IMPROVING THE EVIDENCE BASE FOR TREATMENT DECISION MAKING FOR OLDER ADULTS WITH CANCER:

STUDY DESIGNS TO BENEFIT OLDER ADULTS USING ARCHIVED CLINICAL TRIAL DATA

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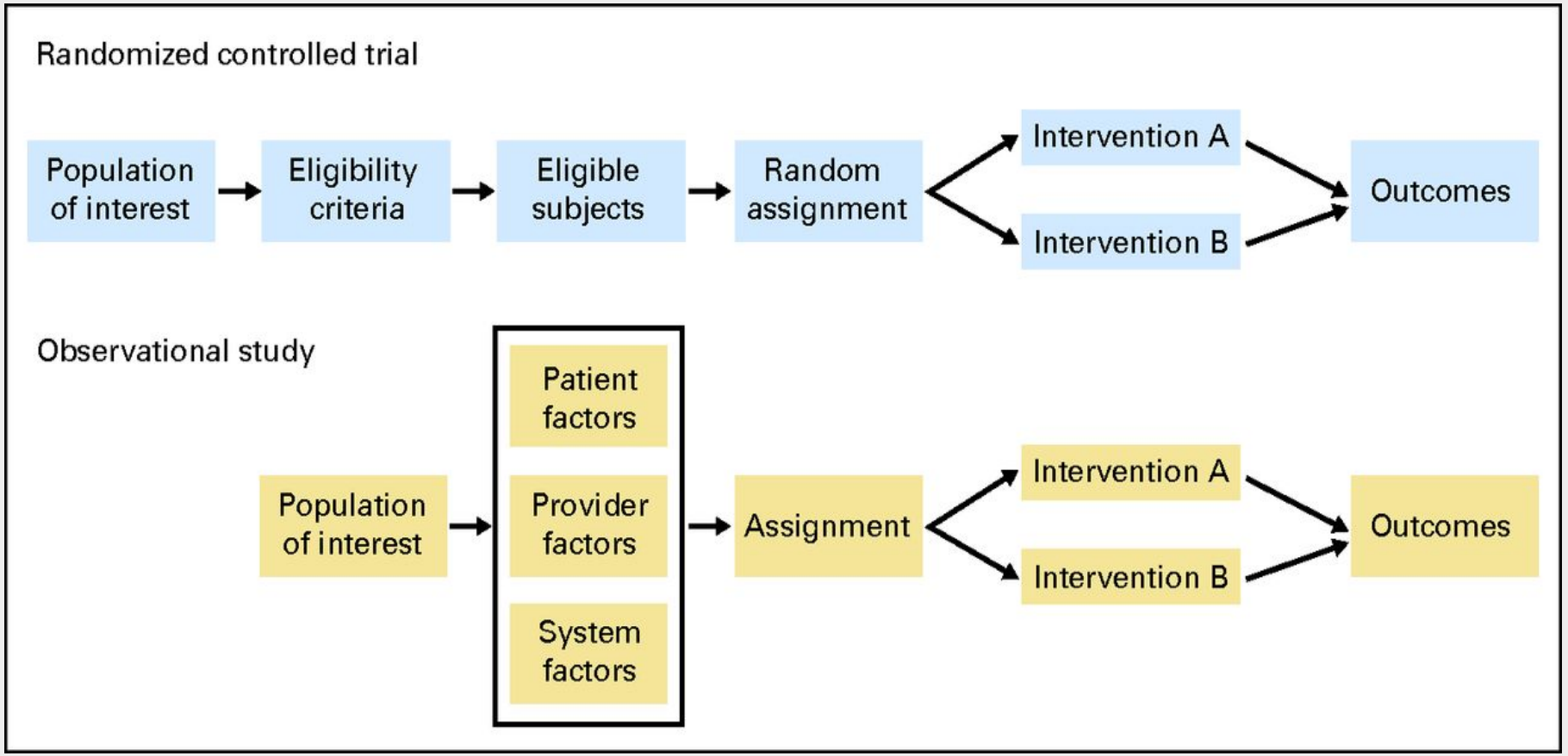
Observational Data VS RCT



Armstrong K. *J Clin Oncol* 2012

Strengths & Limitations of RCT's & Observational Studies

Randomized Clinical Trials

PROS

- Prospective data collection
- Randomized treatment assignment
- Prognostic data collected at baseline

CONS

- Selected patient population
- Strict eligibility Criteria
- Limited baseline / FU data collected
- Limited long-term follow-up after end of intervention
- Take a long time

Observational Data

PROS

- Large numbers
- "Real World"
- Long follow-up
- Lower Cost

CONS

- Selection Bias
- Associations but not causality
- Unknown patient preferences
- lack of detailed information on treatments and prognostic factors
- No data on severity of diagnosis

What about Observational Studies from RCT's?

Benefits

- Randomized treatment assignment
- Known prognostic factors
- Detailed treatment information
- Uniform treatment
- Prospective follow up (PFS, DFS)
- Prospective toxicity data
- NCTN (SWOG, Alliance, NRG, ECOG-ACRIN):
  - Multi-center
  - Community / MU Sites

Combine studies & study special populations

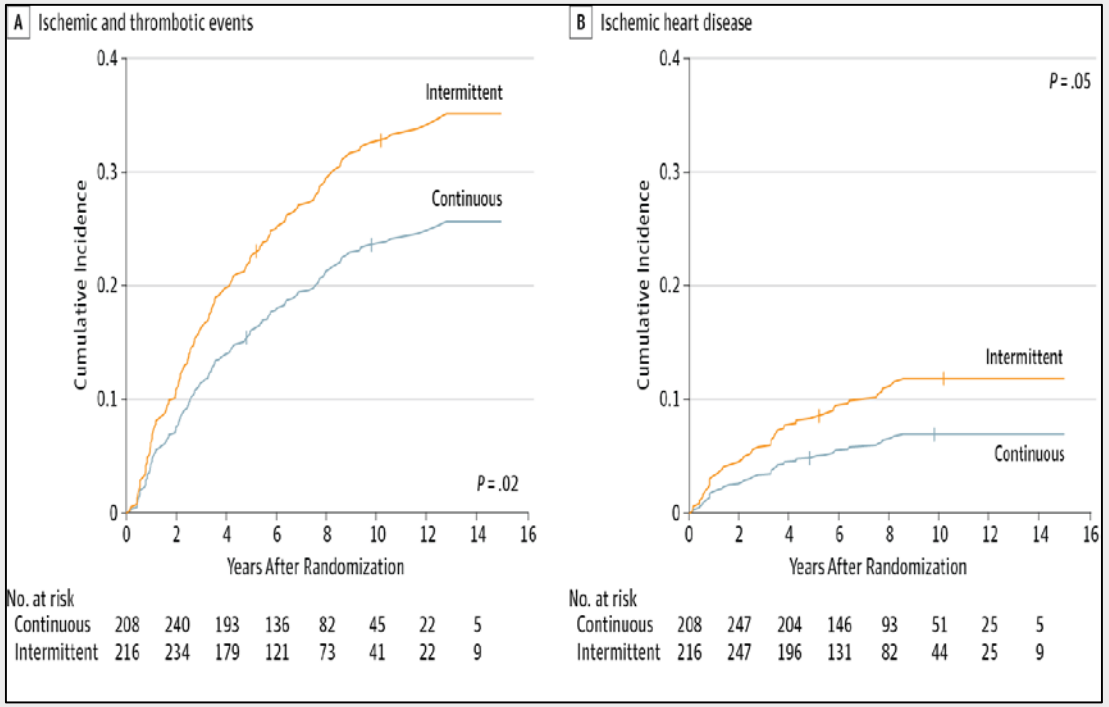
- Elderly
- Race/Ethnicity
- Insurance/Income

Link to claims data (Medicare)

- Long-term follow-up
- Comorbid conditions
- New diagnoses / procedures
- Health utilization and cost data

Long term outcomes in the Elderly:

Adverse Health Effects of Intermittent vs Continuous Androgen Deprivation Therapy for Metastatic Prostate Cancer (S9346)



Predicted Cumulative Incidence of Individual Adverse Health Event by Treatment Arm

Older men on intermittent ADT:

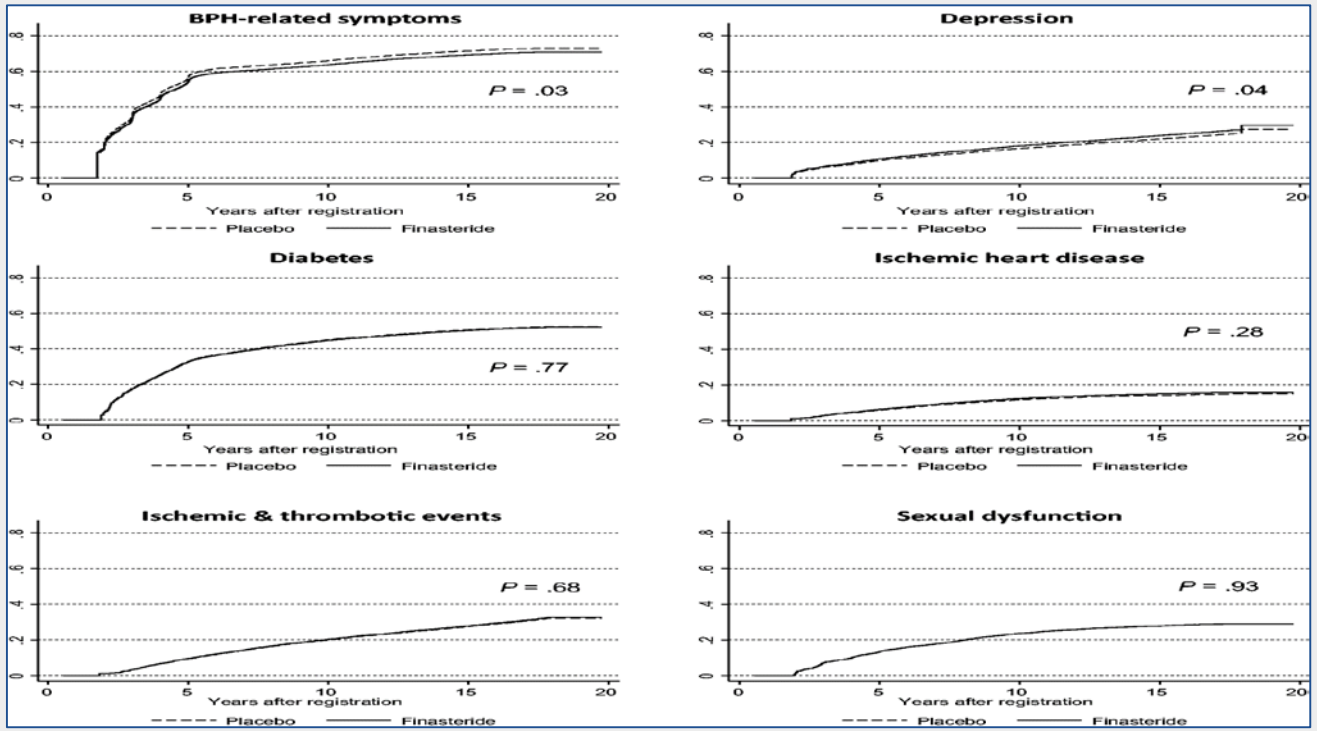
- No apparent reduction in bone, endocrine, or cognitive events
- Increased incidence of ischemic and thrombotic events

IMPLICATIONS: Caution with intermittent therapy

Hershman D, et al, JAMA Onc. 2016

Long term outcomes in the Elderly:

Long-term Consequences of Finasteride vs Placebo in the Prostate Cancer Prevention Trial



Cumulative incidence of selected events by random assignment to finasteride v placebo

- Median SWOG-Medicare linkage follow-up time of 16 years
- Finasteride participants had 10% higher risk for depression (p=.04) and 6% lower risk for BPH-related events
- No other differences were found

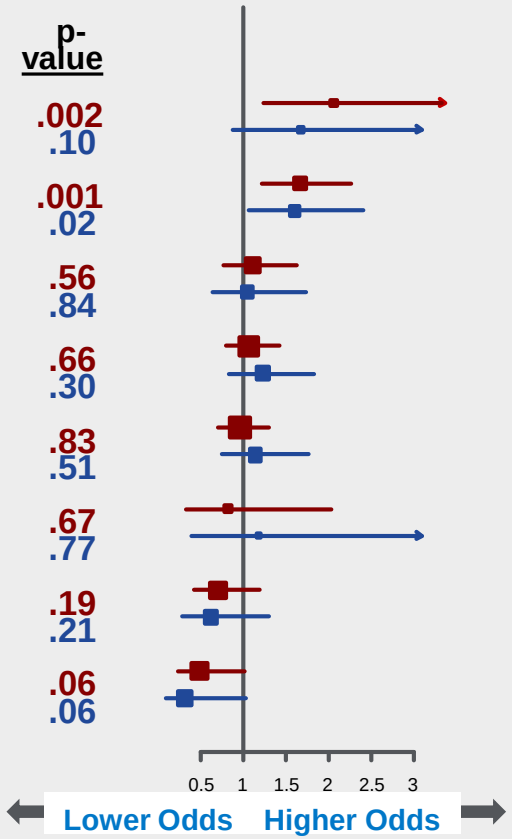
Implications: There is little need to worry about long-term non-cancer consequences of finasteride use

Unger J. et al, JNCI, 2016

Risk of Toxicity in the Elderly:

Comorbidities and Risk of CIPN Among Patients ≥65 Years

Disease Predictor	Neuropathy Grade	Odds Ratio	p-value
Diabetes with Chronic Complications	2-4	2.13	.002
	3-4	1.73	.10
Diabetes with or without Chronic Complications	2-4	1.67	.001
	3-4	1.61	.02
Hypothyroid	2-4	1.12	.56
	3-4	1.05	.84
Hypercholesterolemia	2-4	1.07	.66
	3-4	1.23	.30
Hypertension	2-4	0.97	.83
	3-4	1.15	.51
Varicellazoster	2-4	0.82	.67
	3-4	1.18	.77
Peripheral Vascular Disease	2-4	0.71	.19
	3-4	0.62	.21
Autoimmune Disease	2-4	0.49	.06
	3-4	0.32	.06



Forest plot of the association of neuropathy grade with each comorbid condition

- Neuropathy is a debilitating toxicity associated with various chemotherapy agents
- Examined 1401 patients from 23 studies
- Patients with diabetes complications had >2x the odds of CIPN

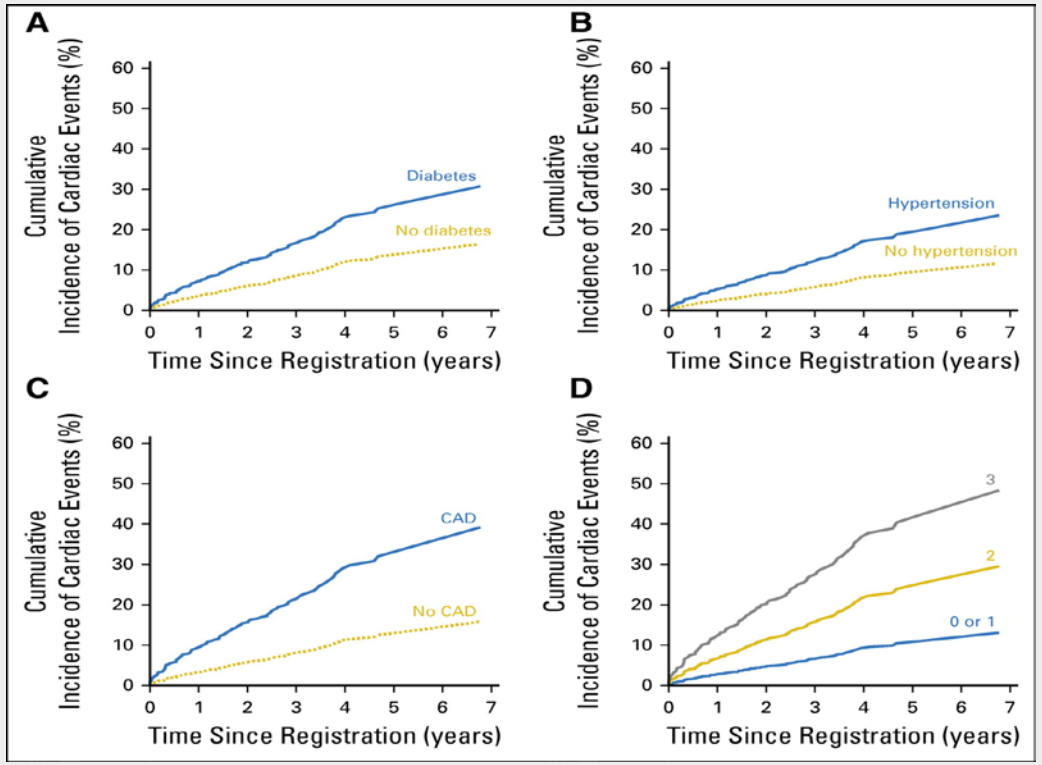
IMPLICATIONS: Elderly with diabetes at higher risk for neuropathy

Hershman DL, et al, JNCI, 2016

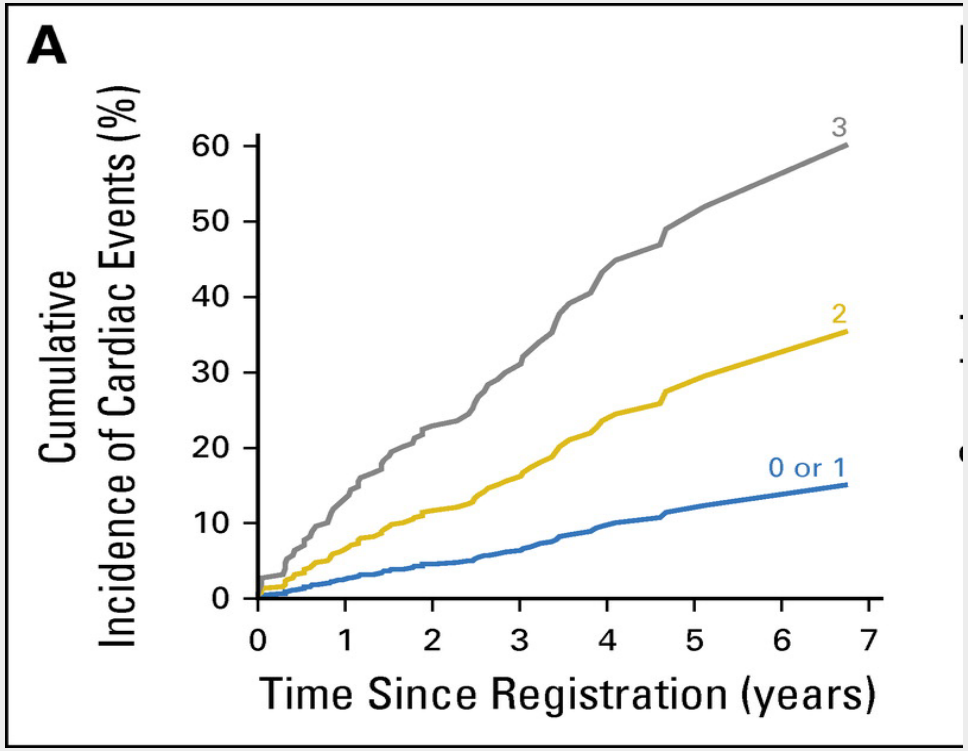
Comorbidity and Outcomes in the Elderly:

Association of Cardiovascular Risk Factors With Cardiac Events and Survival

Cumulative incidence of cardiac events by baseline cardiovascular disease risk factors.



Cumulative incidence of cardiac events by number of cardiovascular disease risk factors

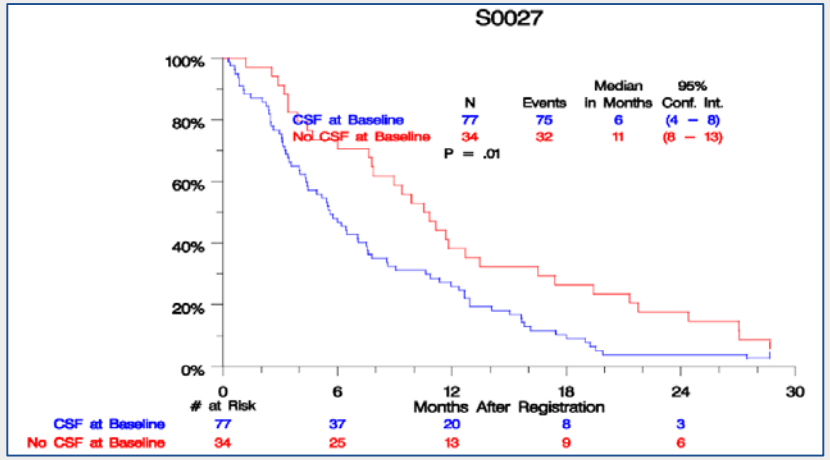


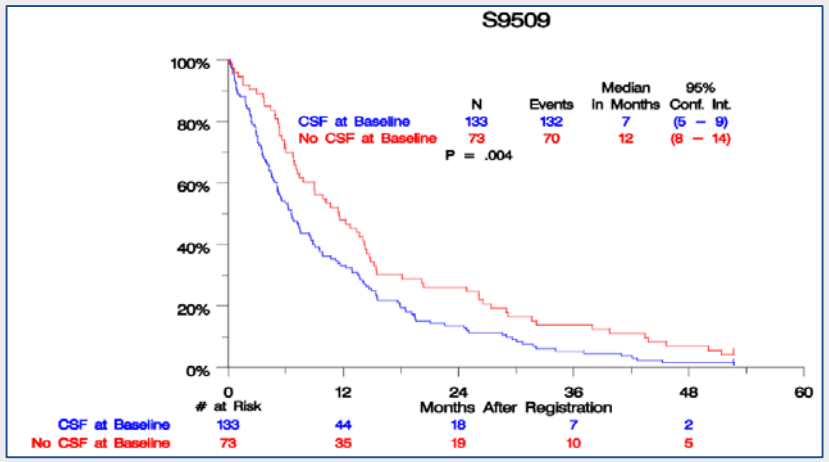
Hershman DL, et al, J. Clin Oncol, 2018

Patient Reported Outcomes and Survival in the Elderly:

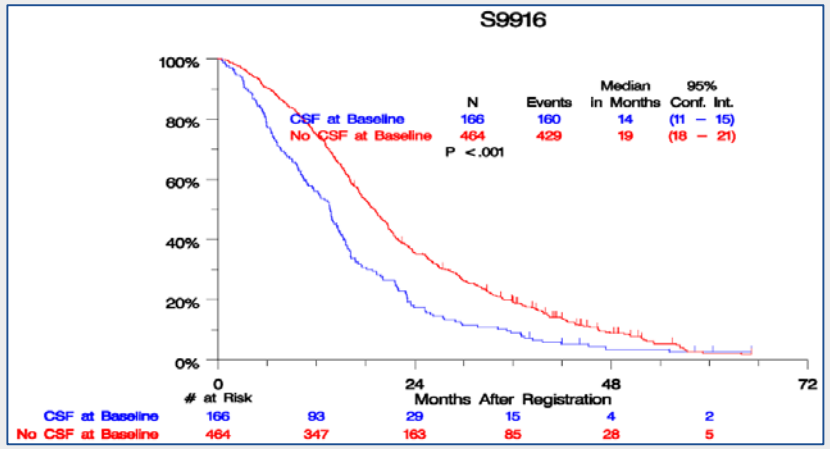
The Association of Patient Fatigue and Outcomes in Advanced Cancer

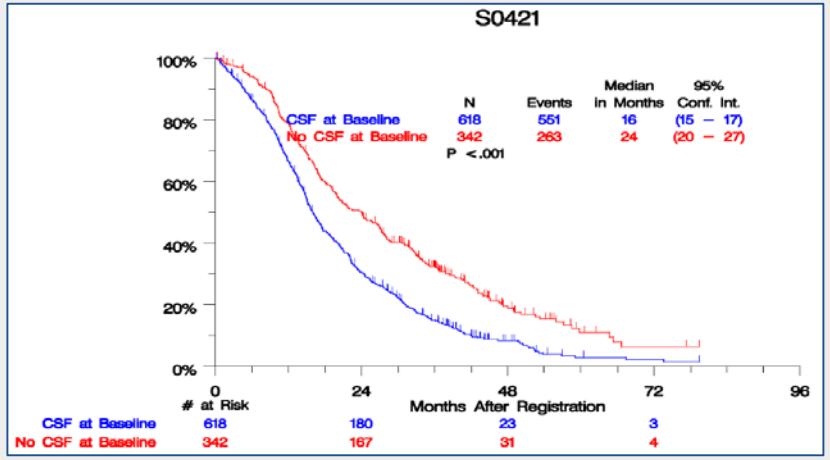
Lung Cancer





Prostate Cancer





- 48% > 70
- 52% with fatigue at baseline

Mo, J et al; ASCO QLTY 2020

USING CLINICAL TRIALS DATA TO INFORM POLICY

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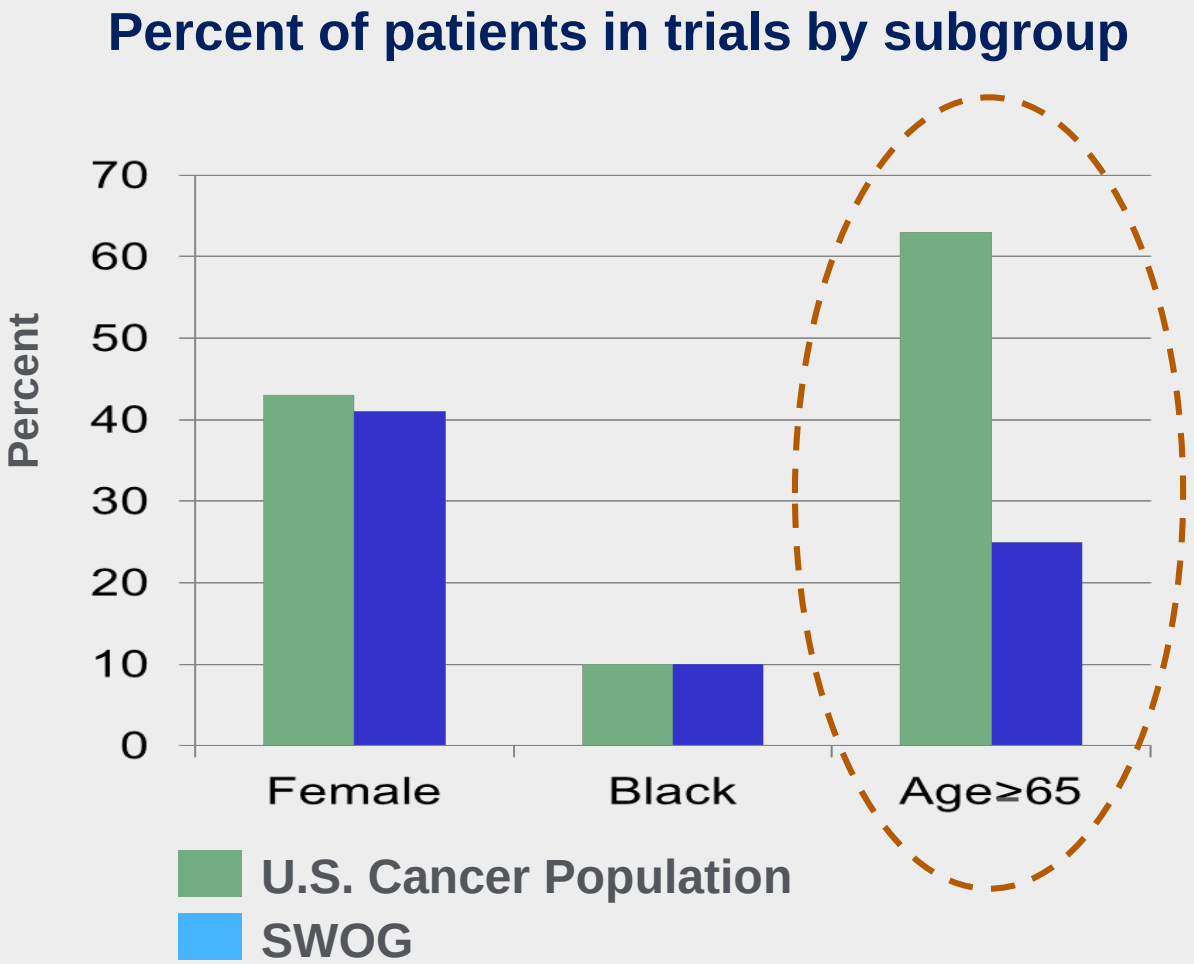
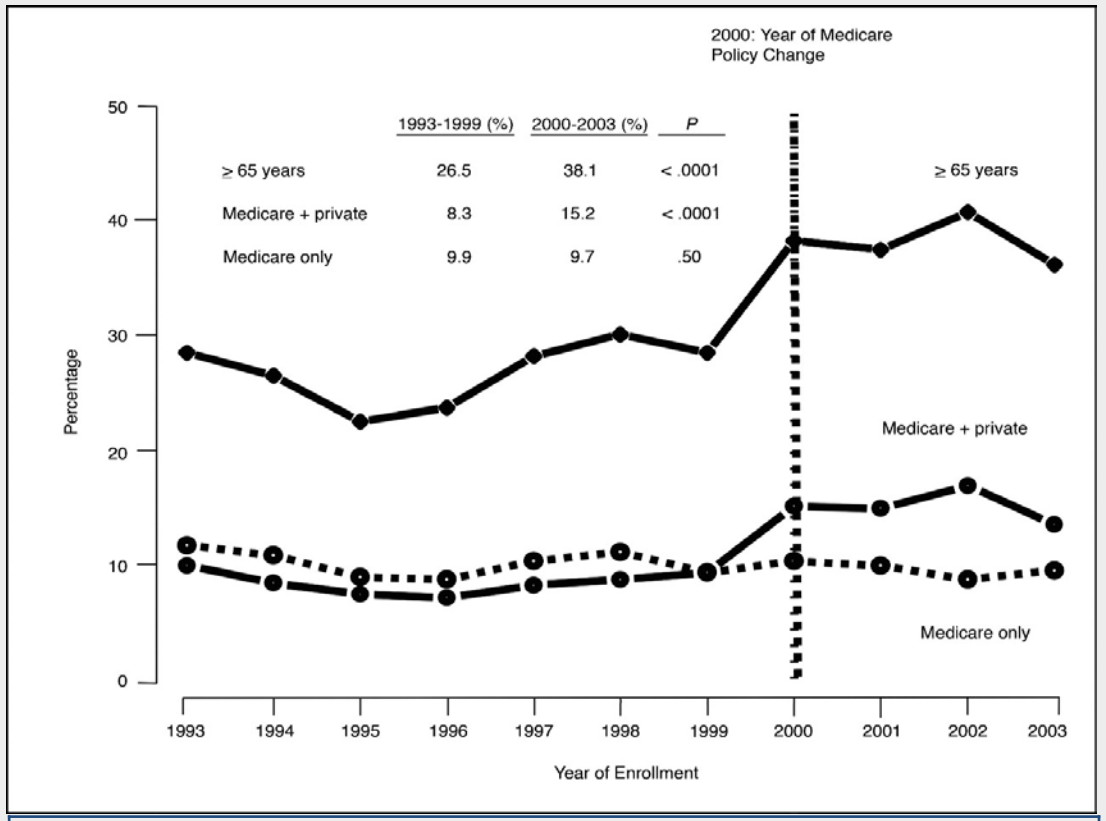
Underrepresentation of patients >65 in cancer trials



- Compared enrollment patterns in SWOG to U.S. cancer population
- Good representation of females and blacks, but dramatic underrepresentation of older patients
- Included in IOM report
- Subsequent policy change by Medicare (in 2000) to cover routine care costs of clinical trials

Hutchins, et al, NEJM, 1999

Impact of the Year 2000 Medicare Policy Change on Older Patient Enrollment to Cancer Clinical Trials



	'93-'99	'00-'03	P-value
% ≥ 65 yrs	26.5%	38.1%	<.0001
% Med+Private	8.3%	15.2%	<.0001
% Med Only	9.9%	9.7%	.50

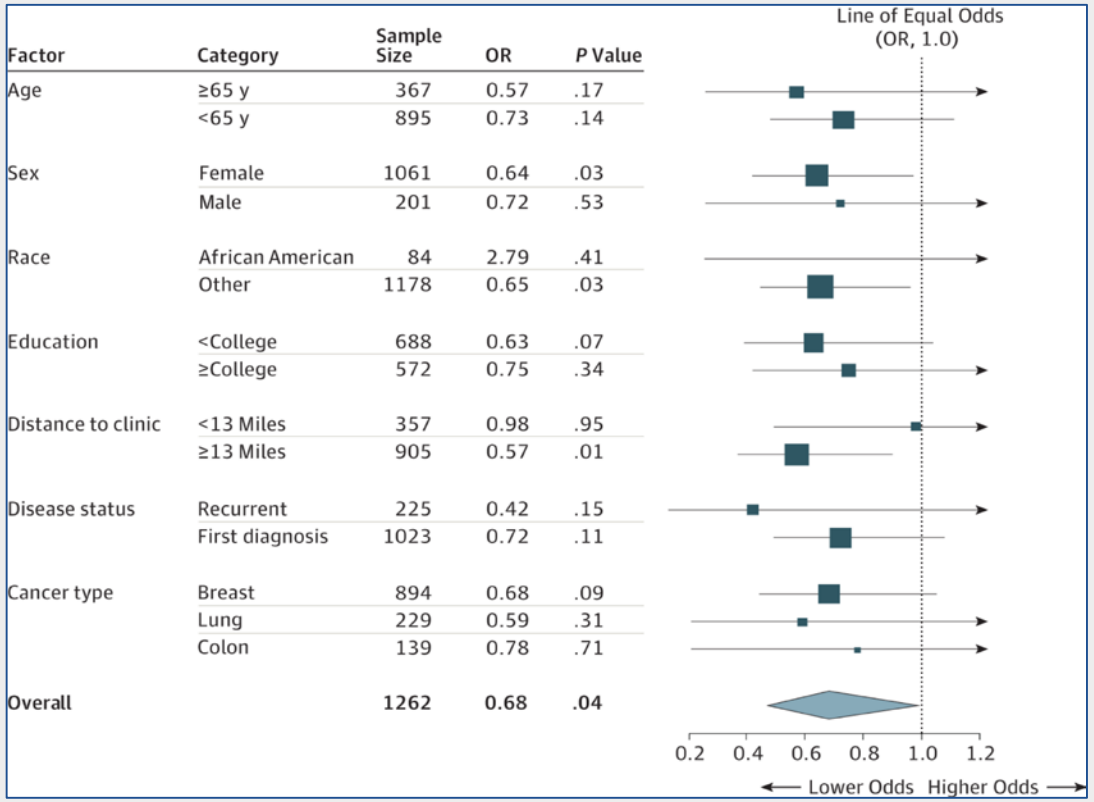
- Examined enrollment patterns by age in SWOG before vs. after the Medicare policy change
- Observed an increase in older patient enrollment overall
- Only among those with Medicare + private insurance

Implications: Marginal additional costs of trial participation (i.e. co-pays, co-insurance) likely still barriers for patients

Unger J. et al, JCO, 2006

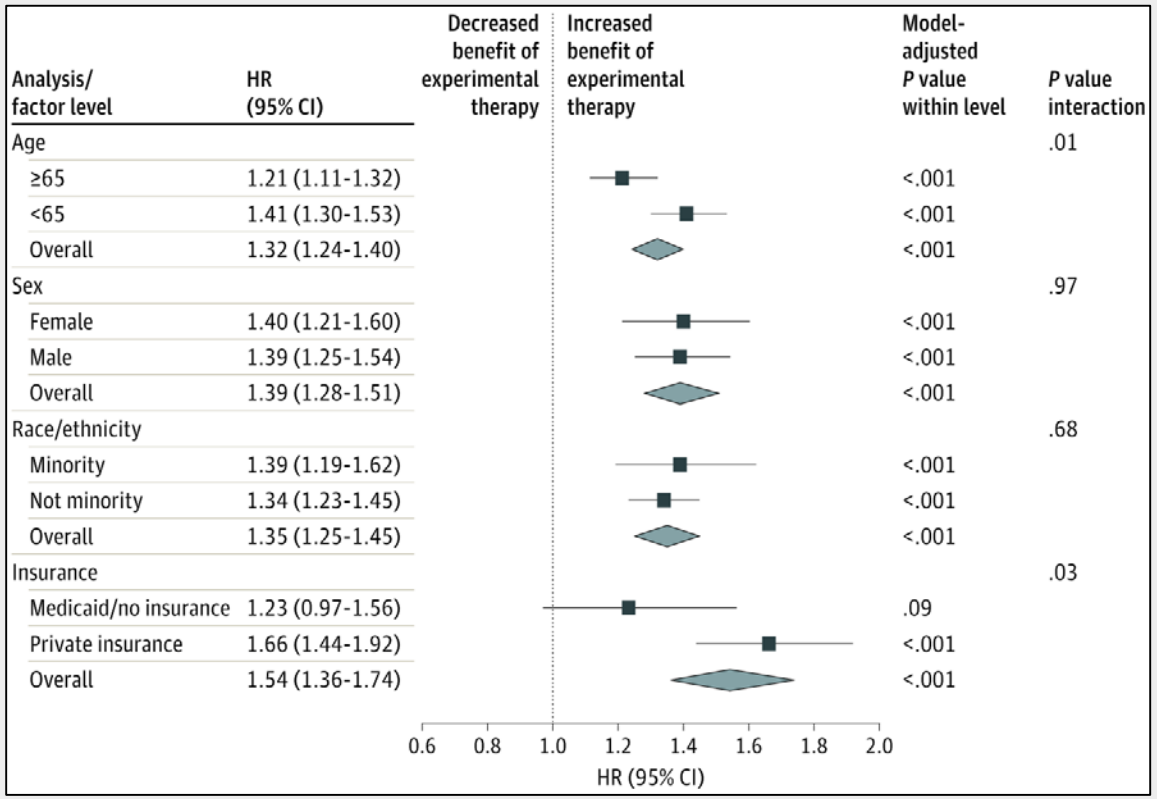
Patient Income Level and Insurance and Cancer Clinical Trial Participation and Outcome

Association of Insurance and Participation



Factor	Category	Sample Size	OR	*P* Value
Age	≥65 y	367	0.57	.17
	<65 y	895	0.73	.14
Sex	Female	1061	0.64	.03
	Male	201	0.72	.53
Race	African American	84	2.79	.41
	Other	1178	0.65	.03
Education	<College	688	0.63	.07
	≥College	572	0.75	.34
Distance to clinic	<13 Miles	357	0.98	.95
	≥13 Miles	905	0.57	.01
Disease status	Recurrent	225	0.42	.15
	First diagnosis	1023	0.72	.11
Cancer type	Breast	894	0.68	.09
	Lung	229	0.59	.31
	Colon	139	0.78	.71
Overall		**1262**	**0.68**	**.04**

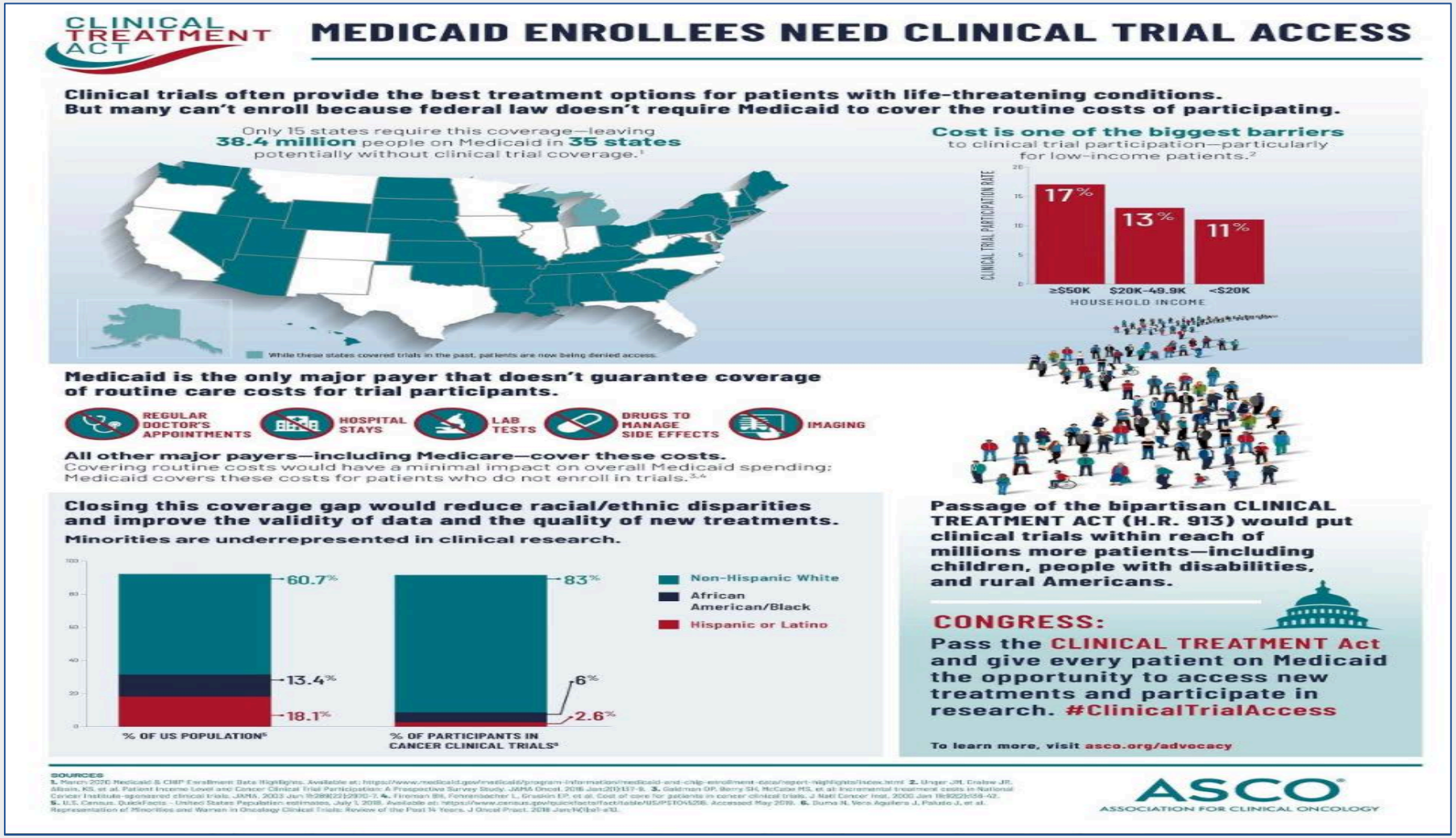
Association of Treatment With Overall Survival



Analysis/ factor level	HR (95% CI)	Model-adjusted *P* value within level	*P* value interaction
Age			.01
≥65	1.21 (1.11-1.32)	<.001	
<65	1.41 (1.30-1.53)	<.001	
Overall	1.32 (1.24-1.40)	<.001	
Sex			.97
Female	1.40 (1.21-1.60)	<.001	
Male	1.39 (1.25-1.54)	<.001	
Overall	1.39 (1.28-1.51)	<.001	
Race/ethnicity			.68
Minority	1.39 (1.19-1.62)	<.001	
Not minority	1.34 (1.23-1.45)	<.001	
Overall	1.35 (1.25-1.45)	<.001	
Insurance			.03
Medicaid/no insurance	1.23 (0.97-1.56)	.09	
Private insurance	1.66 (1.44-1.92)	<.001	
Overall	1.54 (1.36-1.74)	<.001	

Unger, J; JAMA Oncol., 2015.
Unger, J; JAMA Network Open., 2020.

Medicaid to Cover Routine Costs for Patients in Trials



Opportunities

- Many important questions can be answered from trial data from drug development to diffusion of new treatments into the community
- Better understanding of barriers to enrollment is vital for increasing access to trials, interpreting trial results, and understanding their value and impact
- Innovative big data type approaches are necessary to address many of these questions
- Easier and creative ways of making linkages can help

QUESTIONS?