

**Modernizing Clinical Trial Eligibility
ASCO & Friends of Cancer Research**

Lou Fehrenbacher MD

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Modernizing Clinical Trial Eligibility Criteria

Organ Dysfunction, Prior Malignancy, Comorbidity

- **Oncology clinical trials (OCT) determine recommended care**
 - Based on risk:benefit seen in large randomized OCT
- **OCT enrollees are younger and healthier**
- **Similar recommended care is given to patients who:**
 - Could not enroll in OCT re: ineligible
 - are under represented in OCT (older, diverse, rural, poor)
- **? Risk:benefit ratio and toxicity in non OCT patients**
- **Can eligibility criteria be changed to be more inclusive?**

ASCO & Friends of Cancer Research Eligibility Re-Evaluation Process

- **Multi-Disciplinary Working Group**
 - **Trial Design experts**
 - **Clinical Trialists: Academic, Community, Pharmaceutical**
 - **FDA**
 - **Advocates**
- **Multiple meetings:**
 - **Literature Review, data analysis, in depth discussion, consensus development**
 - **Original data collection (Kaiser Permanente)**
 - **Consensus recommendations**

Eligibility Criteria Examined

- **Common Exclusions:**
 - Renal function $\text{GFR} \leq 60\text{cc/min}$
 - Liver function tests
 - Cardiac: CHF/Cardiomyopathy/Hx of MI
 - Prior malignancy ≤ 5 years
 - Comorbidities
- **Uncommon enrollment**
 - Age ≥ 75

Kaiser Permanente Data Extracted

- Kaiser Permanente Northern California: 2013 & 2014
- 12,881 Consecutive cases of:
 - Breast: 5865
 - Colorectal: 2927
 - Lung: 3319
 - Bladder: 770
- Data Base review of peri-diagnosis common eligibility criteria
 - Hx Invasive cancer, Hx CHF/cardiomyopathy/MI, age \geq 75, Charlson
 - Labs: ALT, Bili, GFR,

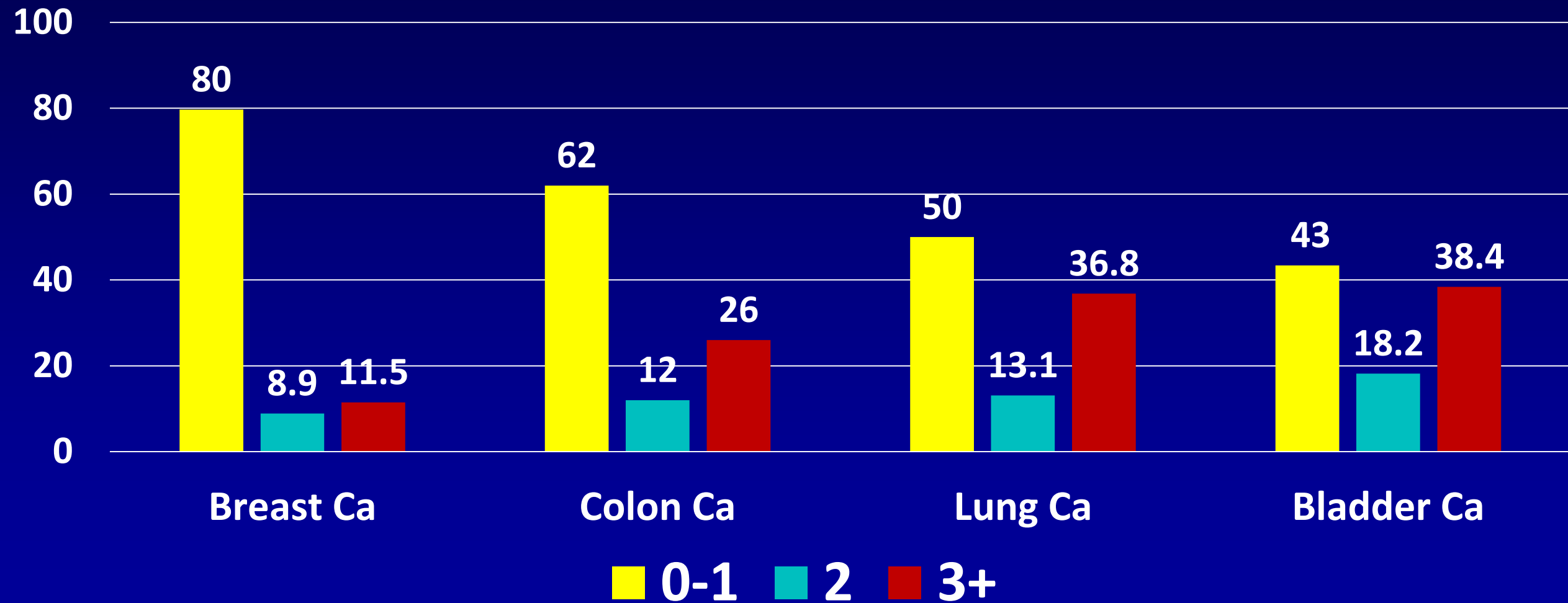
ASCO Working Group- Organ Dysfunction

Kaiser Permanente Population Based Cohort 2013-2014

Ineligibility Rates at Initial Diagnosis

Cancer Site N=12,881	Invasive Cancer <5yr %	CHF/ Card Myop	MI %	HIV+ %	ALT >2.0 X ULN%	Bilirubin >1.5 %	Anti coag %	GFR <60cc /min %	Age >75yo %	Sum of % Ineligible
Breast N=5865	3	5	1	0.05	0.3	0.4	3	15	16	43.7
Colorectal N=2927	5	8	3	0.10	0.9	1	4	18	30	69.9
Lung N=3319	8	11	4	0.27	0.3	0.2	6	20	35	84.7
Bladder N=770	8	11	5	0.39	0.4	1	7	34	45	111.8

Charlson Comorbidity Score % with 0-1, 2, or 3+ By Ca Type KPNC 2013-14, n=13,000+



Modifying Eligibility Criteria Recommendations

- **Renal Function:**
 - Calculated creatinine clearance is the best measurement
 - Unless renal toxicity or renal drug clearance is a clear problem, CrCl <30cc/min should be eligibility criteria in later phase trials
- **Hepatic function:**
 - Mild to moderate dysfunction should be acceptable if pk data and early clinical data show safety
 - Better measurements of function are needed

Modifying Eligibility Criteria Recommendations (cont.)

- **Cardiac Function:**
 - Conservative approach in early phase studies, but broadening criteria as safety becomes evident
 - If QTc prolongation not of concern in early phase I, then criteria should be eliminated in later studies
- **Prior Malignancy:**
 - If prior cancer treatment is completed, risk of recurrence is low, & no endpoint interference, current criteria (<5 years) should change
 - Suggested: 2 years off treatment and no evidence of disease

Goal of Modernizing Eligibility Criteria

- **Increase enrollment:**
 - Greater number of patients
 - Larger percentage of older patients
 - Larger percentage of representative “real life” patients
- **Assess effect in commonly seen subsets, both:**
 - Treatment benefit
 - Treatment toxicity/side effects in subsets

Modernizing Clinical Trial Eligibility Criteria: Recommendations of the American Society of Clinical Oncology–Friends of Cancer Research Organ Dysfunction, Prior or Concurrent Malignancy, and Comorbidities Working Group

Stuart M. Lichtman, R. Donald Harvey, Marie-Anne Damiette Smit, Atiqur Rahman, Michael A. Thompson, Nancy Roach, Caroline Schenkel, Suanna S. Bruinooge, Patricia Cortazar, Dana Walker, and Louis Fehrenbacher

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