

# Barriers and solutions to greater use of single-pill combinations in management of hypertension

Egan BM, et al. *Blood Press.* 2022;31(1):164–168.

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## KEY TAKEAWAY

Greater use of SPC, especially as initial therapy, could improve rates of hypertension control and decrease rates of CVD and death, likely driven by greater adherence.

### PITFALLS TO USE OF SPC



- Majority were **initiated on monotherapy**



- Difficult to **change prescribing behavior**; very high **therapeutic inertia**



- Impractical idea** that initial monotherapy with additional antihypertensives will be as effective as initial SPC if uncontrolled BP is managed more frequently, with prompt intensification; and patients are as adherent with multiple pills as fewer pills

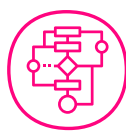
### SOLUTIONS FOR IMPROVED UPTAKE OF SPC



- Inclusion of antihypertensive **SPC on national formularies and recommendations for their use in national hypertension guidelines**



- Ready **availability and affordability of SPC** in the marketplace



- Implementing treatment algorithms** based on **initial use of SPC** along with **ongoing audit and feedback on adherence to the algorithm and hypertension control**

## WHY THIS MATTERS



- While the global burden of hypertension continues to grow, **hypertension control rates remain low globally.**



- Greater **use of antihypertensive SPC** as initial and add-on therapy is relatively **simple and potentially scalable approach for improved hypertension control.**

This article reviewed the **use of SPC**, especially as initial therapy, **vs monotherapy and multiple pill regimens** on adherence, hypertension control, clinical outcomes, population impact and adverse effects.

## KEY RESULTS



### ADHERENCE

- SPC was associated with approximately an absolute **10% higher adherence rate** vs free-equivalent combinations (FEC)
  - Parati G, et al.*: Adherence was found to be significantly greater with SPC vs FEC in 18 of 23 studies, which included **>250,000 individuals on SPC**



### HYPERTENSION CONTROL

STUDY	DOSE OF ANTIHYPERTENSIVE MEDICATIONS	SBP LOWERED
<i>Law MR, et al.</i>	Half-standard doses* of the major classes of antihypertensive medications	<b>~7 mm Hg</b>
	Standard doses of the major classes of antihypertensive medications	<b>~9 mm Hg</b>
	Twice standard doses of the major classes of antihypertensive medications	<b>~11 mm Hg</b>
<i>Salam A, et al.</i>	Half-standard dose of two antihypertensive medication classes	<b>~2.8 mm Hg more</b> than a single medication at standard dose
	Standard dose of two antihypertensive medications	<b>~7.5 mm Hg more</b> than a single medication at standard dose Increased probability of controlling BP <b>42%</b> (RR = 1.42 [95% CI: 1.27–1.58])



### THERAPEUTIC INERTIA

- Individuals **initiated on monotherapy** vs combination therapy were **more likely to remain on monotherapy**, even after three years
- It often takes **two years or more** of uncontrolled hypertension for **addition of antihypertensive medication** or to **increase the dose** of an existing medication

## CLINICAL OUTCOMES (SPC VS ALTERNATIVE THERAPEUTIC APPROACHES)



Initial treatment with SPC could lead to **greater reduction in BP and better hypertension control** vs initial monotherapy



**Quicker time to control** with initial SPC therapy vs initial monotherapy



Most SPC approved for clinical use had approximately **additive antihypertensive effects** vs the prescribed FEC in clinical practice



Hypertensive adults initiated on combination of two antihypertensive medication classes vs monotherapy had **fewer composite CV events**



**Hard clinical outcomes including death were reduced** when equivalent two drug combination therapy was prescribed as a single-pill vs as separate pills



Found to **reduce the composite outcome of ischemic heart disease, stroke, and CKD (ranging from 4.9% to 11.5%)** vs alternative treatment approaches



### KEY FACTORS INFLUENCING UPTAKE OF SPC THERAPY FOR HYPERTENSION ACROSS LOW AND MIDDLE-INCOME COUNTRIES

- Inclusion of antihypertensive SPC on **national essential medications list**
- Recommended use of SPC in **national/regional hypertension guidelines**
- Availability of SPC** on the marketplace – A significant barrier for implementation†

## CONCERNS WITH THE USE OF SPC



- Initiating treatment with a single medication class is appropriate for:
  - Individuals within 10 mm Hg of their SBP goal before treatment
- Older and frail individuals at greater risk** for excessive BP-reductions.
- Determining the **responsible drug causing adverse events** when starting with a SPC may be difficult.
  - However, SPC therapy, especially at standard doses or lower, is known to be well-tolerated with **non-significantly different adverse effects and discontinuation rates** vs those with standard dose monotherapy, which can be easily identified.

For additional details, please refer the source publication [Egan BM, et al.](#)

\* One-quarter maximum recommended dose  
† Due to regional differences in SPC-availability

**ABBREVIATIONS:**  
BP, blood pressure; CI, confidence interval; CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; FEC, free-equivalent combinations; RR, risk ratio; SBP, systolic blood pressure; SPC, single-pill combination.

**REFERENCE:**  
Egan BM, Kjeldsen SE, Narkiewicz K, Kreutz R, Burnier M. Single-pill combinations, hypertension control and clinical outcomes: Potential, pitfalls and solutions. *Blood Press.* 2022;31(1):164–168. doi: 10.1080/08037051.2022.2095254. PMID: 35876172.

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