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## Article

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Operations Research Perspectives

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*Suggested Citation:* Hadid, Majed et al. (2022) : Operations management of outpatient chemotherapy process: An optimization-oriented comprehensive review, Operations Research Perspectives, ISSN 2214-7160, Elsevier, Amsterdam, Vol. 9, pp. 1-29, <https://doi.org/10.1016/j.orp.2021.100214>

This Version is available at:

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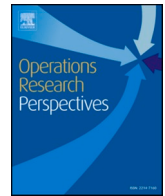
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# Operations management of outpatient chemotherapy process: An optimization-oriented comprehensive review

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## ARTICLE INFO

Edited by Ruiz Ruben

### Keywords:

Outpatient  
Chemotherapy  
Process  
Cancer  
Oncology  
Hematology  
Healthcare  
Patient pathways  
Operations management  
Operations research  
Optimization models  
Content analysis  
Social network analysis

## ABSTRACT

Worldwide, chemotherapy centers that provide outpatient services face significant challenges owing to increased demand and limited resources. Therefore, outpatient chemotherapy process (OCP) optimization has attracted the attention of operations management scholars. This review seeks to provide a comprehensive analysis of existing quantitative optimization-oriented research that addresses OCP problems and identifies departure points for future research.

Various scientific databases were searched to collect the maximum number of OCP optimization-oriented publications. Bibliometric data mining tools were used to provide descriptive analyses of the publications. The OCP optimization-oriented research framework was obtained through social network analysis of the formulation narratives of the models. Content analysis was performed to classify the literature based on several optimization-oriented perspectives. From 1500 publications, 45 studies were screened and included in the review. The current literature lacks a holistic solution to OCP challenges, as most publications are pure optimization studies that consider narrow scopes and idealized problems. This review proposes future research opportunities based on the gaps discovered, which may lead to more insightful results for real-life OCP problems.

## 1. Introduction

Cancer is the second most frequent cause of death worldwide. More than 16% of the current global population deaths are from cancer [1]. According to the most recent world cancer report [2], the total global cancer expenditures were approximately \$1.16 trillion in 2010. This number is expected to increase by 50% as the number of cancer cases diagnosed annually is expected to double by 2040. Cancer treatments include surgery, radiotherapy, chemotherapy, or a combination of the above. Nevertheless, more than half of the global cancer patients required chemotherapy in 2018 [3]. Wilson et al. [4] have predicted a major health crisis driven by unmet chemotherapy demand over the next two decades.

In the past, patients received chemotherapy at the hospital. Today,

most patients visit outpatient chemotherapy centers (OCCs) for a pre-fixed appointment and leave on the same day. The speed at which a patient begins chemotherapy is essential to treatment outcomes, and delays should be avoided whenever possible [5–7]. Therefore, international guidelines specify the maximum delay between the decision to commence chemotherapy and start dates [8]. Starting chemotherapy for a new patient after the maximum allowable delay time is considered to be unacceptable.

The factors that affect delays are directly connected to the downstream daily operation issues in the OCC. Poor utilization of OCC resources owing to demand variety, complex patient pathways, and various uncertainties related to process durations, patient arrival, patient health conditions, and resource availability decreases the actual OCC capacity. In addition to chemotherapy initiation delays, patients

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<https://doi.org/10.1016/j.orp.2021.100214>

Received 14 May 2021; Received in revised form 13 December 2021; Accepted 13 December 2021

Available online 18 December 2021

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often experience long waiting times on the day of treatment. For instance, oncologist consultation and drug administration do not generally start at the scheduled time [9]. Consequently, OCCs have low service quality levels as measured using key performance indicators such as the number of patient complaints [10] and suffer significant cost increases due to drug waste and inefficient resource utilization [11].

Consequently, cancer care challenges are at the top of the global development agenda [12]. The third 2030 sustainable development goal established by the United Nations defined five targets that had to be satisfied to address these challenges [13]. The World Health Organization [1] set the criteria for successful interventions that can be used to achieve these five targets. First, the interventions should be studied from operational and financial perspectives to assess their feasibility. Second, the best available interventions, as supported by the evidence, should be implemented. Moreover, the highest level of intervention-related equality among beneficiaries should be achieved.

In response to this global need, there has been an increase in the number of operations management (OM) research publications related to outpatient chemotherapy process (OCP) optimization. These publications analyzed numerous OCP problems and developed various quantitative models for the proposed interventions. The primary objective of this review is to analyze the content of OCP-related, OM optimization-oriented literature that has been produced during the last decade. The methodology used is described in Section 2. Sections 3 and 4 present the results of the review. Section 5 discusses the potential future research paths. Subsequently, we discuss the necessity of this review.

Publications that address OCP OM have been studied in several literature review papers, as listed in Table 1. The primary focus of these review papers is classified under three categories: (1) outpatient healthcare OM, (2) outpatient and inpatient healthcare OM, and (3) outpatient chemotherapy OM. The first two categories address OM issues related to outpatient and inpatient care in general and contribute to building a foundation for this scientific theme. However, the review papers in these two categories do not provide an in-depth analysis of OCP research.

The two literature review papers in the third category focus on OCP research [14,15]. Planning models are barely mentioned in the narrative review by Heshmat & Eltawil [14]; the authors primarily address scheduling, assignment, and simulation models from only 13 publications. The review by Lamé et al. [15] follows a systematic approach. They studied the contributions to OM in the literature to identify the main features of OCP problems using publications that include quantitative models.

Our work differs from the previous two review papers in the following respects. First, this review focuses on analyzing model formulations to reveal modeling gaps. For this purpose, we developed a scheme for the classification of planning, scheduling, and assignment models based on the included pathway processes, addressed issues, considered complexities, modeling techniques, model solving methods, and appropriate software tools. Hence, in addition to highlighting the

**Table 1**  
Previous review papers.

Reference	Type	Focus	Timespan	Size	Focus
[84]	Narrative	General	1952 to 2001	34	OH
[85]	Narrative	General	1952 to 2008	42	OH
[86]	Systematic	General	Up to 2012	406	OIH
[87]	Narrative	Models	2001 to 2013	64	OIH
[14]	Narrative	Models	2009 to 2015	13	OC
[15]	Systematic	Models	1999 to 2015	25	OC
[88]	Systematic	Models	2003 to 2016	111	OH
[89]	Systematic	Models	Up to 2017	63	OIH
This review	Systematic	Models	2009 to 2021	45	OC

OH: outpatient healthcare OM; OIH: outpatient and inpatient healthcare OM; OC: outpatient chemotherapy OM.

contributions of various publications, comprehensive analyses of existing model formulations are provided. Second, this paper highlights recent advances and research opportunities by including publications for the period after the most recently published review paper.

Furthermore, this review provides a qualitative evaluation of the selected publications using bibliometric analysis software. It also analyzes the model formulations using social network analysis (SNA) methods and tools to derive the OCP research framework for the first time. The data extracted from the reviewed publications were the inputs for SNA. Therefore, this review paves the way for scholars in this domain by answering the following primary research questions:

- What OCP problems are addressed by the current research?
- What leading performance measures are considered when evaluating OCP?
- What mathematical optimization models and solution methods are used to solve OCP problems?
- What are the potential future research topics?

## 2. Research methodology

Our main approach is to provide a structured review of the quantitative OCP models available in the OM research literature. To achieve this, we performed a systematic content analysis that consisted of four primary phases [16]: publication collection, bibliometric analysis, analytical category selection, and publication evaluation.

### 2.1. Publication collection and bibliometric analysis

The primary task in the publication collection phase was the selection of bibliographic databases for a comprehensive search. Publications were collected from the Scopus, Web of Science, PubMed, Digital Science Dimensions, and Cochrane databases. In the next step, the search query terms and Boolean operators were identified. The aim was to collect the maximum number of relevant papers to allow a comprehensive review and in-depth analysis; consequently, a scientific method to identify the search terms was used [17,81].

The search terms were compiled from the relevant literature review papers listed in Table 1. A panel of experts in the OCP research field was consulted to validate the compiled search query, determine the filtering criteria, identify related search terms to the compiled ones, and add appropriate terms to the list. After several trials, the search query listed in Table 2 was used, which consisted of the most relevant keywords to capture the largest number of publications. Table 3 lists the initial filtering criteria for the search results.

Fig. 1 shows the methodology followed to further refine the publications that are studied in this review. After removing duplicates, 1500 publications were considered for the next step. Non-OM-related publications that are not categorized under the scope of this review were also identified among the different publications. After screening the remaining publications, only those that formulated a quantitative optimization model that addressed OCP problems were retained. Consequently, 45 publications satisfying the inclusion criteria were identified. To ensure maximum coverage, backward and forward snowballing approaches were used [82]. Few publications were identified that were not included in the initial set. This supports the comprehensiveness of the search query used. Finally, 45 publications were selected.

**Table 2**  
Search query.

("chemotherapy")
AND ("outpatient*" or "ambulatory")
AND ("plan*" or "schedul*" or "simulat*" or "optimiz*" or "optimis*" or "operate*" or "manage*" or "model*" or "program*" or "appointment")

**Table 3**  
Filtering criteria.

1 Query keywords must exist in the publication title, abstract, or keywords.
2 Only retain publications that satisfy the following conditions:
o Type: Journal article or conference paper
o Language: English
o Time: 2009–2021

2.2. Classification scheme design

The types of OCP problems, performance measures, and modeling approaches were the main aspects that were investigated. They represent the structural dimensions of the questions addressed in this study. The problem structure and classification system used for the content analysis of optimization models are listed in Table 4. Several model classification features were used in the analysis. The scope and improvement levels were extracted from [15]. The remaining features are proposed in this paper. The proposed classification features provide deeper analyses of OCP problems, models, and solutions.

2.3. Material evaluation

The research goals were achieved by analyzing the publication content based on the structural dimensions and analytical scope that have been defined. As shown in Fig. 2, this analysis comprised six steps, including obtaining feedback and re-analyzing the papers. Publication evaluation was performed using the extracted content and designed classification system. This review paper is based on recent advances and research trends in OCP OM.

3. Bibliometric analysis

The literature contains several OM research topics that are related to OCP, as shown in Fig. 3. A considerable increase in the number of publications was observed after 2012. Therefore, a bibliometric analysis was used to capture the status of this research field. The goal is to provide a complete picture of research developments and their primary contributors, as well as to summarize the main research streams through data mining and statistical analysis tools using Biblioshiny software [18].

**Table 4**  
Outpatient chemotherapy process (OCP) quantitative model classification system.

1. Scope
1.1 Optimization problems
1.2 Issues and performance measures
2. Improvement level
2.1 Patient flow versus single process
2.2 Resources
3. Problem definition
3.1 Complexities
3.2 Uncertainties
4. Model formulation and solution techniques
4.1 Uncertainty handling approaches: stochastic and deterministic
4.2 Model types and solving methods
4.3 Validation methods and tools

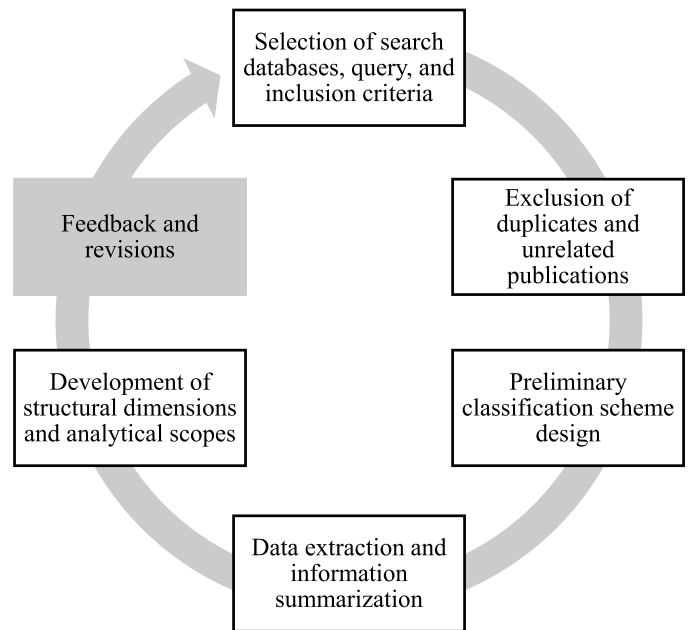


Fig. 2. Research methodology.

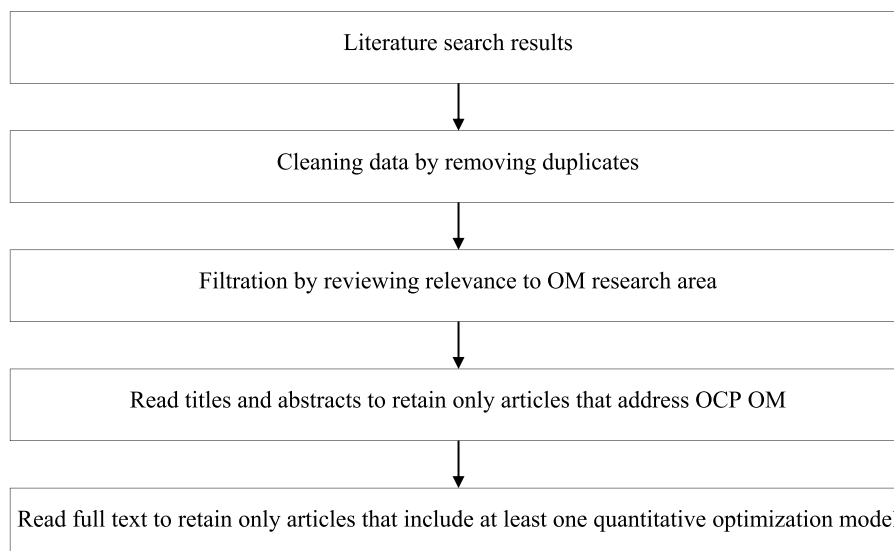


Fig. 1. Refinement of the search results methodology.

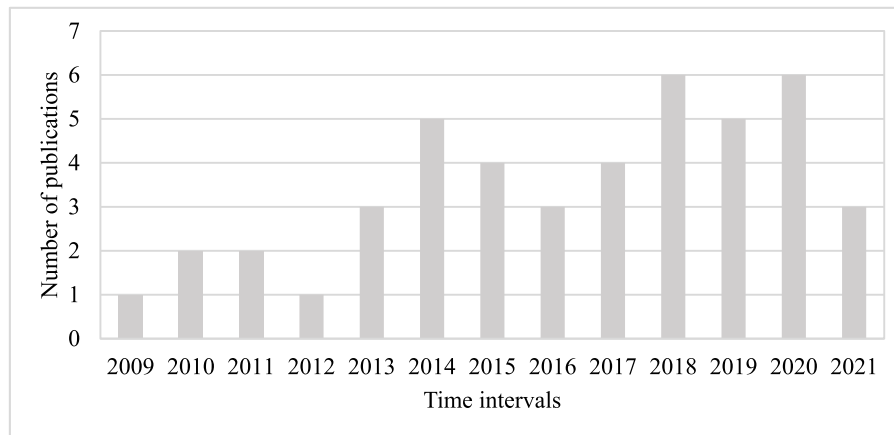


Fig. 3. Distribution of outpatient chemotherapy process (OCP) optimization-oriented publications during the past decade.

### 3.1. Co-citation network of publications

The distribution of the reviewed publications over several journals indicates the importance of this topic. In Fig. 4, lines that connect two

publications indicate that they are cited together by other publications. In bibliometric analysis, this type of citation relationship is called co-citation. The thickness of a line reflects the number of co-citations, which is proportional to the relevance of the publications. The high

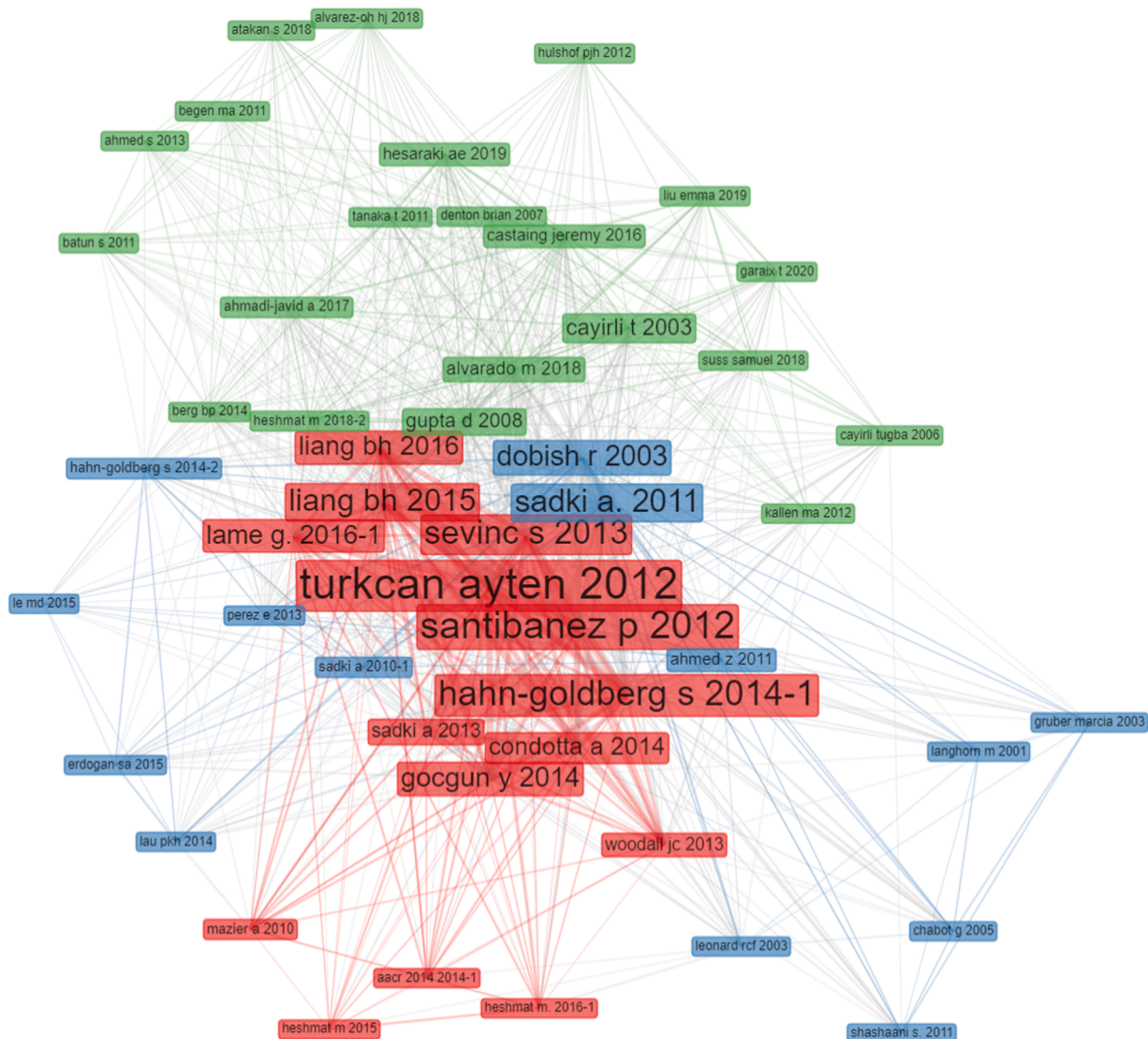


Fig. 4. Co-citation network of publications.

network density indicates the extensive attention given to OCP by various OM scientific sources and the similarity of the OCP-related content in these publications.

### 3.2. High-frequency keywords

Authors use keywords to communicate the main topics in their publications. To summarize the topics in the reviewed publications, we generated the word tree map shown in Fig. 5 using Biblioshiny data mining and visualization tools. The size of a rectangle indicates the keyword frequency.

The highest frequencies were noted for outpatient chemotherapy and optimization, which are the primary focus points of this review. The most frequently used optimization model type is integer programming because the three main OCP problems are selecting patient treatment days, determining patient time slots during each day, and patient resource assignment. The reader can observe that the words “nurse” and “infusion” exist in several rectangles. This highlights that the publications focused extensively on nurse constraints during the drug infusion process.

### 3.3. Outpatient chemotherapy process (OCP) optimization-oriented research framework: social network analysis of the quantitative models

SNA can be used to develop a conceptual model of the topic under investigation [19]. We used SNA to derive the OCP research framework after complete content analysis of the reviewed publications using the classification scheme discussed in Section 2.2. The relationships within the extracted data were then used to develop a quantitative social network model (Fig. 6) using the social structure mapping software VOSviewer [20].

In Fig. 6, a circle represents a model classification feature, while the link between two features indicates their co-existence in a model. The size of a circle is directly proportional to the total number of links to other circles [21]. A high number of links between circles attracts them to each other, and vice versa. Most connected circles are located at the network center. The colors correspond to different subnetworks of connected features. Each subnetwork demonstrates a category of OCP optimization models. For example, the models of the red subnetwork address the patient flow in the OCP by considering the durations of oncologist visits, drug infusions, blood withdrawals, and registrations. Mixed-integer programming is used to reduce the waiting time by

generating optimal medical staff schedules. The next step is to analyze the network and propose a research framework.

As shown in Fig. 7, outpatient chemotherapy pathway involves different processes that provide services for patients such as administration, testing, medical examination, drug preparation, and infusion, which require the resources of receptionists and medical staff. While each process in the patient pathway uses medical and operational information that includes treatment protocols and probability distributions as inputs, the ideal goal is to provide high-quality and cost-effective services.

OCCs encounter major cost, time, and satisfaction issues through its service delivery activities, as listed in Table 6. Modeling and solution approaches are often used to propose improvements to solve the planning, scheduling, and assignment optimization problems that are associated with availability, verity, and duration complexities.

### 3.4. OCP optimization-oriented research chronology

The timeline shown in Fig. 8 was created to highlight the chronology of OCP optimization-oriented research. The rectangles indicate the main problems, techniques, types of modeling, solution methodologies, and improvements. Each color identifies the development of a research path over time.

During the last decade, scholars have developed research paths in four directions: (i) development of medical staff planning, scheduling, and assignment models; (ii) development and improvement of drug preparation and delivery scheduling models; (iii) development and improvement of patient planning, scheduling, and assignment models; and (iv) development and improvement of stochastic models.

For example, the green rectangles represent the second path. The first drug preparation model was developed in 2010 to reduce the patient waiting time. In 2011, objectives related to the cost of drug preparation were considered. Drug preparation and delivery problems were addressed together in 2015. New heuristics were proposed in 2019 and 2021 to enhance the solution and reduce computational time.

## 4. Content analysis

### 4.1. Research scope

The purpose of an OCP model can be propelled by performance measures, which are either quantitative or qualitative. Because

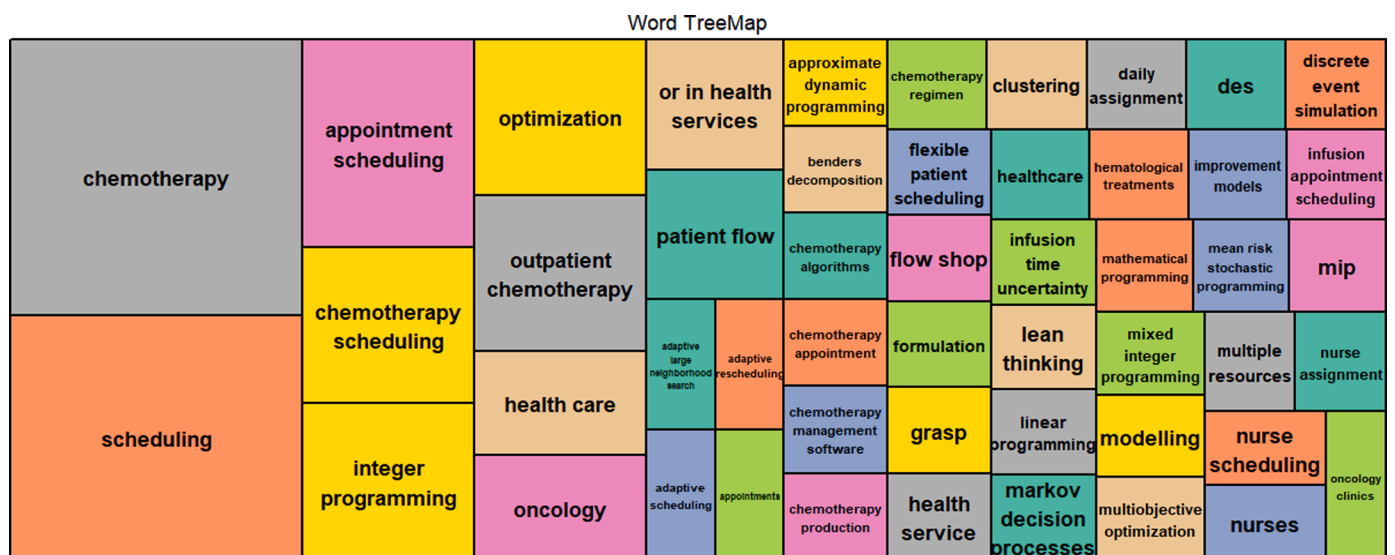


Fig. 5. Word tree map of keywords selected by the authors in the reviewed publications  
des: discrete event simulation; mip: mixed-integer programming.

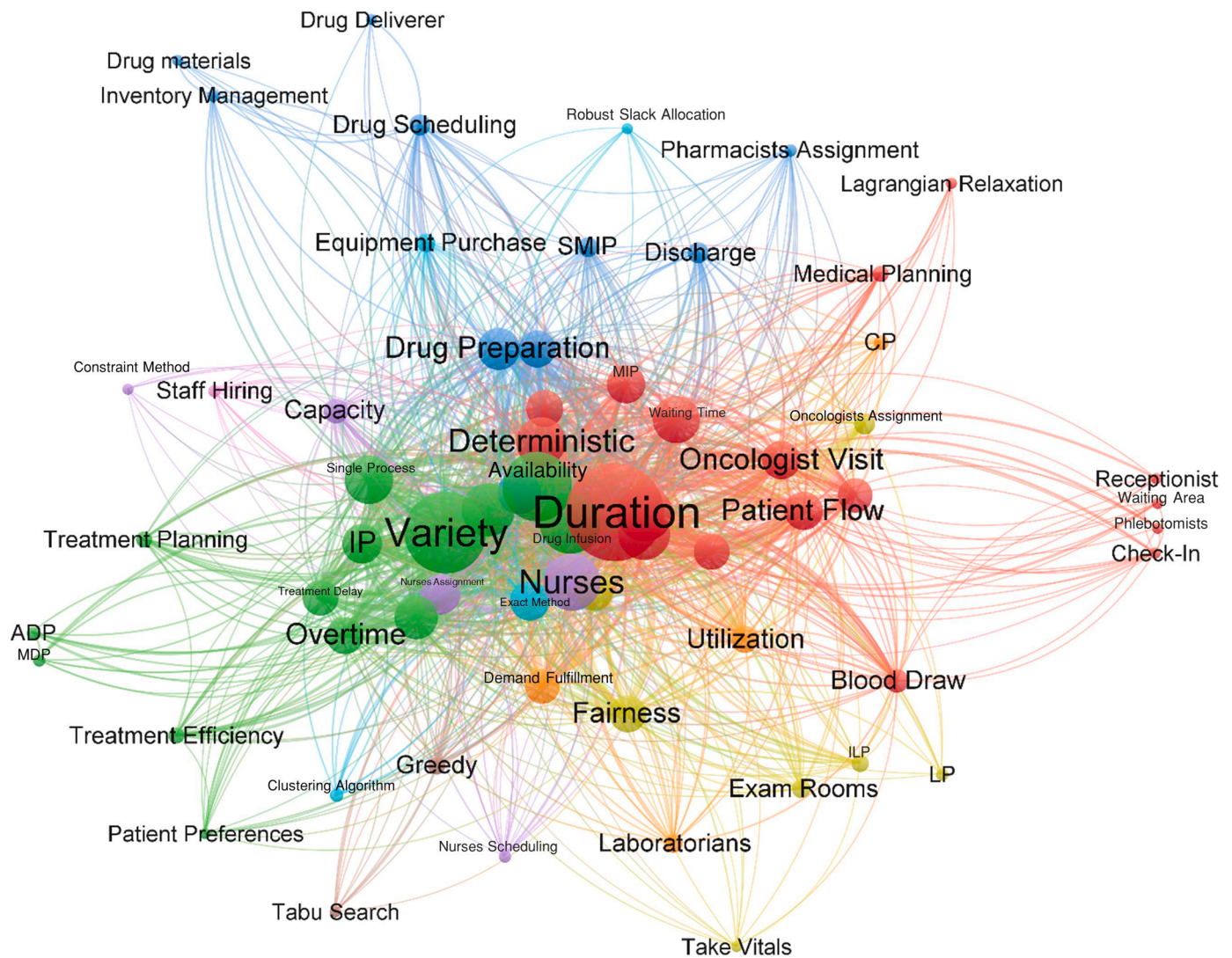


Fig. 6. Social network analysis of the quantitative OCP optimization models.

qualitative objectives can be quantified, all the existing models are quantitative. The publication scope is listed in Table 5. From an OM perspective, the three primary aspects of the OCP problem are planning, scheduling, and assignment optimization.

The planning problems involve day selection decisions. For instance, treatment planning includes the determination of treatment days, recovery days, and the drug doses used each day. Patient planning includes the identification of the most efficient patient distributions when planning horizon days within the constraints defined by the treatment plans. These two planning scopes are related to a third scope, i.e., medical and oncologist planning. This scope balances medical staff workloads and plans the working periods of the oncologist.

Patient planning was the primary planning scope in most publications. This is because we did not consider treatment planning-related publications that did not use an operations planning model. Further, medical and oncologist planning is secondary to patient planning. Interestingly, the studies by Heshmat & Eltawil [41] and Heshmat & Eltawil [59] were the only publications that addressed treatment planning and patient planning scopes simultaneously.

After choosing the treatment days using the planning scope, the exact appointment, drug preparation, and drug delivery times are defined in the scheduling scope. We observed that, in the scheduling scope, significantly more attention is focused on patient scheduling than the scheduling of nurses, drug preparation, and drug delivery. Sadki et al.

[23] presented one of the first attempts to combine patient planning and scheduling scopes.

There is a chain of publications that focus on the scheduling of drug preparation and delivery. Drug preparation scheduling was addressed by Mazier et al. [24] and Billaut [25], while Ta et al. [26], Kergosien et al. [27], Robbes et al. [28], and Robbes et al. [29] studied the scheduling of drug preparation and delivery as a flow shop production and outbound distribution scheduling problem.

The third scope provides the final details by assigning patients to resources (oncologists, nurses, beds/chairs, and pharmacists). In their studies, Turkcan et al. [30], Condotta & Shakhlevich [31], Le et al. [32], Alvarado & Ntaimo [33], Issabakhsh et al. [34], Hooshangi-Tabrizi et al. [35] integrated the three scopes. However, the model proposed by Bouras et al., [36] used the most comprehensive scope. It considers all assignment sub-scopes and patient and drug preparation scheduling sub-scopes, although it does not include the planning scope.

Thus, the major OCP issues include time minimization, cost reduction, workload balance, and satisfaction maximization, as listed in Table 6. An issue can have various scopes of study. Planning and scheduling are the two aspects that address OCP time issues, including treatment delays and waiting time. To satisfy on-time outpatient chemotherapy demands, both treatment days and daily schedules must be determined optimally.

Cost issues are linked primarily to decisions that are related to

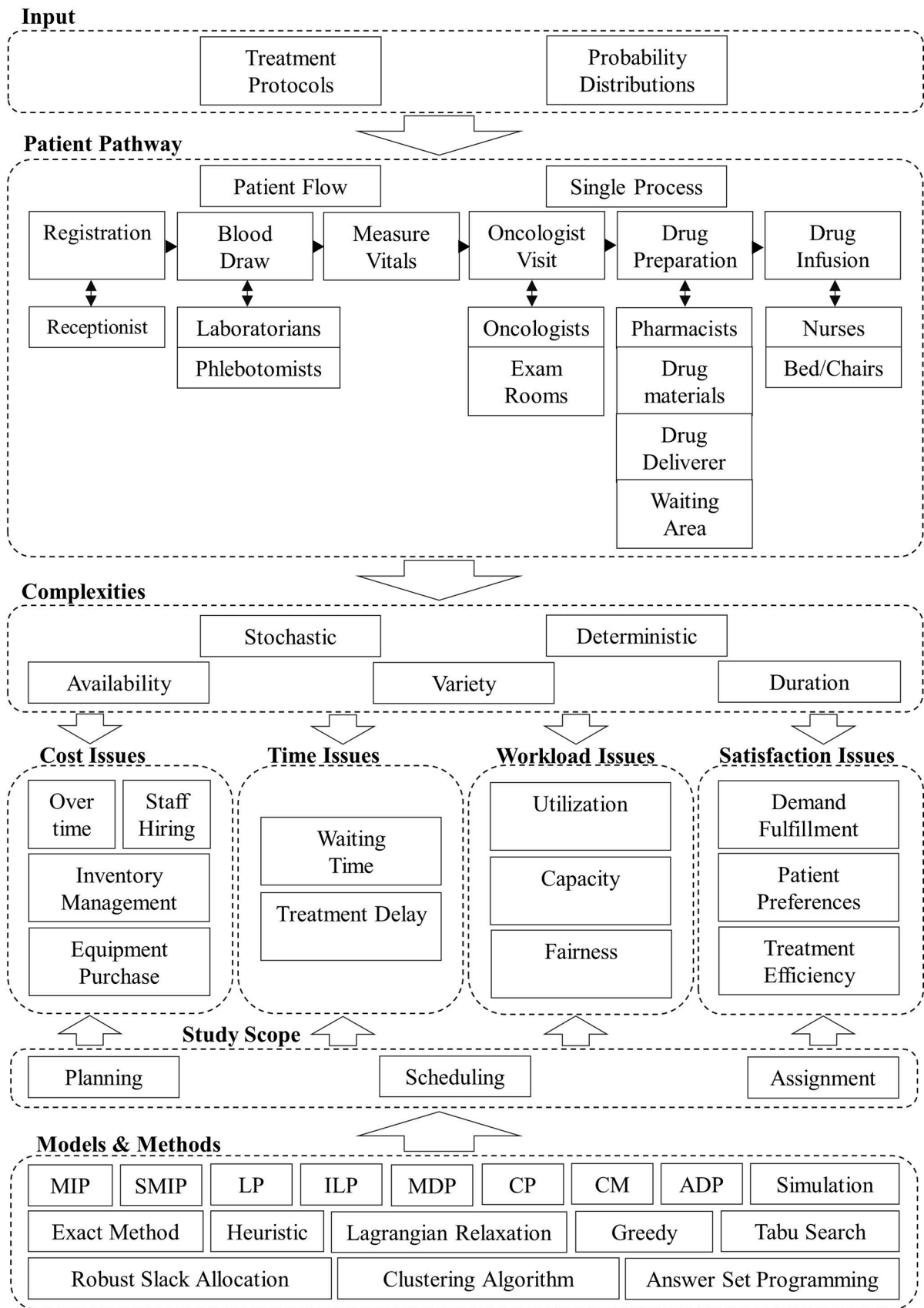


Fig. 7. OCP optimization-oriented research framework

MIP: mixed-integer programming; SMIP: stochastic mixed-integer programming; LP: linear programming; ILP: integer linear programming; MDP: Markov decision process; CP: constraint programming; CM: constraint method; ADP: approximate dynamic programming.

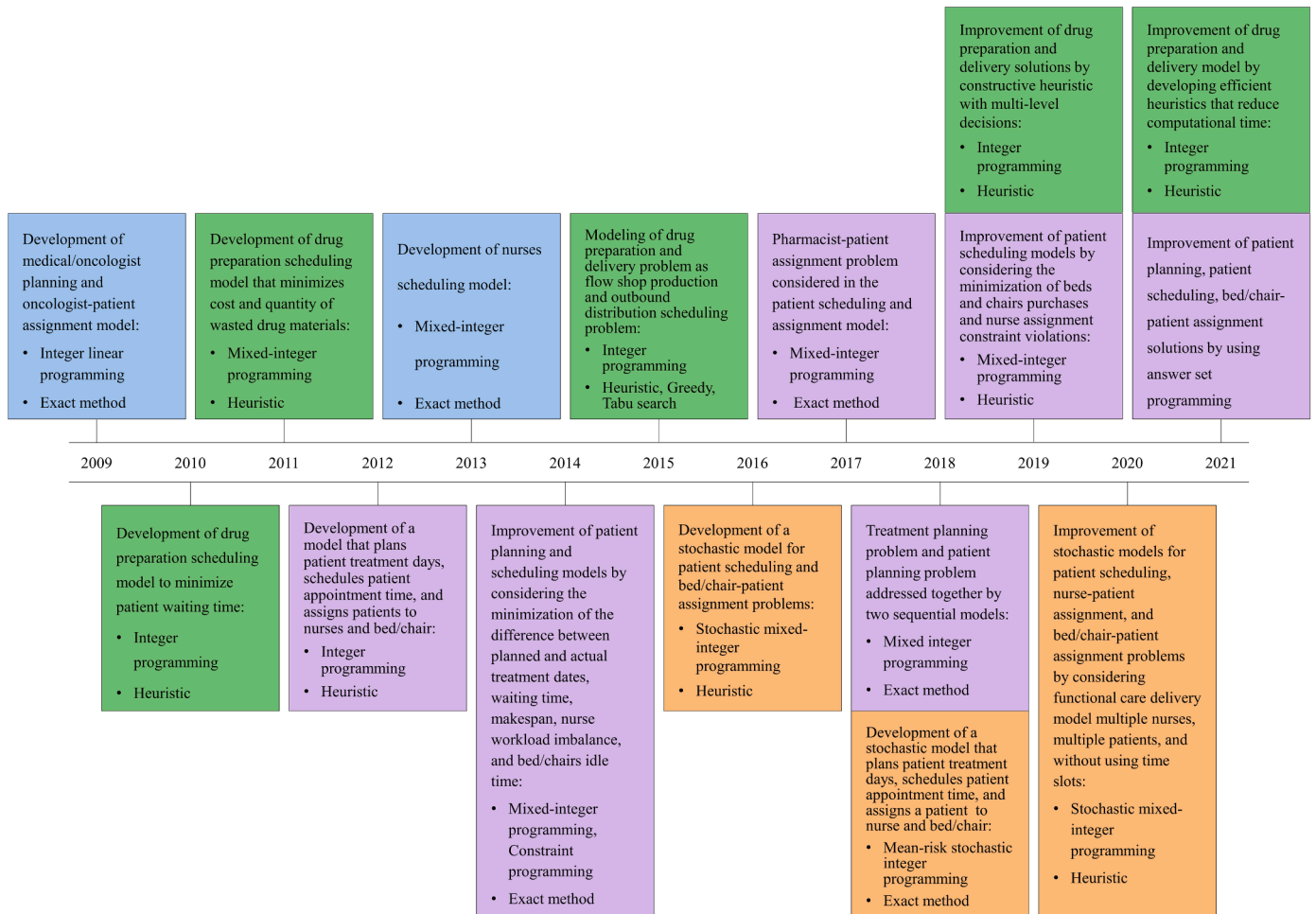


Fig. 8. Chronology of OCP optimization-oriented research.

resource scheduling, including overtime, staff hiring, equipment purchases, and inventory management. The assignment study scope is predominantly related to existing resource workload issues, including fairness, utilization, and capacity considerations.

All three study scopes are used to address satisfaction issues related to demand fulfillment, treatment efficiency, and patient preference.

#### 4.1.1. Time measures

Among the selected publications, 23 studies focused their efforts on waiting time measures, while only 12 addressed treatment delay issues (Table 6). OCP studies have considered various issues that are related to treatment delays or waiting times. In the planning scope, 20% of the reviewed publications had the objective of minimizing the treatment delay for a new patient referred to the OCC after diagnosis.

Contrastingly, the objective of minimizing the difference between the planned day and the day of treatment as specified in the treatment protocol was considered by approximately 11% of the publications. Of these, only one publication attempted to minimize new patient delays and tolerances [37].

From a scheduling scope perspective, the objectives of reducing the total patient waiting time between processes during the treatment day (11 publications) and the total time for completing all processes (11 publications) received considerably more attention than minimization of drug preparation (1 publication) and delivery delays (4 publications). One possible reason for this may be the lack of familiarity of scholars with typical pharmacy operation-related time issues.

#### 4.1.2. Cost measures

Almost 40% of the listed publications address cost measures in their primary or secondary objectives. Interestingly, all these publications were initially concerned about resolving time issues in the planning scope. The focus on cost occurs because the delay reductions that can be achieved are proportional to the cost. Therefore, scholars tend to use a multi-objective function to minimize both time and cost. Existing publications based on treatment delay reduction (planning) that seek to resolve these two significant issues often focus on staff overtime as the major induced cost.

Contrastingly, decisions related to the minimization of staff and equipment assigned to the center are rarely addressed. The human and physical resources considered are nurses, drug materials, and the number of beds or chairs. No publication considers other resource types, such as oncologists, pharmacists, and rooms. This reflects the tendency of OCCs to optimally use available resources instead of increasing or reducing them. Although drug resources, such as raw materials, are essential for OCCs, the cost of drug material inventory is addressed by only one publication. Billaut [25] investigated the objectives of minimizing the total cost and quantity of wasted drug materials.

#### 4.1.3. Workload measures

Differences between the study scopes of workload issues and other OCP issues were readily observed. Workload issues primarily involve the production of detailed daily schedules that assign resources to specific patients. Therefore, OCP workload measures include fairness, utilization, and capacity considerations. Fairness has been predominantly investigated and is discussed in approximately half of the reviewed

**Table 5**  
OCP optimization problems.

Reference	Planning			Scheduling				Assignment			
	Patient	Treatment	Medical/ oncologist	Patient	Nurse	Drug preparation	Drug delivery	Nurse- patient	Oncologist- patient	Bed/ Chair- patient	Pharmacist- patient
Mazier & Xie [61]			●						●		
Sadki et al. [23]	●		●	●					●		
Mazier et al. [24]						●					
Billaut [25]						●					
Sadki et al. [90]			●	●							
Turkcan et al. [30]	●			●				●		●	
Sevinc et al. [50]	●									●	
Woodall et al. [53]					●						
Sadki et al. [66]			●								
Gocgun & Puterman [57]	●										
Hahn-Goldberg et al. [43]				●							
Hahn-Goldberg et al. [80]				●							
Huggins & Pérez [60]				●						●	
Condotta & Shakhlevich [31]	●			●				●			
Le et al. [32]	●			●				●		●	
Ansarifar et al. [44]	●			●							
Liang et al. [38]				●					●	●	
Ta et al. [26]						●	●				
Heshmat & Eltawil [41]	●	●									
Liang & Turkcan [56]				●				●			
Castaing et al. [64]				●						●	
Bouras et al. [36]				●		●		●	●	●	●
Heshmat et al. [91]				●				●		●	
Heshmat & Eltawil [92]	●										
Kergosien et al. [27]						●	●				
Göçgün [51]	●										
Heshmat et al. [22]				●				●		●	
Heshmat & Eltawil [59]	●	●									
Alvarado & Ntaimo [33]	●			●				●		●	
Alabdulkarim [37]	●										
Huang et al. [54]				●				●			
Hesaraki et al. [52]				●				●			
Agnetis et al. [63]				●							
Huang et al. [49]				●				●		●	
Heshmat & Eltawil [65]	●										
Robbes et al. [28]						●	●				
Hesaraki et al. [39]				●	●			●			
Garaix et al. [62]				●							
Benzaid et al. [40]	●			●				●			
Issabakhsh et al. [34]	●			●						●	
Demir et al. [93]				●				●		●	
Hooshangi-Tabrizi et al. [35]	●			●				●		●	
Gul [83]				●				●		●	
Robbes et al. [29]						●	●				
Dodaro et al. [67]	●			●						●	

publications that involve workload issues. In their optimization models, publications address fair human and physical resource workload distribution objectives. For example, several studies considered fairness in daily nurse schedules by minimizing nurse workload imbalances.

Liang et al. [38] addressed human resource workload fairness indirectly by minimizing the difference between the exam room and bed/chair utilization. However, oncologist workload imbalances were rarely considered in OCP models. Maximizing bed and chair utilization is another essential planning and scheduling objective that has received

extensive attention from scholars.

Contrastingly, relatively few publications have included capacity measures directly in their model objectives. Only one publication considered the minimization of violations in the oncologist capacity limit. Hesaraki et al. [39] attempted to maximize the actual nurse capacity by minimizing the number of during-appointment nurse changes instead of restricting them. Alvarado & Ntaimo [33] considered the constraints in nurse acuity levels in their model objective function by minimizing the excess acuity above the maximum nurse acuity level.

**Table 6**  
OCP issues and performance measures.

Reference	Category	Time							Cost				
	Issues	Treatment Delay			Waiting Time				Overtime	Staff Hiring	Equipment Purchases	Inventory Management	
	Scope	Planning			Scheduling				Scheduling				
	Multi-objective	Minimize treatment delay for new patients	Minimize difference between target date and the actual appointment	Minimize difference between the new day and the old one for the patients with a postponed appointment	Minimize patient waiting time	Minimize makespan	Minimize maximum drug preparation delay	Minimize maximum tardiness of delivery from pharmacy to bed or chair	Minimize overtime	Minimize number of nurses	Minimize number of beds/chairs	Minimize total cost of lost drug material	Minimize total quantity of lost drug material
Mazier & Xie [61]													
Sadki et al. [23]													
Mazier et al. [24]							●						
Billaut [25]	●											●	●
Sadki et al. [90]	●				●	●							
Turkcan et al. [30]	●	●							●				
Sevinc et al. [50]	●	●											
Woodall et al. [53]													
Sadki et al. [66]	●												
Gocgun & Puterman [57]			●										
Hahn-Goldberg et al. [43]	●					●							
Hahn-Goldberg et al. [80]	●					●							
Huggins & Pérez [60]													
Condotta & Shakhlevich [31]	●				●								
Le et al. [32]	●								●				
Ansarifar et al. [44]	●	●							●				
Liang et al. [38]	●												
Ta et al. [26]								●					
Heshmat & Eltawil [41]	●	●							●				
Liang & Turkcan [56]	●				●				●				
Castaing et al. [64]	●				●	●							
Bouras et al. [36]					●								
Heshmat et al. [91]						●							
Heshmat & Eltawil [92]		●											
Kergosien et al. [27]								●					
Göçgün [51]	●		●						●				
Heshmat et al. [22]						●							
Heshmat & Eltawil [59]	●	●							●				
Alvarado & Ntaimo [33]	●		●						●				
Alabdulkarim [37]	●	●	●			●							

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Table 6 (continued)

Reference	Category	Time							Cost				
		Treatment Delay			Waiting Time				Overtime	Staff Hiring	Equipment Purchases	Inventory Management	
		Planning			Scheduling				Scheduling				
		Multi-objective	Minimize treatment delay for new patients	Minimize difference between target date and the actual appointment	Minimize difference between the new day and the old one for the patients with a postponed appointment	Minimize patient waiting time	Minimize makespan	Minimize maximum drug preparation delay	Minimize maximum tardiness of delivery from pharmacy to bed or chair	Minimize overtime	Minimize number of nurses	Minimize number of beds/chairs	Minimize total cost of lost drug material
Huang et al. [54]	●										●		
Hesaraki et al. [52]	●				●	●							
Agnetis et al. [63]					●								
Huang et al. [49]	●											●	
Heshmat & Eltawil [65]	●	●				●							
Robbes et al. [28]								●					
Hesaraki et al. [39]	●				●				●				
Garaix et al. [62]	●					●			●				
Benzaid et al. [40]	●									●			
Isabakhsh et al. [34]	●				●	●					●		
Demir et al. [93]	●				●				●				
Hooshangi-Tabrizi et al. [35]	●								●				
Gul [83]	●				●				●				
Robbes et al. [29]								●					
Dodaro et al. [67]	●	●	●	●									

Reference	Workload Fairness Assignment				Capacity				Utilization Planning and Scheduling				
	Minimize nurse workload imbalance	Maximize minimum oncologist workload	Maximize workload balance	Minimize difference between exam rooms utilization	Minimize difference between beds or chairs utilization	Minimize nurse assignment constraint violations	Minimize during-appointment nurse changes	Minimize nurse excess acuity or workload	Minimize oncologist capacity violations	Minimize number of patients who have blood collection at the same time	Minimize bed and chair idle time or maximize bed and chair utilization		
Mazier & Xie [61]		●											
Sadki et al. [23]										●			
Mazier et al. [24]													
Billaut [25]													
Sadki et al. [90]													
Turkcan et al. [30]													
Sevinc et al. [50]	●		●										●
Woodall et al. [53]													
Sadki et al. [66]					●					●			
Gocgun & Puterman [57]													
Hahn-Goldberg et al. [43]													●

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Table 6 (continued)

Reference	Workload Fairness Assignment					Capacity				Planning and Scheduling		Utilization
	Minimize nurse workload imbalance	Maximize minimum oncologist workload	Maximize workload balance	Minimize difference between exam rooms utilization	Minimize difference between beds or chairs utilization	Minimize nurse assignment constraint violations	Minimize during-appointment nurse changes	Minimize nurse excess acuity or workload	Minimize oncologist capacity violations	Minimize number of patients who have blood collection at the same time	Minimize bed and chair idle time or maximize bed and chair utilization	
Hahn-Goldberg et al. [80]												●
Huggins & Pérez [60]												●
Condotta & Shakhlevich [31]	●											
Le et al. [32]	●											
Ansarifar et al. [44]												●
Liang et al. [38]				●	●							
Ta et al. [26]												
Heshmat & Eltawil [41]												
Liang & Turkcan [56]								●				
Castaing et al. [64]												
Bouras et al. [36]												
Heshmat et al. [91]												
Heshmat & Eltawil [92]												
Kergosien et al. [27]												
Göçgün [51]												
Heshmat et al. [22]												
Heshmat & Eltawil [59]												
Alvarado & Ntaimo [33]								●				
Alabdulkarim [37]												
Huang et al. [54]	●							●				
Hesaraki et al. [52]	●											
Agnetis et al. [63]												
Huang et al. [49]	●							●				
Heshmat & Eltawil [65]												
Robbes et al. [28]												
Hesaraki et al. [39]	●							●				
Garaix et al. [62]												
Benzaid et al. [40]												
Issabakhsh et al. [34]												
Demir et al. [93]												●
Hooshangi-Tabrizi et al. [35]	●											
Gul [83]												
Robbes et al. [29]												
Dodaro et al. [67]											●	

Reference	Satisfaction Demand Fulfillment Planning Minimize number of unscheduled appointment requests	Minimize total shortage of nurse hours relative to patient demand	Maximize total number of scheduled appointments	Treatment Efficiency Minimize cancerous cell population at the end of treatment	Assignment Minimize number of patients assigned to floating nurses	Patient Preferences Scheduling Minimize number of patients who do not receive treatment at their preferred time
Mazier & Xie [61]						
Sadki et al. [23]						
Mazier et al. [24]						
Billaut [25]						
Sadki et al. [90]						
Turkcan et al. [30]						
Sevinc et al. [50]						
Woodall et al. [53]		●				
Sadki et al. [66]						
Gocgun & Puterman [57]						
Hahn-Goldberg et al. [43]						
Hahn-Goldberg et al. [80]						
Huggins & Pérez [60]						
Condotta & Shakhlevich [31]						
Le et al. [32]	●					
Ansarifar et al. [44]						
Liang et al. [38]						
Ta et al. [26]						
Heshmat & Eltawil [41]				●		
Liang & Turkcan [56]						
Castaing et al. [64]						
Bouras et al. [36]						
Heshmat et al. [91]						
Heshmat & Eltawil [92]						
Kergosien et al. [27]						
Göçgün [51]						
Heshmat et al. [22]						
Heshmat & Eltawil [59]						
Alvarado & Ntaimo [33]						
Alabdulkarim [37]						
Huang et al. [54]						
Hesaraki et al. [52]						
Agnetis et al. [63]						
Huang et al. [49]						
Heshmat & Eltawil [65]						
Robbes et al. [28]						
Hesaraki et al. [39]						
Garaix et al. [62]						
Benzaid et al. [40]			●			
Issabakhsh et al. [34]						
Demir et al. [93]						
Hooshangi-Tabrizi et al. [35]	●				●	●
Gul [83]						
Robbes et al. [29]						
Dodaro et al. [67]						

#### 4.1.4. Satisfaction-related measures

Satisfaction-related measures that are specific to OCP involve demand fulfillment, treatment efficiency, and patient preferences. Demand fulfillment is the most frequently studied measure because it is critical to patient health. Three out of four studies included objective functions that integrated demand fulfillment with other objectives that are associated with time, cost, or workload [32,35,40].

Because of the challenges related to the improvement of chemotherapy outcomes, treatment efficiency has attracted increased attention. However, relatively few studies have addressed these medical challenges in their OCP models. We identified only two publications that proposed such models. One addresses the treatment planning studies [41], whereas the second is within the scope of assignment studies [35]. The former publication integrates a treatment planning model that aims to maximize the number of cancerous cells killed using a patient planning model. The latter considers care quality by minimizing the number of times a patient does not receive treatment from his primary nurse.

Although ensuring treatment based on patient preferences such as preferred appointment times perform significant roles in patient satisfaction, especially for working patients and those who live far from their OCC, we identified only one patient preference objective in one publication [35].

#### 4.2. Pathway-based classification of publications

The solutions contributed by the reviewed publications for OCP issues varied based on the range of processes and resources considered in their models. On treatment days, patients experience several processes that vary according to their medical requirements. Therefore, not all patients follow the same path on the treatment day. For example, a patient arrives at a prescheduled appointment and then experiences a traditional registration process. If required, the patient undergoes a blood test at the center or brings the test results obtained from an external laboratory. The vital signs are measured, and the patient is examined by an oncologist who determines whether the patient can take the drug during the visit based on the blood test results, vital signs, and physical examination.

According to the literature, 10% of patients are identified to be unfit for treatment [42]; when this occurs, the patient must check out and wait for another appointment. Conversely, patients who can be treated are referred to a waiting area. When a treatment bed or chair is available, the patient drip is prepared, and the drugs are administered when the pharmacy is ready. Certain patients are not required to visit an oncologist; therefore, after registration, their vitals are measured, and they are directed to the waiting area before being transferred to a bed or chair for the infusion. Subsequently, the patient may be required to visit a psychosocial doctor before leaving the chemotherapy center.

From this simple pathway description, one can expect a long patient waiting time between processes. Resource management challenges can also be expected because of the various patient pathways that must be navigated in a single day owing to differences in medical requirements. Table 7 summarizes how the existing literature analyzes pathway processes and resources to improve outpatient chemotherapy services.

##### 4.2.1. Process improvement: patient flow versus individual processes

The improvement levels targeted in existing studies vary with the range of processes considered, and whether patient flow or single process improvement is targeted. We note that 66% of the publications listed in Table 7 attempted to improve a single process. This is because considering multiple processes results in problems that are difficult to solve and drastically increases the computation time for large instances [34,43].

Conversely, no publication that considers patient flow improvement includes a comprehensive system of pathway processes. The maximum number of processes included was four out of seven, and only three publications performed this type of analysis. For example, Ansarifar

et al. [44] improved patient flow during visits that included a blood test, oncologist visit, drug preparation, and infusion pathway processes by comprehensively considering the processes using an integrated planning and scheduling model. They considered the pathway process sequence and maximum allowable waiting time between the processes.

Overall, 93% of scholars focused on improving the drug infusion process, although blood tests, oncologist visits, and drug preparation processes were the main components of the patient pathway. Other processes such as registration, discharge, vital sign measurement, and psychosocial doctor visits were rarely considered. This is because scholars limit the number of pathway processes included in their model based on the next-day scheduling (split scheduling) and advanced drug preparation policies that are successfully applied in many OCCs.

In these centers, the upstream blood test and oncologist visit processes are completed before the day of treatment [45–47] and most drugs are prepared in advance [42,48]. Thus, only the downstream patient infusion process is performed on the day of treatment. These two policies reduce the scope of OCP improvement to only the drug infusion process [33,83,93].

Consequently, the number of patient flow improvement studies remains small (34% of publications) despite the considerable number of patients who prefer to complete all pathway processes in one day to avoid multiple visits to the center [49]. Therefore, there is a need for additional studies that will comprehensively consider the pathway processes.

##### 4.2.2. Process resources

Various human resources, including receptionists, phlebotomists, laboratory technicians, oncologists, pharmacists, drug deliverers, and nurses, are involved in the OCP problem. There are also physical resources such as rooms, drug materials, waiting areas, and beds/chairs. Nurses and beds/chairs have attracted the most attention, although other human and physical resources also perform essential roles. Almost 85% of publications focus primarily on nurses and beds/chairs during the drug infusion process, while fewer publications consider pharmacists and oncologists.

Receptionists, phlebotomists, laboratory technicians, drug deliverers, drug materials, rooms, and waiting areas are typically overlooked. The studies by Sevinc et al. [50] and Ansarifar et al. [44] are the only publications under the planning scope that directly consider laboratory technicians as important resources. Göçgün [51] did not consider specific types of resources; instead, he addressed the total daily resource capacity of the OCC.

The extensive attention given to nurses in the literature can be explained by the characteristics of the tasks that they handle. Nurses are not typically required to stay with patients throughout the infusion process. Depending on the allowed acuity level, the nurse may settle the patient, prepare the infusion, and then leave the patient while serving other patients [52]. As various chemotherapy protocols are used, the periods for completing infusions vary widely. Furthermore, if applied, the primary care delivery system requires the same nurse to serve the patient throughout his treatment journey [35]. Consequently, the drug infusion process is recognized as the bottleneck in the patient pathway, and nurses are the primary limited resource [53].

Beds and chairs are the second most common resource considered in the literature; they are addressed by 71% of the publications. Chairs are associated with nurses based on the acuity levels required by the patients [54]. Assigning patients to staffed chairs requires impractically long computation times [30,32,50]. To reduce the number of variables that cause this computational challenge, Heshmat et al., [22] used clustering algorithms to group patients based on their treatment durations and required acuity levels. Nurses and chairs were then assigned to these groups instead of making individual assignments.

Contrastingly, other scholars have determined that the drug preparation process by the pharmacy is the bottleneck in the pathway [43,55]. Mazier et al. [24] proposed a drug preparation scheduling and

**Table 7**  
OCP improvement levels.

Reference	Level		Process							Resource										
	Patient flow	Single process	Registration	Blood draw	Take vitals	Oncologist visit	Drug preparation	Drug infusion	Discharge	Receptionists	Phlebotomists	Laboratory technicians	Oncologists	Exam rooms	Pharmacists	Drug materials	Drug deliverers	Waiting areas	Nurses	Beds or chairs
Mazier & Xie [61]		●				●		●					●							●
Sadki et al. [23]		●				●		●					●							●
Mazier et al. [24]		●				●	●							●						
Billaut [25]		●					●									●				
Sadki et al. [90]	●					●		●					●							●
Turkcan et al. [30]		●					●	●						●					●	●
Sevinc et al. [50]		●		●		●		●			●		●						●	●
Woodall et al. [53]	●							●											●	
Sadki et al. [66]	●					●		●					●							●
Gocgun & Puterman [57]		●						●											●	
Hahn-Goldberg et al. [43]	●					●	●	●					●		●				●	●
Hahn-Goldberg et al. [80]	●						●	●						●	●				●	●
Huggins & Pérez [60]	●						●	●						●	●				●	●
Condotta & Shakhlevich [31]	●			●	●			●											●	
Le et al. [32]		●						●											●	●
Ansarifar et al. [44]	●			●		●	●	●			●		●	●	●				●	●
Liang et al. [38]	●					●	●	●					●	●					●	●
Ta et al. [26]		●					●							●			●		●	●
Heshmat & Eltawil [41]		●						●											●	●
Liang & Turkcan [56]		●					●	●											●	
Castaing et al. [64]		●						●											●	●
Bouras et al. [36]	●					●	●	●	●				●		●				●	●
Heshmat et al. [91]		●						●											●	●
Heshmat & Eltawil [92]		●					●	●						●	●				●	●
Kergosien et al. [27]		●					●	●						●			●		●	●
Göçgün [51]		●						●											●	●
Heshmat et al. [22]		●						●											●	●
Heshmat & Eltawil [59]		●					●	●						●					●	●
		●						●											●	●

(continued on next page)

Table 7 (continued)

Reference	Level		Process						Resource											
	Patient flow	Single process	Registration	Blood draw	Take vitals	Oncologist visit	Drug preparation	Drug infusion	Discharge	Receptionists	Phlebotomists	Laboratory technicians	Oncologists	Exam rooms	Pharmacists	Drug materials	Drug deliverers	Waiting areas	Nurses	Beds or chairs
Alvarado & Ntaimo [33]																				
Alabdulkarim [37]		●								●									●	●
Huang et al. [54]		●								●					●				●	
Hesaraki et al. [52]		●								●									●	●
Agnētis et al. [63]	●		●	●		●			●	●				●				●	●	●
Huang et al. [49]		●								●									●	●
Heshmat & Eltawil [65]	●						●	●	●					●					●	●
Robbes et al. [28]		●					●	●						●		●				
Hesaraki et al. [39]		●								●									●	
Garaix et al. [62]	●					●		●	●					●					●	●
Benzaid et al. [40]		●				●	●	●						●					●	●
Issabakhsh et al. [34]	●					●	●	●												●
Demir et al. [93]		●								●									●	●
Hooshangi-Tabrizi et al. [35]		●								●									●	●
Gul [83]		●								●									●	●
Robbes et al. [29]		●					●	●						●		●				
Dodaro et al. [67]	●		●	●		●		●												●

assignment method that considers pharmacists as a critical resource. Four papers addressed the transportation problems while delivering the drugs that the pharmacy has prepared to patient locations [26–29]. Drug material inventory management was only considered by Billaut [25].

#### 4.3. Publication classification by problem definition

OCP can be classified as a queuing system with incomparable complexities and uncertainties. The simplest problem definition and formulation occur when all patient demands have similar requirements, i.e., patients and resources are available at predetermined times and the processing durations are stable. The complexity increases as various patient demand requirements are considered. Disturbances occur because of the late arrival of patients or resources, patient no-shows, human resource absences, and breakdowns. Furthermore, pathway processes can consume more or less time than expected because of operational or medical factors.

The existing OCP models are formulated based on various idealized assumptions. Thus, they vary in their consideration of specific complexities and uncertainties. Table 8 compares the models in terms of the complexities and uncertainties that they consider and their approach toward complexity and uncertainty management.

##### 4.3.1. Complexity due to variety

Almost two-thirds of the publications considered the patient acuity level defined in the treatment protocol. The acuity level indicates the time that the nurse must spend on each patient [56]. Marginally fewer publications have considered the flexibility to perform the treatment within a certain range of tolerance days to increase the solution efficiency [57]. However, one-third of the publications considered the number of treatment days in a cycle (frequency of appointments). Chemotherapy drugs destroy cancerous cells and affect normal cells. Therefore, large drug infusions cannot be performed on a single day. Instead, the drug is administered over several days, which are separated by recovery days [58]. The treatment protocols contain information regarding the required treatment and recovery days.

Nevertheless, there are significant drawbacks to the utilization of regime-frequency complexity in several existing planning models. For example, the models by Heshmat & Eltawil [59] and Alabdulkarim [37] do not consider the various treatment and recovery days as inputs. Although they considered the required drug amount and nursing and drug preparation times on all planning horizon days for all patients, their model decides only the first treatment day of the patient based on the resources available on that day. This is a major limitation of the models because the required resources are used on several treatment days depending on different treatment protocols that must be considered [44].

##### 4.3.2. Uncertainty of availability

The availability characteristics of patients and resources at pre-planned appointment times comprise two factors: punctuality and presence. The uncertainty caused by the late arrival of patients to appointments, patient no-shows, and human resource absence is seldom of interest in the OCP literature. These uncertainties were assumed to have low significance [60] or were excluded to simplify the model [52]. However, eight publications considered cancellations or changes in drugs due to patient health conditions on the day of treatment. To avoid the effects of postponements due to cancelation, scholars studied the next-day or split-scheduling model used by OCCs [50] and allowed overbooking [40].

The presence of nurses, oncologists, and pharmacists is addressed moderately in the OCP literature, but no study has considered the presence of receptionists, phlebotomists, and laboratory technicians. Generating nurse and oncologist work schedules that match resources with patient demand has attracted the most attention, although other human resources perform important roles in achieving smooth patient

flow. A few studies have extended this research path by considering the assignment of patients to their referring nurses [35] and oncologists [61] to increase the level of care.

Scholars have focused extensively on bed and chair availability because they are the most important physical resources in the bottleneck process (drug infusion). Other physical resource availability issues, such as those related to exam rooms [38] and drug materials [59] were rarely addressed.

##### 4.3.3. Uncertainty of duration

The duration can be defined as the time required to complete a process or an activity. Most studies assumed homogeneous durations for all processes and activities, except drug infusion, to simplify scheduling problems.

For the second most frequently considered duration (oncologist check), the majority of publications used independently and identically distributed durations for all patients [34,61–63]. Other publications assumed that patient needs during oncologist visits are heterogeneous and modeled them as independently and distinctly distributed durations [36,38,44]. However, almost all publications used independently and distinctly distributed drug infusion durations.

Various types of duration distributions were used in the literature. Many studies depended on empirical data collected from their partner centers to choose the empirical distribution that statistically matches the actual duration distribution [33,39,43]. Scholars rarely addressed processes that appear before the oncologist checks or after drug infusion. Moreover, drug delivery from the pharmacy to the infusion bed or chair, drug expiration periods, and lunch breaks have attracted minimal attention from scholars.

#### 4.4. Classification of publications by model formulation and solution technique

Numerous modeling approaches have been used to solve OCP problems, as listed in Table 9. We classified the models used in these studies into three main categories: the uncertainty handling approach, model type, and solution approach.

##### 4.4.1. Uncertainty handling approaches: stochastic and deterministic

Across all publications, deterministic models represent the most frequently used approach for managing OCP uncertainty. Only four publications used stochastic models, despite the importance of managing uncertainty to produce practical solutions.

Castaing et al. [64] proposed a two-stage stochastic integer program formulation for patient scheduling. They considered a primary care delivery model with a single nurse. In the first stage, the patient sequence was the input, and appointment times were the output. When the researchers restricted patient sequence changes and assumed that one nurse was available, the second stage only revised patient bed and chair assignments to minimize waiting time and makespan.

Alvarado & Ntamo [33] developed more comprehensive three-mean-risk stochastic integer programming models that considered both patient planning and scheduling in the drug infusion process and considered uncertainties in the acuity level, duration, and nurse availability. The first stage identified the patient treatment day, treatment start time, and assigned nurse. After the imposition of drug infusion duration and uncertainty in nurse availability, the second stage minimized nurse overtime, excess acuity, changes in the treatment start time, and overlapping treatments in the same chair by assigning penalties. The model provided a solution for a single patient and used time slots.

A similar formulation was proposed by Demir et al. [93] for a functional care delivery model with multiple nurses, multiple patients, and without using time slots. The outputs of the first stage were patient sequences and appointment times. The second stage assigned patients to beds/chairs and nurses by penalizing patient waiting time, nurse overtime, and idle chair time. Gul [83] restructured the model to balance the

**Table 8**  
OCP complexities and uncertainties.

Reference	Complexity				Uncertainty							
	Variety				Availability							
	Treatment priority	Regime frequencies	Treatment date tolerance	Acuity level	Patients (no-show)	Patient unfit (cancellations) or drug change	Nurses	Physician	Exam rooms	Pharmacists	Drug	Bed and chairs
Mazier & Xie [61]		●						●				●
Sadki et al. [23]		●						●				●
Mazier et al. [24]												
Billaut [25]		●	●								●	
Sadki et al. [90]								●				●
Turkcan et al. [30]	●	●	●	●								●
Sevinc et al. [50]		●				●						●
Woodall et al. [53]				●			●					
Sadki et al. [66]		●						●				●
Gocgun & Puterman [57]	●	●	●				●					
Hahn-Goldberg et al. [43]				●								
Hahn-Goldberg et al. [80]				●								
Huggins & Pérez [60]				●			●			●		●
Condotta & Shakhlevich [31]		●		●								
Le et al. [32]		●	●	●								
Ansarifar et al. [44]	●	●	●	●								●
Liang et al. [38]							●	●	●			●
Ta et al. [26]										●		
Heshmat & Eltawil [41]	●	●	●	●								●
Liang & Turkcan [56]				●			●					
Castaing et al. [64]												
Bouras et al. [36]				●								●
Heshmat et al. [91]				●		●						
Heshmat & Eltawil [92]	●	●	●	●			●			●	●	●
Kergosien et al. [27]										●		
Göçgün [51]		●	●									●
Heshmat et al. [22]				●								
Heshmat & Eltawil [59]	●	●	●	●							●	●
Alvarado & Ntaimo [33]	●	●	●	●			●					
Alabdulkarim [37]	●	●	●	●			●					●
Huang et al. [54]				●								
Hesaraki et al. [52]	●	●	●	●								●
Agnetis et al. [63]												
Huang et al. [49]				●								
Heshmat & Eltawil [65]	●	●	●	●			●			●	●	●
Robbes et al. [28]										●		
Hesaraki et al. [39]				●								
Garaix et al. [62]	●	●										
Benzaid et al. [40]	●	●	●	●			●					●
Issabakhsh et al. [34]		●	●									●
Demir et al. [93]												
Hooshangi-Tabrizi et al. [35]		●	●	●			●					●
Gul [83]												
Robbes et al. [29]										●		
Dodaro et al. [67]	●	●										●

Reference	Uncertainty													
	Duration													
	Registration	Blood draw	Measurement of vitals	Blood test	Oncologist check	Drug expiry period	Drug preparation	Delivery of drug from the pharmacy to the bed or chair	Drug injection	Drug infusion	Drug removal	Nurse overtime	Discharge	Lunch break
Mazier & Xie [61]					●					●				
Sadki et al. [23]														
Mazier et al. [24]						●								
Billaut [25]						●								
Sadki et al. [90]														
Turkcan et al. [30]									●	●	●	●		
Sevinc et al. [50]	●			●	●					●				
Woodall et al. [53]												●		
Sadki et al. [66]					●				●	●	●			
Gocgun & Puterman [57]														
Hahn-Goldberg et al. [43]					●			●	●	●				
Hahn-Goldberg et al. [80]								●	●	●				
Huggins & Pérez [60]								●	●	●				●
Condotta & Shakhlevich [31]														
Le et al. [32]									●	●	●	●		●
Ansarifar et al. [44]	●			●	●			●	●	●	●	●		
Liang et al. [38]					●				●	●				
Ta et al. [26]								●	●					
Heshmat & Eltawil [41]								●	●	●	●	●		
Liang & Turkcan [56]									●			●		
Castaing et al. [64]									●	●	●			
Bouras et al. [36]					●			●	●	●	●			
Heshmat et al. [91]								●	●	●	●			
Heshmat & Eltawil [92]								●	●	●	●			
Kergosien et al. [27]								●	●					
Göçgün [51]														
Heshmat et al. [22]									●	●	●			
Heshmat & Eltawil [59]									●	●	●	●		
Alvarado & Ntaimo [33]										●				
Alabdulkarim [37]														
Huang et al. [54]			●						●	●	●			
Hesaraki et al. [52]									●	●				●
Agnetis et al. [63]	●	●		●	●				●					
Huang et al. [49]			●						●	●	●			

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Table 8 (continued)

Reference	Uncertainty													
	Duration													
	Registration	Blood draw	Measurement of vitals	Blood test	Oncologist check	Drug expiry period	Drug preparation	Delivery of drug from the pharmacy to the bed or chair	Drug injection	Drug infusion	Drug removal	Nurse overtime	Discharge	Lunch break
Heshmat & Eltawil [65]							●		●	●	●		●	
Robbes et al. [28]							●	●						
Hesaraki et al. [39]									●	●	●			
Garaix et al. [62]					●				●	●				
Benzaid et al. [40]					●									
Issabakhsh et al. [34]					●				●	●	●			
Demir et al. [93]									●	●	●			
Hooshangi-Tabrizi et al. [35]												●		●
Gul [83]									●	●	●			
Robbes et al. [29]							●	●						
Dodaro et al. [67]									●	●	●			

workload of patients and assign patients to nurses in the first stage.

Contrastingly, many of the publications that proposed deterministic models considered uncertainty by assuming that the relevant probability distributions are known or can be created using empirical historical data, expert judgment, or both. Scholars have replaced random variables (e.g., types, durations, and arrival rates) with their means ( $\mu$ ) and solved the deterministic models.

Therefore, several different types of probability distributions were used to model the durations [30,34,36,38–40, 50,51,62,65]. New patient arrival rates and types were modeled using uniform [50], stationary [51], triangular [22], and Poisson [31,53,66] distributions.

Furthermore, rescheduling procedures were integrated into the deterministic models to accommodate unpredictable events. Condotta & Shakhlevich [31] and Hooshangi-Tabrizi et al. [35] applied rescheduling to the daily schedule, whereas Dodaro et al. [67] proposed a weekly rescheduling solution.

#### 4.4.2. Model types and solution approaches

We identified model types based on their inputs, constraints, and objective functions. The classification results and solution approaches are listed in Table 9. Mixed-integer programming and integer programming are the most commonly used modeling techniques and are used in more than 77% of publications. Of the forty-five publications reviewed, three proposed stochastic mixed-integer programming, whereas another three proposed integer linear programming models.

Linear, constraint, and mean-risk stochastic integer programming were rarely used. Approximately half of the models produced optimal solutions using the exact method; the rest were typically solved using heuristic approaches.

#### 4.4.3. Solution tools

Scholars have used many different algorithms and tools to execute the solving methods. The first category of software is the solver, where the mathematical formulation is converted into a model that the solver can read using its programming language. As shown in Table 10, the most frequently used solver was CPLEX, which solves only linear and

quadratic problems [68]. More than two-thirds of the studies used real data collected from their study partner center as the input to the solver.

The other one-third generated data to mimic the real data or used data from a published case study [65]. Most of the studies that considered patient flow through the process pathway linked a simulation model with the optimization model to generate data and evaluate solutions [38]. However, the most common approach for model testing and validation was numerical illustration.

### 5. Future research paths

The previous section analyzed the attempts to solve OCP problems in the reviewed publications. Scholars have built upon studies that preceded their work to close various research gaps. However, as listed in Table 11, there are some duplicate research efforts, and several recommended areas have not yet been addressed. The findings of this review for the main research gaps are aggregated in the framework shown in Fig. 9. Furthermore, the main requirements of the solutions were identified. Based on the analyses provided in this paper and the proposed solution framework, we present the following potential future research paths.

#### 5.1. Comprehensive optimization studies

Treatment planning, nurses scheduling, pharmacist-patient assignment are important research problems that have received low attention in existing literature, as listed in Table 5. Interesting research questions can be answered by integrating treatment planning with other operational planning models. Detailed studies are needed on how to coordinate the work of nurses and pharmacists, which is a foundation to guarantee the global performance of OCP by controlling drug preparation jobs and infusion supervision.

There is a need for a comprehensive model that simultaneously covers all planning, scheduling, and assignment scopes. Various connected departments (administration, labs, pharmacy, medical, etc.) deliver outpatient chemotherapy services. Therefore, an efficient

**Table 9**  
OCP model types and solving methods.

Reference	Uncertainty Handling		Model Type						
	Stochastic	Deterministic	Mixed-integer programming	Stochastic mixed-integer programming	Integer programming	Integer linear programming	Mean-risk stochastic integer programming	Linear programming	Constraint programming
Mazier & Xie [61]		●				●			
Sadki et al. [23].		●	●						
Mazier et al. [24].		●			●				
Billaut [25]		●	●						
Sadki et al. [90].		●	●						
Turkcan et al. [30].		●			●				
Sevinc et al. [50].		●			●				
Woodall et al. [53].		●	●						
Sadki et al. [66].		●	●						
Gocgun & Puterman [57]		●							
Hahn-Goldberg et al. [43].		●	●						●
Hahn-Goldberg et al. [80].		●							●
Huggins & Perez [60]		●	●						
Condotta & Shakhlevich [31]		●				●			
Le et al. [32].		●			●				
Ansarifar et al. [44].		●			●				
Liang et al. [38].		●				●		●	
Ta et al. [26].		●			●				
Heshmat & Eltawil [41]		●	●						
Liang & Turkcan [56]		●			●				
Castaing et al. [64].	●			●					
Bouras et al. [36].		●	●						
Heshmat et al. [91].		●			●				
Heshmat & Eltawil [92]		●			●				
Kergosien et al. [27].		●			●				
Gocgun [51]		●			●				
Heshmat et al. [22].		●			●				
Heshmat & Eltawil [59]		●	●						
Alvarado & Ntaimo [33]	●						●		
Alabdulkarim [37]		●	●						
Huang et al. [54].		●							
Hesaraki et al. [52].		●	●						
Agnētis et al. [63].		●	●						
Huang et al. [49].		●			●				
Heshmat & Eltawil [65]		●			●				
Robbes et al. [28].		●			●				
Hesaraki et al. [39].		●	●						
Garaix et al. [62].		●							
Benzaid et al. [40].		●	●		●				
Issabakhsh et al. [34].		●	●						
Demir et al. [93].	●			●		●			

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Table 9 (continued)

Reference	Uncertainty Handling		Model Type						
	Stochastic	Deterministic	Mixed-integer programming	Stochastic mixed-integer programming	Integer programming	Integer linear programming	Mean-risk stochastic integer programming	Linear programming	Constraint programming
Hooshangi-Tabrizi et al. [35].	●			●					
Gul [83].									
Robbes et al. [29].		●			●				
Dodaro et al. [67].		●			●				

Reference	Solving Method											
	Exact method	Lagrangian relaxation problem	Markov decision process	Heuristic	Greedy	Tabu search	Simulated annealing	Constraint method	Robust slack allocation	Clustering algorithm	Approximate dynamic programming	Answer set programming
Mazier & Xie [61].	●											
Sadki et al. [23].				●								
Mazier et al. [24].				●	●							
Billaut [25].	●											
Sadki et al. [90].		●		●								
Turkcan et al. [30].				●								
Sevinc et al. [50].				●								
Woodall et al. [53].	●											
Sadki et al. [66].				●								
Gocgun & Puterman [57].			●	●							●	
Hahn-Goldberg et al. [43].	●											
Hahn-Goldberg et al. [80].	●											
Huggins & Perez [60].	●											
Condotta & Shakhlevich [31].	●											
Le et al. [32].					●	●						
Ansarifar et al. [44].				●								
Liang et al. [38].	●											
Ta et al. [26].				●	●	●						
Heshmat & Eltawil [41].												
Liang & Turkcan [56].								●				
Castaing et al. [64].				●								
Bouras et al. [36].	●											
Heshmat et al. [91].	●									●		
Heshmat & Eltawil [92].	●									●		
Kergosien et al. [27].				●								
Göçgün [51].			●								●	
Heshmat et al. [22].	●									●		
Heshmat & Eltawil [59].	●											
Alvarado & Ntaimo [33].	●											
Alabdulkarim [37].	●											
Huang et al. [54].												
Hesaraki et al. [52].				●								

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Table 9 (continued)

Reference	Solving Method											
	Exact method	Lagrangian relaxation problem	Markov decision process	Heuristic	Greedy	Tabu search	Simulated annealing	Constraint method	Robust slack allocation	Clustering algorithm	Approximate dynamic programming	Answer set programming
Agnetis et al. [63].	●											
Huang et al. [49].	●											
Heshmat & Eltawil [65]	●											
Robbes et al. [28].				●								
Hesaraki et al. [39].				●								
Garaix et al. [62].				●	●							
Benzaid et al. [40].	●											
Issabakhsh et al. [34].				●			●		●			
Demir et al. [93].				●								
Hooshangi-Tabrizi et al. [35].	●											
Gul [83]	●											
Robbes et al. [29].				●	●							
Dodaro et al. [67].												●

decision support system must provide synchronized solutions to the OCP problems of various OCC departments to ensure operational harmony. The utilization of simulation-based optimization methods that can comprehensively and simultaneously handle the complexity, uncertainty, and optimization of this system appears promising.

5.2. Performance measures

Even though existing publications have considered a wide range of performance measures, the majority of these measures are neglected by most studies. As listed in Table 6, time and cost measures have received more attention than workload and satisfaction measures. However, there are still time and cost measures that are not sufficiently considered. Consequently, research that investigates the significance of different performance measures provides a valuable starting point for future research.

Current research can be extended to include performance measures that have not yet been analyzed. For instance, future studies can include congestion measures, such as the number of patients in the queue or system. Furthermore, future studies should extend fairness performance measures to resolve patient-related issues, such as the mean waiting times for various processes and variance in waiting times and queue sizes.

Furthermore, in the time performance measurement category, the assumption of a linear relationship between the patient waiting time and cost of waiting should be replaced with more realistic assumptions that can capture the heterogeneous effects of waiting for different patients. Moreover, tradeoffs between performance measures, such as satisfying patient demand and operational costs, should be reassessed.

5.2.1. Application in developing countries

OCP problems are directly connected to country-related contexts. Most of the reviewed studies were researched in developed countries. Therefore, they focused on OM issues in the context of developed countries. Only one publication considered the availability of sufficient drug quantities on the day of treatment. These types of issues exist in

developing countries because of limited resources and poor infrastructure. In 2040, low- and middle-income countries will bear immense cancer-related burdens because 70% of the global cancer deaths will occur in these countries [1]. Therefore, there is an urgent need for optimization-oriented research in developing countries to analyze and solve OCP issues specific to their contexts.

5.3. Generic models

Although receptionists, phlebotomists, and laboratory technicians play significant roles in OCP, they are often neglected in existing studies (Table 7). Considering all human resources while modeling OCP to capture their effect is an important research question. In most studies, scholars defined the problems and created models based on the environment of their partner centers. They compared the improvements produced by their models to the actual results obtained from the partner centers. Therefore, the current models lack generalizability. This prevents them from being used to satisfy the requirements of different centers. One promising research path would be to combine these models into a generic model that includes all outpatient chemotherapy processes, resources, policies, complexities, and uncertainties across a wide range of chemotherapy center-based environments.

5.4. Problem definition and assumptions

Several refinements must be applied to the existing literature to provide precise definitions of OCP problems and adopt realistic assumptions. In Table 11, one direct refinement is to consider the disruptive effect of late patient arrival to appointments, patient no-shows, and unexpected staff absences. For instance, it is easy to expect drug waste when the pharmacy anticipates drug preparation, but the patient does not arrive for treatment. These are critical issues that future research should consider when providing recommendations for reducing patient waiting times while limiting the cost of wasted drugs and optimizing the use of center resources.

Furthermore, future research should consider variance in the patient

time required for all standard processes (e.g., blood draw, oncologist check, drug preparation) by relaxing the assumption that patients are homogeneous.

### 5.5. Modeling and solution approaches

The existing OCP literature assumes independence between unplanned occurrences and human resource behavior. Thus far, scholars have connected only discrete-event simulations to optimization models. However, agent-based simulations can be adapted to determine the effects of the psychological reactions of human resources on performance [69,70]. For example, if several patients are waiting because of unexpected events, the oncologist may act subconsciously to finish the patient examination process more quickly [71].

However, real OCP problems are complex. Thus, hybrid modeling approaches are required to produce realistic solutions. None of the reviewed publications examined the usefulness of combining game theory with other modeling approaches in the OCP environment. Game theory can be used to model patient and human resource behavior and capture the effects of conflicting interests. For instance, a patient may come earlier or later than the specified appointment time to avoid waiting. In parallel, human resources may be unavailable because they do not expect punctual patient arrival. Future research should consider game theory to explore practical managerial insights for OCP improvement.

Moreover, the reviewed publications predominantly focused on a proactive operational model, which depends on prediction to generate the best possible solution. Therefore, future research should focus on reactive operational countermeasures. The few studies that used stochastic modeling limited its use to handling uncertainty in drug infusion durations and nurse availability. However, several other sources of uncertainty, such as human resource availability, patient availability, and processing duration, exist in the pathway processes.

The high variability of these stochastic parameters reduces the service performance of OCCs. Simultaneous modeling of all these stochastic parameters is quite complex and makes solving the model within a reasonable computation time difficult. Therefore, the formulation of a comprehensive, generic, stochastic OCP model and developing fast, easy heuristics to solve it represents a challenging potential future research path.

### 5.6. Healthcare Industry 4.0 technologies and data analytics

There is a vast gap between outpatient chemotherapy OM research and the application of Industry 4.0 to the healthcare industry (referred to as Health 4.0). The transformational technologies in Health 4.0 enable several OCP-related research opportunities [72,73]. Existing optimization-oriented OCP research can be extended to assess the incorporation of cloud computing, big data, the internet of everything, augmented reality, and other Health 4.0 cyber-physical system technologies for OCP automation and optimization. The literature models only mimic actual practices that occur in OCCs. Health 4.0 technologies have not been integrated into the models to investigate their usefulness and feasibility.

Heshmat & Shehata [74] proposed a framework to integrate chemotherapy planning and scheduling stages with patient databases using a mobile application and an online cloud. The paradigm of the internet of services has the potential to improve decision making and achieve higher service performance via innovative physical devices and intelligent connections among people (patients, admins, managers, medical staff, and logistics staff), data (patients electronic records, real-time health status, and tests results), and things (smartphones, self-registration devices, pharmacy machines, oncologist examination tools, and infusion beds or chairs). Therefore, new revisions of the existing OCP operational models are necessary to accommodate the changes in Health 4.0.

Another vital future research path that coincides with Health 4.0 technologies is data analytics. Recent advances in artificial intelligence (AI) and machine learning (ML)-based approaches have enabled the characterization of the root causes of issues in outpatient clinics, identification of critical points along the patient pathway, development of complex predictive models, and cost-effective preventative intervention recommendations [75].

The reviewed publications assume that uncertain events, such as altered processing durations, patient actions, and resource unavailability, are independently and identically distributed. However, factors such as age, area of residence, behavioral history, and cancer type can be used as uncertainty-related risk-increasing and risk-mitigation indicators [76]. These indicators can help OCCs to implement countermeasures that can reduce or eliminate the burden of uncertainties [77,78]. Thus, there are several research opportunities associated with integrating OCP optimization models with AI, ML, and other trending data analytics research methods.

### 5.7. Implementation

Although all the reviewed publications validated their models using either numerical examples or simulation results, there is a lack of emphasis on the change management methodology required to develop and apply OCP optimization models in real environments.

In the list of publications reviewed, only one study [63] considers change management using multiple methodologies (lean thinking and mathematical optimization). In other studies, the OCP issues were addressed as pure optimization problems. This approach is the primary source of weakness in OM-optimization-oriented research [79]. Consequently, the value of combining methodologies from soft OM science with optimization-oriented OCP research has not been fully explored.

## Conclusion

This systematic review paper provides content analysis of the quantitative optimization models developed in various OM studies to solve OCP problems. Several research databases were used to maximize the number of identified publications. The inclusion criteria allowed the acceptance of publications using quantitative models. After screening, 45 publications were selected for the review. A classification scheme and material evaluation steps were defined for the analysis.

The bibliometric analysis showed that several scientific journals are interested in OCP optimization-oriented research. Nevertheless, only a few countries have researched this field. Few studies were conducted in developing countries and certain developed countries. The narrative of the quantitative models was analyzed using the SNA approach to develop a conceptual model. The OCP optimization-oriented research framework was subsequently derived from SNA results.

Content analysis revealed the three main intervention categories proposed by the publications: decision support systems for planning, scheduling, and resource assignment. The models used many performance measures to solve time, cost, workload, and satisfaction issues. More than half of the publications addressed these issues by optimizing a single process. However, scholars who considered patient flow have developed multi-process optimization models. Nurses and beds/chairs were the bottleneck resources in most of the OCCs considered in the studies. Twenty-two sources of OCP uncertainty and four sources of OCP complexity were considered in the models. Because different problems require different modeling techniques, scholars have used seven model types and eleven solution methods to solve the models within reasonable computational time using various software.

Existing attempts to optimize the OCP through scientific research are in the development stage, as several research gaps remain uncovered. Analysis of the limitations of the reviewed publications identified eight main future research paths with many potential sub-directions. Formulating a comprehensive, generic OCP optimization model that

**Table 10**  
Validation type and tools.

Reference	Illustration Type		Data Source		Solver													Simulator		Languages					
	Numerical	Simulation	Real data	Generated data	Lingo	Clingo	CPLEX	Gurobi	GAMS	GNU	Spreadsheet	MATLAB	GLPK	Microsoft SQL Server	COMET	MAXHS	OPEN-WBO	RC2	AnyLogic	Arena	C++	Python	Julia/0.5.2	AMPL	
Mazier & Xie [61]	●		●	●			●																		
Sadki et al. [23]	●		●	●			●																		
Mazier et al. [24]	●		●	●			●		●																
Billaut [25]	●			●									●												
Sadki et al. [90]	●		●	●																			●		
Turkcan et al. [30]	●		●				●																		
Sevinc et al. [50]		●	●										●												
Woodall et al. [53]	●	●	●								●														●
Sadki et al. [66]	●		●				●																		
Gocgun & Puterman [57]	●	●	●				●								●										
Hahn-Goldberg et al. [43]	●		●				●																		
Hahn-Goldberg et al. [80]	●		●																						
Huggins & Pérez [60]		●	●					●																	●
Condotta & Shakhlevich [31]	●		●				●																		
Le et al. [32]	●		●																						●
Ansarifar et al. [44]	●			●																					
Liang et al. [38]	●	●	●																						●
Ta et al. [26]	●			●																					
Heshmat & Eltawil [41]	●			●																					
Liang & Turkcan [56]	●			●																					●
Castaing et al. [64]	●																								●
Bouras et al. [36]	●	●	●																						●
Heshmat et al. [91]	●		●																						●
Heshmat & Eltawil [92]	●			●																					●

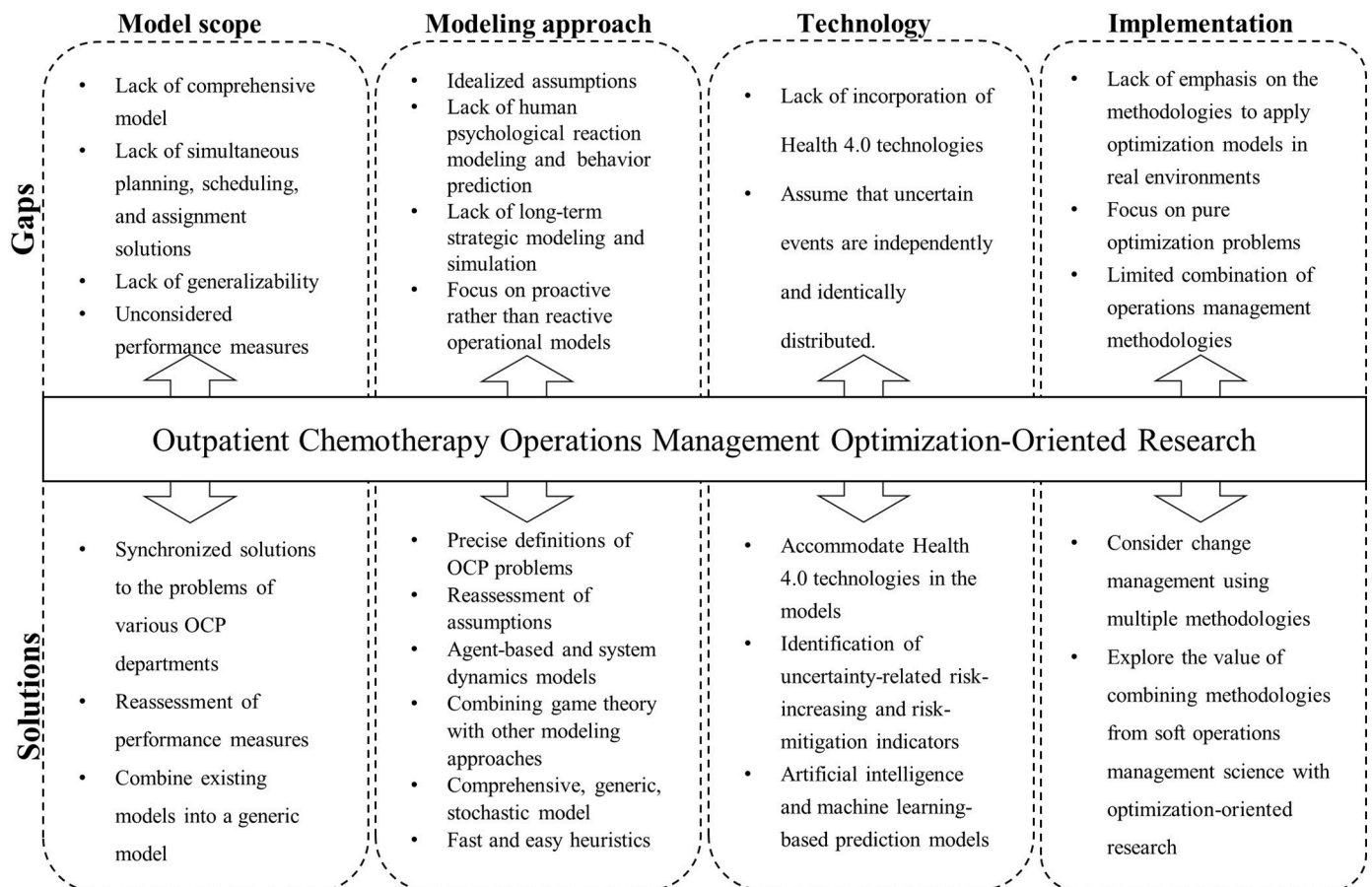
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Table 10 (continued)

Reference	Illustration Type		Data Source		Solver													Simulator		Languages					
	Numerical	Simulation	Real data	Generated data	Lingo	Clingo	CPLEX	Gurobi	GAMS	GNU	Spreadsheet	MATLAB	GLPK	Microsoft SQL Server	COMET	MAXHS	OPEN-WBO	RC2	AnyLogic	Arena	C++	Python	Julia/0.5.2	AMPL	
Kergosien et al. [27]	●			●			●																		●
Göçgün [51]	●	●					●																		●
Heshmat et al. [22]	●		●				●				●														
Heshmat & Eltawil [59]	●			●	●																				
Alvarado & Ntaimo [33]		●	●																						
Alabdulkarim [37]	●			●			●																		
Huang et al. [54]	●		●																						
Hesaraki et al. [52]	●		●				●																	●	
Agnētis et al. [63]		●	●				●													●					
Huang et al. [49]	●		●																						
Heshmat & Eltawil [65]	●	●		●			●													●					
Robbes et al. [28]	●			●																		●			
Hesaraki et al. [39]	●		●																						
Garaix et al. [62]	●	●	●	●																	●				
Benzaid et al. [40]	●	●		●			●													●				●	
Issabakhsh et al. [34]	●		●																						
Demir et al. [93]	●		●				●														●				
Hooshangi-Tabrizi et al. [35]	●		●				●														●				
Gul [83]	●		●				●														●				
Robbes et al. [29]	●			●																	●				
Dodaro et al. [67]	●		●			●		●										●	●	●					

**Table 11**  
OCP research development.

Suggested Research		Suggested by	Addressed by	
Dimension	Direction			
<b>Optimization problem</b>	Patient scheduling	[22,66]	Refer to Table 5	
	Drug preparation scheduling	[66]	[24,25,36,27]	
	Nurse-patient assignment	[30]	[22,31–33,35,36,40,49,52,54,56,83,91]	
<b>Performance measures</b>	Minimize makespan	[22]	[90,43,43,64,91,59,37,52,65,62,34]	
	Minimize number of nurses	[22]	[40]	
	Minimize nurse workload imbalance	[30,38]	[50,31,32,54,52,49,39,35]	
	Maximize oncologist workload balance	[30,66]	[61,50]	
	Minimize number of patients assigned to floating nurses	[30]	[35]	
	<b>Improvement level Complexities and uncertainties</b>	Patient flow	[64,22,62,66]	[53,43,43,60,31,44,38,36,63,65,34]
		Treatment priority	[30] [66]	[22,33,37,40,41,44,52,57,62,65]
Acuity level		[30,38]	[53,43,43,60,31,32,44,41,56,36,91,22,59,33,37,54,52,49,65,39,40,35]	
Variety in raw material package volume		[25]	Non	
Non-punctual patient arrival		[43,52,63]	Non	
Patient no-show		[61,51,52,35]	Non	
Patient unfit (cancellation) or drug change		[23,30,43,44,36,27,35]	[33,34,40,50–52,62]	
Physician availability		[61,23]	[90,66,38]	
Pharmacist availability		[24]	[60,27,65]	
Bed or chair availability		[61]	[23,90,30,66,50,60,44,38,41,22,37,65,40,34,35]	
Blood test duration		[30,44,49,93]	[50,63]	
Duration for oncologist checks		[34,49,93]	[61,50,66,43,44,38,36,63,62,40]	
Drug preparation duration		[24,35] [66]	[43,43,60,44,36,27,65]	
Drug injection duration	[30,43,44,49,62]	Refer to Table 8		
Drug infusion duration	[30,43,44,49,62]			
Drug removal duration	[30,43,44,49,62]			
<b>Model type</b>	Stochastic	[44,52,63,62]	[33,64,83,93]	



**Fig. 9.** Framework of Gaps and Solution Approaches.

can achieve higher performance measures without simplification assumptions can no longer be neglected. Consequently, the development of fast heuristics to solve complex OCP models is a major future research challenge. Finally, extensive process improvement research is required to close the gap between OCP optimization-oriented research and practice.

### Declaration of Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### Acknowledgment

This article was made possible by National Priorities Research Program -Standard (NPRP-S) Twelfth (12th) Cycle grant# NPRP12S-0219-190108, from the Qatar National Research Fund (a member of Qatar Foundation). The findings herein reflect the work, and are solely the responsibility, of the author[s].

Open Access funding provided by the Qatar National Library.

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