

# Systematic review of the cost-effectiveness of interventions in patients with multimorbidity

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## ABSTRACT

**Background:** Multimorbidity is becoming increasingly prevalent and has become a major challenge for healthcare systems. Conducting a systematic review of the cost-effectiveness of interventions in patients with multimorbidity is essential to support resource allocation decisions and optimize integrated care models. **Objectives:** A Systematic Review of the Cost-Effectiveness of Interventions in Patients with Multimorbidity. **Materials and methods:** The systematic review was conducted following PRISMA 2020 guidelines, with searches performed in PubMed, Cochrane, Embase, and Vietnamese health science journals up to October 31, 2025. Eligible studies were screened, quality-assessed using the CHEERS 2022 checklist, and all cost and ICER data were converted to 2024 USD. **Results:** The systematic review identified 21 articles with 20 primary studies, including 12 organizational and integrated care models, of which the majority (9/12 studies) reported cost-effective interventions. Reported costs ranged from savings of USD 3,393 to additional costs of USD 3,679, accompanied by improvements in QALYs from 0.007 to 0.298 compared with usual care. Five interventions focusing on behavior change, enhanced self-management, and digital health support showed considerable variation in costs, ranging from savings of USD 3,588 to additional costs of USD 287,946, and QALY changes from -0.030 to +0.031, with most ICER values falling below the willingness-to-pay threshold (4/5 studies). Three interventions evaluating rational medication use and optimization of treatment processes demonstrated that all included studies found these interventions to be dominant or cost-effective compared with their comparators (3/3 studies). **Conclusion:** The systematic review demonstrates the cost-effectiveness of interventions for patients with multimorbidity, providing an evidence base to inform the selection and implementation of future interventions in Vietnam.

**Keywords:** systematic review, multimorbidity, cost-effectiveness

## 1. INTRODUCTION

Multimorbidity refers to the condition in which a patient simultaneously has two or more chronic diseases. It is considered a serious public health challenge - not only adversely affecting physical health, self-care capacity, and quality of life, but also substantially increasing the burden on the healthcare system and the socio-economic environment [1]. According to estimates from the World Health Organization, more than one-third of the global adult population has at least two chronic diseases. The prevalence is particularly high among individuals aged  $\geq 60$  years and varies considerably across regions: high-income countries have generally reached a stable state, whereas developing countries continue to observe an upward trend [2]. Moreover, evidence from long-term cohort studies indicates that multimorbidity is

not only highly prevalent but is also associated with higher mortality risk and substantial health burdens in the adult population [3]. In Vietnam, a study conducted at the Central Geriatric Hospital found that 87.8% of elders had at least two chronic diseases, with the most common being hypertension (78.1%), osteoarthritis (35.8%), diabetes (30.3%), and ischemic heart disease (29.5%) [4]. Multimorbidity also leads to increased healthcare utilization and medical costs, with economic burdens tending to rise proportionally with the number of coexisting chronic conditions - thereby increasing pressure not only on the healthcare system but also on society as a whole [6]. Due to its complexity and multidimensional burden, the management of patients with multimorbidity requires coordination between

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many disciplines, individualized treatment plans, and continuous monitoring - demands that traditional care models often fail to meet. The study by Soley-Bori and colleagues in the United Kingdom reported that annual direct medical costs for patients with multimorbidity can vary significantly, from \$800 up to \$150,000, depending on the type of comorbid conditions and country context [5]. Internationally, numerous health systems have implemented integrated care models, self-management support, and telehealth initiatives to optimize clinical outcomes, enhance quality of life, reduce hospital readmissions, and mitigate healthcare expenditures. Although several economic evaluations have assessed the cost-effectiveness of such interventions, no systematic review has synthesized the overall evidence to date. Accordingly, the present study aims to consolidate and appraise the scientific evidence regarding the cost-effectiveness of interventions for patients with multimorbidity, with the intention of informing the selection and implementation of optimal and context-appropriate strategies within the Vietnamese healthcare setting. The study was

undertaken with two specific objectives:

1. To identify studies analyzing the cost-effectiveness of interventions for patients with multimorbidity.
2. To describe the characteristics and findings of studies evaluating the cost-effectiveness of interventions for patients with multimorbidity.

## 2. METHODS

### 2.1. Study subjects

All studies assessing the cost-effectiveness of interventions targeting patients with multimorbidity.

### 2.2. Study methods

#### 2.2.1. Study design

A systematic review was conducted based on the PRISMA 2020 guidelines for systematic reviews [7].

#### 2.2.2. Study content

##### Research question

Research question: "What is the cost-effectiveness of interventions for patients with multimorbidity?"

The PICOS research question is presented in Table 1.

**Table 1.** PICOS question

P (Populations)	Patients with multimorbidity
I (Intervention)	All types of therapeutic interventions
C (Comparator)	All types of therapeutic interventions
O (Outcome)	Cost-effectiveness indicators (ICER, ICUR)
S (Study)	Pharmacoeconomic evaluations (CEA, CUA)

#### Literature search methods

A comprehensive search process was conducted electronically across international and domestic healthcare databases and scientific journal platforms up to October 31, 2025. *Vietnamese sources*: Vietnam Medical Journal, Ho Chi Minh City Journal of Medicine, Hong Bang International University Journal of Science, Journal of Pharmaceutical Research and Drug Information.

*English sources*: PubMed, Cochrane, and Embase.

To maximize search results, search strategies were developed using keyword combinations such as: "multimorbidity", "chronic multiple conditions", "cost-effectiveness", "cost and cost analysis", "cost-benefit analysis", "cost-utility analysis", together with Boolean operators AND, OR, NOT.

Identified studies were then screened and excluded based on the criteria listed in Table 2.

**Table 2.** Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
- Population: patients with multimorbidity	- Studies without full text
- Intervention: all types of interventions	- Case reports, commentaries, letters, expert opinions, systematic reviews
- Outcomes: ICER, ICUR	- Full text not available in English or Vietnamese
- Study design: CEA, CUA	

Two researchers independently screened titles, abstracts, and full texts. Results were compared, and any discrepancies were resolved through

discussion, with consultation from a third researcher if necessary.

#### Quality assessment

The CHEERS 2022 checklist was used to evaluate the quality of included studies. The checklist contains 28 criteria across seven sections: title, abstract, introduction, methods, results, discussion, and other information [8]. Each reporting criterion was scored based on completeness. Criteria with fully reported content are scored 1 point, reported incompletely - 0.5 points, not reported - 0 points, with no criterion weighted more heavily than another. Criteria not applicable in the assessment were marked as "not applicable" and not scored.

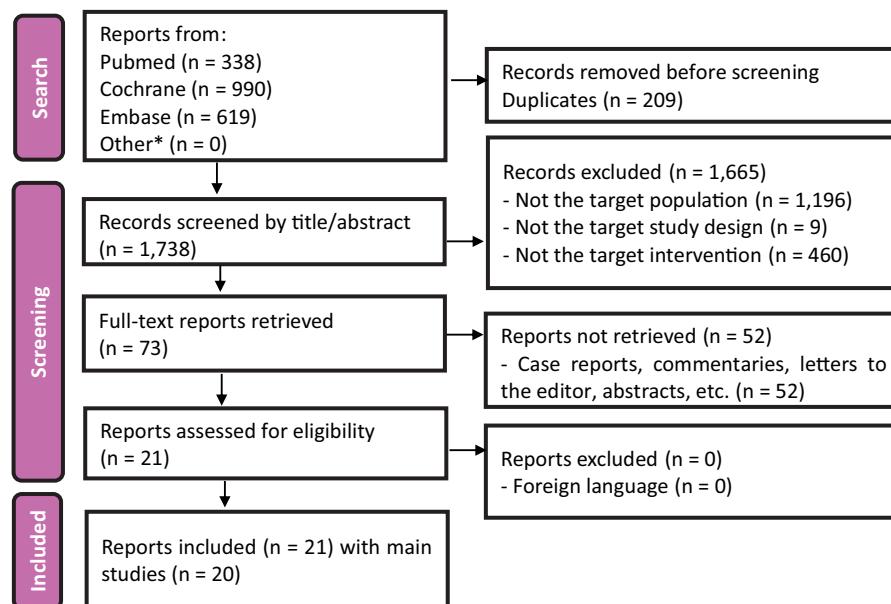
#### *Data extraction and analysis*

After obtaining eligible data, detailed information regarding study characteristics, methods, and pre-specified outcomes was extracted. Cost and ICER estimates were standardized to a common currency unit (USD) using the CCEMG-EPPI-Centre Cost Converter, which applies inflation adjustment based on the Consumer Price Index (CPI) and Purchasing Power Parity (PPP) to convert all monetary values to 2024 USD [9].

### 3. RESULTS

#### 3.1. Selection of cost-effectiveness studies on interventions for patients with multimorbidity

Using the keywords and search strategies described in the Methods section, the study identified 1,947 records from three electronic databases - PubMed, Cochrane, and Embase - in both English and Vietnamese, along with additional sources from domestic medical journals. After removing 209 duplicates, 1,738 records remained for screening. During screening, 1,665 records were excluded for not meeting the eligibility criteria, leaving 73 records for full-text review. Among these, 52 records were conference abstracts or commentary/letter-to-editor articles and were therefore excluded. Therefore, the systematic review included 21 articles, 20 of which were selected as primary studies for overall cost-effectiveness assessment: 12 studies on organizational and integrated care models, 5 studies on interventions focused on behavior-change, enhanced self-care, and digital health support, and 3 studies on interventions assessing rational medicine use and treatment process optimization.



**Figure 1.** PRISMA flow diagram

*Note: \*: Vietnam Medical Journal, Ho Chi Minh City Journal of Medicine, Hong Bang International University Journal of Science, Journal of Pharmaceutical Research and Drug Information*

**Table 3.** Characteristics of studies on interventions based on organizational and integrated care models

No.	Author (year)	Country	Intervention	Comparator	Perspective	Discount
1	Hui-Min Hsieh et. al. (2023) [10]	Taiwan	Pay-for-Performance (P4P) program	Usual care	Third-party payer	3%
2	Itziar Lanzetaa et. al. (2016) [11]	Spain	Integrated Care Model (ICM)	Usual care	Societal	NA
3	Elizabeth M. Camacho et. al. (2018) [12]	UK	Collaborative care model	Usual care	Healthcare system	NA

No.	Author (year)	Country	Intervention	Comparator	Perspective	Discount
4	Walter Bruce Vogel et. al. (2021) [13]	USA	Wellness Incentives and Navigation (WIN) program	Usual care	Payer	5%
5	Bridget Kiely et. al. (2024) [14]	Ireland	Social prescribing link workers	Usual care	Healthcare system	NA
6	Yanshang Wang et. al. (2025) [15]	USA	Community-based Integrated Care for Patients with Diabetes and Depression (CIC-PDD)	Usual care	Healthcare system, third-party payer, societal	NA
7	Stewart W. Mercer et. al. (2016) [16]	UK	CARE Plus - whole-system enhancement of primary care	Usual care	Healthcare system	3.5%
8	Lani Zimmerman et. al. (2017) [17]	USA	Home-Based Care Transition Intervention (HBCTI)	Usual care	Societal	NA
9	Heini Kari et. al. (2022) [18]	Finland	People-centred Care Model (PCCM)	Usual care	Healthcare system	NA
10	Martina Lundqvist et. al. (2018) [19]	Sweden	Comprehensive Geriatric Assessment (CGA) in an Ambulatory Geriatric Unit (AGU)	Usual care	Healthcare system	Costs: 3%; Effects: 3.5%
11	Joanna Thorn et. al. (2020) [20]	UK	“3D Approach” (Dimensions of Health, Depression, Drugs)	Usual care	Payer	3.5%
12	Irma H. J. Everink et. al. (2018) [21]	Netherlands	Integrated Care Pathway in geriatric rehabilitation	Usual care	Societal	NA

Note: NA: Not Applicable

The systematic review found that the interventions evaluated for cost-effectiveness were highly diverse, with no overlap in intervention types across the studies, and all studies used usual care as the comparator. The systematic review was conducted across countries in Europe (the United Kingdom, Ireland, the Netherlands, Finland, Sweden, and Spain), Asia (Taiwan), and the Americas (the United States). Among the 12 studies, 6 were conducted from the healthcare system perspective, 4 from the societal perspective, 2 from the payer perspective, and 2 from the third-party payer perspective, with

the study by Yanshang Wang et al. (2025) [15] evaluating multiple perspectives. Discount rates in the included studies generally ranged from 3% to 5%, with one study additionally applying a 3.5% discount rate for effectiveness. Five out of the 12 studies did not clearly report the discount rate used.

#### *Between interventions based on behavior-change, enhanced self-care, and digital health support*

The synthesized characteristics of studies on interventions based on behavior-change, enhanced self-care, and digital health support are presented in Table 4.

**Table 4.** Characteristics of studies on interventions based on behavior-change, enhanced self-care, and digital health support

No.	Author (year)	Country	Intervention	Comparator	Perspective	Discount
1	Erja Oksman et. al. (2017) [22]	Finland	Telephone Health Coaching	Usual care	Healthcare system, societal	NA
2	Paddy Gillespie et. al. (2022) [23]	Ireland	OPTIMAL Program (Occupational Therapy-led Self-Management Support)	Usual care	Healthcare system	NA
3	Rafael N Miranda et. al. (2022) [24]	Canada	Electronic Patient-Reported Outcomes Tool (ePRO)	Usual care	Healthcare system	NA

No.	Author (year)	Country	Intervention	Comparator	Perspective	Discount
4	Garry Alan Tew et. al. (2024) [25, 31]	UK	Gentle Years Yoga (GYY) for older adults	Usual care	Payer	NA
5	Maria Panagioti et. al. (2018) [26]	UK	Telephone Health Coaching	Usual care	Healthcare system	NA

Note: NA: Not Applicable

The systematic review recorded that 2 out of 5 studies evaluated telephone health coaching interventions, and all studies used usual care as the comparator. The studies were conducted in Europe (Finland, Ireland, the UK) and North America (Canada), of which three studies adopted a healthcare system perspective, one adopted a payer perspective, and one adopted both the

healthcare system and societal perspectives. None of the studies applied a discount rate.

#### *Between interventions assessing rational medicine use and treatment process optimization*

The synthesized characteristics of studies on interventions assessing rational medicine use and treatment process optimization are presented in Table 5.

**Table 5.** Characteristics of studies on interventions assessing rational medicine use and treatment process optimization

No.	Author (year)	Country	Intervention	Comparator	Perspective	Discount
1	Paola Salari et. al. (2022) [27]	Ireland	Chronic Disease Self-Management Program (CDSMP)	Usual care	Healthcare system, societal	NA
2	Paddy Gillespie et. al. (2024) [28]	Ireland	OPTIMAL Program (Occupational Therapy-led Self-Management Support)	Usual care	Healthcare system	NA
3	Ji-Hee Youn et. al. (2019) [29]	UK	Standard pharmacologic treatments (to optimize therapy)	No treatment	Healthcare system	Cost: 3.5% Effects: 3.5%

Note: NA: Not Applicable

The systematic review found that two out of the three included studies were conducted in Ireland, and no overlap in the types of interventions was observed across studies. Two of the three comparisons used usual care as the comparator. All three studies adopted a healthcare system perspective, with one additionally incorporating a societal perspective. One of the three studies applied discounting at a rate of 3.5% for both

costs and health outcomes.

#### *3.2.3. Synthesis of research methods*

##### *Between interventions based on organizational and integrated care models*

The synthesis of research methods for interventions based on organizational and integrated care models is presented in Table 6.

**Table 6.** Research methods of interventions based on organizational and integrated care models

No.	Author (year)	Study design	Time horizon	Cycle	Cost type	Outcome measure	Sensitivity analysis
1	Hui-Min Hsieh et. al. (2023) [10]	RCT	4	NA	Direct medical	QALY	PSA
2	Itziar Lanzetaa et. al. (2016) [11]	RCT	1	NA	Direct medical	QALY	PSA
3	Elizabeth M. Camacho et. al. (2018) [12]	RCT	2	NA	Direct medical	QALY	PSA, DSA
4	Walter Bruce Vogel et. al. (2021) [13]	RCT	3	NA	Direct medical	QALY	PSA, DSA
5	Bridget Kiely et. al. (2024) [14]	RCT	0.08	NA	Direct medical	QALY	PSA, DSA

No.	Author (year)	Study design	Time horizon	Cycle	Cost type	Outcome measure	Sensitivity analysis
6	Yanshang Wang et. al. (2025) [15]	RCT	1	NA	Direct medical, indirect	QALY	PSA
7	Stewart W. Mercer et. al. (2016) [16]	RCT	1 Scenario: 2	NA	Direct medical	QALY	PSA, scenario
8	Lani Zimmerman et. al. (2017) [17]	RCT	0.5	NA	Direct medical	QALY	NA
9	Heini Kari et. al. (2022) [18]	RCT	2	NA	Direct medical	QALY	DSA
10	Martina Lundqvist et. al. (2018) [19]	Model-based	Lifetime	1 year	Direct medical	QALY	PSA, scenario
11	Joanna Thorn et. al. (2020) [20]	RCT	1.25	NA	Direct medical	QALY	DSA, PSA
12	Irma H. J. Everink et. al. (2018) [21]	Prospective cohort	0.75	NA	Direct medical, indirect	QALY	PSA

Notes: NA: Not Applicable; RCT: Randomized Controlled Trial; DSA - Deterministic Sensitivity Analysis; PSA - Probabilistic Sensitivity Analysis; QALY - Quality-Adjusted Life Year

The systematic review found that 10/12 studies were randomized controlled trials, with follow-up durations ranging from 0.08 to 4 years, the longest being 4 years (Hui-Min Hsieh et. al., 2023) [10]. One study used a lifetime Markov model with a 1-year cycle (Martina Lundqvist et. al., 2018) [19], and one study adopted a prospective cohort design with a 0.75-year follow-up period (Irma H.J. Everink et. al., 2018) [21]. Most studies (10/12) evaluated direct medical costs, and 2/12 assessed both direct medical and indirect costs. Most studies (10/12)

evaluated direct medical costs, and 2/12 assessed both direct medical and indirect costs. All studies used QALY as the outcome measure. PSA was conducted in 10/12 studies, DSA in 5/12, and one study did not perform sensitivity analysis.

*Between interventions based on behavior-change, enhanced self-care, and digital health support*

The synthesis of research methods for interventions based on behavior-change, enhanced self-care, and digital health support is presented in Table 7.

**Table7.** Research methods of behavior-change, enhanced self-care, and digital health support interventions

No.	Author (year)	Study design	Time horizon	Cycle	Cost type	Outcome measure	Sensitivity analysis
1	Erja Oksman et. al. (2017) [22]	RCT	1	NA	Direct medical	QALY	PSA
2	Paddy Gillespie et. al. (2022) [23]	RCT	0.5	NA	Direct medical	QALY	PSA
3	Rafael N Miranda et. al. (2022) [24]	RCT	1.25	NA	Direct medical	QALY	PSA, DSA
4	Garry Alan Tew et. al. (2024) [25] [31]	RCT	1	NA	Direct medical	QALY	PSA, scenario
5	Maria Panagioti et. al. (2018) [26]	Prospective cohort	1.5	NA	Direct medical	QALY	PSA

Notes: NA: Not Applicable; RCT: Randomized Controlled Trial; DSA - Deterministic Sensitivity Analysis; PSA - Probabilistic Sensitivity Analysis; QALY - Quality-Adjusted Life Year

The review identified that 4 out of 5 studies employed a randomized controlled trial (RCT) design, except for the study by Maria Panagioti et al. (2018), which used a prospective cohort design

[26]. All five studies had evaluation periods ranging from 0.5 to 1.5 years and assessed both healthcare costs and effectiveness in terms of QALYs. All five studies conducted probabilistic sensitivity

analyses (PSA), with the study by Garry Tew et al. (2024) additionally performing deterministic sensitivity analysis (DSA), and the study by Maria Panagioti et al. (2018) combining PSA with scenario analysis.

*Between rational medicine use and treatment process optimization interventions*

The synthesis of research methods for interventions assessing rational medicine use and treatment process optimization is presented in Table 8.

**Table 8.** Research methods of interventions assessing rational medicine use and treatment process optimization

No.	Author (year)	Study design	Time horizon	Cycle	Cost type	Outcome measure	Sensitivity analysis
1	Paola Salari et. al. (2022) [27]	RCT	1	NA	Direct medical, indirect	QALY	PSA
2	Paddy Gillespie et. al. (2024) [28]	RCT	0.5	NA	Direct medical	QALY	PSA, scenario
3	Ji-Hee Youn et. al. (2019) [29]	Model-based	Lifetime	NA	Direct medical	QALY	PSA

Notes: NA: Not Applicable; RCT: Randomized Controlled Trial; PSA - Probabilistic Sensitivity Analysis; QALY - Quality-Adjusted Life Year

The systematic review found that two out of the three studies employed a randomized controlled trial (RCT) design with study durations ranging from 0.5 to 1 year, while the remaining study used a modeling approach over a lifetime horizon. All studies adopted a cost-utility framework using QALYs and direct medical costs; the study by Paola Salari et al. (2022) additionally incorporated indirect costs [27]. All studies conducted probabilistic sensitivity

analyses (PSA), and the study by Paddy Gillespie et al. (2024) further performed scenario analyses [28].

### 3.2.4. Synthesis of study findings

*Between interventions based on organizational and integrated care models*

The main findings of studies on interventions based on organizational and integrated care models are presented in Table 9.

**Table 9.** Main findings of studies on interventions based on organizational and integrated care models

No.	Author (year)	Cur. (study year)	Incremental cost		IE	ICER		WTP (study year)	Conclusion
			Study year	USD 2024		Study year	USD 2024		
1	Hui-Min Hsieh et. al. (2023) [10]	TWD (2021)	-42,850	-3,393	0.085	Dominant		24,000	Dominant
2	Itziar Lanzetaa et. al. (2016) [11]	EUR (2016)	1,036	1,996	-0.076	Dominated		25,000 - 30,000	Dominated
3	Elizabeth M. Camacho et. al. (2018) [12]	GBP (2016)	517	964	0.140	13,069	24,356	20,000 - 30,000	Cost-effective
4	Walter Bruce Vogel et. al. (2021) [13]	USD (2020)	3,728	3,006	0.298	12,511	14,832	50,000 - 100,000	Cost-effective
5	Bridget Kiely et. al. (2024) [14]	EUR (2020)	1,195	1,704	0.015	79,683	113,605	45,000	Not cost-effective
6	Yanshang Wang et. al. (2025) [15]	USD (2023)	263	269	0.003	10,207	10,439	13,064 - 39,192	Cost-effective*
			266	272	0.003	10,342	10,576		Cost-effective**
			295	302	0.003	11,478	11,738		Cost-effective***
7	Stewart W. Mercer et. al. (2016) [16]	GBP (2013)	929	1,799	0.076	12,224	23,674	20,000 - 30,000	Cost-effective

No.	Author (year)	Cur. (study year)	Incremental cost		IE	ICER		WTP (study year)	Conclusion
			Study year	USD 2024		Study year	USD 2024		
8	Lani Zimmerman et. al. (2017) [17]	USD (2016)	489	624	-0.170	Dominated		50,000	Dominated
9	Heini Kari et. al. (2022) [18]	EUR (2017)	-2,139	-28,811	0.029	Dominant		30,000	Dominant
10	Martina Lundqvist et al. (2018) [19]	EUR (2016)	24,678	3,679	0.540	45,987	34,838	50,000	Cost-effective
11	Joanna Thorn et. al. (2020) [20]	EUR (2016)	126	235	0.070	18,499	34,476	20,000	Cost-effective
12	Irma H. J. Everink et. al. (2018) [21]	EUR (2014)	-11,605	-19,154	0.010	Dominant		50,000	Dominant

Notes: IE - Incremental effectiveness; ICER - Incremental cost-effectiveness ratio; WTP - willingness-to-pay threshold; \*healthcare system perspective; \*\*payer perspective; \*\*\*societal perspective.

The systematic review found that the incremental cost between the studied interventions and the comparator interventions ranged from a reduction of 28,811 USD to an increase of 3,679 USD. Incremental effectiveness ranged from a decrease of 0.170 QALY to an increase of 0.540 QALY. Among the 12 studies, 6 out of 12 studies were cost-effective, with ICER values ranging from 10,439 to 34,838 USD/QALY, and 3 out of 12 studies reported that the studied intervention was dominant, producing cost savings (from 2,139 to 42,850 USD)

together with improved effectiveness (0.010 to 0.085 QALY). Two of 12 studies found the studied intervention to be dominated, and one of 12 studies was not cost-effective, with an ICER value of 113,605 USD/QALY - exceeding the willingness-to-pay threshold (45,000 USD/QALY).

*Between interventions based on behavior-change, enhanced self-care, and digital health support*  
The main findings of studies on interventions based on behavior change, enhanced self-care, and digital health support are presented in Table 10.

**Table 10.** Main findings of studies on interventions based on behavior change, enhanced self-care, and digital health support

No.	Author (year)	Cur. (study year)	Incremental cost		IE	ICER		WTP (study year)	Conclusion
			Study year	USD 2024		Study year	USD 2024		
1	Erja Oksman et. al. (2017) [22]	EUR (2017)	432	582	0.009	48,000	64,656	50,000	Cost-effective
2	Paddy Gillespie et. al. (2022) [23]	EUR (2019)	-2,548	-3,588	0.031	Dominant		20,000	Dominant
3	Rafael N Miranda et. al. (2022) [24]	CAD (2020)	1,710	1,703	-0.030	Dominated		50,000	Dominated
4	Garry Alan Tew et. al. (2024) [25, 31]	GBP (2021)	81	134	0.018	4,545	7,560	20,000 - 30,000	Cost-effective
5	Maria Panagioti et. al. (2018) [26]	GBP (2014)	151	288	0.019	8,050	15,393	20,000 - 30,000	Cost-effective

Notes: IE - Incremental effectiveness; ICER - Incremental cost-effectiveness ratio; WTP - willingness-to-pay threshold

The systematic review recorded that the incremental cost between the studied interventions and the comparator interventions ranged from a reduction of 3,588 USD to an increase of 287,946

USD, while incremental effectiveness ranged from a decrease of 0.030 QALY to an increase of 0.031 QALY. Among the five studies, 3/5 studies were cost-effective with ICER values ranging from 7,560 USD to

64,656 USD; 1/5 study reported that the evaluated intervention was dominant over the comparator (-3,588 USD and 0.031 QALY); 1/5 study reported that the evaluated intervention was dominated by the comparator (1,703 USD and -0.030 QALY).

*Between interventions, evaluating rational medicine use and treatment process optimization*  
The main findings of studies evaluating rational medicine use and treatment process optimization are presented in Table 11.

**Table 11.** Main findings of studies evaluating rational medicine use and treatment process optimization are presented

No.	Author (year)	Cur. (study year)	Incremental cost		IE	ICER		WTP (study year)	Conclusion
			Study year	USD 2024		Study year	USD 2024		
1	Paola Salari et. al. (2022) [27]	CHF (2018)	-3,588	-5,222	0.025	Dominant		NA	Dominant
2	Paddy Gillespie et. al. (2024) [28]	EUR (2019)	-401	-565	0.014	Dominant		20,000 - 45,000	Dominant
3	Ji-Hee Youn et. al. (2019) [29]	GBP (2013)	847	1,640	0.236	3,583	6,939	20,000	Cost-effective*
			840	1,627	0.234	3,582	6,937		Cost-effective**
			408	790	0.280	1,458	2,824		Cost-effective***

*Notes:* NA: Not Applicable; IE - Incremental effectiveness; ICER - Incremental cost-effectiveness ratio; WTP - willingness-to-pay threshold; \* Linked model with correlations incorporated; \*\* Independently linked mode; \*\*\* Individual disease models.

The systematic review found that the incremental cost ranged between the studied interventions and the comparator interventions ranged from a reduction of 3,588 USD to an increase of 847 USD, while incremental effectiveness ranged from 0.014 QALY to 0.236 QALY. Among these, 2/3 of the studies demonstrated that the intervention dominated the comparator, while 1/3 of the studies reported that the intervention was cost-effective.

#### 4. DISCUSSION

From three online databases - PubMed, Cochrane, and Embase - together with domestic journal sources, a total of 1,947 records were identified and recorded. After removing duplicates and screening based on the inclusion and exclusion criteria, 21 articles (20 primary studies) were eligible for data extraction and analysis of characteristics, methods, and results. The systematic review identified 12 organizational and integrated care models, 5 interventions based on behavior-change, enhanced self-care, and digital health support, and 3 interventions assessing rational medication use and treatment processes optimization.

Interventional studies comparing integrated care and coordinated care models have been conducted across various countries, with clinical trial-based methods predominantly applied. The systematic review indicates that organizational and integrated

care models were superior or cost-effective compared with usual care in studies with longer follow-up durations. Likewise, the systematic review by Rocks et al. (2020), which examined 34 economic evaluations of integrated care interventions for chronic conditions across multiple countries up to December 2019, also reported that studies with follow-up periods exceeding one year demonstrated cost-effectiveness, with significantly reduced costs (0.87; 95% CI: 0.80 - 0.94) compared with usual care and improved clinical outcomes (1.15; 95% CI: 1.11 - 1.18). These interventions contributed to reduced healthcare utilization costs, including hospitalization rates and length of stay, while simultaneously improving health outcomes such as quality of life and disease control [32]. Integrated interventions, which are comprehensive and address multiple dimensions (physical, psychological, and social), align well with the multidimensional nature of multimorbidity. However, heterogeneity in intervention models (in terms of structure and processes) makes generalization difficult, and most evidence originates from high-income countries. Therefore, careful consideration is needed when applying these models in the Vietnamese health system, which differs substantially in cost structures and workforce capacity.

Studies on behavior-change interventions, self-management enhancement, and digital health support

demonstrated wide variations in costs, ranging from cost savings of USD 3,588 to additional costs of USD 287,946, and QALY changes from -0.030 to +0.031, with the majority of ICER values falling below the willingness-to-pay threshold (4 out of 5 studies). These findings are consistent with the systematic review by Gentili et al. (2022), which examined economic evaluations of digital health interventions for chronic disease management and reported highly variable clinical and economic outcomes. Clinical improvements ranged from mild to moderate and were not consistent across technology types, while economic results exhibited substantial heterogeneity. Among the 18 economic evaluations, 12 studies (66.7%) concluded that these interventions were cost-effective, particularly for respiratory diseases and diabetes [33]. This group of interventions is characterized by flexibility, scalability, and low maintenance costs, and is especially suitable in the context of rising chronic disease burden and growing demand for patient self-management. However, their effectiveness heavily depends on patient adherence, and implementation requires robust technical infrastructure and adequate digital accessibility for patients.

Interventions focusing on rational medication use and optimization of treatment processes consistently demonstrated superiority or cost-effectiveness compared with the comparator interventions (3 out of 3 studies). A systematic review on the economic evaluation of pharmacist-led interventions for outpatient medication management in chronic diseases (hypertension, type 2 diabetes, dyslipidemia) similarly reported that most interventions were cost-effective or dominant (10 out of 11 studies), indicating that medication optimization strategies—particularly those involving clinical pharmacists—provide clear economic benefits across various healthcare settings [34]. Strengths of

this intervention group include low implementation costs and ease of adoption in hospital or clinic models, especially given Vietnam's ongoing efforts to strengthen the role of clinical pharmacists. However, the number of studies in this area remains limited, and most were conducted in countries with well-developed electronic medical record systems, whereas Vietnam is still in the early stages of development and implementation.

This systematic review was conducted following PRISMA guidelines, and study quality was assessed using the CHEERS checklist to ensure transparency, consistency, and reproducibility. The data extraction process was systematic and included information on study design, participant characteristics, analytical methods, and key economic outcomes. Additionally, all costs and incremental cost-effectiveness metrics were standardized to 2024 USD, enhancing comparability and analytical reliability. The findings provide a comprehensive overview of the cost-effectiveness of interventions in managing multimorbidity, supporting future pharmacoeconomic research and cost-effectiveness assessments within the Vietnamese multimorbidity context. However, the study still has certain limitations, as the literature search was restricted to selected databases and two primary languages (English and Vietnamese), meaning that relevant studies published elsewhere or in other languages may have been missed.

## 5. CONCLUSION

In the context where the implementation of interventions for patients with multimorbidity in Vietnam remains limited, this systematic review demonstrates the cost-effectiveness of such interventions, thereby providing a foundation for the selection and deployment of new interventions for patients with multimorbidity in the future.

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## Tổng quan hệ thống chi phí - hiệu quả của các can thiệp trên người bệnh đa bệnh đồng mắc

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### TÓM TẮT

**Đặt vấn đề:** *Đa bệnh đồng mắc (ĐBĐM) ngày càng phổ biến và trở thành thách thức lớn đối với hệ thống y tế, việc thực hiện tổng quan chi phí - hiệu quả của các can thiệp trong nhóm đối tượng này là cần thiết nhằm hỗ trợ ra quyết định phân bổ nguồn lực và tối ưu hóa mô hình chăm sóc tích hợp.* **Mục tiêu:** *Tổng quan hệ thống chi phí - hiệu quả của các can thiệp trên người bệnh đa bệnh đồng mắc.* **Đối tượng và phương pháp:** *Tổng quan hệ thống được thực hiện theo hướng dẫn PRISMA 2020, tìm kiếm trên PubMed, Cochrane, Embase và các tạp chí khoa học sức khỏe tại Việt Nam đến ngày 31/10/2025. Các nghiên cứu đủ điều kiện được sàng lọc, đánh giá chất lượng bằng bảng kiểm CHEERS 2022, và quy đổi toàn bộ dữ liệu chi phí, ICER sang USD năm 2024.* **Kết quả:** *Tổng quan ghi nhận 21 bài báo với 20 nghiên cứu chính được chọn bao gồm 12 mô hình tổ chức và chăm sóc tích hợp ghi nhận tính chi phí - hiệu quả của các can thiệp ở phần lớn nghiên cứu (9/12 nghiên cứu) với chi phí dao động từ tiết kiệm 3,393 USD đến gia tăng 3,679 USD cùng với QALY cải thiện từ 0.007 đến 0.298 QALY so với chăm sóc thông thường; 5 can thiệp dựa trên thay đổi hành vi, tăng cường tự chăm sóc và hỗ trợ bằng công nghệ số cho thấy chi phí dao động đáng kể từ tiết kiệm 3,588 USD đến chi phí tăng thêm 287,946 USD và QALY từ giảm 0.030 đến tăng 0.031 với phần lớn giá trị ICER thấp hơn ngưỡng chi trả (4/5 nghiên cứu); 3 can thiệp đánh giá sử dụng thuốc hợp lí và tối ưu hóa quá trình điều trị cho thấy toàn bộ nghiên cứu đều ghi nhận các can thiệp này vượt trội hoặc đạt chi phí - hiệu quả so với can thiệp so sánh (3/3 nghiên cứu).* **Kết luận:** *Tổng quan hệ thống cho thấy tính chi phí - hiệu quả của các can thiệp trên người bệnh ĐBĐM, cung cấp cơ sở cho việc lựa chọn, triển khai các can thiệp mới tại Việt Nam trong tương lai.*

**Từ khóa:** *tổng quan hệ thống, đa bệnh đồng mắc, chi phí - hiệu quả*

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