

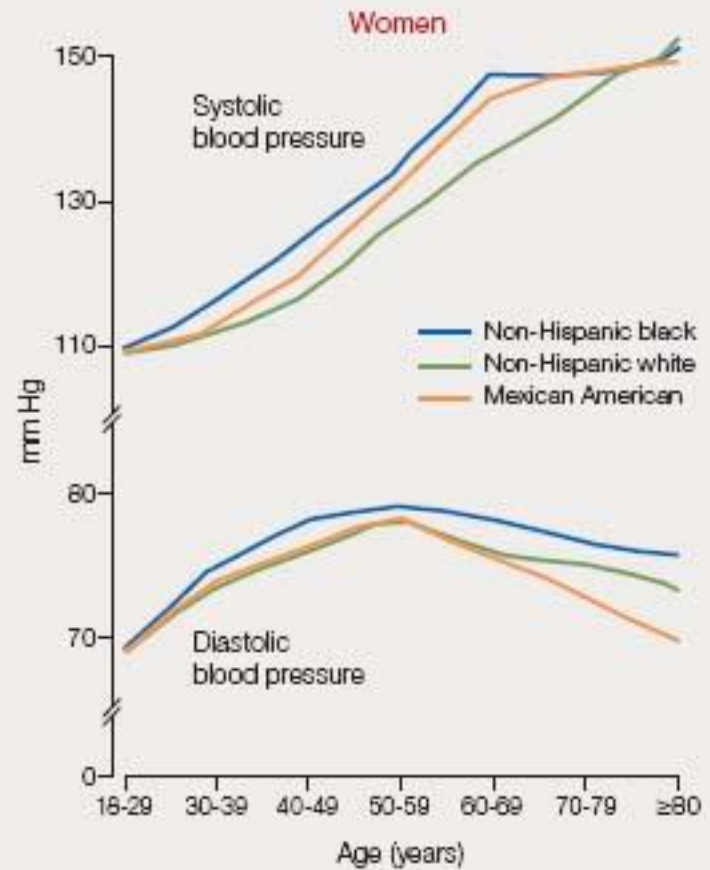
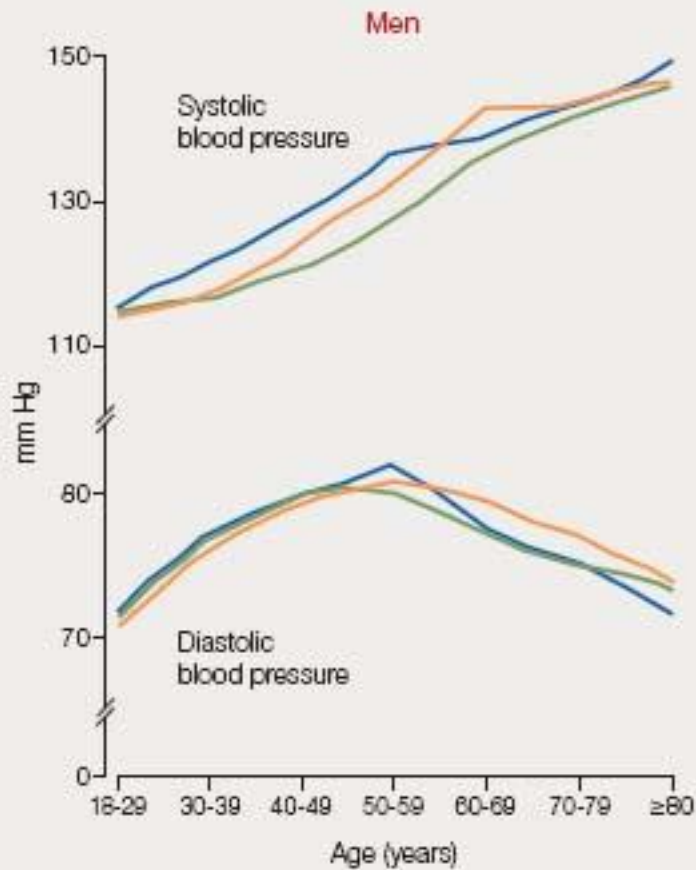
# Hypertension targets in the elderly

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September 2016

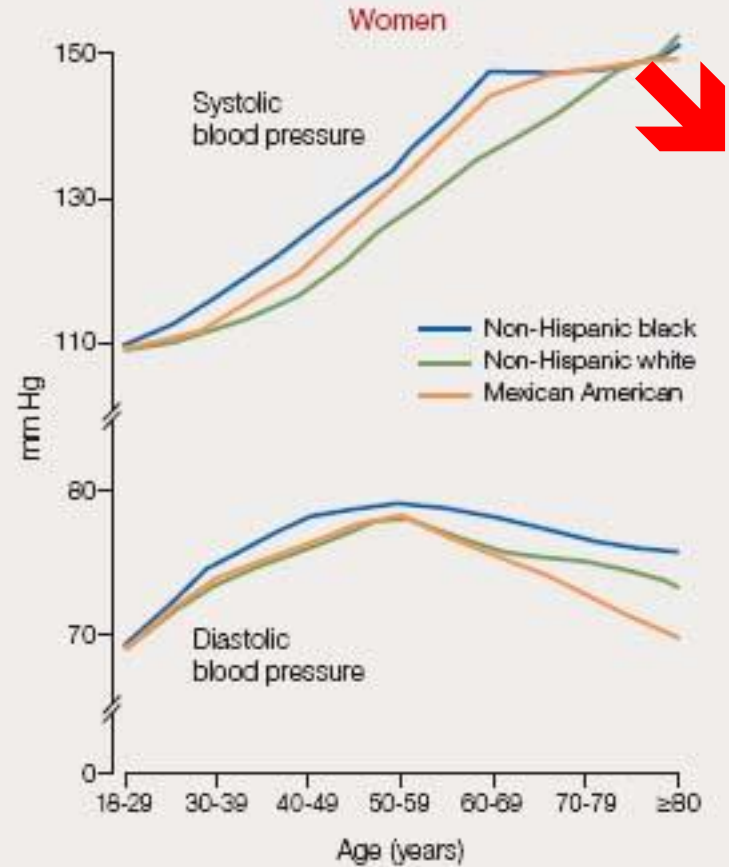
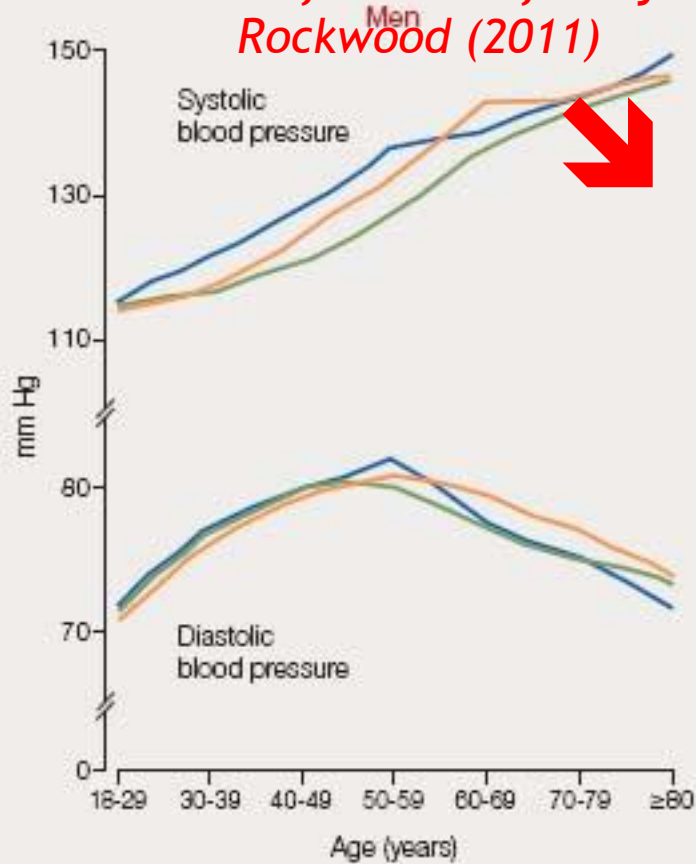
- NICE (2011)
  - Aim for a target clinic blood pressure below 150/90 mmHg in people aged 80 years and over [new 2011]
  - (<140/80 if diabetic)
- QOF
  - % of patients with hypertension (of any age) whose last recorded BP is < 150/90
  - (and <140/80 if diabetic)

# Examples

- 1. 82 year old woman, no other co-morbidity, globe-trotting, golf-playing
  - Target <150/90
- 2. 84 year old man, COPD / diabetes / TIA / mild cognitive impairment, mobile short distances with a stick
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*BP falls with frailty*  
*Rockwood (2011)*



Does high BP harm older people as much as younger people?

# High BP is associated with..

- RR 2.0 for cardiac failure
- Hypertension said to account for more than half of CCF in the elderly
  - Strongest contributor to CCF risk in the elderly

# High BP is associated with..

- Doubled risk of CKD across all ages
- In most age groups blood pressure control slows rate of renal decline
  - Tight BP control important to prevent progression to ESRF
- As people age, life expectancy falls and contribution of BP to renal outcomes also falls
  - Old people (>85) with established CKD are more likely to die than develop ESRF

O'Hare (2007)



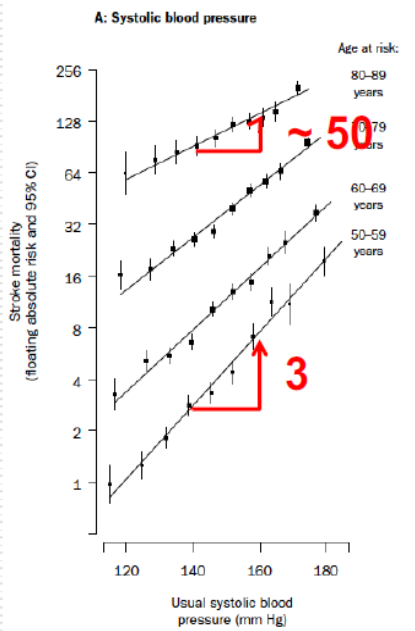
# High BP is associated with..

- Doubling of stroke risk for every increase of 20/10 mmHg over 115/75 mmHg
- In young people BP the main risk factor for stroke:
  - Steep slope of stroke risk vs BP
- In older people age is the main risk factor
  - Slope is less steep
  - Individual risk higher
  - Small increases in BP associated with significant extra risk
  - Most strokes occur in older people with high normal BPs

Lewington 2002

# High BP is associated with..

## SBP vs stroke mortality risk relationship



- No apparent threshold
- Stroke mortality risk doubles for every 20/10 mm Hg increase above 115/75
- 20 mm Hg increase associated with a 10-fold larger annual absolute stroke risk in 80s vs. 50s.

# High BP is associated with..

- RR 1.5 for dementia (overall)
- Higher risk for mid-life hypertension
  - Dementia the end result of often decades of damage
- Complicated relationship in elderly
  - Late-life hypertension overall lower risk, but
  - Hypertension associated with stroke, and post-stroke dementia quite common
  - Low BPs also risk cognitive decline in frailty
  - ‘U-shaped curve’

Kennelly, 2009

Brett, 2015

Ogliari, 2015

# Summary: is hypertension harmful in the elderly?

- In the elderly high BP is associated with higher risks of
  - Stroke
  - CKD
  - Dementia (probably)
  - CCF (certainly)
- But contribution of BP is lower
- Age itself a stronger risk factor for all but CCF

# Evidence base for guidelines

# 1. HYVET (2008)

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- Indapamide ±perindopril
- 3845 people, average age 84 (73% 80-84 years, 5% 90+)
  - Exclusions: CCF, dementia, creat >150
  - “healthier than gen pop”: lower rate of strokes etc
- Baseline average SBP 173
  - Intervention group average reduction of 15 mm Hg more
    - mean SBP ≈140

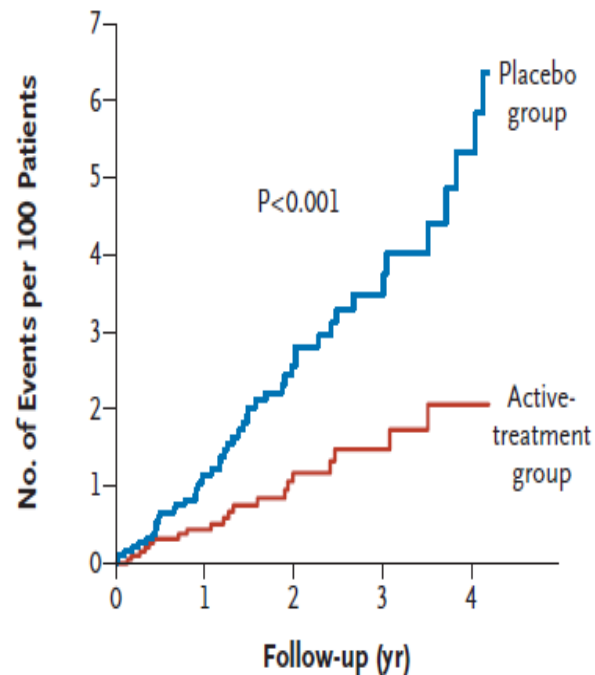
# 1. HYVET (2008)

- Stroke risk 30% lower in treatment group
- MIs 34% lower in treatment group



# 1. HYVET (2008)

## Heart Failure

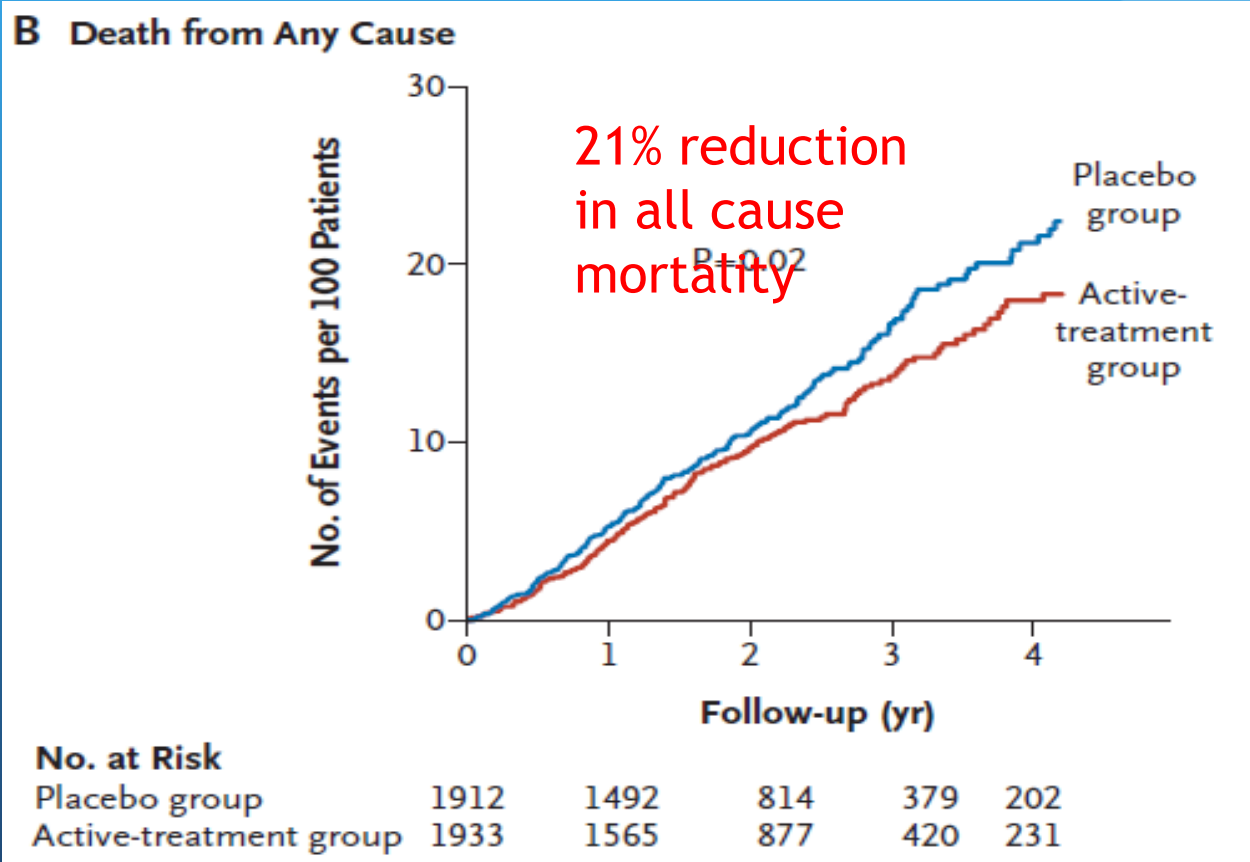


64% reduction in heart failure

### No. at Risk

Placebo group	1912	1480	794	367	188
Active-treatment group	1933	1559	872	416	228

# 1. HYVET (2008)



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- Positive outcomes across the board
- But note study population:
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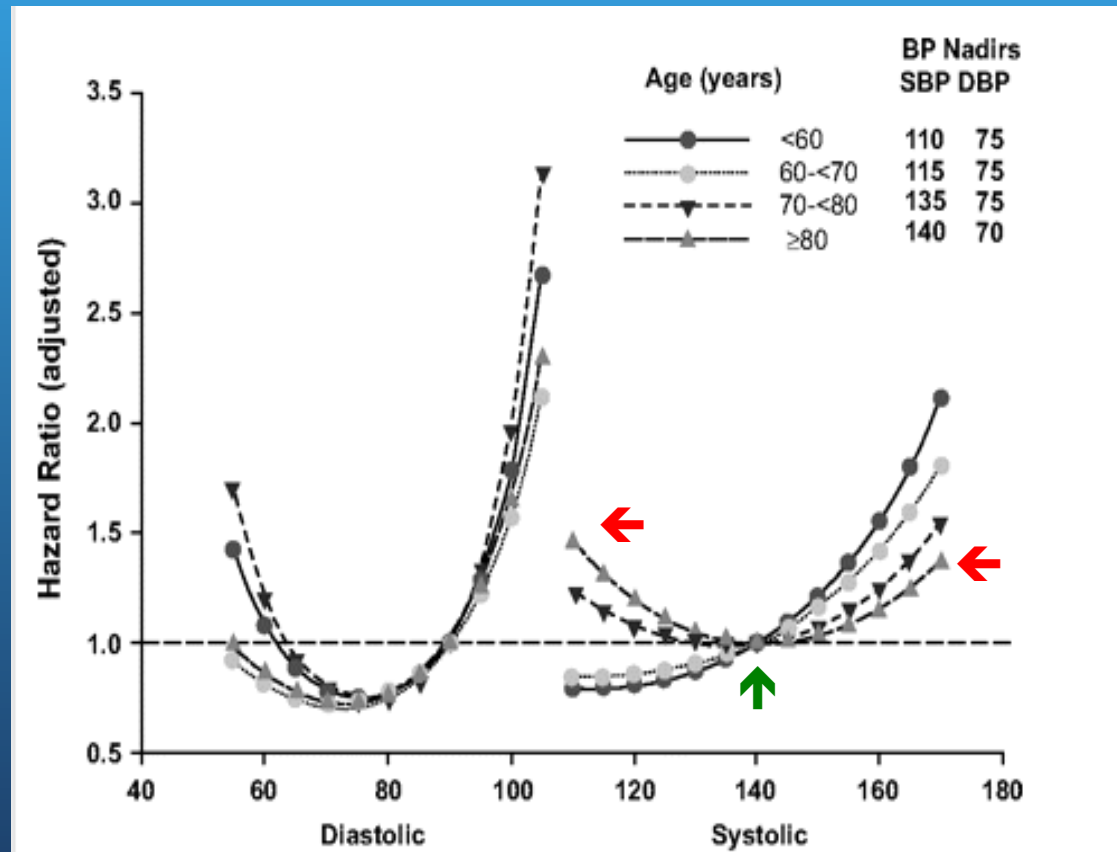
- Positive outcomes across the board
- But note study population: **Fit, young elderly**  
↓
- 3845 people, average age 84 (73% 80-84 years, 5% 90+)
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- Baseline average SBP 173
  - Intervention group average reduction of 15 mm Hg more
    - **mean SBP ≈140**

**High starting BP, modest reduction**



## 2. INVEST subgroup (2010)

## 2. INVEST subgroup (2010): Death/MI/CVA vs BP in people with **coronary artery disease**



Denardo  
(2010)

### 3. ACCORD (2010)

- Intensive BP control in type 2 diabetes (SBP <120) vs standard therapy (<140)
- Reduction in stroke - RR 0.6 - but event rate low: need to treat 89 people for 5 years to reduce 1 stroke
- No effect on mortality
- Serious adverse side effects of treatment in 3.3% intensive vs 1.3% standard treatment
- Under 80s only

# Summary: evidence for current guidelines

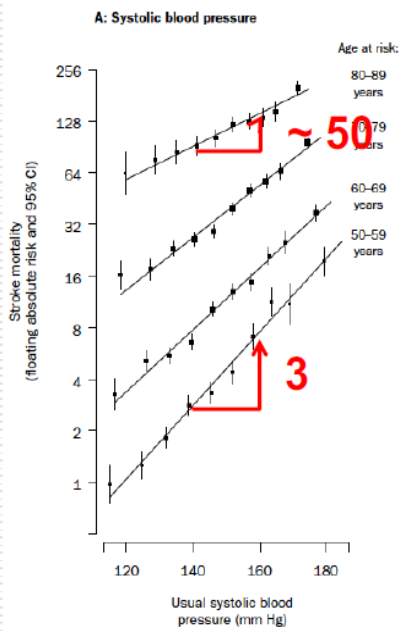
- All studies are of fit, young elderly. In these:
- High BP associated with higher stroke / CKD / dementia / CCF risk in elderly
- HYVET trial suggests lowering SBP to target 140 is safe and effective in a fit, younger subset of elderly
  - INVEST subgroup suggests optimal SBP in >80s with coronary artery disease is 140 too
- Evidence for aggressive targets in diabetics (ACCORD trial) to reduce stroke risk did not include > 80s



**How low should we go?**

# Stroke risk vs BP

## SBP vs stroke mortality risk relationship



- No apparent threshold
- Stroke mortality risk doubles for every 20/10 mm Hg increase above 115/75
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# SPRINT senior (2016)

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- 2636 patients > 75 years, average 79 years
- Target SBP <120; **achieved 123mmHg**
  - but different method so clinic BPs likely higher than this
- Excluded:
  - DM/stroke/eGFR<20/dementia/CCF/standing SBP<110
  - Non-ambulatory or living in care home
- Attempt made to address frailty issue:
  - calculated frailty index, gait speed, collected falls data

# 3. SPRINT senior (2016)

## Conclusions

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(Trialists slide)

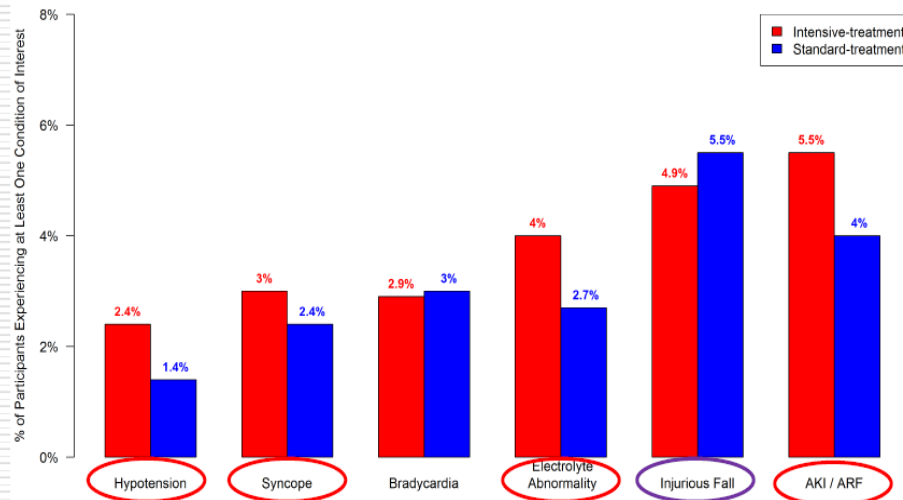
- ❑ The SPRINT-Senior cohort is representative of community dwelling older adults
- ❑ Rates of hypotension, syncope, electrolyte abnormalities, kidney injury were higher in the intensive arm, but not rates of injurious falls or orthostatic hypotension
- ❑ Overall, benefits of more intensive BP lowering – 33% reduction in primary CV outcome and 32% reduction in total mortality – exceeded the potential for harm, even among the most frail older patients

# SPRINT senior (2016)

- 27 treated for 3.14 years to prevent composite end point (vascular event / decompensated CCF / death)
- 41 treated for 3.14 years to prevent a death (RR 0.66)
- No increase in orthostatic hypotension (20%) / syncope / falls
- Small increase in electrolyte abnormalities, AKI

# 3. SPRINT senior (2016)

## Conditions of Interest for Participants > 75 Years



# SPRINT senior (2016)

- Reductions in stroke risk and mortality in >75s
- But:
  - Relatively small numbers with overlap in outcomes
  - Despite claims, not very frail (average FI 0.18; frail if > 0.21)
  - Starting SBP low (143)
    - Unlikely to be able to treat to target 120 from eg. 170 without adverse effects
  - BP measurements were different to real life
  - Postural BP measurements different to real life
  - Mostly under 80s, with major exclusions



# Summary: how low should we go?

- In the fittest (young) elderly without coronary artery disease, lowering SBP slowly to  $< 120$  is likely to lower stroke risk and possibly mortality
- 0% had adverse effects of treatment, however

**What do you think the targets should be?**

# Examples

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**Is there evidence in less  
selected elderly people?**

# BP and mortality

- In > 80s, SBP > 139 and DBP > 89 associated with lower 5 year mortality
- In > 80s, no relationship between mortality and uncontrolled hypertension

Oates 2007

# Postural hypotension predicts death in ambulatory older men

- Postural hypotension predicts increased risk of death (RR 1.64) during 4 year follow up in older men
  - Despite adjusting for BMI, smoking, activity, medications etc
- Increased drop associated with increased risk

Masaki, 1998

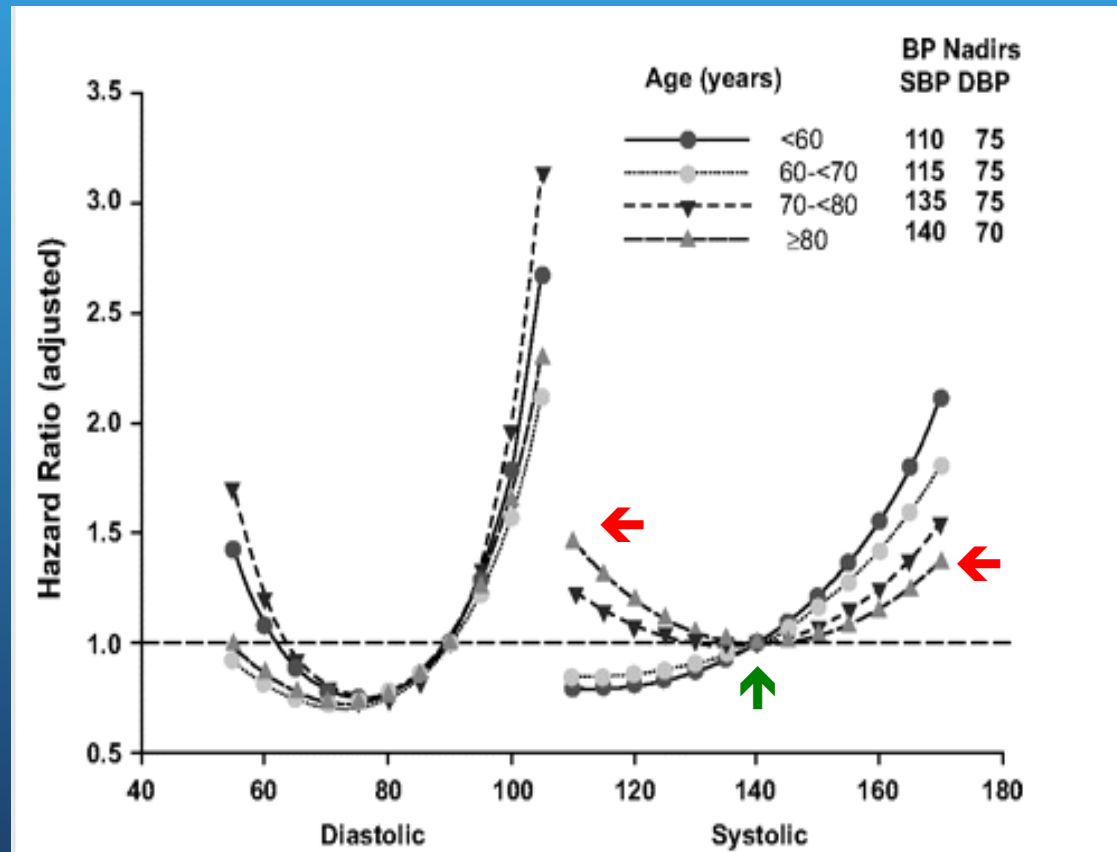
# Diastolic hypotension predicts death in over 85s

- 835 people followed for 5-7 years
  - DBP < 65mmHg 88% died
  - DBP > 100mmHg 59% died

Boshuizen, 1998



# INVEST subgroup: Death/MI/CVA vs BP in people with coronary artery disease



Denardo  
(2010)

# BP, mortality and gait speed

- 2340 people >65 years, followed 6 years
- In fast walkers
  - higher SBP = more likely to die (RR 1.35)
- In slower walkers
  - no relationship BP and mortality
- In those who couldn't walk 6m
  - elevated SBP > 140 associated with lower risk of death (RR 0.38)

Odden, 2012

# J shaped curve BP and stroke

- Stroke risk increased in orthostatic hypotension
  - RR 2.0

Eigenbrodt, 2000

- In untreated hypertensives, linear association increasing BP and stroke risk
- In treated hypertensives, J shaped relationship
  - Low BPs also associated with stroke

Voko, 1999

# Hypotension and cognitive decline

- Hypotension and postural hypotension associated with dementia and risk of developing dementia Kennelly, 2009  
Brett, 2015  
Ogliari, 2015
- Small white matter lesions associated with low systolic and diastolic BPs
- In those with treated hypertension, risk of dementia decreases with increasing BP
  - Ie over-treated hypertension associated with dementia

Ruitenbergh 2001

# Diastolic BP and stroke

- For those with ADL limitation
  - high DBP protective against stroke
    - RR 0.65 for DBP 66-80
    - RR 0.49 for DBP > 80
- For those with ADL limitation
  - lowest mortality with DBP 66-80 (RR 0.72)

# Anecdotally

- Complications of anti-hypertensives prevalent in hospital, where elderly patients more likely to be hypo than hypertensive
  - Falls, fractures
    - Low BP or postural hypotension
  - AKI
    - Often precipitated by sepsis / bleeding
      - Sepsis and bleeding seem to be poorly tolerated in frail elderly on anti-hypertensives
  - Electrolyte disturbance

# Summary of evidence in frailty

- In less selected elderly populations, hypotension and especially over-treated hypertension are associated with poor outcomes:
  - Dementia
  - Stroke
  - Mortality in those dependent for ADLs / unable to walk 6m
- Gait speed helps to decide on aggressiveness of BP treatment
  - Aggressive treatment beneficial in fast elderly walkers

# Examples

- 1. 82 year old woman, no other co-morbidity, globe-trotting, golf-playing
  - Target?
- 2. 84 year old man, COPD / diabetes / TIA / mild cognitive impairment, mobile short distances with a stick
  - Target?
- 3. 89 year old woman, living alone with qds carers, mobile with ZF, recurrent falls, undiagnosed cognitive impairment
  - Target?



# Bottom line

- Over 80s too heterogeneous for blanket BP recommendations
  - Large BP trials favour the fit and relatively young
- In fittest, NICE targets may not be aggressive enough
  - Though development of postural hypotension with aggressive treatment likely to be harmful
  - Gait speed helps to identify fittest
- In frailest, hypotension likely to be more harmful than hypertension
  - And beware the underlying (falling) BP trajectory