OPTIMIZATION

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The evidence behind your decisions

Outline

- Introduction
- Optimization model
- Case studies in healthcare using optimization
  - Eye clinic layout planning
  - Optimal ATD drug dosage (personalized medicine)
  - Shift capacity planning for nursing staff

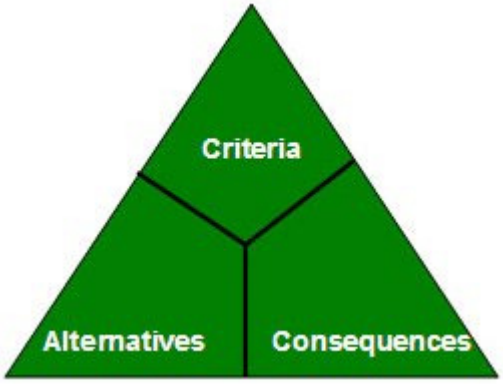
Introduction -- what is optimization?

Optimization (mathematical programming) is the *selection* of a *best* element with regard to some *criteria* from some set of available *alternatives*.

Optimization is to find the best solution from all feasible solutions

Maximize

Minimize



What is an optimization problem?

1. You have some value that you want to optimize [Objective]

2. To do that, you need to choose the values of some variables, which determine such outputs as total cost, revenue, and profit [Decision variables], eg, what stock to buy, which route to choose

3. You typically have certain restrictions (physical, logical, economic) [Constraints], eg, budget, timeline, people

Optimization models answer the question: "what decision values give the best outputs?"

Fundamental concepts

Optimisation problem consists of **three ingredients:**

- **objective function,** to be maximized or minimized

$$f(x)$$

- **decision variables,** to be calculated

$$x$$

- **constraints,** to be respected

$$g(x) = 0 \text{ (equality constraints)}$$

$$h(x) \geq 0 \text{ (inequality constraints)}$$

Applications in healthcare using optimization

- **Healthcare planning:** location selection (healthcare centres, emergency vehicles), capacity planning, facility layout planning
- **Healthcare management and logistics:** patient scheduling, resource scheduling (nurse staffing, nurse scheduling, operating room scheduling), hospital logistics
- **Healthcare practice:** disease diagnosis, treatment planning, optimal drug dosage
- **Specialized and preventive healthcare:** organ donation and transplant, prevention of diseases

A simple optimization example

- Suppose a clinic has a choice to treat certain numbers of private and subsidised patients, so as to maximize its total revenue
- Revenue from a private patient is $63 and $45 from a sub patient
- Doctor consultation times for a private and sub patient are 35 min & 20 min, respectively
- A private /sub patient takes 8 /10 min of nurses time, respectively
- The clinic has 7900 min of doctors' consultation time and 3000 min of nurses time
- From population profile analysis, it is known that the number of sub patients will be between 180 and 250

Optimization model (2 decision variables)

Decision variables

numbers of private patients & subsidised patients, ***x, y***

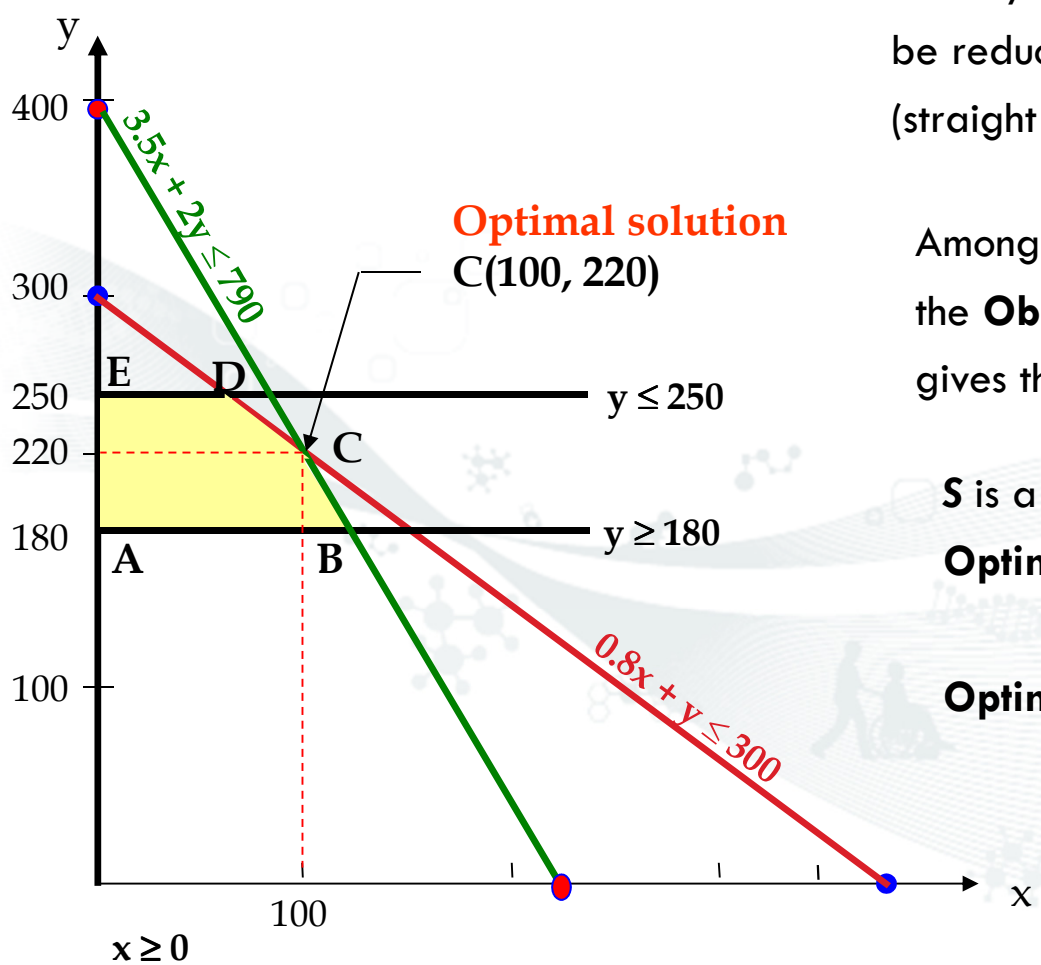
Objective

maximize the total revenue, ***maximize 63x + 45y***

Constraints

1. $8x + 10y \leq 3000$; (nurses time constraint)
2. $35x + 20y \leq 7900$; (consultation time constraint)
3. $y \leq 250$; (upper bound of number of subsidised patients)
4. $y \geq 180$; (lower bound of number of subsidised patients)
5. $x \geq 0$. (nonnegative number of private patients)

Solve the problem: graphical solution



The x-y space marks the **possible choices**, to be reduced by the sets of **constraints** (straight lines)

Among the **feasible region S**, the point where the **Objective** function reaches the maximum gives the **optimal** point

S is a polyhedral set, i.e., ABCDE

Optimal solution:

x=100, y=220

Optimal value:

63x100 + 45x220 = $16,200

Some insights

- Constraints, decision variables may be multiple
- The optimal solution can be found at the intersection of some constraints (called corner points). Hence at optimality, some constraints are binding and some might not
- The optimal solution can be unique, finite/infinite, or even does not exist
- Adding constraints to a problem shall not improve the objective value

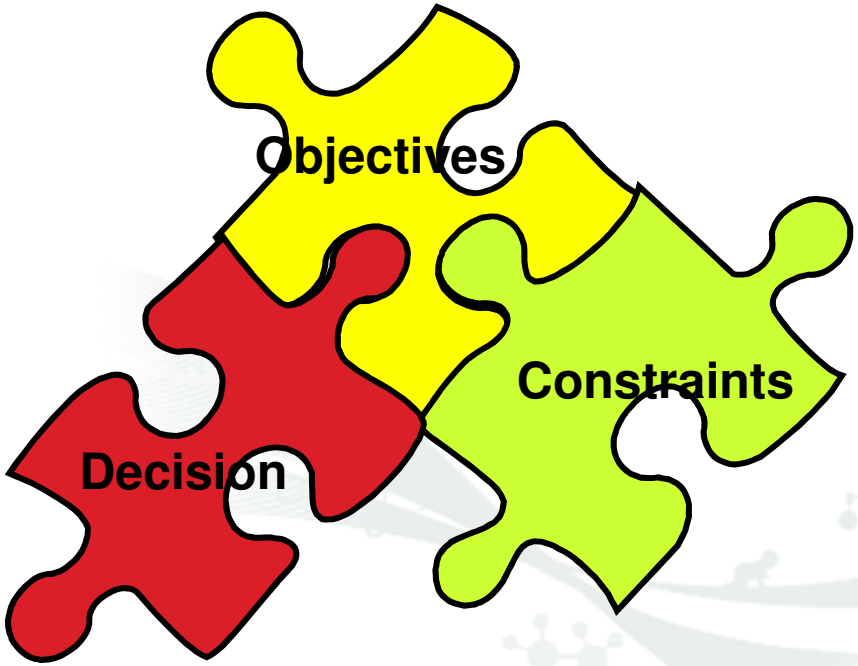
Optimization

- Choice of best strategy
- Choice of best estimate
- Choice of best design parameters
- Choice of best combinations of scenarios

Criteria for optimization

- Performance index
- Value function, e.g., time, distance
- Cost function
- Fitness function

Optimization Framework: Decision, Objectives, Constraints



I. Decision (Do what)
   + Basic option to be chosen (who, what, when, where)

II. Objectives (Optimise what)
   + Criteria to maximize or minimize (utilization or cost, etc)

III. Constraints (Feasibility)
   + Policy (subsidy, private)
   + Legacy (culture now = culture before)
   + Physical limits (usable space ≤ max space)
   + Demand (meet current operating load)
   + Conservation (inflow = outflow)

Optimization model

Minimize (or maximize) an *objective function*

with respect to some *decision variables*

subject to some *constraints*

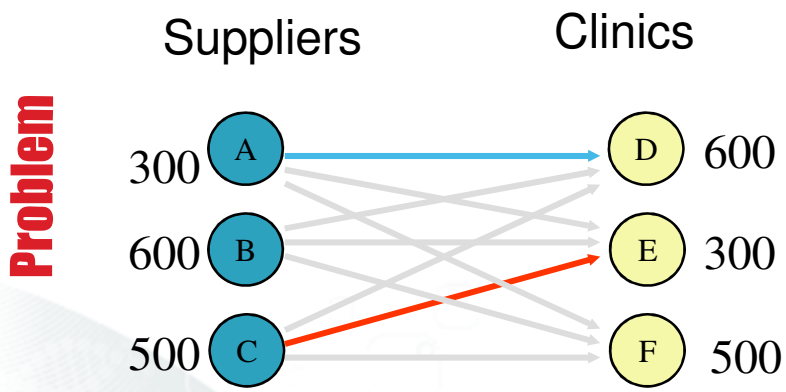
Example

$$
\begin{aligned}
\min \quad & 2x_1 + 3x_2 \\
\text{s.t.} \quad & x_1 - 10x_2 + 7 \leq 0, \\
& x_1 + 4x_2 - 5 = 0.
\end{aligned}
$$

Most common optimization models

Optimization models	Linear programming (LP)	Integer programming (IP)	Mixed integer programming (MIP)
Objective	Linear function	Linear function	Linear function
Constraints	Linear functions	Linear functions	Linear functions
Decision variables	Nonnegative	Nonnegative, All variables are integers	Nonnegative, Some variables are integers

Medical items delivery plan with the least total shipping cost



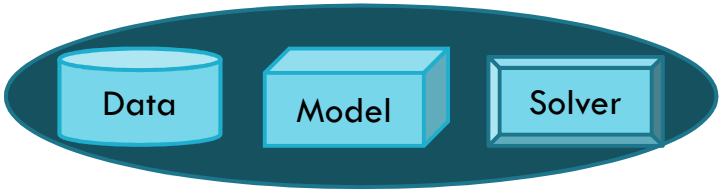
	D	E	F
A	$0	$4	$1
B	$1	$6	$3
C	$3	$7	$6

Delivery cost matrix (per unit)

Declarative approach

+ State the data
+ State decision variables, objective, constraints
+ Formulate the model
+ Solve the model

Structure problem



Data: number of suppliers & clinics, delivery cost per unit, capacity of each supplier, demand from each clinic

Decision variables: Number of items shipped from suppliers to clinics

Objective: Minimise the total delivery cost

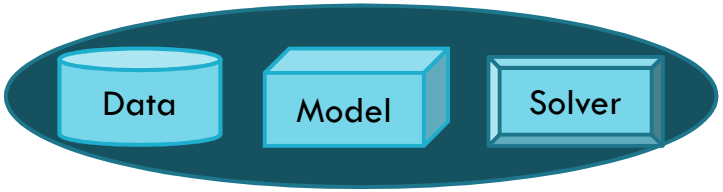
Constraints

1. For each supplier, can only ship what quantity of items **>=** quantity shipped
2. For each clinic, total quantity of items received **=** its demand
3. Quantities of items in delivery **>=0**

Math model

$$
\begin{aligned}
\min \quad & \sum_{i=1}^{3}\sum_{j=1}^{3} c_{ij}x_{ij} \\
\text{s.t.} \quad & \sum_{j=1}^{3} x_{ij} \le s_i, \quad i = 1,2,3, \\
& \sum_{i=1}^{3} x_{ij} = d_j, \quad j = 1,2,3, \\
& x_{ij} \ge 0, \ i = 1,2,3; j = 1,2,3.
\end{aligned}
$$

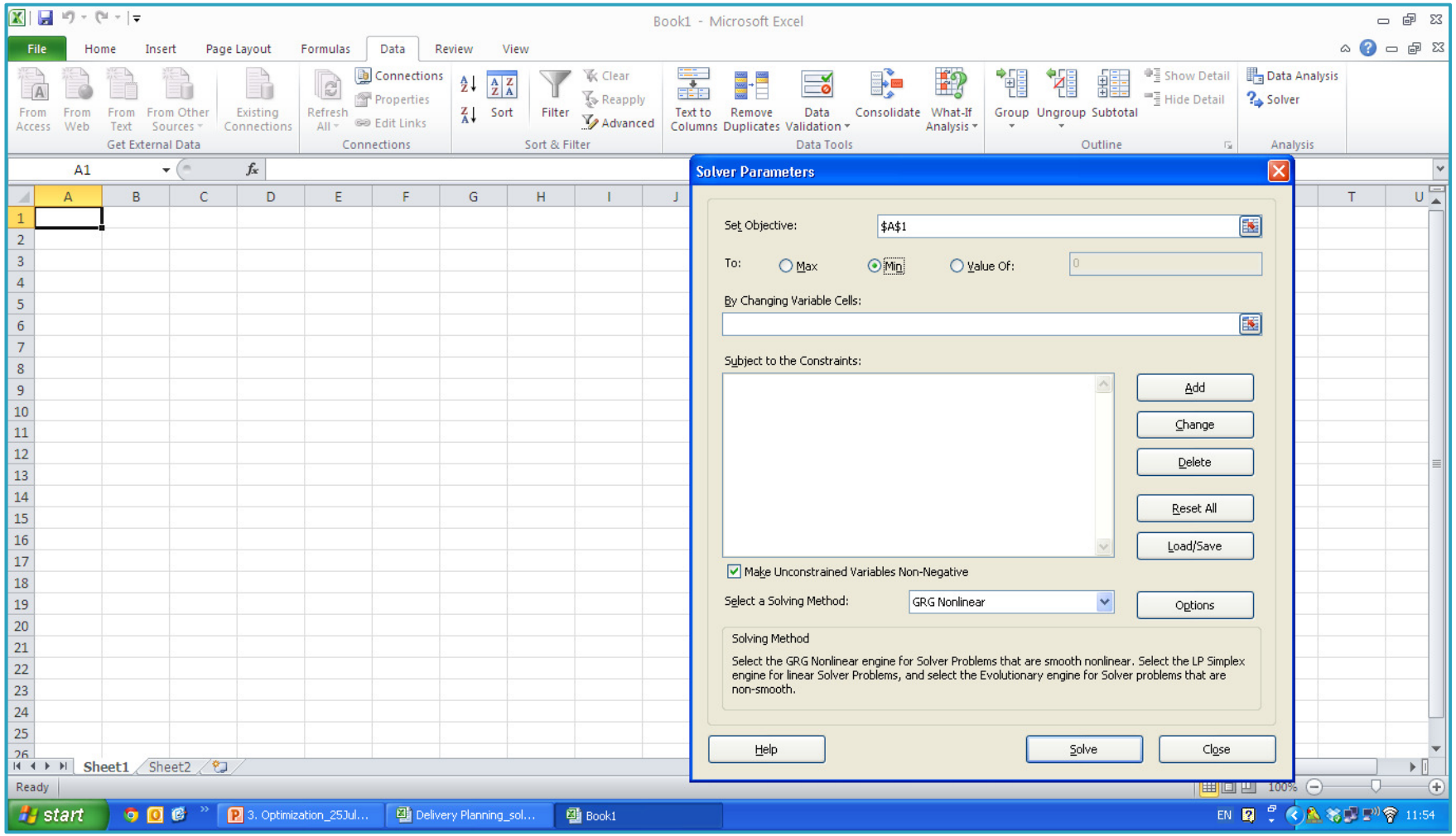
Solve optimization model



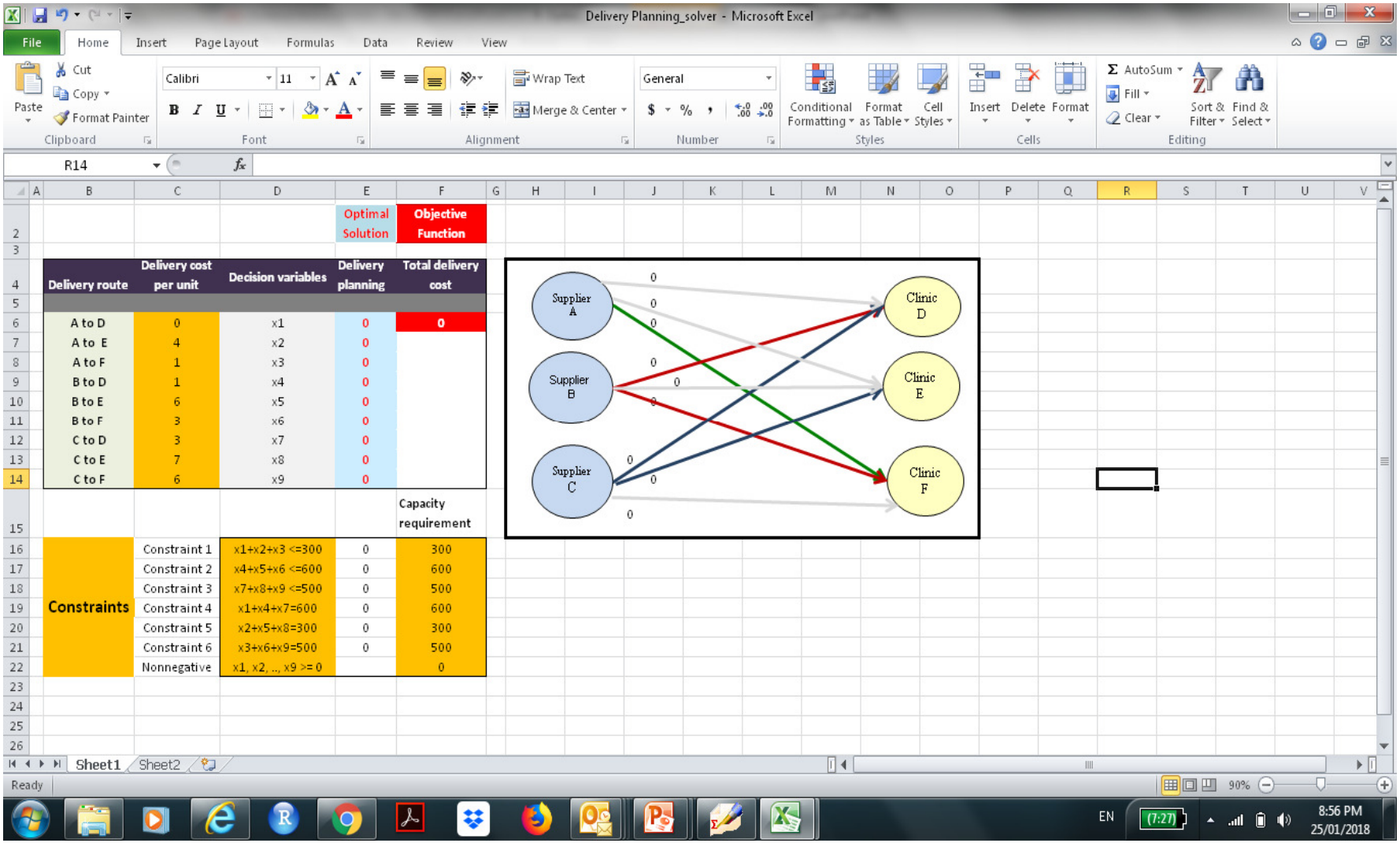
Solve optimization model

- MS Excel optimization solver (applicable to small scale problems)
- Other commercial software
  - AMPL, CPLEX, Gurobi, LINDO API, LINGO, Maple, Mathematica, MATLAB, OPL Studio

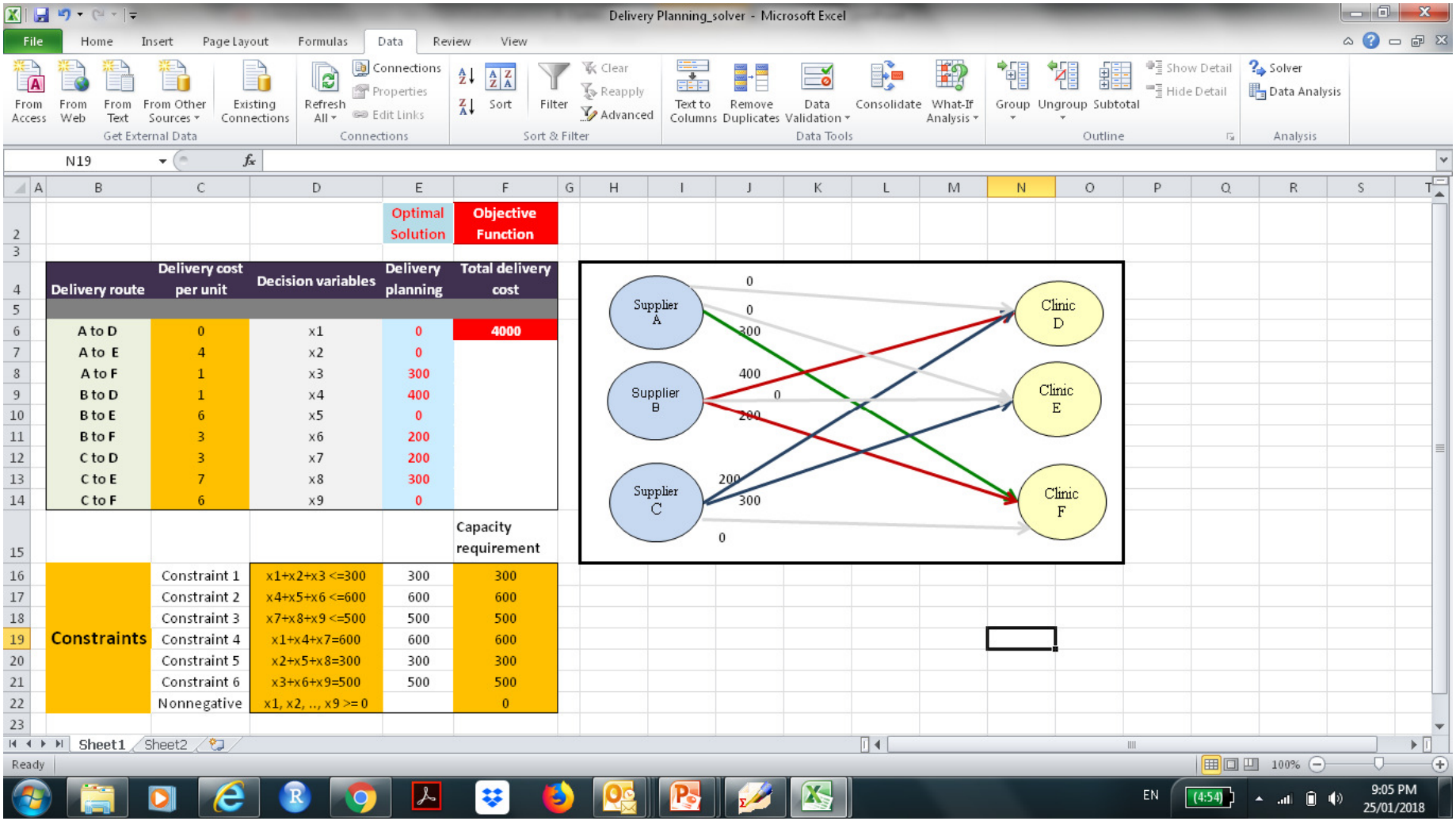
Excel optimization solver to solve least cost transport plan



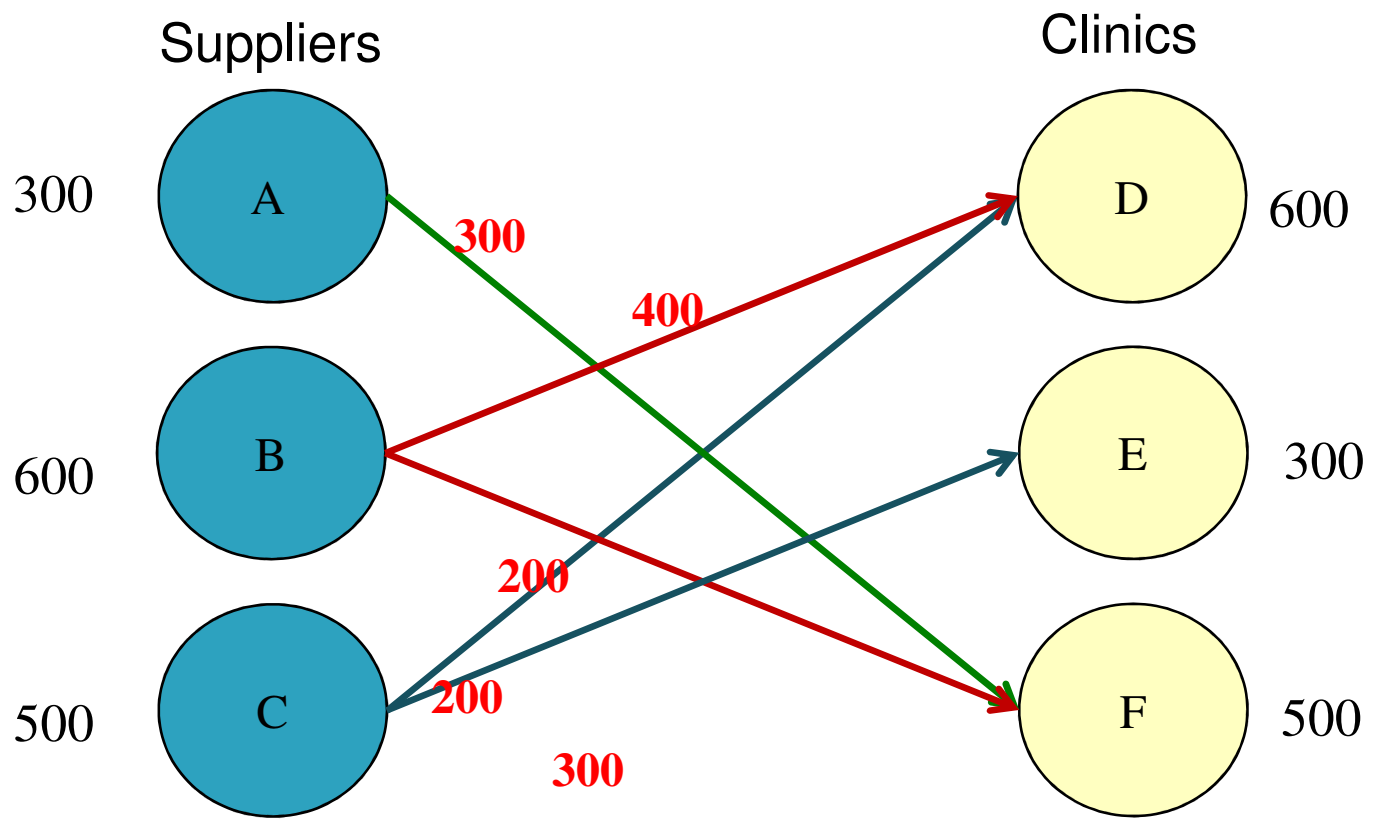
Excel optimization solver



Excel optimization solver



Optimal delivery plan (the minimum delivery cost: $4,000)



Case studies in healthcare using optimization

Case study 1: facility layout planning for an eye clinic

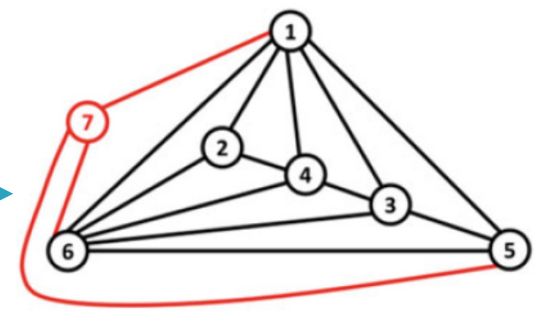
- **Facility layout problem** originates from industrial applications, e.g., planning the location of different machines of an assembly line to manufacture a product.
- Facility layout planning is to decide the **relative positions of units** inside a building, i.e., which units should be adjacent in the layout.
- In general, hospital layout planning problem aims to minimize the travel distance (or time) for patients and personnel.
- For the eye clinic layout design, we use graph theory to construct the layout design which can be modelled to find a ***maximum weight planar subgraph*** of a graph based on patient flow information (i.e., the association matrix).

An illustrative facility layout example

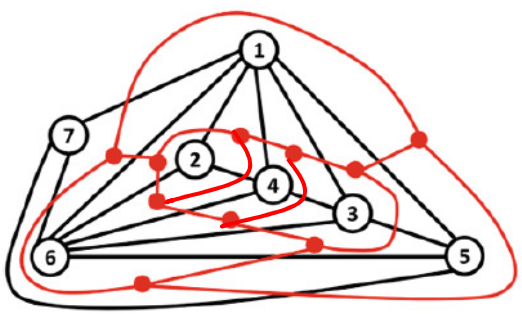
Given an adjacency matrix of 6 facilities/stations as below

highest connectivity

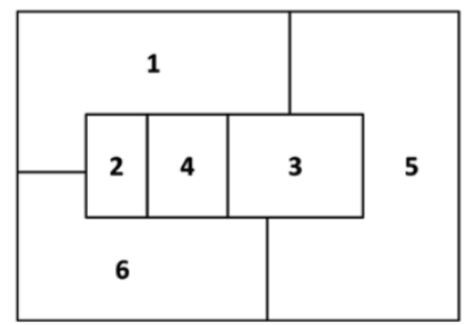
$$U = \begin{array}{c} \begin{array}{cccccc} 1 & 2 & 3 & 4 & 5 & 6 \end{array} \\ \begin{pmatrix} - & 4 & 7 & 1 & 7 & 10 \\ 4 & - & 2 & 5 & 2 & 4 \\ 7 & 2 & - & 8 & 8 & 1 \\ 1 & 5 & 8 & - & 1 & 3 \\ 7 & 2 & 8 & 1 & - & 5 \\ 10 & 4 & 1 & 3 & 5 & - \end{pmatrix} \end{array} \begin{array}{c} 1 \\ 2 \\ 3 \\ 4 \\ 5 \\ 6 \end{array}$$



Primal planar graph with an additional node 7



Dual graph



Block layout

Optimization model to find a maximal planar graph

- Given a graph $G' = (V, E')$ with an adjacency matrix $U = (u_{ij})$, the weight u_{ij} of edge (i, j) represents the demand (connectivity) between node i and j

- **Optimization model:**

$$\max_{\boldsymbol{x}} \sum_{(i,j)\in E'} u_{ij} x_{ij}$$

$$E = \{(i, j) \in E' \mid x_{ij} = 1\}.$$

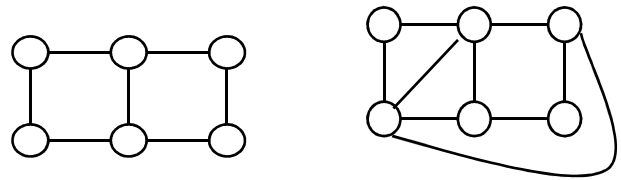
$s.t.$ $G = (V, E)$ is a planar subgraph of $G' = (V, E')$ with

- **Objective**: to maximize the sum of edge weights (i.e., the corresponding entries of the adjacency matrix)
- **Decision variables**: $x_{ij} = 1$ if edge $(i, j) \in E'$; $x_{ij} = 0$, otherwise.

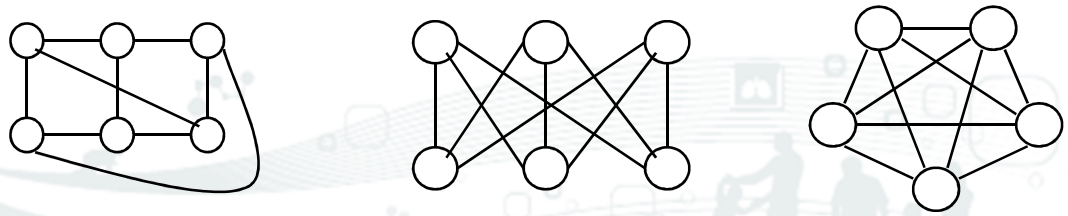
Basic notions in graph theory

A graph $G = (V, E)$ with n nodes and m edges is called a ***planar graph*** if it can be drawn on a plane without crossing edges.

- Planar graph



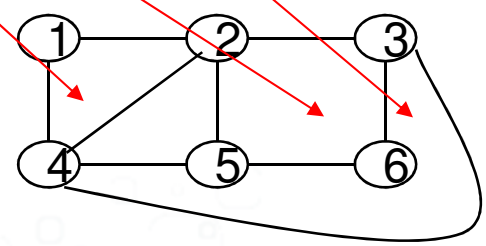
- Nonplanar graph



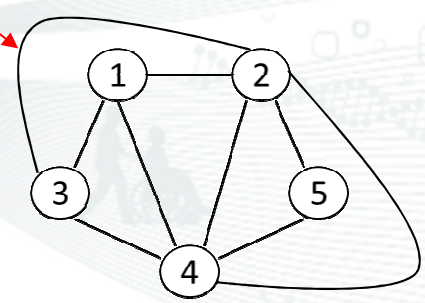
- A planar graph is called a **maximally planar graph** if no edge can be added without making the graph nonplanar.

Facet and deltahedron

- **A facet** γ of a planar graph is an area in the plane bounded by nodes and edges, such as, $\gamma_{1,2,4}$, $\gamma_{2,3,5,6}$, $\gamma_{3,4,5,6}$



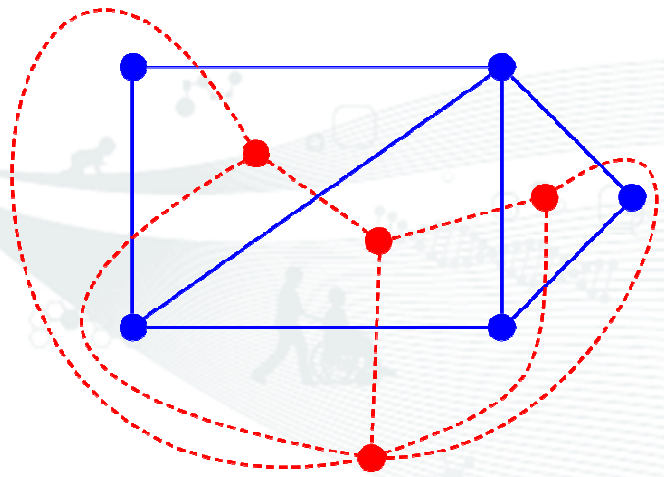
- A facet γ is called a **triangle** if it is bounded by three nodes and three edges. Eg. $\Delta(1,2,4)$, $\Delta(2,4,5)$,
- A planar graph is called a **deltahedron** if all facets of the graph are triangles.



- **Theorem**: A planar graph is **maximal** if and only if it is a **deltahedron.**

Dual graph

- A **dual graph** $G^* = (V^*, E^*)$ of the planar graph G =*(V, E)* is a graph that has a node for each facet of G.
- The number of nodes in G (primal graph) is the same number of facets in G^* (dual graph), and vice versa.
- The dual of G^* is graph G.



The red graph is the dual graph of the blue graph, and vice versa

Graph-theoretic approach to constructing a maximal planar graph

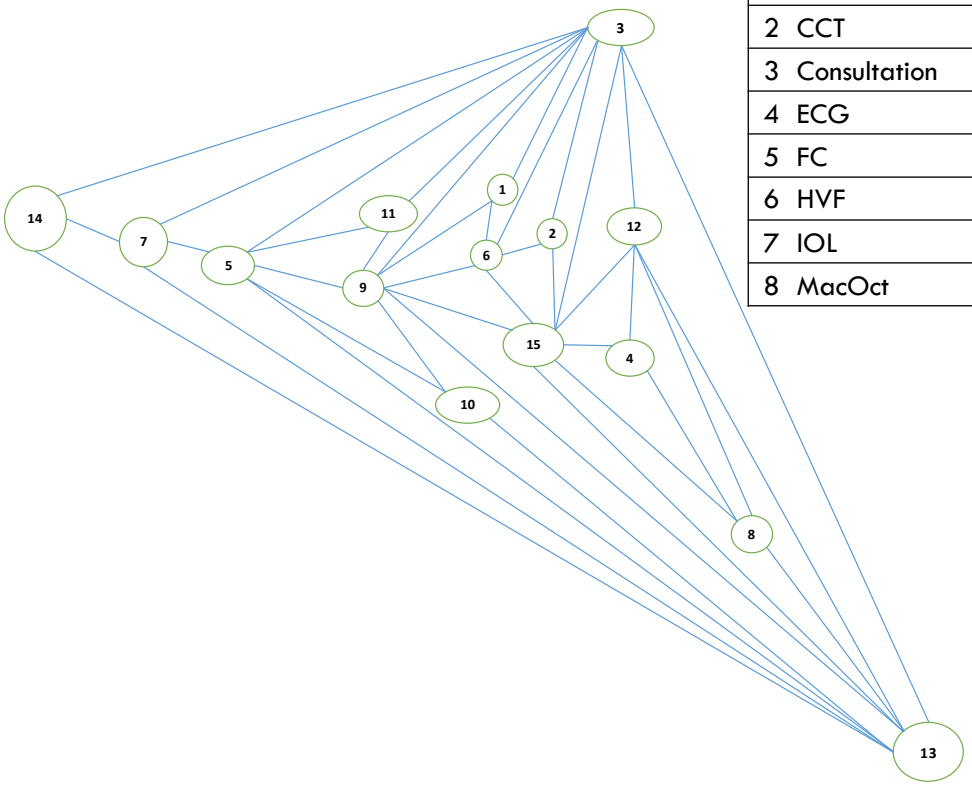
Heuristic Procedure

1. Calculate the row sums of adjacency matrix U; sort them in the decreasing order
2. Initialization: build an initial deltahedron using *four nodes* with the highest row sum
3. Iterations: integrate the remaining nodes into the deltahedron in the decreasing order of row sums. Always include the node into the triangle facet where the objective value is maximum
4. Build the primal planar graph with an additional node
5. Construct the dual graph and the block layout from the dual graph

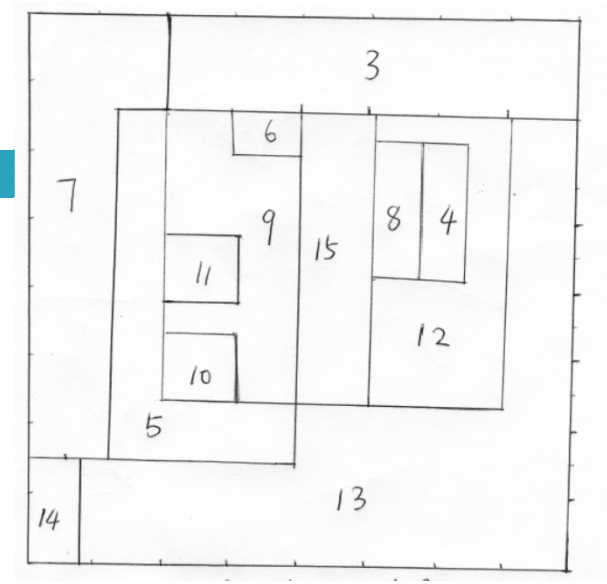
References

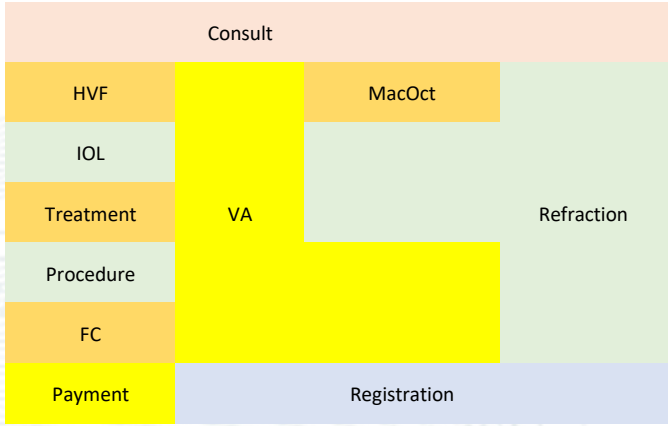
1. Arnolds, Ines and Stefan Nickel, "Layout Planning Problems in Health Care." Applications of location analysis (pp 109-152). Springer, Cham
2. Janny Leung, (1992) A New Graph-Theoretic Heuristic for Facility Layout. *Management Science* 38(4):594-605. http://dx.doi.org/10.1287/mnsc.38.4.594

Block layout with AH eye clinic data



1	Autokeratometry	9	Payment
2	CCT	10	PFE
3	Consultation	11	Procedure
4	ECG	12	Refraction
5	FC	13	Registration
6	HVF	14	Treatment
7	IOL	15	VA
8	MacOct		





This study suggests some ideas for Alex hospital eye clinic layout planning, according to the data of patient flows among different service stations. The derived layout is for logical planning, but not physical.

Case study 2: optimal drug dosage for patients with Graves' disease

INTERFACE

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Research

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Hyperthyroidism in the personalized medicine era: the rise of mathematical optimization

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- Graves' disease is an autoimmune disorder, the most common cause of hyperthyroidism.
- Each year, 0.02% - 0.05% newly diagnosed with Graves' disease
- **Three treatment methods**
  - Antithyroid drugs (ATD): to block the production of thyroid hormones
  - Radioactive iodine: to destroy the thyroid gland
  - Thyroidectomy: to remove the thyroid gland surgically
- Multiple factors, e.g., patient preference & risk of relapse, are involved in determining the treatment method

Background

- Two regimens to adopt ATD treatment
  - **Titration regimen:** adjust ATD dosage based on thyroid tests such that the patient achieves euthyroidism at the lowest dosage of ATD
  - **Block-and-replace regimen:** give patients a high dosage of ATD to suppress production of thyroid hormones
  - Both have comparable effectiveness. Titration regimen has less adverse effects to patients but with more frequent clinician visits

Current practice of titration of ATD treatment

- based on thyroid function trend of individual patient
- arbitrary and time-consuming, requiring multiple clinic monitoring visits before an optimal ATD dose is found

Aim

To develop a personalized medicine model that facilitates optimal drug dosing via the titration regimen

Method

Variables

- y: free thyroxine concentration (pmol/L)
- d: antithyroid drug dosage (mg)
- t: time (day)

Parameters

- A: synthesis rate of y
- C: constant decay rate
- IC_{50}: dosage of ATD that reduces y by half

- Analyze patients' thyroid function tests (TFT) data, consisting of drug dosage, time period, and the value of serum free thyroxine (FT4)

- Use ordinary differential equation (ODE) to describe the dynamic behavior of FT4 concentration as below, which is Bernoulli equation with the order of 2.

$$\frac{dy}{dt} = A\left(1 - \frac{d}{\mathrm{IC}_{50} + d}\right)y - Cy^2$$

Solution method

- Develop an optimization model to estimate parameters of synthesis rate, decay rate and IC_{50} in FT4 equation with individual patient's data

$$\min_{A,C,\mathrm{IC}_{50},C_1} \quad \frac{1}{m-1}\sum_{i=2}^{m}\left(\frac{\frac{A\times \mathrm{IC}_{50}}{\mathrm{IC}_{50}+\tilde{d}_i}e^{\frac{A\times \mathrm{IC}_{50}\times t_i}{\mathrm{IC}_{50}+\tilde{d}_i}}}{C\times e^{\frac{A\times \mathrm{IC}_{50}\times t_i}{\mathrm{IC}_{50}+\tilde{d}_i}}+\frac{A\times \mathrm{IC}_{50}\times C_1}{\mathrm{IC}_{50}+\tilde{d}_i}}-y_i\right)^2$$

$$\text{subject to} \quad A-\ y_1(C+A\times C_1)=0, \qquad \text{(initial condition)}$$

$$Ce^{\frac{A\times \mathrm{IC}_{50}\times t_i}{\mathrm{IC}_{50}+\tilde{d}_i}}+\frac{A\times \mathrm{IC}_{50}\times C_1}{\mathrm{IC}_{50}+\tilde{d}_i}>0, i=1,\dots,m,$$

$$A>0, C>0, C_1<0, 0<\mathrm{IC}_{50}\le 150,$$

- Establish the closed-form time- and dose-dependent solution, which allows explicit estimates of predicted FT4

$$y(t)=\frac{A\left(1-\frac{d}{\mathrm{IC}_{50}+d}\right)e^{A\left(1-\frac{d}{\mathrm{IC}_{50}+d}\right)t}}{Ce^{A\left(1-\frac{d}{\mathrm{IC}_{50}+d}\right)t}+A\left(1-\frac{d}{\mathrm{IC}_{50}+d}\right)C_1}$$

Descriptive statistics of TFT data (*N*=49)

Item	Review visit (time)	FT4 value (pmol/L)	Review interval (day)
Mean	6.9	20.7	73.5
Standard deviation	4.7	16.0	33.9
Median	5	15	70
Minimum	2	1	5
Maximum	24	91	210

- **Data set**: TFT data with first x-visit; with at most x-visit, x=3, 4, 5
- **Parameters**: synthesis rate; decay rate; IC_{50}
- Estimated parameters are acceptable if the predicted FT4 value is within a tolerance of 4.5 pmol/L

Use MATLAB built-in solver *fmincon* to solve the optimization model

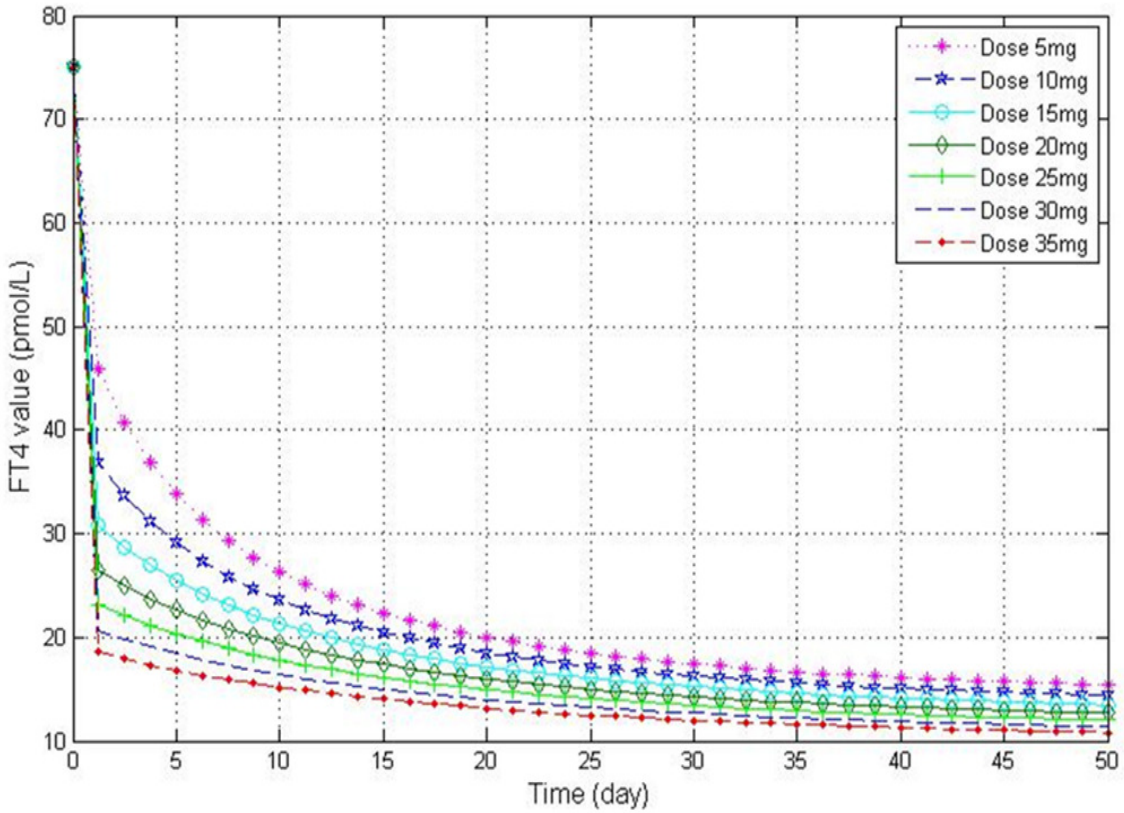
Personalized FT4 formula & estimation accuracy rates

Patient S/N	Visit times	A	IC_{50}	C	C_1	FT4 formula
2	9	0.052	58.151	0.003	-0.051	$\tilde{y}(t,d)=\frac{\frac{3.024}{58.151+d}e^{\frac{3.024t}{58.151+d}}}{0.003e^{\frac{3.024t}{58.151+d}}-\frac{0.154}{58.151+d}}$
16	3	5.194	72.901	0.371	-0.001	$\tilde{y}(t,d)=\frac{\frac{378.648}{72.901+d}e^{\frac{378.648t}{72.901+d}}}{0.371e^{\frac{378.648t}{72.901+d}}-\frac{0.379}{72.901+d}}$
23	4	4.237	35.062	0.246	-0.033	$\tilde{y}(t,d)=\frac{\frac{148.558}{35.062+d}e^{\frac{148.558t}{35.062+d}}}{0.246e^{\frac{148.558t}{35.062+d}}-\frac{4.902}{35.062+d}}$

Data set	Number of patients	Number of patients meeting the tolerance	Estimation accuracy rate
First 3-visit	48	37	77.1%
At most first 3-visit	49	38	77.6%
First 4-visit	36	27	75.0%
At most first 4-visit	49	36	73.5%
First 5-visit	31	26	83.9%
At most first 5-visit	49	35	71.4%

Drug dosages for targeted FT4 value & predicted FT4 curves for different drug dosages

Targeted FT4 value	Time period (day)	Dose (mg)
12	35	44.1
	49	36.6
	63	32.1
15	35	22.3
	49	15.4
	63	12.0
17	35	12.7
	49	6.3
	63	3.5



- The higher the dose, the steeper the FT4 curve in the decline phase
- Patients with the lower drug dose would take a longer time to achieve the same FT4 target

Some key points

1. We introduced ODE to describe the dynamic behavior of FT4 concentration
2. We developed an optimization model to estimate parameters including synthesis rate, decay rate, IC_{50} with the TFT data of each patient
3. We derived the closed-form solution of the ODE and explicit personalized estimation of FT4
4. We derived favorable accuracy rate (**77.1%, 75.0%, and 89.9%**) of predicted FT4 using data from the first 3, 4 and 5 visits respectively, compared against actual FT4 data within a tolerance of 4.5 pmol/L.

Case study 3: shift capacity planning for nursing staff in ED

Pacific Journal of Optimization

SHIFT CAPACITY PLANNING FOR NURSING STAFF IN EMERGENCY DEPARTMENT USING MIXED INTEGER PROGRAMMING

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Background

- Workload in ED changes by day-of-week and time-of-day. Patients flow into different areas of ED depending on their needs.
- The ED nurses are one critical component in the management of the patients. The nurses have different skill sets and are deployed at different functional areas of ED, and work in shifts.
- Matching the workload with the staffing can thus be a complex issue.

Aim

- To develop a mathematical model for nurse capacity planning

Shift capacity planning for nurse staffing in ED

Areas in ED

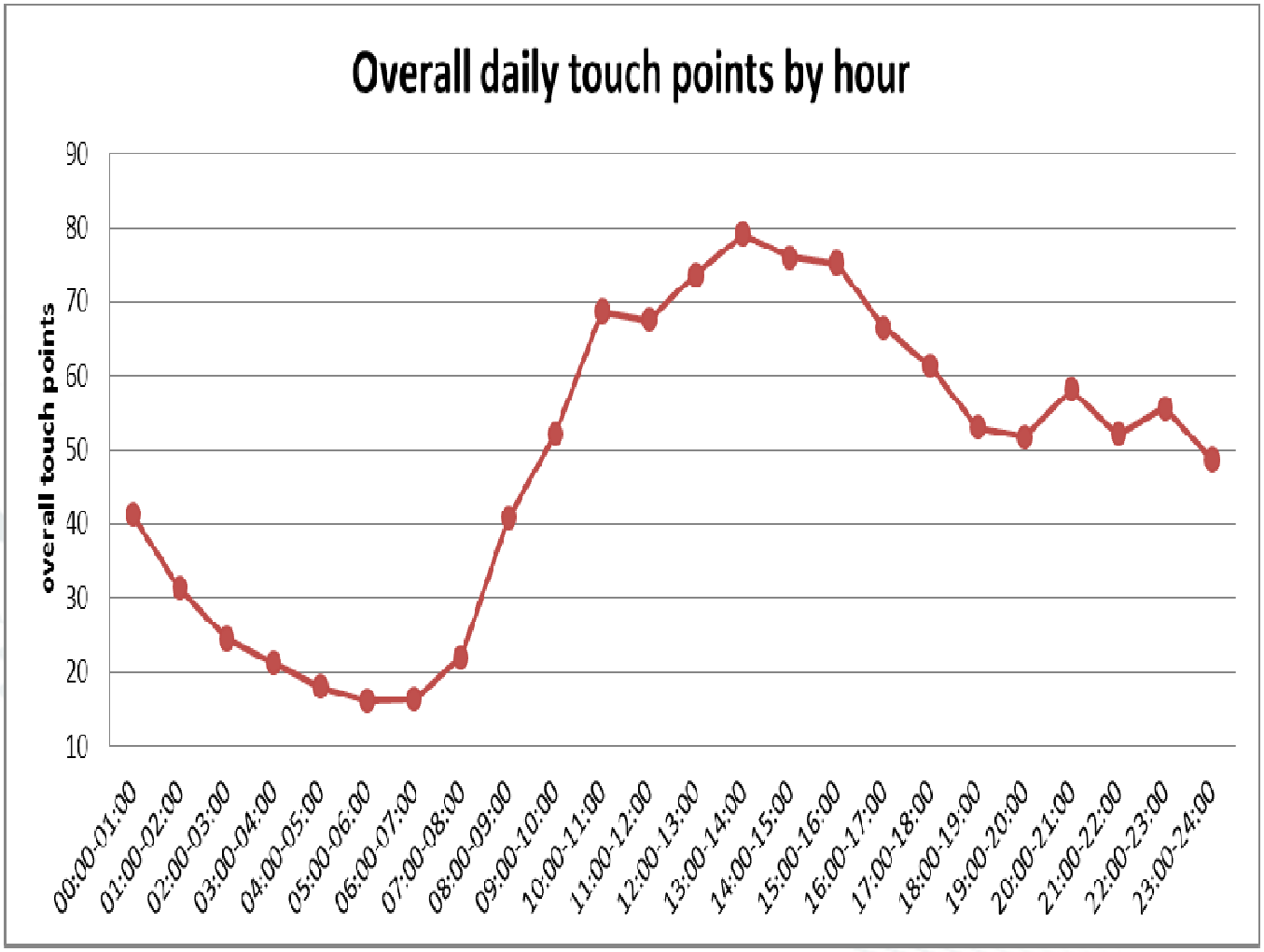
- Triage; Consult; AUC; Resus; Decon; EDC Obs; EDX consult, EDX Obs & EDX Iso; EDTC.

Shifts in ED

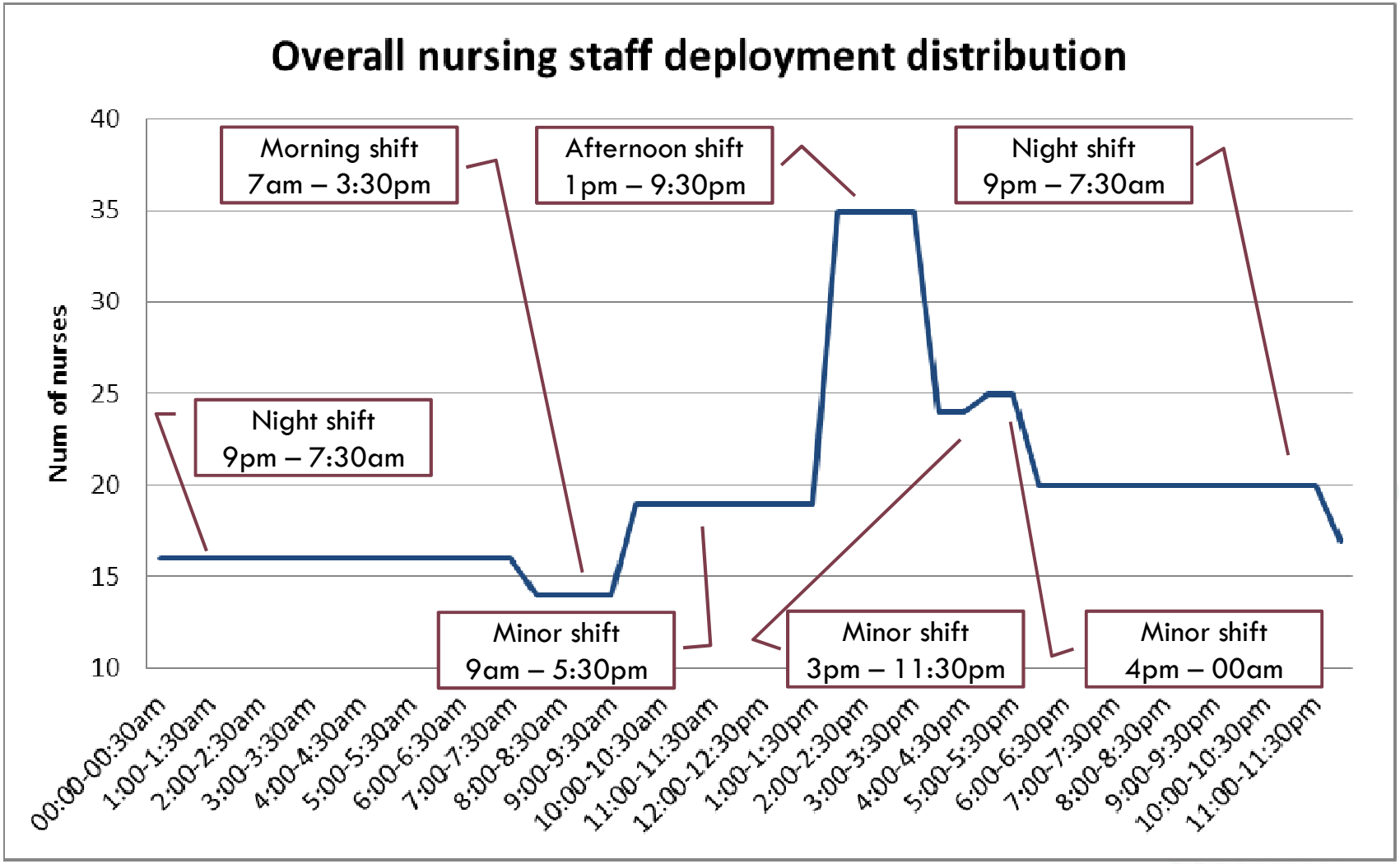
- *3 major shifts*:
  - ❑ morning shift (7am-3:30pm)
  - ❑ afternoon shift (1pm-9:30pm)
  - ❑ night shift (9pm-7:30am)
- *3 minor shifts:*
  - ❑ minor shift 1 (9am-5:30pm)
  - ❑ minor shift 2 (3pm-11:30pm)
  - ❑ minor shift 3 (4pm-00am)

Daily demand/touch points

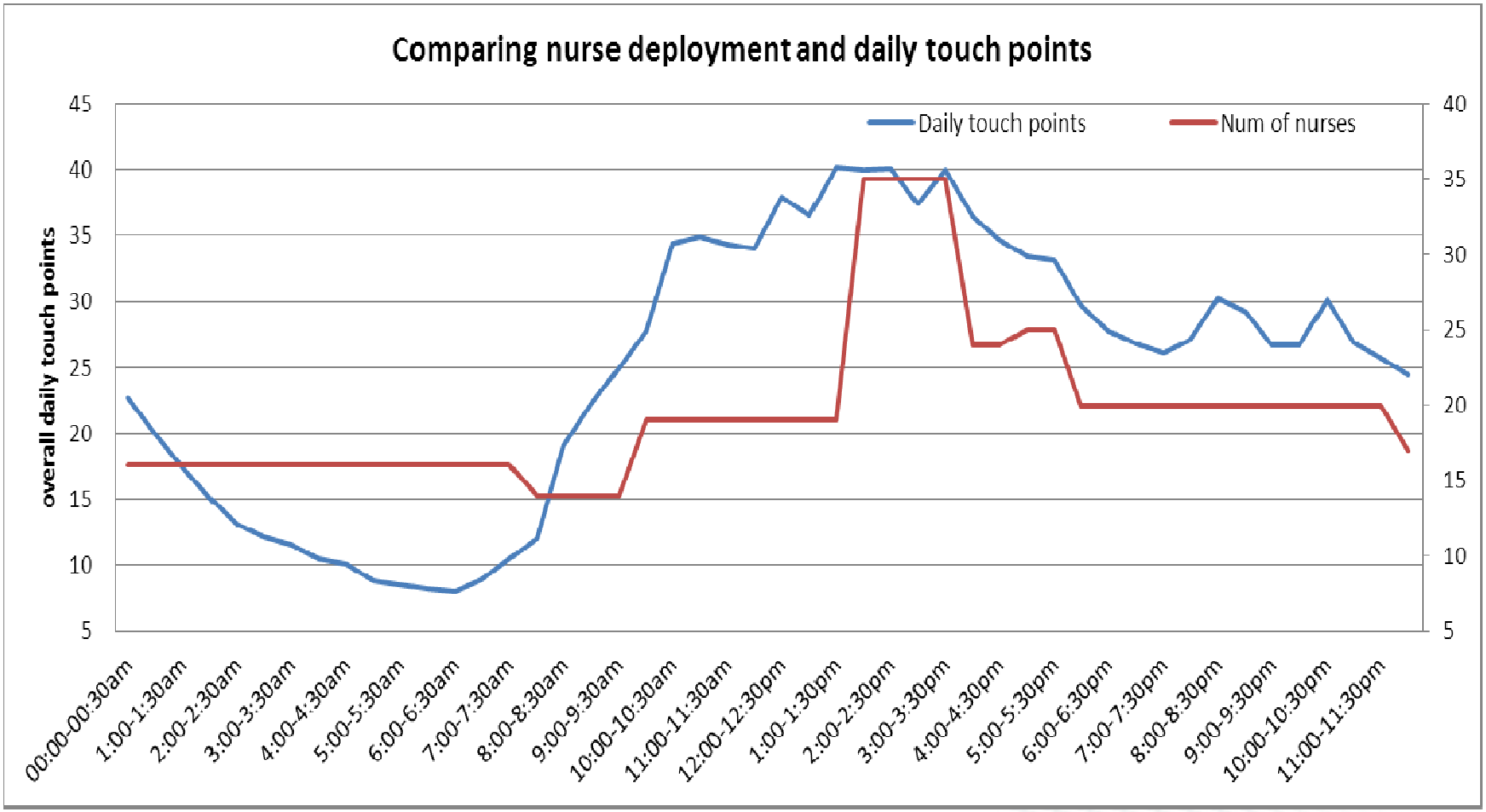
Area	Daily touch Points
Triage	449
Consult	205
AUC	192
EDC Obs	169
EDX Consult	76
EDX Obs	41
Resus	26
Decon	12
EDX Iso	3



Overall nursing staff deployment



Comparison of touch points and nursing staff deployment



Optimization model for shift capacity planning

Assumption

- Current total manpower supply is unchanged
- Current shift times are unchanged

Objective

- To balance the overall workload during a day, i.e., to minimize the mean deviation of workload during the 48 half an hour intervals of a day

Decision variables

- Numbers of nursing staff of 6 shifts

Optimization model for shift capacity planning

$$
\begin{aligned}
\min \quad & \frac{1}{J}\sum_{j=1}^{J}\left|\frac{y_j}{d_j} - \frac{1}{J}\sum_{k\in\mathcal{T}}\frac{y_k}{d_k}\right| \\
\text{s. t.} \quad & \mathbf{1}'x \le C, \\
& l \le x \le u, \\
& y = A'x, \\
& y_j \ge \rho d_j, \quad j = 1,\dots,J, \\
& y_j \ge C_j, \quad j = 1,\dots,J, \\
& z_1 = z_2 = z_3 = 1, \\
& \sum_{i=4}^{S+3} z_i \le \gamma, \\
& x_i \le M_0 z_i, \quad i = 4,\dots,S+3, \\
& z_i \le x_i, \quad i = 4,\dots,S+3, \\
& x_i \in Z^+,\ z_i \in \{0,1\},\ i = 1,\dots,S+3,\ \ y_j \in Z^+,\ j = 1,\dots,J.
\end{aligned}
$$

Decision variables

- x_i: number of nursing staff in shift M_i, $\quad i = 1,\dots,S+3$
- y_j: number of nursing staff in time interval T_j, $j = 1,\dots,J$
- z_i: 0-1 binary variable, $i = 4,\dots,S+3$. For each $\mathrm{M}_i \in \mathcal{K}_2$,

$$
z_i := \begin{cases} 1, & \text{if minor shift } \mathrm{M}_i \text{ is selected for capacity planning,} \\ 0, & \text{otherwise.} \end{cases}
$$

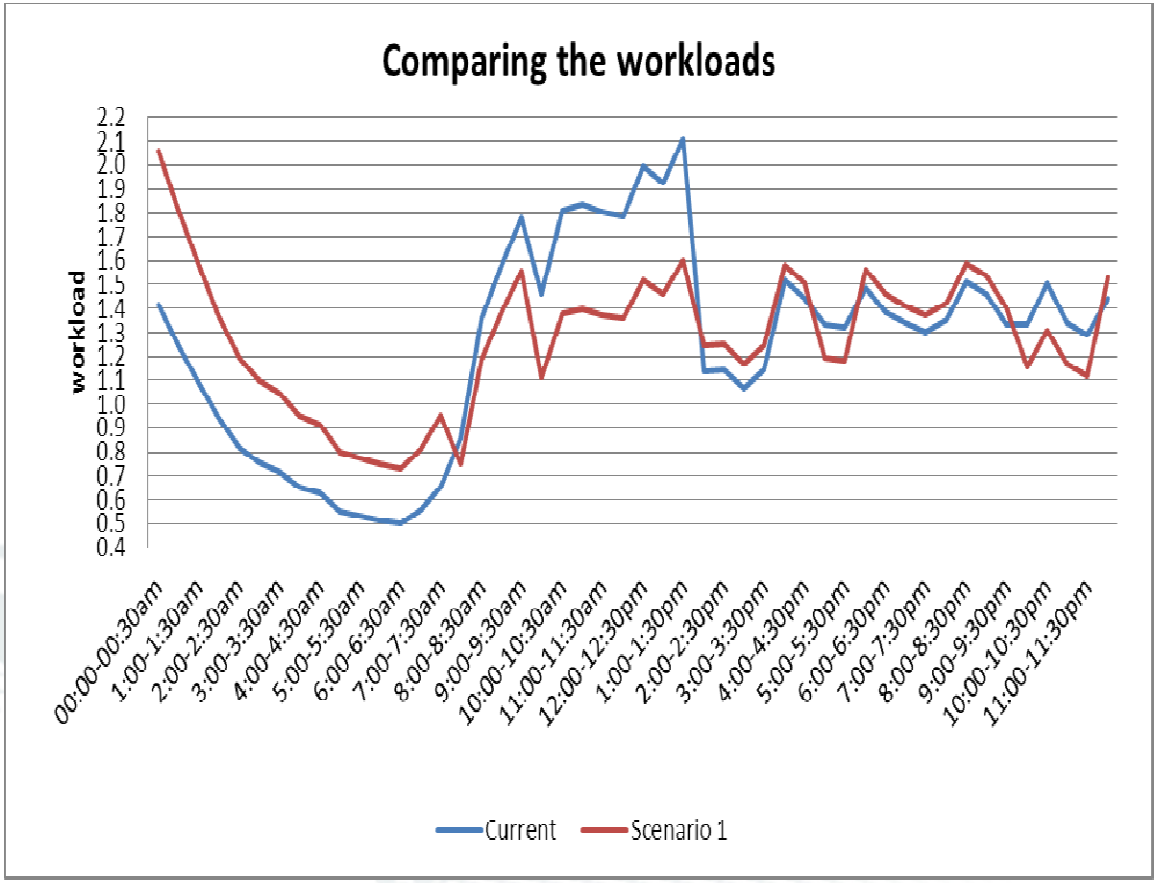
Scenarios for shift capacity planning

- **Scenario 1**
  - no constraint on the number of nurses for each shift;
  - the maximum workload <= current maximum workload.
- **Scenario 2**
  - current nurse capacity of major shifts may decrease/increase *x* nurses;

    where x= 1, 2, 3, 4, 5, 6.
- **Scenario 3**
  - number of nurses of night shift is unchanged.

Results of scenario 1

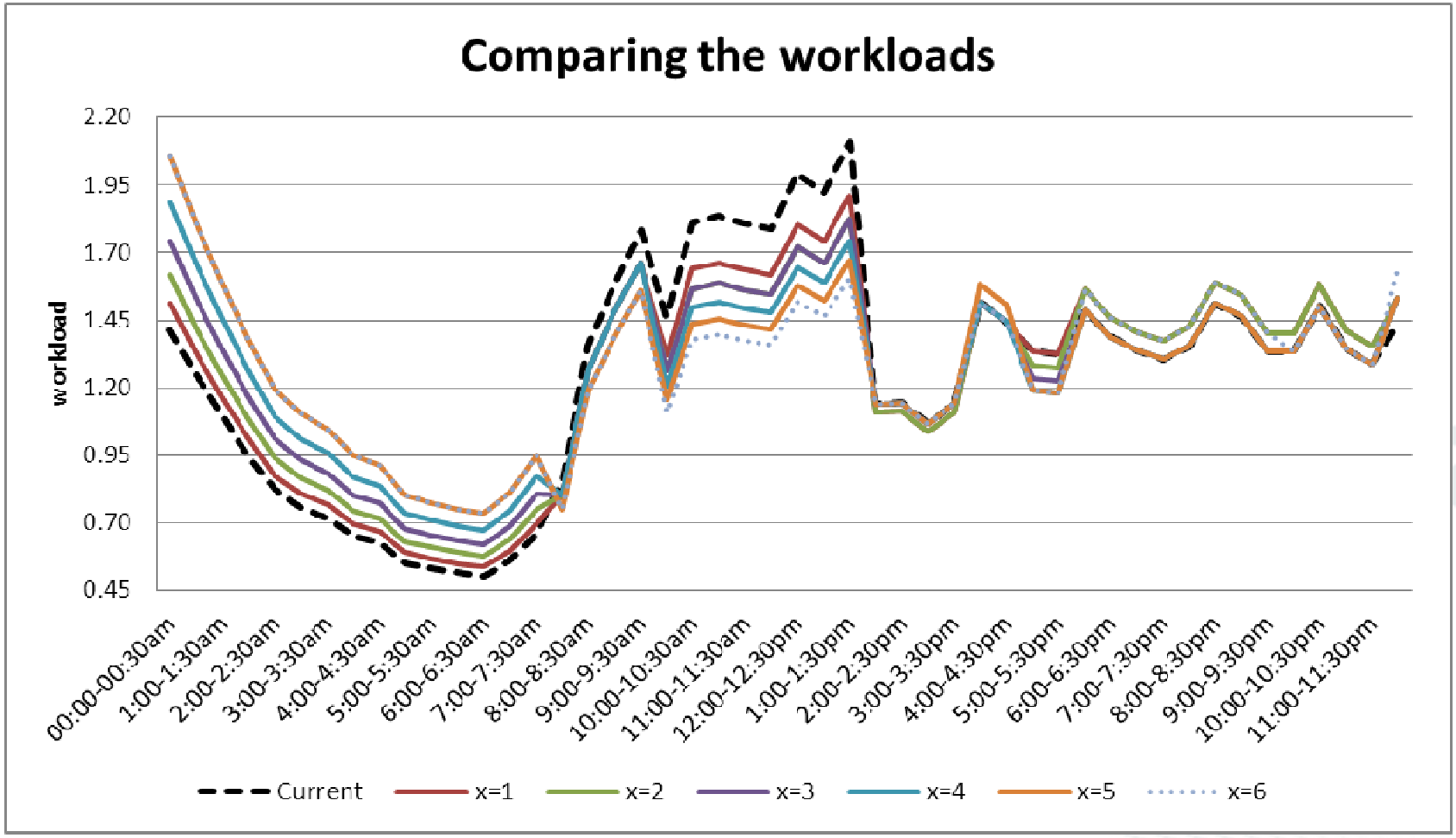
	Current	Scenario 1
Morning shift	14	16
Afternoon shift	16	7
Night shift	16	11
Minor shit 1	5	9
Minor shift 2	3	7
Minor shift 3	1	5
Total capacity	55	55
Mean of workload	1.25	1.28
Mean deviation	0.34	0.23
Mean deviation reduction		32.4%
max WL - min WL	1.61	1.33



Results of scenario 2

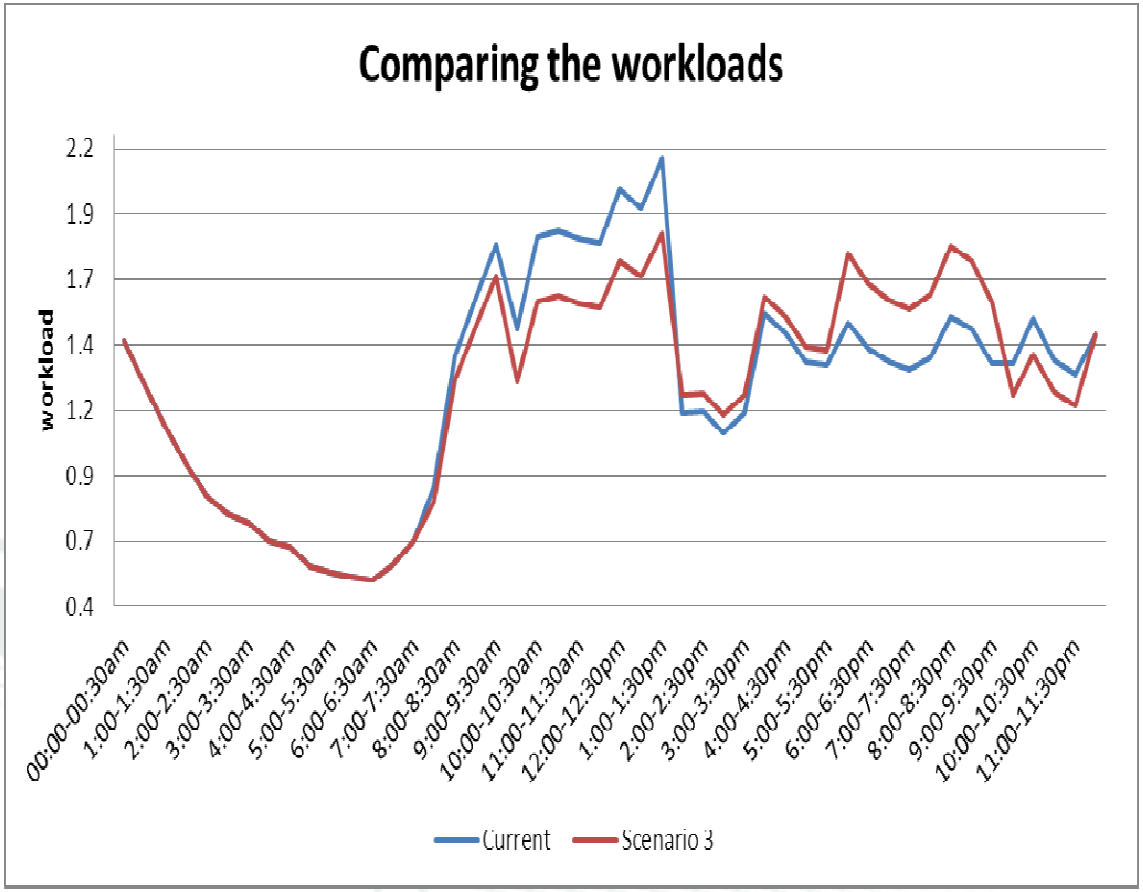
	Current	x=1	x=2	x=3	x=4	x=5	x=6
Morning shift	14	15	15	15	15	16	16
Afternoon shift	16	15	14	13	12	11	10
Night shift	16	15	14	13	12	11	11
Minor shit 1	5	6	7	7	8	8	9
Minor shift 2	3	3	3	4	4	4	5
Minor shift 3	1	1	2	3	4	5	4
Total capacity	55	55	55	55	55	55	55
Mean workload	1.25	1.25	1.25	1.26	1.27	1.28	1.28
Mean deviation	0.34	0.32	0.30	0.27	0.25	0.24	0.24
Mean deviation reduction		5.8%	13.0%	21.4%	26.1%	30.1%	28.9%
max WL - min WL	1.61	1.37	1.25	1.20	1.22	1.33	1.33

Results of scenario 2



Results of scenario 3

	Current	Scenario 3
Morning shift	14	15
Afternoon shift	16	11
Night shift	16	16
Minor shit 1	5	7
Minor shift 2	3	5
Minor shift 3	1	1
Total capacity	55	55
mean of workload (7:30am-00am)	1.47	1.46
mean deviation (7:30am-00am)	0.21	0.19
mean deviation reduction (7:30am-00am)		11.5%
max WL - min WL (7:30am-00am)	1.25	1.02



Other examples using optimization

1. Facility location
   - Where should we place the service points, e.g. hospitals, Polyclinics, to provide sufficient service and minimise distance travelled?
2. Roster
   - Staff roster for a team, e.g. doctor, nurse, etc
3. Bed allocation
   - Given current inpatient beds, how many beds should be given to each department? where should the beds be?
4. Inventory planning
   - Inventory (e.g. gloves, drugs) that needs to be stored, used, purchased
   - How many to buy, when to buy?

Some of our papers & other references

1. Hyperthyroidism in the personalized medicine era – the rise of mathematical optimization. *Journal of the Royal Society Interface* **16**, 20190083, doi: 10.1098/rsif.2019.0083, 2019 (Meng FW et al)
2. Applying gravity model to predict demand of public hospital beds. *Operations Research for Health Care.* https://doi.org/10.1016/j.orhc.2017.09.006 2017 (Teow KL et al)
3. Shift capacity planning for nursing staff in emergency department using mixed integer programming. *Pacific Journal of Optimization* **12**, 635-648, 2016 (Meng FW et al).
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5. Intelligent analysis of acute bed overflow in a tertiary hospital in Singapore. *Journal of Medical Systems* **36**, 1873-1882, 2012 (Teow KL et al)
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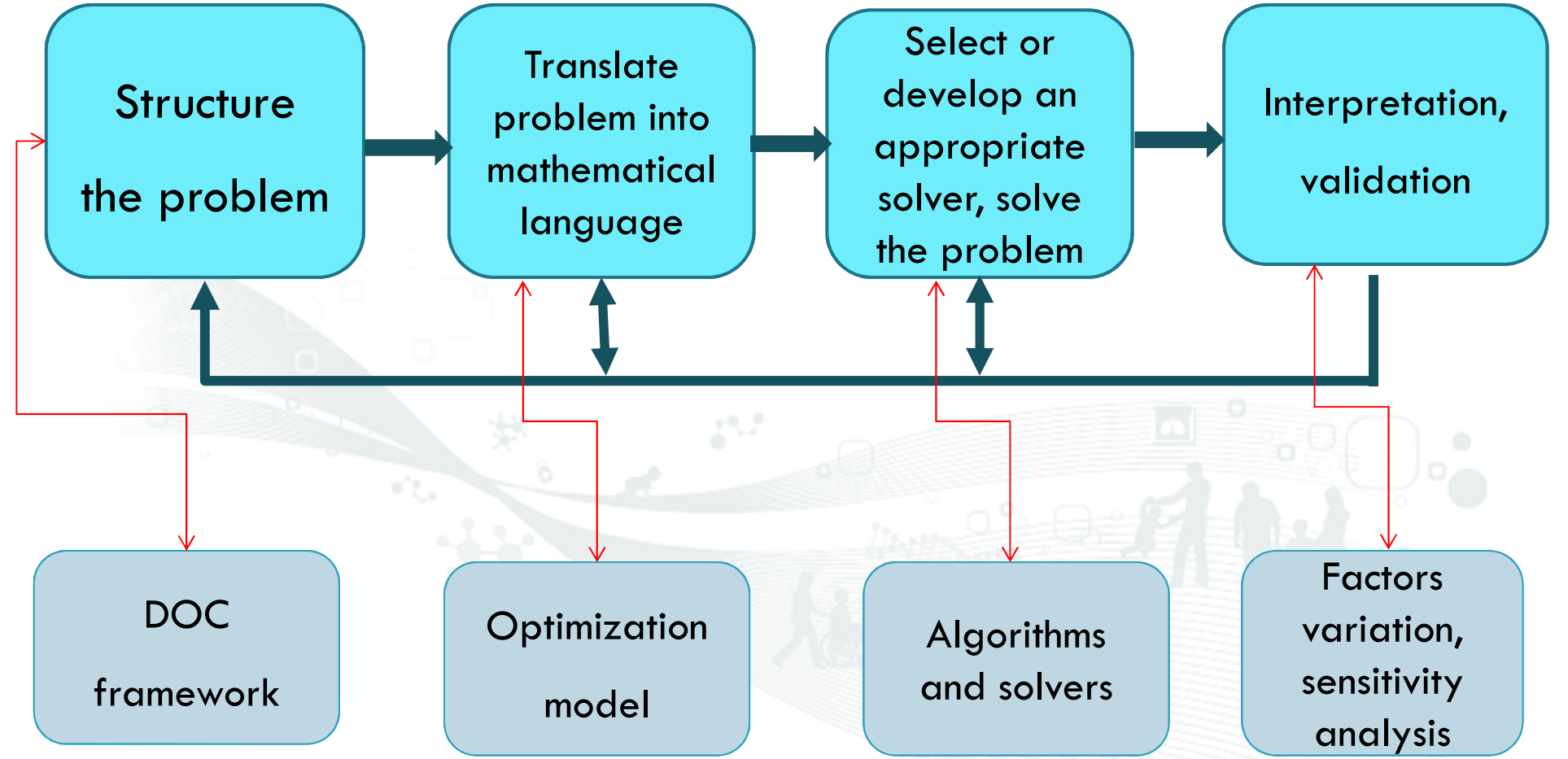
9. Mixed integer programming approaches to treatment planning for Brachytherapy – application to permanent prostate implants. *Annals of Operations Research* **119**, 147-163, 2003 (Lee EK et al)
10. Optimization of operating room allocation using linear programming techniques. *Journal of American College of Surgeons* **197**, 889-895, 2003 (Kuo PC et al)

Summary -- optimization modeling system