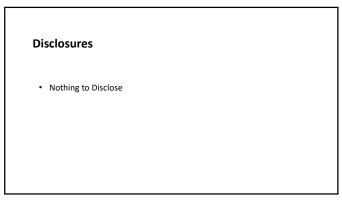
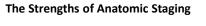
Prognostic Markers Beyond TNM: They Are Here to Stay (What are they and how do they affect staging?

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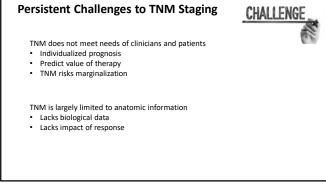
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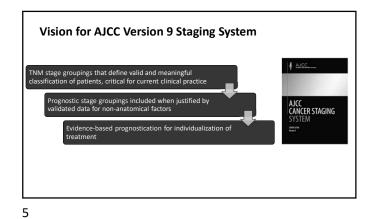


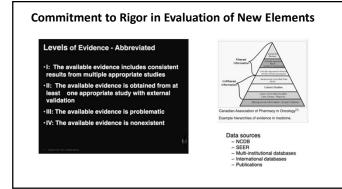


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- Common language of patient classification across the global cancer community Patient care
 Research
- Basis of historical cancer data comparisons Relates contemporary patients to like patients in past 70 years, allowing tracking of changing management approaches and outcomes
- Common denominator of classification of cancer cases, achievable for nearly all patients
 Sole source of patient classification in low- and middle-income countries
- · Utility as cornerstone of evaluation and treatment decisions
- Anatomic stage codified by TNM remains the strongest prognostic factor for solid tumors.







AJCC Version 9 Sites That Incorporate Non-anatomic Factors Chapter Name Prognostic Factor

As quality data has accrued to provide statistical and clinical significance, AJCC has empanelled experts to update *both anatomical and non-anatomical factors* within a framework that is globally applicable.

Add non-anatomic factor(s) to the historical BIN model (breast)

or

• Use non-anatomic factor(s) to define separate staging systems (oropharynx)

Primary Cutaneous Lymphoma Peripheral Blood Involvement

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Implications of Adding Non-anatomical Prognostic Factors to Breast Cancer Staging

In a large data set, application of prognostic stage groups changed the stage of 40% of patients.

Application of prognostic stage groups "led to a better prognostic distribution of the (TNM stage) group and more precise individual prognostication." - Hortobagyi, Edge, Giuliano. ADCO Educational Book, 2018.

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Breast Cancer Staging Update for Version 9 in Progress

- Expert panel assembled under Dr. Stephen Edge
- Updated Version 9 expected implementation on 1/1/2026
- Expected additions:
 - 1. Staging system for de novo metastatic cancer
 - Per NCDB/SEER data, survival clearly segregates into 4 groups
 - Stage groupings for post-neoadjuvant therapy

 Response to neoadjuvant therapy is a major prognostic factor
 - 3. No change in current prognostic staging (clinical / pathologic)

	TNM Stage	Primary Tumour	Lymph Metastasis	Distant Metastasis
The Bin Model of	0	TIS	N0	M0
TNM	I	T1	N0	M0
		T2	NO	M0
Stage Groupings	п	T3	N0	M0
Are "Bins" of		T4	N0	M0
All the Possible	IIIA	T1,2	N1	M0
ombinations of T, N, and M	IIIB	T3,4	N1	M0
i, ii, and iii	IIIC	Any T	N2	M0
	IV	Any T	Any N	M1
	Bin model is inflexible: a calculator becomes a necessity			

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Classifier vs. Calculator: Roles in Precision Medicine

 For the 8th Edition, the Personalized Medicine Core of the AJCC offered an additional perspective: individualized prognosis and computational approaches.

Classifiers group patients into ordered risk strata with probability-estimate cut-points.

- TNM = a classifier with ordered strata (I, II, III, IV) of increasingly poor prognosis.
- Classifiers are constrained by the number of categories that are manageable.

• Classifiers are limited by the variability of prognosis of patients within a given risk class.

• Risk calculators are prognostication tools are with individualized probability estimates.

- Algorithm: designed for more precise estimate of outcome for an individual patient through computational integration of a variety of patient-specific data elements.
- AI may be deployed for this task.

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Anal	Analysis of Prognostication Tools: State of the Science					
0-++ ± ±+-0	PMC undertook an intensive search to locate all exiting prognostication tools.	Initial observations: wide variation in quality, consistency, outcome assessed, inclusion of validation (internal or external)				
稟	PMC developed and published guidelines for prognostication tool quality.	Kattan et al. CA Can J Clin 2016; 66:370-4.				
¢ 0	PMC evaluated all identified tools accordin	g to published quality guidelines.				
	Results published in 8 th Edition chapters, as appropriate.					

AJCC Endorsed Prognostication Tools

- 30 prognostication models/tools were identified and critically reviewed.
- At that time, only two were found to have met all predefined AJCC inclusion and none
 of the exclusion criteria, and both have been externally validated.
 - · Adjuvant! Online (currently unavailable)
 - PREDICT-Plus
- Adjuvant! Online: developed to assist decision-making about adjuvant therapy in $\mathit{early-stage}$ disease
 - Probability estimates made according to a proprietary system
- PREDICT-Plus developed to predict outcome in women treated for *early-stage* breast cancer in the United Kingdom
 - Open system

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Going Forward

- AJCC encourages the development of calculators that are backed up by the AJCC content management system as the single source of truth and quality control.
- AJCC encourages the development of high-quality prognostication tools by the community using the AJCC published quality criteria will serve as a guideline.
 - Kattan MW, et American Joint Committee on Cancer acceptance criteria for inclusion of risk models for individualized palrognosis in the practice of precision medicine. CA Can J Clin 2016; 66:370-4.

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Key Takeaways

- The TNM staging system continues to be the single most robust prognosticator for solid malignancies.
- The TNM staging system based on anatomical factors remains fundamental to patient classification for clinical management and for research worldwide.
- The AJCC is committed to evidence-based inclusion of validated non-anatomical prognostic factors of clinical relevance to refine prognosis and support current clinical practice.
- The AJCC is committed to maintaining a framework that permits worldwide application of TNM when analysis of non-anatomical factors may not be possible.

Thank you

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