Appendix 1: Methodology

1   Description of problem

In order to establish a hyper-acute stroke unit (HASU) model for emergency stroke care across England, all HASUs (providing thrombolysisis) should ideally have a minimum of 600 yearly admissions of confirmed strokes. Comprehenisve stroke centres (providing thrombolysis and thrombectomy) should perform a minimum of 150 thrombectomy proecures per year (10% of stroke patients are assumed to receive thrombectomy). No unit should be infeasibly large, and we have taken the current largest unit with ~2,000 stroke admissions per year as our upper target, though the algorithm also explores use of larger units.

The problem involves looking for solutions that can place any number of hospitals in any of 127 locations. There are therefore 2^{127} or 10^{38} possible solutions. Each solution requires looking up road travel times from each of 31,171 patient locations to all open hospitals to allocate patients to their closest hospital. There are 13 possible objectives to try to achieve or trade-off (see section 3.1).

This type of problem is termed 'NP-hard' - it cannot be solved explicitly in reasonable time. And as there are multiple-objectives that trade-off against each other there is no single solution to the problem (as there is no way to objectively determine the weighting of different objectives); rather we are looking for a population of solutions which demonstrate the trade-off between different objectives.

With NP-hard problems there are often a range of different heuristic algorithms which search for good solutions to the problem, while never guaranteeing an optimal solution is found. One set of general purpose heuristic methods are a family of algorithms known as 'genetic algorithms', due to their inspiration coming from the theory of evolution. Here we describe the specific genetic algorithm used in our study.

2   Code and data repository

Data and code used for the model are available at:
https://github.com/MichaelAllen1966/1805_thrombectomy_location

Note: The code contains a bespoke Genetic Algorithm written in Python/NumPy. No Genetic Algorithm libraries were used.

3   Multi-objective problem

3.1 Pareto dominance

When solving an optimisation problem based on one objective, the optimal solution is given by the configuration with the best (highest or lowest) objective value. In the case of multi-objective optimisation, comparing several solutions requires to reference to the notion of dominance: a vector a of the objective space dominates another vector b if all criteria of a are better or equal to criteria of b and $a \neq b$[1]. Then, a solution is non-dominated if there are no other solutions at least equal in all objectives and better in at least one objective. At the end of the optimisation process, there is no

single best solution but a set of non-dominated solutions, called the Pareto Front. An example of a Pareto Front using two objectives is shown in figure 1.
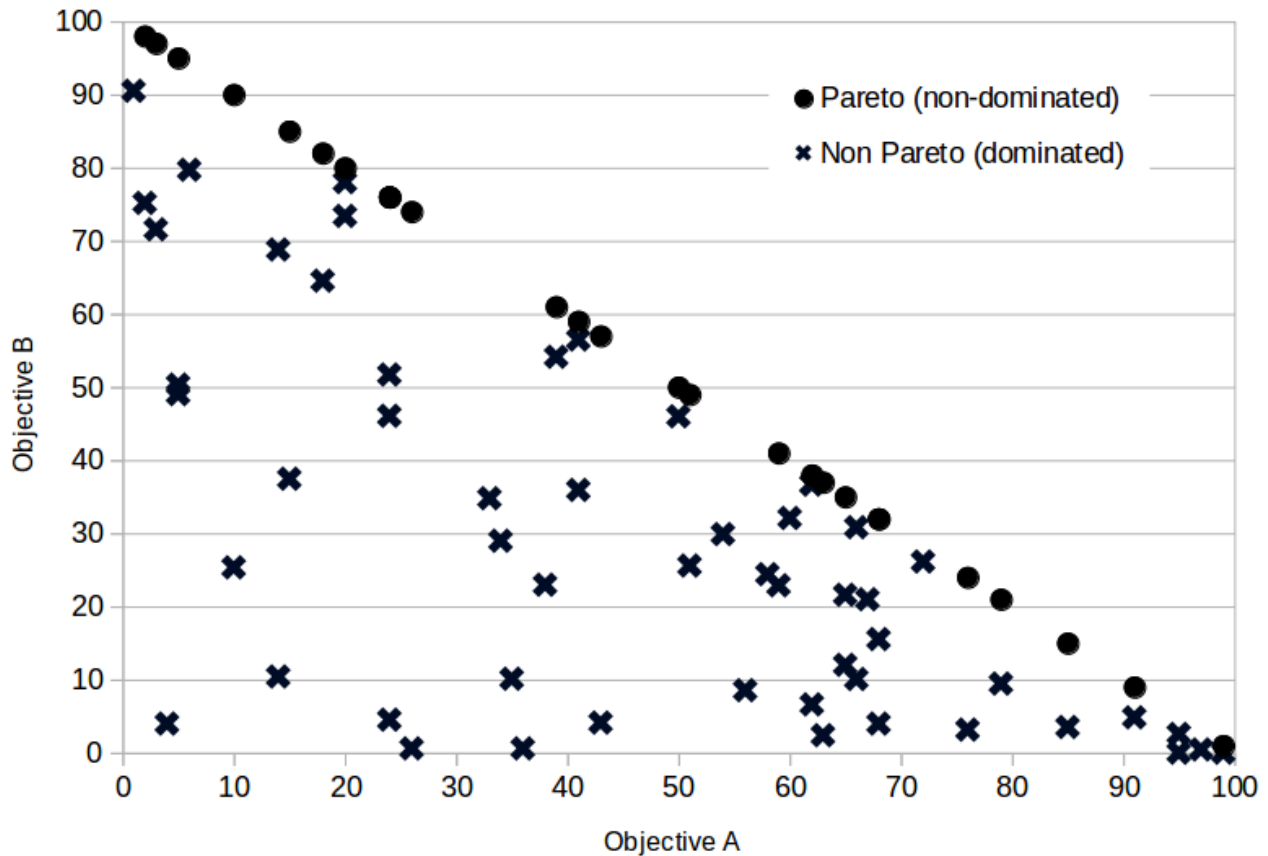

Figure 1: Example of identification of Pareto front (non-dominated) points when comparing two objectives.

The greater the number of objectives on the Pareto Front the lower the chance that a point will be dominated by another. If there is no correlation between objectives and solutions are entirely random then the chance of a single point being dominated by another single point picked at random is $0.5^{\wedge}n_{obj}$.

3.2 Algorithm code and data

The algorithm code and data used may be downloaded from.

https://github.com/MichaelAllen1966/1805_thrombectomy_location

(Note: A general version of this algorithm is also available here: https://github.com/MichaelAllen1966/1802_acute_healthcare_location_algorithm)

The algorith was run in two stages:

1) Identify best locations of thrombolysis/thrombectomy centres (this is all that is neeed for the mothership model).

2) For drip'n'ship models, fix the location of thrombectomy centres and identify best locations of thrombolysis-only centres.

Initial algoithm runs focussed on a reduced criteria set of reduce the number of hospitals used, reduce average distance, minimise the the nunebr of admissions to the smallest unit, maximise the size of the smallest unit. This limited approach has two advantages: 1) it finds solutions that are

independnent of specific taregts for distance or admission numbers, and 2) it provdes more praid progress of the algorithm. This progressive extension of objectives is an established general methodology for genetic algorithms [2]. After the initial limited run is complete the numebr of objectives is enlarged (though the algorithm allows for three different target travel times, the next expansion used only one target travel time, with a final run of the algorthm expandinf solutions based on all objectives).

4 Genetic algorithms

Genetic algorithms manage a population of individuals encoded as vectors through a given number of generations. At each generation, 'good' parents are selected from the population according to their fitness (any measure of superiority over other potential parents). Parents are then combined, using a cross-over operator, to create children which are finally mutated. Genetic algorithms differ in the parent selection process, in the cross-over and mutation processes, and in the way the population is archived.

4.1 Representation

Solutions are coded as binary string of genes with either 1 for an open location or 0 for closed. For instance, 001011 would be six genes that represent hospitals 3, 5 and 6 being open and 1, 2 and 4 being closed. In this study, vectors represent the 127 hospitals (SSNAP acute admitting stroke units).

4.2 Selection

The selection operator chooses a part of the population to become parents. The better individuals in terms of objective values are more likely to become parents. The selection probability can be proportionate to fitness by roulette-wheel sampling[3] or stochastic universal sampling[4]. The sigma scaling method normalises the fitness by its variance in the population, so that the individuals with the highest fitness always have a higher probability than others to produce children. However, these approaches focus on exploitation of existing population rather than exploration of the decision space and they can lead to premature convergence.

Other selection methods rely on ranking rather than fitness value. With ranking selection, individuals are ranked according to their fitness and their probability to become parents is function of their rank[5]. Similarly, the tournament selection creates random pairs of individuals and keeps the one with the highest fitness value with a given probability[3]. Such methods allow the algorithm to keep some individuals with low fitness values (with the advantage of keeping a broader gene pool).

Finally, the Boltzmann selection[6] controls the selection rate via a temperature. At the beginning, all individuals have a similar probability to be selected. As the temperature decreases, the selection focusses on high-fitness individuals.

4.3 Cross-over

The cross-over is the process which exchanges genes from parents to create new children. The simplest option is the single-point cross-over which selects one locus and exchanges the blocks of parents before and after that locus. For instance, a crossover at point five would perform the following:

Parent A:	1 1 1 1 1 1	
Parent B:	0 0 0 0 0 0	
Child A: =	1 1 1 1 0 0	
Child B:	0 0 0 0 1 1	

The choice of the single-point location can be made by a uniform distribution. In the case of binary vectors, the single-point cross-over is less likely to exchange the endpoints of vectors [2]. To reduce this effect, the cross-over can rely on two or more exchange points.

4.4   Mutation

Mutation changes the gene value of each locus, with a very small probability for each individual each generation. According to [7], the mutation process avoids the loss of diversity in the population.

4.5   Archive

Genetic algorithms also vary by the way solutions are archived and if the population size is variable. The simple option is to keep only children. However, it assumes that children are better than parents which are lost. Several methods build an archive which is union of parents and children. If the population size is variable, an option is to keep the Pareto Front of this archive. However, the size of this Pareto Front can increase dramatically, in particular with many objective functions. Then, individuals from the archive are ranked, based on their Pareto dominance and another metric. NSGA-II [8] and SPEA2 [9] both rank individuals by combining dominance and spread metric in order to maximise population diversity.

4.6   The NSGA-II method

In NSGA-II [8] the archive and the new population are merged and all individuals are ranked according to a two-step mechanism. In the first step, the merged population is split into layers of non-dominated fronts, the first layer being the Pareto Front (the second layer being the next Pareto Front after removal of the first layer). In the second step, the spread of the population is measured by the crowding distance which gives the distance from an individual to its nearest neighbour. To keep the size of the population constant, a given number of individuals is selected from the merged population, preferably from the upper layers and with the largest crowding distance.

NSGA-II has the advantage to keep not only optimal solutions but also near-optimal solutions in lower layers. However, to do so, the population must be large enough. The second advantage is to provide a diverse population in terms of score values, thanks to the crowding distance ranking.

The NSGA-II was chosen for this study after a pilot comparison with SPEA2[9], MOEAD[10], and HypE[11] which showed that NSGA-II provided similar objective performances with a more diverse population.

4.7   Convergence indicator

Population diversity can be monitored using average Hamming distance. The Hamming distance between any two solutions is the proportion of genes that are different. Average Hamming distance

is the mean Hamming distances for all pairwise comparisons in the population (after first Pareto Front selection).

4.8 Description of our genetic algorithm

The code contains a bespoke implementation of a genetic algorithm, based on NSGA-II[8]. Our method evolves solutions based on multiple objectives, but without any weighting of objectives. In each generation, the Pareto Front of non-dominated solutions is identified. Larger populations may be selected by picking subsequent Pareto Fronts (re-evaluation the Pareto Front after removal of the previous Pareto Front identified). The population size is maintained in the interval $\left[P_{min} ; P_{max} \right]$.

The steps of the algorithm are:

1) Identify which combination of objectives to use for selection in algorithm (may be from 2 objectives to all objectives).

2) Set up initial population of solutions (a typical starting population is 10,000 solutions).

   i) Randomly choose number of hospitals to open in each solution.

   ii) Randomly assign open hospitals.

   iii) A library of solutions may be imported instead of, or in addition to, a random population of solutions.

   iv) Non-unique solutions are removed.

3) Breed solutions:

   i) Choose pairs of solutions at random from the population.

   While NSGA-II selects parents with the tournament method based on weighted criteria, our method selects parents randomly to avoid weighting any objective.

   ii) Select a single crossover point at random within the solution binary string.

   iii) Apply the cross-over operator to produce children.

   iv) Randomly mutate children with a probability per element of 0.002.

   v) Combine parents and children into a new population.

   vi) Remove non-unique solutions and any solutions where all hospitals are closed.

4) Calculate the performance of all solutions against the objectives used for selection.

5) Identify all non-dominated (Pareto Front) solutions

   i) If the number of selected solutions is greater than the maximum permitted population size then reduce the number of solutions by either

   (1) picking the required number of solutions at random, or

   (2) pick two solutions at random and use tournament selection based on crowding distance

   ii) If the number of selected solutions is lower than the target population then remove the previously selected non-dominated solutions and repeat the Pareto selection until sufficient solutions have been identified.

6) Repeat steps 3-5 until the maximum number of generations is reached or the algorithm is stopped by another indicator:

> i) Stop the algorithm when there is a change of <0.001 in average Hamming distance across 5 generations.

Note: The minimum and maximum number of solutions to pass on to the next generation may be the same number to keep solution size constant. Alternatively, a range of population size may be acceptable (e.g. a minimum number of 1,000 solutions may be chosen, but a maximum number of 5,000 solutions may be permitted. In this case Pareto selection is repeated until at least 1,000 solutions have been selected, but restriction on the number of solutions only occurs if the number of solutions chosen exceeds 5,000).

The time taken to reach convergence depended on the the number of objectives in the Pareto Front. Typical populations sizes and run times were:

- For 3-4 objectives: population sizes of 2,500 to 5,000 were used. Typical run time to convergence on a single core of a 2GHz processor was 48hrs.

- For 8-12 objectives: population sizes of 5,00 to 10,000 were used. Typical run time to convergence on a single core of a 2GHz processor was 4-7 days.

Note: algorithms may be speeded up by restricting solutions to a smaller range of acceptable number of hospitals (strict filters may be introduced into the algorithm to remove unacceptable solutions before identifying the Pareto Front).

5 References

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