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Robert Aarhus and Edward Huang, George Mason University

Use of a Multidisciplinary Design Optimization Approach to Model Treatment Decisions in Oropharyngeal Cancer

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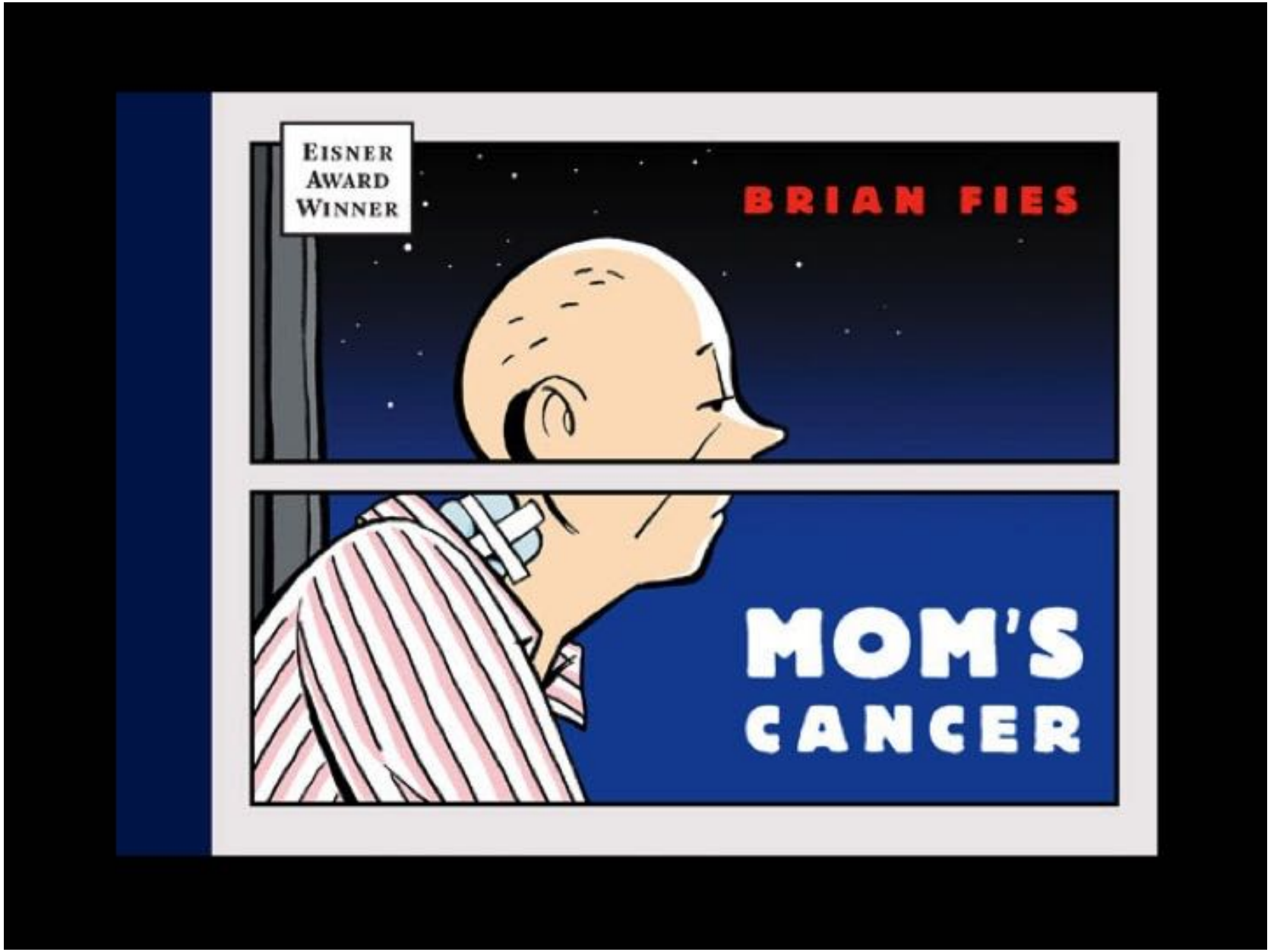
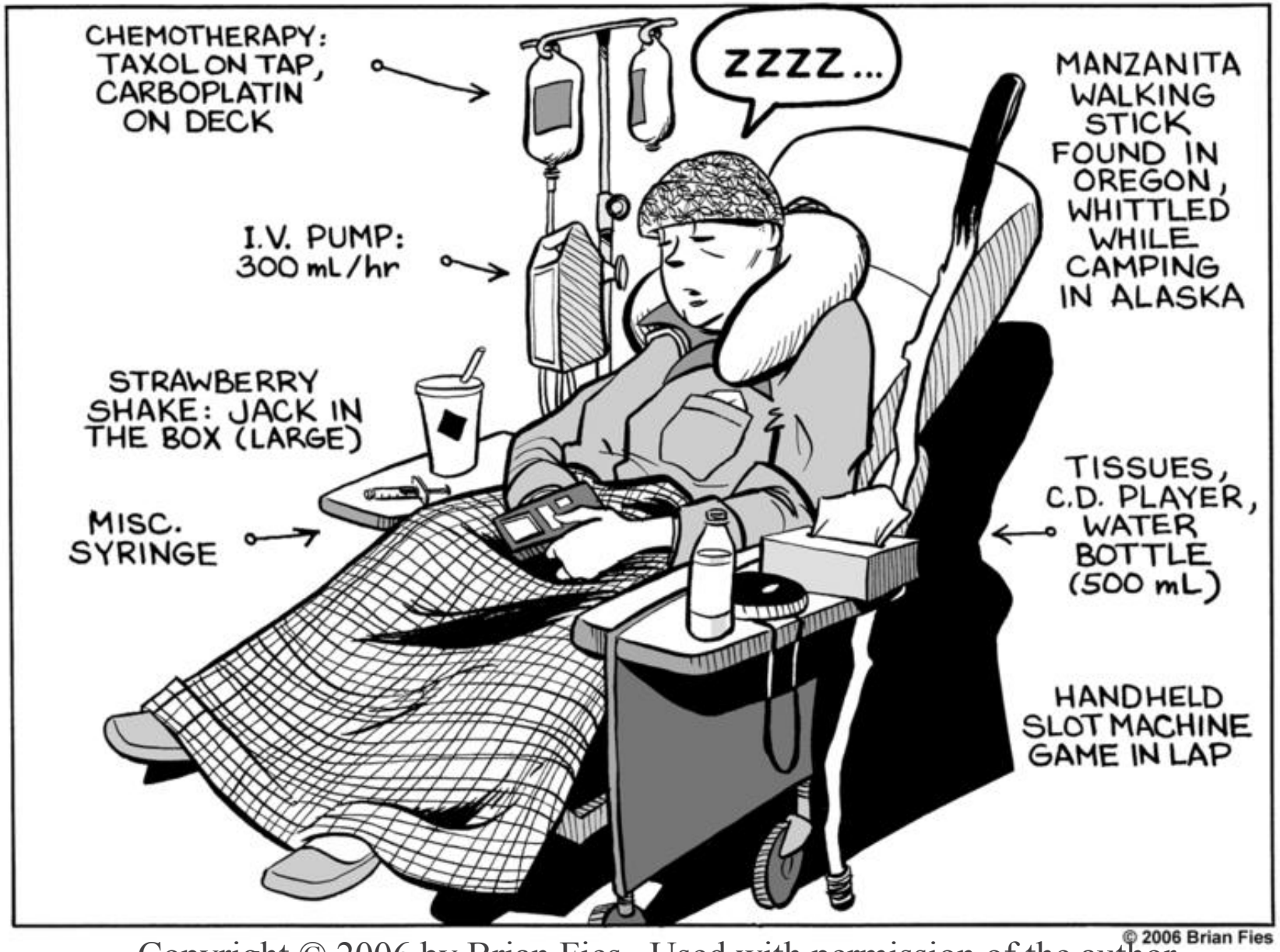
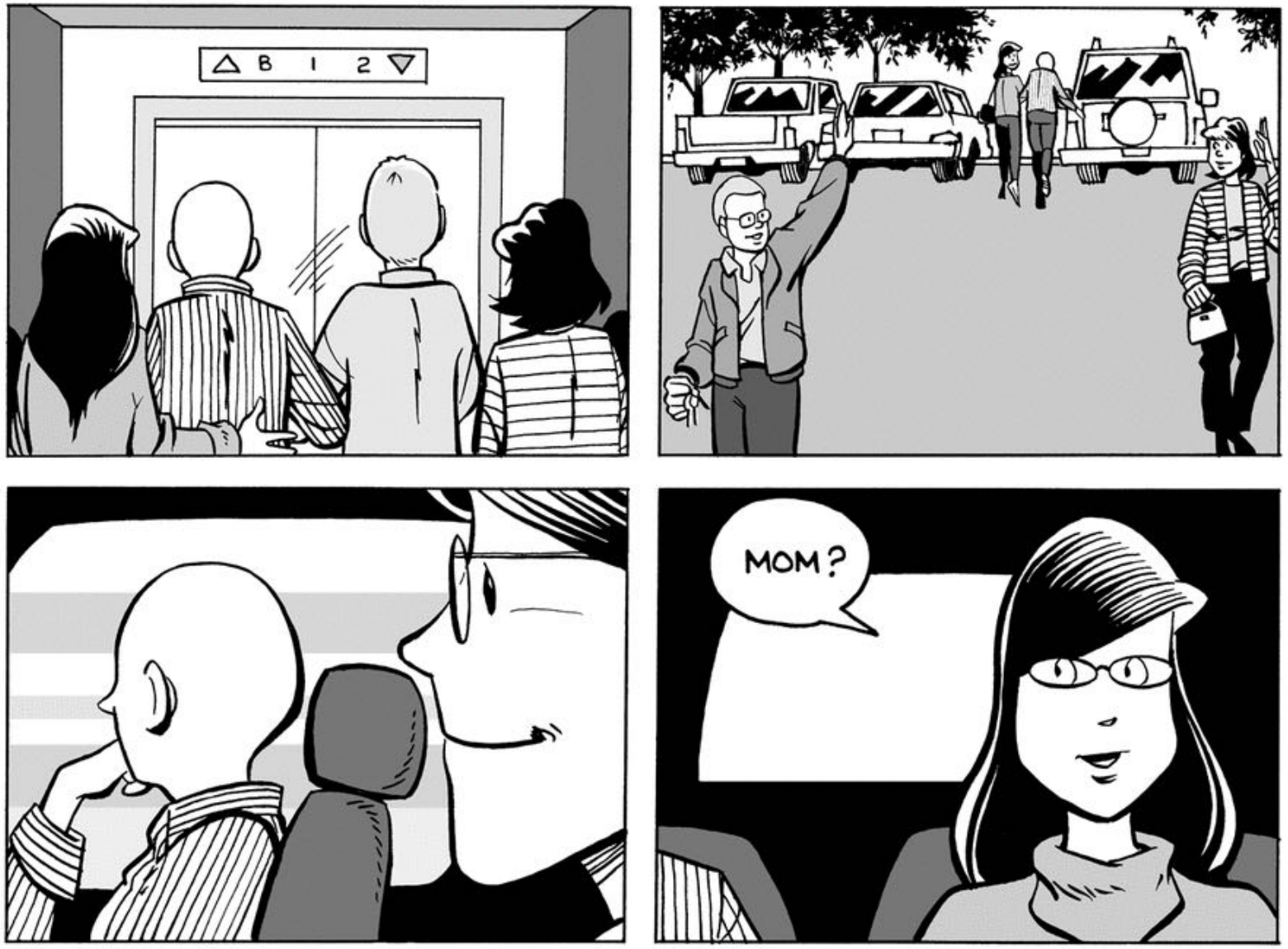




The Five Percent Solution

The Five Percent Solution (con't)



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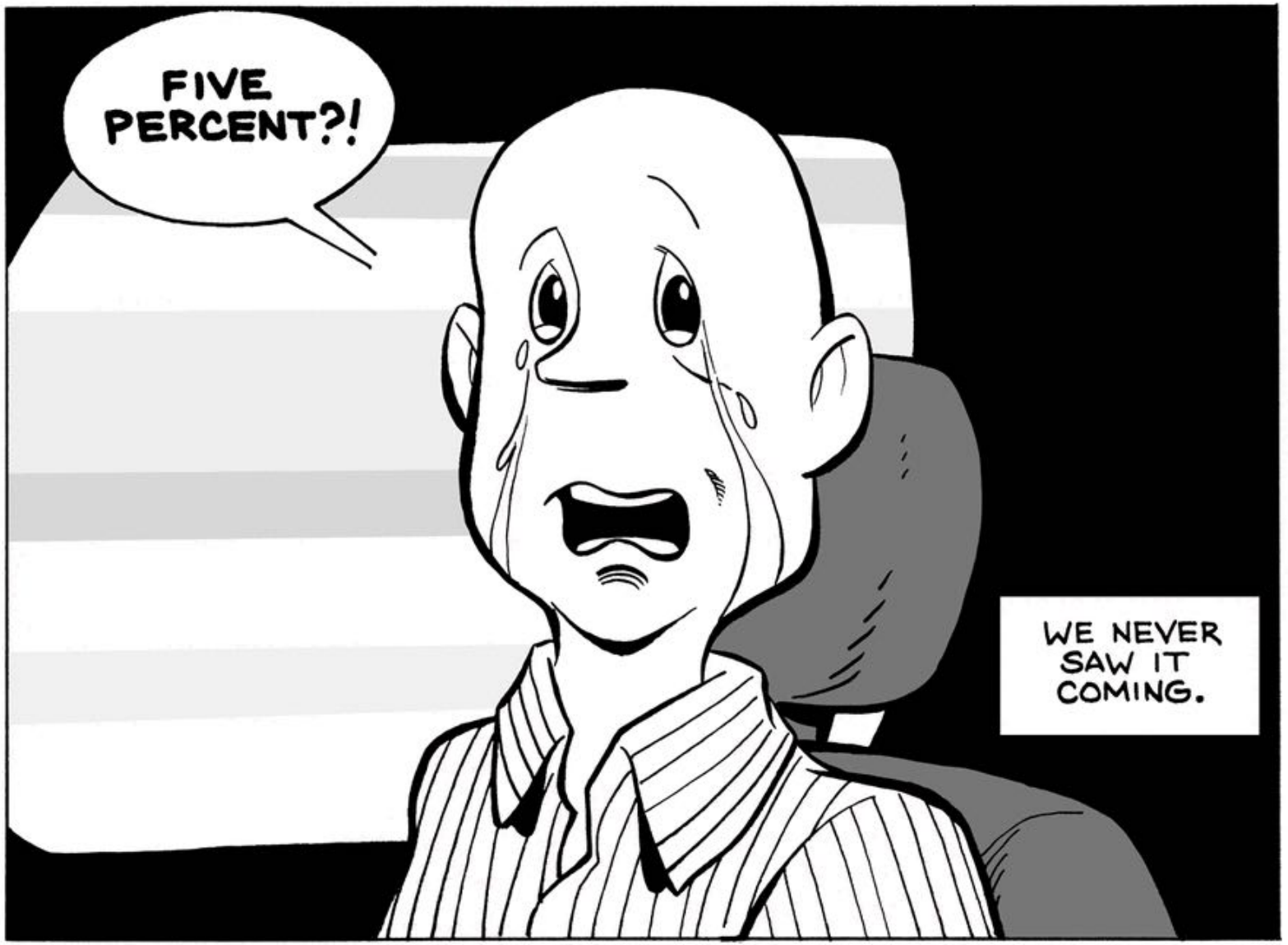


The Five Percent Solution (con't)

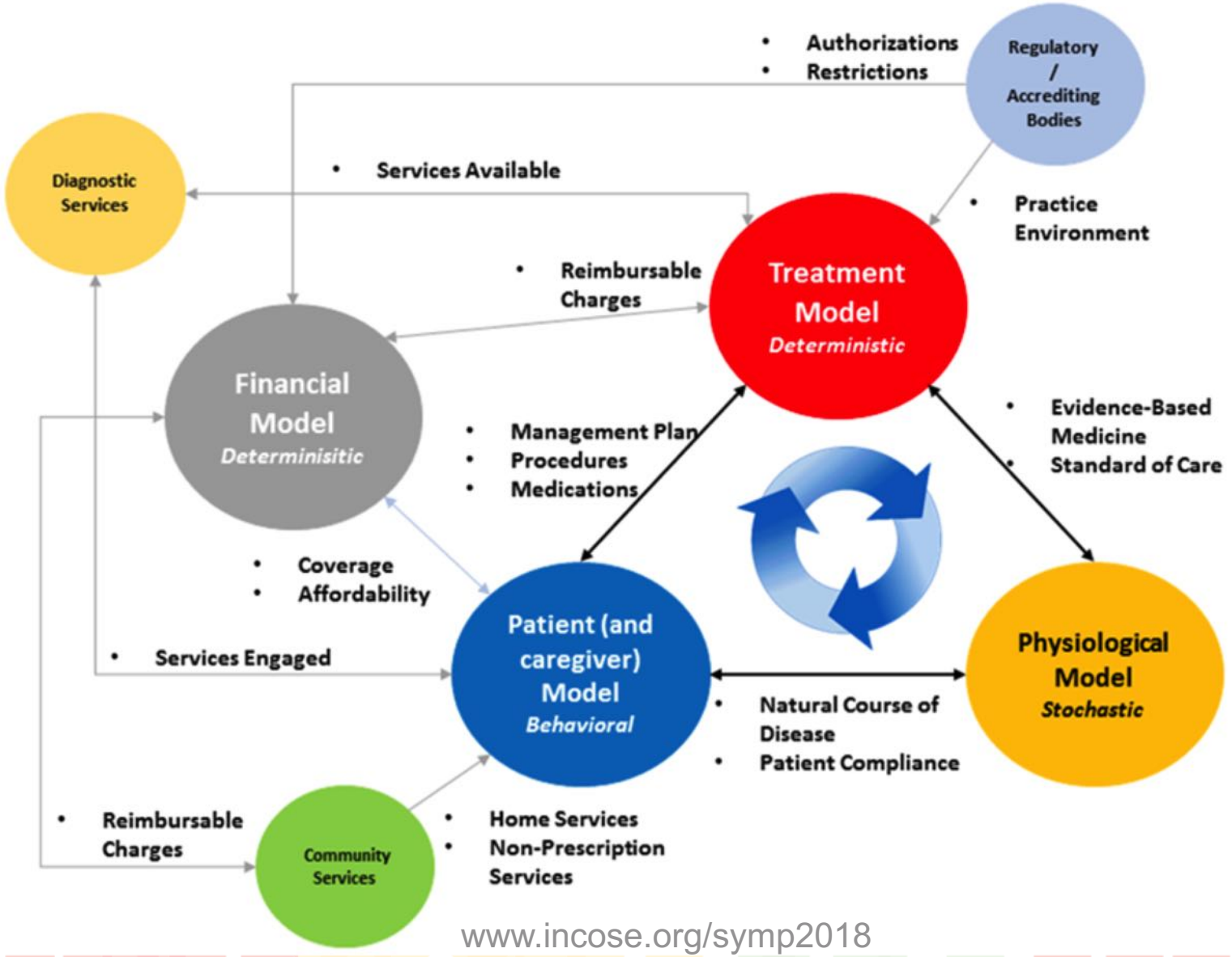
MOM'S CANCER

- Not an unusual scenario for patients (and families) struggling with cancer or life-threatening chronic illness – understanding:
  - What is the likelihood of success of various treatment pathways?
  - Which one should I/we take?
  - When should I/we stop?

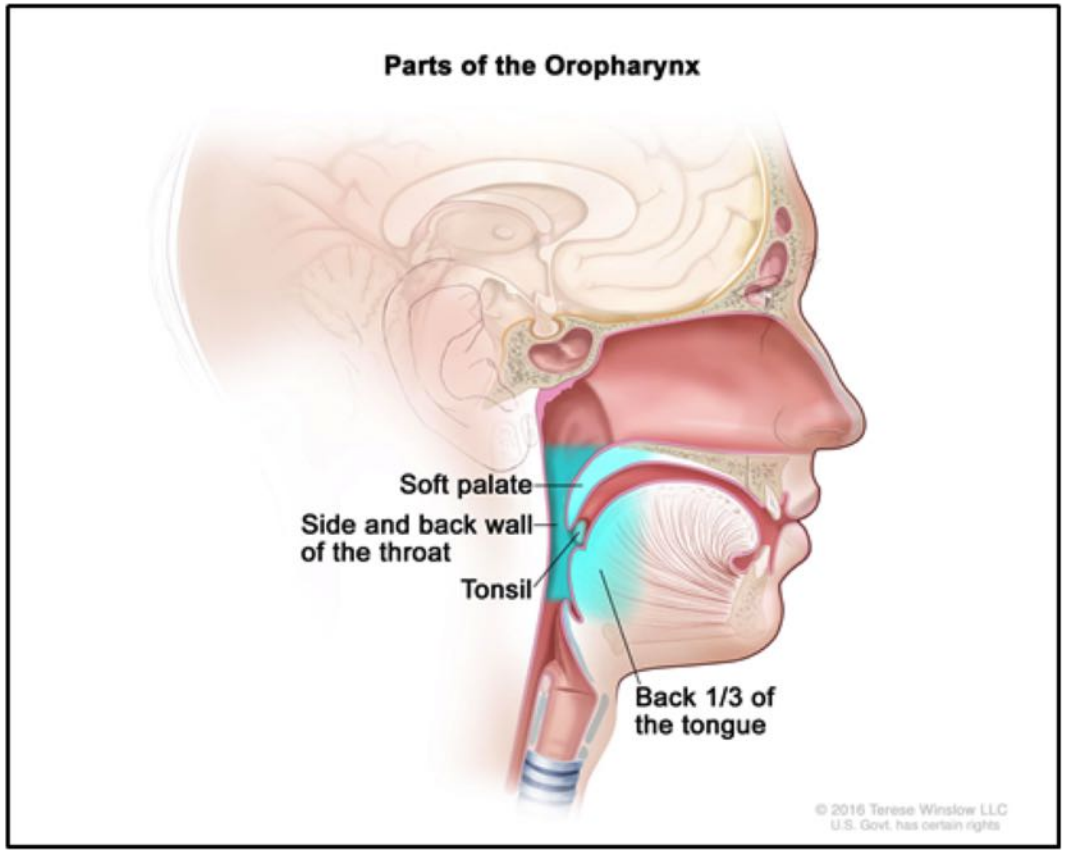
- Not all patients are like Mom
  - Some will try anything to extend their life, even if chances of recovery are remote
  - Others will have specific conditions they want to avoid

- We are developing a decision aid for cancer patients.
- But we are discovering that the true system boundary extends far beyond the patient-physician dynamic.

The (Simplified) Medical Decision Making Domain



Oropharyngeal Cancer: An Emerging Crisis



National Cancer Institute, Oropharyngeal Cancer Treatment. Retrieved November 20, 2017, from https://www.cancer.gov/types/head-and-neck/patient/oropharyngeal-treatment-pdq

- Human Papillomavirus (HPV)-positive oropharyngeal squamous cell carcinoma (OPSCC, hereinafter OPC) is becoming an epidemic among younger patients
- Traditional approaches for non-HPV OPC are accompanied by a high degree of toxicity
  - No treatment option has been found to be substantially superior in terms of mortality
- HPV-positive tumors are more responsive to therapy; therefore, de-intensification strategies are currently under study in clinical trials

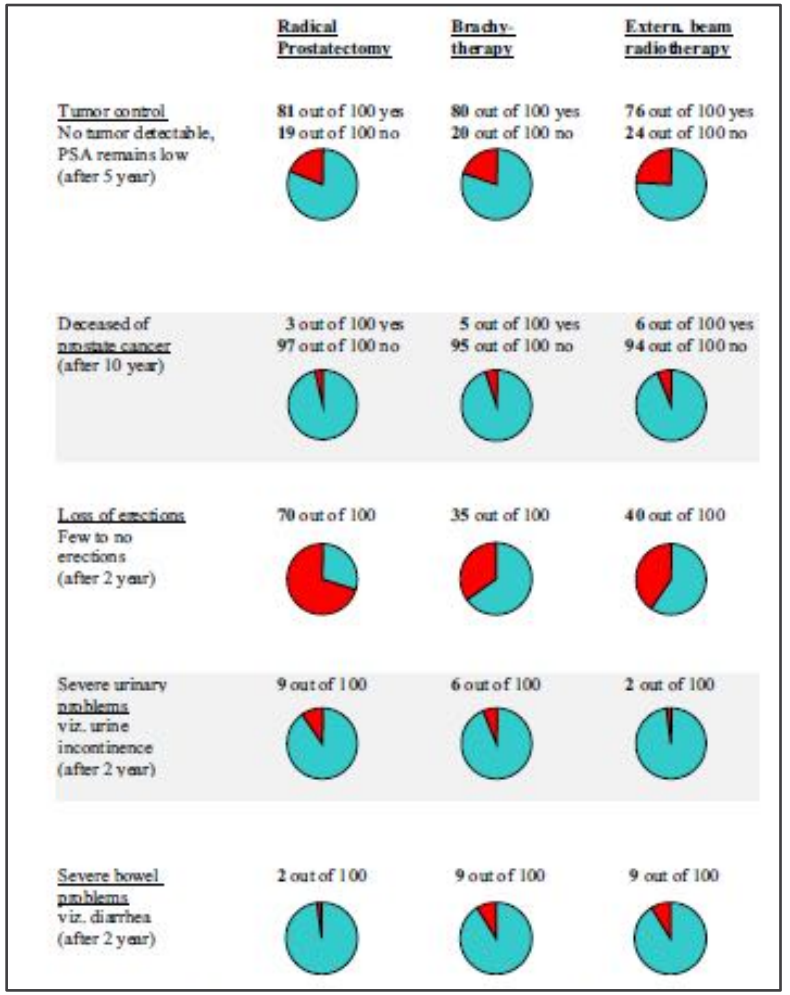
Treatment Options for OPC

Intervention	Comments	Selected Complications
Surgery	Open surgery through jaw or neck Transoral (but only for early stage disease)	Potentially disfiguring scars Difficulty swallowing Nerve damage Changes in speech Tracheostomy
Radiation	Intensity-modulated radiotherapy (IMRT) Conformal RT	Difficulty swallowing Dry mouth Feeding tube dependence Hearing loss Skin reactions/burns Secondary malignancies
Chemotherapy	Usually given in conjunction with or as an adjuvant to a primary treatment; cisplatin is agent of choice	Fatigue Anemia Hair loss Opportunistic infections

Cohen E. E. W., et al. American Cancer Society Head and Neck Cancer Survivorship Care Guideline. *CA Cancer J Clin*. 2016;66(3):204–39.

Shared Decision Making

- Shared Decision Making (SDM) is an interaction between health provider and patient designed to involve both parties in the process of treatment choice and informed consent
- Studies (such as Pollard, 2015) have demonstrated that in some – but not all – clinical scenarios, physicians generally support SDM
- SDMs can be guided by use of a Decision Aid



van Tol-Geerdink, et al. Does a decision aid for prostate cancer affect different aspects of decisional regret, assessed with new regret scales? A randomized, controlled trial. Health Expect. 2016;19(2):459–70.

Decision Regret – An important patient-centered outcome in some disease processes

Authors	Definition
Brehaut et al., 2003	"...remorse or distress over a decision."
Gill et al., 2011	"The negative, cognitively based emotion that we experience when realizing or imagining that our present situation would have been better had we acted differently."
Hernandez et al., 2014	"...the difference between the utility of an action taken and utility of an alternative action"

Characteristics of Decision Regret: A Summary of the Literature

- Experienced by patients, surrogate decision makers, medical staff
- Disease-dependent
  - Usually occurs in chronic or serious disease, particularly cancer
  - Higher in Prostate, Head and Neck Cancer (~20%/~15% Moderate to Severe)
  - Low in Breast Cancer (but higher in post-mastectomy reconstruction)
- Positively correlated with Decisional Conflict
  - Too little (or too much) information
  - Lack of participation (although some patients prefer this)
  - Differing decision-making role expectations between provider and patient
- Stable over time?
  - Breast cancer: yes [Martinez et al., 2015]
  - Prostate cancer: probably increases over time [Aning et al., 2012, and other studies]

Characteristics of Decision Regret, cont'd

- May be reduced using patient Decision Aids through Shared Decision Making
  - In RCTs, generally reduce decision regret (often by lowering decisional conflict)
  - Not universal – some decision aids have no effect, or increase DR
- Higher levels of Decision Regret often result in depression, distrust of the medical system
- The Curse of the Counterfactual Narrative

Motivation for a Decision Aid that includes Decision Regret factors

- "Regret, a negative conscious and emotional reaction to personal past acts, decisions, or behaviors, is commonly experienced in everyday life. This is often considered in the context of economics and finance under the terms of opportunity loss, buyer remorse, or buyer regret. However, **differences between expected and actual outcomes** as well as **assumptions related to alternative consequences if a different course of action had been chosen** are increasingly important in medical decision making. Importantly, in the realm of surgical procedures the often irreversible nature of the chosen step can have important implications for satisfaction and future health care decisions." [Lorenzo et al., 2014, emphasis added]

Evaluating Patient Status

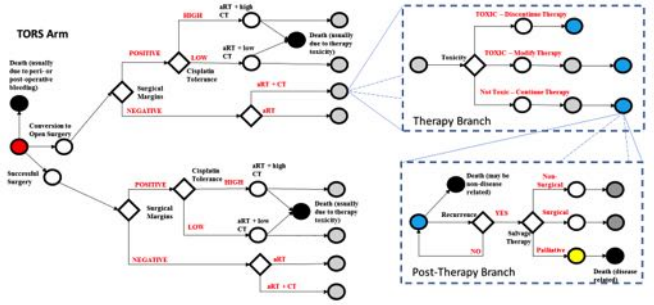
- Initial Assessment
  - Performance Status Baseline (ECOG, EORTC QLQC-30/H&N35)
    - Pain
    - Dysphagia
  - Clinical or Pathological Tumor staging (TNM)
    - Physical exam
    - Endoscopy with biopsy
    - Chest X-ray / CT / PET scan
  - Demographics (age, gender, race)
  - Comorbidities (diabetes, vascular disease)
  - Behavioral practices (tobacco, alcohol)
- These values allow us to determine the likelihood of success of various interventions based on historical values

Quantifying Patient Health States

- Patient-Identified Outcome Concerns
  - Pain
  - Dysphagia (difficulty swallowing)
  - Xerostomia (dry mouth)
  - Speech
  - Appearance
  - [Temporary] surgical interventions (tracheostomy, feeding tube)
- Model implementation values
  - Longevity
  - Quality of Life (derived from patient outcome preferences)
  - Regret Risk (a function of the difference between physician-defined expectation and alternative pathway experience)

Model Structure (Oropharyngeal Cancer)

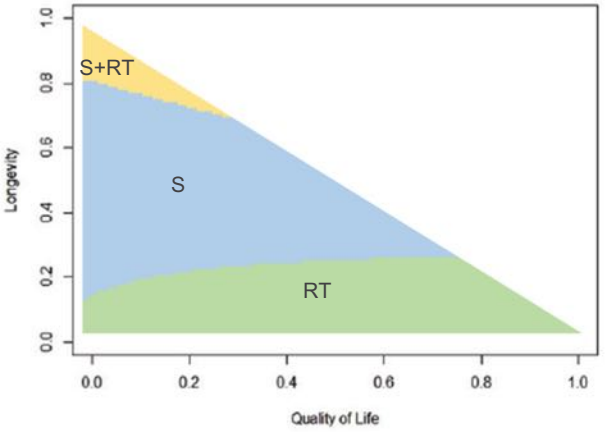
Clinical pathways (based on TNM staging and therapies available to the patient) with transition probabilities and outcome expectations



Provider receives graphic sensitivity analysis of primary treatment choices

Patient current health and performance status, and physical/social outcome preferences (speech, appearance, swallowing, etc.)

Stochastic Dynamic Program – Find best policy (that is, series of treatment choices) for a given set of patient preferences and state weights

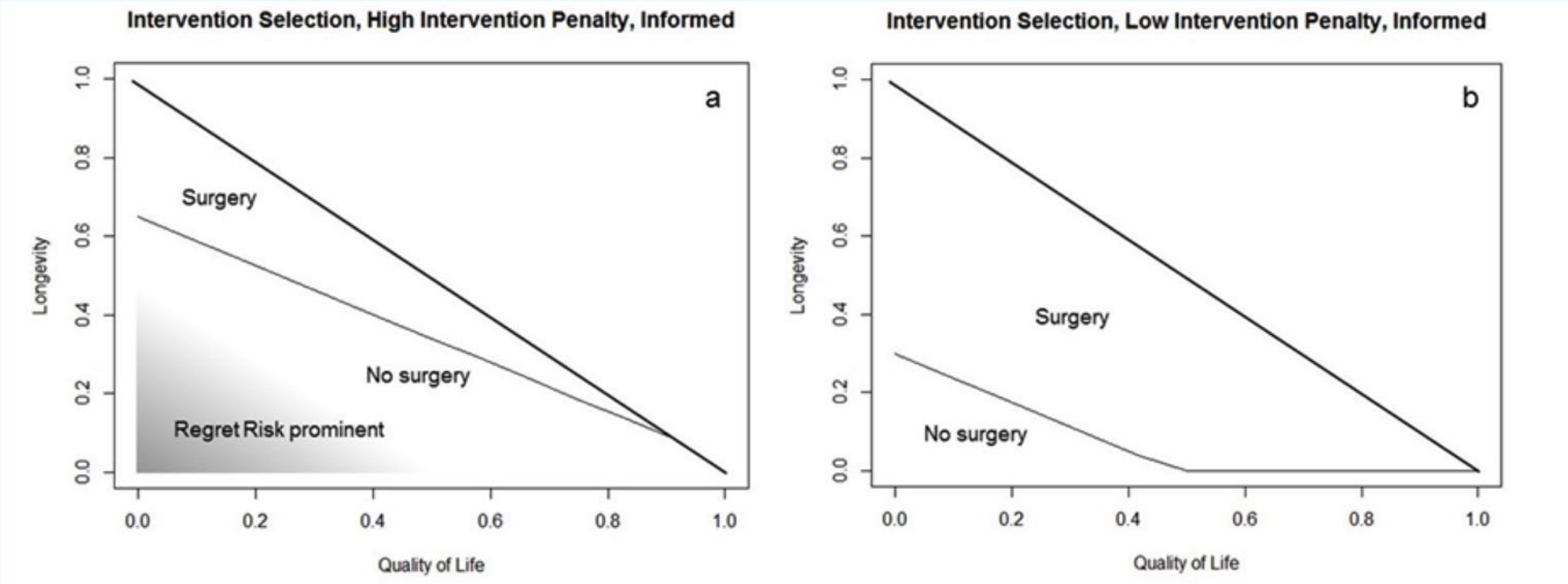


State factor weighting for all values where

$$w_L + w_{QOL} + w_{RR} = 1$$

Implementation Example

A middle-aged patient with advanced OPC (HPV-negative) is trying to decide between surgery and no-surgery; with surgery, life expectancy is approximately 3.2 years, without surgery it is 1.2 years. Depending on patient weights for longevity, quality of life, and regret risk, the patient's decision profile will change. Longitudinal effects, including intervention timing, are taken into account.



THE CHANGING MEDICAL LANDSCAPE

The NEW ENGLAND JOURNAL of MEDICINE

JULY 19, 2012

Radical Prostatectomy versus Observation for Localized Prostate Cancer

ABSTRACT

“Among men with localized prostate cancer detected during the early era of PSA testing, radical prostatectomy did not significantly reduce all-cause or prostate-cancer mortality, as compared with observation, through at least 12 years of follow-up.” (*NEJM*, July, 2012)

NARRATIVE MATTERS

A Failing Heart And The Downside Of Life-Prolonging Technology

“With so much to lose, doctors have to be able to predict and communicate to patients when it makes sense to count on the best possible outcome (accepting the limits and potential downsides of treatment) and when no intervention (that is, palliative or supportive care only) may ultimately be the best approach.” (*Health Affairs,* August, 2015)

“What if I decide to just do nothing?” (Time, October, 2015)

Robot to the Rescue?

OPC Location	Base of Tongue[1]	Tonsillar[1]	Mixed[2]
Intervention	Open Surgery	Open Surgery	TORS
5-year survival	49%	47%	[~90% 2 yr][3]
Severe Complications	32%	23%	~10%
Fatal Complications	3.5%	3.2%	<0.3%

Photograph: Shah S, Goldenberg D. Robotic surgery for oropharyngeal cancer. Rambam Maimonides Med J. 2014;5(2):e0014.

1. National Cancer Institute, Oropharyngeal Cancer Treatment (adult). March 28, 2018. Retrieved at https://www.cancer.gov/types/head-and-neck/hp/adult/oropharyngeal-treatment-pdq#section/_49.
2. Multiple sources.
3. Note: disproportionate number of cases were HPV-positive

Outcome Differences in Underserved Populations

- Both survival and decision regret in various cancer therapies differ by race and socioeconomic status
  - Survival differences have been attributed to tumor genetics, lack of early detection due to insurance status/access to care, mistrust of healthcare systems, adherence to treatment regimens [Aizer et al., 2014]
- Survival outcome racial disparities in prostate cancer have been shown to vary substantially between US cities [Benjamins et al., 2016]
  - This in part validates our contention that factors exogenous to the patient-provider decision-making model have an important role in determining treatment success
  - "All healthcare is local" – variations in access and quality could be sources
- These factors do not, however, explain the increase in decision regret in underserved populations
  - Sometimes attributed to cultural and communication barriers – if so, our model cannot represent these, nor could it simulate institutionalized antagonisms
  - Perhaps partially attributable to emergent behavior of the system?

Multidisciplinary Design Optimization

- Used to explore design space for simultaneous optimal solution(s) among multiple interests
- Typical implementation is in engineering design (aerospace, automotive) where different engineering disciplines and computational complexity dominate
- Aggregating our individual model to the community level provides necessary demand factors which influence infrastructure and policy decisions

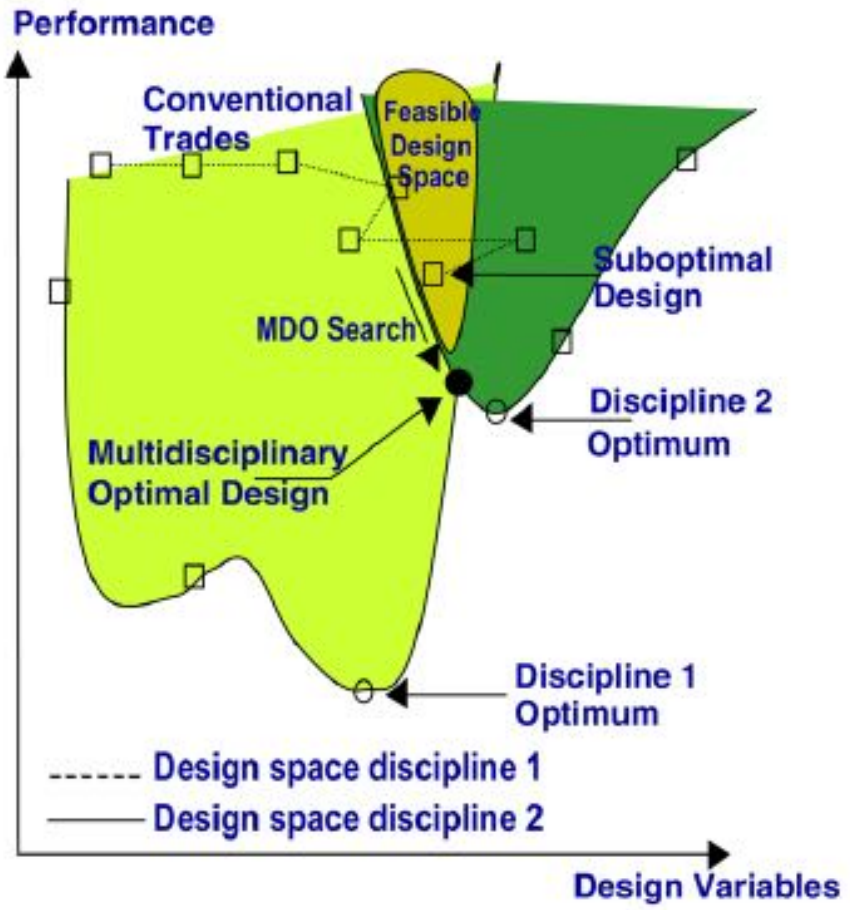
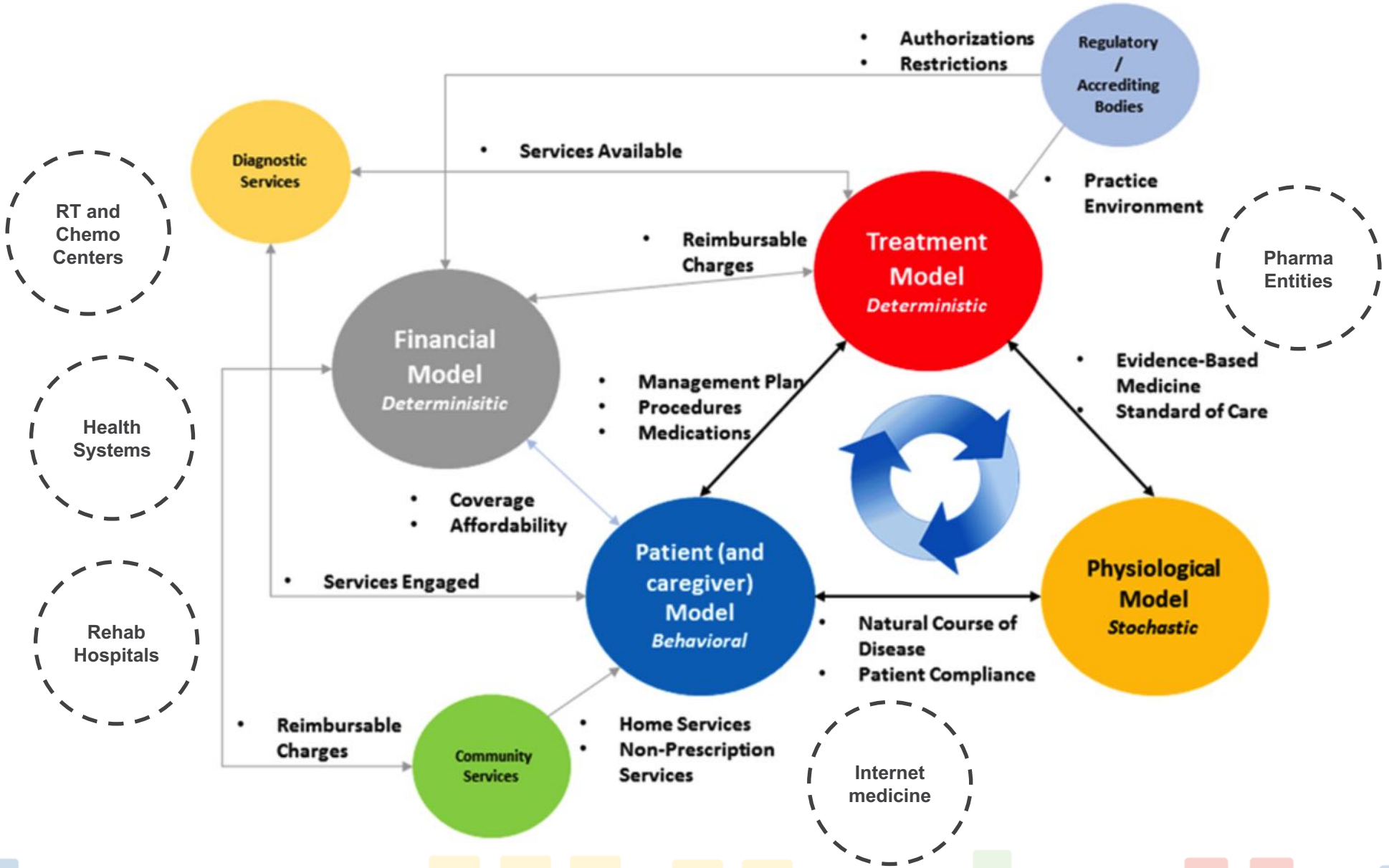


Image: Simpson and Martins, 2011

Opportunities and Drawbacks

- Opportunities
  - Allows exploration of optimal frontiers recommending changes in public policy or payor financing to encourage deployment of advanced technologies (e.g. TORS)
  - Could contribute to a better understanding of factors influencing underserved outcomes in chronic disease and cancer
- Drawbacks
  - Unlike engineering, models for exogenous disciplines may not exist or would have to be modified
  - Because of the longitudinal focus of our model, the dynamic nature of health networks and facilities (mergers, hospital closures) require assumptions about future states
    - Blue Sky: a sufficiently detailed economic model might serve as a useful tool for anticipating shifts in market demand that drive medical infrastructure decisions

The (Revisited, but still Simple) MDM Domain



Initial Forays into the “Big Picture”

- Individual model assumes access to all treatment pathways but is easily modified to account for availability and accessibility according to insurance status, income, and geographical location
- Motivations of the Treatment module apart from institutional objectives are more difficult to discern – do the actions of a an overzealous surgeon or disorganized receptionist need to be represented?

Summary

Healthcare decision-making for complex and chronic diseases, including cancer, is a systems engineering problem. Interventions used to treat these medical conditions frequently require the coordination of multiple specialty entities that define available action space. At the same time, considerations for the preferences of patients in a shared decision-making environment introduce alternatives that magnify computational complexity. In this research, we consider the opportunities and drawbacks of Multidisciplinary Design Optimization (MDO) to address an emerging healthcare issue – Human Papillomavirus (HPV)-positive oropharyngeal cancer (OPC) – to evaluate the conformity of various interventions that may reduce treatment burden while pursuing patient longevity for this unique disease. An implementation of the proposed algorithm demonstrates behavior consistent with regret avoidance, while a more robust model will allow both patient-physician and healthcare system feedback in optimizing treatment policies.

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BACKUP SLIDES

Overview

- Cancers (and certain chronic conditions) differ from many other disease processes in that they involve
  - Multiple healthcare providers, specialties, and facilities over months/years
  - Many decision points longitudinally where patient preferences can play a part
- Because of this, a systems perspective beyond the patient-physician relationship is needed when considering best treatment pathways
  - Availability, Accessibility, Financing
- Medicine is facing an emerging epidemic of Human Papillomavirus (HPV)-mediated Oropharyngeal Cancer (OPC)
  - We propose using a Multidisciplinary Design Optimization (MDO) approach to informing both Shared Decision Making (SDM) and local/regional healthcare infrastructure decisions to address this crisis

Healthcare (and MDM) as a Complex Engineered System (CES) [after Complexity Labs]

Characteristic	Definition	Context in MDM
Open System	High level of interaction with environment; boundaries are difficult to define	Factors exogenous to the patient-physician relationship (insurance companies, regulatory bodies) influence medical decisions
Nonlinear	Many processes in parallel, a system of systems	Modern healthcare systems are complex enterprises, with each entity potentially having their own governance structure and accreditation or certification bodies
Interactive	The decisions of one organization impact another, often in a complimentary fashion (but not always)	Decisions made in one entity may be coordinated and executed in another; for example, a patient may be diagnosed in a clinic, referred to a surgeon in a different practice, undergo procedures at a hospital, and recover at a rehabilitation facility. (Shuman 2017)
Emergent	Separate pieces work together for an overall positive effect	A set of longitudinal decisions will almost always involve a number of entities with differing global objectives, but whose effect will be the promotion of the health of the individual patient
Composite	Heterogeneous components that function independently	While many components work together more seamlessly than in other disciplines, certain portions of the spectrum (i.e. insurance companies, government agencies) may not focus on the patient's outcome as their primary objective
Autonomous	Systems evolved bottom-up from earlier, independent systems rather than being built de novo	A large portion of the existing medical system has evolved from the acquisition and assimilation of existing systems; even today, however, these systems have issues with interoperability and remuneration, which may limit decision space for patient treatment


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Clinical Pathway Regret Risk Differences Between Affluent and Underserved Populations
Translating Clinical Decision Support to Practice
Robert Aarhus
George Mason University, Department of Systems Engineering and Operations Research

Hypothesis – Action Space

- At the individual level, the available choices of treatments and facilities for both primary and subsequent treatments – the action space – will differ according to geographic location, insurance status, offered services – factors outside the immediate patient-provider relationship
- Hypothesis: limitations on action space increase outcome variance and therefore increase regret risk
  - Example: TORS
- Initial Results from the treatment model
- Future Work

Summary for the Individual Module

- OPC is a disease process that is increasing in frequency due to spread of HPV
- Therapies are generally the same in terms of survival; therefore, patient outcome preferences are an important consideration
- Shared decision making (SDM) is an important factor in OPC treatment; we are constructing a decision aid to assist physicians
- Our model includes consideration of Decision Regret – elevated in Head and Neck cancers – as a consideration

Authors

Robert Aarhus is a retired US Army Medical Service Corps officer with over 35 years experience across emergency medicine, military field medicine, clinical laboratory science, medical information management, clinical software acquisition and development, and hospital construction disciplines. He is DAWIA Level III Certified in Program Management. He holds a BS in Biology from Carnegie-Mellon University and an MS in Biomedical Engineering from the University of North Carolina, Chapel Hill.

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