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An integrated discrete event simulation and particle swarm optimisation model for optimising efficiency of cancer diagnosis pathways☆

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ABSTRACT

The National Health Service (NHS) constitution sets out minimum standards for rights of access of patients to NHS services. The 'Faster Diagnosis Standard' (FDS) states that 75% of patients should be told whether they have a diagnosis of cancer or not within 28 days of an urgent GP referral. Timely diagnosis and treatment lead to improved outcomes for cancer patients, however, compliance with these standards has recently been challenged, particularly in the context of operational pressures and resource constraints relating to the COVID-19 pandemic. In order to minimise diagnostic delays, the National Physical Laboratory in collaboration with the Royal Free London (RFL) NHS Foundation Trust address this problem by treating it as a formal resource optimisation, aiming to minimise the number of patients who breach the FDS. We use discrete event simulation and particle swarm optimisation to identify areas for improving the efficiency of cancer diagnosis at the RFL. We highlight capacity-demand mismatches in the current cancer diagnosis pathways at the RFL, including imaging and endoscopy investigations. This is due to the volume of patients requiring these investigations to meet the 28-day FDS target. We find that increasing resources in one area alone does not fully solve the problem. By looking at the system as a whole we identify areas for improvement which will have system-wide impact even though individually they do not necessarily seem significant. The outcomes and impact of this project have the potential to make a valuable impact on shaping future hospital activity.

1. Introduction

The National Health Service (NHS) constitution sets out minimum standards for rights of access of patients to NHS services [1]. For cancer patients there are nine operational standards which cover the whole treatment pathway from receipt of referral to treatment. Compliance with these standards has recently been challenged, particularly in the context of operational pressures and resource constraints relating to the COVID-19 pandemic. However, delivering timely treatment for cancer is now more important than ever since it is evident that a significant number of cancer patients throughout the pandemic have been delayed in their presentation to services [2].

Symptoms with positive predictive value of cancer have been used to create NICE guidance for urgent referral to be seen within 2 weeks [3]. Additionally, in April 2020 a new 'Faster Diagnosis Standard' (FDS) [4,5] was introduced which states that patients should be told whether they have a diagnosis of cancer or not within 28 days of an urgent GP referral. This target is currently set at 75%. The overall standard for cancer diagnosis and treatment is 85% of patients starting treatment within 62 days of an urgent GP referral [6]. Evidence suggests that timely diagnosis and treatment leads to improved outcomes for cancer patients [7–9]. To achieve the FDS standard evidence-based Timed Diagnostic Pathways have been developed and provide milestones for most appropriate sequence and combination of investigations [10].

The Royal Free London (RFL) NHS Foundation Trust is a large provider of cancer treatment in North London, with a catchment area reach including specialised services of 2.5 million patients, and receives the second largest volume of urgent GP referrals for suspected cancer in the NHS [11]. Ensuring there is sufficient capacity to diagnose and treat incoming referrals in line with national targets is a priority which presents challenges. Meeting this challenge is critical as modelling suggests a likely increase in the number of cancer deaths due to diagnostic delays caused by the pandemic [12].

In order to minimise diagnostic delays, the National Physical Laboratory (NPL) in collaboration with the RFL has proposed addressing this problem by treating it as a resource optimisation problem, aiming

☆ Using cancer diagnosis process data to identify bottlenecks and areas for improving efficiency within a London hospital trust.

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to minimise the number of patients who breach the FDS. Although the FDS for cancer diagnosis is that 75% of patients receive a diagnosis within 28 days of urgent GP referral, the RFL set an internal target, which we use in this study, of 85% in order to align with the target for timely treatment. This also aligns with the overall standard for care target of 85% of patients starting treatment within 62 days of urgent GP referrals.

1.1. Literature review

Various aspects can lead to delays in cancer pathways, such as the impact of patients moving between secondary and tertiary centres. Methods have been used to investigate or explain these delays using audits [13], qualitative methods [14], and mixed methods [15]. A shift in resources required to prioritise urgent referrals may increase the waiting times for non-urgent referrals, causing delays. Similarly, diversion of resources to one pathway with high volume of referrals such as skin cancer may result in loss from other cancer pathways unless all cancer pathways are considered simultaneously. Furthermore, referral patterns are not static but change stochastically, as a result of awareness-raising campaigns and other influences. Seasonal variations in presentation of cancers have been observed [16], impacting on relative utilisation of resources.

A particular challenge within healthcare is that re-design often must occur whilst services are still running. Being able to explore the potential impact of changes prior to implementation may help minimise the likelihood of changes having unintended consequences [17]. Simulation modelling to help understand resource allocation issues and explore different scenarios may therefore be of value for operational management of cancer pathways [18].

Discrete event simulation is a computer-based modelling approach that can be used to address such challenges in demand capacity modelling [19]. For example, examining diagnostic pathways for lung cancer in Wales demonstrated that ensuring the patient attends their first outpatient appointment within 7 days and streamlining the diagnostic tests would have the potential to remove approximately 20 days, resulting in a 20–25% increase of patients receiving treatment within 62 days. If patients begin their treatment within 21 days of diagnosis almost all patients would meet the 62-day target [20]. Streamlining interdependent pathways such as cancer referrals is a challenging task due to their high dimensionality and complex dependencies.

Optimisation theory is an interdisciplinary research area which draws techniques from Mathematics, Physics, Computer Science, and Engineering [19] and is well suited to solving high dimensional and interdependent tasks. Optimisation theory has applications in scheduling [20], resource allocation [21], communications [22], and data science [23] and has also led to numerous successes in industrial applications such as in manufacturing, where supply chains and factory floor layouts have been optimised to achieve cost savings and improved efficiency [24].

Particle swarm optimisation (PSO) is a type of optimisation algorithm that is widely applied to real-world optimisation [25,26]. The PSO algorithm was originally developed to simulate the collective behaviour of swarms of social animals such as fish [26]. The basis of the algorithm is that potential solutions to a given problem (such as parameter or weight values) are coded as individuals within a swarm. These potential solutions are typically randomly initialised and updated through successive iterative learning cycles [27]. For PSO, the individuals in the swarm have an associated position, the potential solution, and velocity in the search space [28]. During the learning cycles each individual is evaluated against the objective function. The algorithm retains the best solution from each particle and the best solution found by the swarm. The position and velocity of each individual is then updated based on the best values to balance local and global searching. PSO has been shown to converge faster than other common optimisation algorithms such as genetic algorithms [29] and simulated annealing [30] which is an essential requirement for methods to be clinically useful.

Some applications of optimisation in a clinical context have been used, e.g. to assign blocks in the operating room to reduce overcrowding in patient beds [31], for choosing the optimal location for new facilities [32] or for optimising operating room scheduling [33] but have been historically less widespread than in other application areas such as manufacturing and supply chain design [34].

PSO is a popular algorithm for optimisation problems due to its high performance and search efficiency for obtaining optimal solutions [35]. As such, they have been used in number of relevant application areas including disease detection and diagnosis [36–38], medical data analysis [39–41], resource allocation [42], task assignment [43] and scheduling problems [44,45].

1.2. This paper

In this work we formulate a resource allocation optimisation problem using PSO to optimise the efficiency of cancer diagnosis at the RFL. This paper describes how the problem was formulated and presents the optimised resources needed for the RFL to comply with diagnostic targets.

Data of current referral and diagnostic resource activity from hospital services in RFL were translated into a model which has subsequently been validated and optimised. Our aim is to create an optimal model which will provide a total service solution for all pathways simultaneously, compensating for any potential negative impact of resource allocation from one pathway on another. Here we present our work and discuss how this model was constructed and how it may be applied in the context of the NHS, which is now meeting the dual challenges of recovery from the first waves of the pandemic whilst maintaining heightened provision of care for patients affected by COVID-19.

2. Proposed model

This Section describes the formulation of the resource allocation optimisation problem, including the data provided, the way it was visualised and interpreted, the set-up of the model and the optimisation runs that were carried out. Firstly, we define the main concepts and variables used throughout the paper.

2.1. Main concepts and variables within the model

Throughout the rest of this paper, we frequently use some key terms and concepts. For clarity and ease of reference, we define these concepts in this Section.

Investigation: any step in the diagnostic pathway to the point of discharge or multi-disciplinary team (MDT) discussion at which the diagnosis of cancer is confirmed or refuted (e.g., Outpatient Appointment (OPA) Clinic, Ultrasound (US), Biopsy (Bx), . . . , MDT for breast, discharge).

Capacity: how many investigation slots are available in the model definition of a working day.

Current capacity values were calculated for each investigation type as follows:

- For imaging investigations (CT, MRI, PET, Ultrasound), the capacity was calculated using the number of scanners in the trust and the percentage of scanner time allocated to cancer patients for each scanner.
- For endoscopy investigations, the capacity was calculated using data about the number of endoscopy rooms running lists in the trust and number of points per list.
- For radiology and pathology reports and clinics, the capacities were estimated such that targets are achieved — e.g., biopsy reporting target is 7 calendar days.

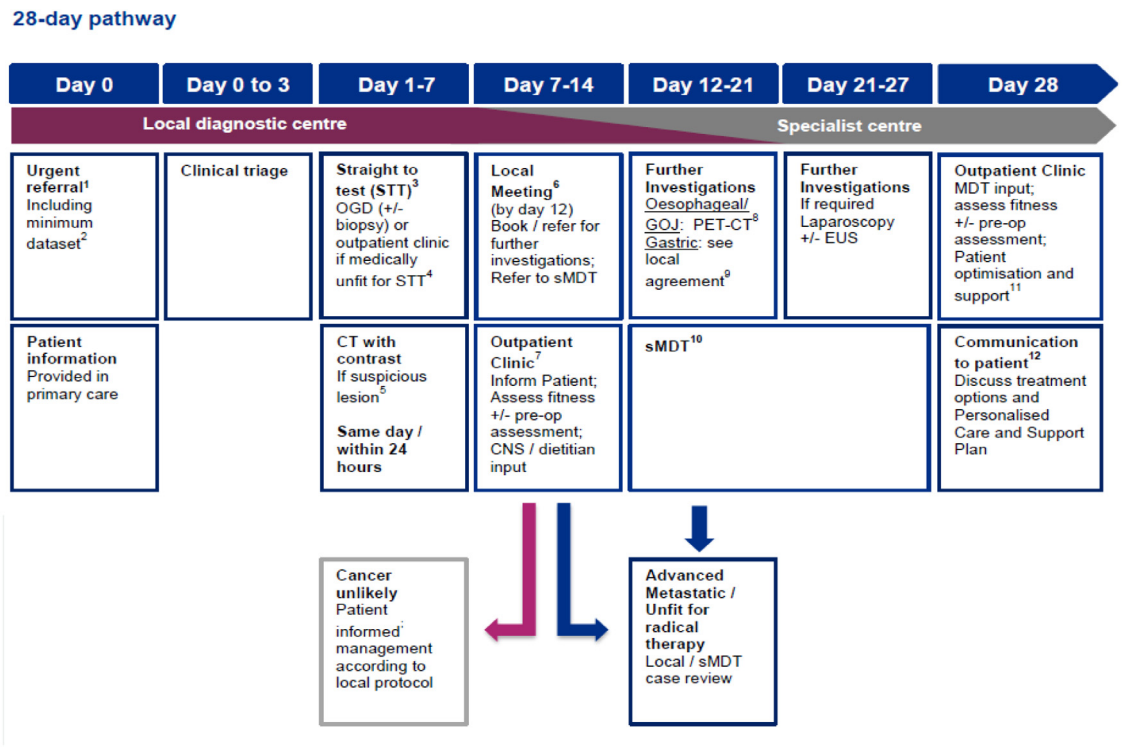


Fig. 1. Timed pathway map for Oesophageal cancer produced by NHS England [46].

- For remaining investigations, where no relevant data was available, numbers were set in consultation with relevant clinicians as far as possible (e.g., for examinations under anaesthetic (EUA)) or the capacity was set to an arbitrarily high number if the investigation was not a constraining factor (e.g., for referrals).

Optimised capacity values per investigation are an output of the optimisation model.

Timing: actual duration of each investigation per patient.

The timing values were calculated where possible per investigation using the activity data provided, as follows:

- For imaging investigations, the timings per investigation per tumour site were calculated from historical imaging activity data. The median and range of timings for each imaging modality are shown in Table 1. The minimum, median and maximum times were calculated from these data and weighted by how much time is available for cancer imaging compared to other examination types (elective, emergency, routine, etc.) — e.g., the median time for a lung CT is of the order of 15 min, but with the calculated weighting it is 2.6 h.
- For endoscopy investigations, a point system was used — each tumour site endoscopy has a certain number of points associated with it and each point equals 15 min.
- For the rest of the investigations, a well-informed estimation in consultation with clinicians was used as a timing.

Patients seen per day: calculated as capacity over timing per investigation.

Breach: when a patient has not received a diagnosis or otherwise of cancer by 28 days from referral and thus breaches the FDS standard

Working day: the model assumes a 7-day working week with 12-hour working days, but the model outputs have then been converted to a 5-day working week with 12-hour working days to reflect that > 90% of investigations are completed Monday–Friday.

Table 1
Timings from historical imaging activity data showing the median time used for each modality, and the range of times. The range shows the 10th to 90th interpercentile range to avoid extreme outliers.

Modality	Median scan time (min)	Time range (min)
CT	15	11–15
MRI	37	22–45
Mammography	15	6–15
PET CT	30	18–30
Ultrasound	20	8–20

2.2. Data provided

In order to formulate the resource allocation optimisation problem, a range of retrospective data from the Trust was provided that covered a period of one year (from April 2019–March 2020 inclusive), including:

- Monthly volume of referrals for each tumour site taken from the cancer information system — Somerset Cancer Registry (SCR) (see Table 2)
- Pathway maps that outline the typical sequence of steps for patients referred to a particular cancer pathway, provided for all cancer types that are diagnosed at the RFL (see Fig. 1)
- Activity data from the radiology information system, Computerised Radiology Information System (CRIS), along with hours of operation and number of scanners for each of the imaging modalities
- Activity data from the endoscopy information system, Unisoft, along with data on available capacity
- Activity data from the pathology information system, WinPath
- Historic performance against cancer access standards

No patient-identifiable information was included in formulating or running the resource allocation optimisation.

Hospital resources are finite and allocating resource between pathways is an interrelated problem as altering resources for one pathway

Table 2
Volume of urgent cancer referrals, per month, to each of the speciality teams at RFL from April 2019–March 2020. Data are taken from the Somerset Cancer Registry.

Period	2019/20 Q1				2019/20 Q2				2019/20 Q3				2019/20 Q4			
Sub-Category	Apr	May	Jun	Quarter	Jul	Aug	Sep	Quarter	Oct	Nov	Dec	Quarter	Jan	Feb	Mar	Quarter
Anal	<5	<5	<5	**<15**	<5	<5	<5	**<15**	<5	<5	<5	**<15**	<5	<5	<5	**<15**
Bladder	156	142	118	**416**	156	147	130	**433**	132	129	123	**384**	121	113	107	**341**
Brain/Central Nervous System	36	47	47	**130**	47	30	48	**125**	32	47	37	**116**	41	31	32	**104**
Breast	827	785	808	**2420**	882	706	721	**2309**	871	806	914	**2591**	818	856	627	**2301**
Dermatology	746	792	814	**2352**	949	925	898	**2772**	919	849	662	**2430**	788	636	663	**2087**
Gynaecological	313	298	277	**888**	304	280	274	**858**	292	294	308	**894**	293	176	233	**702**
Haematological	67	54	52	**173**	54	49	49	**152**	60	52	51	**163**	48	53	63	**164**
Head and Neck	226	256	219	**701**	261	220	242	**723**	279	248	237	**764**	239	264	229	**732**
HPB-HPB	8	10	5	**23**	6	10	10	**26**	18	9	14	**41**	5	11	5	**21**
Lower Gastrointestinal	607	626	554	**1787**	538	596	540	**1674**	677	636	550	**1863**	571	533	603	**1707**
Lung	117	127	129	**373**	120	106	117	**343**	133	160	134	**427**	126	140	81	**347**
Oesophago-gastric	207	214	196	**617**	217	204	225	**646**	271	247	223	**741**	248	199	203	**650**
Prostate	132	146	107	**385**	147	118	127	**392**	142	122	154	**418**	160	155	164	**479**
Renal	15	12	13	**40**	23	19	23	**65**	18	18	19	**55**	13	16	15	**44**
Testicular	8	14	7	**29**	15	9	18	**42**	12	11	12	**35**	11	15	15	**41**

may impact on another. For example, increasing the number of CT scans to deal with a spike in lung cancer referrals may lead to a decrease in the available capacity of CT scans for patients on a lower gastrointestinal pathway. For each cancer tumour site there is typically an optimal pathway that describes the ideal sequence of investigations and steps along a patient's cancer pathway, an example of which is outlined in Fig. 1 [46].

2.3. Model set up

The base resource allocation model was set up as a discrete-event simulation with fixed-increment time progression. In this model, patients are simulated with assigned cancer types, distributed according to the historical numbers seen by the RFL. They are then passed through the appropriate diagnostic pathway given their cancer type. For each stage of the pathway, e.g., investigations such as a CT scan or a biopsy being taken, there is an associated capacity (number of patients who may be seen at once) and time to complete. Once the patient completes their pathway, their total time in the system is logged. The model runs over a defined period of time, currently set to 24 weeks including 12 weeks of "warm-up" time to allow the system to fill with patients and stabilise, and every 28 days calculates the number of patients who breach the FDS. The 12-week warm up time was established by monitoring the system over a longer period of time and checking when the system started showing a stable output between consecutive 28-day windows. The base model run on a 64-bit Windows OS with 1.6 GHz CPU takes 5–10 min to complete.

This base model may be run with current capacities from the RFL to validate against their known breach numbers. It may then be run with an optimisation algorithm (described in Section 2.6) to minimise the output number of breaches by changing the capacities for each investigation.

Appendix A gives a more detailed description of the notation used in the code and an outlined pseudo-code.

In reality, the procedures and investigations needed by cancer patients do not always run to plan. Scanners break down, appointments get rearranged, and patients do not attend for various reasons. In the model this was taken into account by allowing for a random probability that a patient would be assigned to an investigation but not actually undergo the procedure. This probability, the "investigation not performed" rate, was set to 4.4% based on historical data from the RFL.

2.4. Data visualisation and problem formulation

Using the historical patient referral numbers (Table 2) and the recommended pathways for different cancer types (Fig. 1), a visualisation of the system where all pathways can be seen in a Sankey diagram is presented in Fig. 2. The width of each line is proportional to the number of patients referred for each type of cancer. Cancer referral types are colour coded. This shows that some investigations are only undertaken by patients with a single cancer type, and thus have relatively low patient numbers (e.g., orchidectomy in the testicular cancer pathway). Fig. 2 gives a clearer picture of where bottlenecks – i.e., investigations required by larger numbers of patients – might be.

All patients in this case were assumed to start their pathway at an out-patient "two-week wait" (2WW) clinic, and end with a (specialist) multi-disciplinary team meeting ([S]MDT) which resulted in a diagnosis of cancer, or not. In practice, some patients will enter their pathway by proceeding straight to an investigation and enter the clinic later. Similarly, some patients may be discharged before the MDT meeting. These fixed points are used here to simplify the model.

The data provided in the cancer pathways as described in Section 2.2 and Fig. 1 outline the order of investigations usually needed by patients with a given suspected cancer. In consultation with the RFL, some adaptations were made from the diagram in Fig. 2 in the problem formulation: in practice, rectal examinations are typically undertaken within the 2WW clinic, so these have been combined for the purposes of the model. Similarly, pathology as seen in Fig. 2 was combined with biopsy in the model as this is the same investigation at different times for the gynaecology pathway. Orchidectomy was removed due to the low patient numbers and limited scope for resource management.

For the model, the pathways were translated into a format that could be inputted into the optimisation model. We illustrate how this was achieved in Fig. 3. Each step in a given pathway is numbered sequentially — e.g., in the lung pathway, a Positron Emission Tomography/Computed Tomography (PETCT, #4) is always carried out before a biopsy (#6). Steps with the same order number also have a tag indicating whether the investigations are carried out in an arbitrary order, or only one/some of the investigations are needed – e.g., in the brain pathway, a patient could have a CT (#2) and CT report (#3) or an MRI (#2) and MRI report (#3). Tags also exist to indicate if a given investigation is always done, or only for some patients.

2.5. Validation

Before optimising any investigation capacities, the model was run with the RFL's current capacities (or estimates where exact figures were unavailable) to validate the output timings and number of expected breaches. The model output showed expected breaches of 33% with a range of approximately 0.5% either side of the median, i.e., 67% of patients were expected to be diagnosed within 28 days of referral. The historical numbers from the RFL for timely diagnosis range between 54%–76% with a median of 68%. This suggests that the timing and capacity numbers used in the model are reasonable estimates for the true values, with the median values matching very closely.

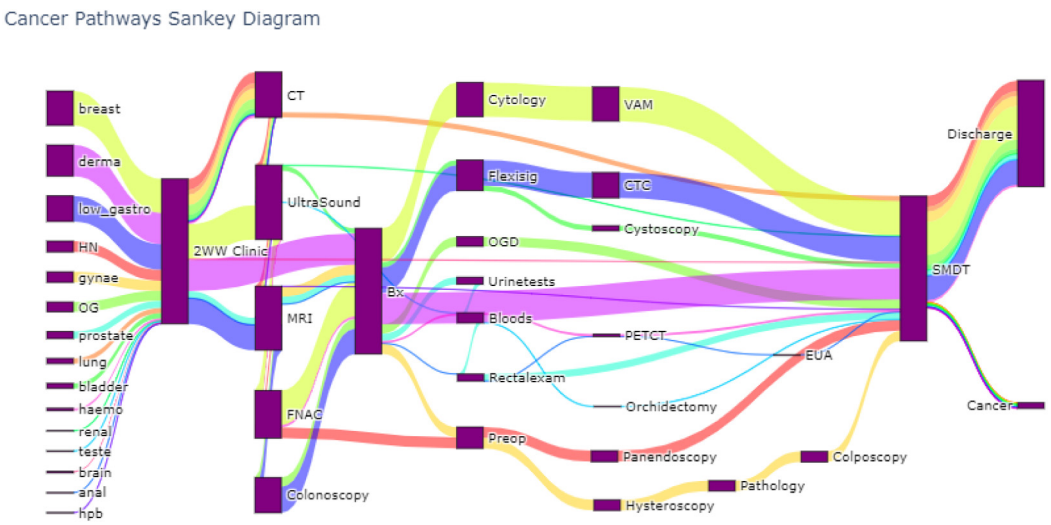
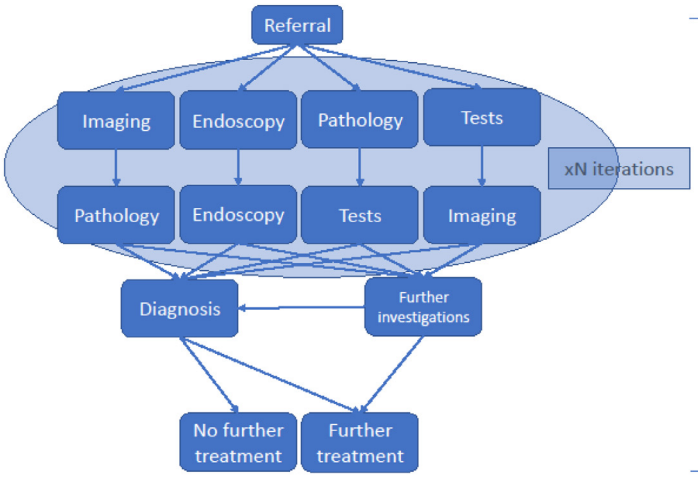


Fig. 2. A Sankey flow diagram depicting the various routes through cancer diagnosis pathways taken by patients. Purple blocks show investigations in the pathways; their height represents the number of patients requiring that investigation. Coloured ribbons show routes taken by patients with different suspected cancer types; the width of the lines represents the number of patients. HN here refers to head and neck cancers, OG refers to oesophago-gastric cancers.



		Referral	Imaging	Endoscopy	Pathology	Tests	Diagnosis	Further investigations	Treatment
Cancer type	Investigation needed and ordering	1	2	2	3	3	4	5	6
	Tag	Always	Always – order not important	Always – order not important	Sometimes – either/or	Sometimes – either/or	Always	Sometimes – 50% of time	Sometimes - 30% of time

Fig. 3. The translation of the cancer diagnosis pathways into a format readable by the optimisation model. Each step in a given pathway is numbered sequentially. Steps with the same order number also have a tag indicating whether the investigations are carried out in an arbitrary order, or only one/some of the investigations are needed. Tags also exist to indicate if a given investigation is always done, or only for some patients.

The optimisation outputs a capacity for each investigation. However, capacity is not measured in the same way for all investigations, e.g., physical number of scanners, staffing levels, room availability. To directly compare all investigations, we therefore convert the output capacity into patients seen per day. For this we assume a 12-hour working day, as historical data from the RFL shows 99% of cancer patients are seen between 08:00 and 20:00. We also assume a 5-day working week as fewer than 10% of cancer investigations are performed at weekends.

The optimisation outputs a capacity, C, i.e., the number of slots which may be used by patients. The unit for this is $[C]$ = patients (we use square bracket notation to define units). We convert this to patients seen per day by dividing it by the time it takes to process a single patient: T_1, where $[T_1]$ = days. Thus, the number of patients seen per day, N, is given by Eq. (1) and $[N]$ = patients/day. As an illustrative example, if the hospital had one CT scanner ($C = 1$ patients) and each patient took 0.1 days (1.2 h in a 12-hour day) to have a CT scan ($T_1 = 0.1$ days), then the number of patients seen in CT per day is $N = 1/0.1 = 10$ patients/day.

$$N = \frac{C}{T_1} \tag{1}$$

All results in Section 3 are presented as number of patients that are required to be able to be seen per day (N) in a 5-day working week in order to meet the 28-day FDS.

2.6. Optimisation to minimise breaches

The aim of optimising the model is to lower the number of patients breaching the FDS. The base model has 29 different, interconnected investigations with capacities which may be changed. This means that there may be many possible solutions (local minima) which achieve the aim of reducing breach numbers to fewer than 15%.

Each configuration of capacities input into the model will produce a value of a quality metric (the objective), i.e., number of breaches. By changing the capacities, we can search for a particular set of capacities which is optimal, in this case lowering the number of breaches to fewer than 15%. As there are 29 different investigations, and therefore capacities, which may be changed, it would be infeasible to check the number of breaches for all possible combinations. We therefore use an optimisation algorithm to check solutions, measure the quality metric, and return better solutions more quickly and efficiently.

There are different approaches which may be used to search for optimised solutions. In this problem, we use a stochastic approach for the following reasons: the objective function cannot easily be expressed explicitly in an algebraic form, the search space is high-dimensional, and it is simpler to include constraints on the various capacities. In particular, we use a stochastic PSO algorithm to optimise capacities. PSO was chosen as the number of combinations of the capacity for all 29 investigations is too large to feasibly check every possible combination. PSO instead checks a sample of random solutions and then iterates towards those that provide better solutions. We run the PySwarms [47] global-best PSO algorithm with cognitive parameter = 0.4, social parameter = 0.6, and inertia = 0.8 to allow for exploration of different solutions.

In this case, each particle represents a vector of different capacities for each investigation in the diagnostic pathways. The PSO algorithm is run on the base model with each particle and the output, number of breaches per 28-day window, recorded. All the solutions are then evaluated, the best ones noted, and the particle "positions" (capacities of each investigation) are changed to try to move towards better solutions. The algorithm iterates for a given number of trials, and the best generated solution is returned at the end. We then check if this solution is successful, i.e., one for which there were fewer than 15% patient breaches per 28-day window. If the best solution returns more than 15% breaches, we do not accept the results.

As we do not expect a single, global optimum, we run the optimisation algorithm multiple times with the same starting parameters to show the range of possible solutions due the stochastic nature of both the model, and the optimisation algorithm. The optimisation process was run 25 times in total. This number of runs was chosen as high enough to show the range of solutions, but low enough that it could be run in a timely manner without the need for high performance computing; the optimisation process takes about an hour to complete on a 64-bit Windows OS with 1.6 GHz CPU.

This allows the RFL to select different results based on feasibility of, for example, changing resources in a given area. This is also useful for the RFL to be able to test different conditions and scenarios (for example, procurement of a new scanner) or re-optimise in the case of unexpected shortages or increases in resourcing.

3. Results

Different scenarios of patients flowing through the diagnosis pathways over the course of 6 months were run and validated against actual performance at the RFL, using the data described in Section 2.2. The model was optimised using the PSO algorithm to see where capacity might need to be increased to improve patient flow through the system to reduce the number of patients breaching the FDS to less than 15%. Note that given 29 inter-connected model variables, corresponding to each of the investigations, there is no single optimised solution but instead a subset of possible optimal solutions, as can be seen in Fig. 4.

Fig. 5 shows the same plot as Fig. 4, but with each run of the optimisation highlighted, with the output numbers listed. This information is now allowing the RFL to select where capacity can be increased. Different optimised solutions may then be selected based on the RFL's capacities and the impact on needs in other areas such as urgent care and non-cancer patients. The RFL is also able to create business cases for further resources where required.

Table 3 shows a table summarising the results of all 25 optimisation runs. Figs. 4 and 5 omit some investigations such as biopsy for clarity due to the large scale of these numbers. We note that biopsy reports take a significantly longer time than the biopsies hence the daily capacity is much lower. Additionally, US reports are completed immediately after the US investigation hence are omitted. We report the numbers for these omissions in Table 3. Table 3 just shows the minimum, maximum and median values for each investigation from all optimisation runs as the full solutions from each run are shown in Fig. 5. Note that using simply the minimum values for all investigations will not result in the RFL meeting the FDS as the investigations are all inter-connected (Figs. 4 and 5). Also listed are the RFL's current capacities for comparison. Each row is highlighted to show whether the current capacity is sufficient for requirements or less than required for all optimisation runs. The red and yellow highlighted investigations are priority areas for improvement in order to minimise breaches and achieve the FDS.

4. Discussion

In this study, we have demonstrated a model which will allow optimisation of available diagnostic capacity for patients on urgent cancer pathways and highlighted the areas where increased capacity is required in order to meet the 28-day FDS standard even with optimal efficiency.

The novelty of the approach presented is in the application area. As mentioned briefly in Section 1, the use of mathematical optimisation in a healthcare context is not as common as in other application areas and, furthermore, not many of the methods in healthcare have been applied to optimising disease diagnostic pathways [48]. The work developed here offers an improvement to efficiently diagnosing cancer pathways formulated as a mathematical problem in comparison to other methods such as case management [49].

We have shown some capacity demand mismatches in the current cancer diagnosis pathways at the RFL. Examples include imaging investigations such as CT scans and ultrasounds, and endoscopy investigations such as oesophago-gastro-duodenoscopy (OGD). This is due to the volume of patients and the number of different cancer pathways requiring these investigations within the timeframe to meet the 28-day FDS target.

Previous work has addressed patient diagnosis time in a single cancer pathway [50,51]. In this work, we have examined all cancer diagnosis pathways as a complete system. Figs. 4 and 5 show that changing resource in any one investigation impacts the resources needed in other investigative areas. This suggests that studies which look at individual areas may miss the wider context, and not necessarily improve overall patient diagnosis times. Looking at the system as a whole, we identified areas for improvement which will have system-wide impact. In other areas, provision exceeds the optimal level, informing future resource planning and realignment that can provide benefit to these and other areas.

Additional use of mathematical optimisation in healthcare would have a further benefit — it lays a solid foundation for the successful rollout of AI interventions [52]. After systematic changes to healthcare workflows and processes through mathematical optimisation, AI techniques can further enhance these systems. Examples of the use of AI in a healthcare context include improving the efficiency of the operating room environment with an optimisation and machine learning model [53] and improving patient flow on mental health in-patient units [54].

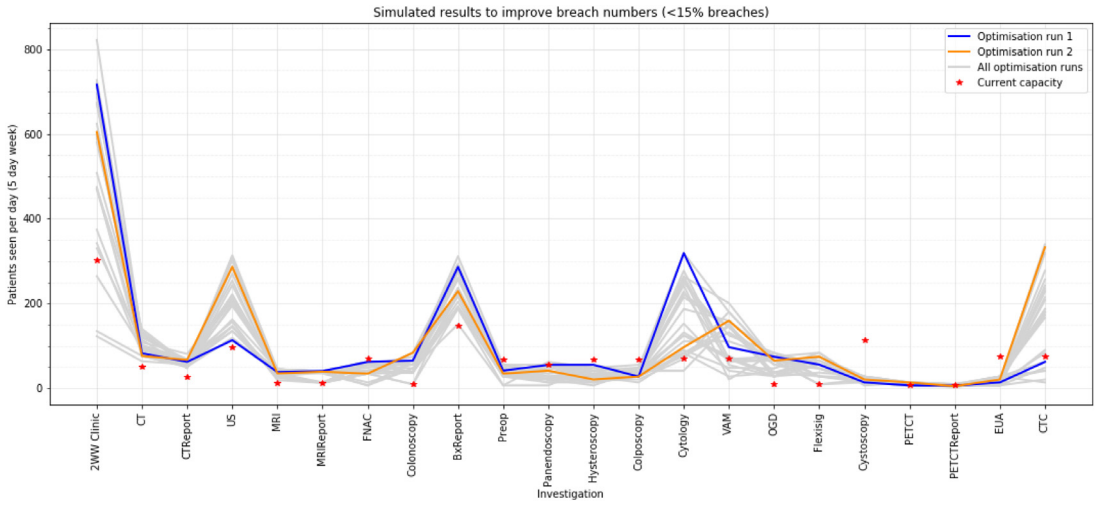
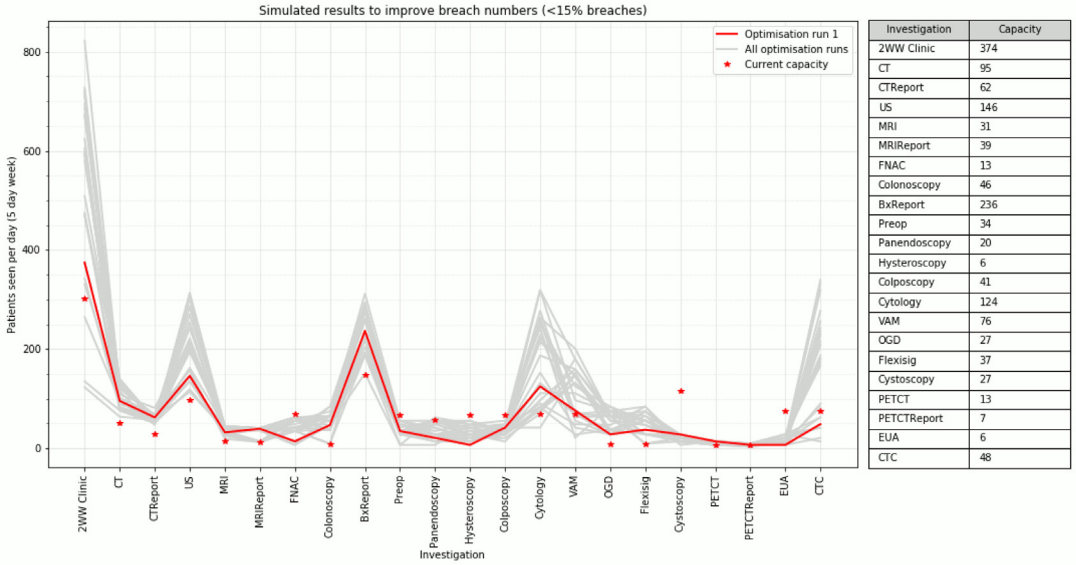


Fig. 4. Results from 25 optimisation runs showing the capacity of patients needing to be seen for each investigation in a 5 day (12 h per day) working week. Each grey line represents a solution which results in fewer than 15% of patients breaching the 28-day gold standard for diagnosis. Highlighted are two runs to show the spread in results and the importance of optimising all investigations simultaneously. By lowering capacity in one investigation, capacity must be increased elsewhere to meet targets. The red stars show the current working capacity at the RFL.



Investigation	Capacity
2WW Clinic	374
CT	95
CTReport	62
US	146
MRI	31
MRIReport	39
FNAC	13
Colonoscopy	46
BxReport	236
Preop	34
Panendoscopy	20
Hysteroscopy	6
Colposcopy	41
Cytology	124
VAM	76
OGD	27
Flexisig	37
Cystoscopy	27
PETCT	13
PETCTReport	7
EUA	6
CTC	48

Fig. 5. Animation/plots of the results from 25 optimisation runs showing the capacity of patients needing to be seen for each investigation in a 5 day (12 h per day) working week. Each grey line represents a solution which results in fewer than 15% of patients breaching the 28-day gold standard for diagnosis. Coloured lines highlight each run individually and the corresponding numbers are shown in the table to the right. The red stars show the current working capacity at the RFH. An animated version of this figure is available in the supplementary material.

These ideas and models are also applicable in other medical areas where there are pathways to follow/flow through. For example, pharmaceutical processes [55], diabetes [56] or dementia [57] diagnosis pathways, emergency department flow [58], or major trauma pathways [59].

The model comes with its limitations: we are assuming the efficiency of the hospital is as described, i.e., we are assuming constant efficiency of scanners, procedures and clinics and do not account for variation in operational efficiencies in practice. Future implementations will also seek to include different start and endpoints for different patient pathways. Furthermore, we have not included human factors such as staff being unwell or staff reacting to changing situations, for example. Our model relies on broad statistics, and the fact that these issues might balance out on average over time, but it is not a true representation of an individual patient's trajectory through the diagnostic pathway.

5. Conclusions

The collaboration between NPL and the RFL is ongoing. Future work will consider further refinement of the model based on new data; validation against real-world scenarios within the RFL; adapting the model to use real-time data direct from the RFL systems; and expansion to other hospitals/trusts. In particular, future investigation may look at the distribution of breach numbers by cancer type. Careful consideration needs to be taken towards ensuring there are no biases introduced by the optimisation. For example, increasing resources for faster treatments to reduce breaches in a single area, rather than across the board.

The outcomes and impact of this project have the potential to make a valuable impact on shaping future hospital activity. This project has demonstrated the utility of a collaboration between a national government laboratory and an NHS hospital in the unprecedented and

Table 3
Summary of results from all 25 optimisation runs. Shown are the current capacities for each investigation, and the lowest, highest, and median capacities output by the optimiser. Note that no single optimisation results in all the lower values, these numbers simply show the range of results produced. The colours indicate whether the current capacity is higher than required by any optimised run (blue), sufficient for requirements (green), slightly less than required by most optimisation runs (yellow), or severely less than required for all optimisation runs (red). Rows shown in white were unconstrained as these investigations are not usually a limiting factor in patients' pathways. Note that reporting for ultrasound (USReport) is highly correlated with ultrasound (US) as the reporting is undertaken immediately after the investigation by the same member of staff.

	Current capacity (patients per day)	Optimised capacity (lower)	Optimised capacity (upper)	Optimised capacity (median)
Referral	Unconstrained	Unconstrained	Unconstrained	Unconstrained
2WW Clinic	302	134	821	589
CT	51	76	133	108
CTReport	28	50	69	57
US	97	118	302	186
USReport	97	118	302	186
MRI	15	19	35	31
MRIReport	12	12	39	12
FNAC	73	6	62	38
Colonoscopy	9	37	83	60
Bx	2599	1247	5517	4384
BxReport	148	192	294	259
Preop	67	27	55	34
Panendoscopy	56	13	55	38
Hysteroscopy	67	6	55	31
Colposcopy	67	13	48	34
Cytology	69	41	277	138
VAM	69	27	180	72
OGD	9	27	74	46
Flexisig	9	9	83	55
Cystoscopy	114	13	27	20
Urinetests	Unconstrained	Unconstrained	Unconstrained	Unconstrained
Bloods	Unconstrained	Unconstrained	Unconstrained	Unconstrained
PETCT	7	6	13	10
PETCTReport	7	2	9	7
EUA	75	6	27	13
CTC	75	20	277	183
MDT	Unconstrained	Unconstrained	Unconstrained	Unconstrained
Discharge	Unconstrained	Unconstrained	Unconstrained	Unconstrained

extreme situations of the COVID-19 global pandemic. The project has been an important example of two disparate areas of the health system coming together with a joint determination to improve outcomes for patients.

CRediT authorship contribution statement

Elizabeth A. Cooke: Codesigned the study, Verified the data, Carried out the modelling, Data analysis with contributions from ST, Verified the results, Wrote the manuscript, Interpretation of results. **Nadia A.S. Smith:** Codesigned the study, Verified the data, Carried out the modelling, Data analysis with contributions from ST, Verified the results, Wrote the manuscript, Interpretation of results. **Spencer A. Thomas:** Codesigned the study, Wrote the manuscript, Interpretation of results, Contributed to the modelling and Data Analysis. **Carolyn Ruston:** Codesigned the study, Interpretation of results. **Sukhraj Hothi:** Codesigned the study, Gathered and provided the data, Verified the data, Verified the results, Wrote the manuscript, Interpretation of results. **Derralynn Hughes:** Codesigned the study, Wrote the manuscript, Interpretation of results.

Declaration of competing interest

EAC, NS, ST, CR and SH declare no conflict of interest exist. DH declares that she is the clinical co-director of the NCL cancer alliance.

Data sharing

Data collected for this work will not be made available beyond what is reported in this paper.

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All authors had access to the data, critically reviewed the paper before publication, and had final responsibility for the decision to submit the research for publication.

Appendix A. Pseudo-code

Notation

- M = number of investigations
- A = number of cancer types
- C = (Mx1) vector of capacity for each scanner

- W = (MxAx3) matrix of time for each investigation for each cancer for each of [min, median, max] timings. To allow for additional cleaning measures in place during the COVID-19 pandemic, we add 10 mins to each of these: W = W+10
- P = matrix of virtual "patients". This should be in a randomised order to mimic patients arriving at the hospital and so that all patients of a single cancer type do not enter the system consecutively
- S = vector of investigations containing information on the investigation type and how many patients are currently undergoing each investigation
- t = time index that will increase through the loop
- dt = time increment to increase by on each loop (e.g., half a day, 15 mins, 1 min). The smaller this is, the longer the code will run (larger loops), but the more "resolution" obtained on investigation times. For example, a procedure taking 15 minutes will not be well-resolved if the time step is 1 hour
- tau = window size, e.g., 28 days
- L = number of windows over which to calculate breaches
- B = number of breaches (Lx1) vector
- n = patient index, number of patients currently in the system

Method

- Initialise: set up S based on C and W. Set up initial P
- Loop from 1 to L (windows) in steps of 1:
    - Loop from 1 to tau in steps of dt (days in window):
        - Add new patients, patients currently in system is n
        - Loop from 1 to n in steps of 1: (add patients to an investigation where possible)
            - If patient P(n) is not currently occupied (in an investigation), check if all investigations are done and remove to list of "complete" patients or select next investigation required from list
            - Check if the investigation is available in S. If True, send patient to investigation & update investigation time_required_to_complete based on cancer type
        - Increase t
        - Loop from 1 to n in steps of 1: (check all patients currently in an investigation)
            - If patient P(n) is in an investigation, check time and whether they are done. Remove from investigation if done, else leave
            - Add random probability that patient completes the investigation but is not noted as complete in the system to account for "investigation not performed"
    - Calculate B
- Calculate average B
- Update C and repeat to minimise avg(B)

Appendix B. Supplementary data

Supplementary material related to this article can be found online at https://doi.org/10.1016/j.health.2022.100082.

References

[1] Handbook to the NHS Constitution for England, 2021, [Online]. Available: https://www.gov.uk/government/publications/supplements-to-the-nhs-constitution-for-england/the-handbook-to-the-nhs-constitution-for-england (Accessed May 2021).

[2] A.G. Lai, L. Pasea, A. Banerjee, G. Hall, S. Denaxas, W.H. Chang, M. Katsoulis, B. Williams, D. Pillay, M. Noursadeghi, D. Linch, D. Hughes, M. Forster, Estimated impact of the COVID-19 pandemic on cancer services and excess 1-year mortality in people with cancer and multimorbidity: near real-time data on cancer care, cancer deaths and a population-based cohort study, BMJ Open 10 (2020).

[3] National Institute for Health and Care Excellence, Suspected cancer: recognition and referral, 2015, [Online]. Available: AccessedJuly2022.

[4] N.H.S. England, 2022. [Online]. Available: Accessed04July2022.

[5] N.H.S. England, Achieving world-class cancer outcomes: a strategy for England 2015–2020, 2016, [Online]. Available: https://www.cancerresearchuk.org/sites/default/files/achieving_world-class_cancer_outcomes_-_a_strategy_for_england_2015-2020.pdf (Accessed July 2022).

[6] N.H.S. England, National cancer waiting times monitoring dataset guidance, 2020.

[7] R. Neal, P. Tharmanathan, B. France, N. Din, S. Cotton, J. Fallon-Ferguson, W. Hamilton, A. Hendry, M. Hendry, R. Lewis, U. Macleod, E. Mitchell, M. Pickett, T. Rai, K. Shaw, N. Stuart, M. Tørring, C. Wilkinson, B. Williams, N. Williams, J. Emery, Is increased time to diagnosis and treatment in symptomatic cancer associated with poorer outcomes? Systematic review, Br. J. Cancer 112 (2015) S92–S107.

[8] K. Robinson, K. Christensen, B. Ottesen, A. Krasnik, Diagnostic delay quality of life and patient satisfaction among women diagnosed with endometrial or ovarian cancer: A nationwide Danish study, Qual. Life Res. 21 (2012) 1519–1525.

[9] M. Tørring, P. Murchie, W. Hamilton, P. Vedsted, M. Esteva, M. Lautrup, M. Winget, G. Rubin, Evidence of advanced stage colorectal cancer with longer diagnostic intervals: a pooled analysis of seven primary care cohorts comprising 11 720 patients in five countries, Br. J. Cancer 117 (2017) 888–897.

[10] C. Harrison, R. Spencer, D. Shackley, Transforming cancer outcomes in England: earlier and faster diagnoses pathways to success, and empowering alliances, J. Healthc. Leadersh. 11 (2019) 1–11.

[11] N.H.S. England, Provider based cancer waiting times statistics, 2020, [Online]. Available: https://www.england.nhs.uk/statistics/statistical-work-areas/cancer-waiting-times/quarterly-prov-cwt/2020-21-quarterly-provider-based-cancer-waiting-times-statistics/provider-based-cancer-waiting-times-for-q3-2020-21-provisional/. (Accessed April 2021).

[12] C. Maringe, J. Spicer, M. Morris, A. Purushotham, E. Nolte, R. Sullivan, B. Rachet, A. Aggarwal, The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England UK: A national, population-based, modelling study, Lancet Oncol. 21 (2020) 1023–1034.

[13] P. Spurgeon, F. Barwell, D. Kerr, Waiting times for cancer patients in England after general practitioners' referrals: retrospective national survey, BMJ 320 (7238) (2000) 838–839.

[14] E. Kaltenthaler, A. McDonnell, J. Peters, Monitoring the care of lung cancer patients: linking audit and care pathways, J. Eval. Clin. Pract. 7 (1) (2001) 13–20.

[15] H. Ip, T. Amer, M. Dangoor, A. Zamir, D. Gibbings-Isaac, R. Kochhar, T. Heymann, Managing patient pathways to achieve lung cancer waiting time targets: mixed methods study, JRSM Short Rep. 3 (10) (2012) 1–15.

[16] J.Y. Yoon, M.S. Kwak, H.I. Kim, J.M. Cha, Seasonal variations in the diagnosis of the top 10 cancers in Korea: A nationwide population-based study using a common data model, J. Gastroenterol. Hepatol. 36 (2021) 3371–3380.

[17] S. Mohiuddin, J. Busby, J. Savović, A. Richards, K. Northstone, W. Hollingworth, J.L. Donovan, C. Vasilakis, Patient flow within UK emergency departments: a systematic review of the use of computer simulation modelling methods, BMJ Open 7 (5) (2017).

[18] J.M. Tyler, B.J. Murch, C. Vasilakis, R.M. Wood, Improving uptake of simulation in healthcare: User-driven development of an open-source tool for modelling patient flow, J. Simul. (2022) 1–18.

[19] J. Vázquez-Serrano, R. Peimbert-García, L. Cárdenas-Barrón, Discrete-event simulation modeling in healthcare: A comprehensive review, Int. J. Environ. Res. Publ. Health 18 (22) (2021) 12262.

[20] T.J. England, P.R. Harper, T. Crosby, D. Gartner, E.F. Arruda, K.G. Foley, I.J. Williamson, Examining the diagnostic pathway for lung cancer patients in Wales using discrete event simulation, Transl. Lung Cancer Res. 10 (3) (2021).

[21] P. Gill, W. Murray, M. Wright, Practical Optimization, London Academic Press, 1982.

[22] G.C. Goodwin, M.M. Seron, D.Q. Mayne, Optimisation: A key tool for advanced design in scheduling estimation and control, IFAC Proceedings Volumes 40 (2007) 3–16.

[23] L.W. Krakow, L. Rabiet, Y. Zou, G. Iooss, E.K. Chong, S. Rajopadhye, Optimizing dynamic resource allocation, Procedia Comput. Sci. 29 (2014) 1277–1288.

[24] M.H. Zafar, I. Khan, M.O. Alassafi, An efficient resource optimization scheme for D2D communication, Digit. Commun. Netw. (2022).

[25] Y. Shi, R. Eberhart, A modified particle swarm optimizer, IEEE Int. Conf. Evol. Comput. Proc. (1998) 69–73.

[26] R. Eberhart, J. Kennedy, A new optimizer using particle swarm theory, in: MHS'95, Proceedings of the Sixth International Symposium on Micro Machine and Human Science, 1995, pp. 39–43.

[27] P. Cazzaniga, M.S. Nobile, D. Besozzi, The impact of particles initialization in PSO: Parameter estimation as a case in point, in: 2015 IEEE Conference on Computational Intelligence in Bioinformatics and Computational Biology, CIBCB, 2015, pp. 1–8.
[28] M. Meissner, M. Schmuker, G. Schneider, Optimized particle swarm optimization (OPSO) and its application to artificial neural network training, BMC Bioinformatics 7 (1) (2006) 125.
[29] F.D. Wihartiko, H. Wijayanti, F. Virgantari, Performance comparison of genetic algorithms and particle swarm optimization for model integer programming bus timetabling problem, IOP Conf. Ser. Mater. Sci. Eng. 332 (2018) 012020.
[30] S.A. Ethni, B. Zahawi, D. Giaouris, P.P. Acarnley, Comparison of particle swarm and simulated annealing algorithms for induction motor fault identification, 2009.
[31] A.C. Zenteno, T. Carnes, R. Levi, B.J. Daily, P.F. Dunn, Systematic OR block allocation at a large academic medical center comprehensive review on a data-driven surgical scheduling strategy, Ann. Surg. 264 (6) (2016) 973–981.
[32] W. Crown, N. Buyukkaramikli, P. Thokala, A. Morton, Y. Mustafa, D.A. Marshall, J. Tosh, W.V. Padula, M.J. Ijzerman, P.K. Wong, K.S. Pasupathy, Constrained optimization methods in health services research—An introduction: Report 1 of the ISPOR optimization methods emerging good practices task force, Value Health 20 (2017) 310–319.
[33] W.C. Levine, P.F. Dunn, Optimizing operating room scheduling, Anesthesiol Clin. 33 (4) (2015) 697–711.
[34] D.J. Garcia, F. You, Supply chain design and optimization: Challenges and opportunities, Comput. Chem. Eng. 81 (2015) 153–170.
[35] R. Cheng, Y. Jin, A competitive swarm optimizer for large scale optimization, IEEE Trans. Cybern. 45 (2) (2015) 191–204.
[36] S. Pervaiz, Z. Ul-Qayyum, W.H. Bangyal, L. Gao, J. Ahmad, A systematic literature review on particle swarm optimization techniques for medical diseases detection, Comput. Math. Methods Med. 2021 (2021) 5990999.
[37] W. Srisukkham, L. Zhang, S.C. Neoh, S. Todryk, C.P. Lim, Intelligent leukaemia diagnosis with bare-bones PSO based feature optimization, Appl. Soft Comput. 56 (2017) 405–419.
[38] N. Zeng, H. Qiu, Z. Wang, W. Liu, H. Zhang, Y. Li, A new switching-delayed-PSO-based optimized SVM algorithm for diagnosis of Alzheimer's disease, Neurocomputing 320 (2018) 195–202.
[39] S. Raj, K.C. Ray, ECG signal analysis using DCT-based DOST and PSO optimized SVM, IEEE Trans. Instrum. Meas. 66 (3) (2017) 470–478.
[40] Y. Li, X. Bai, L. Jiao, Y. Xue, Partitioned-cooperative quantum-behaved particle swarm optimization based on multilevel thresholding applied to medical image segmentation, Appl. Soft Comput. 56 (2017) 345–356.
[41] Z. Zhu, J. Zhou, Z. Ji, Y.-H. Shi, Dna sequence compression using adaptive particle swarm optimization-based memetic algorithm, IEEE Trans. Evol. Comput. 15 (5) (2011) 643–658.
[42] Y.-J. Gong, J. Zhang, H.S.-H. Chung, W.-N. Chen, Z.-H. Zhan, Y. Li, Y.-H. Shi, An efficient resource allocation scheme using particle swarm optimization, IEEE Trans. Evol. Comput. 16 (6) (2012) 801–816.
[43] S.-Y. Ho, H.-S. Lin, W.-H. Liauh, S.-J. Ho, OPSO: Orthogonal particle swarm optimization and its application to task assignment problems, IEEE Trans. Syste. Man Cybern. A 38 (2) (2008) 288–298.
[44] S. Nguyen, M. Zhang, M. Johnston, K.C. Tan, Automatic programming via iterated local search for dynamic job shop scheduling, IEEE Trans. Cybern. 45 (1) (2015) 1–14.
[45] T.-L. Lin, S.-J. Horng, T.-W. Kao, Y.-H. Chen, R.-S. Run, R.-J. Chen, J.-L. Lai, I.-H. Kuo, An efficient job-shop scheduling algorithm based on particle swarm optimization, Expert Syst. Appl. 37 (3) (2010) 2629–2636.
[46] N.H.S. England, Rapid cancer diagnostic and assessment pathways, 2018, [Online]. Available: https://www.england.nhs.uk/publication/rapid-cancer-diagnostic-and-assessment-pathways/. (Accessed December 2021).
[47] L. Miranda, Pyswarms: a research toolkit for particle swarm optimization in python., J. Open Source Softw. 3 (21) (2018) 433.
[48] W. Crown, N. Buyukkaramikli, Y. Mustafa, P. Thokala, A. Morton, D.A. Marshall, J.C. Tosh, M.J. Ijzerman, W.V. Padula, K.S. Pasupathy, Application of constrained optimization methods in health services research: Report 2 of the ISPOR optimization methods emerging good practices task force, Value Health 21 (9) (2018) 1019–1028.
[49] C.N. Wulff, M. Thygesen, J. Søndergaard, P. Vedsted, Case management used to optimize cancer care pathways: a systematic review, BMC Health Serv. Res. 8 (2008).
[50] B. Berg, B. Denton, H. Nelson, H. Balasubramanian, A. Rahman, A. Bailey, K. Lindor, A discrete event simulation model to evaluate operational performance of a colonoscopy suite, Med. Decis. Making 30 (3) (2010) 380–387.
[51] E.F. Arruda, P. Harper, T. England, D. Gartner, E. Aspland, F.O. Ourique, T. Crosby, Resource optimization for cancer pathways with aggregate diagnostic demand: a perishable inventory approach, IMA J. Manag. Math. 32 (2) (2021) 221–236.
[52] A. Reddy, D. Scheinker, The case for mathematical optimization in health care: Building a strong foundation for artificial intelligence, 2020, [Online]. Available: https://www.healthaffairs.org/do/10.1377/forefront.20201110.585462/full/. (Accessed 04 July 2022).
[53] M. Fairley, D. Scheinker, M.L. Brandeau, Improving the efficiency of the operating room environment with an optimization and machine learning model, Health Care Manag. Sci. 22 (2019) 756–767.
[54] F.M. Dawoodbhoy, J. Delaney, P. Cecula, J. Yu, I. Peacock, J. Tan, B. Cox, AI in patient flow: applications of artificial intelligence to improve patient flow in NHS acute mental health inpatient units, Heliyon 7 (5) (2021).
[55] F. Delfani, H. Samanipour, H. Beiki, A.V. Yumashev, E.M. Akhmetshin, A robust fuzzy optimisation for a multi-objective pharmaceutical supply chain network design problem considering reliability and delivery time, Int. J. Syst. Sci. Oper. Logist. 9 (2020) 155–179.
[56] I. Contreras, J. Vehi, Artificial intelligence for diabetes management and decision support: Literature review, J. Med. Internet Res. 20 (5) 2018.
[57] J. Bae, J. Stocks, A. Heywood, Y. Jung, L. Jenkins, V. Hill, A. Katsaggelos, K. Popuri, H. Rosen, M. Faisal Beg, L. Wang, Transfer learning for predicting conversion from mild cognitive impairment to dementia of Alzheimer's type based on a three-dimensional convolutional neural network, Neurobiol. Aging 99 (2021) 53–64.
[58] W.G. Allihaibi, M. Masoud, M. Elhenawy, S.Q. Liu, J. Burke, A. Karim, Solving the emergency care patient pathway by a new integrated simulation-optimisation approach, IEEE Access 9 (2021) 100895–100910.
[59] Trauma overview, National institute for health and care excellence, 2021, [Online]. Available: https://pathways.nice.org.uk/pathways/trauma#path=view%3A/pathways/trauma/trauma-overview.xml&content=view-index. (Accessed November 2021).