumbar drainage catheters were reported as risk factors [20]. Therefore, recommendations to resume these activities not only depend on the extent of the approach (routine vs. extended), but also on the occurrence of intraoperative CSF-leak during routine procedures.

CPAP

Obstructive sleep apnea (OSA) is frequent in patients with pituitary disorder: Particularly in acromegaly, OSA is a frequent presenting symptom, and can be resolved by successful TSS [21]. Many patients with OSA are treated by using a CPAP-device. Affected patients benefit from the use of CPAP or bilevel positive airway pressure (BiPAP) after any kind of surgical procedures. However, both methods could cause pneumocephalus after TSS [22, 23]. Unless contraindicated by the surgical procedure, the use of CPAP-device early after surgery is generally recommended if it was already used by the patients preoperatively [24, 25]. However, currently no consensus exists for the management of OSA patients undergoing transsphenoidal operations [26]. In a series of 469 patients undergoing TSS, 105 were at risk for OSA, and 10 of them developed postoperative hypoxemia which was treated with low-flow oxygen using face mask. However, three of them required a CPAP device not earlier than 2 days after surgery. None of them had an intraoperative CSF-leak, and no complications occurred after application of CPAP [27]. In another retrospective review the use of CPAP was re-initiated in 25 of 323 patients undergoing 349 TSS early after surgery. The only 2 cases with postoperative pneumocephalus in this series did not belong to the subgroup using CPAP postoperatively, leading these authors to the assumption that resuming CPAP early after TSS might be less dangerous than previously stated [28].

Diving

While pituitary surgeons are often faced with patients using a CPAP-device for treatment of OSA, the question when to resume scuba diving after TSS is asked rarely. This may explain the diversity of pituitary surgeons' primary statements in this survey. Moreover, only one of the authors has personal experience with scuba diving. Therefore, the authors included the advice of several consultants for diving medicine especially for this topic. Diving at the surface using a snorkel is supposed to be equivalent to crawling. In greater depth problems with pressure gradients may occur between solid tissues and gas containing cavities, such as sinuses. Normal pressure at the sea level is 1 bar. Air in a diver's body air spaces will be compressed as pressure increases and expand as pressure decreases. During scuba dive descending leads to a linear pressure increase (1 bar per 10 meter depth). Diving at 10 m depth means a pressure increase of 1 bar and an absolute pressure of 2 bars (relative change of 100 %). As a consequence, any gas volume in the body is compressed to the half of its initial volume, thus producing a negative pressure gradient in case of entrapment. In scuba diving any communicating gas compartment is equilibrated to ambient pressure. Therefore, no pressure gradients will develop. Thus, the problems with pressure gradients in scuba diving arise only with trapped air compartments, wherever they may be. In apnea diving

(breathhold diving) by definition any air filled compartments are enclosed air compartments unless flooded and therefore location of relevant pressure gradients.

The pressure in the paranasal sinus and middle ear rises if the gas cannot escape properly. TSS is associated with swelling of the nasal mucosa and impairs ventilation of the middle ear through the Eustachian tube and of the paranasal sinuses. In a retrospective cohort of 306 divers, who were treated by otorhinolaryngologists, 46 % had problems with the middle ear, 18 % with the inner ear, and 17 % with the nose and sinuses [29]. Sinus barotrauma from scuba diving is self-limiting in almost all cases, and frequently results from nasal pathology [30, 31]. Two of the consultants argued, that as long as a normal outflow of gas from the paranasal sinuses is given, there should be no pressure gradient between this and the sella or the cranial cavity, which would allow diving even with incomplete bony closure after 3 months or 6 months, respectively. On the other hand it has been claimed recently, that sphenoid sinus barotrauma may be underreported and misdiagnosed [32], and limitation of local ventilation may be overlooked. After sphenoid sinus barotrauma sinusitis and abscess formation [33], intrasellar air collection [34] and even subarachnoid pneumatocephalus with severe persistent neurological deficit [35] have been reported. The latter two cases showed spontaneous bony defects of the sphenoidal wall, which may be equivalent to the postoperative state after TSS in many cases. In conclusion, after surgeon's statement on the stability of the skull base scar, postoperative sinusitis especially of the sphenoid sinus and any trapped air should be ruled out by ENT physicians before scuba diving is resumed after TSS. However, ambitious apnoe diving with persistent bony defect of the skull base should be omitted lifelong.

Flying on an airplane

Barometric changes also play a role in the question regarding the recommendation to resume flying on an airplane [36, 37]. At a height of 10.000 m, the air pressure is approximately ¼ of the pressure on ground. However, the cabin pressure appears to be unproblematic. According to Lufthansa, the maximum cabin pressure in an aircraft corresponds to the pressure in a height of approximately 2500 m (depending on aircraft type cabin pressure can be lower). Nasal swelling could impair ventilation of the paranasal sinuses and middle ear after TSS and make flying painful. While air can more easily escape from the sinuses or the middle ear during ascent of an aircraft even if the mucosa is swollen, the flow of air into the paranasal sinuses during descent and landing is more problematic and can cause heavy pain.

Our permission to resume flying in an aircraft as early as one week after surgery definitely requires the exclusion of intracranial air by CT or MRI in order to prevent space-occupying pneumatocephalus. Particular attention is required following an extended transsphenoidal approach.

Risk of cerebral fits

Driving a motor vehicle

The recommendation to resume driving a car as early as 5 days after TSS in uncomplicated cases without any involvement of brain surface by tumor or surgery seems to be applicable when the patient feels well, has neither neurological nor ophthalmological deficit,

and hyponatremia is ruled out. One has to keep in mind and instruct the patient, that the latter may also occur in the second week after TSS and even later, and may cause seizures [38–41]. It is very important to instruct the patient that in case of secondary malaise after discharge, driving a motor vehicle is prohibited. In case of postoperative seizures fitness to drive is assessed according to neurological standards.

If extended TSS involves brain tissue, driving a car is not allowed for 3 months according to the regulations following craniotomy.

Mental and physical condition

Work live

The recommendations concerning resumption of work life in this manuscript focus on the operative approach and its consequences only. Any neurological and ophthalmological problem may profoundly change the advices given. The same is true for the endocrinological state. In Cushing's disease or acromegaly, the co-morbidities could represent a limitation to resume work after TSS.

Conclusions

Despite the diversity of opinions, the audit provides important information on expert opinions and their customs in patients' counselling with the power of about 1.000 transsphenoidal procedures performed per year. Together with information from the meaningful literature the data of our survey provide a basis for elaboration of joint recommendations for patients' conduct and to minimize the approach-related postoperative risks after TSS.

Acknowledgements

Further participating neurosurgeons: Martin Bettag, Trier, Marcus Czabanka, Berlin, Christian Ewelt, Münster, Andreas Jödicke, Berlin, Jürgen Kreutzer, Nürnberg, Walter Rachinger, München, Mukesch Johannes Shah, Freiburg, Peter Vajkoczy, Berlin, Germany.

Participating consultants: Eckhart Altenmüller, professor for music physiology and musician's medicine, Hannover, Julian Brade, neurosurgeon, Minden, Helmut Landgraf, professor for aviation medicine, Berlin, Tim Christopher Lenzian, anesthesiologist, Bünde, Claus-Martin Muth, professor for anesthesiology, Ulm, Peter Schellinger, professor for neurology, Minden, Martin Schrader, professor for otorhinolaryngology, Minden, Hendrik Schröder, industrial medicine and diving medicine consultant, Minden, Ulrich Van Laak, diving and hyperbaric medicine consultant GTÜM/EDTC/ECHM, Kronshagen, Germany.

Funding

This research did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.

Conflict of Interest

No conflict of interest has been declared by the authors.

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Supplementary Material

AGREE Reporting Checklist 2016

This checklist is intended to guide the reporting of clinical practice guidelines.

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
DOMAIN 1: SCOPE AND PURPOSE		
1. OBJECTIVES <i>Report the overall objective(s) of the guideline. The expected health benefits from the guideline are to be specific to the clinical problem or health topic.</i>	☒ Health intent(s) (Le., prevention, screening, diagnosis, treatment, etc.) ☒ Expected benefit(s) or outcome(s) ☒ Target(s) (e.g., patient population, society)	1,2,10
2. QUESTIONS <i>Report the health question(s) covered by the guideline, particularly for the key recommendations.</i>	☒ Target population ☒ Intervention(s) or exposure(s) ☐ Comparisons (if appropriate) ☐ Outcome(s) ☐ Health care setting or context	1 – 10
3. POPULATION <i>Describe the population (i.e., patients, public, etc.) to whom the guideline is meant to apply.</i>	☐ Target population, sex and age ☒ Clinical condition (if relevant) ☐ Severity/stage of disease (if relevant) ☐ Comorbidities (if relevant) ☐ Excluded populations (if relevant)	1 – 10
DOMAIN 2: STAKEHOLDER INVOLVEMENT		
4. GROUP MEMBERSHIP <i>Report all individuals who were involved in the development process. This may include members of the steering group, the research team involved in selecting and reviewing/rating the evidence and individuals involved in formulating the final recommendations.</i>	☒ Name of participant ☒ Discipline/content expertise (e.g., neurosurgeon, methodologist) ☒ Institution (e.g., St. Peter's hospital) ☒ Geographical location (e.g., Seattle, WA) ☒ A description of the member's role in the guideline development group	title page, 2, 10,11
5. TARGET POPULATION PREFERENCES AND VIEWS <i>Report how the views and preferences of the target population were sought/considered and what the resulting outcomes were.</i>	☐ Statement of type of strategy used to capture patients'/publics' views and preferences (e.g., participation in the guideline development group, literature review of values and preferences) ☒ Methods by which preferences and views were sought (e.g., evidence from literature, surveys, focus groups) ☐ Outcomes/information gathered on patient/public information ☒ How the information gathered was used to inform the guideline development process and/or formation of the recommendations	2,3
6. TARGET USERS <i>Report the target (or intended) users of the guideline.</i>	☒ The intended guideline audience (e.g. specialists, family physicians, patients, clinical or institutional leaders/administrators) ☒ How the guideline may be used by its target audience (e.g., to inform clinical decisions, to inform policy, to inform standards of care)	table, 6 – 10

DOMAIN 3: RIGOUR OF DEVELOPMENT

7. SEARCH METHODS <i>Report details of the strategy used to search for evidence.</i>	☒ Named electronic database(s) or evidence source(s) where the search was performed (e.g., MEDLINE, EMBASE, PsychINFO, CINAHL) ☐ Time periods searched (e.g., January 1, 2004 to March 31, 2008) ☐ Search terms used (e.g., text words, indexing terms, subheadings) ☐ Full search strategy included (e.g., possibly located in appendix)	3
8. EVIDENCE SELECTION CRITERIA <i>Report the criteria used to select (i.e., include and exclude) the evidence. Provide rationale, where appropriate.</i>	☒ Target population (patient, public, etc.) characteristics ☐ Study design ☐ Comparisons (if relevant) ☐ Outcomes ☐ Language (if relevant) ☐ Context (if relevant)	3 n.a.
9. STRENGTHS & LIMITATIONS OF THE EVIDENCE <i>Describe the strengths and limitations of the evidence. Consider from the perspective of the individual studies and the body of evidence aggregated across all the studies. Tools exist that can facilitate the reporting of this concept.</i>	☐ Study design(s) included in body of evidence ☐ Study methodology limitations (sampling, blinding, allocation concealment, analytical methods) ☐ Appropriateness/relevance of primary and secondary outcomes considered ☐ Consistency of results across studies ☐ Direction of results across studies ☐ Magnitude of benefit versus magnitude of harm ☐ Applicability to practice context	n.a.
10. FORMULATION OF RECOMMENDATIONS <i>Describe the methods used to formulate the recommendations and how final decisions were reached. Specify any areas of disagreement and the methods used to resolve them.</i>	☒ Recommendation development process (e.g., steps used in modified Delphi technique, voting procedures that were considered) ☒ Outcomes of the recommendation development process (e.g., extent to which consensus was reached using modified Delphi technique, outcome of voting procedures) ☐ How the process influenced the recommendations (e.g., results of Delphi technique influence final recommendation, alignment with recommendations and the final vote)	3, 6 – 10
11. CONSIDERATION OF BENEFITS AND HARMS <i>Report the health benefits, side effects, and risks that were considered when formulating the recommendations.</i>	☐ Supporting data and report of benefits ☒ Supporting data and report of harms/side effects/risks ☐ Reporting of the balance/trade-off between benefits and harms/side effects/risks ☐ Recommendations reflect considerations of both benefits and harms/side effects/risks	6 – 10
12. LINK BETWEEN RECOMMENDATIONS AND EVIDENCE <i>Describe the explicit link between the recommendations and the evidence on which they are based.</i>	☐ How the guideline development group linked and used the evidence to inform recommendations ☐ Link between each recommendation and key evidence (text description and/or reference list) ☐ Link between recommendations and evidence summaries and/or evidence tables in the results section of the guideline	n.a.

13. EXTERNAL REVIEW <i>Report the methodology used to conduct the external review.</i>	☐ Purpose and intent of the external review (e.g., to improve quality, gather feedback on draft recommendations, assess applicability and feasibility, disseminate evidence) ☐ Methods taken to undertake the external review (e.g., rating scale, open-ended questions) ☒ Description of the external reviewers (e.g., number, type of reviewers, affiliations) ☐ Outcomes/information gathered from the external review (e.g., summary of key findings) ☐ How the information gathered was used to inform the guideline development process and/or formation of the recommendations (e.g., guideline panel considered results of review in forming final recommendations)	3,11
14. UPDATING PROCEDURE <i>Describe the procedure for updating the guideline.</i>	☐ A statement that the guideline will be updated ☐ Explicit time interval or explicit criteria to guide decisions about when an update will occur ☐ Methodology for the updating procedure	n.a.
DOMAIN 4: CLARITY OF PRESENTATION		
15. SPECIFIC AND UNAMBIGUOUS RECOMMENDATIONS <i>Describe which options are appropriate in which situations and in which population groups, as informed by the body of evidence.</i>	☐ A statement of the recommended action ☐ Intent or purpose of the recommended action (e.g., to improve quality of life, to decrease side effects) ☒ Relevant population (e.g., patients, public) ☐ Caveats or qualifying statements, if relevant (e.g., patients or conditions for whom the recommendations would not apply) ☒ If there is uncertainty about the best care option(s), the uncertainty should be stated in the guideline	2,3,8
16. MANAGEMENT OPTIONS <i>Describe the different options for managing the condition or health issue.</i>	☐ Description of management options ☒ Population or clinical situation most appropriate to each option	3 – 10
17. IDENTIFIABLE KEY RECOMMENDATIONS <i>Present the key recommendations so that they are easy to identify.</i>	☒ Recommendations in a summarized box, typed in bold, underlined, or presented as flow charts or algorithms ☐ Specific recommendations grouped together in one section	table
DOMAIN 5: APPLICABILITY		
18. FACILITATORS AND BARRIERS TO APPLICATION <i>Describe the facilitators and barriers to the guideline's application.</i>	☐ Types of facilitators and barriers that were considered ☐ Methods by which information regarding the facilitators and barriers to implementing recommendations were sought (e.g., feedback from key stakeholders, pilot testing of guidelines before widespread implementation) ☐ Information/description of the types of facilitators and barriers that emerged from the inquiry (e.g., practitioners have the skills to deliver the recommended care, sufficient equipment is not available to ensure all eligible members of the	n.a.

	☐ population receive mammography} ☐ How the information influenced the guideline development process and/or formation of the recommendations	
19. IMPLEMENTATION ADVICE/TOOLS <i>Provide advice and/or tools on how the recommendations can be applied in practice.</i>	☒ Additional materials to support the implementation of the guideline in practice. For example: <ul style="list-style-type: none"> ○ Guideline summary documents ○ Links to check lists, algorithms ○ Links to how-to manuals ○ Solutions linked to barrier analysis (see Item 18) ○ Tools to capitalize on guideline facilitators (see Item 18) ○ Outcome of pilot test and lessons learned 	table
20. RESOURCE IMPLICATIONS <i>Describe any potential resource implications of applying the recommendations.</i>	☐ Types of cost information that were considered (e.g., economic evaluations, drug acquisition costs) ☐ Methods by which the cost information was sought (e.g., a health economist was part of the guideline development panel, use of health technology assessments for specific drugs, etc.) ☐ Information/description of the cost information that emerged from the inquiry (e.g., specific drug acquisition costs per treatment course) ☐ How the information gathered was used to inform the guideline development process and/or formation of the recommendations	n.a.
21. MONITORING AND AUDITING CRITERIA <i>Provide monitoring and/or auditing criteria to measure the application of guideline recommendations.</i>	☐ Criteria to assess guideline implementation or adherence to recommendations ☐ Criteria for assessing impact of implementing the recommendations ☐ Advice on the frequency and interval of measurement ☐ Operational definitions of how the criteria should be measured	n.a.
DOMAIN 6: EDITORIAL INDEPENDENCE		
22. FUNDING BODY <i>Report the funding body's influence on the content of the guideline.</i>	☐ The name of the funding body or source of funding (or explicit statement of no funding) ☐ A statement that the funding body did not influence the content of the guideline	n.a.
23. COMPETING INTERESTS <i>Provide an explicit statement that all group members have declared whether they have any competing interests.</i>	☒ Types of competing interests considered ☐ Methods by which potential competing interests were sought ☐ A description of the competing interests ☐ How the competing interests influenced the guideline process and development of recommendations	title Page

From:

Brouwers MC, Kerkvliet K, Spithoff K, on behalf of the AGREE Next Steps Consortium. The AGREE Reporting Checklist: a tool to improve reporting of clinical practice guidelines. *BMJ* 2016;352:i1152. doi: 10.1136/bmj.i1152.

For more information about the AGREE Reporting Checklist, please visit the AGREE Enterprise website at <http://www.agreetrust.org>.