APPENDIX

ADAPTE Process for the Chemoprevention of Breast Cancer

Eastern Health Breast Disease Site Group

Phase I - Setup

The Breast Disease Site Group was formed in the fall of 2006 with representatives from Eastern Health's Cancer Care Program. It is a coalition of health professionals composed of pathologists, radiologists, radiation oncologists, medical oncologists, surgeons, genetics, and representatives of the provincial screening program, pharmacists, nursing, and administration.

The purpose of the group is to develop evidence-based clinical practice guidelines for diagnosis, care, and treatment of individuals with breast disease in the province of Newfoundland and Labrador.

The objectives of the group include:

1. determining priorities for guideline development
2. reviewing national/international guidelines and providing direction for local adaptation
3. approving practice guidelines for local/provincial use
4. providing direction for dissemination and evaluation of guidelines
5. developing strategies for collection and analysis of breast cancer data within Eastern Health.

Limited resources were a significant challenge to the objectives of the group though provincial funding had procured a clinical practice guideline coordinator position, while our expert members of other specialties volunteered generously of their time from busy work schedules. Therefore, a small subcommittee or guidelines team was created to oversee the adaptation process where applicable. It consisted of an oncologist, a pharmacist, the guidelines coordinator, and occasionally member(s) of the Disease Site Group with a particular interest in a guideline topic.

All panel members in the guideline development process have completed declarations of conflict of interest. Authorship of all adapted guidelines will be acknowledged as that of the Eastern Health Breast Disease Site Group. Once the draft guideline (either adapted or de novo) has been developed, it is reviewed at the monthly meeting of the group. Feedback is welcomed, any revisions are carried out and consensus, where possible, is reached. The guideline is then circulated to select target users for feedback, and revisions made accordingly. The guideline is then presented to the administrative body of Eastern Health for approval. Upon said approval, it will be distributed to appropriate health care providers in the province.

This guideline will be reviewed and/or updated every 3-5 years, unless new research requires an earlier review.

Phase II – Adaptation

Question: What is the optimal chemoprevention management offered to women at high risk of developing breast cancer?

PIPOH

Population concerned – women at high risk of developing breast cancer

Interventions of interest – chemoprevention

Professionals whom guideline is targeted – family doctors, general practitioners, pharmacists, nurses, other health care specialists

expected Outcomes – decrease in the rate of breast cancer occurrence

Health care setting – outpatient clinics.

The search for existing guidelines and other relevant documents concerning chemoprevention of breast cancer have revealed the following:

1. Chemoprevention of breast cancer: a joint guideline from the Canadian Task Force on preventative health care and the Canadian Breast Cancer Initiative's Steering Committee on clinical practice guidelines for the care and treatment of breast cancer. 2001;
2. Chemoprevention of breast cancer: a summary of the evidence for the United States Preventative Services Task Force. 2002;
3. American Society of Clinical Oncology technology assessment of Pharmacologic interventions for breast cancer risk reduction including tamoxifen, raloxifene and aromatase inhibition. 2002;
4. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Breast cancer risk reduction. 2008.

Table for Summarizing Guideline Characteristics

Title	Publisher	Country, language	Publication date	End of search date	Comments
Chemoprevention of breast cancer: a joint guideline from the Canadian Task Force on preventative health care and the Canadian Breast Cancer Initiative's Steering Committee on clinical practice guidelines for the care and treatment of breast cancer.	Canadian Medical Association Journal	Canada, English	June 2001	August 2000	This is a Canadian guideline which would elevate its status as a desirable choice but unfortunately is too old and potentially out-of-date.
Chemoprevention of breast cancer: a summary of the evidence for the United States Preventative Services Task Force.	Annals of Internal Medicine	United States, English	July 2002	December 2001	Good analysis of recorded clinical trials but does not include the results of the CORE or STAR trials since both were published after this guideline.
American Society of Clinical Oncology technology assessment of pharmacologic interventions for breast cancer risk reduction including tamoxifen, raloxifene and aromatase inhibition.	Journal of Clinical Oncology	United States, English	August 2002	March 2002	Good analysis of recorded clinical trials but also did not include the CORE or the STAR trials since both were published after this guideline.

NCCN clinical practice guidelines in oncology: breast cancer risk reduction.	National Comprehensive Cancer Network	United States, English	February 2008	unknown	Good analysis of all pertinent clinical trials. Recent, up-to-date.

Table for Summarizing Guideline Content

		Joint Canadian Guideline CPG 1	United States Preventative Services Task Force CPG 2	ASCO CPG 3	NCCN CPG 4
What is the optimal chemoprevention management offered to high risk patients?		**yes**	**yes**	**yes** **risk reduction**	**yes** **risk reduction**
Population	**Women who are deemed to be at high risk of developing breast cancer.**	**yes**	**yes**	**yes**	**yes**
Intervention(s)	**Chemoprevention or pharmaceutical management**	**yes**	**yes**	**yes**	**yes, but also includes risk reduction strategies i.e. surgery**
Professionals/patients	**Target users are family physicians, general practitioners, other specialists and health care professionals**	**yes**	**yes**	**yes**	**yes**
Outcome	**Decreased number of breast cancer occurrences**	**yes**	**yes**	**yes**	**yes**
Healthcare setting	**Outpatient setting**	**yes**	**yes**	**yes**	**yes**

Assess guideline quality

Use of the AGREE (Appraisal of Guidelines Research and Evaluation) provides the framework for assessing the quality of clinical practice guidelines. Each of the four selected guidelines were evaluated with the AGREE instrument.

Guideline currency

Only one of the four identified guidelines would be deemed as current, this being the NCCN breast cancer risk reduction guideline. New evidence has been presented since the publication of the remaining three guidelines which doesn't invalidate their recommendations but offers further options.

Guideline content

A recommendation matrix was created to help assess the content of each of the identified guidelines and compare their recommendations.

Recommendation Matrix

RECOMMENDATIONS	CANADIAN CPG #1	USPSTF CPG #2	ASCO CPG #3	NCCN CPG #4
Clinical Trials	Four clinical trials reviewed: NSABP P-1, Italian Tamoxifen Prevention Study, Royal Marsden Hospital Study, and the MORE trial	Four clinical trials reviewed: Royal Marsden, Italian Tamoxifen Prevention Study, NSABP P-1, and the MORE trial.	Five clinical trials reviewed: NSABP P-1, IBIS -1, Royal Marsden, Italian Tamoxifen Prevention Study, And the MORE trial.	Seven clinical trials reviewed: NSABP P-1, Royal Marsden, IBIS-1, Italian Tam. Prev. Study, MORE trial, CORE trial, and the STAR trial.
Role of Tamoxifen	Women at high risk should be offered and counseled of risks/benefits of Tamoxifen for 5 years.	Women at high risk should be offered Tamoxifen for 5 years if at low risk of adverse events.	Women at high risk may be offered Tamoxifen for 5 years to reduce short term risk.	Tamoxifen to be offered as an option for both premenopausal and post- menopausal women. at high risk and those who have had LCIS.
Role of Raloxifene	No role outside of a clinical trial setting	Not enough evidence to Support its use.	Use not recommended for lowering risk.	Raloxifene to be offered as an option for post-menopausal women at high risk and those who have had LCIS.

Guideline consistency

Table of Criteria for Assessing the Quality of Study Search and Selection

	Canadian CPG #1			USPSTF CPG #2			ASCO CPG#3			NCCN CPG#4		
	Yes	**Unsure**	**No**	**Yes**	**Unsure**	**No**	**Yes**	**Unsure**	**No**	**Yes**	**Unsure**	**No**
Overall, was the search for evidence comprehensive?	X			X			X				X	
The authors had a clearly focused question (population, intervention, outcome)	X			X			X			X		
Appropriate databases were searched for source guidelines	X			X			X				X	
Internet sites were searched for source guidelines		X			X			X		X		
Years covered in search	X			X			X				X	
Languages covered in search	X			X				X			X	
Keywords used	X					X	X				X	
Combinations of keywords	X					X	X				X	
Detailed search strategies are provided with the guideline	X			X			X					X
Snowball methods were used		X		X				X			X	
A hand search of the reference lists was completed	X				X			X			X	
Local experts and/or societies were asked for guideline recommendations		X			X			X		X		
	Yes	**Unsure**	**No**	**Yes**	**Unsure**	**No**	**Yes**	**Unsure**	**No**	**Yes**	**Unsure**	**No**
Overall, was bias in the selection of articles avoided?			X			X			X	X		
Inclusion and exclusion criteria reported			X	X			X					X
The number of persons who selected and analyzed the data is documented			X	X					X			X
The procedure to solve disagreement is described			X	X					X	X		
The number of references analyzed is documented	X			X					X			X
The number of excluded references is documented			X	X					X			X

The reasons for excluding references are given	X	X	X	X
The criteria for inclusion and exclusion are clinically and methodologically valid	X	X	X	X
The reasons for exclusion conform to the selection and exclusion criteria	X	X	X	X
The process for selection of evidence is adequately described	X	X	X	X

Table for Recording Evaluations of Consistency between Evidence, it's Interpretation, and Recommendations

What is the optimal chemoprevention management offered to high risk patients?	**Canadian CPG#1**	**USPSTF CPG#2**	**ASCO CPG#3**	**NCCN CPG#4**
	Yes Unsure No	**Yes Unsure No**	**Yes Unsure No**	**Yes Unsure No**
Overall, the evidence was valid	X	X	X	X
Given the search strategy, the risk that relevant evidence has been missed is low	X	X	X	X
The criteria for selecting the evidence is explicit	X	X	X	X
Settings and protocols of selected studies fit the health question	X	X	X	X
Outcomes were clinically sound	X	X	X	X
The criteria used for assessing the quality and validity of the selected studies are adequately reported	X	X	X	X
The risk that biased evidence has been reported is low	X	X	X	X
The outcomes were considered clinically sound	X	X	X	X
When a meta-analysis was performed, statistical analysis were appropriate. Sensitivity analysis and test of heterogeneity was performed	X	X	X	X

Coherence between the evidence and recommendations	**X**	**X**	**X**	**X**
The evidence was direct. Patients and interventions included in the studies were comparable to those targeted by the recommendation	**X**	**X**	**X**	**X**
Conclusions were supported by data and/or the analysis; results were consistent from study to study. When inconsistencies existed in data, considered judgment was applied and reported	**X**	**X**	**X**	**X**
The conclusions were clinically relevant	**X**	**X**	**X**	**X**
The conclusions derived from data point to effectiveness/ ineffectiveness of the intervention and the recommendation is written accordingly	**X**	**X**	**X**	**X**
There is some justification to recommend/not recommend the intervention even though the evidence is weak	**X**	**X**	**X**	**X**
The hierarchy of strength of evidence is adequately described	**X**	**X**	**X**	**X**
Overall, the scientific quality of this recommendation does not present risks of bias	**X**	**X**	**X**	**X**
The strength of evidence attributed to the recommendation is adequately described and justified	**X**	**X**	**X**	**X**
Risks and benefits have Been weighed	**X**	**X**	**X**	**X**

Acceptability and Applicability of the Recommendations

Health question	Canadian CPG#1	USPSTF CPG#2	ASCO CPG#3	NCCN CPG#4
What is the optimal chemoprevention management offered to high risk patients?	Yes Unsure No	Yes Unsure No	Yes Unsure No	Yes Unsure No
Overall, the recommendation is acceptable	X	X	X	X
The strength of evidence and the magnitude of effect adequately support the grade of the recommendation	X	X	X	X
There is sufficient benefit of the intervention, compared with other available management	X	X	X	X
The recommendation is compatible with the culture and values in the setting where it is to be used	X	X	X	X
Overall, the recommendation is applicable	X	X	X	X
The intervention is applicable to patients in the context of use	X	X	X	X
The intervention/equipment is available in the context of use	X	X	X	X
The necessary expertise is available in the context of use	X	X	X	X
There are no constraints, legislation, policies, or resources in the health care setting of use that would impede the implementation of the recommendation	X	X	X	X

Decision and Selection

The AGREE tool indicated that source guidelines #1 and #4 received this highest scores for quality. The assessment of currency suggests that only source guideline #4 is up-to-date and current while the other three are out of date. The recommendations matrices indicate that though the recommendations are similar for the use of tamoxifen across all source guidelines, recommendations for the use of raloxifene is not consistent due to availability of more up-to-date literature for guideline source #4. Ironically, the most current of the guidelines, #4, did not provide a detailed account of the search strategy as the other three but did have an overview of the development process. There was also a relative consistency between the evidence and its interpretation and between the interpretation and the recommendations for all four guideline sources, taking into account the available evidence at the time. Any of the source guidelines can easily be applied to the target population and has shown to be worthy of implementation.

After careful consideration, the guidelines team elected to use guideline source #4, the NCCN's Breast Cancer Risk Reduction guideline since it was the most current evaluation of the available literature. The decision was made to ACCEPT just those specific recommendations pertaining to the use of drugs in the prevention of breast cancer.

Checklist of Adapted Guideline Content

Guideline section	When to be completed/Completed
1. Overview material **- Structured abstract including:** **o Guideline's release date** **o Status (adapted)** **o Print and electronic sources** **- Adapter and source guideline developer** **2. Introduction and background** **3. Scope and purpose** **4. Target audience of the guideline** **5. Health questions** **6. Recommendations** **- Risks and benefits associated with the recommendations** **- Specific circumstances under which to perform the recommendation** **- Strength of recommendation (if assigned)** **7. Supporting evidence and information for the recommendations** **- Panel rational behind the recommendations** **- Presentation of additional evidence** **- How and why existing recommendations were modified** **8. External review and consultation process** **- Who was asked to review the guidelines** **- What process was followed** **- Discussion of feedback** **- Feedback incorporated into the final document** **9. Plan for scheduled review and update** **10. Algorithm or summary document** **11. Implementation consideration** **12. Glossary (for unfamiliar terms)** **13. References of all materials used in creating the guideline** **14. Acknowledgement of source guideline developers and permission granted (where necessary)** **15. List of panel members and their credentials, declarations of conflicts of interest** **16. List of funding sources** **17. Appendix describing adaptation process including:** **- Guideline search and retrieval including list of guidelines and whether they were included/excluded, with rationale** **- Guideline assessments including a summary of results for each assessment (including AGREE domain scores)** **- Decision process followed by panel** **- Results, and decisions of each evaluation**	

Table for Reporting on Results of Update Process

Health question	Recommendation in original guideline(s)	End date of literature search	New evidence (references)	Final recommendation	Comments
What is the optimal chemoprevention management offered to high risk patients?					