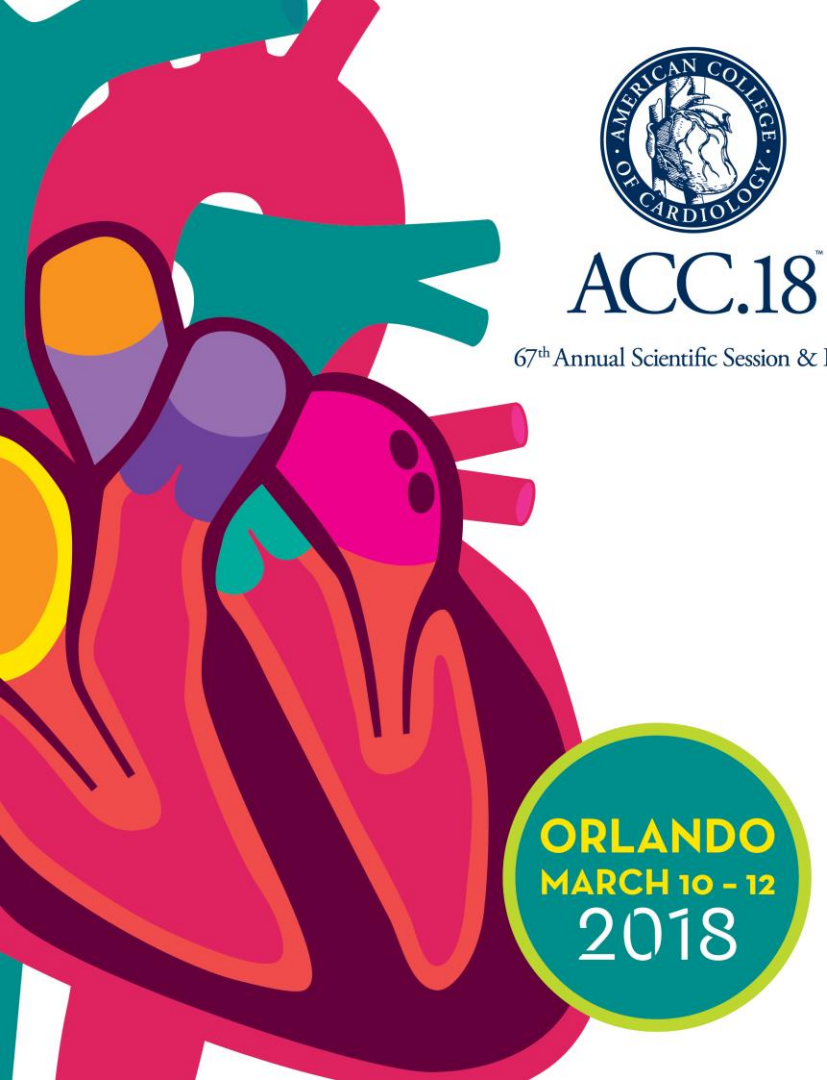


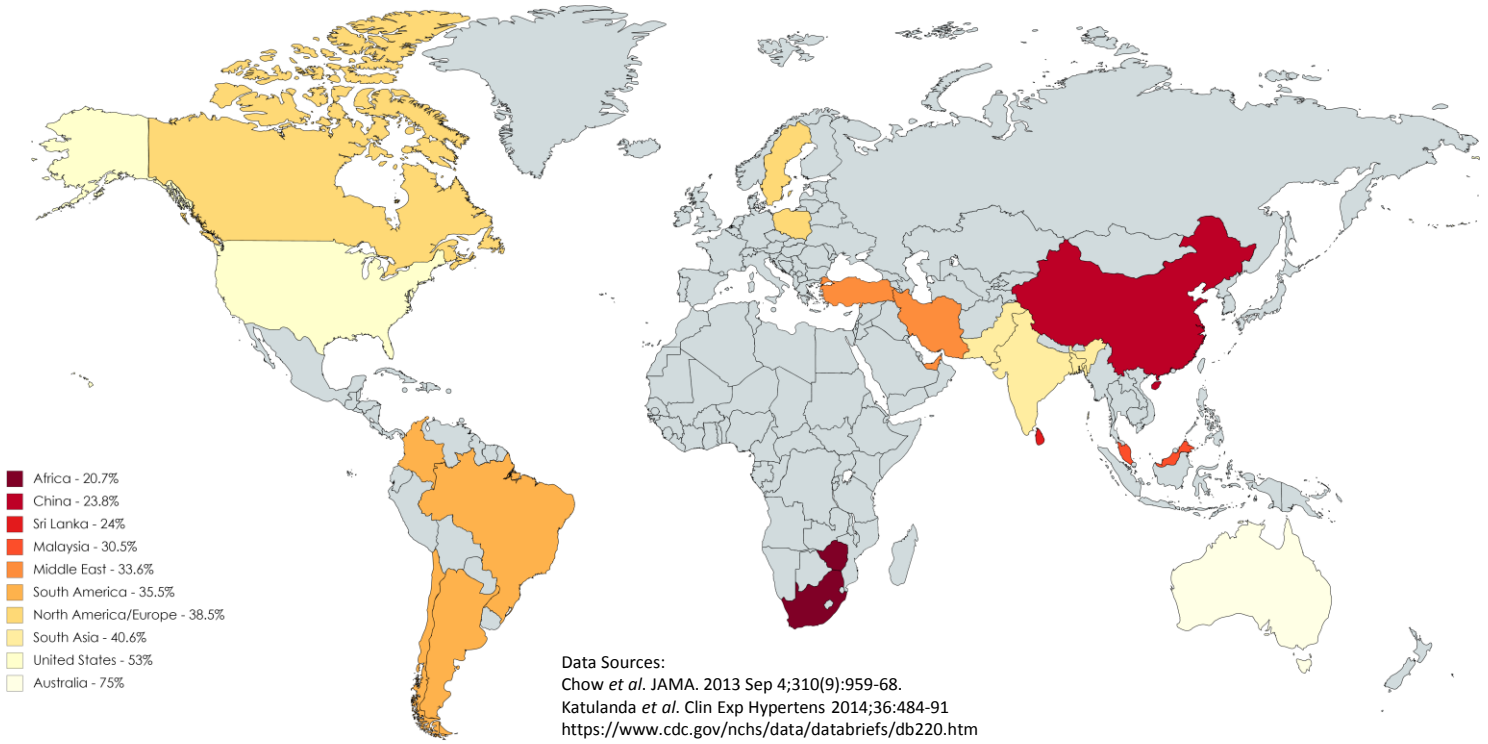
TRIple pill vs. Usual care Management for Patients with mild-to-moderate Hypertension

The TRIUMPH study

Dr Ruth Webster, PhD, MBBS, MIPH, BMedSc

Global control rates for hypertension

BP < 140/90 among those receiving treatment



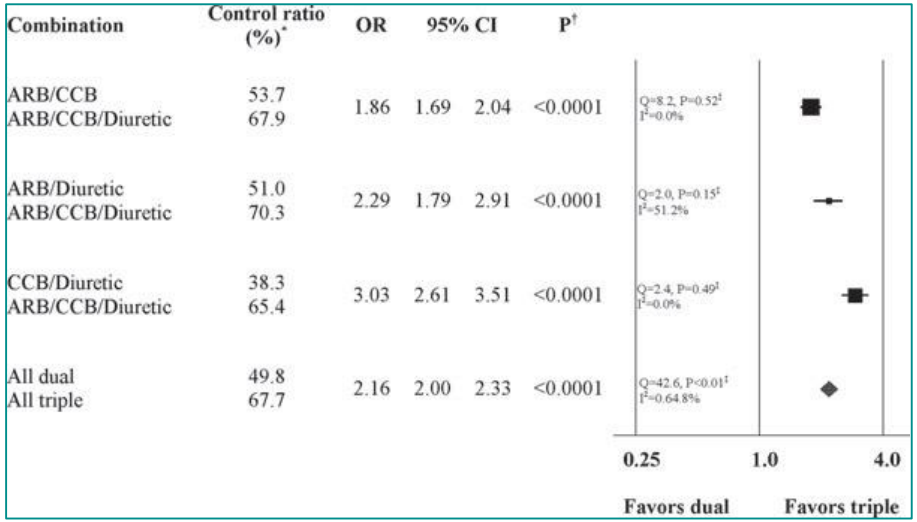
Data Sources:
Chow *et al*. JAMA. 2013 Sep 4;310(9):959-68.
Katulanda *et al*. Clin Exp Hypertens 2014;36:484-91
https://www.cdc.gov/nchs/data/databriefs/db220.htm
https://www.heartfoundation.org.au/about-us/what-we-do/heart-disease-in-australia/high-blood-pressure-statistics

Potential advantages of low-dose combinations

- Additive benefits of multiple drug classes
- Low dose minimizes adverse effects
- Compared to standard dose, about 80% BP lowering efficacy achieved at ½ dose
- Fixed-dose combination pills may:
  - Improve patient adherence
  - reduce physician inertia to up-titration

Previous trials

- Currently guidelines recommend
  - Dual combination therapy for patients with blood pressure >20/10 mmHg above target
  - Triple therapy for patients uncontrolled on maximal dual therapy
- No trial has evaluated a triple low dose pill for early treatment of hypertension



Kizilirmak *et al*, J Clin Hypertens 2013;15:193-200.

Objectives

To assess whether a strategy of initial or early treatment with fixed low-dose triple combination therapy would safely achieve better blood pressure (BP) control, compared with usual care.

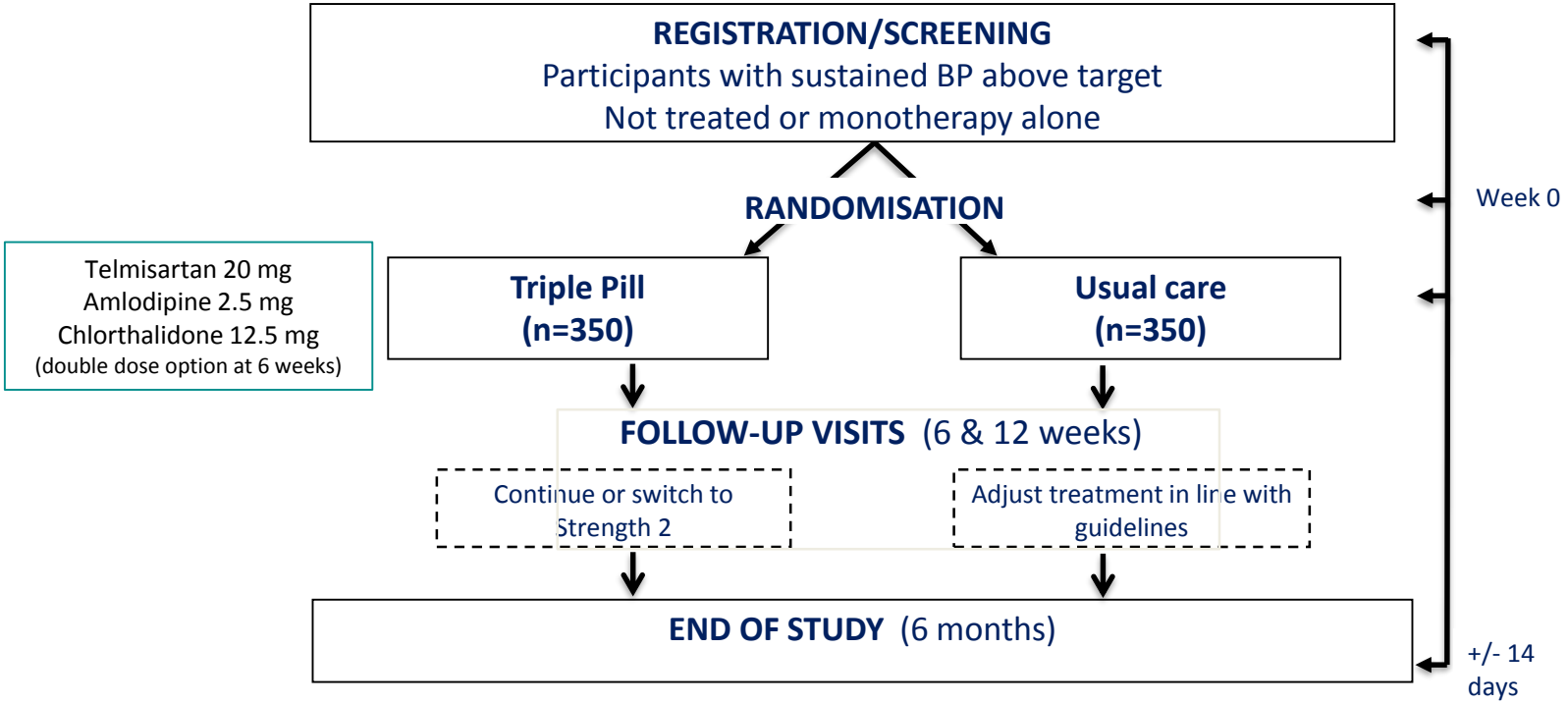
Study participants - inclusion

- Adults ≥18 years of age.
- Persistent hypertension (SBP >140 mm Hg and/or DBP >90mmHg; or SBP >130 mm Hg and/or DBP > 80 mm Hg in patients with diabetes mellitus or chronic kidney disease)
- requiring pharmacological treatment:
  - Initiation among patients not currently taking drug therapy, or
  - up-titration in patients taking single drug therapy

Study participants - exclusion

- On two or more BP lowering drugs.
- Severe (SBP>180 and/or DBP >110 mmHg) or accelerated hypertension.
- Contraindication to any of the components of the Triple Pill.
- Pregnancy, breast feeding, childbearing potential without effective contraception.
- Unstable medical condition or known situation where medication regimen might be altered for a significant length of time.
- Participants with clinically significant abnormal laboratory value judged to be unsuitable for trial participation by the investigator.

Study schema



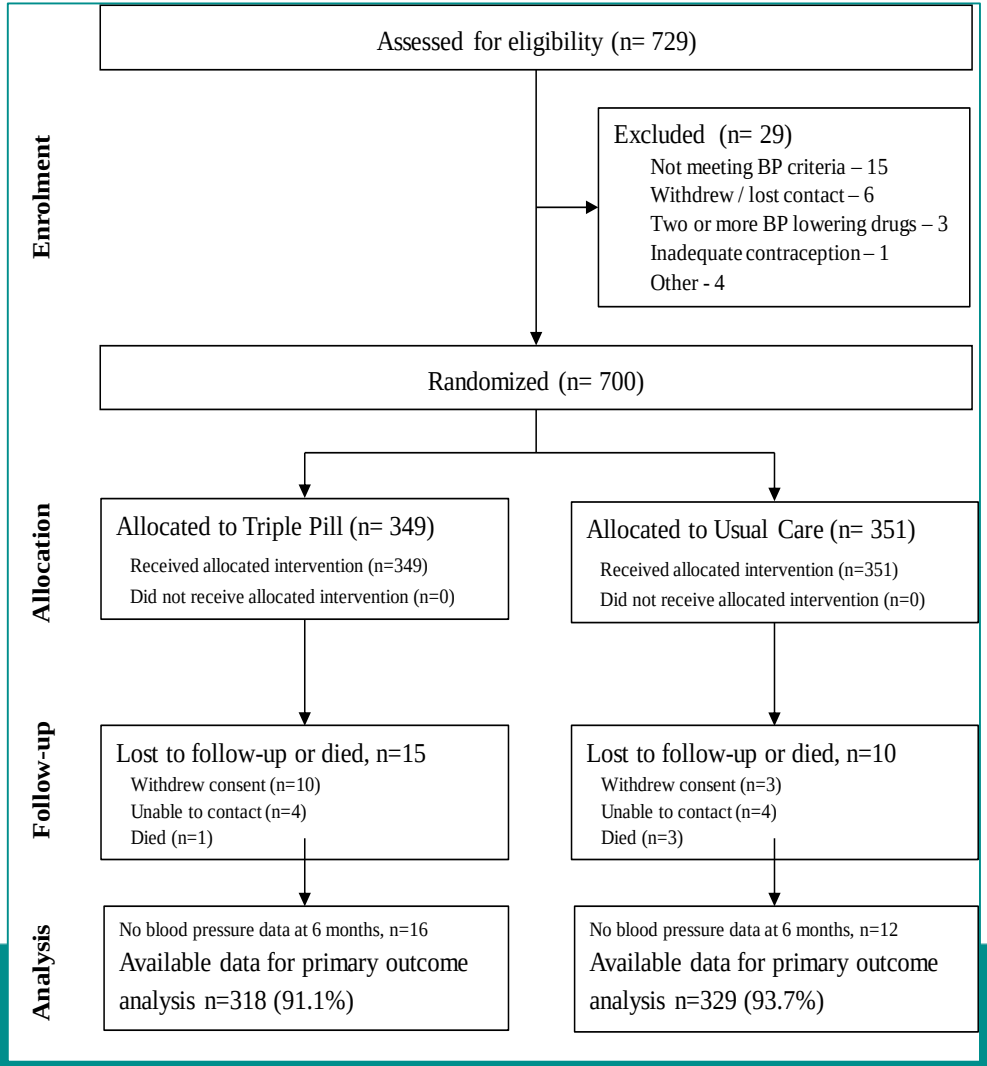
Outcomes

Primary outcome

BP control at 6 months (<140/90 mmHg; <130/80mmHg diabetes and/or chronic kidney disease).

Secondary outcomes

- BP control at 6 and 12 weeks
- Mean change in SBP and DBP at 6 months
- Tolerance to treatment at 6 months
- Self-reported BP lowering medication use

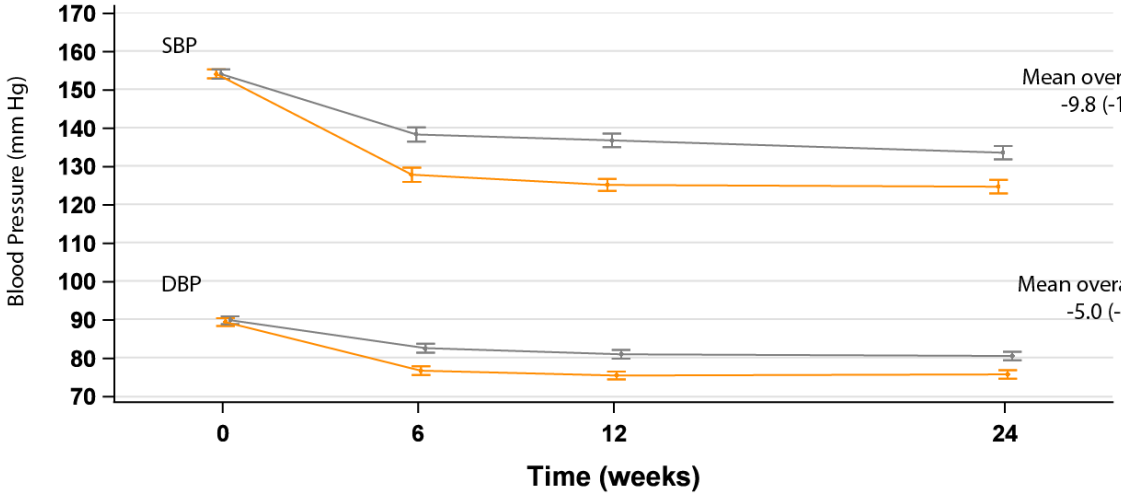

Assessed for eligibility (n= 729)
Excluded (n= 29)
Not meeting BP criteria – 15
Withdrew / lost contact – 6
Two or more BP lowering drugs – 3
Inadequate contraception – 1
Other - 4
Randomized (n= 700)
Enrolment
Allocation
Follow-up
Analysis
Allocated to Triple Pill (n= 349)
Received allocated intervention (n=349)
Did not receive allocated intervention (n=0)
Allocated to Usual Care (n= 351)
Received allocated intervention (n=351)
Did not receive allocated intervention (n=0)
Lost to follow-up or died, n=15
Withdrew consent (n=10)
Unable to contact (n=4)
Died (n=1)
Lost to follow-up or died, n=10
Withdrew consent (n=3)
Unable to contact (n=4)
Died (n=3)
No blood pressure data at 6 months, n=16
Available data for primary outcome analysis n=318 (91.1%)
No blood pressure data at 6 months, n=12
Available data for primary outcome analysis n=329 (93.7%)

Baseline characteristics

Characteristic	Triple Pill (N=349)	Usual Care (N=351)
Age – yr	56.4 ± 11.3	56.0 ± 10.7
Female sex (%)	59.3	55.8
Blood pressure (mmHg)	154/90	154/90
Not taking BP lowering treatment (%)	59.9	58.1
Current tobacco use. (%)	11.2	9.7
Known coronary artery or cerebrovascular disease (%)	11.5	8.3
Chronic kidney disease (%)	2	0.9
Diabetes mellitus (%)	30.4	27.6

Primary outcome and Change in blood pressure

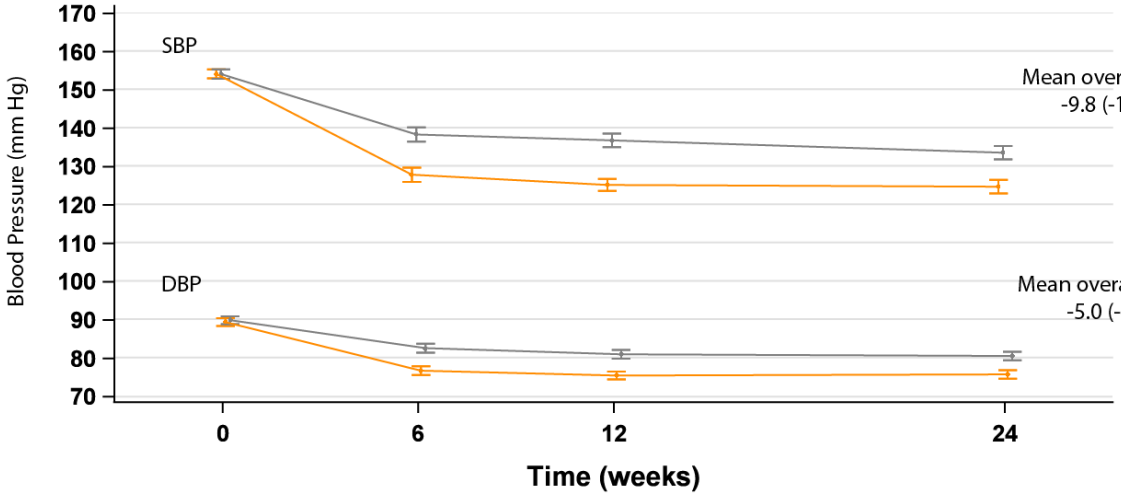
Proportion reaching target at 6 months:
69.5% vs 55.3%
RR 1.23 (1.09, 1.39)
P=0.0007



No with BP data				
Triple Pill	349	329	329	318
Usual Care	351	344	340	329
Mean No of BP classes				
Triple Pill	0.4	2.8	2.8	2.8
Usual Care	0.4	1.2	1.3	1.4
Mean Sum of Standard Doses of BP drugs per participant				
Triple Pill	0.5	1.5	1.5	1.5
Usual Care	0.5	1.3	1.5	1.6

Primary outcome and Change in blood pressure

Proportion reaching target at 6 months:
69.5% vs 55.3%
RR 1.23 (1.09, 1.39)
P=0.0007



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Usual Care	0.4	1.2	1.3	1.4
Mean Sum of Standard Doses of BP drugs per participant				
Triple Pill	0.5	1.5	1.5	1.5
Usual Care	0.5	1.3	1.5	1.6

Secondary outcomes

	Triple Pill (N=349)	Usual Care (N=351)	Treatment Effect (95% CI)	P value
Reaching target Week 6	67.8%	43.6%	1.53 (1.33, 1.76)	<0.001
Reaching target Week 12	72.6%	47.4%	1.51 (1.32, 1.72)	<0.001
Mean change in SBP at 6 months – mm Hg	-29.1	-20.3	-8.8 (-11.2, -6.4)	<0.001
Mean change in DBP at 6 months – mm Hg	-13.9	-9.3	-4.6 (-6.0, -3.1)	<0.001
Adherence (%)	95.0%	94.6%	1.00 (0.97, 1.04)	0.82

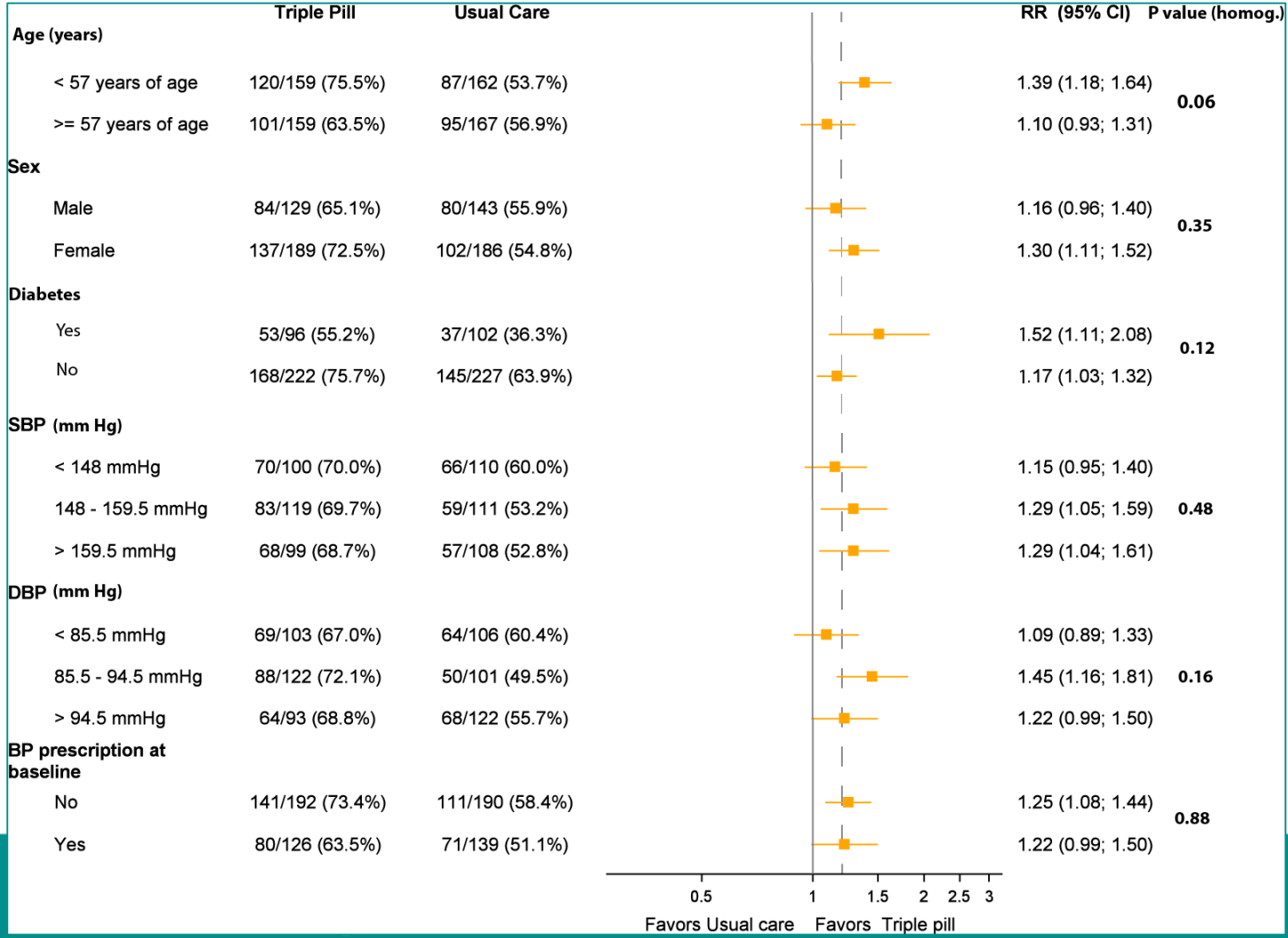
Safety

	Triple Pill (N=349)	Usual Care (N=351)	Treatment Effect (95% CI)	P Value
Adverse events	38.1%	34.5%		0.51
Serious adverse event (%)	7.7%	6.0%	1.28 (0.74 to 2.22)	0.37
Withdrawal due to adverse event (%)	6.6%	6.8%	0.97 (0.56, 1.7)	0.92

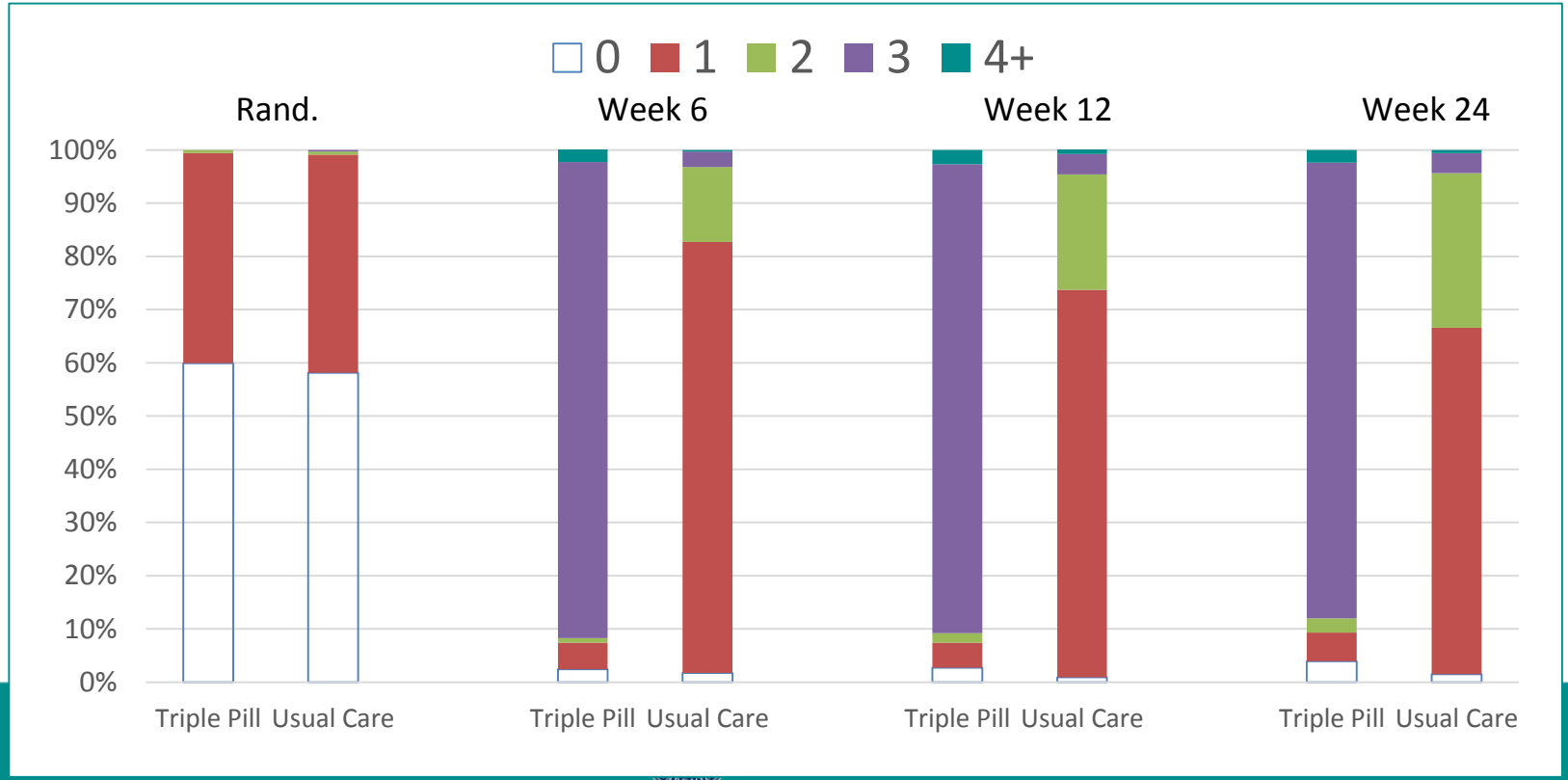
Laboratory parameters – change from baseline

	Triple Pill (N=349)	Usual Care (N=351)	Treatment Effect (95% CI)	P Value
LDL – mg/dL	-4.8	-12.9	8.1 (2.2, 14.1)	0.007
HDL – mg/dL	1.0	1.1	-0.1 (-1.5, 1.3)	0.88
Triglycerides – mg/dL	-27.2	-26.9	-0.3 (-8.1, 7.4)	0.93
Creatinine – mg/dL	0.07	0.03	0.04 (-0.06, 0.14)	0.47
Glucose – mg/dL	0.5	-1.8	2.4 (-3.8, 8.5)	0.45

Subgroup Analysis



Changes in BP treatment over time



Conclusions

- Early use of a low dose 3 in 1 combination BP lowering pill is safe and provides faster, better control of blood pressure compared to usual care
- Strongly supports the strategy of early use of low-dose triple combination therapy in all settings
- Most urgent need is effective implementation and scale up in low and middle-income countries with greatest disease burden

Acknowledgements

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