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REVIEW

# Application of Discrete Event Simulation Models for COPD Management: A Systematic Review

Liu Shuai[1], Chunni Zhou[1], Jinyi Zhou[2], Hao Hu[3], Yunfeng Lai[4], Lijun Fan[1], Wei Du[1], Meng Li[1]

[1]School of Public Health, Southeast University, Nanjing, People's Republic of China; [2]Department of Non-Communicable Chronic Disease Control, Jiangsu Provincial Center for Disease Control and Prevention, Nanjing, People's Republic of China; [3]State Key Laboratory of Quality Research in Chinese Medicine, Institute of Chinese Medical Sciences, University of Macau, Macao, People's Republic of China; [4]School of Public Health and Management, Guangzhou University of Chinese Medicine, Guangzhou, People's Republic of China

Correspondence: Meng Li, School of Public Health, Southeast University, 87, Dingjiaqiao Road, Gulou District, Nanjing, 210009, People's Republic of China, Email meng-li@seu.edu.cn



**Background:** This systematic review aims to comprehensively assess the current application of discrete event simulation (DES) models in managing chronic obstructive pulmonary disease (COPD). By synthesizing and analyzing multiple studies, we incorporate the latest evidence, evaluate research quality, identify gaps, and provide recommendations for the future application of DES in COPD management.

**Methods:** We systematically searched six electronic databases including PubMed, Web of Science, Embase, Cochrane, Econlit, and China National Knowledge Infrastructure (CNKI) for articles published up to August 22, 2024. Reference lists of the included articles were also manually checked. Depending on the study type, we assessed quality using either the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) 2022 checklist or the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Practice Guidelines.

**Results:** Out of the 273 records identified, nine studies met the inclusion criteria. All of these studies focused on health economic evaluations using DES in COPD management, and were conducted in high-income countries. The studies were divided into three groups based on the modeling systems they used: cost-effectiveness analyses of different pharmacological treatments (n=3), economic evaluations of case detection strategies (n=3), and assessments of various interventions on COPD healthcare services (n=3). All studies reported model validation methods (n=9); however, only two studies performed subgroup analysis.

**Conclusion:** This review highlights the current use of DES in COPD management and suggests avenues for future research and resource allocation to enhance the effectiveness of COPD interventions.

**Keywords:** discrete event simulation, chronic obstructive pulmonary disease, personalized medicine, systematic review

## Introduction

Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable respiratory disease characterized by persistent airflow limitation, and symptoms such as shortness of breath, coughing, and sputum production.[1,2] Over 350 million people worldwide are affected by COPD, with 3.2 million deaths annually, making it the third leading cause of death globally.[3] COPD not only imposes a severe disease burden but also incurs substantial economic costs.[4] It is projected that from 2020 to 2050, COPD will cost the global economy INT$4.3 trillion (International Dollar).[5] With advancements in epidemiological research, increasing evidence suggests that in-depth research into the prevention and management of COPD is of significant public health and economic importance.

Decision analysis models (DAMs) are an essential branch of operations research.[6] These models integrate and analyze various data sources, using mathematical and logical relationships to abstract the uncertain real world, thus allowing for the quantitative assessment of different decisions.[7,8] In public health, DAMs are widely used to provide scientific evidence for policy-making.[9] With the continuous advancement in research on COPD, DAMs have become an

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indispensable tool in managing COPD.[10] This is because DAMs can simulate hypothetical scenarios and offer practical evaluation and optimization strategies, especially when real-world resources are limited and clinical trial costs are high.[11]

Currently, the most commonly used DAMs in COPD are Markov models and decision trees.[12] These methods mainly address disease management at the population level, with limitations in handling patient heterogeneity and complex interactions. However, COPD is highly heterogeneous and comorbid.[13,14] To better address individual differences and complexity, discrete event simulation (DES) models are gaining attention from researchers.[15]

The DES model, also known as the event occurrence time model, is an individual-level operational research technique characterized by its ability to flexibly simulate the dynamic behavior of complex systems and the interactions between individuals, groups, and the environment.[16,17] Therefore, the DES model is ideal for addressing complex chronic diseases like COPD. This simulation tool can overcome the limitations of traditional modeling approaches, helping researchers to gain a deeper understanding of the natural disease progression of COPD, thereby better supporting decision-making and the implementation of health policies.[18,19]

This article aims to systematically summarize the current application status of DES in COPD research, revealing their potential in disease management and treatment effect evaluation. It will also propose possible future research directions and issues requiring further attention. While some studies have preliminarily explored the application of DES in COPD management, a systematic review and evaluation are still lacking. Hopefully, this review will provide valuable references for researchers and promote the development of personalized treatment and precise management of COPD.

# Methods

This systematic review strictly adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure the transparency and reliability of the research.[20] The review has been registered in the International Prospective Register of Systematic Reviews (PROSPERO: CRD42024563296). The complete review protocol, including detailed research questions, inclusion and exclusion criteria, and data extraction methods, can be accessed in this database.

## Inclusion and Exclusion Criteria

Selecting appropriate inclusion and exclusion criteria is crucial. By strictly defining these criteria, we can maximize the relevance and quality of the included studies, thereby enhancing the credibility and scientific rigor of the systematic review. The specific inclusion criteria are: (i) studies that utilize formal decision analysis methods and implement DES in the COPD population, (ii) studies that focus on applying DES in the domain of COPD.

The exclusion criteria are: (i) lack of a clear association between the DES model and COPD, (ii) qualitative studies, pure abstract papers, or purely methodological studies, and (iii) systematic reviews and/or meta-analyses. Studies that meet the above inclusion criteria will be included in this review, while those that meet any of the exclusion criteria will be excluded.

## Data Sources and Search Strategy

Six databases, PubMed, Web of Science, Embase, Cochrane, Econlit, and China National Knowledge Infrastructure (CNKI), were searched. Additionally, we manually searched the references of included articles to identify any relevant articles that might have been missed during the systematic search. The search period covered from the inception of each database up to August 22, 2024.

The keywords and accessible terms used for the search included “Chronic Obstructive Pulmonary Disease” and “discrete event simulation” OR “(discrete event) AND (computer simulation* OR model*)”.[21] Boolean operators OR/AND were employed to diversify the search terms. The search results were downloaded into Endnote,[21] and Appendix 1 provides a detailed summary of the search strategy.

## Study Selection

After removing duplicate records using literature management software and manual verification, articles were screened based on titles and abstracts to exclude those irrelevant to the research objectives. Subsequently, full-text reviews were performed on eligible studies to ensure they met the predefined criteria. Finally, disagreements were resolved through consensus discussions between two reviewers, resulting in the final selection of included articles.

## Data Extraction

Data extraction was performed by one author and verified by another to ensure accuracy. The extraction followed a pre-designed strategy, encompassing the following details: (i) Basic study information: title, first author, publication year and country, abstract, and source of the literature, (ii) Research methodology: study population, data sources, model structure, parameter settings, model validation, simulation software, perspective, sensitivity analysis, and intervention scenarios, (iii) Outcome measures: health-related indicators, cost-effectiveness indicators, and study conclusions.

## Quality Assessment

To ensure the quality of the included studies, we used different quality assessment tools based on the study type. Two independent reviewers scored all the studies and resolved differences through discussion. The final quality assessment results were recorded and reported to ensure transparency and reliability of the research.

### Quality Assessment Using the CHEERS 2022 Checklist

Given that the articles included in this study are related to health economics, the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) recommends evaluating health economics research according to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS).[22] In this study, two authors used the CHEERS 2022 checklist to assess the quality of the publications, each CHEERS item was described as "reported", "not reported", or "not applicable." CHEERS does not provide a specific scoring mechanism.[23] As defined by Zhou et al, studies meeting 100% of the relevant CHEERS items are classified as demonstrating excellent quality, those meeting 75%–99% are high quality, 50%–74% are medium quality, and those meeting less than 50% as poor quality.[24]

### Quality Assessment Using ISPOR Practice Guidelines

Since one of the included studies was a Budget Impact Analysis (BIA), which falls outside the scope of CHEERS quality assessment, we used the ISPOR Good Practices for BIA guidelines to evaluate the quality of this study.[25] Two authors independently assessed the study based on the nine items outlined in the ISPOR practice guidelines: perspective, time horizon, interventions and comparators, target population, data sources, cost inclusions, sensitivity analysis, discounting, and validation.[26]

# Results

Figure 1 illustrates the literature identification, screening, and final inclusion process. Through standardized searches across six databases and manual searches of reference lists, a total of 274 articles were obtained. After removing duplicates, 237 articles (86.5%, 237/274) remained. Subsequently, titles and abstracts were screened, excluding 222 articles (93.7%, 222/237) because their topics were not concentrated on DES and COPD-related research.

Fifteen articles underwent full-text review, of which six articles (40.0%, 6/15) were excluded for the following reasons: two articles were systematic reviews, one article was a purely methodological study, and three articles only had abstracts available. Ultimately, nine articles were determined to be included.

## Characteristics of the Included Studies

The characteristics of the selected studies are summarized in Table 1, which are further detailed below.

### Baseline Characteristics

This systematic review included nine studies. These studies were conducted in the UK (n=4),[27,33–35] Canada (n=3),[30–32] and France (n=1).[28] Additionally, the study by Hoogendoorn et al was conducted across Finland, Sweden, and the Netherlands.[29] All studies were published in or after 2019, distributed as follows: three studies in 2019,[27,28,30] one in 2020,[33] three in 2021,[29,31,34] one in 2022,[35] and one in 2023.[32]

According to the research objectives, the included studies are classified into three distinct model lineages. A detailed examination of the specific distinctions among these lineages is provided in the subsequent Model Lineage section.

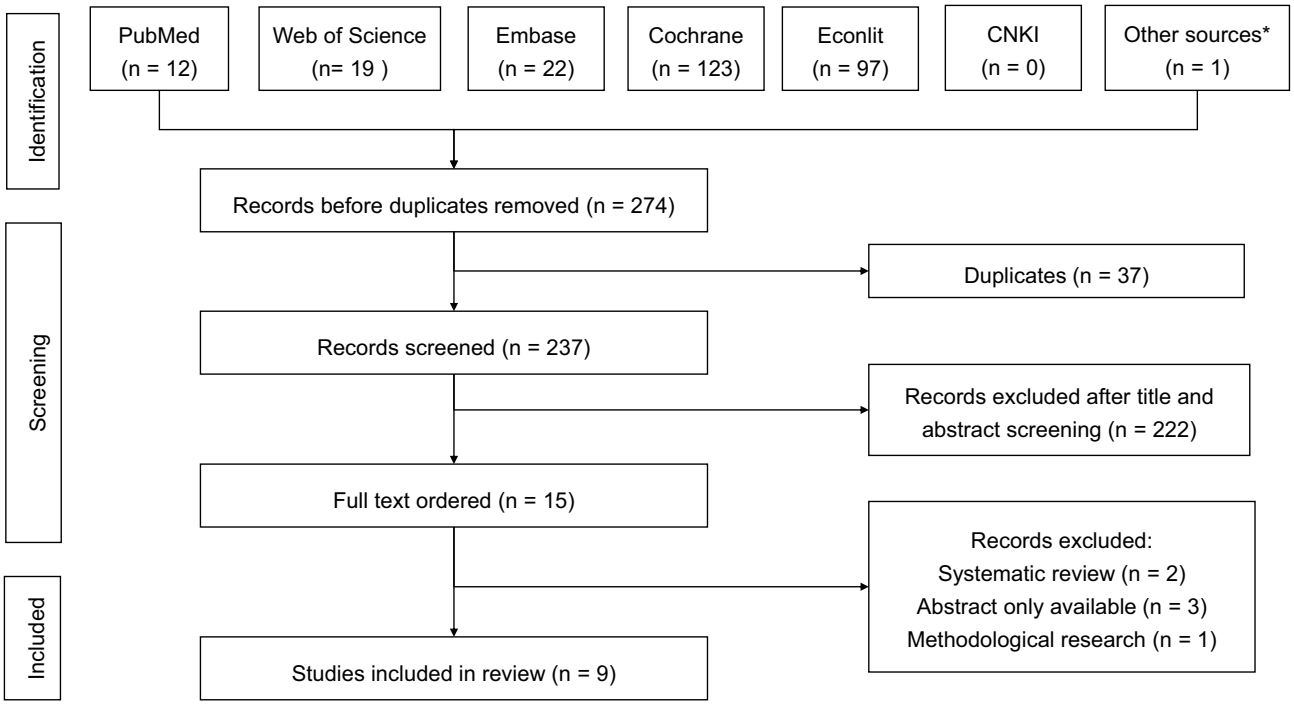


**Figure 1** PRISMA flowchart of study selection.
**Note**: *Other sources, Additional records identified through references.

## Model Design

Population: Six selected studies focused on COPD patients as their target population,[27–29,33–35] while three studies targeted the general population aged 40 and older.[30–32] The sample sizes varied significantly depending on the research objectives, ranging from 563 individuals to the entire target population.

Simulation software: During the modelling process, researchers selected different modelling software. Six studies used general-purpose scripting languages (C++/R) for modelling,[27–32] while three other studies employed specific DES software (Simul8).[33–35] General-purpose scripting languages offer greater flexibility but require coding and extensive debugging. In contrast, specialized software overcomes the limitations of programming languages, making the modelling process more streamlined and efficient.

Time horizon: Among the nine included studies, eight reported the simulation time horizons, ranging from one year to a lifetime. Three studies covered a lifetime.[27–29] One study evaluated 20 years, a duration that can be considered equivalent to a lifetime span given that COPD is typically diagnosed in older individuals with shorter lifespans.[31] The remaining four studies had time horizons between one and five years.[32–35]

Cost-effectiveness of interventions and associated uncertainty: Among the nine included studies, three studies used only scenario sensitivity analysis (SSA),[33–35] while two studies used only deterministic sensitivity analysis (DSA).[31,32] A more comprehensive approach was adopted by three studies, combining probabilistic sensitivity analysis (PSA) with SSA[27,29] or DSA.[28] Notably, one study did not conduct any sensitivity analysis.[30] These diverse methods provide varying degrees of robustness in capturing uncertainties and evaluating potential variations in intervention outcomes.

Results validation: All nine studies validated their results. Three studies conducted internal validation only,[28,34,35] while six studies combined both internal and external validation.[27,29–33] These validation methods enhance the robustness and reliability of the study findings.

## Economic Evaluation

Type of health economic evaluation: After conducting a literature search on the application of DES in COPD, it was found that all included studies belong to the field of health economics. Specifically, these studies provide information to decision-makers by quantitatively assessing the short-term and long-term effects of different interventions under various

**Table 1** General Characteristics of the Included Studies

| First Author (Year) | Country | Model Lineage | Population (Sample Size) | Software | Time Horizon | SA | Validation | Perspective | Final Outcomes | Discount Rate | Included Costs | EE Type | Application (Interventions Type) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hoogendoorn et al (2019)[27] | UK | DPM | COPD patients (5000) | R | Lifetime | PSA, SSA | Internal, external | Healthcare | QALYs | Effects and costs (3.5%) | Medication, maintenance, exacerbations, pneumonia | CUA | Pharmacological therapy(tiotropium) |
| Hoogendoorn et al (2019a)[28] | France | DPM | COPD patients (15000) | R | Lifetime | PSA, DSA | Internal | Healthcare payer, societal | QALYs | Effects and costs (4% years 1–30, 2% thereafter) | Medication, maintenance, exacerbations, pneumonia | CUA | Pharmacological therapy (tiotropium monotherapy and T/O) |
| Hoogendoorn et al (2021)[29] | Finland, Sweden, Netherlands | DPM | COPD patients (2000) | R | Lifetime | PSA, SSA | Internal, external | Finland (healthcare payer), Sweden and Netherlands (societal) | QALYs | Finnish and Sweden (effects and costs: 3%), Netherlands (effects: 1.5%, costs: 4%) | Medication, maintenance, exacerbations, pneumonia | CUA | Pharmacological therapy (tiotropium monotherapy, T/O, and LABA/ICS) |
| Sadatsafavi et al (2019)[30] | Canada | SM | Population aged ≥ 40 years(all) | C++/R | NR | NR | Internal, external | NR | QALYs | NR | Maintenance, exacerbations | CUA | Modeling(EPIC) |
| Johnson et al (2021)[31] | Canada | SM | Population aged ≥ 40 years (routine primary care visit | C++/R | 20 years | DSA | Internal, external | Healthcare | QALYs | Effects and costs (1.5%) | Case detection and diagnosis, medication, maintenance, exacerbations | CUA | Case detection (16 strategies) |
| Mountain et al (2023)[32] | Canada | SM | Population aged ≥ 40 years(all) | C++/R | 5 years | DSA | Internal, external | Healthcare payer | Budget, diagnosis rate | Costs (0%) | Case detection and diagnosis, medication, maintenance, exacerbations | BIA | Case detection (8 strategies) |
| Yakutcan et al (2020)[33] | UK | HCSO | COPD patients (563) | Simul8 | 3 years | SSA | Internal, external | Healthcare | QALYs | NR | Staff, PR, occupied bed day | CUA | Service management (PEPR) |
| Yakutcan et al (2021)[34] | UK | HCSO | COPD patients (1540) | Simul8 | 3 years | SSA | Internal | Healthcare payer | QALYs, net benefits | Effects and costs (3.5%) | Staff, PR, occupied bed day, monetary value of QALY, annual drug and indirect | CUA, CBA | Service management (PR) |
| Yakutcan et al (2022)[35] | UK | HCSO | COPD patients (1600) | Simul8 | 1 year | SSA | Internal | Healthcare | QALYs | NR | NR | CER | Service management (COVID-19) |

**Abbreviations**: DPM, disease progression model; SM, screening model; HCSO, health and care system operations; SA, sensitivity analysis; DSA, deterministic sensitivity analysis; PSA, probabilistic sensitivity analysis; SSA, scenario sensitivity analysis; NR, not reported; QALYs, quality-adjusted life years; EE, economic evaluation; CUA, cost-utility analysis; BIA, budget impact analysis; CBA, cost-benefit analysis; CER, comparative effectiveness research; T/O, tiotropium/olodaterol; EPIC, Evaluation Platform in COPD; PEPR, post-exacerbation pulmonary rehabilitation; PR, pulmonary rehabilitation.

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hypothetical scenarios, aiming to maximize public health benefits. Based on the study outcomes of interest to the researchers, these studies were categorized into different types. Among them, six studies focused on cost-utility analysis (CUA),[27–31,33] two studies conducted BIA and comparative effectiveness research, respectively,[32,35] and one study combined CUA and cost-benefit analysis.[34] Quality-Adjusted Life Years (QALYs) was the primary outcome measure used in the studies, with some also measuring other outcomes, including diagnostic rates, budget increments due to detection case strategies,[32] and net benefits arising from different hypothetical scenarios.[34]

Perspective: From a research perspective, four studies adopted the healthcare perspective,[27,31,33,35] three studies adopted the healthcare payer perspective,[31,32,34] and two studies considered both the healthcare payer perspective (such as National Sickness Fund or a limited payer) and the societal perspective.[28,29]

Discount rates: The discount rates used in different studies vary. Specifically, five studies reported discount rates for effects and costs, ranging from 1.5% to 4%.[27–29,31,34] Due to the relatively short time horizon of 5 years in one study, the discount rate for costs was 0%.[32] There were three studies that did not report whether and how costs and effects were discounted.[30,33,35]

Costs: Among the nine studies, eight reported the composition of costs, with researchers including different costs based on their specific research objectives and perspectives. Three pharmacoeconomic studies considered not only the cost of the target drug but also the costs associated with pneumonia, which helps decision-makers make more accurate policy and resource allocation decisions.[27–29] Additionally, some studies also accounted for specific costs related to pulmonary rehabilitation(PR) programs and case screening.[30,32–34]

## Interventions

Among the selected studies, a variety of interventions were analyzed. These interventions can be classified into three broad categories, which are summarized below and visually represented in Figure 2.

Pharmacological therapy: Three studies explored the impact of different pharmacological treatment regimens on COPD patients.[27–29] One study primarily evaluated the long-term cost-effectiveness of tiotropium across various hypothetical scenarios and subgroups, revealing significant effects in reducing acute exacerbations and improving quality of life.[27] Additionally, two other studies compared the health outcomes and overall healthcare costs of tiotropium/olodaterol fixed-dose combination (LAMA+LABA) therapy with both tiotropium monotherapy and the combination of long-acting β2

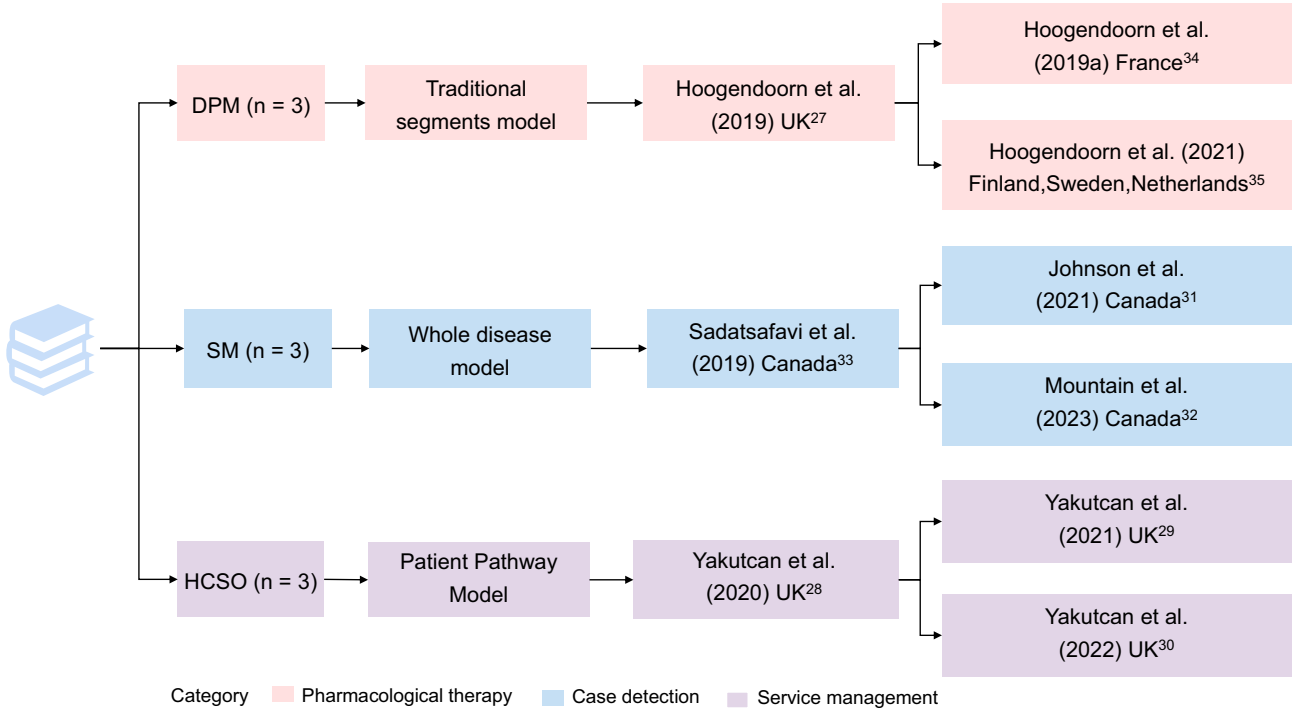


**Figure 2** Evolution of the DES simulation model for COPD.
**Abbreviations**: DPM, disease progression model; SM, screening model; HCSO, health and care system operations.

agonists/inhaled corticosteroids (LABA/ICS).[28,29] The findings indicated that, for specific populations, tiotropium/olodaterol also significantly improved lung function and quality of life and demonstrated superior long-term cost-effectiveness. These studies provide robust economic evidence for stratified and personalized treatment of COPD.

Disease detection: Sadatsafavi et al provided a detailed account of the development and validation process of the EPIC assessment platform.[30] Subsequently, two additional studies built upon this foundation by integrating early screening components and progressively explored the cost-effectiveness and budget impact of various early detection strategies.[31,32] These screening strategies considered different risk populations and screening tools and various screening intervals. The findings indicate that, under a specific willingness-to-pay threshold, conducting COPD diagnostic questionnaires (CDQ) for all asymptomatic individuals is the most cost-effective option, though it requires a substantial budget. In contrast, screening high-risk individuals with a smoking history (aged ≥50) with CDQ achieves a better balance between cost-effectiveness and budget.

Service management: Three studies focused on the healthcare departments providing services to COPD patients through HCSO, considering patient dynamics readmissions.[33–35] Among these, two studies explored and analyzed the impact of non-pharmacological PR strategies on COPD patient outcomes. They analyzed their role in capacity planning and resource reallocation within healthcare departments.[33,34] The first study assessed post-exacerbation pulmonary rehabilitation (PEPR) strategies, aiming to provide decision-makers with more effective methods for COPD care while maintaining and improving care quality.[33] The second study evaluated PR strategies under varying referral volumes, finding through different scenario simulations that increasing PR utilization is cost-effective and improves patient and operational outcomes.[34] The third study incorporated pandemic-related components, using DES combined with regression models to assess the impact of different stringency indices on healthcare services for COPD patients during the pandemic.[35] This study is valuable for understanding strategies to optimize healthcare service delivery during the pandemic.

## Model Lineage

Once a disease model is developed, it is frequently adapted for various purposes through multiple iterations of expansion, revision, and version updates. Based on the fundamental structure of the model, different versions gradually emerge over time.[36]

In this systematic review, researchers applied varying parameters to construct DES models, resulting in the formation of three primary categories: the disease progression modeling, which utilizes traditional segmented methods to describe the natural history of diseases;[27–29] the screening modeling, which employs a comprehensive disease framework to assess the benefits of different screening strategies;[30–32] and the health and care system operations, which describes patient movement trajectories between healthcare departments.[33–35] These categories are inspired by previous classifications.[37,38] As illustrated in Figure 2, we present a lineage diagram of DES models in the study of COPD, incorporating publication dates, authors' statements, and citation relationships from the included studies. Different colors are used to distinguish the application areas of these categories, demonstrating how foundational models have been continuously updated and expanded over time to address various research needs.

## Quality Assessment

### Quality Assessment Using the CHEERS 2022 Checklist

Of the included studies, eight were evaluated based on the CHEERS 2022 evaluation criteria.[27–31,33–35] Table 2 shows the quality scores of each study, with scores ranging from 67.9% to 85.7%. According to the criteria defined by Zhou et al,[24] seven studies were classified as high quality (achieving 75%-99% of the items),[27–29,31,33–35] and only one study was rated as medium quality (achieving 50%-74%).[30] No studies were rated as poor quality. Overall, the included studies performed well in terms of quality assessment.

Nevertheless, these studies still have some shortcomings. Analysis shows a severe lack of comprehensive reporting in several key areas. Only two studies conducted a heterogeneity analysis.[27] Moreover, none of the studies described the health economic analysis plan (HEAPs), distribution effects, or the effect of engagement with patients and others affected by the survey. The detailed assessment results can be referred to Table S1 in Appendix 2. These deficiencies are further illustrated in Figure 3, which details the reporting of different CHEERS items in the included literature. It can be seen that items such as title and discount rate were also insufficiently reported in many studies.

**Table 2** Assessment of the CHEERS 2022 Checklist on Study Level

| Study | CHEERS Items Satisfied | CHEERS Items Not Satisfied | Relevant CHEERS Items | Percent (%) Satisfied | Quality |
|---|---|---|---|---|---|
| Hoogendoorn et al (2019)[27] | 24 | 4 | 28 | 85.7 | High |
| Hoogendoorn et al (2019a)[28] | 23 | 5 | 28 | 82.1 | High |
| Hoogendoorn et al (2021)[29] | 23 | 5 | 28 | 82.1 | High |
| Sadatsafavi et al (2019)[30] | 19 | 9 | 28 | 67.9 | Medium |
| Johnson et al (2021)[31] | 24 | 4 | 28 | 85.7 | High |
| Yakutcan et al (2020)[33] | 22 | 6 | 28 | 78.6 | High |
| Yakutcan et al (2021)[34] | 22 | 6 | 28 | 78.6 | High |
| Yakutcan et al (2022)[35] | 21 | 7 | 28 | 75.0 | High |

### Quality Assessment Using ISPOR Practice Guidelines

Based on the ISPOR working group guidelines, we evaluated the quality of the remaining study using nine specific items.[26] The comprehensive evaluation indicated that the study met all nine items, indicating that the overall quality was high.[32] The detailed assessment results can be referred to Table S2 in Appendix 2.

## Discussion

In this systematic review, we identified nine studies published since March 2019. This indicates that, with the increasing focus on personalized treatment for COPD patients in recent years,[39] the publication rate of DES-based models in COPD management has significantly increased. This aligns with the rapid growth trend of DES in the healthcare field.[40] Most current research is concentrated in high-income countries rather than low- and middle-income countries (LMICs). However, 90% of COPD-related deaths occur in LMICs. Due to limited epidemiological and clinical data in these regions, as well as a shortage of medical resources,[41] there is currently no research from these areas, highlighting a significant research gap in the literature. Therefore, considering the generalizability of evaluation results and the specific medical and economic contexts of different countries, there is a need for targeted evaluations based on the conditions of each country in the future.[5]

Research has found that the application of DES in COPD management falls under the category of health economics evaluation. There are three main reasons for this. First, DES is particularly well-suited for simulating complex medical processes and decision-making scenarios, allowing for patient-level modeling and analysis of COPD disease progression and care pathways.[42] Given the limited healthcare resources in the real world, decision-makers often face conflicts when making decisions.[43] In such cases, DES provides a systematic approach to evaluate the cost-effectiveness of different treatment options, helping to make optimal choices.[44] Therefore, DES holds significant value in health economics evaluation. Second, as one of the most prevalent and costly diseases globally, COPD not only imposes a severe health burden but also creates substantial financial pressure.[45,46] Thus, the health economics evaluation of COPD is important. Finally, this is in line with current research trends, as health economics evaluation has become an increasingly common research topic for DES in the healthcare field.[21]

For chronic diseases like COPD, the choice of time horizon is crucial.[47] Yakutcan et al,[35] when assessing the impact of various policies on COPD management during the pandemic, chose a one-year time horizon to allow decision-makers to make rapid adjustments in a dynamic and rapidly changing environment.[48] Mountain et al,[32] in their assessment of screening strategies using BIA, they selected a five-year time horizon, which aligns with the one to five years recommended by relevant guidelines.[25] Standard CEA guidelines suggest using a sufficiently long (lifetime) time horizon to capture all outcomes.[49] However, Yakutcan's team chose a three-year time horizon for their studies on the PR and PEPR projects,[33,34] as these were not lifetime solutions for COPD and could not assess lifetime benefits indefinitely.[50] Overall, the choice of time horizon for DES in COPD management exhibits considerable heterogeneity but is consistent with the research objectives and application contexts.

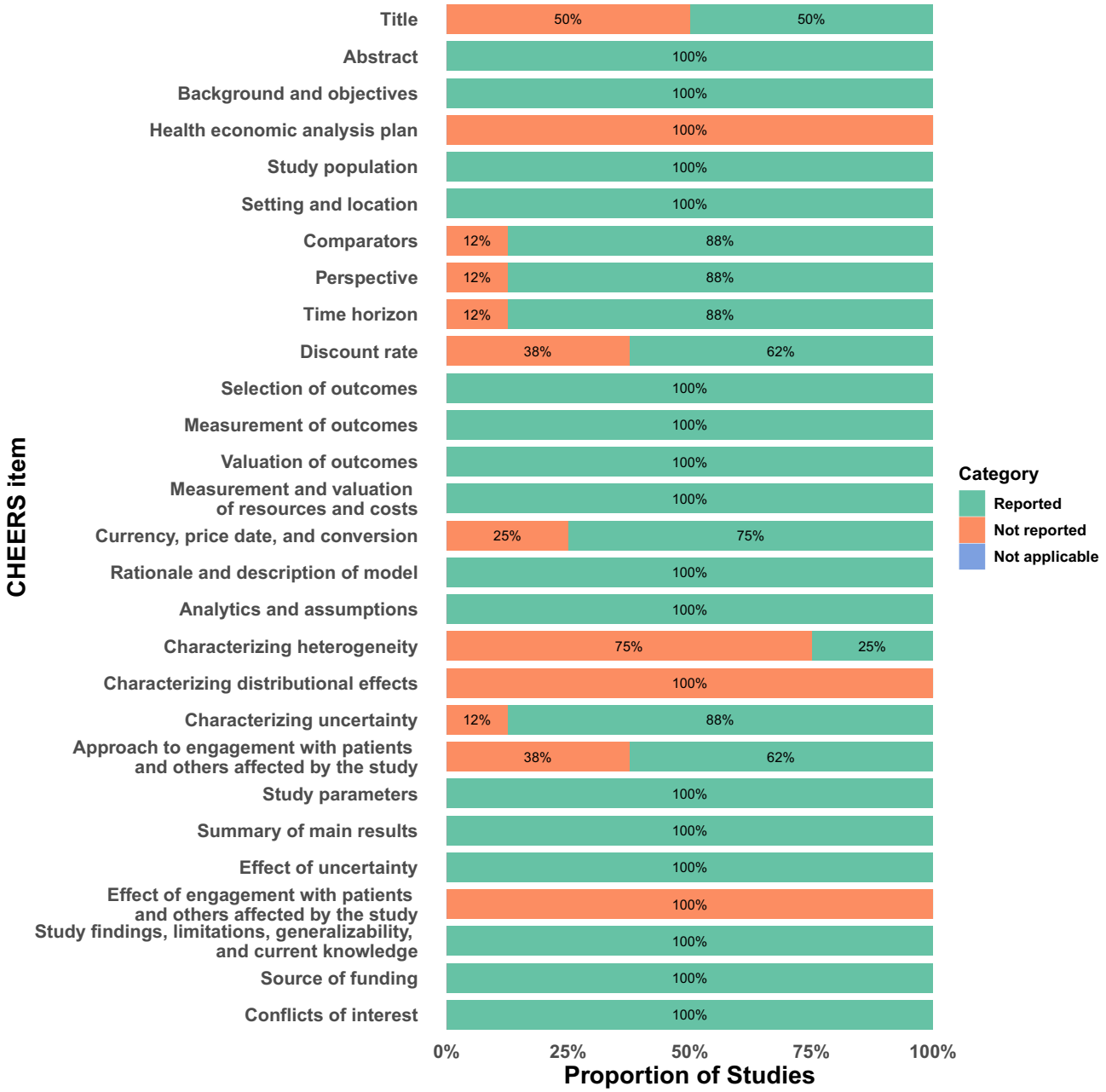


**Figure 3** Overview of the percentage of studies reporting a specific item of the CHEERS checklist.

Studies on pharmacological interventions cover common categories of medications for COPD, ranging from monotherapy to combination therapy. All treatment options can improve patients' lung function and quality of life, each with its applicable range and advantages. This is consistent with the GOLD 2024 guidelines.[2] The studies included vary in their selected settings and perspectives, leading to differences in cost composition.[27–29] However, they all reach a consistent conclusion that LAMA+LABA has significant advantages in improving health outcomes and reducing treatment costs for COPD patients and is thus recommended as a preferred treatment option, aligning with the NICE guidelines.[51]

However, current research does not consider triple therapy (LABA+LAMA+ICS). Although existing studies have demonstrated that triple therapy can improve lung function and reduce exacerbations, its target population is high-risk patients and requires clinical review before use.[52,53] Current studies mainly focus on patients with moderate to severe

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airflow obstruction.[27–29] Therefore, future research on COPD drug interventions should address a broader patient population and evaluate the application of triple therapy.

Previous studies have shown that DES screening modeling has been widely applied in various disease areas, such as lung cancer and diabetes.[54–56] However, its application in COPD is relatively limited, which may be due to the considerable heterogeneity of existing screening strategies.[57,58] The studies included suggest that the most cost-effective scenario involves conducting CDQ screening every three years for all individuals aged 40 and above.[31] In contrast, the US Preventive Services Task Force (USPSTF) tends to favor targeted case finding rather than population-wide screening.[59,60] A recent study based in China, however, suggests that population screening strategies can be cost-effective.[61] Overall, there is no global consensus on which populations (general vs high-risk) should undergo COPD screening or how screening should be conducted (screening frequency, screening tools) at the primary and specialty care levels.[62] Nonetheless, it is undeniable that case screening is a potential strategy for identifying undiagnosed COPD, leading to early interventions that can improve long-term health outcomes.[63]

In summary, when choosing an optimal strategy for COPD case finding, the criteria, accuracy, feasibility, and cost-effectiveness of approaches must be considered in relation to the operating environment, such as low-income versus high-income countries or different healthcare settings.[64]

COPD is a chronic disease, and patients may be hospitalized multiple times over a period.[65] Yakutcan's team developed an innovative approach that combines DES with the concept of patient readmission, demonstrating that the two critical non-pharmacological therapies, PR and PEPR, not only improve patients' quality of life but also impact hospital healthcare management by reducing hospital stay and readmission rates, thereby enhancing overall hospital operational efficiency.[33,34] This is consistent with current evidence on the effectiveness of PR and PEPR in treating COPD.[66–68] Despite substantial evidence supporting the effectiveness of PR, its application remains significantly underutilized.[69] The main reasons are insufficient awareness among professionals, payers, and patients regarding PR, as well as inadequate implementation of PR programs in healthcare facilities.[70] Therefore, future efforts should focus not only on increasing awareness of PR but also on promoting broader delivery methods, such as community-based or home-based PR.[71,72]

During the COVID-19 pandemic, digital technology developed rapidly, and traditional face-to-face communication services gradually shifted to remote care.[73] As a result, the telemedicine market became a safer alternative for COPD management. This phenomenon also validated McKinstry's earlier conclusion that global telemedicine has enormous potential in the field of COPD management.[74]

Based on the CHEERS 2022 evaluation standards, seven studies were rated as high quality. The original CHEERS statement comprised 24 items,[75] while the revised version incorporated an additional four items, totaling 28 items.[23] In our review of the included literature, although some studies considered the approach to engagement with patients and others affected by the study, none adequately addressed the other three newly added items: HEAPs, distributional effects, and the effect of engagement with patients and others affected by the study.[23] This omission is primarily due to the fact that most of the included studies were published before 2022 and thus did not fully adhere to the CHEERS 2022 evaluation standards. Future research should refer to the latest CHEERS statement to enhance the comprehensiveness and applicability of evaluations. For example, adopting the core elements of HEAPs as determined by expert Delphi consensus and making them publicly available as supplementary information can enhance the transparency and practicality of the research.[76] Additionally, adopting patient and public involvement approaches could further strengthen the quality of the research.[77]

Although this study has comprehensively and systematically assessed the potential of DES models in the management of COPD, their real-world application continues to face several challenges. Firstly, DES modeling is inherently complex, particularly in the context of chronic progressive diseases such as COPD. Modelers are required to abstract real-world processes and make numerous decisions,[78] which directly influence both the construction of the model and the evaluation of outcomes. However, due to the abstract nature of the modeling process, researchers are often unable to capture all relevant details, which limits the transparency and reproducibility of the results.[79] Secondly, DES operates at the individual level, necessitating not only high-quality and comprehensive data,[80] but also placing greater demands on researchers. In addition to clinical expertise, proficiency in simulation and programming is essential.[81] Nevertheless, in

practice, the accessibility and completeness of data are frequently limited, presenting challenges for researchers seeking to implement DES.[82] Furthermore, many interventions, such as PR, telemedicine, and screening strategies, require substantial infrastructure investments. In resource-constrained countries and regions, the shortage of funding and equipment often constitutes a significant barrier to the implementation of these interventions.[41] Lastly, although comorbidities play a critical role in COPD management, the studies included in this review generally fail to adequately address the impact of comorbid conditions. Comorbidities significantly influence both the outcomes and treatment effectiveness in COPD,[83] therefore, future research should prioritize the inclusion of comorbidities to enhance the external validity of the models.

In summary, this systematic review is the first to address the application of DES models in the management of COPD. By systematically evaluating and synthesizing the available evidence, this review offers a novel perspective on the role of DES in improving COPD management and identifies key areas for future research.

## Conclusions

In conclusion, this review analyzes the current status of DES applications in the management of COPD and proposes future improvements, providing valuable information for research and resource allocation. The study results indicate that publications on the application of DES in COPD management have been steadily increasing since 2019, primarily focusing on interventions such as pharmaceuticals, screening strategies, and health service management from a health economics perspective. However, these studies are predominantly concentrated in a few high-income countries, which may limit the applicability of their results to low- and middle-income countries. Additionally, while the methods and reporting quality of these studies are generally adequate, there is still room for further improvement. We recommend that future researchers use the CHEERS 2022 checklist to improve the modeling process, ensuring the transparency and credibility of their research.

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## Disclosure

The authors declare no competing interests in this work.

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