

Advantages of Fixed-Dose Combination (FDC) Products over Loose-Dose Combination (LDC) Products: A Systematic Literature Review (SLR)

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INTRODUCTION

- Fixed-dose combination products (FDC),¹ also known as single-tablet combination therapies (STCT), integrate multiple drugs into one dose, making administration more convenient and streamlining the process of obtaining prescriptions at the pharmacy. Previous work has linked the use of FDCs with improved treatment adherence and persistence in patients with chronic diseases,²⁻³ but it is less clear how FDC use affects health economics, clinical outcomes, and health-related quality of life (HRQoL).

OBJECTIVE

The aim of this study was to conduct a systematic literature review (SLR) to better understand the impact of FDCs for patients with chronic diseases.

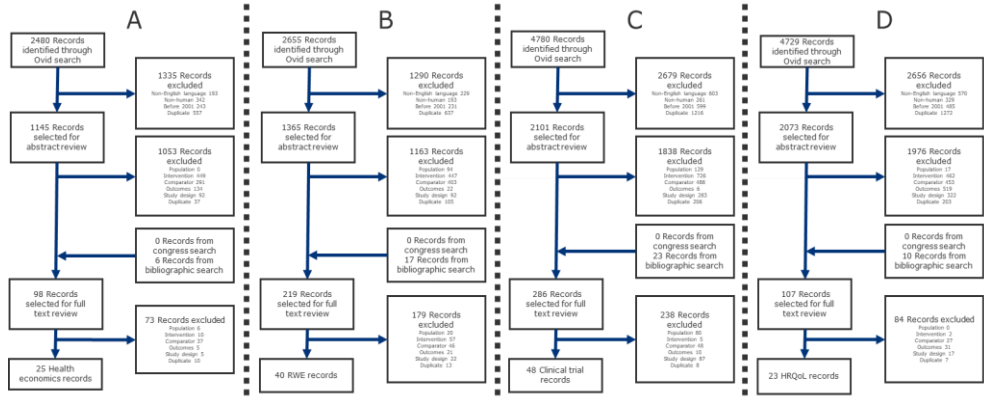
METHODS

- The SLR identified studies that compared the effects of FDCs and equivalent loose-dose combination products (LDC) across four evidence domains:
 - Health economic studies
 - Real-world studies (RWE)
 - Clinical trials
 - HRQoL
- Database and registry records published from January 2001 to December 2021 were searched on December 3, 2021 following PRISMA guidelines.⁴ Databases included Ovid MEDLINE® ALL, Cochrane, American College of Physicians Journal Club, National Health Service Economic Evaluation Database, Embase, and EconLit. Searches, screening, and data extraction were performed by two independent reviewers, with all conflicts resolved by a third reviewer or consensus-based discussion. Search terms included “fixed or single pill,” related terms, and validated study design filters. Included studies compared economic or clinical outcomes, adherence, persistence, compliance, or HRQoL with FDC and LDC products.

RESULTS

In total, 109 original studies across 44 countries were identified (Figure 1 and Figure 2); 27 studies contained evidence relevant to more than one research domain. Cardiovascular, respiratory, and eye diseases were among the most frequently included indications (Figure 3).

FIGURE 1: PRISMA diagram of health economics (A), RWE (B), clinical trial (C), and HRQoL (D) searches



Note: Twenty-seven studies contained evidence from more than one SLR.

RESULTS (cont.)

Health economic studies

- Of the 25 health economic studies identified, all reported cost savings or reduced healthcare resource use (HCRU) with FDCs.
- All 6 cost-effectiveness, cost-utility, or cost-minimization studies (Figure 4) reported that FDCs dominated LDCs.
- All 4 budget impact analyses (Figure 5) reported cost savings with FDCs.
- Medical costs and/or HCRU were reported in 16 studies. Lower medication costs (n=9), hospitalization rates (n=3), and emergency department visit rates (n=3) were reported for FDCs.

FIGURE 2: Locations of identified studies

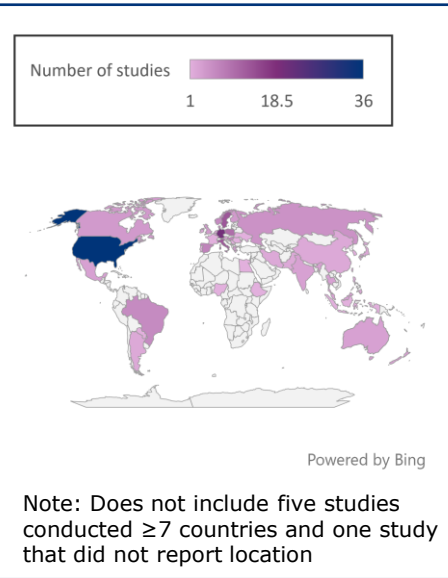
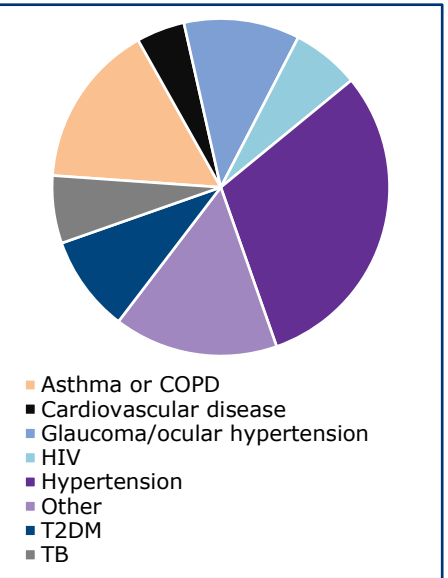


FIGURE 3: Indications in identified studies



RWE studies

- Of the 40 RWE studies that were identified, 20 reported adherence outcomes. FDCs were associated with significantly (n=16) and numerically (n=2) higher adherence.
- All 18 studies that examined persistence reported a significantly (n=16) or numerically (n=2) higher persistence with FDCs in at least one study arm. Higher compliance was reported with FDCs in three of four studies.
- Eleven of the 14 studies (79%) that reported clinical outcomes described a numeric (n=5) or significant (n=6) improvement with FDCs, most commonly, blood pressure control (n=4), a reduced need for add-on medication (n=3), and glycemic control (n=2).
- In 6 studies, improved clinical outcomes were reported alongside an increase in adherence, persistence, or compliance with FDCs.
- In RWE studies that reported adherence, persistence, or compliance outcomes using the same metrics, the overall mean 1-year persistence was 50.8% for FDCs and 32.9% for LDCs (Figure 6); FDCs were associated with improvement in 21 of 24 study arms (Figure 7).

Clinical trials and HRQoL studies

- In the 48 identified clinical trials, adherence and compliance were similar with FDCs and LDCs in 9 of 13 and 4 of 4 studies, respectively. None of the 23 identified HRQoL studies evaluated the pill burden for patients. In one study of patients with hypertension, there was a statistically significant HRQoL benefit with FDCs compared with LDCs.

FIGURE 4: Economic findings from all cost comparison studies

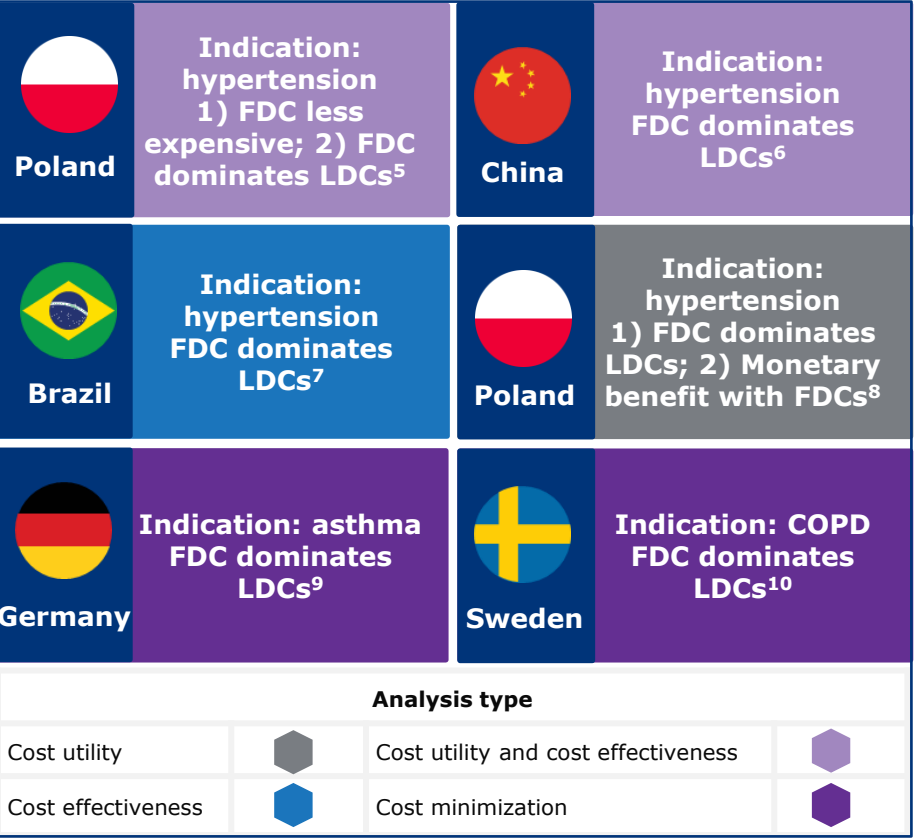


FIGURE 5: Economic findings from all budget impact analyses

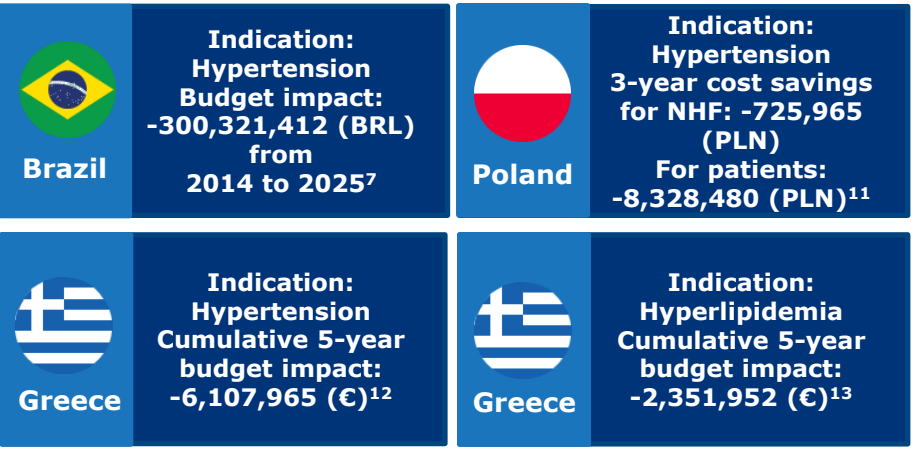


FIGURE 6: Mean 1-year persistence with FDCs vs LDCs in RWE studies (n=13)

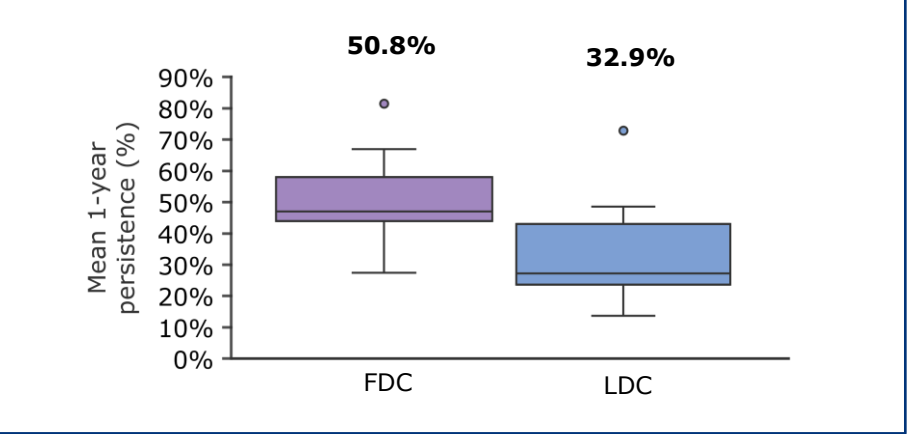
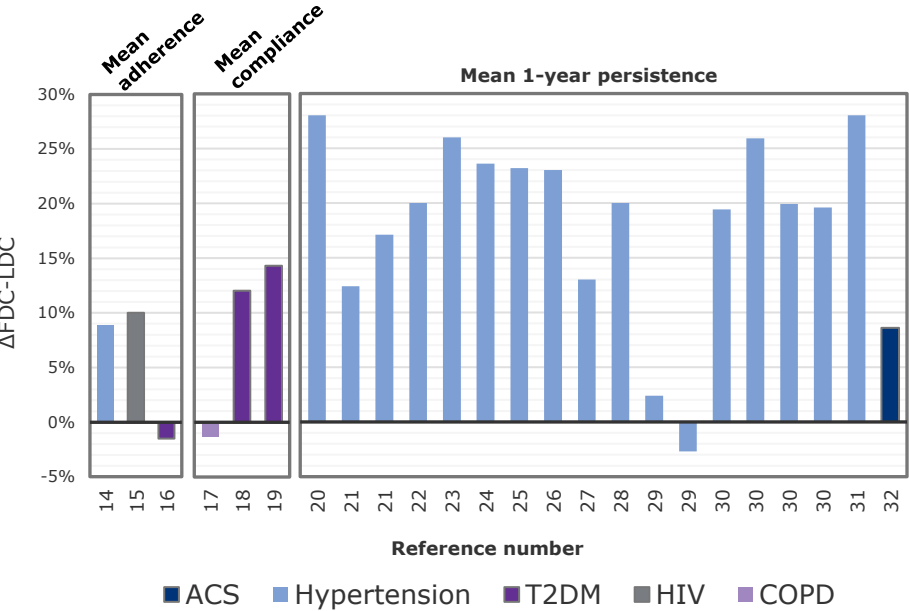


FIGURE 7: Adherence, compliance, and persistence outcomes across comparable RWE studies



CONCLUSIONS

Economic studies and RWE consistently reported the advantages of FDCs over LDCs across various chronic disease indications and economic markets. FDCs were associated with better adherence and persistence, improved clinical outcomes, and reduced costs and HCRU.

- In total, 109 studies were identified across the research domains of RWE, clinical trials, HRQoL studies, and health economics.
- All 25 economic studies reported cost savings or HCRU reductions with FDCs, including 4 budget impact analyses and 6 cost comparison studies.
- The findings from RWE studies pointed toward improved adherence, compliance, and persistence with FDCs, leading to better clinical outcomes.
- Future studies can build upon these findings by including patients from additional countries, and by using drug-administration focused HRQoL measures, such as the Treatment Satisfaction Questionnaire for Medication.³³

Abbreviations

ACS, acute coronary syndrome; BRL, Brazilian real; COPD, chronic obstructive pulmonary disease; FDC, fixed-dose combination product; HIV, human immunodeficiency virus; HCRU, healthcare resource use; HRQoL, health-related quality of life; LDC, loose-dose combination product; PLN, Polish zloty; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta Analyses; RWE, real-world evidence; SLR, systematic literature review; STCT, single-tablet combination therapies; T2DM, type 2 diabetes mellitus; TB, tuberculosis

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