

# Inclusion/Exclusion Criteria for Elderly populations in NIH-funded Clinical Studies

EA WG

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# Proposal:

- Proposal:
  - Address inclusion/exclusion of older individuals from NIH-funded clinical studies.
- Aim:
  - To explore the representation of elderly populations in clinical research and what type of research may exclude this population.

# Definitions and Rationale:

- Definitions
  - For the purposes of this analysis “older/elderly” persons are defined as 65 years or older.
    - Some consensus that 65 years old is either 1) roughly the age when a person may receive retirement benefits, 2) is eligible for Medicare, or 3) a cut off age for clinical trials
  - Upper age limit or age capped- clinical studies that have defined age limits (e.g. 21-69 yrs old)
- Rationale:
  - Studies have demonstrated that elderly persons are considerably excluded from disease treatment based clinical trials (Dobson, 2007; Hadbavna et al, 2013, Zulman *et al.* 2011, Wildiers *et al.* 2007)
  - Examined diseases based on the higher prevalence in older/elderly adults

# Questions to be addressed

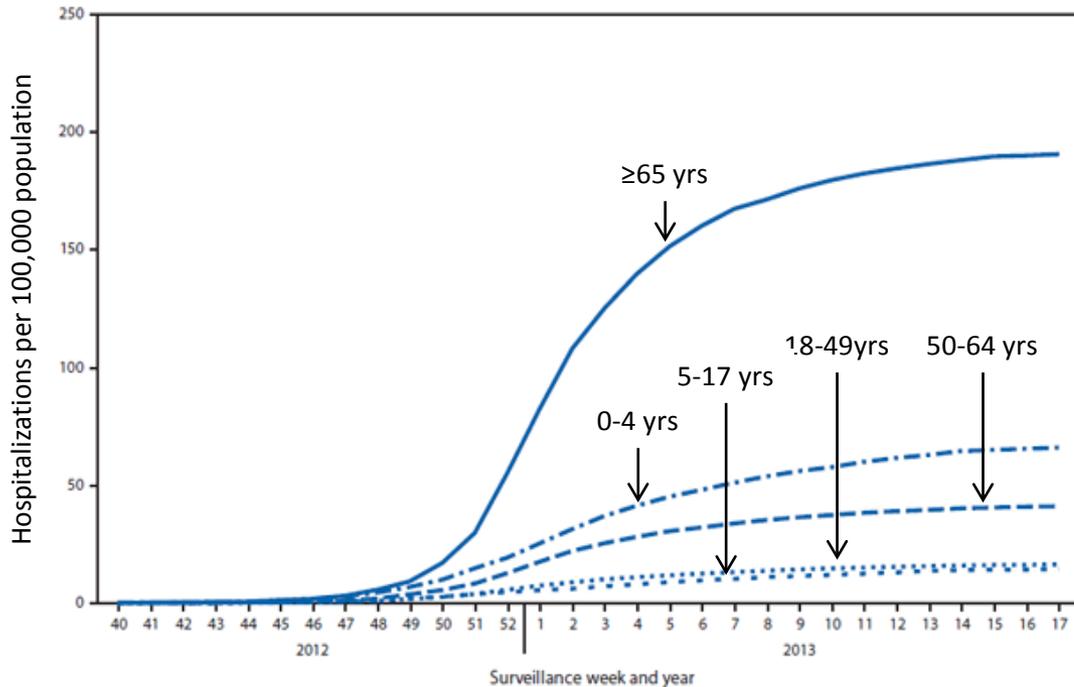
- Does age of participants in clinical studies reflect the prevalence of the target condition in the population?
- What criteria may exclude older adults?

# Methods

- Collect a random sampling of **NIH-funded Phase 3** clinical studies
  - Analyzed data on age, exclusion criteria, and prevalence
  - Data sources: QVR records, [www.clinicaltrials.gov](http://www.clinicaltrials.gov), and associated publications
- Randomly sampled up to 50 studies in each category (or all studies if < 50)

# Pneumonia: Prevalence vs. Clinical Studies

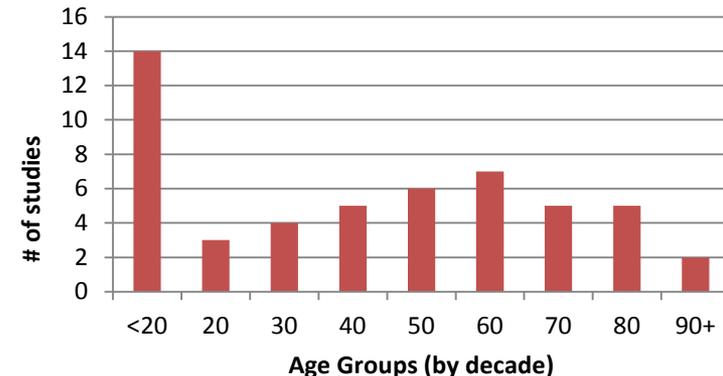
## Prevalence of Influenza Pneumonia by Age



Cumulate hospitalization rates for laboratory-confirmed influenza, by age group, surveillance week, and year (<http://www.cdc.gov/mmwr>).

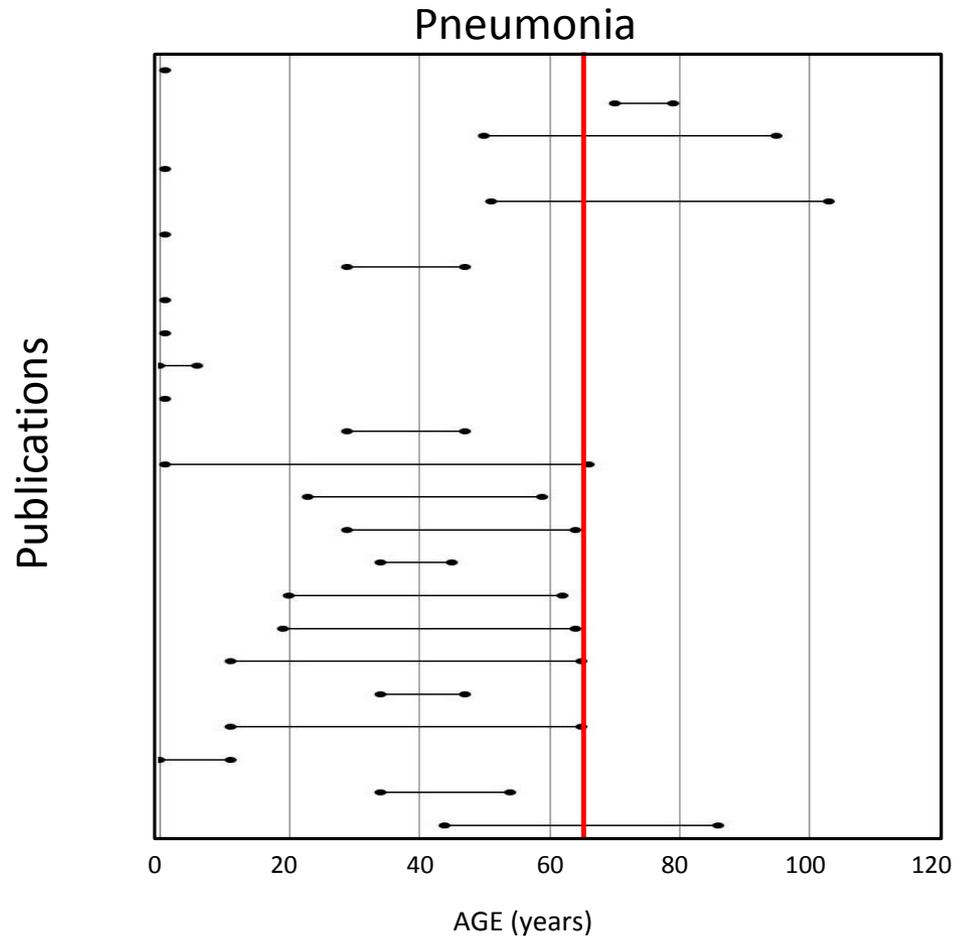
*Weekly June 14, 2013 / 62(23); 473-479*

## Pneumonia Phase 3 Clinical Trials with defined age caps



Phase 3 clinical studies with upper age limit (e.g. 21- 60years) n=19 (40%)

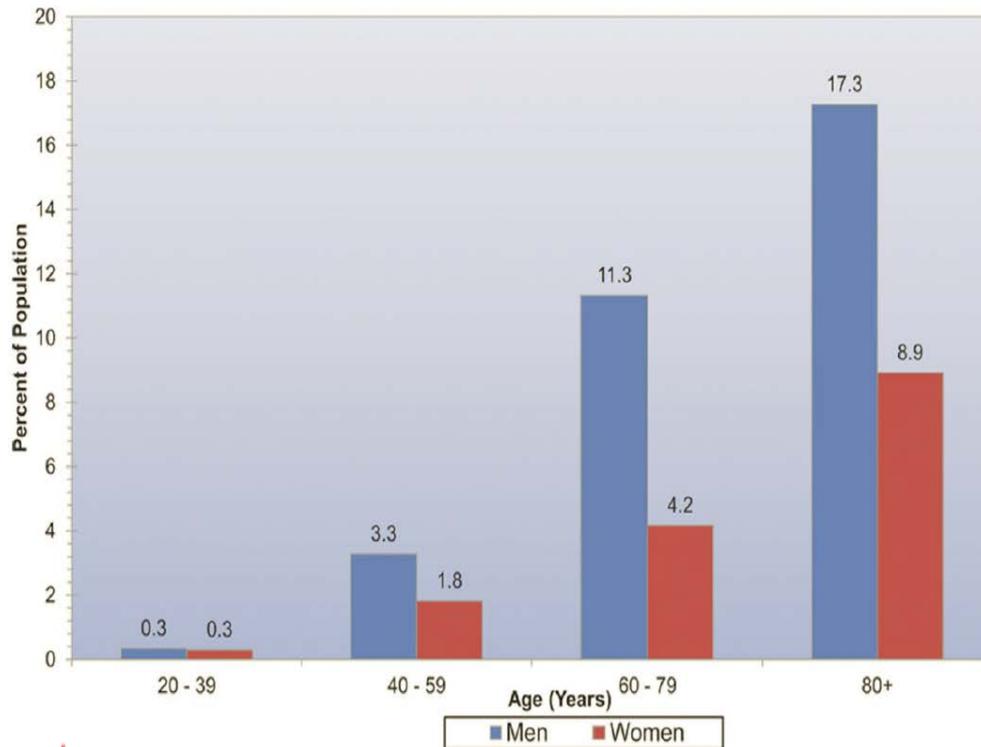
# Age Ranges from Publications associated with clinical trials



Analysis of age range reported in publications for clinical studies in cohort. n=24 (45%). (e.g. 21- 62 yrs old) Red line=approx. 65yrs

# Heart Attack: Prevalence vs. Clinical Studies

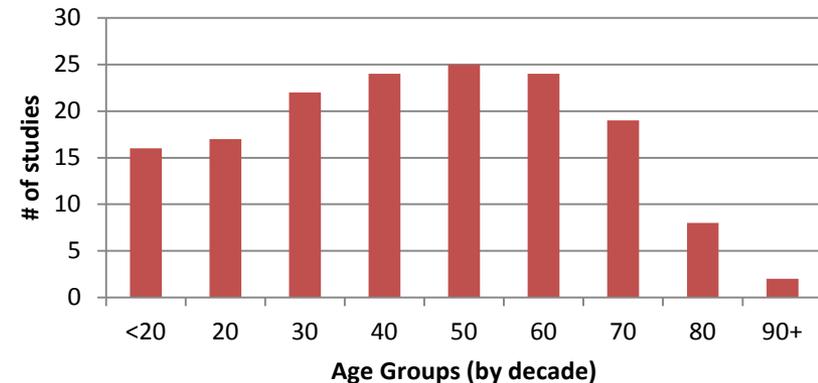
## Prevalence of Myocardial infarction by age and sex



Mozaffarian D et al. *Circulation*. 2015;131:e29-e322  
National Health and Nutrition Examination Survey 2009-2012

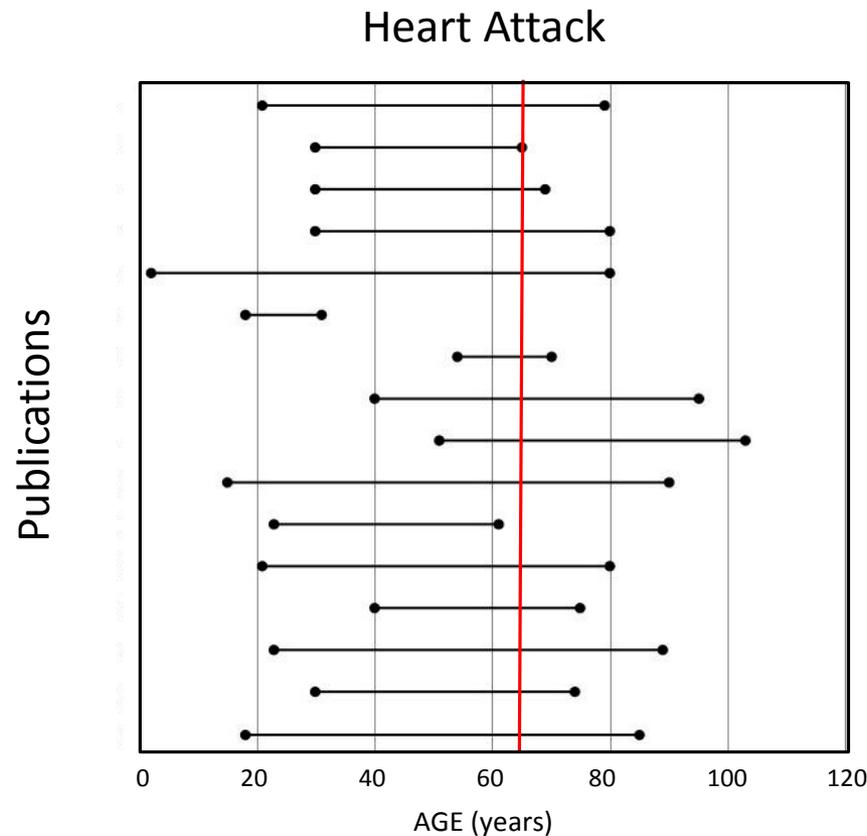
[https://www.heart.org/idc/groups/heart-public/@wcm/@sop/@smd/documents/downloadable/ucm\\_449846.pdf](https://www.heart.org/idc/groups/heart-public/@wcm/@sop/@smd/documents/downloadable/ucm_449846.pdf)

## Heart Attack Phase 3 Clinical Trials with defined age caps



Phase 3 clinical studies with upper age limit (e.g. 21- 60years) n=27 (54%)

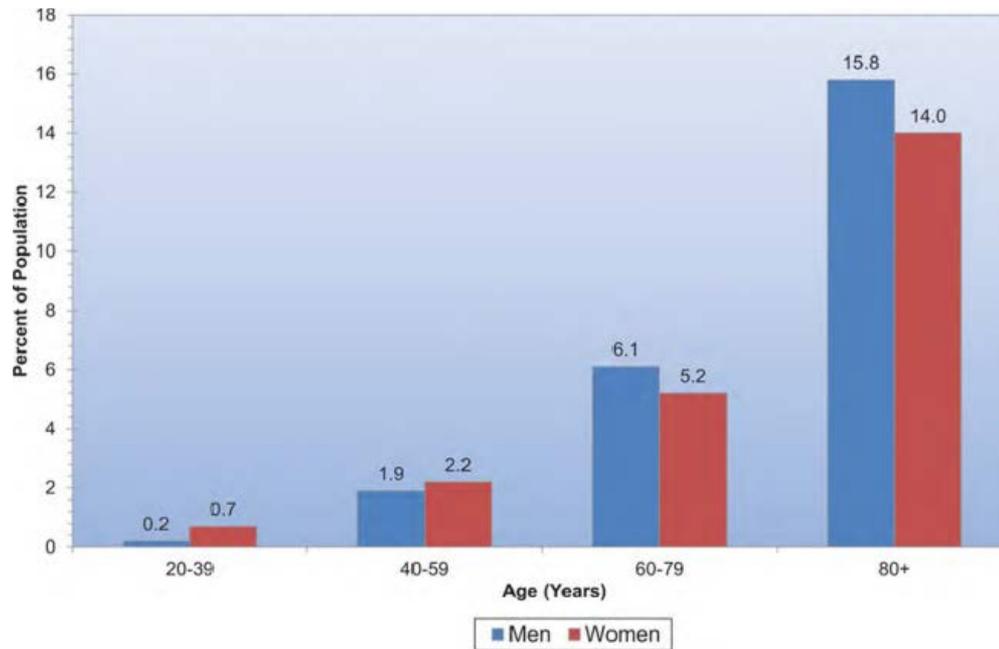
# Age Ranges from Publications associated with clinical trials



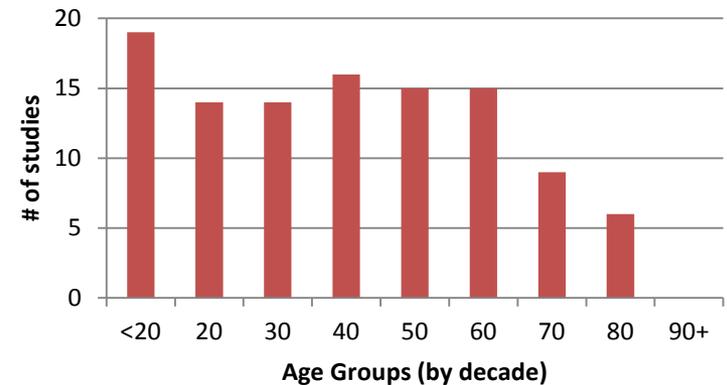
Analysis of age range reported in publications for clinical studies in cohort. n=16 (32%). (e.g. 21- 62 yrs old) Red line=approx. 65yrs

# Stroke: Prevalence vs. Clinical Studies

## Prevalence of stroke by age and sex



## Stroke Phase 3 Clinical Trials with defined age caps



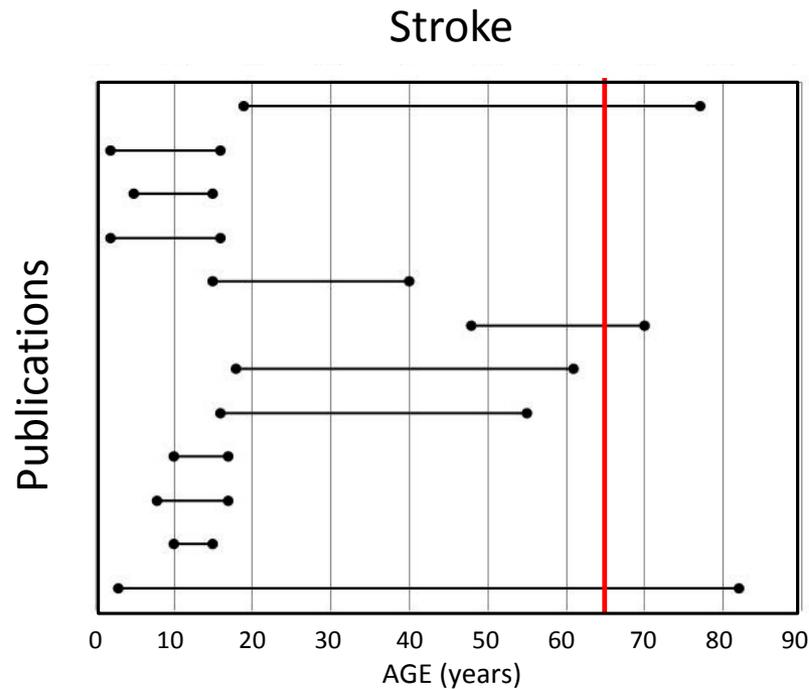
Phase 3 clinical studies with upper age limit (e.g. 21- 60years) n=24 (46%)



Mozaffarian D et al. Circulation. 2015;131:e29-e322

(National Health and Nutrition Examination Survey: 2009–2012)

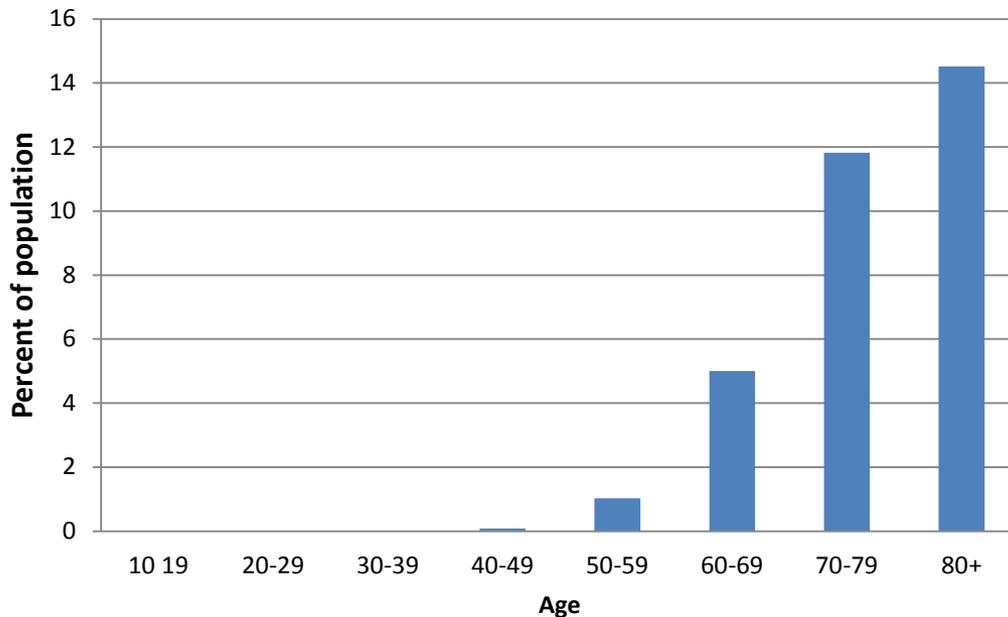
# Age Ranges from Publications associated with clinical trials



Analysis of age range reported in publications for clinical studies in cohort. n=12 (23%) (e.g. 21- 62 yrs old) Red line=approx. 65yrs

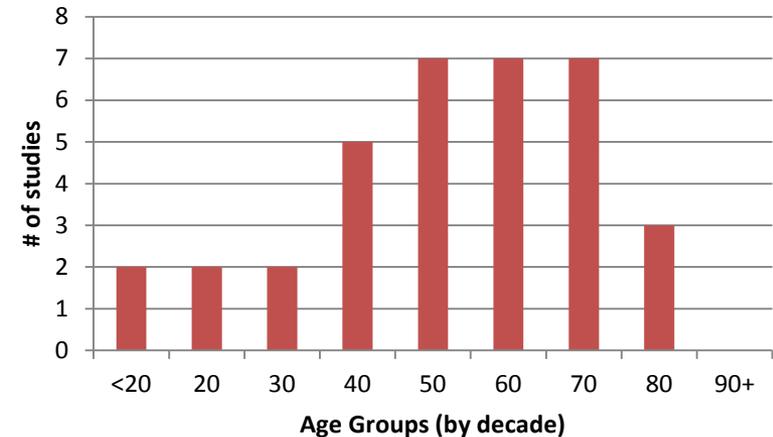
# Prostate Cancer: Prevalence vs. Clinical Studies

## Prevalence of Prostate Cancer by Age



Estimated prevalence percent on January 1, 2011, of the SEER population diagnosed in the previous 19 years SEER NCI, Cancer.gov

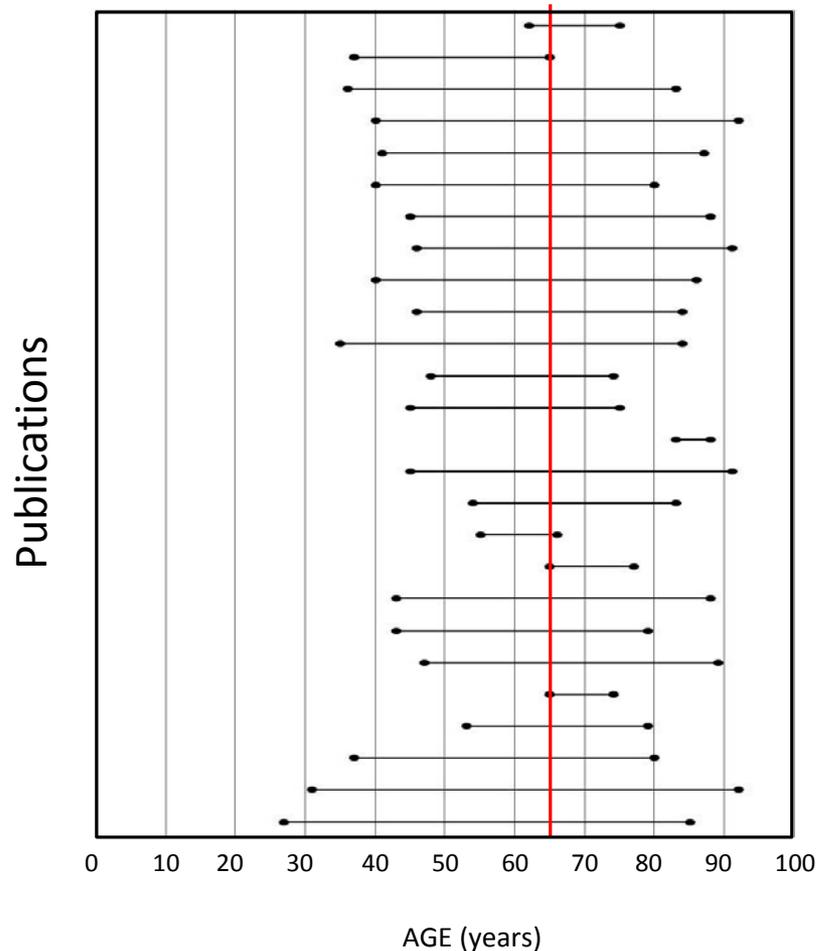
## Prostate Cancer Phase 3 Clinical Trials with defined age caps



Phase 3 clinical studies with defined “age caps” (e.g. 21- 60years). n=13 (26%)

# Age Ranges from Publications associated with clinical trials

Prostate Cancer



Analysis of age range reported in publications for clinical studies in cohort. n=26 (52%) (e.g. 21- 62 yrs old) Red line=approx. 65yrs

# Inclusion/Exclusion Criteria

- Clinical studies publish inclusion and exclusion criteria for participants
- Analyzed the types of exclusion factors associated with these clinical studies

<u>Exclusion Criteria</u>		
Cancer (active)	GI/Liver	Reduced life expectancy
Cancer (history/past case)	Hypertension	Pulmonary disease
Cardiovascular	Neurological	Renal
Congestive Heart Failure	Pain	Stroke
Diabetes	Physical Disability	Nursing Home
Polypharmacy/ concomitant medication	Cognitive Impairment/ Psychosis	

# Exclusion Criteria by disease category in Phase 3 studies

## Exclusion Criteria

	<u>Hypertension</u>	<u>Diabetes</u>	<u>Poly-pharmacy</u>
Congestive Heart Failure	12%	12%	29%
Pneumonia	7%	7%	33%
Coronary Atherosclerosis	32%	16%	22%
Cardiac Dysrhythmias	4%	4%	42%
Heart Attack	14%	33%	12%
Osteoarthritis	---	---	24%
Stroke	6%	8%	35%
COPD	6%	6%	13%
Lung Cancer	8%	4%	31%
Prostate Cancer	4%	4%	22%

Disease

Study protocols were reviewed and examined for specific criteria that would exclude a patient from a particular study. Shown as percent of studies that exclude based on specific criteria.

# Summary

- Is exclusion for older adults appropriate?
- What are the primary reasons for exclusion?
- Are exclusion criteria framed within specific types of studies (drug intervention, device, behavioral, etc.)?
- Is inclusion/exclusion of older adults with poly-pharmacy and/or comorbidities appropriate?

# Acknowledgements

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