Contextual differences considered in the Tunisian ADOLOPMENT of the European Guidelines on Breast Cancer Screening

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Abstract

Background Breast cancer is a common disease in Tunisia and is associated with high mortality rates. The “Instance Nationale de l’Evaluation et de l’Accréditation en Santé” (INEAS) and the Tunisian Society of Oncology decided to develop practice guidelines on the subject. While the development of de novo guidelines on breast cancer screening is a demanding process, guideline adaptation appears more appropriate and context sensitive. The objective of this paper is to describe the adaptation process of the European Guidelines on Breast Cancer Screening and Diagnosis to the Tunisian setting in terms of the methodological process, contextual differences between the source and adoloped guideline, and changes in the recommendations.

Methods We used the GRADE-ADOLOPMENT methodology to prioritize the topic, select the source guideline, and prioritize the questions and the outcomes. Once the source guideline was selected- the European Breast Cancer Guidelines- the European Commission´s Joint Research Centre shared with the project team in Tunisia all relevant documents and files. In parallel, the project team searched for local studies on the disease prevalence, associated outcomes’ baseline risks, patients’ values and preferences, cost, cost-effectiveness, acceptability and feasibility. Then, the adoloping panel reviewed the GRADE evidence tables and the Evidence to Decision tables and discussed whether their own judgments were consistent with those from the source guideline or not. They based their judgments on the evidence on health effects, the local evidence and their own experiences.

Results The most relevant contextual differences between the source and adoloped guidelines were related to the perspective, scope, prioritized questions, rating of outcome importance, baseline risks, and indirectness of the evidence. The ADOLOPMENT process resulted in keeping 5 out of 6 recommendations unmodified. One recommendation addressing “screening versus no screening with ultrasound in women with high breast density on mammography screening” was modified from ‘conditional against’ to ‘conditional for either’ due to more favorable ratings by the adoloping panel in terms of equity and feasibility.

Conclusion This process illustrates both the feasibility of GRADE-ADOLOPMENT approach and the importance of consideration of local evidence. It also highlights the value of collaboration with the organization that developed the source guideline.

Background

Breast cancer represents the second most prevalent cancer in the world affecting 2.1 million women each year. [1] According to the latest GLOBOCAN estimates, the incidence has increased by more than 20% and mortality by 14% in 4 years. The incidence rates are higher in the most developed countries, but mortality rates remain much higher in low-income countries, reflecting a gap in the early detection and access to treatment. In Tunisia, it represents the most common type of cancer; among 100,000 women, there are 32.2 incident cases and 10.3 related deaths each year. [1]

In order to address this public health problem, the “Instance Nationale de l’Evaluation et de l’Accréditation en Santé” (INEAS) and the Tunisian Society of Oncology decided to develop practice guidelines on the subject. Indeed, guidelines can enhance evidence-based practice and reduce variability in practice. [2]

However, developing guideline de novo (i.e., ‘from scratch’) can be a demanding process in terms of time, human, and financial resources. Alternative options to de novo development include adopting or adapting guidelines developed by others. [3, 4] While adoption of a guideline can be done quickly and with fewer resources, it might be inappropriate when contextual differences between the original and target setting exist. In these cases, adaptation of guidelines is a more appropriate approach as it takes into account contextual differences. [4]

A methodological survey identified eight methodologies for the adaptation of health guidelines. [4] The GRADE-ADOLOPMENT, one of these methodologies, combines the advantages of adoption, adaptation and de novo guideline development which allows the creation of recommendations appropriate to the context [3]. GRADE-ADOLOPMENT is based on three cornerstones: (1) identifying and prioritizing credible existing relevant guidelines or evidence syntheses (2) evaluating and completing the GRADE Evidence to Decision (EtD) frameworks for each of the recommendations; and (3) deciding on a final adoption, adaptation or de novo development for each of the recommendations. [5]

The objective of this paper is to describe the project in terms of the methodological process, contextual differences between the source and adoloped guideline, and changes in the recommendations.

Methods

Overall process

The process of this project is based on the steps of the Guidelines 2.0 checklist, [6] and the GRADE-ADOLOPMENT approach. [3] We used the GRADEpro-GDT software [7] to develop GRADE evidence tables and Evidence to Decision (EtD) frameworks. [5] The GRADE evidence table provides the effect estimates for each outcome of interest and the associated certainty of evidence [8].

The EtD table includes information on the following criteria: desirable and undesirable effects, certainty of evidence, certainty about or variability in values and preferences, cost, and cost-effectiveness, equity, feasibility, and acceptability. [9-11] The information included for each EtD criterion consists of judgment, research evidence, and additional considerations. Figure 1 shows this information displayed in columns for one of the factors (cost effectiveness used as an illustrative example)[12]).

We describe below the methodological aspects of the project most relevant to the ADOLOPMENT process.

Contributors

INEAS is an independent public authority that contributes to the regulation of the health system in Tunisia through quality and efficiency. The guideline project was a collaborative effort between INEAS and the Tunisian Society of Oncology. The Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ) GmbH funded the study, while the American University of Beirut GRADE (Grading of Recommendations Assessment, Development and Evaluation) center provided the methodological support.

Two major groups were involved: the project team and the guideline panel. The project team consisted of four members from INEAS (ABB, HO, HG, MH) and two members of the AUB GRADE center (LK, EA). The guideline panel consisted of 12 local experts including medical and surgical oncologists, gynecologists, family medicine, radiologists, guideline methodologists, and governmental representatives. None of the panelists had financial conflict of interest.

Prioritization of the topic

The project team initially considered the following four topics: breast cancer screening, colorectal cancer screening, hypertension, and management of pain. The team then conducted a priority setting exercise to prioritize one of those topics. [13, 14] The factors considered for priority setting included: public health burden; avoidable mortality and morbidity; economic burden on the health care system and patient; emerging diseases or emerging care options; potential impact of intervention on health outcomes, economy, health care system, and equity; variation in clinical practice; and rapidly changing evidence. [13, 14] Eventually, the project team prioritized the topic of breast cancer screening as it was rated the highest.

Selection of the source guideline

The project team systematically searched for existing guidelines on breast cancer screening published after 2016, to ensure they were up to date. The group searched MEDLINE, GuidelineCentral, Guideline International Network (GIN) database, and websites of guideline producing agencies such as the National Institute for Health and Care Excellence (NICE), National Comprehensive Cancer Network (NCCN), Scottish Intercollegiate Guidelines Network (SIGN), World Health Organization (WHO), Belgian Health Care Knowledge Center (KCE), and Agency for Healthcare Research and Quality (AHRQ).

The search identified 124 unique citations. The title and abstract screening yielded seven citations as potentially eligible (on breast cancer). The full-text screening of the seven citations identified two relevant guidelines that were based on systematic reviews and developed using the GRADE approach. [15, 16] Two members from INEAS (HO, ABB) independently assessed the methodological rigor and transparency of each of the two guidelines using the AGREE II tool. [17] The project team selected the breast cancer screening guidelines developed by the European Commission Initiative on Breast cancer (ECIBC) as it scored the highest on the AGREE II tool as shown in figure 2. [18]

Prioritization of questions and outcomes

For prioritizing the questions and the outcomes, the project team organized a face-to-face panel meeting in September 2018. The panelists anonymously rated the importance of each of the nine screening

questions addressed in the source guideline at the time this ADOLOPMENT process was started. They used a scale of 1-9 (least important - most important) and considered the relevance of the populations and interventions addressed by each question. Then, the panel discussed the rating results and selected the final set of questions through consensus.

Similarly, the panel rated the importance of the outcomes defined in each of the questions of the source guideline on a scale of 1-9 (7–9 indicates outcome is critical for decision-making, 4–6 indicates it is important, and 1–3 indicates it is not important for decision-making). [6]

Gathering the evidence

For the evidence on health effects, the ECIBC team (ZSP) shared with the project team the evidence syntheses reports and other relevant documents from the source guideline, including the GRADEpro files for GRADE evidence tables and Evidence to Decision (EtD) frameworks. As the ADOLOPMENT took place relatively shortly after the publication of the source guideline, there was no need to update the evidence.

For the local evidence, the project team searched for local studies on the disease prevalence, associated outcomes' baseline risks, patients' values and preferences, cost, cost-effectiveness, acceptability, and feasibility. As the team did not identify much of the needed data from published studies, it solicited them from panel members and searched for studies from contexts similar to that of Tunisia (i.e., Arabic countries of North African countries). The local baseline risk was integrated in the evidence summary tables and the rest of the criteria were integrated in the Evidence to Decision (EtD) framework.

Finalizing the recommendations

In December 2018, the panel reviewed the GRADE evidence tables and the EtD frameworks reproduced in full from the source guideline. In other terms, the panelists were able to view the judgments made by the original panel. For each question, and for each judgment, the panel discussed whether their own judgments were consistent with those from the source guideline or not. They based their judgments on the evidence on health effects, the local evidence and their own experiences as displayed in figure 3.

Results

Contextual differences between source and adoloped guidelines

We present below and summarize in table 1 below the most relevant contextual differences between the source and ADOLOPMENT guidelines: perspective, scope, prioritized questions, rating of outcome importance, baseline risks, and indirectness of the evidence.

- Perspective: the source guideline had a population (public health) perspective and the recommendations addressed organized mammography screening The Tunisian panel opted for an individual (clinical) perspective as no mammography screening programs are available in Tunisia. As a result, reference to organized programs was removed from all the adoloped recommendations.

- Scope: while the source guideline addressed both breast cancer screening and diagnosis, the Tunisian panel preferred to focus on screening only. This decision was driven by feasibility considerations, and by the fact that this project was the first ADOLOPMENT experience for INEAS.
- Prioritized questions: out of a total of nine screening questions in the source guideline at the time the ADOLOPMENT process was begun, the panel dropped three questions on tomosynthesis screening. While the technology is available in Tunisia, it is not used as a screening tool.
- Rating of outcome importance: the panel changed the rating of the importance of two outcomes: (1) 'all-cause mortality' from not important (in the source guideline) to important; and (2) 'overdiagnosis from critical to important. These changes in ratings reflect moving from a population perspective to an individual perspective, where patients' values have a relatively higher weight.
- Baseline risks: the panel assumed a lower incidence of breast cancer but higher breast cancer mortality rate in the Tunisian setting compared to the numbers used by the source guideline. Thus, overall, the baseline risk of breast cancer mortality in Tunisia was assumed to be similar to that in Europe. These assumptions were not based on peer reviewed data but on local unpublished data.
- Indirectness of the evidence: The panel considered whether the certainty of the evidence for different outcomes from the source guideline should be rated down for indirectness when considered in the Tunisian setting. The judgement of indirectness considered whether any differences in the characteristics of populations or intervention in the Tunisian setting compared to the setting of the source guideline, would lead to different relative effects. In addition, the panel considered potential differences in the quality of health care systems, and the linkage to care of screening-detected disease. The ultimate judgment was not to rate down the certainty of evidence from the source guideline for indirectness.

Changes in the recommendations

Figure 4 indicates whether the judgments made by the source panel were modified by the adoloping panel for the different EtD criterion and the recommendation statements, for each of the six questions. The ADOLOPMENT process resulted in keeping 5 out of 6 recommendations unmodified. The modified recommendation addressed "screening versus no screening with ultrasound in women with high breast density on mammography screening". The panel modified the recommendation from 'conditional against' to 'conditional for either' due to more favorable ratings by the adoloping panel in terms of equity and feasibility.

For each the five remaining unmodified recommendations, the adoloping panel had different judgments (relative to the source guideline) for at least one the EtD criteria (range 2-4 criteria).

Table 1: Contextual differences between the source (ECIBC) and adoloped (Tunisian) guidelines

Guideline Item	ECIBC Guideline	Tunisian Guideline	Rationale for change by Tunisian panel
Perspective	Population	Individual	Organized mammography screening programs not available in Tunisia
Scope	Screening and diagnosis	Screening	Feasibility considerations; first ADOLOPMENT experience
Prioritized questions	9	6	Tomosynthesis not used in Tunisia as a screening tool
Rating of outcome importance	'all-cause mortality' important; 'overdiagnosis' critical	'all-cause mortality' not important; 'overdiagnosis' important	Change in perspective (from population to individual)
Baseline risks	Breast cancer incidence and breast cancer mortality rate from the meta-analysis control arm data	Lower breast cancer incidence, higher breast cancer mortality rate	The Tunisian panel made assumptions based on local evidence
Indirectness of the evidence	Judgment of indirectness made in the source guideline	Judgment of no (further) rating down of certainty of evidence for indirectness	Based on the consideration of how the characteristics of the populations or the interventions in the Tunisian setting compare to the setting of the source guideline

Discussion

The ADOLOPMENT of the European Guidelines on Breast Cancer Screening and Diagnosis to the Tunisian setting illustrates the feasibility of carrying out this process with limited resources and in a short period of time (3 months). We have highlighted the complete methodological process followed which led to six contextual differences between the source guideline and the Tunisian one, and changes in the recommendations.

A major facilitator to this ADOLOPMENT project was the collaboration between the two teams of the source and ADOLOPMENT guidelines. The ECIBC guideline project team allowed the unrestricted use of their recently published guideline and related material as the basis for the ADOLOPMENT process [18].

Another major facilitator is the fact that the two guideline efforts used the same methodology (i.e., GRADE), and the same tools (e.g., RevMan, GRADEPro-GDT). On the other hand, one major challenge was the lack of published local evidence from Tunisia for values and preferences, and economic implications. The judgments made for those criteria relied mainly on the panelists' expert opinion.

A clear advantage of guideline adaptation is the ability to present the adoloping panel with evidence that has already been synthesized for the source guideline. However, it is not clear whether the panel should be also presented with the EtD sections completed by the source guideline' panel. These sections include 'judgments' and 'additional considerations' made for the different EtD criteria, and the final 'recommendation'. In principle, there are three approaches to sharing information from the source guideline with the adoloping panel, as illustrated in table 2 below.

Table 2: Three approaches to sharing with the adoloping panel information from the source guideline.

Approach	Local evidence	Information from the source guideline			
		For each EtD criterion			Recommendation
		Synthesized evidence	Judgment	Additional considerations	
A	x	x	x	x	x
B	x	x	x	x	
C	x	x			

Approach A would allow the panel to build on the source guideline's full information and decide whether to modify any of the judgments or recommendation.

Approach B would allow the panel to build on the source guideline's information except for the recommendation. The panel would decide whether to modify any of the judgments but develop the recommendation independently.

Approach C would allow the panel to make their judgments and develop the recommendations independently, taking into account only the evidence synthesized for the source guideline and the local evidence.

While we have used the third approach in previous ADOLOPMENT projects [19-24], we opted to go for the second approach in this project. The decision was driven by the preference of the adoloping panel, and by the scarcity of local evidence from Tunisia.

Based on this experience, we suggest that the structure of EtDs used in guideline ADOLOPMENT include the following:

1. for each EtD criterion, the synthesized evidence, judgments, and additional considerations already made by the source guideline panel (reproduced from the source guideline);
2. for each EtD criterion, the local evidence, judgments, and additional considerations, to be made by the ADOLOPMENT guideline panel;
3. the recommendation developed by the source guideline panel (reproduced from the source guideline);
4. the recommendation to be developed by the adoloping panel.

However, including the elements from the source guideline (#1 and #3 above) would be optional to allow the panelists select one of the three approaches discussed above (table 2).

For the information from the source guideline, we suggest reproducing it as is and not allowing its edition to reflect the source guidelines' panel's input. For the adoloped guideline, we suggest providing a blank section to allow the project team to add any local evidence, and the adoloping panelists to include their own judgment, their own additional considerations, and their own recommendation. We show in table 3 below more detailed suggestions for the structure of EtDs used in guideline ADOLOPMENT. These different approaches could be reproduced in guideline development software, such GRADEpro-GDT software.

Table 3: Detailed suggestions for structure of EtDs used in guideline ADOLOPMENT.

	Research evidence	Judgement	Additional considerations	Recommendation
Source guideline	Reproduced from the source guideline	Reproduced from the source guideline	Reproduced from the source guideline	Reproduced from the source guideline
Adoloped guideline	Project team adds any local evidence	Highlight judgments modified by the panel	Provide justification for any change	Provide justification for any change

Implications for practice

This project illustrates a number of facilitators for guideline ADOLOPMENT, including (1) collaboration with the organization that developed the source guideline; (2) same methodology (GRADE) used for the source guideline development and the adoloped guideline; (3) availability of local evidence; (4) availability of an adaptation module in a guideline development tool (e.g., GRADEPro- GDT); and (5) engagement of panelists in the ADOLOPMENT process.

Implications for research

As illustrated by figure 4, the adoloping panel might change several judgments for some EtD criteria, without leading to a change in the recommendation. It would be interesting to explore to what extent this observation applies to other guideline adaptation efforts. In addition, there is a need to evaluate the feasibility of the three approaches of sharing with the adoloping panel information from the source guideline, and their acceptability by the panelists and methodologists. Finally, it would be helpful to develop an extension to the G-I-N-McMaster checklist for guideline development [6], to support groups adapting guidelines.

Declarations

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Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Competing interests

The authors report intellectual conflict of interest being members of the GRADE working group (LAK, EAA).

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Figures

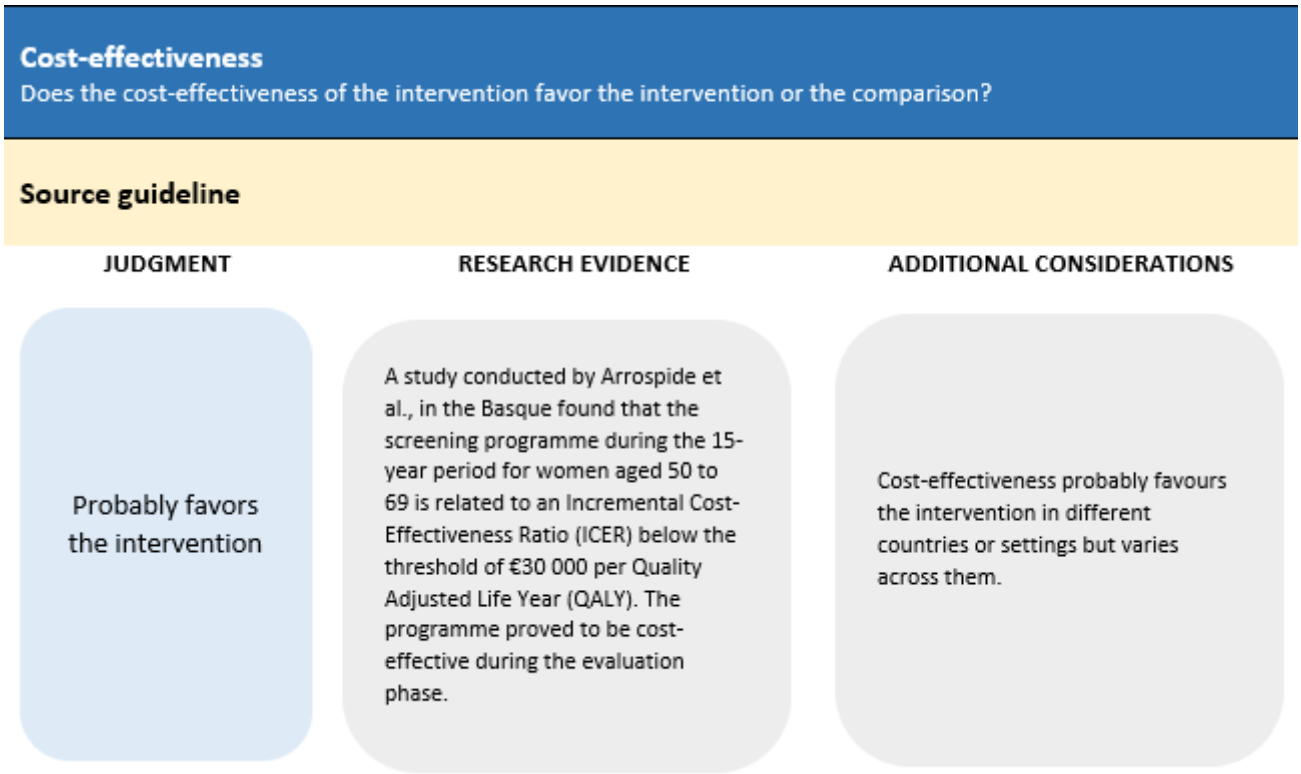

Figure 1

Example for the cost-effectiveness section from an EtD framework from the ECIBC guideline

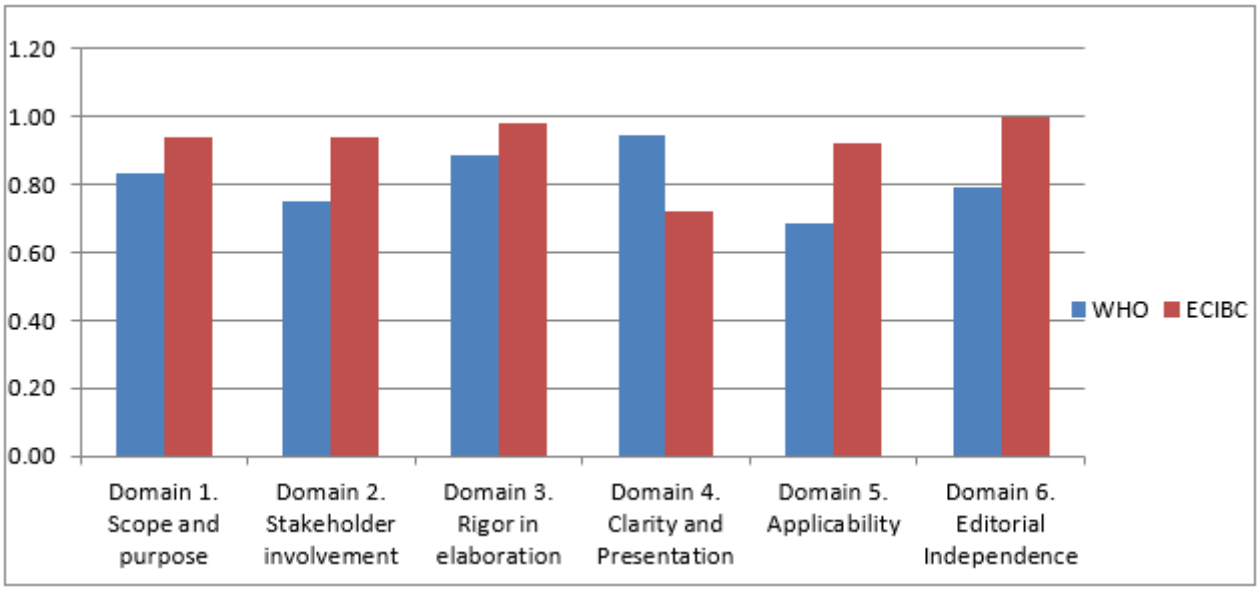

Figure 2

Scoring of the two potentially eligible guidelines as per the AGREE II tool Abbreviations: WHO: World Health Organization; ECIBC: European Commission Initiative on Breast Cancer

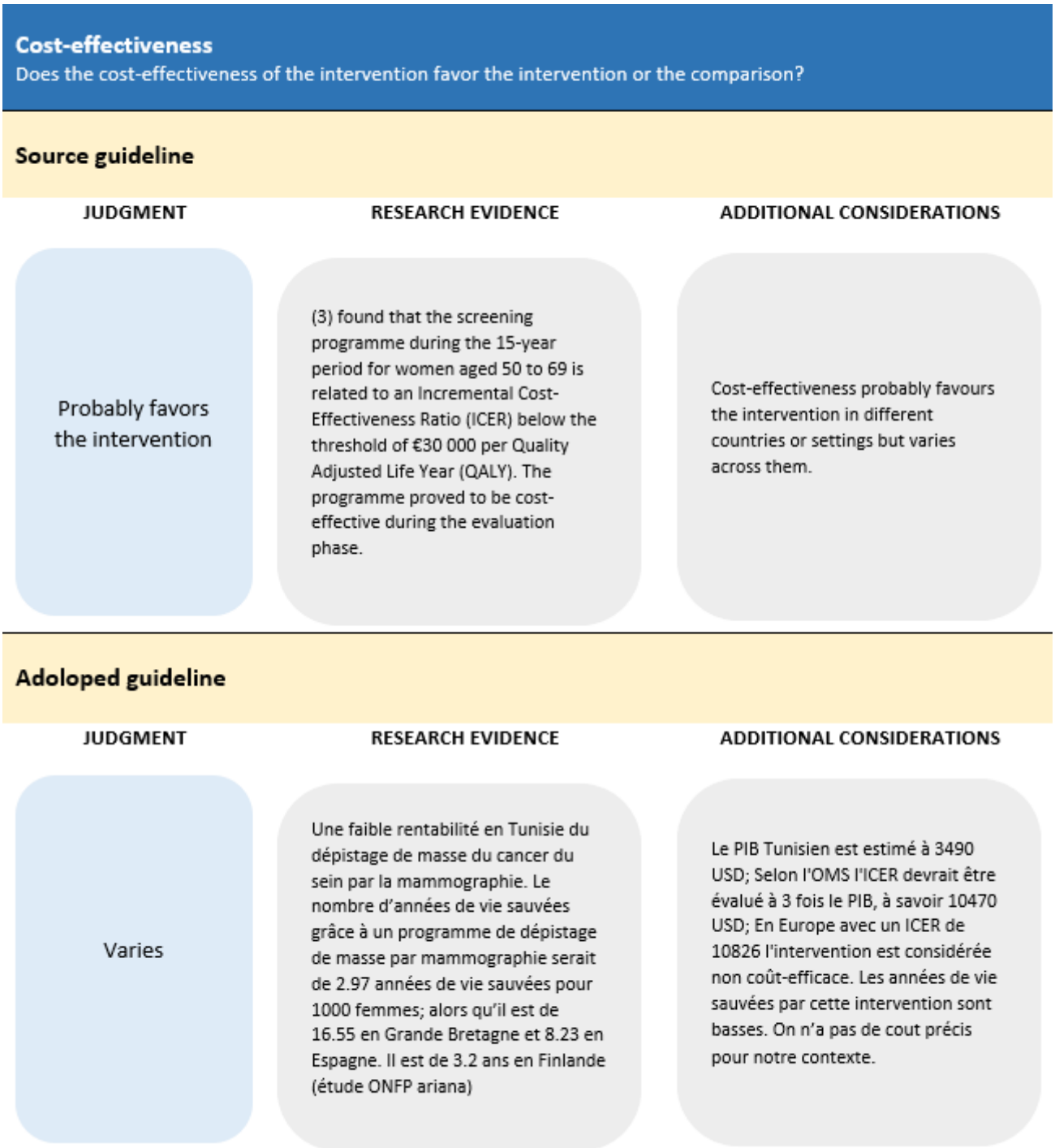

Figure 3

Display of EtD framework

	Desirable effect	Undesirable effect	Certainty of the evidence	Values and preferences	Balance of effect	Resource required	Cost-effectiveness	Equity	Acceptability	Feasibility	Rec
Q1								+		+	
Q2								+		+	
Q3							-	+		+	
Q4								+		+	
Q5	-		-	+			-	+		+	+
Q6	-							-			

The blue shade refers to the changes made by the adoloping panel to the judgments made by the source guideline panel for the different EtD criterion and the recommendation statements, for each of the six questions
+ refers to the change in judgment that made the corresponding factor more favorable
- refers to the change in judgment that made the corresponding factor less favorable

Figure 4

Changes made by the adoloping panel to the judgments made by the source guideline panel for the different EtD criteria and the recommendation statements, for each of the six questions