

## Publication

### Cost-effectiveness of a structured medication review approach for multi-morbid older adults: Within-trial analysis of the OPERAM study

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**Author(s)** Salari, Paola; O'Mahony, Cian; Henrard, Séverine; Welsing, Paco; Bhadhuri, Arjun; Schur, Nadine; Roumet, Marie; Beglinger, Shanthi; Beck, Thomas; Jungo, Katharina; Byrne, Stephen; Hossmann, Stefanie; Knol, Wilma; O'Mahony, Denis; Spinewine, Anne; Rodondi, Nicolas; Schwenkglenks, Matthias

**Author(s) at UniBasel** [Salari, Paola](#) ; [Schwenkglenks, Matthias](#) ; [Bhadhuri, Arjun](#) ; [Schur, Nadine](#) ;  
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Background: Inappropriate polypharmacy has been linked with adverse outcomes in older, multimorbid adults. OPERAM is a European cluster-randomized trial aimed at testing the effect of a structured pharmacotherapy optimization intervention on preventable drug-related hospital admissions in multimorbid adults with polypharmacy aged 70 years or older. Clinical results of the trial showed a pattern of reduced drug-related hospital admissions, but without statistical significance. In this study we assessed the cost-effectiveness of the pharmacotherapy optimisation intervention. Methods: We performed a pre-planned within-trial cost-effectiveness analysis (CEA) of the OPERAM intervention, from a healthcare system perspective. All data were collected within the trial apart from unit costs. QALYs were computed by applying the crosswalk German valuation algorithm to EQ-5D-5L-based quality of life data. Considering the clustered structure of the data and between-country heterogeneity, we applied Generalized Structural Equation Models (GSEMs) on a multiple imputed sample to estimate costs and QALYs. We also performed analyses by country and subgroup analyses by patient and morbidity characteristics. Results: Trial-wide, the intervention was numerically dominant, with a potential cost-saving of CHF 3'588 (95% confidence interval (CI): -7'716; 540) and gain of 0.025 QALYs (CI: -0.002; 0.052) per patient. Robustness analyses confirmed the validity of the GSEM model. Subgroup analyses suggested stronger effects in people at higher risk. Conclusion: We observed a pattern towards dominance, potentially resulting from an accumulation of multiple small positive intervention effects. Our methodological approaches may inform other CEAs of multi-country, cluster-randomized trials facing presence of missing values and heterogeneity between centres/countries.

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