The Impact of Single Pill Combinations versus Free Dose Equivalents on Outcomes in Patients with Hypertension and/or Dyslipidaemia: A Systematic Review

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INTRODUCTION

- Good medication adherence is necessary to realise the benefits of a treatment.[1]
- Patients with chronic illnesses often take multiple pills per day, which may lead to poor adherence to therapy, defined as taking less than 80% of the prescribed dose.[1]
- Simplified treatment regimens are needed to improve adherence in patients with chronic conditions and taking multiple tablets per day.[2]

OBJECTIVE

- To assess the impact of single-pill combination (SPC) treatments on clinical and economic outcomes and quality of life (QoL), in patients with hypertension and/or dyslipidaemia relative to their free-equivalent combination (FEC).

METHODS

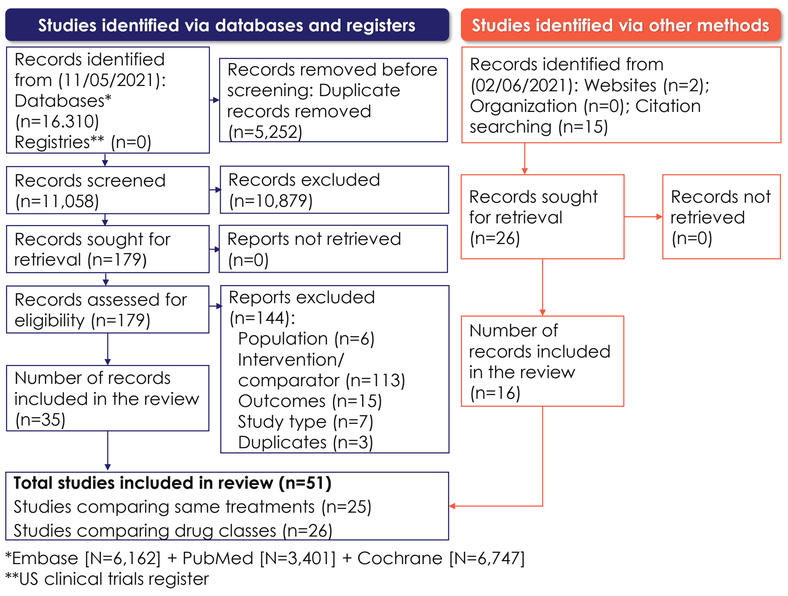
- A systematic literature review was conducted covering studies identified from EMBASE, PubMed-Medline, and Cochrane from inception to 16 May 2021.
- We included studies that compared adherence, persistence, clinical outcomes, QoL, and economic outcomes among patients with hypertension and/or dyslipidaemia treated with an SPC versus an FEC.
- No country or language restrictions were applied.

RESULTS

Study Characteristics

- 16,310 publications were identified. Of 51 studies that met inclusion criteria, 38 were on hypertension, 7 on hypertension and dyslipidaemia, and 6 were on dyslipidaemia alone (**Fig. 1**).
- The majority of included studies were real-world evidence (RWE) (69%) with ≥1,000 patients (59%) and a follow-up >7 months (61%).
- Studies were predominantly published in the US (35%), Europe (25%), and Asia (24%), followed by Australia (10%) and multi-country studies (6%).

Figure 1. PRISMA diagram for study selection



*Embase [N=6,162] + PubMed [N=3,401] + Cochrane [N=6,747]
**US clinical trials register

Patients with Hypertension

- 38 studies reported outcomes of interest for patients with hypertension (see **Table 1**).
- 12 out of 13 studies reported significant improvements in adherence in SPC-treated patients compared to FEC-treated patients; one study reported non-significant improvement in adherence.
- All studies assessing persistence (n=12) consistently reported significant improvements in SPC-treated patients compared with FEC-treated.
- Most studies reported greater reductions in BP in SPC-treated patients compared to FEC-treated patients, either significantly (n=3) or non-significantly (n=8). Four studies reported greater reductions in BP in FEC-treated patients compared to SPC-treated patients, of which three (75%) were not significant.
- Four studies reported reductions in the incidence of CV events in patients treated with an SPC versus an FEC.
- Lower HRU was reported in SPC-treated patients compared to FEC-treated patients in nearly all studies (n=9/10).
- One study reported QoL results in patients with hypertension using the 36 item Short Form (SF-36) questionnaire.
  - Significantly improved QoL was reported in SPC-treated patients compared to patients treated with FEC.

Table 1. Overall summary of hypertension studies

Outcome	Study type	Common definition	Positive significant	Positive non-significant	Negative non-significant	Negative significant
Adherence	RWE	PDC ≥ 80%	10	1	-	-
	RCT	PDC/MPR ≥ 80%	2	-	-	-
Persistence	RWE	A gap in therapy of 30 or 60 days	12	-	-	-
	RCT	Not defined	-	-	-	-
Change in BP	RWE	Difference between baseline and follow-up	1	1	1	1
	RCT		2	7	2	-
CV complications	RWE	Incidence of CV events	3	1	-	-
	RCT		-	-	-	-
HRU	RWE	Direct costs/resource use	7	1	-	1*
	RCT	Decrease in costs	-	1	-	-
QoL	RWE	SF-36	1	-	-	-
	RCT	-	-	-	-	-

*Study reported only drug costs
Abbreviations: CV- cardiovascular; HRU- healthcare resource use; MPR- medication possession ratio; PDC- proportion days covered; QoL- quality of life; RCT- randomised controlled trial; RWE- real-world evidence;

>10 studies 5-10 studies <5 studies >10 studies 5-10 studies <5 studies

Patients with Hypertension and Dyslipidaemia

- Seven studies reported outcomes of interest for patients with hypertension and dyslipidaemia (see **Table 2**).
- Consistent improvements in adherence were reported in all five studies, where three reported significant improvements, whilst two reported non-significant improvements for SPC-treated versus FEC-treated.
- One study reported significant improvements in persistence for patients treated with an SPC versus an FEC.
- Higher decrease in BP or cholesterol levels was reported across three studies in SPC-treated versus FEC-treated patients.
- Two studies reported lower HRU for SPC-treated patients versus FEC-treated.
- No studies reported results for incidence of CV events or QoL in patients with hypertension and dyslipidaemia.

Table 2. Overall summary of hypertension and dyslipidaemia studies

Outcome	Study type	Common definition	Positive significant	Positive non-significant	Negative non-significant	Negative significant
Adherence	RWE	PDC ≥ 80%	3	-	-	-
	RCT	PDC/MPR ≥ 80%	-	2	-	-
Persistence	RWE	A gap in therapy of 30 or 60 days	1	-	-	-
	RCT	Not defined	-	-	-	-
Change in BP or cholesterol levels	RWE	Difference between baseline and follow-up	-	-	-	-
	RCT		1	2	-	-
CV complications	RWE	-	-	-	-	-
	RCT		-	-	-	-
HRU	RWE	Direct costs/resource use	1	1	-	-
	RCT	Decrease in costs	-	-	-	-
QoL	RWE	-	-	-	-	-
	RCT	-	-	-	-	-

Patients with Dyslipidaemia

- Six studies reported outcomes of interest for patients with hypertension (see **Table 3**).
- Four out of five studies reported significant improvements in adherence in SPC-treated patients compared to FEC-treated patients; one study reported non-significant improvements in adherence.
  - Improvements in adherence were reported for treatment-naïve patients with dyslipidaemia treated with an SPC versus an FEC.
- Out of the three studies investigating persistence, two reported significant improvements in SPC-treated versus FEC-treated and one reported significant improvements for FEC-treated versus SPC-treated patients.
  - Persistence results followed similar trends as the ones observed for adherence.
- One study reported numerically higher decrease in cholesterol levels for patients treated with an SPC versus an FEC and one study reported lower incidence of CV events in SPC-treated patients versus those on FECs.
- Two studies consistently reported significantly lower HRU and total direct costs for patients treated with an SPC versus and FEC.
- No studies reported results for QoL in patients with dyslipidaemia.

Table 3. Overall summary of dyslipidaemia studies

Outcome	Study type	Common definition	Positive significant	Positive non-significant	Negative non-significant	Negative significant
Adherence	RWE	PDC ≥ 80%	4	1	1	-
	RCT	PDC/MPR ≥ 80%	-	-	-	-
Persistence	RWE	A gap in therapy of 30 or 60 days	2	-	-	1
	RCT	Not defined	-	-	-	-
Change in cholesterol levels	RWE	Difference between baseline and follow-up	-	-	-	-
	RCT		-	1	-	-
CV complications	RWE	Incidence of CV events	-	1	-	-
	RCT		-	-	-	-
HRU	RWE	Direct costs/resource use	2	-	-	-
	RCT	Decrease in costs	-	-	-	-
QoL	RWE	-	-	-	-	-
	RCT	-	-	-	-	-

CONCLUSIONS

- SPC treatment leads to improvements in adherence and persistence compared to FEC treatment in patients with hypertension and/or dyslipidaemia.
- Consistently, SPC treatment was associated with lower total direct healthcare costs compared to FEC treatment in patients with hypertension and/or dyslipidaemia.
- Collected evidence suggests a potential association between improved adherence, improved BP control and reduced risk of CV events and lower HRU in patients with hypertension.
- This work provides the foundation for a subsequent meta-analysis, that will assess adherence and persistence in patients with hypertension and/or dyslipidaemia with SPC treatment compared to FEC treatment.

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DISCLOSURES

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