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MULTI-DEPOT GENERAL COLORED TRAVELING SALESMAN PROBLEM WITH TIME WINDOWS IN HOME HEALTHCARE SYSTEM: A MEDICATION DELIVERY EXAMPLE

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This paper focuses on the problem of medication delivery, specifically addressing meeting the medication demands of patients by different pharmacies. Medication delivery, along with the distribution of vaccines and test kits, is a crucial component of home healthcare services, primarily aiming to serve elderly patients and those with physical or psychological disabilities. A significant aspect of these services is the direct delivery of medications from pharmacies to patients' homes. The importance of home healthcare services has grown, particularly during the pandemic, as many patients faced difficulties accessing both prescribed and over-the-counter medications during lockdowns. The medication delivery problem under consideration is modeled as a Multi-Depot General Colored Traveling Salesman Problem with Time Windows (MD-GCTSP-TW). To solve this problem, a mixed integer mathematical model and a metaheuristic algorithm were designed. The effectiveness of these methods was tested on a variety of test problems, demonstrating the metaheuristic's efficiency through promising results.

Keywords: General Colored Traveling Salesman Problem; Home Healthcare System; Medication Delivery; Mixed Integer Mathematical Model; Variable Neighborhood Descent Algorithm.

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1. INTRODUCTION

Home healthcare has become an integral part of modern medical services, supported extensively by medication distribution systems that deliver medications directly from pharmacies to patients' homes (Watson, 2014; Suwatcharachaitiwong *et al.*, 2020). This form of healthcare focuses on providing medical services within the home environment, with medication delivery being one of the key services offered. The growth of home healthcare can be attributed to factors such as an aging population, changes in family dynamics, an increase in chronic diseases, advancements in medical technology, the introduction of new medications, and government initiatives to expand healthcare access. The goal is to enable elderly individuals, people with physical or psychological disabilities, and those with illnesses to live as independently as possible in their own homes.

Medication delivery services can operate through a combination of home delivery and customer pickup options. Medications may be delivered directly to patients' homes or nearby pickup points like lockers or convenience stores (Suwatcharachaitiwong *et al.*, 2020; Veenstra *et al.*, 2018). These services are particularly beneficial for individuals with chronic illnesses, the elderly, disabled persons, and those requiring regular prescriptions or over-the-counter medications. During events like a pandemic lockdown, home delivery becomes even more essential. However, providing this service requires visiting each patient's home, leading to significant transportation costs.

Effective route planning for home healthcare visits is critical in healthcare logistics. Optimizing vehicle routes for visiting all patients is challenging, and failure to do so can result in longer routes and increased delivery costs. The Vehicle Routing Problem (VRP) is commonly applied to address such logistical challenges in home healthcare delivery. At this point, since VRP is a challenging problem to solve, approaches like the Modified Sweeping Algorithm were proposed to improve the efficiency of solving it, particularly for cases with radial clustered patterns (Altarawneh and Kwon, 2023).

When considering medication delivery with sufficient vehicle capacity, the problem can be addressed as a Traveling Salesman Problem (TSP), where a single route must be planned for visiting all patients with the minimum total cost or distance. When multiple routes are involved, it becomes a Multiple Traveling Salesman Problem (m-TSP). TSP and its various forms have been widely studied in the literature. For instance, in the study by Liu *et al.* (1999), the problem of optimizing

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drilling routes in multi-layer printed circuit boards (PCBs) was modeled as a TSP. In our study, the problem encountered in medication delivery is the Colored Traveling Salesman Problem (CTSP), a specialized version of the *m*-TSP. This research addresses the most general form of CTSP, known as the Multi-Depot General Colored Traveling Salesman Problem with Time Windows (MD-GCTSP-TW).

In home healthcare systems, many pharmacies provide services to patients. However, compatibility constraints must be considered since each pharmacy may not have the specific pharmaceutical goods to satisfy all patient demands or may be unable to send a vehicle to the area where a particular patient is located. These constraints can arise from factors such as pharmacy operating hours, geographical challenges, medication stock, and demand variations. As a result, not every pharmacy can serve every patient, and multiple pharmacies may serve some patients. Moreover, in real-world applications, patients have specific time windows during which they wish to receive services, and pharmacies must deliver the required services within these time frames. Therefore, to handle the challenges encountered in home healthcare services, this study addresses the medication delivery problem as the MD-GCTSP-TW. This approach considers both the multi-depot structure and the time window constraints for patients. Furthermore, MD-GCTSP-TW can also address real-world applications with its compatibility constraints.

In this study, we propose a mixed integer mathematical model as an exact solution method and the Variable Neighborhood Descent (VND) algorithm as a metaheuristic method to solve the MD-GCTSP-TW in the context of medication delivery. Our solution approaches are tailored for distributing over-the-counter medication and healthcare supplies to individuals who are disabled, elderly, or require healthcare at home, especially during potential lockdown situations. Moreover, these solution approaches effectively satisfy all the conditions of the MD-GCTSP-TW, and they provide obtaining high-quality solutions. To validate our proposed methods, we generated ten different test scenarios. Using these test scenarios, the performance of the proposed VND algorithm was compared with the Reduced Variable Neighborhood Search (RVNS) algorithm from the literature. On examining the results, it was found that the VND algorithm significantly outperforms in terms of solution quality. Therefore, the proposed VND algorithm and its components are successful in solving the MD-GCTSP-TW.

The remainder of this paper is structured as follows: Section 2 presents a literature review. Section 3 provides an overview of the TSP and m-TSP, followed by an introduction to CTSP and GCTSP. The significance of medication delivery in healthcare is then discussed. Section 4 gives detailed information about the proposed solution approaches. Section 5 provides computational results. Section 6 details the performance of the proposed solution approaches. Finally, Section 7 concludes the paper and offers recommendations for future research.

2. LITERATURE REVIEW

There are many studies about the home healthcare system in literature. Fikar and Hirsch (2017), Grieco *et al*. (2021), Goodarzian *et al*. (2023), and Chabouh *et al*. (2023) conducted significant literature reviews that provided detailed information about home healthcare. These papers are quite useful for researchers interested in home healthcare systems. In this section, papers related to this study are presented.

Harms (2013) focused on the delivery of pharmaceutical products from a retail pharmacy to customers. In this study, pharmaceutical products are delivered from a single retail pharmacy to customers. Therefore, this problem is considered a Single-Depot Vehicle Routing Problem (SD-VRP). Harms used the Petal algorithm (a heuristic method) to solve SD-VRP.

Liu *et al*. (2014) focused on the Periodic Home Health Care Pickup and Delivery Problem (PHHPDP), which is a significant issue in Home Health Care (HHC) logistics. They considered four different logistics demands in PHHPDP: distribution of medical devices from the HHC pharmacy to patients' homes, collection of unused medical devices from patients' homes to the depot, delivery of special drugs from the hospital to patients, and pickup of blood samples from patients' home to the lab. Since the items, such as boxes of medicine and blood samples, are small, they assumed that vehicle capacity is unlimited in PHHPDP. Therefore, they highlighted that PHHPDP is a special case of the Traveling Salesman Problem with Time Windows (TSP-TW). To solve the problem, they used the Tabu Search metaheuristic algorithm.

Linfati *et al*. (2018) studied the problem of scheduling visits to customers and vehicle routing for the home delivery of medications. They proposed a two-phase heuristic algorithm to solve this problem. In the first phase of the algorithm, the problem of scheduling visits to customers in clusters was addressed and solved using an integer linear programming model. In the second phase, the Vehicle Routing Problem with service time was considered. They developed a hybrid metaheuristic algorithm that combines Simulated Annealing and Record-to-Record algorithms to solve the Vehicle Routing Problem with service time.

Ji (2019) considered three different demand types in the HHC logistics problem: delivery from pharmacy to patient, delivery from hospital to patient, and pickup from patient to pharmacy. In this problem, the pharmacy and patients were defined as the depot and customers, respectively. Based on this structure, the HHC problem was discussed as the Vehicle Routing Problem with Simultaneous Delivery and Pickup and Time Windows (VRPSDPTW). To get optimal scheduling, a mixed integer mathematical model was proposed. The objective function of the mathematical model is to minimize the total distance traveled by vehicles.

Ouiss *et al*. (2021) addressed the problem of delivering medication to a set of patients using a fleet of drones launched from multiple depots. This problem encountered in healthcare delivery was defined as the Multiple Depot Vehicle Routing Problem with Drones. In this problem, the payload capacity and maximum flight range of the drones are considered, and the objective is to minimize the total distance traveled by the drones. To obtain high-quality solutions within reduced execution time, a parallel genetic algorithm was used.

Bagheri Tofighi *et al*. (2024) addressed the problem of delivering pharmaceutical products from distribution centers to hospital pharmacies. They developed a two-step clustering method to optimize the Multi-Depot Vehicle Routing Problem (MD-VRP) in pharmaceutical distribution in Tehran. In the first step, the K-means algorithm was used to determine the optimal distribution centers. In the second step, the K-means algorithm was applied to obtain sub-clusters considering vehicle capacities and demand values. Then, the vehicle routes for serving these sub-clusters were obtained by solving the TSP.

Examining the papers in the literature, it is seen that the medication delivery problem in home healthcare systems was studied with a multi-depot structure or by considering patients' time windows. However, no study was found that addresses the medication delivery problem in home healthcare systems with multiple depots, patients' time windows, and compatibility constraints. The compatibility constraints refer to the condition that pharmacies can only serve specific patients. Therefore, some patients are classified as shared patients, meaning they can be served by multiple pharmacies, while others must receive service from a specific pharmacy. This condition increases the complexity of the medication delivery problem. While deciding which pharmacies will serve the shared patients, it is also necessary to obtain vehicle routes for the patients assigned to each pharmacy and ensure that all patients are served within their time windows. To the best of our knowledge, there is no study in the literature that discusses the home healthcare medication delivery problem as MD-GCTSP-TW. In this study, the medication delivery problem is covered following the characteristics and constraints of the home healthcare system. Furthermore, an exact solution method and a metaheuristic algorithm were designed to solve the MD-GCTSP-TW. The performance of these solution approaches was evaluated using another metaheuristic algorithm from the literature. Moreover, a subset of a real-world problem was considered and solved using the developed solution methods.

3. MULTI-DEPOT GENERAL COLORED TRAVELING SALESMAN PROBLEM WITH TIME WINDOWS

The Traveling Salesman Problem (TSP) is one of the most extensively studied combinatorial optimization problems (Laporte, 1992). The goal of the TSP is to determine the shortest possible route that allows a salesman to visit *n* cities and return to the starting city. By optimizing the route, the total distance traveled, time spent, or cost incurred is minimized, thereby meeting the salesman's objectives. When there are m salesmen, each responsible for visiting a subset of the n cities and starting and ending at the same depot, the problem is referred to as the multiple traveling salesman problem (m-TSP). The m-TSP is a generalization of the classic TSP, accommodating multiple salesmen in the solution (Bektas, 2006).

The Colored Traveling Salesman Problem (CTSP), a special variant of the m-TSP, was introduced by Li *et al*. (2014) to address scenarios where multiple salesmen not only have individual tasks but also share a subset of tasks. In the CTSP, each salesman is associated with a specific color, and each city may be assigned one or more colors depending on the problem type. Each city must be visited exactly once by a salesman of the corresponding color. Li *et al*. (2015) identified two types of city groups: exclusive city groups, where each city is visited by only one salesman of a specific color, and shared city groups, where multiple salesmen can visit the same city. A schematic representation of the CTSP is shown in Figure 1 (Li *et al*., 2014).

The CTSP can be categorized as serial (S-CTSP), radial (R-CTSP), or general, based on the color assignment of each city. In S-CTSP, each city has one or two colors, while in R-CTSP, a city can have one or all colors. The general CTSP (GCTSP) extends the concepts of S-CTSP and R-CTSP (Xu *et al.*, 2021). The color assignments in R-CTSP and S-CTSP have significant theoretical and practical implications regarding city accessibility for salesmen. Li *et al*. (2014) initially applied the CTSP to optimize the routing of dual-bridge waterjet cutting machines. The CTSP has since been used in other areas, such as collision-free scheduling in multi-bridge machine systems and rice harvesting (Li *et al*., 2017). However, Meng *et al.* (2018) pointed out that neither R-CTSP nor S-CTSP is suitable for home healthcare scheduling due to the need for more diversified city accessibility. To the best of our knowledge, to date, no studies have applied any version of the CTSP to healthcare problems, particularly the MD-GCTSP-TW.

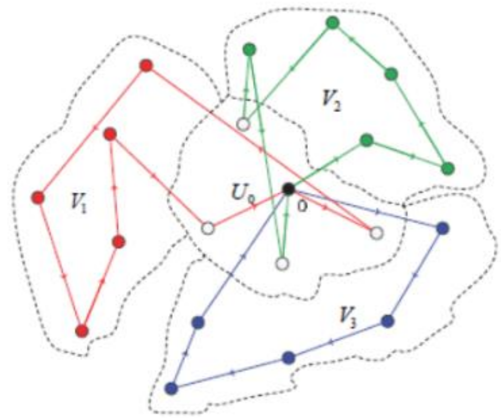

Figure 1. Example of a CTSP with one shared city set.

This research focuses on the delivery of medications from community pharmacies to patients' homes. With the increasing use of smartphones, home delivery has become popular across many sectors, including the pharmacy sector, which is crucial during pandemics. While medications are the primary product of pharmacies, they are closely linked to broader healthcare system issues. Delivery speed and order accuracy are critical factors in pharmaceutical delivery systems. Revadekar *et al.* (2020) noted that optimizing delivery routes in scenarios involving multiple sources and destinations significantly increases problem complexity. Therefore, we considered the MD-GCTSP-TW for this study. The primary motivations behind this research include:

- Introducing a novel approach by addressing the multi-depot and time windows variant of the general colored traveling salesman problem, representing a significant advancement in the field.
- Proposing a unique solution to the medication delivery problem by modeling it as an MD-GCTSP-TW for the first time.
- Developing a tailored mathematical model specifically for the MD-GCTSP-TW, demonstrating originality in problem-solving methodologies.
- Innovatively designing components of a metaheuristic algorithm, specifically the Variable Neighborhood Descent Algorithm, to effectively manage the complexities of the MD-GCTSP-TW, thereby advancing optimization techniques.

Although pharmacy structures and education vary by country, a pharmacy is generally classified as one of the following types: (https://www.rasmussen.edu/degrees/health-sciences/blog/types-of-pharmacies/)

- Retail pharmacy
- Hospital pharmacy
- Clinical pharmacy
- Homecare pharmacy
- Mail order pharmacy
- Assisted living and long-term care pharmacy
- Compounding pharmacy

This study focuses on the retail pharmacy structure, where community (retail) pharmacies are predominantly independent, locally owned businesses. During the pandemic, reliance on these pharmacies increased, exacerbating access issues for many patients needing prescribed and over-counter medications, particularly during lockdowns. This situation led to prolonged recovery times for many patients or unmet immediate health needs. Consequently, home delivery of medications has become more prominent, particularly in home healthcare systems where pharmacies deliver medications directly to patients' homes, meeting the needs of disabled individuals, elderly individuals, and those requiring home-based healthcare.

The application of MD-GCTSP-TW for medication delivery is illustrated in Figure 2. Features of this medication delivery problem are also provided through this illustration.

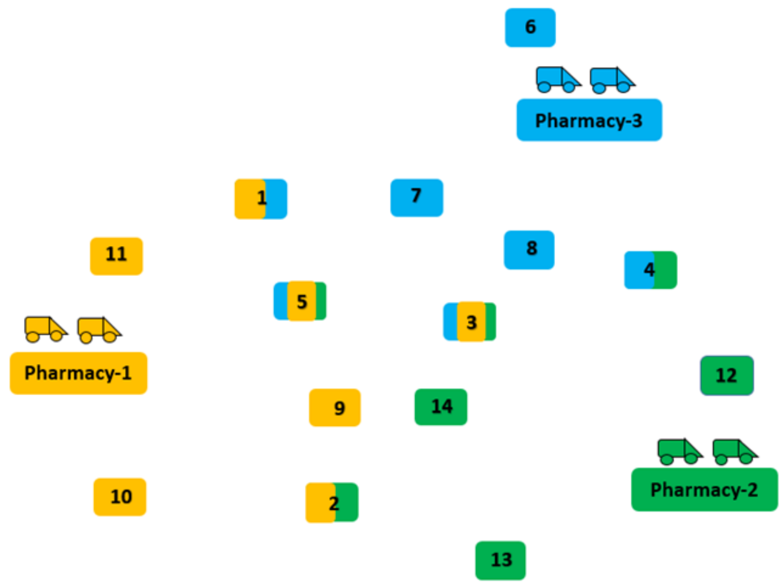

Figure 2. A sample problem for the medication delivery.

In Figure 2, there are 14 patients and three pharmacies. To distinguish between pharmacies and patients, patients are denoted by the number. Each pharmacy acts as a depot, leading to a total of three depots. The medication needs of patients must be met by these three pharmacies. However, not every pharmacy can serve every patient. Some patients are exclusive to a single pharmacy, while others are shared among multiple pharmacies. Patients who can only be served by a specific pharmacy are represented by the same color as that pharmacy. For instance, patients 9, 10, and 11 are served only by Pharmacy-1, patients 12, 13, and 14 only by Pharmacy-2, and patients 6, 7, and 8 only by Pharmacy-3.

On the other hand, patients 1, 2, 3, 4, and 5, who can be served by multiple pharmacies, are represented by the colors of the respective pharmacies. For example, patient-1 can be served by either Pharmacy-1 or Pharmacy-3, patient-2 by either Pharmacy-1 or Pharmacy-2 and patient-4 by either Pharmacy-2 or Pharmacy-3. Patients 3 and 5, shown with three colors, can be served by any of the three pharmacies.

Additionally, each pharmacy has two vehicles available to serve patients, though it is not mandatory to use all available vehicles. Each vehicle is color-coded according to its corresponding pharmacy, ensuring that it adheres to the service constraints of that pharmacy. Patients are assigned specific time windows within which their medication must be delivered, requiring vehicles to fulfill these needs within the allocated times to ensure timely service.

Thus, the medication delivery problem is modeled as an MD-GCTSP-TW involving multiple depots (pharmacies) with multiple vehicles at each depot. While not all vehicles need to be used, the goal is to meet the medication needs of patients within their specified time windows. The objective is to optimize vehicle routes, minimizing the total distance traveled while satisfying these constraints.

The real-world application of the MD-GCTSP-TW problem is discussed using data from home healthcare medication delivery services provided by two independent retail pharmacies of the same company in Indiana, USA. A subset of the patients served by these pharmacies is considered to analyze a real-world application example. Due to company policy and privacy concerns, the company name, patient addresses, and their exact locations on the map are not directly disclosed. Instead, a mapping was created based on the information obtained from the company, and parameter values such as the distance matrix, time matrix, service time, and compatibility constraints for pharmacies were derived. This medication delivery problem is presented in Figure 3.

In Figure 3, there are two pharmacies and 13 patients that need to be served by these pharmacies. Patients numbered 1, 2, 3, 4, and 9 are served by Pharmacy-1, while patients numbered 5, 6, 7, 8, and 11 are served by Pharmacy-2. The remaining patients, numbered 10, 12, and 13, can be served by either pharmacy. Moreover, each patient has a specific time window that they want to get the service, and the pharmacies must complete the deliveries within these time frames. This scenario represents the real-world application of the MD-GCTSP-TW problem. This problem can be solved using the solution approaches presented in this study.

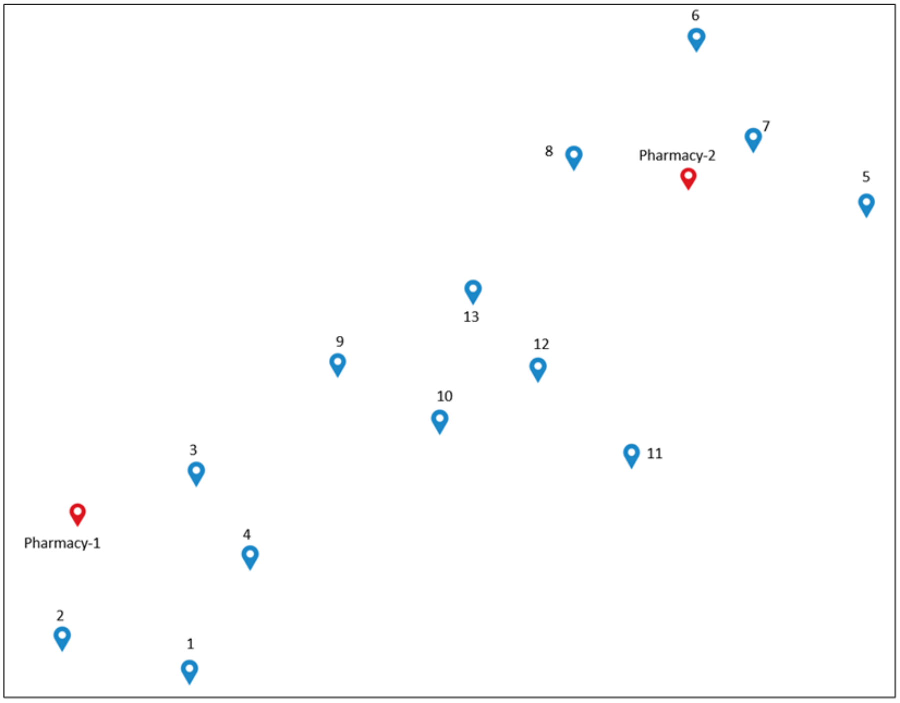

Figure 3. A real-world problem for medication delivery.

4. PROPOSED METHODS FOR MD-GCTSP-TW

In this section, two solution approaches for the MD-GCTSP-TW are presented, including an exact solution method and a metaheuristic method. First, a mixed integer mathematical model is defined and presented as the exact solution method. Then, an in-depth explanation of the Variable Neighborhood Descent algorithm is given. This algorithm is a metaheuristic method with components specifically designed for this problem.

4.1 Mixed Integer Mathematical Model

To address the multi-depot general colored traveling salesman problem with time windows (MD-GCTSP-TW), consider the following mixed integer programming model.

Indices

i, j, l	Node index.
k	Vehicle index.

Sets

V	The set of nodes.
V_c	The subset of patients' nodes. ($V_c \subset V$)
V_d	The subset of depots' (pharmacies) nodes. ($V_d \subset V$)
K	The set of vehicles.
K_i	The subset of vehicles assigned to depot (pharmacy) i. ($K_i \subset K$)

Parameters

d_{ij}	Distance between node i and node j.
a_{ik}	Patient–vehicle color matrix. This matrix consists of binary values {0,1}. If $a_{ik} = 1$, it implies that vehicle k is of the same color as patient i, signifying that vehicle k can serve patient i. Conversely, if $a_{ik} = 0$, it indicates that vehicle k and patient i are of different colors, and vehicle k cannot serve patient i.
f_i	Service time at patient i.
b_i	The earliest service time of patient i.
c_i	The latest service time of patient i.
t_{ij}	Travel time between node i and node j.
M	Very large positive number.

Decision Variables

$$\mathrm{x_{ijk}} = \begin{cases} 1, & \text{if vehicle k travels from node i to node j} \\ 0, & \text{otherwise} \end{cases}$$

$\mathrm{s_i}$ = Arrival time at patient i.

In the mathematical model's d_{ij} parameter, the i and j indices can be patient or pharmacy. Therefore, the d_{ij} parameter represents the distance between patients and pharmacies in the problem. The parameter a_{ik} is essentially a compatibility matrix. Therefore, if vehicle-k is suitable to serve patient-i, the parameter a_{ik} takes the value of 1; otherwise, it takes the value of 0. The parameters f_i, b_i, and c_i in the model represent the time window values for patient-i. The service for patient-i must be completed within the time window defined by the values b_i, and c_i. Another time-related parameter is t_{ij}, which represents the travel time between nodes i and j (patients and pharmacies). In terms of decision variables, $\mathrm{x_{ijk}}$ is a binary variable that gets the value of 1 if vehicle k traverses between nodes i and j, and 0 otherwise. The indices i and j in $\mathrm{x_{ijk}}$ variable can refer to the patient and pharmacy. Another decision variable, s_i, represents the arrival time of the vehicle at patient-i. This time must fall within the interval defined by the parameter values b_i and c_i in the model.

Model

$$Min\ z = \sum_{i \in V} \sum_{j \in V} \sum_{k \in K} d_{ij} * x_{ijk} \tag{1}$$

Subject to

$$\sum_{i \in V} \sum_{k \in K} x_{ijk} = 1 \qquad \forall j \in V_c, i \neq j, a_{ik} = 1, a_{jk} = 1 \tag{2}$$

$$\sum_{j \in V} \sum_{k \in K} x_{ijk} = 1 \qquad \forall i \in V_c, i \neq j, a_{ik} = 1, a_{jk} = 1 \tag{3}$$

$$\sum_{i \in V} x_{ilk} - \sum_{j \in V} x_{ljk} = 0 \qquad \forall l \in V, \forall k \in K, i \neq l, j \neq l \tag{4}$$

$$\sum_{j \in V_c} x_{ijk} \leq 1 \qquad \forall i \in V_d, \forall k \in K_i, a_{jk} = 1 \tag{5}$$

$$\sum_{i \in V_c} x_{ijk} \leq 1 \qquad \forall j \in V_d, \forall k \in K_j, a_{ik} = 1 \tag{6}$$

$$\sum_{i \in V_c} x_{ijk} = 0 \qquad \forall j \in V_d, \forall k \notin K_j \tag{7}$$

$$\sum_{j \in V_c} x_{ijk} = 0 \qquad \forall i \in V_d, \forall k \notin K_i \tag{8}$$

$$s_i + f_i + t_{ij} - s_j \leq (1 - x_{ijk}) * M \qquad \forall i \in V, \forall j \in V_c, \forall k \in K \tag{9}$$

$$s_i + f_i + t_{ij} - s_j \geq -(1 - x_{ijk}) * M \qquad \forall i \in V, \forall j \in V_c, \forall k \in K \tag{10}$$

$$b_i \leq f_i + s_i \leq c_i \qquad \forall i \in V \tag{11}$$

$$x_{ijk} \in \{0,1\}, s_i \geq 0 \qquad \forall i \in V, \forall j \in V, \forall k \in K \tag{12}$$

The objective function (1) of this model is to minimize the total distance traveled by vehicles. Constraints (2) and (3) ensure that each patient is visited exactly once by a vehicle of the corresponding color. Constraint (4) maintains flow conservation and ensures route continuity. Constraints (5) and (6) stipulate that each vehicle can depart from or return to its depot (pharmacy) no more than once, and when doing so, the vehicle must travel to or from a patient of the same color. Due to these constraints, not all vehicles at each depot are required to be used. Constraints (7) and (8) prevent vehicles from beginning or ending their routes at depots other than their designated ones. Constraints (9) and (10) specify the relationships among x_{ijk}, s_i and s_j. Therefore, these constraints ensure that if the vehicle travels from patient i to patient j, the arrival time of the vehicle at patient j is equal to $(s_i + f_i + t_{ij})$. Constraint (11) ensures that each patient is served within a certain time window. Constraint (12) indicates the sign constraints of the decision variables.

4.2 Variable Neighborhood Descent Algorithm

The MD-GCTSP-TW is an NP-hard problem. Therefore, as the problem size of the MD-GCTSP-TW problem increases, the computation time increases exponentially. To obtain high-quality solutions in a short amount of time, we employed a metaheuristic algorithm. The Variable Neighborhood Search (VNS) algorithm has proven effective in various routing problems, as demonstrated by Hansen *et al*. (2019) and Lan *et al*. (2021). Therefore, we utilized a version of the VNS algorithm in this study, specifically, the VND algorithm (Hansen and Mladenović, 1999). The pseudo-code for the VND is provided below, following the notation used in the algorithm.

k : neighbor search operator
N_k : the set of neighbor search operators
s : initial solution
$f(s)$: objective function value of the initial solution
s' : neighbor solution
$f(s')$: objective function value of the neighbor solution

The initial solution was generated randomly while considering the service delivery constraints, specifically the patient-vehicle color matrix. In the algorithm's structure, a multidimensional list is used to represent the solution. Each depot is associated with a separate list, and each list contains patients of the same color as the depot who can be served by the depot. To explore different neighbor solutions, the algorithm utilizes four distinct neighbor search operators and one shaking operator. The set of neighbor search operators includes swap, insert, reverse, and drop/add. For the swap, insert, and reverse operators, a depot is first selected randomly. In the swap operator, two randomly chosen patient nodes within the selected depot are exchanged. The insert operator involves placing a randomly selected patient node into a random position within the selected depot's list. The reverse operator reverses the direction of the path between two randomly chosen positions in the selected depot list. The drop/add operator is used for shared patients who can be serviced by multiple vehicles, allowing the randomly selected shared patient to be transferred from the current list to another depot list from which the patient can also be serviced. The number of neighbors evaluated in the algorithm's sixth step is set to three. Thus, it is aimed to achieve a balance between computational efficiency and solution quality.

The shaking operator is implemented using the k-drop/add mechanism in the sixth line of the algorithm. This involves executing the drop/add operator k times, selecting k random shared patients, and inserting them into the lists of different depots where they can receive service. This process introduces significant changes to the current solution. The shaking step is performed once every 100 iterations. The goal is to avoid getting stuck in local optima.

Pseudo-code of the Variable Neighborhood Descent Algorithm

1. N_k choose the set of neighbor search operators
$(k = 1,2, \ldots, k_{max})$
2. Generate initial solution (s).
3. **Repeat**
4. $k := 1$
5. **Repeat**
6. Obtain the best neighbor s' of s ($s' \in N_k(s)$).
7. **If** $f(s') < f(s)$;
8. $s := s'$ and $k := 1$
9. **Otherwise**;
10. $k := k + 1$
11. **If** $f(s') < f(s_{best})$;
12. $s_{best} := s'$ and $f(s_{best}) := f(s')$
13. **Until** $(k := k_{max})$
14. **Until** (Stopping Criteria)
15. The best-obtained solution s_{best}, $f(s_{best})$

A feasible solution is generated based on the sample problem presented in Figure 2 and its compatibility constraints. This solution is shown in Figure 4. On examining the solution presented in Figure 4, it is seen that Pharmacy-1 serves patients 5, 10, 9, 11, and 2; Pharmacy-2 serves patients 14, 3, 13, 12, and 4; and Pharmacy-3 serves patients 7, 8, 1, and 6.

Position	0	1	2	3	4	0	1	2	3	4	0	1	2	3
Current Solution	5	10	9	11	2	14	3	13	12	4	7	8	1	6
Pharmacy	Pharmacy-1					Pharmacy-2					Pharmacy-3			

Figure 4. The current solution of the sample problem presented in Figure 2.

The solution presented in Figure 4 is considered as the current solution in the VND algorithm. Based on this current solution, the neighbor search operators and the shaking mechanism used in the structure of the algorithm are visually explained in Figures 5.a, 5.b, 5.c, 5.d, and 5.e, respectively.

Randomly Selected Pharmacy	2	
Randomly Selected Positions	1	3

Position	0	1	2	3	4	0	1	2	3	4	0	1	2	3
Current Solution	5	10	9	11	2	14	3	13	12	4	7	8	1	6

Position	0	1	2	3	4	0	1	2	3	4	0	1	2	3
Neighbor Solution	5	10	9	11	2	14	12	13	3	4	7	8	1	6

Figure 5.a. Illustration of swap operator.

Randomly Selected Pharmacy	1	
Randomly Selected Positions	2	0

Position	0	1	2	3	4	0	1	2	3	4	0	1	2	3
Current Solution	5	10	9	11	2	14	3	13	12	4	7	8	1	6
Position	0	1	2	3	4	0	1	2	3	4	0	1	2	3
Neighbor Solution	9	5	10	11	2	14	3	13	12	4	7	8	1	6

Figure 5.b. Illustration of insert operator.

Randomly Selected Pharmacy	2	
Randomly Selected Positions	1	4

Position	0	1	2	3	4	0	1	2	3	4	0	1	2	3
Current Solution	5	10	9	11	2	14	3	13	12	4	7	8	1	6
Position	0	1	2	3	4	0	1	2	3	4	0	1	2	3
Neighbor Solution	5	10	9	11	2	14	4	12	13	3	7	8	1	6

Figure 5.c. Illustration of the reverse operator.

Randomly Selected Shared Patient	1	
Randomly Selected Pharmacy and Position	1	3

Position	0	1	2	3	4	0	1	2	3	4	0	1	2	3
Current Solution	5	10	9	11	2	14	3	13	12	4	7	8	1	6
Position	0	1	2	3	4	5	0	1	2	3	4	0	1	2
Neighbor Solution	5	10	9	1	11	2	14	3	13	12	4	7	8	6

Figure 5.d. Illustration of drop/add operator.

Randomly Selected Shared Patient	1			2			3			4			5	
Randomly Selected Pharmacy and Position	1	0		2	3		1	4		3	0		3	2

Position	0	1	2	3	4	0	1	2	3	4	0	1	2	3
Current Solution	5	10	9	11	2	14	3	13	12	4	7	8	1	6
Position	0	1	2	3	4	0	1	2	3	0	1	2	3	4
Neighbor Solution	1	10	9	3	11	14	13	2	12	4	7	5	8	6

Figure 5.e. Illustration of shaking mechanism.

In the VND pseudo-code, the acceptance criterion function is found on the seventh line. The generic VND acceptance criterion does not allow the acceptance of solutions that do not improve the current solution, as it only accepts better solutions based on the objective function value. This restriction can limit the search space and increase the likelihood of becoming trapped in local optima. To address this, we revised the generic acceptance criterion by replacing it with a function proposed by Dueck (1993) to obtain higher-quality solutions.

The objective function value of the best solution found during the search is referred to as the record, denoted by $f(s_{best})$. The deviation parameter is represented by D. The new acceptance criterion function is expressed as follows (Equation 13):

$$\mathrm{f(s') < \ Record + D} \tag{13}$$

Then, the record value is updated according to the objective function value of the best solution $f(s_{best})$. This dynamically adjusts the acceptance threshold for neighbor solutions, allowing the exploration of inferior solutions to reduce the chances of getting trapped in local optima.

Since the number of vehicles to be used is not yet certain, the list is not divided into specific vehicle routes at this stage. A mechanism is needed to create vehicle routes from the patients assigned to each depot while also satisfying the time window constraints. To achieve this, the splitting method is incorporated into the variable neighborhood search algorithm. The splitting method allows a sequence to be divided into multiple routes, optimizing the separation to minimize total costs (Beasley, 1983; Prins, 2004). This method ensures feasible solutions for patients assigned to each depot in every iteration of the VND. The splitting method consists of two phases: the splitting procedure and the extraction of feasible vehicle routes. The pseudo-code of this method, along with the necessary notation, is provided below.

n	: Number of patients.
Sp_i	: Value of the shortest path from the depot to patient i.
$Tdistance$	: Total distance value.
$Ttime$	: Total time value.
$Pred_j$	: Predecessor of patient j.
S_i	: The i[th] member in the sequence of patients.

The First Step of the Splitting Method: The Splitting Procedure

```
Sp_0 := 0
For i := 1 to n:
    Sp_i := +∞
endfor
While (i ≤ n):
    Tdistance := 0, Ttime := 0, j := i
    While (j ≤ n and Ttime − t_{S_j 0} ≤ c_{S_j}):
        If (i == j):
            Tdistance := d_{o S_j} + d_{S_j 0}
            Ttime := t_{o S_j} + t_{S_j 0} + f_{S_j}
        Else:
            Tdistance := Tdistance − d_{S_{j−1} 0} + d_{S_{j−1} S_j} + d_{S_j 0}
            Ttime := Ttime − t_{S_{j−1} 0} + t_{S_{j−1} S_j} + t_{S_j 0} + f_{S_j}
        endif
        If (Ttime − t_{S_j 0} ≤ c_{S_j}):
            If (Sp_{i−1} + Tdistance < Sp_j):
                Sp_j := Sp_{i−1} + Tdistance
                Pred_j := i − 1
            endif
            j := j + 1
        endif
    endwhile
    i := i + 1
endwhile
```

The Second Step of the Splitting Method: Extracting Feasible Routes

For $\mathbf{i} \coloneqq \mathbf{1}$ **to** $\mathbf{n}$:
  $Route_i \coloneqq \emptyset$
endfor
$t \coloneqq 0$
$j \coloneqq n$
While $(\mathbf{i} \neq \mathbf{0})$:
  $t \coloneqq t + 1$
  $i \coloneqq Pred_j$
  For $\mathbf{k} \coloneqq \mathbf{i} + \mathbf{1}$ **to** $\mathbf{j}$:
    $enqueue(Route_t, S_k)$
  endfor
  $j \coloneqq i$
endwhile

The algorithm's termination is based on the number of iterations. Once the specified maximum number of iterations is reached, the algorithm is terminated, and the best solution identified during the search process is reported.

5. COMPUTATIONAL RESULTS

Ten test problems of different sizes were created to assess the performance of the proposed mixed integer programming model and the VND algorithm in addressing the problem. The specific characteristics of these test problems are outlined in Table 1.

Table 1. Characteristics of the test problems

Problem	Number of Patients	Number of Shared Patients	Number of Depots (Pharmacies)	Number of Vehicles in Each Depot (Pharmacy)
P-1	10	3	2	2
P-2	14	5	3	2
P-3	17	4	2	2
P-4	22	3	2	2
P-5	30	6	3	3
P-6	40	8	3	4
P-7	50	10	4	4
P-8	70	15	4	4
P-9	100	20	5	4
P-10	200	50	8	6

The test problems outlined in Table 1 incorporate several additional parameters beyond those previously mentioned. These include:

- The distance matrix between nodes (patient-patient, patient-pharmacy),
- The patient-vehicle color matrix,
- The travel time between nodes,
- The service time for each patient,
- The earliest and latest service times for each patient.

The distance matrix is symmetric, with values randomly generated between 5 and 100. The patient-vehicle color matrix consists of binary values {0,1}. Among the test problems, P-10 is the most challenging, comprising 200 patients, 50 shared patients, 8 depots (pharmacies), and 6 vehicles per depot (pharmacy). This problem was specifically designed to evaluate the problem-solving capabilities of the developed metaheuristic algorithm. (The test problems listed above in Table 1 are available at https://dataandresults.wixsite.com/darp).

This study addresses the MD-GCTSP-TW under certain assumptions. These assumptions are stated below.

- The travel time between nodes was calculated, which vehicles travel one unit of distance in one unit of time.
- Each patient's service time was set to five units of time.
- While no specific restrictions were placed on the earliest service time for patients, the latest service time was considered with random values generated for this parameter.
- Since over-the-counter medications and healthcare supplies are delivered from pharmacies to patients, it is assumed that the capacity utilization rates for these supplies are low. Therefore, it is assumed that the vehicle capacities are sufficient for the patients assigned to them. However, the critical point to consider here is that even though vehicle capacities are sufficient, multiple vehicles are required to ensure that patients are served within their time windows.

The components of the VND metaheuristic algorithm used to solve the test problems were designed as follows. The initial solution for all test problems was generated randomly, considering the patient-vehicle color matrix. This random initialization strategy was intended to enhance the algorithm's exploration capability by starting the optimization process from different regions of the solution space. Four distinct neighbor search operators—swap, insert, reverse, and drop/add—were employed across all test problems to generate neighbor solutions from the current one. These operators are crucial in the local search phase of the VND algorithm and play a significant role in intensifying the search process.

During the shaking phase of the algorithm, the k-drop/add operator was used, with the value of k set to 5 for problems P-1, P-2, P-3, P-4, P-5, and 10 for problems P-6, P-7, P-8, P-9, P-10. This approach ensures the effective execution of the k-drop/add operator, scaling appropriately with problem size. It also bolsters the algorithm's diversification mechanism, enabling a more comprehensive exploration of the solution space, particularly in the context of the complex and challenging characteristics of the MD-GCTSP-TW. The stopping criterion for the algorithm, based on the number of iterations, was tailored to the size and complexity of each problem: 5,000 iterations for P-1 and P-2; 10,000 for P-3; 50,000 for P-4, P-5, P-6, and P-7; 75,000 for P-8; 150,000 for P-9 and 200,000 for P-10. The deviation value in the acceptance criterion function (Equation 13) was determined to balance exploration and exploitation in the search space. Therefore, this value was specified as 10 for P-1, P-2, P-3, and P-4, and 25 for P-5, P-6, P-7, P-8, P-9, and P-10.

The proposed mixed integer mathematical model and the metaheuristic algorithm were implemented using Python 3.7 programming language. The Gurobi solver was utilized in Python 3.7 to solve the mixed integer mathematical model. These methods were executed on an Intel Core i9 2.5 GHz computer with 32 GB of RAM. The results obtained using these methods are summarized in Table 2. Additionally, the proposed metaheuristic algorithm was run 10 times for each test problem, and the best results obtained are presented.

Table 2. Computational Results of the Test Problems

Problem	**Mixed Integer Mathematical Model**		**Variable Neighborhood Descent Algorithm**	
	Total Distance	**Computation Time (second)**	**Total Distance**	**Computation Time (second)**
P-1	312	0.5	312	1.5
P-2	562	40.9	562	2.7
P-3	377	5.3	377	5.1
P-4	600	1,108.2	600	31.2
P-5	N/A	10,800	678	35.6
P-6	N/A	10,800	776	58.9
P-7	N/A	10,800	1,096	63.7
P-8	N/A	10,800	1,347	124.9
P-9	N/A	10,800	1,681	355.4
P-10	N/A	10,800	2,723	1412.5

The mixed integer mathematical model was executed with a time limit of 10,800 seconds. Within this time frame, optimal solutions were obtained for four problems (P-1, P-2, P-3, and P-4), all of which can be classified as small-scale. As the problem size increases, with more patients, depots (pharmacies), and vehicles, the time required to solve the problem also increases. For problems P-5 and larger, optimal solutions could not be achieved within the 10,800-second limit, reflecting the NP-hard nature of the MD-GCTSP-TW.

In contrast, the proposed metaheuristic method successfully obtained high-quality solutions for all the problems within realistic computation times. A comparison of the two methods, particularly for the first four problems, shows that the metaheuristic algorithm reached the optimal solutions much faster. Additionally, a high-quality solution for the largest test problem, P-10, was obtained in approximately 24 minutes. This is remarkable, considering that the problem involves 200 patients (including 50 shared patients), eight depots (pharmacies), and six vehicles per depot (pharmacy), all while accounting for time window constraints and the service constraints inherent to the CTSP. This outcome highlights the effectiveness and practical applicability of the metaheuristic algorithm for the MD-GCTSP-TW. Figure 6 provides a detailed depiction of the optimal vehicle routes corresponding to the objective function of problem P-2.

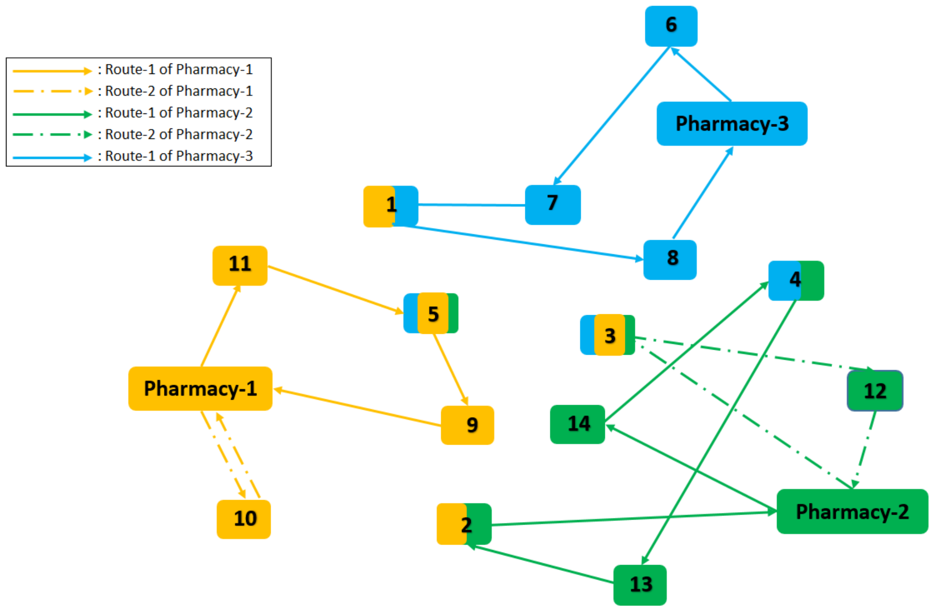

Figure 6. Vehicle routes obtained for P-2.

Figure 6 illustrates the vehicle routes departing from each pharmacy, using the same color scheme as the respective pharmacy. If two vehicles are dispatched from the same pharmacy, the second vehicle's route is represented with dashed lines, although it retains the same color as the pharmacy. In the optimal solution for problem P-2, patient medication needs are met using a total of five vehicles: two from Pharmacy-1, two from Pharmacy-2, and one from Pharmacy-3. The resulting vehicle routes are as follows:

Pharmacy-1 (1st vehicle route): (Pharmacy-1) – (11) – (5) – (9) – (Pharmacy-1).
Pharmacy-1 (2nd vehicle route): (Pharmacy-1) – (10) – (Pharmacy-1).
Pharmacy-2 (1st vehicle route): (Pharmacy-2) – (14) – (4) – (13) – (2) – (Pharmacy-2).
Pharmacy-2 (2nd vehicle route): (Pharmacy-2) – (3) – (12) – (Pharmacy-2).
Pharmacy-3 (1st vehicle route): (Pharmacy-3) – (6) – (7) – (1) – (8) – (Pharmacy-3).

An evaluation of these routes reveals that patients are serviced by the pharmacies best suited to their needs. Among the shared patients, Pharmacy-1 serves patient-5, Pharmacy-3 serves patient-1, and Pharmacy-2 serves the other patients (2, 3, 4). The service constraints inherent to the CTSP, such as patient service requirements, are satisfied by the routes obtained. Additionally, the routes were designed to respect each patient's time window, ensuring that their medication needs were met within the designated times.

As an example, we can examine the route of the first vehicle in Pharmacy-1. The pharmacies are assumed to start their service at 09:00. The latest service times (c_i: The latest service time of patient i) for patients on this route are $c_{11} = 09{:}35$, $c_5 = 10{:}40$, and $c_9 = 10{:}15$. When the obtained route is analyzed, the times when the vehicle meets the demands of the relevant patients and completes its service are 9:31 for patient-11, 10:00 for patient-5 and 10:14 for patient-9. The patients' demands were met before the latest service time, and the patients' time window constraints were satisfied.

The total distances traveled by vehicles from Pharmacy-1 are 94 and 48 units, respectively. For Pharmacy-2, the distances are 95 and 148 units, and for Pharmacy-3, the total distance is 177 units. In summary, the medication needs of 14 patients were met by three pharmacies using five vehicles, covering a total distance of 562 units.

The number of iterations used as the stopping criterion and the deviation parameter in the acceptance criterion function (Equation 13) are discussed above. These parameter values were determined based on the size of the test problems and to provide a balanced operation of exploration and exploitation mechanisms during the search phase. Hence, the goal is to explore different solution areas in the search space and deeply investigate high-quality solution areas to obtain optimal solutions. Each test problem was solved using different numbers of iteration and deviation values. The appropriate parameter values were determined by considering the solution quality and computation time. For example, the large-scale test problem P9 was solved with the VND algorithm using different numbers of iteration and deviation values. VND algorithm was run 10 times for each parameter value, and results of the parameter analysis for P9 are presented in Figures 7a, 7.b, and 7.c.

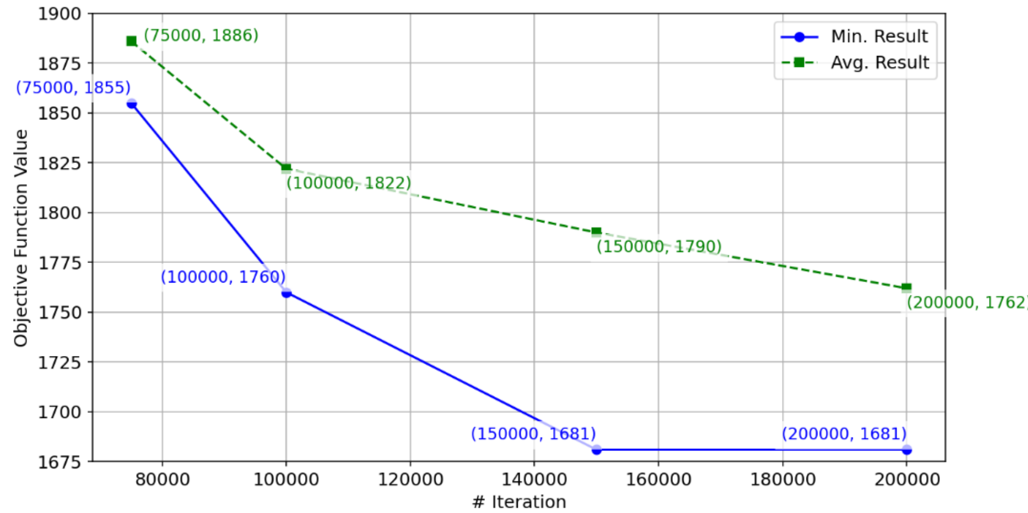

Figure 7.a. Solution quality analysis with different number of iterations for P9.

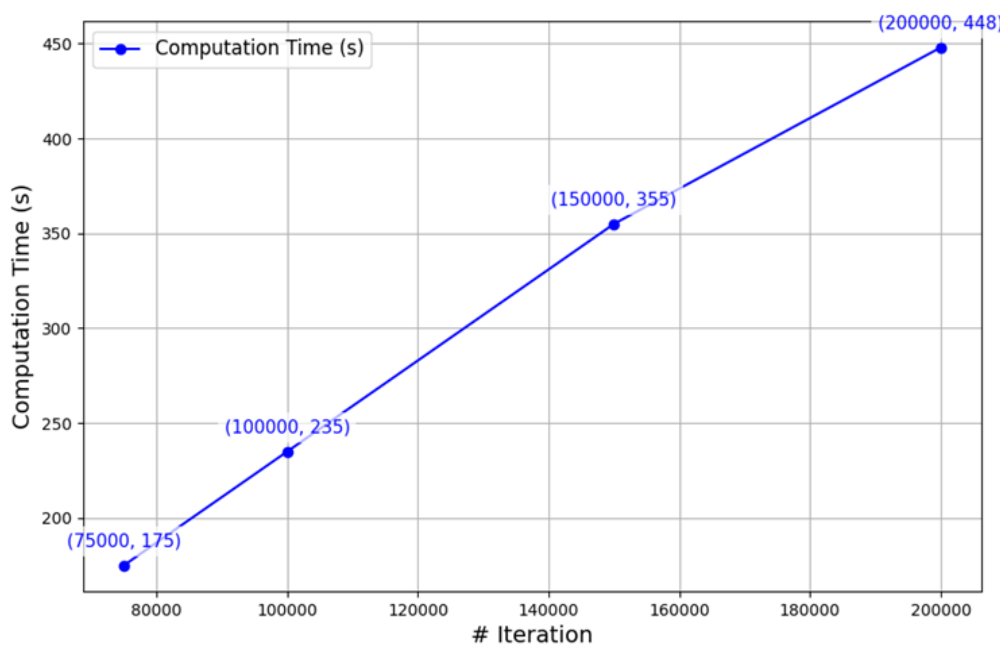

Figure 7.b. Solution quality analysis with different number of iterations for P9.

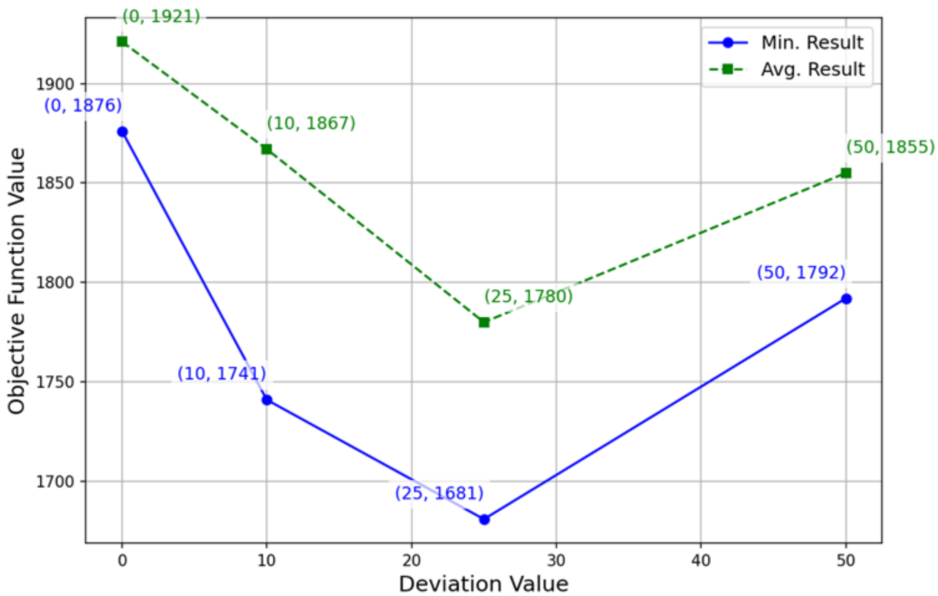

Figure 7.c. Solution quality analysis with different number of iterations for P9.

In Figure 7.a, the deviation value is fixed at 25, and the minimum and average objective function values obtained with different iterations are presented. For example, at 75,000 iterations, the minimum objective function value is 1,855, while the average objective function value is 1,886. At 100,000 iterations, these values are 1,760 and 1,822, respectively. Thus, it is evident that as the number of iterations increases, the algorithm obtains better results. However, an important point to note is that the same minimum objective function value (1681) was obtained at both 150,000 and 200,000 iterations. This indicates that increasing the number of iterations more does not improve solution quality. Therefore, the number of iterations for the P9 problem is set to 150,000.

An analysis was also conducted regarding computation time for different numbers of iterations, and the results are presented in Figure 7.b. For instance, when the VND algorithm is run for 75,000 iterations, the computation time is 175 seconds, whereas for 100,000 iterations, the computation time increases to 235 seconds. This analysis shows that as the number of iterations increases, the computation time also increases. However, since solution quality does not improve beyond 150,000 iterations, further increasing the number of iterations is unnecessary.

In Figure 7.c, the number of iterations is fixed at 150,000, and the minimum and average objective function values obtained with different deviation values are presented. Examining this graph, when the deviation value is set to 10, the minimum and average results are 1,741 and 1,867, respectively. On the other hand, the deviation value is set to 25, and these values are 1,681 and 1,780, respectively. Therefore, considering the results obtained for all deviation values, the best solution is obtained when the deviation value is set to 25. For this reason, the deviation parameter is determined as 25.

The parameter values for the real-world application example presented in Figure 3 are shared at https://dataandresults.wixsite.com/darp. This problem was solved using the mixed integer mathematical model and the VND algorithm. In the VND algorithm, the deviation value was set to 1,000, and the number of iterations was set to 10,000 for this problem. The other mechanisms of the algorithm were applied as described above. The vehicle routes obtained for this problem are presented in Figure 8.

The optimal solution for the presented real-world problem was obtained with both solution approaches. The computation time for the mixed integer mathematical model is 2.5 seconds, while the computation time for the VND algorithm is 1.5 seconds. Analyzing the optimal vehicle routes (as presented in Figure 8), a single vehicle from Pharmacy-1 served patients 1, 4, 10, 9, 3, and 2, respectively. The total distance traveled by this vehicle was obtained as 21,448.11 meters. Pharmacy-2 used two vehicles: the first vehicle served patients 7, 8, 6, and 5, while the second vehicle served patients 13, 12, and 11. The distances traveled by these two vehicles were 17,148.14 meters and 23,629.88 meters. Consequently, the total distance traveled by all vehicles (i.e., the objective function value) was 62,226.13 meters. In this problem, patients 10, 12, and 13 could be served by either pharmacy. Based on the optimal solution, patients 12 and 13 were served by Pharmacy-2, while patient 10 was served by Pharmacy-1.

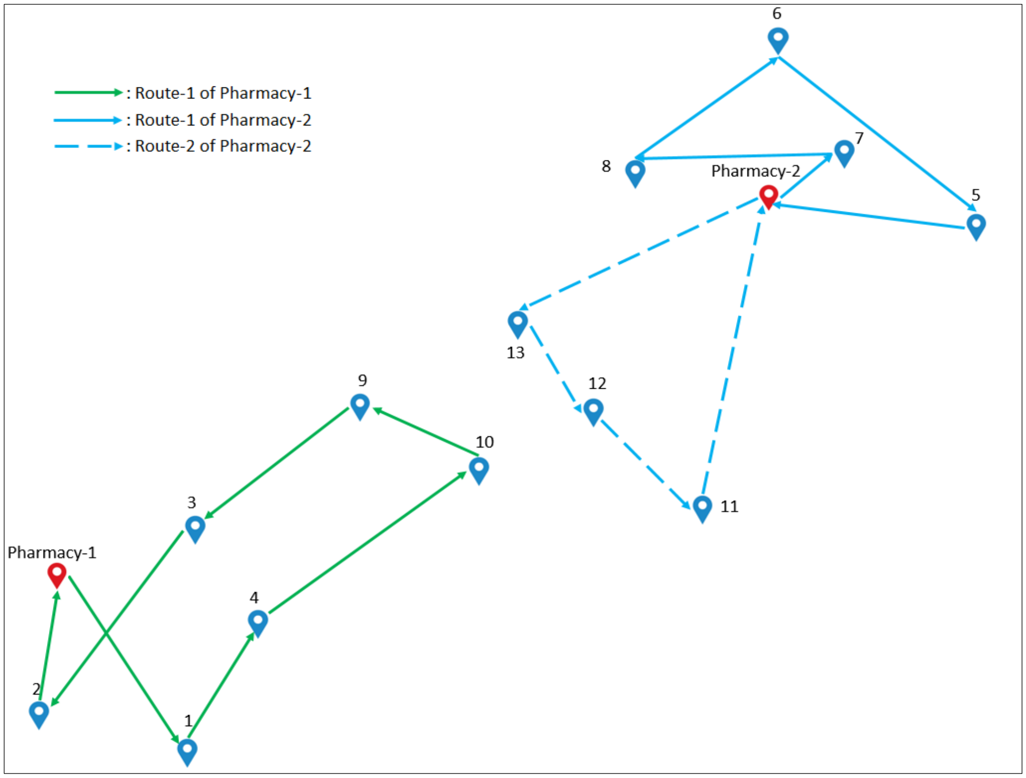

Figure 8. Vehicle routes obtained for a real-world example.

6. COMPARISON OF SOLUTION METHODS

In this study, a mixed integer mathematical model and a VND algorithm were used to solve the MD-GCTSP-TW. Detailed information on these solution approaches is presented above. In this section, the performance of the proposed solution approaches was compared. The performance of the mixed integer mathematical model and VND algorithm was compared in terms of solution quality and computation time based on the results obtained from the test problems and is shown in Figure 9.

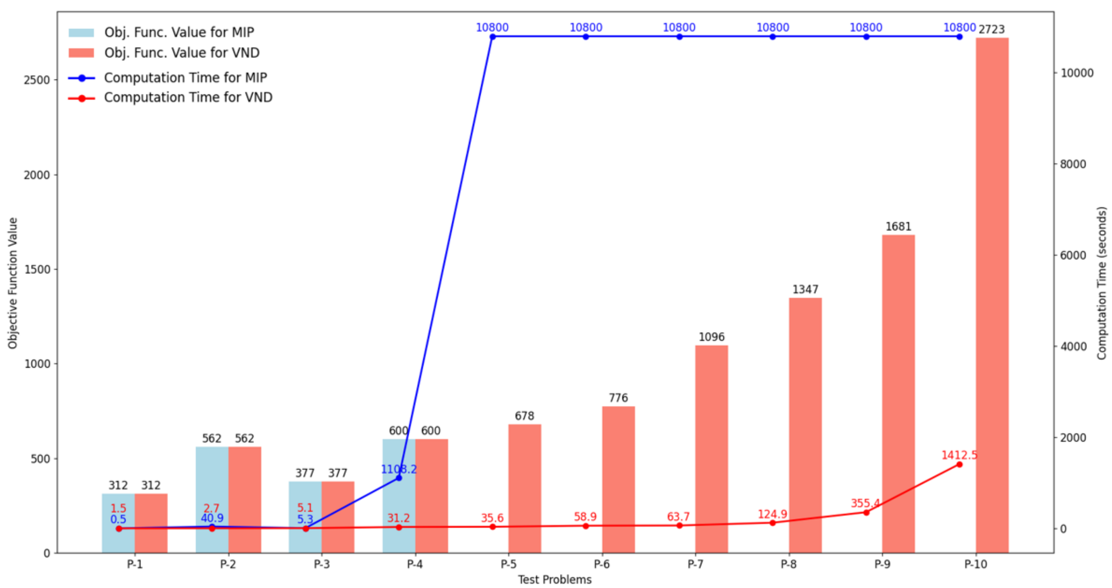

Figure 9. Performance analysis of mixed integer mathematical model and VND algorithm.

Examining the data shown in Figure 9, since MD-GCTSP-TW is NP-hard, the mixed integer mathematical model could only obtain optimal solutions for small-sized problems (P-1, P-2, P-3 and P-4) within reasonable computation times (10,800 seconds). On the other hand, with the VND algorithm, optimal results were obtained for small-sized problems, and quality results were achieved for medium and large-sized problems in reasonable computation times. In this case, it becomes necessary to use another metaheuristic algorithm to evaluate the performance of the VND algorithm. Therefore, to evaluate the performance of the VND algorithm for medium- and large-sized problems, the RVNS algorithm was used. The RVNS algorithm was introduced in 1999 by Hansen and Mladenovic as one of the variants of the Basic Variable Neighborhood Search (BVNS) algorithm. Unlike BVNS, the local search phase is omitted in the RVNS algorithm. Below are the steps of the RVNS algorithm (Hansen *et al*., 2019).

Pseudo-code of the Reduced Variable Neighborhood Search Algorithm

Select the set of neighborhood structures N_k for $k = 1, \dots, k_{max}$ that will be used in the search.
Generate an initial solution.
Choose a stopping condition.
Repeat
    Set $k \leftarrow 1$
    Repeat
        Generate a point x' at random from the kth neighborhood of $x(x' \in N_k(x))$
        If this point is better than the current solution, move there $(x \leftarrow x')$, and continue the search with $N_1(k \leftarrow 1)$; otherwise, set $k \leftarrow k + 1$;
    Until $(k = k_{max})$
Until $(stopping\ condition\ is\ met)$

The RVNS algorithm's key feature is its speed and ability to use several neighbor search operators. Removing a local search phase provides the getting of quality solutions quickly. To compare the performance of both algorithms appropriately, the neighbor search operators and stopping condition in the RVNS algorithm are set to the same as those used in the VND algorithm. Each test problem was solved 10 times using both algorithms, and the best results obtained are presented in Table 3.

Table 3. Computational Results of the metaheuristic algorithms

Problem	Variable Neighborhood Descent Algorithm		Reduced Variable Neighborhood Search Algorithm	
	Total Distance	Computation Time (second)	Total Distance	Computation Time (second)
P-1	312	1.5	312	0.4
P-2	562	2.7	562	1.2
P-3	377	5.1	377	2.7
P-4	600	31.2	622	13.5
P-5	678	35.6	696	16.1
P-6	776	58.9	838	27.3
P-7	1,096	63.7	1,206	30.7
P-8	1,347	124.9	1,536	55.9
P-9	1,681	355.4	1,945	155.4
P-10	2,723	1412.5	3,188	611.6

When the computational results presented in Table 3 are examined, it is observed that the VND algorithm provides better-quality solutions than the RVNS algorithm. For example, for the P-10 problem, the total distance (objective function value) obtained with the VND algorithm is 2,723, while the total distance obtained with the RVNS algorithm is 3,188. Therefore, the result of the RVNS algorithm is approximately 17% worse than the result of the VND algorithm for P-10. On the other hand, for the P-1, P-2, and P-3 problems, the same results were obtained with both algorithms, while for other test problems, better solutions were achieved with the VND algorithm. The only advantage of the RVNS algorithm is the shorter computation time. However, the VND algorithm demonstrated superior performance compared to the RVNS algorithm in terms of solution quality.

7. CONCLUSIONS AND FUTURE WORKS

Medication distribution is a critical component of home healthcare, particularly during lockdowns when access to medication becomes challenging for individuals who are elderly, physically or psychologically disabled, or otherwise need assistance. These individuals often strive to live independently in their homes, making the delivery of medication essential. This study addresses the medication delivery problem by modeling it mathematically using the Multi-Depot Generalized Colored Traveling Salesman Problem with Time Windows.

To tackle this problem, we developed a mixed integer mathematical model and a metaheuristic algorithm, the Variable Neighborhood Descent. We generated ten test problems to evaluate the performance of these proposed methods. While the mixed integer model successfully reached optimal solutions for small-sized problems, it was unable to do so for medium- and large-sized problems within a 10,800-second time limit due to the problem's complexity. Therefore, we employed the VND algorithm, which was specifically tailored to address the intricacies of the MD-GCTSP-TW. The VND algorithm proved highly effective, delivering high-quality solutions in a remarkably short time. Even for the largest test case, P-10, which involved 200 patients, eight depots (pharmacies), and six vehicles per depot (pharmacy), a high-quality solution was obtained in just 24 minutes. This highlights the efficiency and robustness of the algorithm in solving complex problems.

Based on the computational results, the performance of the VND algorithm was compared with the RVNS algorithm from the literature. The solution quality obtained using the proposed VND algorithm was never worse than that obtained by the RVNS algorithm for any test instance. Especially, for the large-sized test problems P-8, P-9, and P-10, the solutions obtained using the VND algorithm were approximately 15% better. This indicates that the components of the VND algorithm were effectively designed for the MD-GCTSP-TW. The only disadvantage of the VND algorithm compared to the RVNS algorithm is its higher computational time. However, considering that even the largest test problem was solved within approximately 24 minutes, this period is considered acceptable. Besides, a real-world application of the problem was discussed using data from two retail pharmacies in Indiana, USA. This problem was solved by using both the VND algorithm and the mixed integer mathematical model. The optimal solution was obtained with both solution methods. Therefore, the effectiveness of the proposed solution approaches in addressing real-world problems was clearly demonstrated.

In this study, MD-GCTSP-TW was considered under some assumptions. When these assumptions are examined in terms of practical implications, the following comments can be made.

- The assumption that one unit of distance is equal to one unit of time provides a scalable and understandable structure for calculating travel time. In addition, in real-world problems, this structure can be adjusted by incorporating parameters such as traffic congestion, which changes travel times. In this case, the proposed solution approaches can still provide solutions suitable for the new parameter values.
- To simplify operations and planning, a fixed service time was used in this study. In real scenarios, this duration may vary based on patient needs and can be used flexibly. In such cases, the parameter value of service time should be updated.
- The latest service time parameter used in this study is highly compatible with real-life constraints. In real scenarios, patients expect pharmacies to provide services at the promised time and following service agreements.
- Assuming low capacity utilization due to the nature of the supplies aligns with real-world cases where over-the-counter medications are lightweight and compact. Therefore, we assume that the vehicle capacities are sufficient for the patients assigned to them.

The VND algorithm developed in this study has potential applications across various home healthcare services. Future research could extend the problem addressed here (i.e., medication delivery) to other scenarios, such as distributing test kits or vaccines. Given the similar setup of depots and patients, it is anticipated that the proposed algorithm will continue to perform effectively in these contexts, as demonstrated in this study.

Moreover, future research could explore the use of the collaboration of drones and vehicles for medication delivery based on MD-GCTSP-TW. Investigating the feasibility, efficiency, and safety of drone-based delivery systems could lead to innovative solutions that enhance global healthcare accessibility.

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