Operations Research in Medicine and HealthCare

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What we do

- Operations Research –
  - World War II – target precision, ground logistics and planning and resource supply-chain, health medical plans and execution, soldiers’ well-being (meal planning) and rescue
  - Name – military mission – Operations *Reseach*
- Mathematical Programming –
  - Mathematical models + software programs
- A rich class of mathematics and computational tools (theory and computation)
- Some examples of my work –
  - Information and decision technology/tools for medicine and healthcare, biodefense and public health planning, telecommunication, transportation networks, scheduling ad routing, finance and economics, intelligence and mission-critical logistics

Introduction

- **GT – Health Systems Program, oldest in the country**
- The **Center for Operations Research in Medicine and Healthcare (1998 -) http://www.isye.gatech.edu/~evakylee/medicalor**
  - a collaborative education and research center between OR and medical/public health researchers
  - Mission: to foster interdisciplinary education and research efforts involving the development and application of sophisticated techniques from the field of Operations Research to problems in medicine and healthcare.
- **Center research focuses on the design of novel mathematical modeling and advanced computational algorithms**
  - Health risk prediction
  - Disease prediction and early diagnosis
  - Optimal therapeutics design and novel drug delivery
  - Treatment outcome analysis and monitoring
  - Planning, operation and process efficiency and cost-effectiveness

Center Specific Objectives

- Operations Research – developing realistic models and achieving theoretical, computational and engineering advances for systems, operations, and process improvement.
- HealthCare and Medicine
  - Patient-oriented
  - Early diagnosis
  - Optimal treatment and delivery
  - Cost savings
  - Global and network efficiency (logistics and planning)
- Decision support systems for cost-savings and efficiency achievement in the healthcare-chain:
  - diagnosis, treatment, medical decision making, outcome monitoring, healthcare operations and logistics, and operational and strategic planning

Center Focus: within healthcare and medicine

Develop mathematical models and computer algorithms for:

Modeling, Informatics, and Computing

I. Early Detection, Diagnosis and Monitoring

II. Optimal Treatment & Therapeutics Design

III. Optimal Resource Allocation and Strategic Responses

General Schema

- ***Understand problem and collect data*** for application in hand
- Develop realistic ***mathematical models*** for the application based on the data
- Design and implement ***software programs*** to solve the models developed
- ***Interpret solutions*** to end-users*
- ***Re-engineer*** based on feedback

Tools: **Mathematics, computer science, engineering**

End product: **Decision support system, feedback control device etc…**

IOM/NAE Report (2005)

July 20, 2005 Prepublication Workshop

- The health care industry has devoted relatively little technical talent and intellectual effort to optimizing its operations (particularly at higher levels of systems-hospitals, regional networks, etc.) or to measuring its performance in terms of quality and productivity.

- This neglect has contributed to the development of a high-cost delivery system with poor operational processes and performance measures that provides highly uneven quality of care and limited coverage/reach of quality care.

HealthCare Issues

Some Issues

- Costs
- Quality
- Technology
- Access/deliverability
- Social Infrastructure
- Aging population (chronic condition)
- Social Security/Medicare Financial Crisis

Generic Optimization Models

Max/Min $f_1{}^t x, f_2{}^t x, f_3{}^t x$

subject to $gx <= b$

x *decision variables*

- Multiple objectives (conflicting)
- Linear/nonlinear/discrete objective functions, constraints
- Deterministic, probabilistic, stochastic
- Continuous variables, **discrete variables**

Optimization in HealthCare

It is everywhere…..

process efficiency and quality, cost, preventive care, diagnosis, treatment, disease management and monitoring, e-health, facility network, decision-making, risk-assessement, process design, scheduling…….

Optimizing HealthCare Systems

- **Diagnosis**
- **Predictive/preventive care**

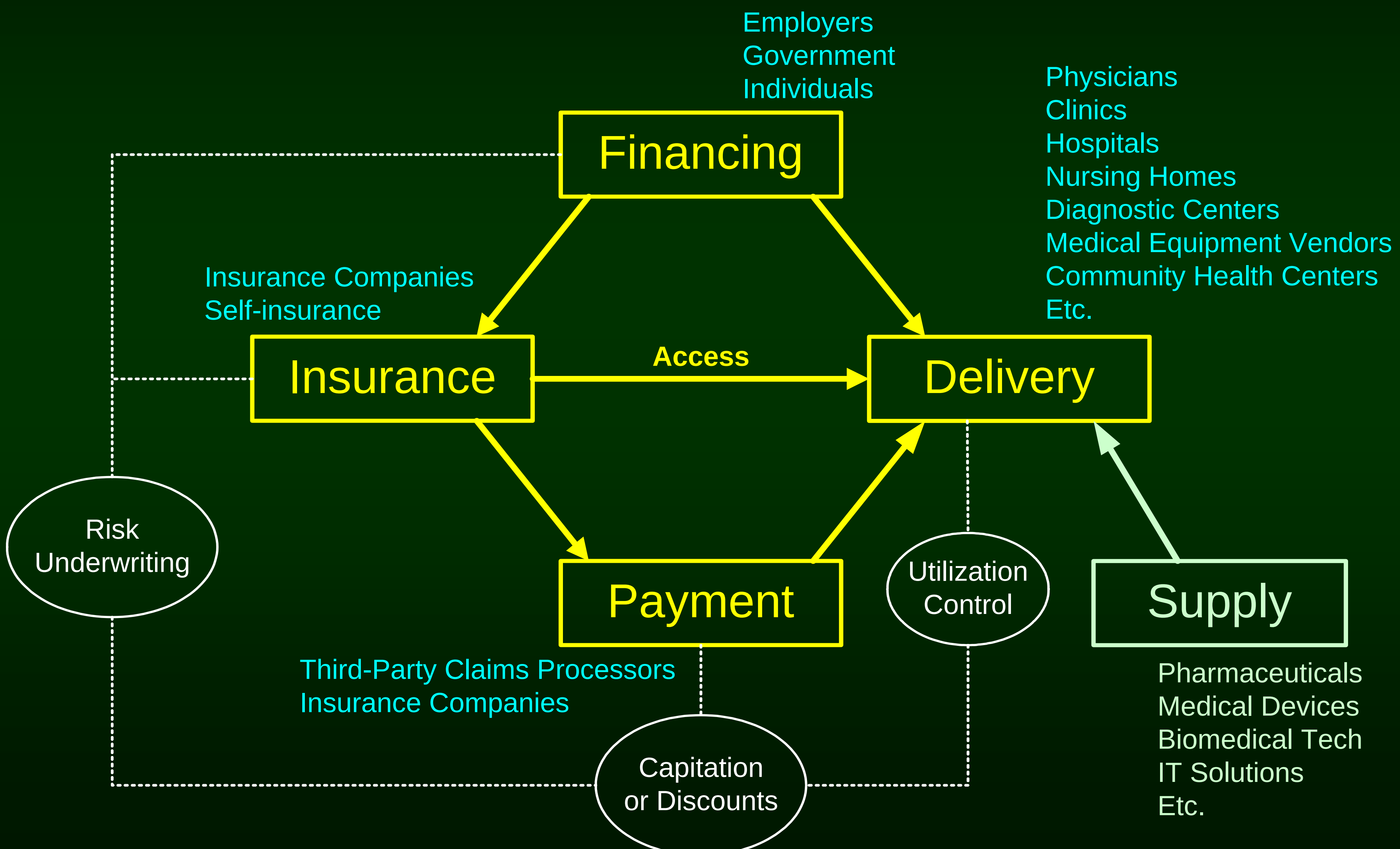
- **Quality Treatment**
- **Cost-effectiveness**

- **Drug Design**
- **Supply Chain & logistics**

- **Medical Device**
- **Accessibility**

- **Individualized Treatment**
- **Quality Pediatric Care**
- **Accurate Diagnosis**
- **Efficient Monitoring and Followup**

Backend – A Complex & Dynamic Operations & Logistics System in Healthcare



Some Experience

This talk will focus on experience of our team in building various successful models and solution engines for real applications --

- Medical Diagnosis
- Optimal Treatment Design and Drug Delivery
- Vaccine design and schedule
- Public health infrastructure and efficient dispensing and treatment operations

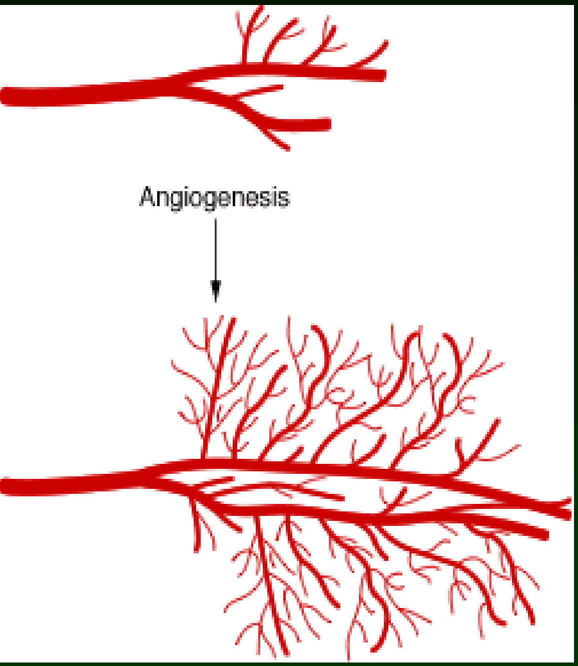
I. Medical Diagnosis & Treatment

- Quality
- Technology
- Cost
- Access

- Not totally transparent
- More biological and clinical oriented
- Challenges –

Medical Diagnosis

- Use information from patients whose statuses are known to develop predictive rule.
- Tests that are relatively inexpensive and unobtrusive; clinical and laboratory observations are frequently available for analysis
- Identify "hidden" patterns in large data set in order to explain, classify or predict; identify discriminatory attributes from these observations to develop a rule that allows one to discriminate one group from another
- Can assist in early detection and intervention



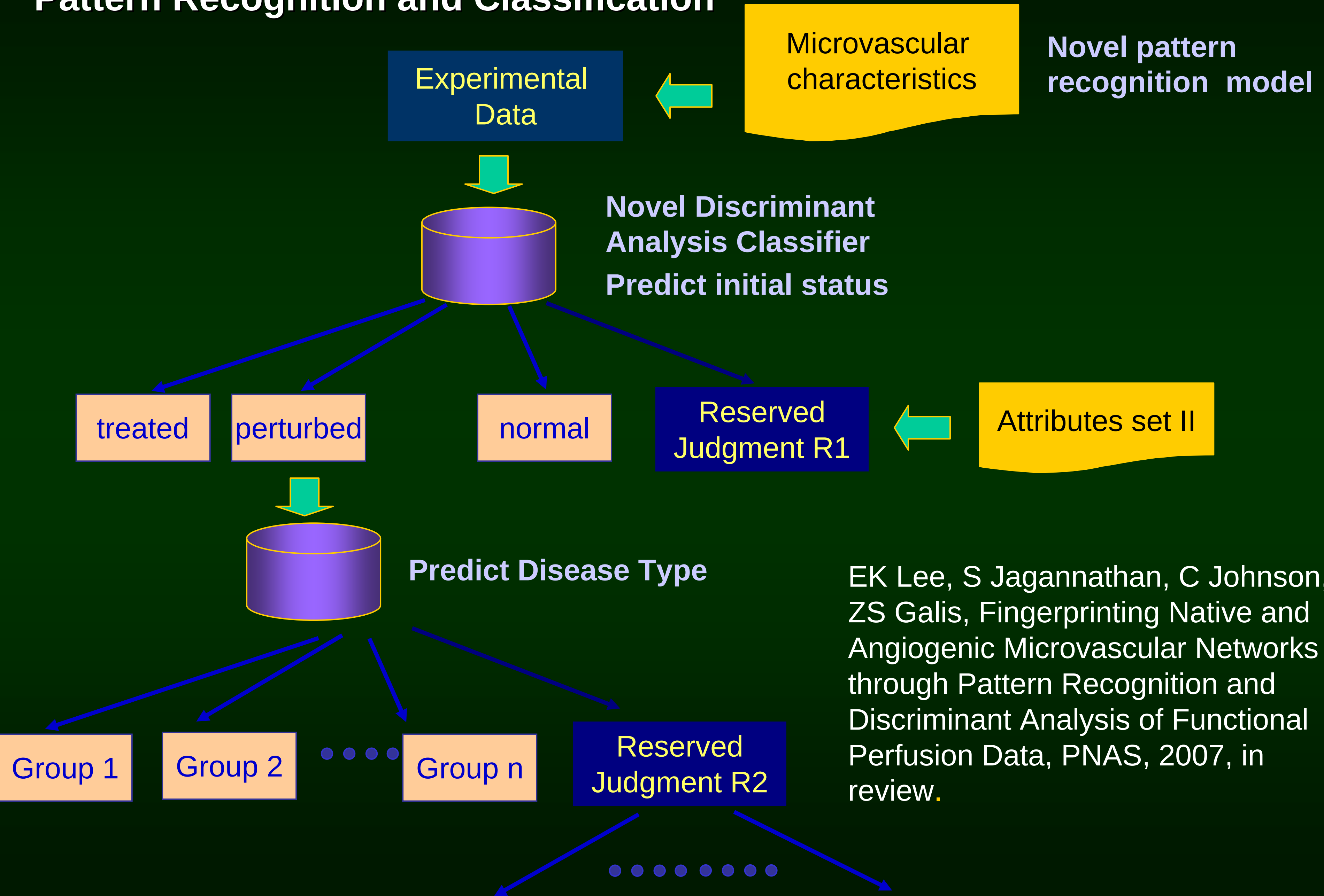
Angiogenesis and its Medical Importance

- Microvascular networks could be used to investigate the potential perturbing effects of conditions such as cardiovascular disease, aging, genetic deficiency, diabetes, and cancer on the microvascular structure in relevant tissues.

- "Angioprinting" will contribute to the understanding of angiogenic mechanisms, and could be utilized in the early diagnosis of microvascular deficiencies, as well as for monitoring and allowing for design of a better therapeutic regimen.

- The study offers novel approaches for
  - **Early disease diagnosis and intervention**
  - **Treatment monitoring and prognosis**
  - **Novel therapeutic approach**

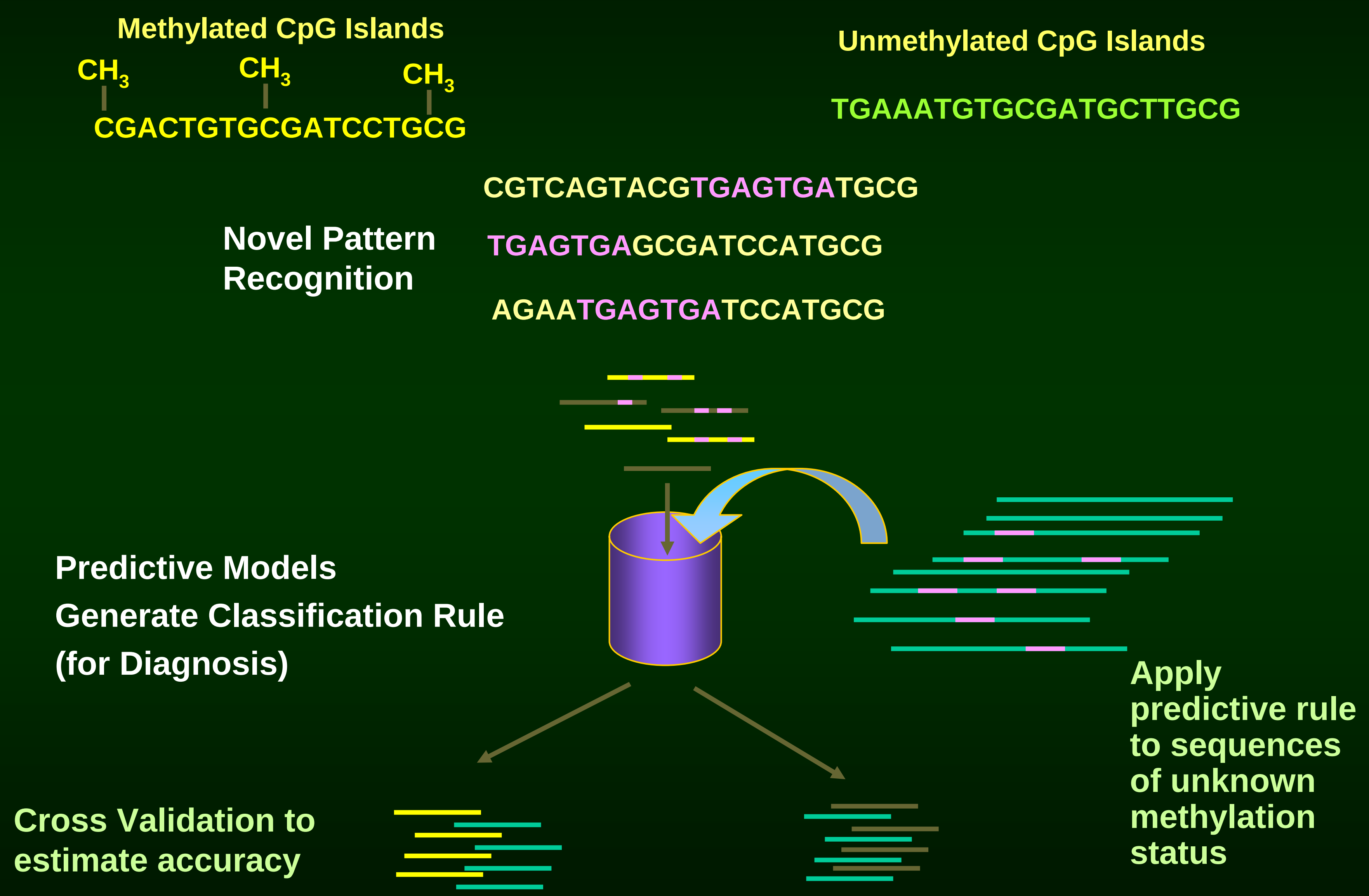
Fingerprinting Native and Angiogenic Microvascular Networks via Pattern Recognition and Classification



EK Lee, S Jagannathan, C Johnson, ZS Galis, Fingerprinting Native and Angiogenic Microvascular Networks through Pattern Recognition and Discriminant Analysis of Functional Perfusion Data, PNAS, 2007, in review.

Predicting CpG Island Methylation (Cancer)

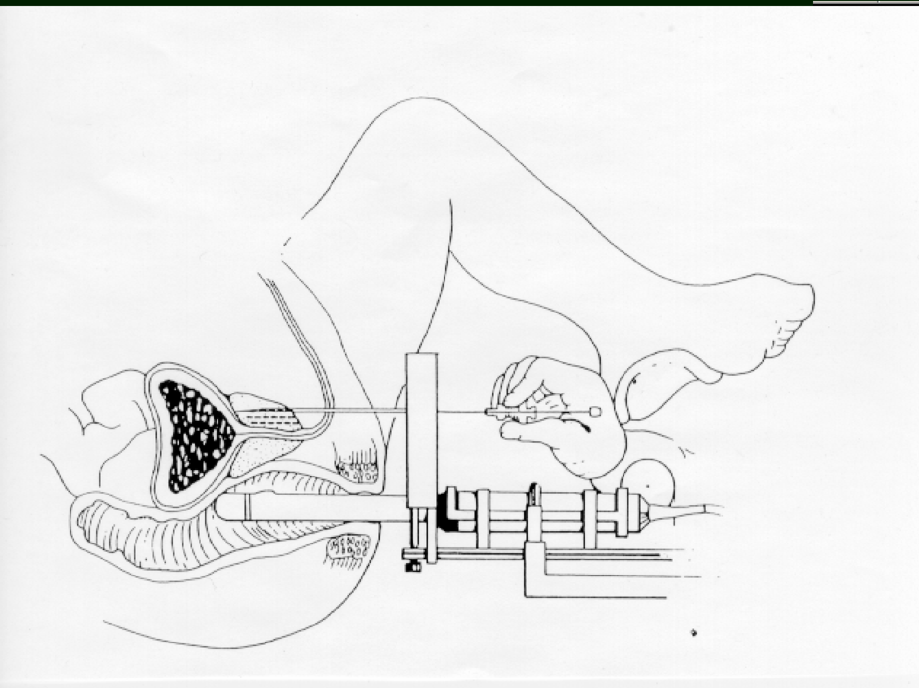
FA Feltus, EK Lee, JF Costello, C Plass, PM Vertino, Predicting Aberrant CpG Island Methylation, Proceedings of the National Academy of Sciences (PNAS), 100(21): 12253-12258, 2003.

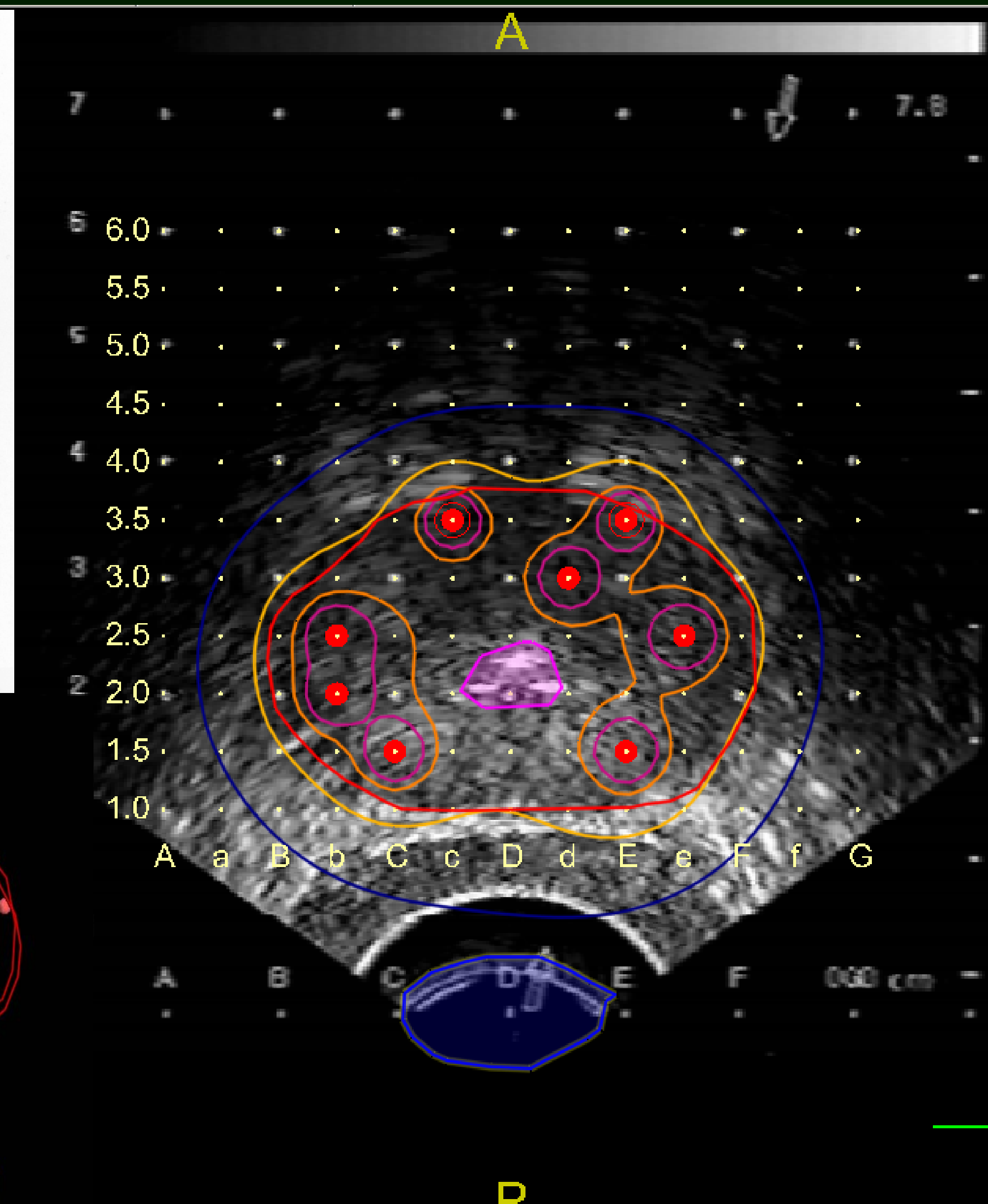


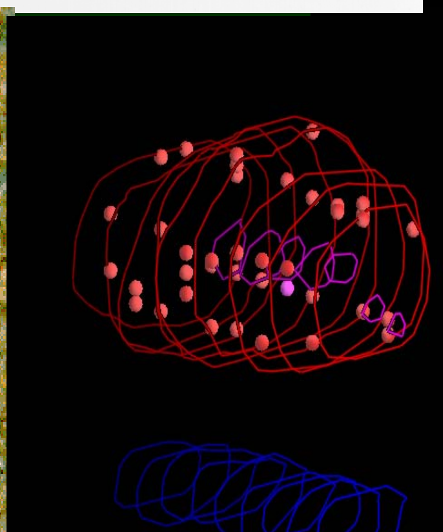
Medical Treatment Designs

- Problems to Tackle
  - Individualized/population treatment design
    - Optimal drug regimen
    - Radiation therapy
    - Combined modality
    - Thermo-ablation
  - One example to focus here:

Optimal Cancer Treatment







Challenges

- **Determine optimal radioactive source locations for best individualized treatment**
- **Many more for optimal cancer treatment…..**

- Ref: EK Lee, M Zaider, Intra-Operative Dynamic Dose Optimization in Permanent Prostate Implants. 2002. Int J Radiat Oncol Biol Phys., 56(3): 854-861, 2003.
- EK Lee, M Zaider, Mixed Integer Programming Approaches to Treatment Planning for Brachytherapy – Application to Permanent Prostate Implants. Annals of Operations Research. 119: 147-163, 2003.
- EK Lee, M Zaider, Determining an Effective Planning Volume for Permanent Prostate Implants. Int J Radiat Oncol Biol Phys., 49(4): 1197-1206, 2001
- M Zaider, M Zelefsky, EK Lee, K Zakian, HA Amols, J Dyke, J Koutcher, Treatment Planning for Prostate Implants Using MR Spectroscopy Imaging. Int J Radiat Oncol Biol Phys., 47(4): 1085-96, 2000.
- EK Lee, RJ Gallagher, D Silvern, CS Wuu and M Zaider, Treatment Planning for Brachytherapy : an Integer Programming Model, Two Computational Approaches and Experiments with Permanent Prostate Implant Planning. Phys Med Biol., 44, No.1, 145-165, 1999.

Traditional Computer-aided Planning Procedure

- Simulation ultrasound/CT scan done days (sometimes weeks) in advance of actual implantation
- Trial-and-error approach to selecting seed positions and viewing on computer
- Graphically examine plans
- Attempt to match prescription isodose contours to target volume contours
- Limit dose to neighboring healthy tissue & organs

Limitations of Traditional Planning

- Labor Intensive Process! (~4-8 hours)
- Cannot impose clinically desirable properties
  - coverage, conformity, number of needles used, multiple seed types
- Non-uniform plan quality
  - High rate of normal tissue complication
  - Poor tumor control
- Hot spots in urethra; cold spots to parts of target volume

Implantation Difficulties

- Reproducibility
  - unable to duplicate patient position
  - unable to duplicate transducer angulation
- Geometry
  - volume changes, organ motion, rectum contraction, bladder/rectum content
- Implementation (feasibility)
  - Pre-plan needle site blocked by bone
  - Pre-plan needle too close to urethra
  - Other tissue structures not registered on pre-plan US images

Current Planning System

Original Clinical Input Data

. US Images
. Anatomy
. Prescription

→

Computer-aided Treatment Planning

Trial-and-error approach to design a plan during simulation session
•Plan evaluation (DVHs, isodose curves, figures of merit)

→

•Radiation Oncologists

•Urologists

OR Modeling and Computation Breakthroughs

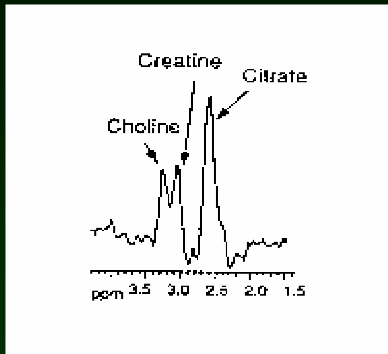
- Plans obtained within less than 5 minutes
- Superior coverage and conformity
- Reduce rectum dose by 15%
- Reduce urethra dose by 25%
- Bonuses: Use fewer seeds (~20-30%) and needles (15%)

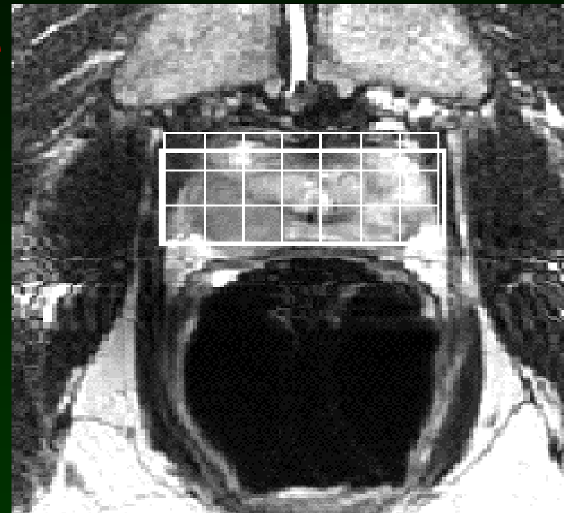
Clinical Significance

- We developed an optimization tool which can incorporate any known constraints of clinical significance, and **solve the problem in real time for the operating room**.
- Saves **~450 million** US dollars in no-longer-needed pre- & post-operation procedures (imaging, hospital usage, labor) for prostate cancer alone in USA.

Advanced System

MRS-Image Engine





MRS data for a patient with Gleason score 7, PSA = 8 ng/ml. The spectral voxels correspond to the grid overlaid on the image

Dose-Control Engine

Extended dose constraints for 30 day period are Imposed to control dose delivered to the prostate, urethra and rectum

Original Clinical Input Data

. US Images
. Anatomy
. Prescription

Auotmated Treatment Planning Engine

- Discretization module
- Dose calculation module
- Treatment plan modeling component with graphical user interface
- Optimization engine
- Plan evaluation (DVHs, isodose curves, figures of merit)

- **Radiation Oncologists**
- **Urologists**

General Challenges – Optimal Treatment

- Objectives are complex, competing
- Biological and clinical objectives are not readily available nor easily incorporated
- Computational advances are needed for complex treatment design
- Elements of uncertainty is very high (clinical outcome)
- Biological advances appear to be critical
- High translational value… but must be patient and persistent….

I. Medical Diagnosis & Treatment

- Quality
- Technology
- Cost
- Access

- Not totally transparent
- More biological and clinical oriented
- Challenges –

Quality, Technology, Cost, Accessibility

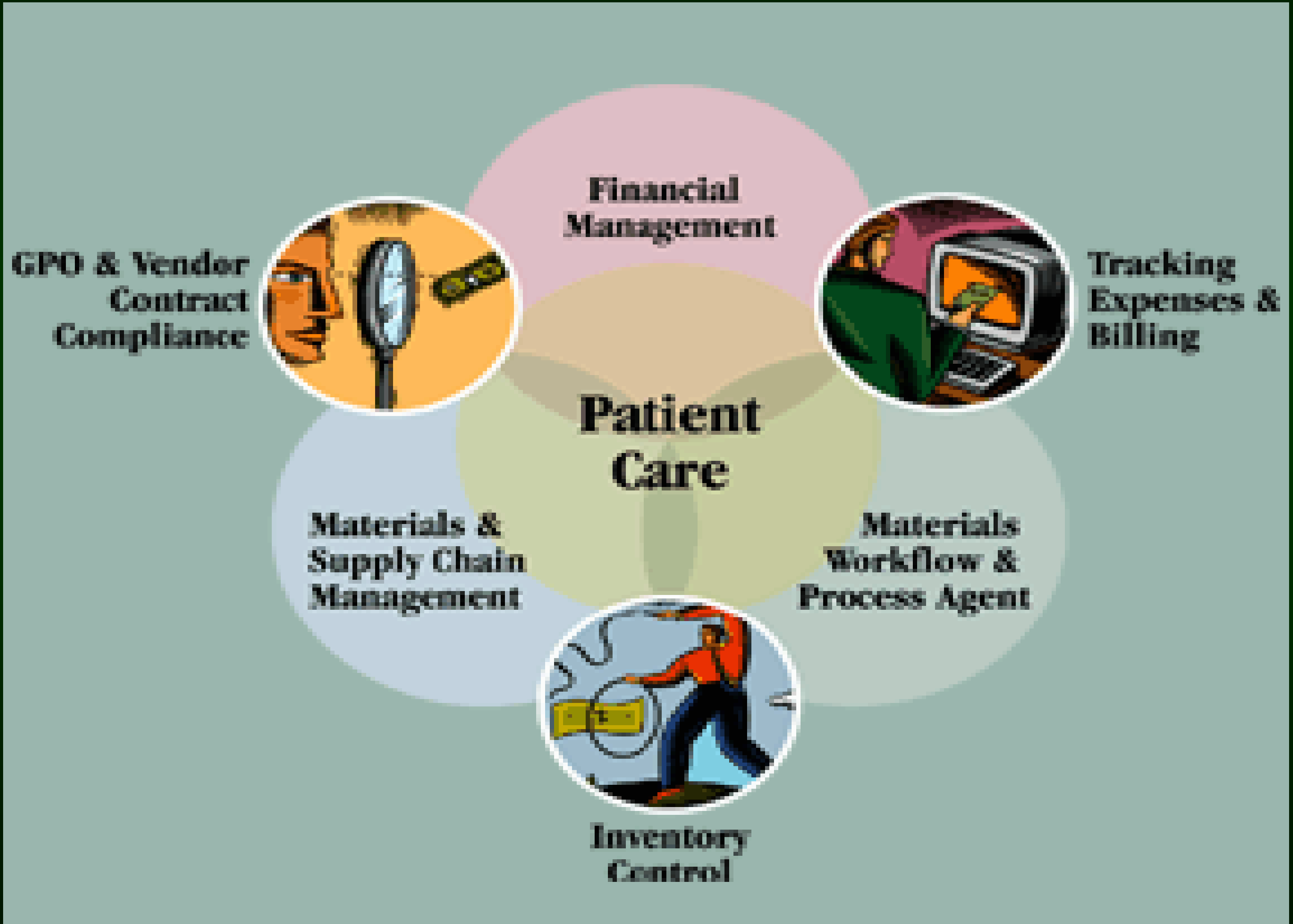
- Improve accuracy and power of diagnosis
- Diagnosis, treatment design no longer operator-dependent
- Predictive, treatment models and parameters are far more complex and realistic than existing ones
- Cost saving in terms of labor time, cost of treatment, and hospital facilities usage
- Objective analysis of clinical improvement

II. Delivery, Operations & Logistics

- Costs
- Quality
- Technology
- Access
- Social Security/Medicare Financial Crisis

- Traditional OR technologies are readily available
- Similar to their applications to other industrial applications
- Challenges –

A Complex & Dynamic Operations & Logistics System in Healthcare



Designing Pediatric Formularies for Childhood Immunization Using Integer Programming Models – Optimal Drug Deliver Schedule

Excerpt from course taught by Lee: OR in Medicine and HealthCare, Spring 2006.

Problem with Vaccine Development

Galloping advance of bio-technology

+

Complexity of the United States recommended childhood immunization schedule

=

Opportunity in process improvement

As vaccine manufacturers develop new vaccine for childhood immunization, and the Advisory Committee on Immunization Practice (ACIP) adds these vaccines to the recommended childhood immunization schedule, the plethora of choices presented to health-care providers, health insurance companies and parents has created a combinatorial nightmare for the already complex immunization schedule.

Vaccine Scheduling

DEPARTMENT OF HEALTH AND HUMAN SERVICES • CENTERS FOR DISEASE CONTROL AND PREVENTION

Recommended Childhood and Adolescent Immunization Schedule UNITED STATES • 2006

Vaccine ▼ / Age ▶	Birth	1 month	2 months	4 months	6 months	12 months	15 months	18 months	24 months	4–6 years	11–12 years	13–14 years	15 years	16–18 years
Hepatitis B[1]	HepB	HepB		*HepB[1]*	HepB				HepB Series					
Diphtheria, Tetanus, Pertussis[2]			DTaP	DTaP	DTaP		DTaP			DTaP	Tdap	Tdap		
Haemophilus influenzae type b[3]			Hib	Hib	*Hib[3]*	Hib								
Inactivated Poliovirus			IPV	IPV	IPV					IPV				
Measles, Mumps, Rubella[4]						MMR				MMR	MMR			
Varicella[5]						Varicella			Varicella					
Meningococcal[6]							Vaccines within broken line are for selected populations		MPSV4		MCV4	MCV4	MCV4	
Pneumococcal[7]			PCV	PCV	PCV	PCV			PCV / PPV					
Influenza[8]					Influenza (Yearly)				Influenza (Yearly)					
Hepatitis A[9]						HepA Series								

This schedule indicates the recommended ages for routine administration of currently licensed childhood vaccines, as of December 1, 2005, for children through age 18 years. Any dose not administered at the recommended age should be administered at any subsequent visit when indicated and feasible. ▭ Indicates age groups that warrant special effort to administer those vaccines not previously administered. Additional vaccines may be licensed and recommended during the year. Licensed combination vaccines may be used whenever any components of the combination are indicated and other components of the vaccine are not contraindicated and if approved by the Food and Drug Administration for that dose of the series. Providers should consult the respective ACIP statement for detailed recommendations. Clinically significant adverse events that follow immunization should be reported to the Vaccine Adverse Event Reporting System (VAERS). Guidance about how to obtain and complete a VAERS form is available at www.vaers.hhs.gov or by telephone, 800-822-7967.

▭ Range of recommended ages ▭ Catch-up immunization ▭ 11–12 year old assessment

The overcrowded 2006 Childhood Immunization Schedule

General Challenges

- Complex models required for optimal vaccine development (biological, logistical, clinical trials and approval)
- On schedule deliverability
- Affordability, convenience, comfort of delivery
- Special care -- deliver to the poor

DTPa-HIB-HBV-IPV Vaccine

Optimal Pediatric Vaccine Formula

Visit Age	Scheduled Vaccine
 months	DTPa-HIB-HBV-IPV (Unspec. MFG) + PNUcn-7 (WYE)
 months	DTPa-HIB-HBV-IPV (Unspec. MFG) + PNUcn-7 (WYE)
 months	DTPa-HIB-HBV-IPV (Unspec. MFG) + PNUcn-7 (WYE)
 2-18 onths	**DTPa-HIB-HBV-IPV (Unspec. MFG) + MMR (MRK) + VAR (MRK) + PNUcn-7 (WYE)**
 -6 years	DTPa-HIB-HBV-IPV (Unspec. MFG) + MMR (MRK)
 1-12 ears	Td (AVP)

Schedule designed by GT students:
Ahmet Xareooglon, Yen Duong, with Faculty advisor, EK Lee

And INF
Vaccine yearly

Large-Scale Public Health Logistics

- EK Lee, S Maheshwary, J Mason, W Glisson, Large-scale dispensing for emergency response to bioterrorism & infectious disease outbreak. Interfaces -- OR Applications for Homeland Defense, 36(6): 591-607, 2006.
- EK Lee, S Maheshwary, J Mason, Real-Time staff allocation for emergency treatment response of biologic threats and infectious disease outbreak. Medical Decision Making 2005. Selected as INFORMS William Pierskalla Best Paper Award on research excellence in HealthCare and Management Science, Nov 2005

Some Challenges to Tackle

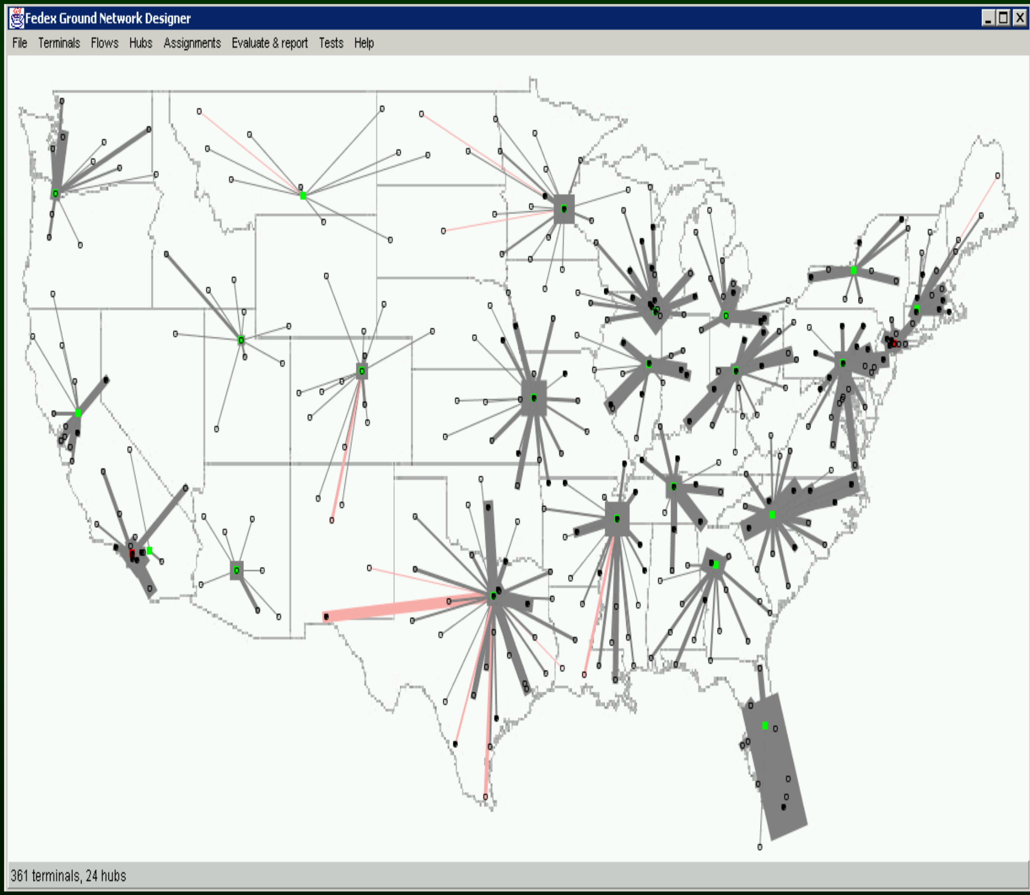
National Level

- Supply/delivery networks
  - **Efficient Infracstructure:** Facility location, Hub-and-spoke design
  - **Efficient Transportation network:** routing and operational design
  - Ref: Bartholdi JJ, III, D Dave, EK Lee, Computing optimal load plans in less-than-truckload freight networks. Advances in Manufacturing, Logistics, and Supply Chain Management: Proceedings of the International Workshop in IT-Enabled Manufacturing, Logistics, and Supply Chain Management, Bangalore, India, 1-22, 2003.

Strategic Planning

- Provide high level view of network design
- Sensitivity in operation costs, and shipment flows on hub-and-spoke assignments
- Overview of patterns of freight flows
- Techniques:
    - Frontend java graphical user interface
    - Backend large-scale optimization (MIP) engine for facility locations planning

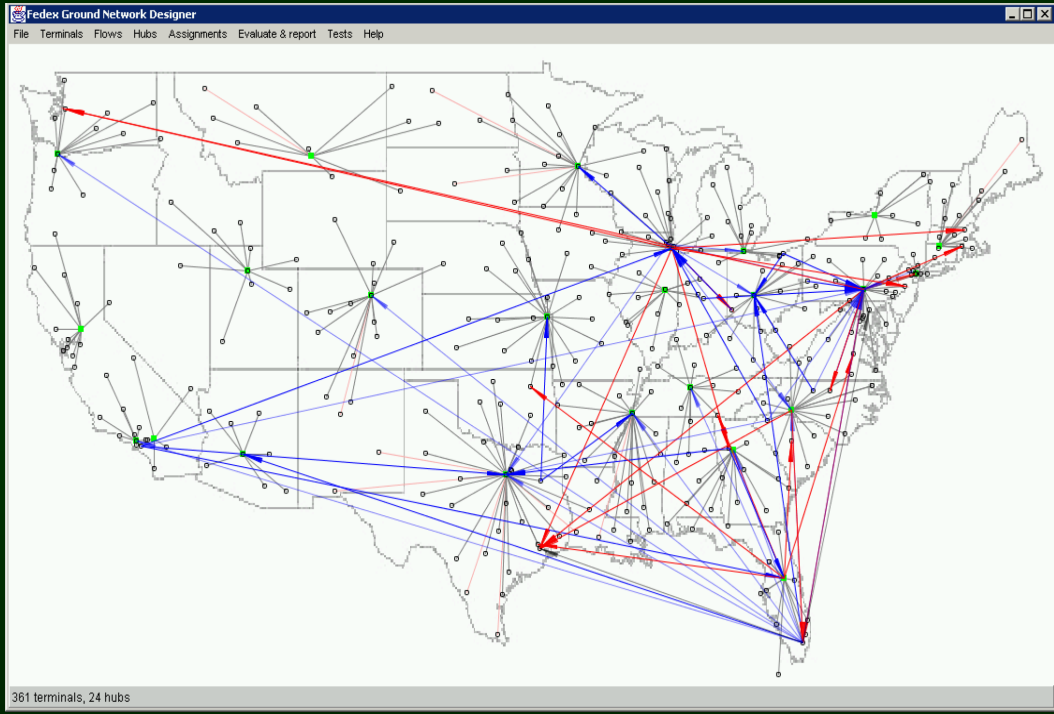
Hub-and-Spoke Network Design



Operational Planning

- Provide operational planning for handling day-to-day (or month-to-month) load planning
- Sensitivity in flow/cost based on sorting / transportation through different possible routes
- Daily patterns of freight flows, forecast of patterns over long period for feedback to strategic hub-and-spoke design

Load Planning



- Techniques:
    - Frontend: java graphical interface
    - Backend: MIPs, parallel algorithms, heuristic routines

Some Challenges to Tackle

Regional Level – At local facility

- Individual access
- Efficient staffing for cost-effective and quality service

- Ref: EK Lee, S Maheshwary, J Mason, Real-Time staff allocation for emergency treatment response of biologic threats and infectious disease outbreak. Medical Decision Making 2005. Selected as INFORMS William Pierskalla Best Paper Award on research excellence in HealthCare and Management Science, Nov 2005.
- EK Lee, S Maheshwary, J Mason, W Glisson, Large-scale dispensing for emergency response to bioterrorism & infectious disease outbreak. Interfaces -- OR Applications for Homeland Defense, 36(6): 591-607, 2006.
- EK Lee, Y Zhang, F Pietz, B Benecke, Facility locations and multi-modality mass dispensing for biodefense and infectious disease outbreaks, 2007, submitted.

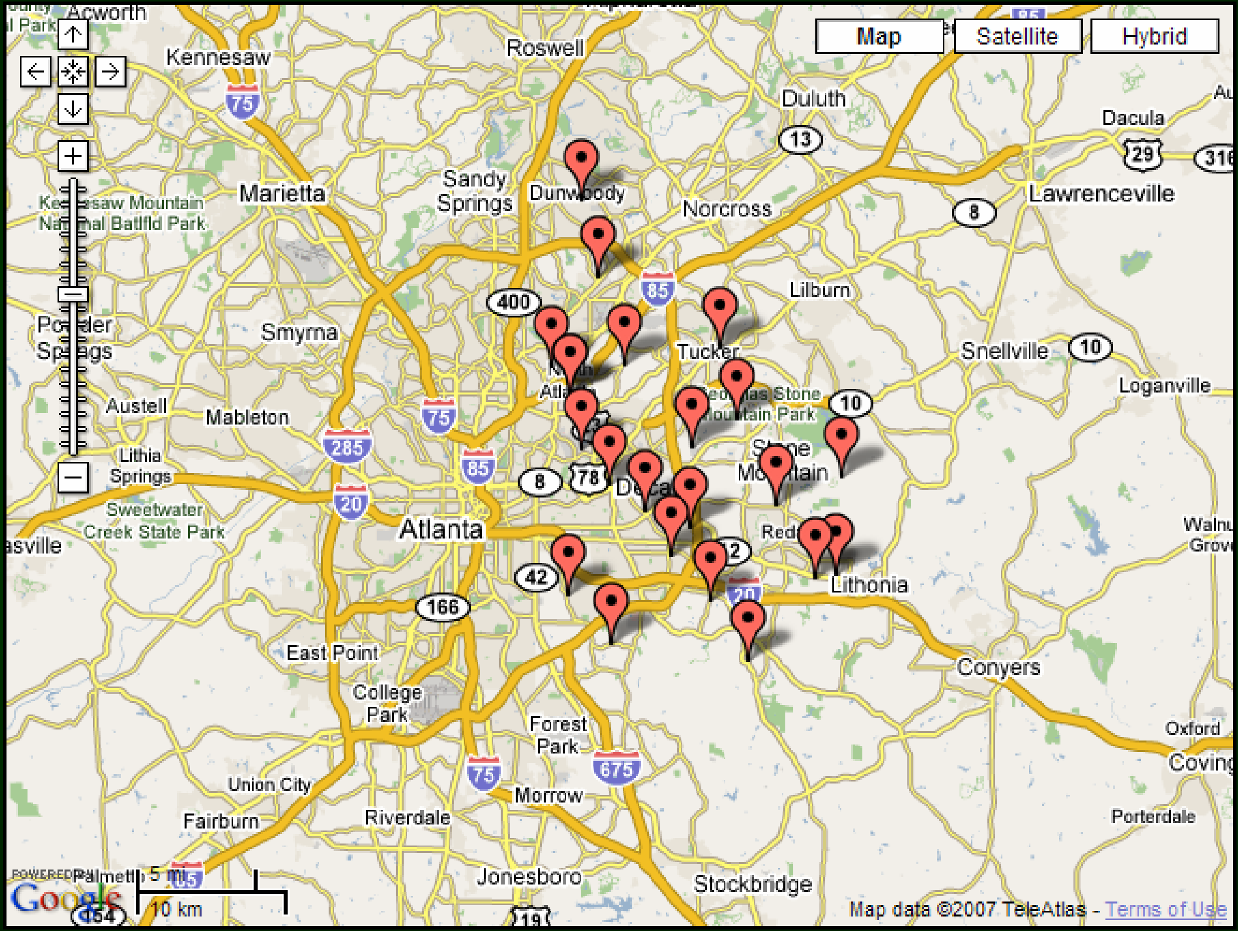
Local Planning & Logistics

- A county with 10 population regions
- 3 Assembly Points
- 7 Points-of-Dispensing (POD, healthcare facilities)
- A given amount of labor resources
- Objectives
  - Determine how many assembly points and PODs are needed and where to set them up
  - Determine the best assignment/routing of individuals to assembly points
  - Determine best assignment/routing of individuals from assembly point to POD
  - Determine the minimum resources needed to provide dispensing for the entire regional population without a time constraint.

Local Planning and Logistics

- Given a regional population, determine where and how many facilities are needed for optimal operations
- Determine optimal assignment of individuals to various facilities
- Determine optimal staffing/resources needed at each facilities for required throughput

Potential Facility Locations

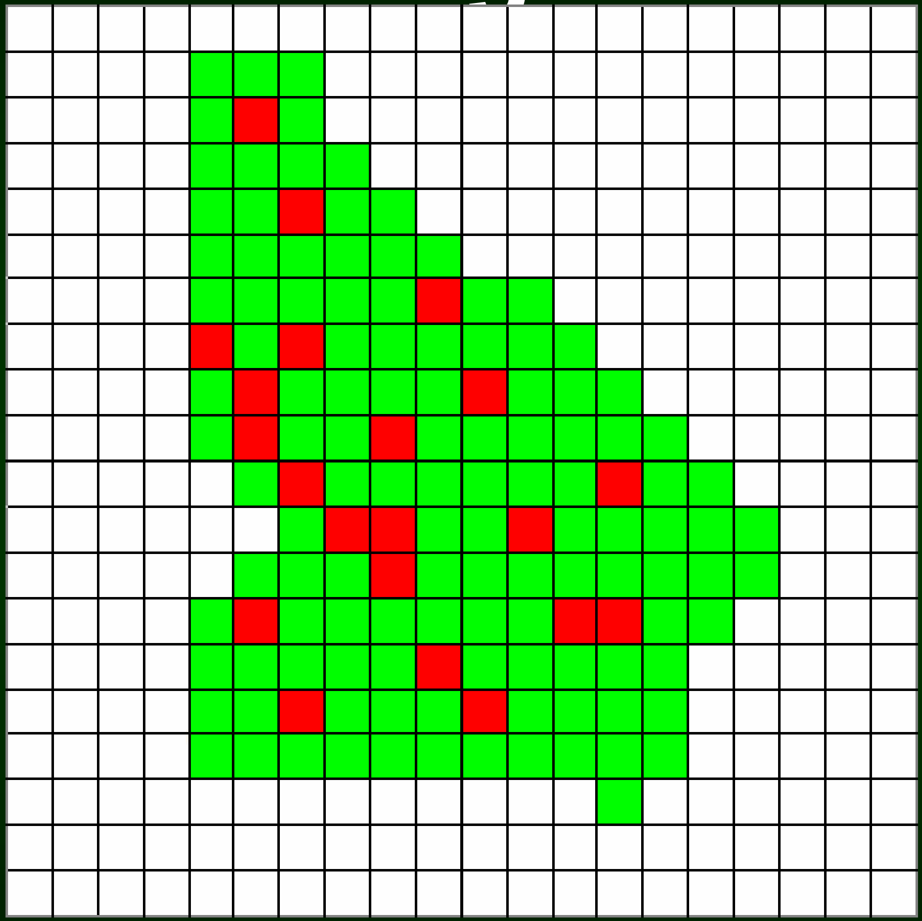


highlighted locations

Strategic Planning

- Given a regional population, determine where and how many facilities are needed for optimal operations
- How to direct residents to these locations?
- Multiple-Objective: minimize average distance to the closest dispensing location, as well as minimize facility set-up cost.

Facility-Location Determination in a Region



Optimization Model

Task for RealOpt©: Study the impact of the number of dispensing locations on the average travel distance. Model has many variations.

Objective(s): Minimize distance travel by each household and total facility setup costs

Constraints:

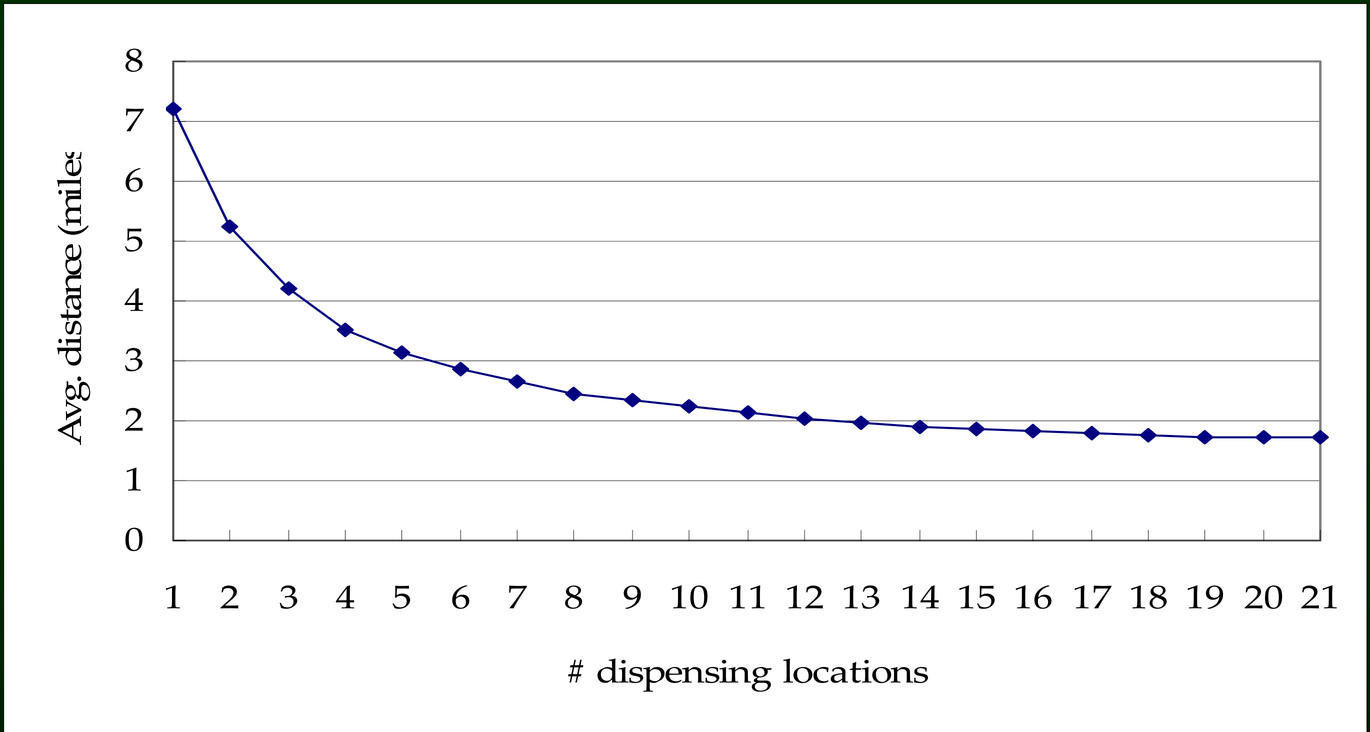
-Each household is assigned to exactly one facility

-Only a limited number of facilities can be opened (due to setup resource limitation)

-Every household must be served

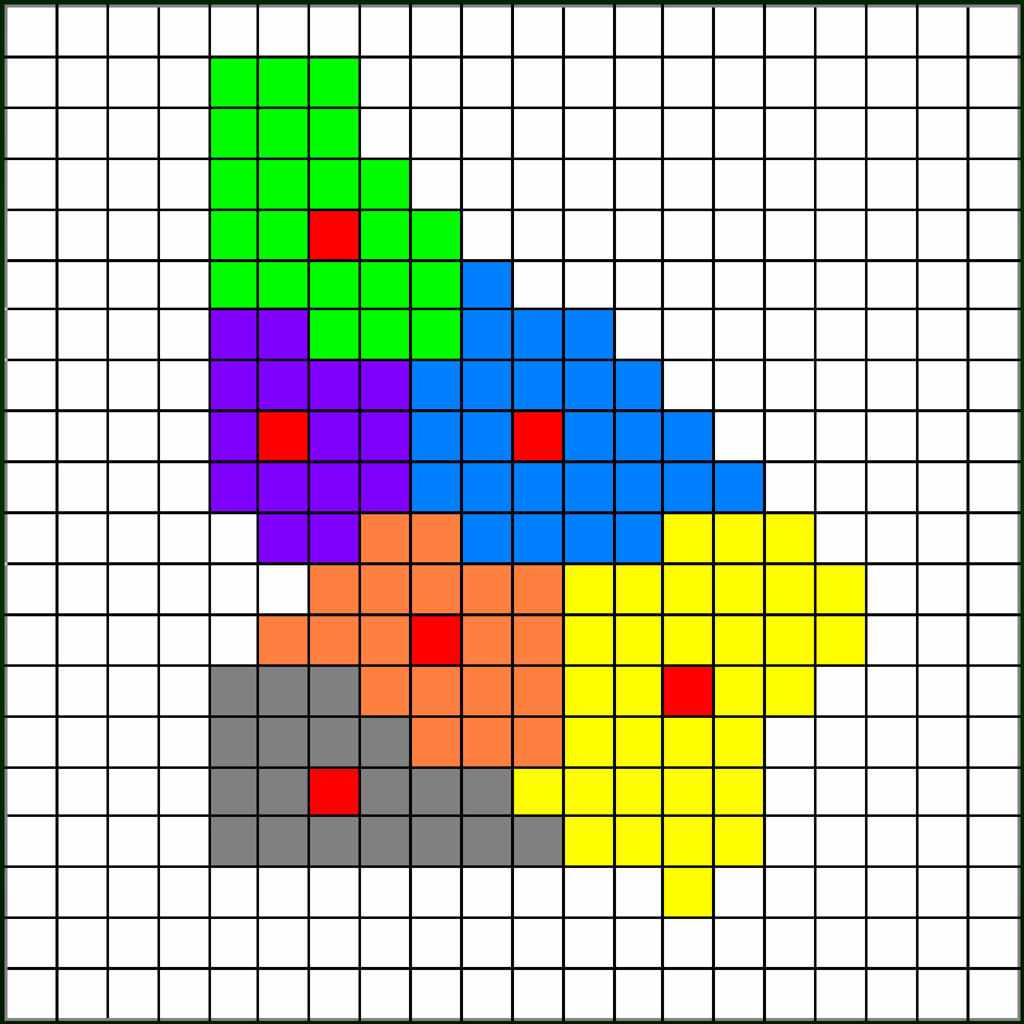
Computational Study

Table: Average distance to the closest facility location versus number of locations



Optimal number of facilities: We can setup 6 facilities.

Optimal Facility Locations



Next Step

- Given a regional population, determine where and how many facilities are needed for optimal operations
- Determine optimal assignment of individuals to various facilities
- Determine optimal staffing/resources needed at each facility for required throughput

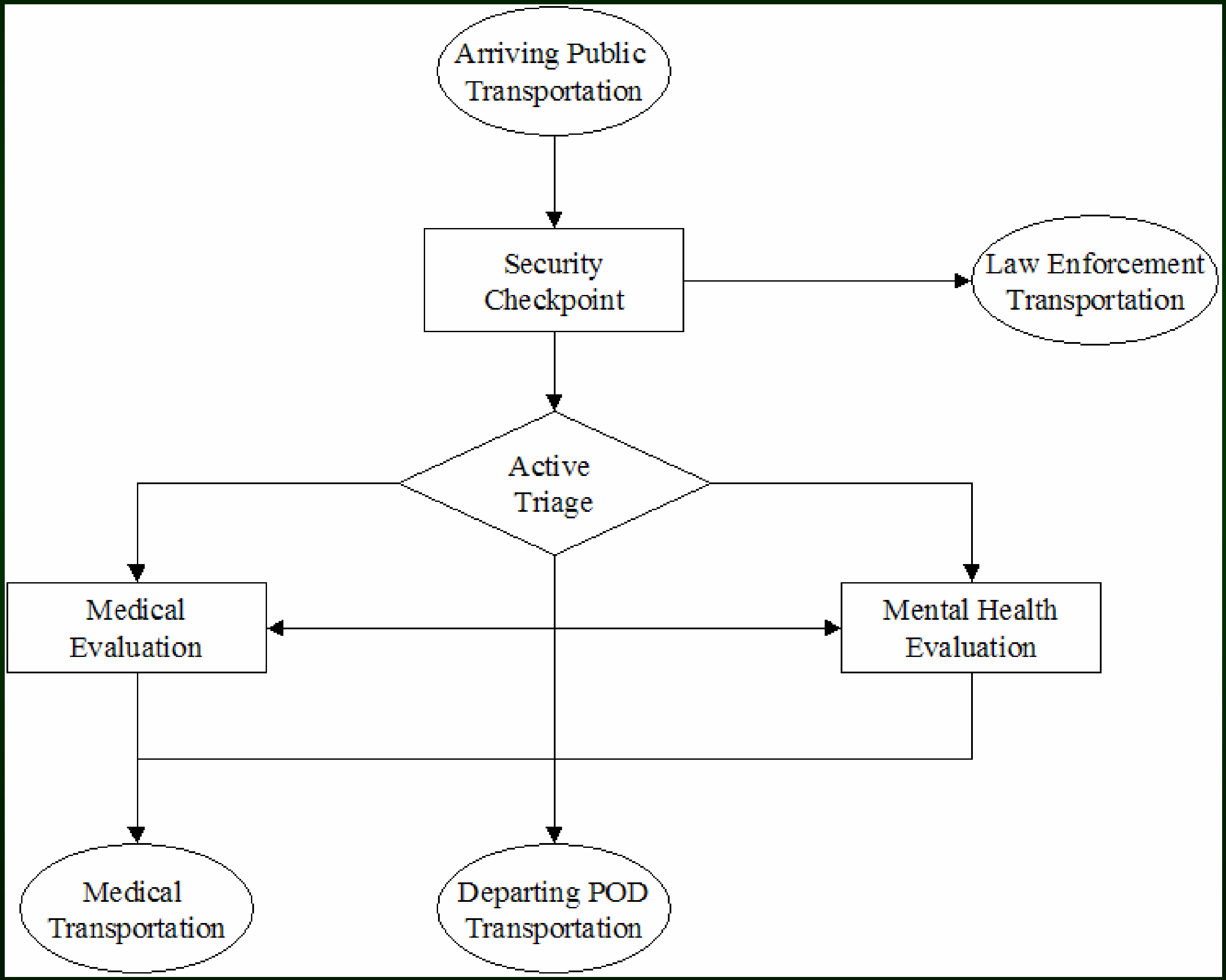
Resource Allocation Problem

- Let *S* be the set of workstations, *T* the set of worker-types
- Let x_{ij} be the number of workers of type *i* assigned to station *j*
- Let *mij* and <u>*mij*</u> be max and min no. of workers of type *i* assigned to station *j*
- Let w_j, q_j, u_j be the average wait time, queue length and utilization rate of station *j*, respectively
- Let *c* be the average cycle time, and *b* be the average throughput for the entire system

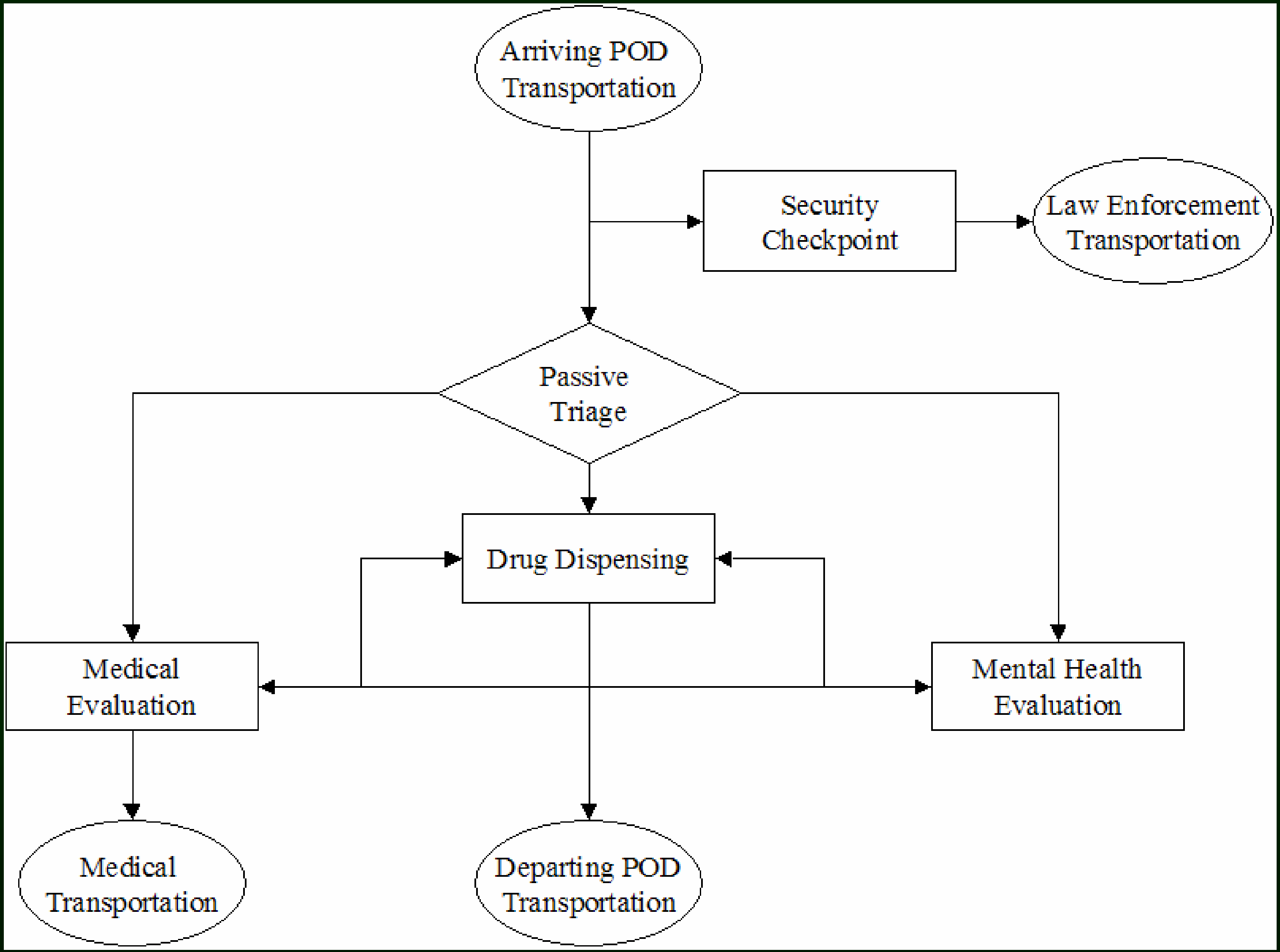
Resource Allocation Problem

- Cost of each station j: $g_j\,(k_{ij}x_{ij}, w_j, q_j, u_j)$
- Facilitate multiple objectives:
  - Minimize total labor/cost: $\sum_j (g_j, c, b)$
  - Maximize throughput
  - Equalize utilization at each station
  - Minimize max wait time
- Constraints:
  - min utilization rate, max wait time, max queue length, min/max worker-type assignment, *etc*
- Objective not a closed-form; facility need not achieve steady-state

Anthrax Clinic – Assembly Point



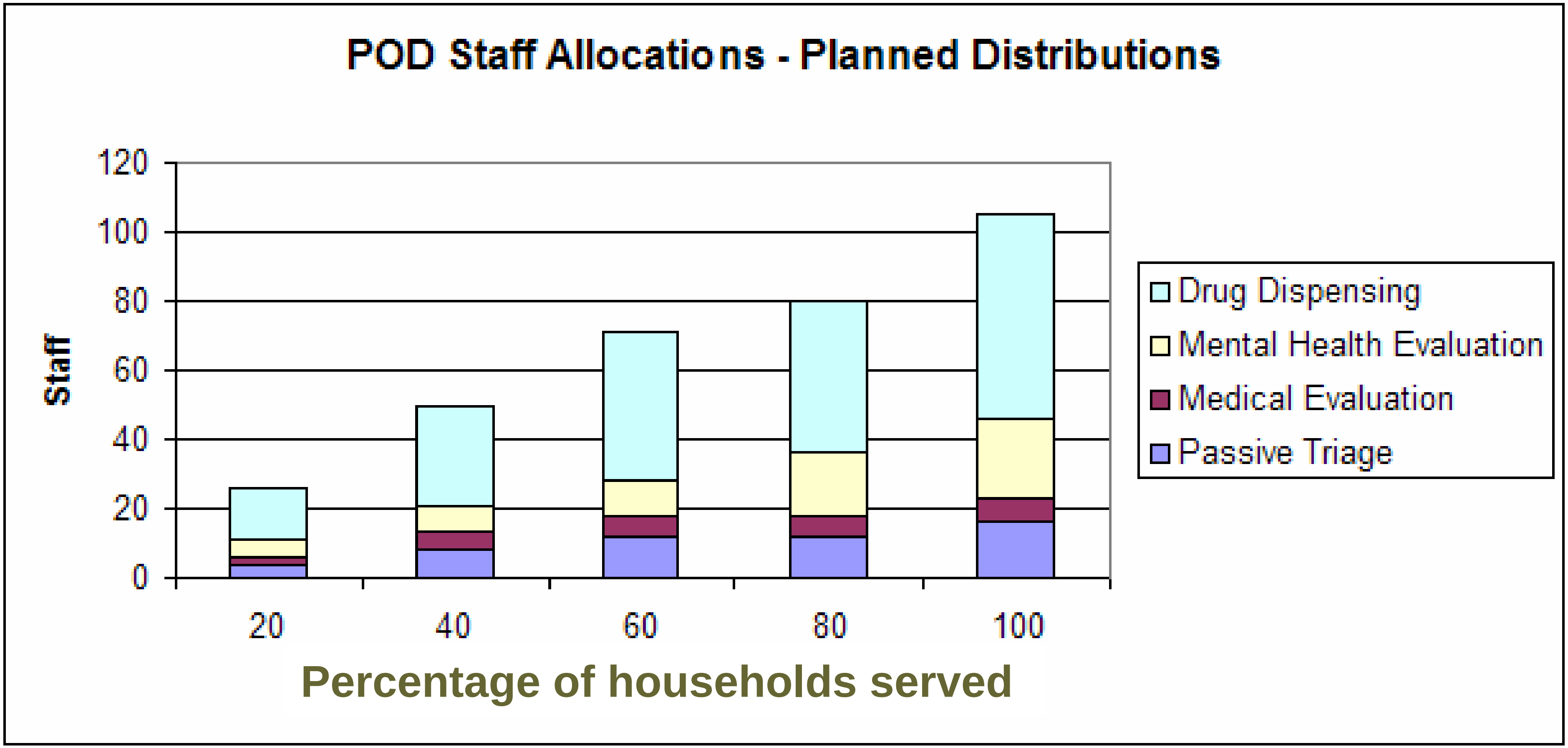
Anthrax Clinic – Point-of-Dispensing



Target Dispensing Level

- 864,000 households
- 3 Assembly-point, 7 POD pairs are used
- Workers work in 8 hour-shifts
- Goal: complete dispensing for entire population within 24 hours
- Task for RealOpt©: Determine the minimal resources required to man each station within each assembly point and POD.

Labor Resources Required for each facility for each 8-hour shift



RealOpt© Capability

- Design to determine healthcare facilities and labor needs to effectively serve a region (can handle population in order of millions)
- Can be used for regular (e.g. daily, monthly, seasonal, yearly) clinic/facility resource determination, e.g., running an HIV clinic, setting up healthcare facilities in Africa and other countries.
- Critical: System output offers optimal efficiency under *scare resources*

Summary

- Systems approach to analyze a problem
- A powerful modeling and algorithmic design for decision making/analysis
- Requires close collaboration with domain experts
- Final system used in practice (companies, government, clinics, public health)

Engineering Health Care Delivery Systems

- Systems Approach
  - Information & Decision Support Systems
  - Operations research, systems modeling
  - Advanced information and communication technologies
- Modeling, Analysis, Management and Control tools, techniques and theories
- Major forces changing the health care environment provide OR experts with even greater opportunities to improve healthcare delivery system

The End