

# When Less is More: Optimizing Prescription **ALERTS** under Fatigue

**Hossein Piri**

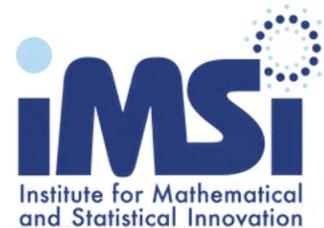
Assistant Professor

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Feb 2026

**Michael Lingzhi Li**

Assistant Professor

Harvard Business School

Harvard University



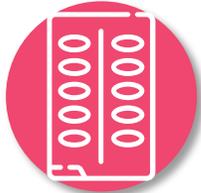
**Harvard  
Business  
School**



**Research Motivation**



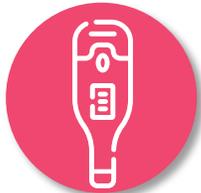
**Literature Review**



**Model Framework & Structure**



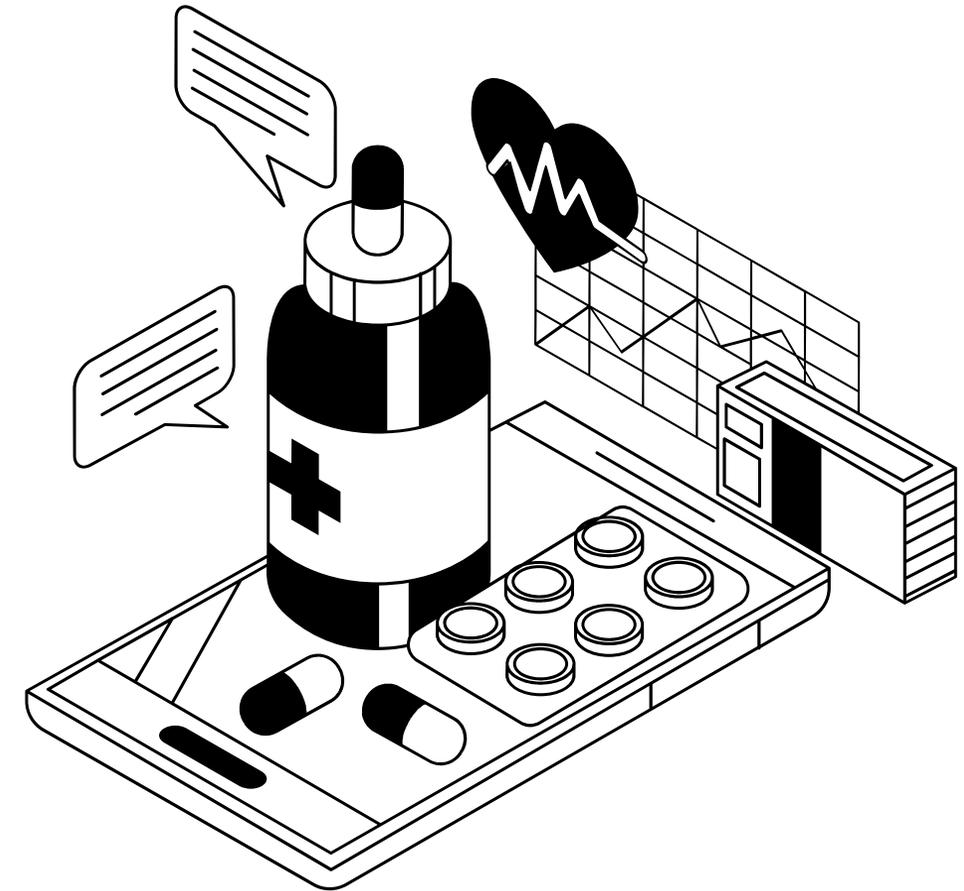
**Special Case in the Real World**



**Case Study**



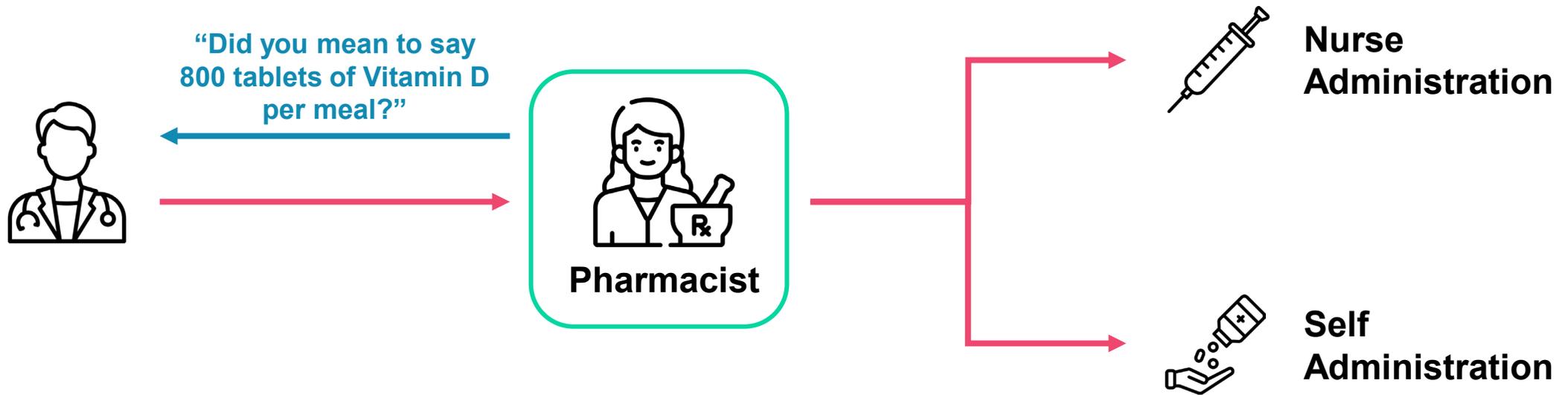
**Conclusion**



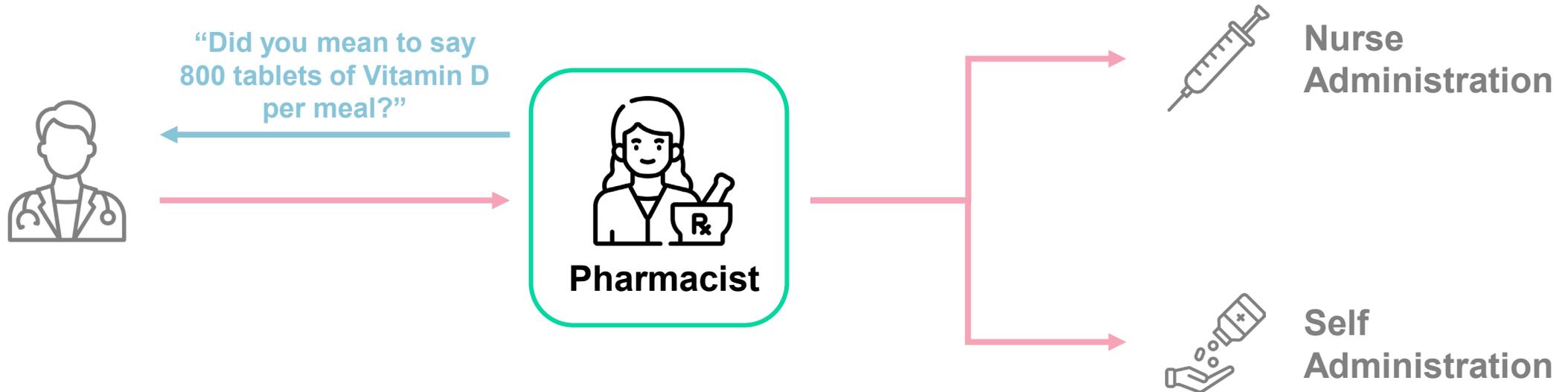


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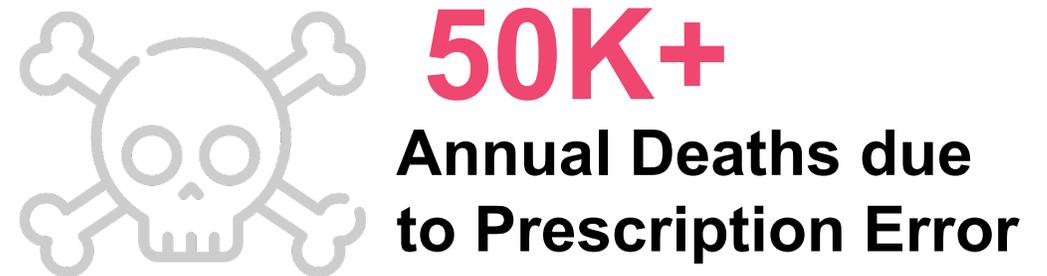
# Overview of the Prescription Workflow



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**Pharmacists** act as the last line of defence



(Naserallah et al. 2020)

(AHRQ 2015)

# Computer Provider Order Entry (CPOE) Systems

Web Page Dialog

**Warning**

**You are ordering: HYDROCHLOROTHIAZIDE**

**Drug - Allergy Intervention**

Alert Message	Keep New Order - select reason(s)
The patient has a probable allergy: Sulfa. Reaction(s): Itching, Rash.	<input type="radio"/> Patient does not have this allergy, will D/C pre-existing allergy
	<b>Reasons for override:</b>
	<input type="checkbox"/> Patient has taken previously without allergic reaction
	<input type="checkbox"/> Low risk cross sensitivity, will monitor
	<input type="checkbox"/> No reasonable alternatives
	<input type="checkbox"/> Other <input type="text"/>

**Therapeutic Duplication Intervention**

Alert Message	Keep New Order - select reason(s)
Patient is currently on ZESTORETIC (LISINAPRIL/HYDROCHLOROTHIAZIDE) 10-12.5 SL QD . Both drugs are Hydrochlorothiazide containing medications and should not be used together.	<input type="radio"/> Will D/C pre-existing drug
	<b>Reasons for override:</b>
	<input type="checkbox"/> Pt on long term therapy with combination
	<input type="checkbox"/> Transitioning from 1 drug to the other
	<input type="checkbox"/> New evidence supports duplicate therapy of this type
	<input type="checkbox"/> Advice from a consultant
	<input type="checkbox"/> Other <input type="text"/>

**Drug - Lab Contraindication**

Alert Message	Keep New Order - select reason(s)
HYDROCHLOROTHIAZIDE is contraindicated	<b>Reasons for override:</b>

http://ppd.partners.org/mar/test/popup/Modellauncher.html?http%3A/ppd.partners.org/scripts/phsweb.m Internet

## A Tier 1 (most severe)

Medication Warnings

Current Warnings Report

Current Warnings (1 unfiltered, 1 overridden inline)

**Drug-Drug: SUMatriptan and phenelzine**  
Increased levels of rizatriptan, sumatriptan or zolmitriptan.(1-10)  
Details

Very High

Override Reason...

Associated Orders

SUMatriptan (IMTREX) 50 MG tablet Prescription: New.	Remove
phenelzine (NARDIL) 15 mg tablet Prescription: Active.	Discontinue

## B Tiers 2 (moderate) and 3 (least severe)

Medication Warnings

New Warnings Report

New Warnings (1 unfiltered, 2 filtered)

**Drug-Drug: warfarin and ciprofloxacin HCl**  
Concurrent use of quinolones may increase the hypoprothrombinemic effects of anticoagulants, which may result in an increased risk of bleeding.  
Details

High

Override Reason...

Associated Orders

warfarin (COUMADIN) 1 MG tablet Prescription: New.	Remove
ciprofloxacin HCl (CIPRO) 500 MG tablet Prescription: Reordered.	

**Filtered Warnings (2)**

**Drug-Drug: warfarin and aspirin**  
The concurrent use of anticoagulants and salicylates leads to blockade of two distinct coagulation pathways and may increase the risk for bleeding.  
Details

Medium

Filtered by system settings

**Drug-Drug: oxyCODONE and ciprofloxacin HCl**  
The concurrent administration of a CYP3A4 inhibitor may result in elevated levels of and toxicity from alfentanil, fentanyl(1,2) and oxycodone(3), including somnolence and potentially fatal respiratory depression.  
Details

Medium

Filtered by system settings

oxyCODONE 5 MG immediate release tablet  
Prescription: Active.

Discontinue

Immediately override all warnings:  Benefit outweighs risk  Per protocol  Inaccurate warning  Does not apply to patient  Patient tolerated before  Will monitor  Override All Warnings...

Show filtered warnings (2)  Override and Accept  Cancel

Error Reduction by **50%+**

# How much of a good thing is TOO much?



**7-15**

Average # of Alerts  
per Prescription



**100-1000**

Average # of Alerts  
per Shift



**90%+**

Time Spent Dealing  
with Alerts



**96%**

Override

*“A hospitalized teenager received 38x overdose of antibiotic because clinician advised to ‘ignore all alerts.’”  
-AHRQ Patient Network*

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**GOAL:** Understand optimal alerting strategy under fatigue.

## Research Question

**How to optimize CPOE alerts to balance between providing essential alerts and minimizing unnecessary interruptions?**



# Literature Review

# Literature Review

## Behavioral Dimension

- **Fatigue ↓ compliance in clinicians**
- **Repeated interruptions → lower responsiveness**
  - Nanji et al. 2014
  - Dai et al. 2015
  - Ancker et al. 2017
  - Schwartz et al. 2021
  - Joseph et al. 2021
  - Bavafa and Jonasson 2024
- **Probability of a favorable parole among judges: 65% → ~0%**
  - Danziger et al. 2011

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## Clinical Approaches

- **Tiering/context filters; adjust severity/frequency**
- **Rule-based threshold tuning can reduce burden (often manual/static)**
  - Cash 2009
  - Del Beccaro et al. 2010
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  - Naeem et al. 2022
  - Chan 2022

# Literature Review

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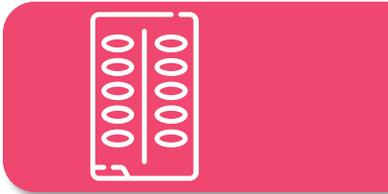
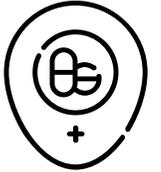
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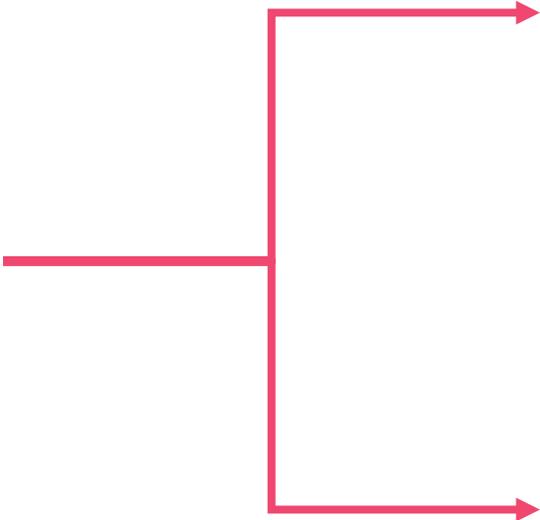
## Machine Learning / Statistical Approaches

- **Predict/suppress low-value alerts (overrides/outcomes)**
- **Personalize relevance (patient/clinician-specific models)**
  - Malone et al. 2023
  - Chen et al. 2024
  - Martell 2019; Poly et al. 2020
  - Graafsma et al. 2024



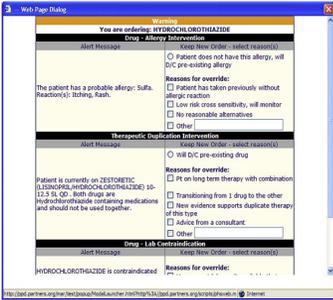
# Model Framework & Structure

# Why is this difficult?



**Don't Show**

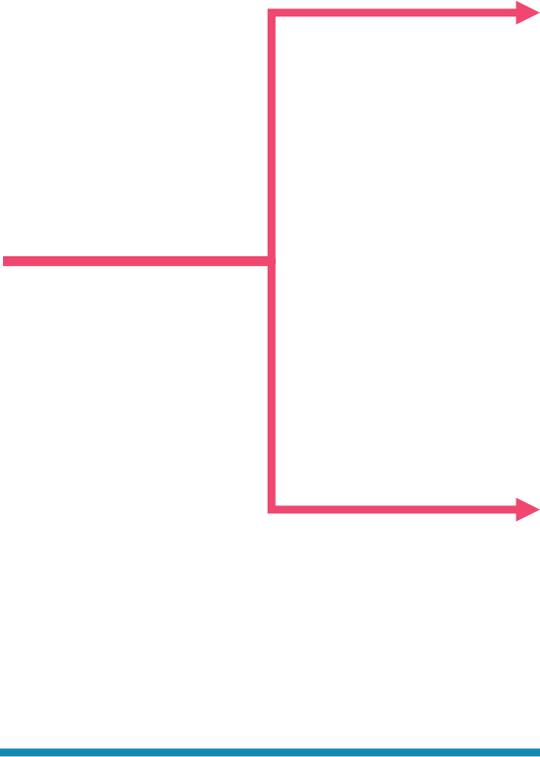
→ **Patient Risk**



**Show**

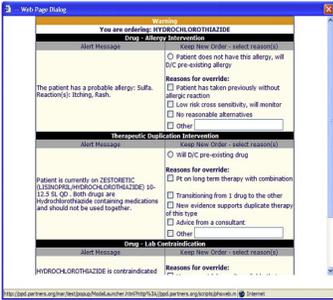
→ **Patient Risk Fatigue**

# Why is this difficult?



Don't Show

→ Patient Risk

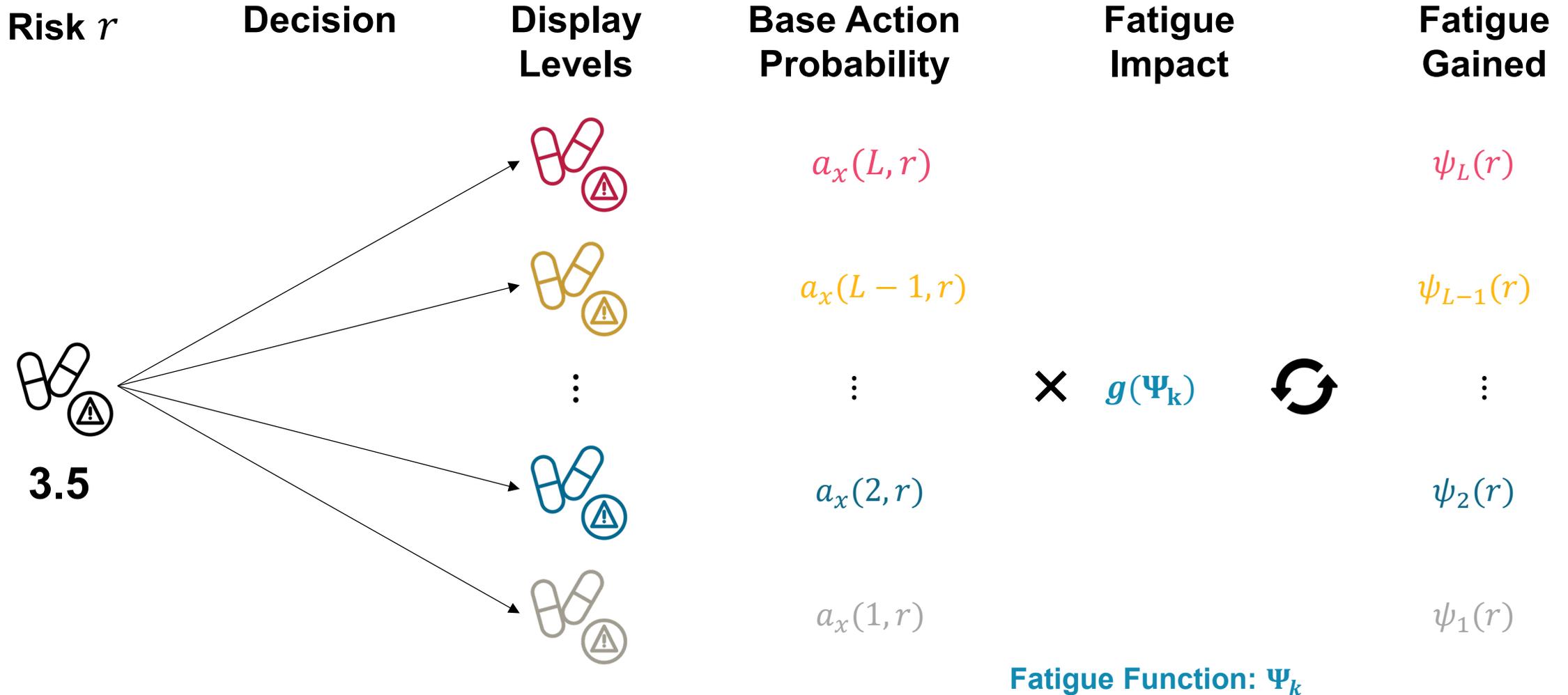


Show

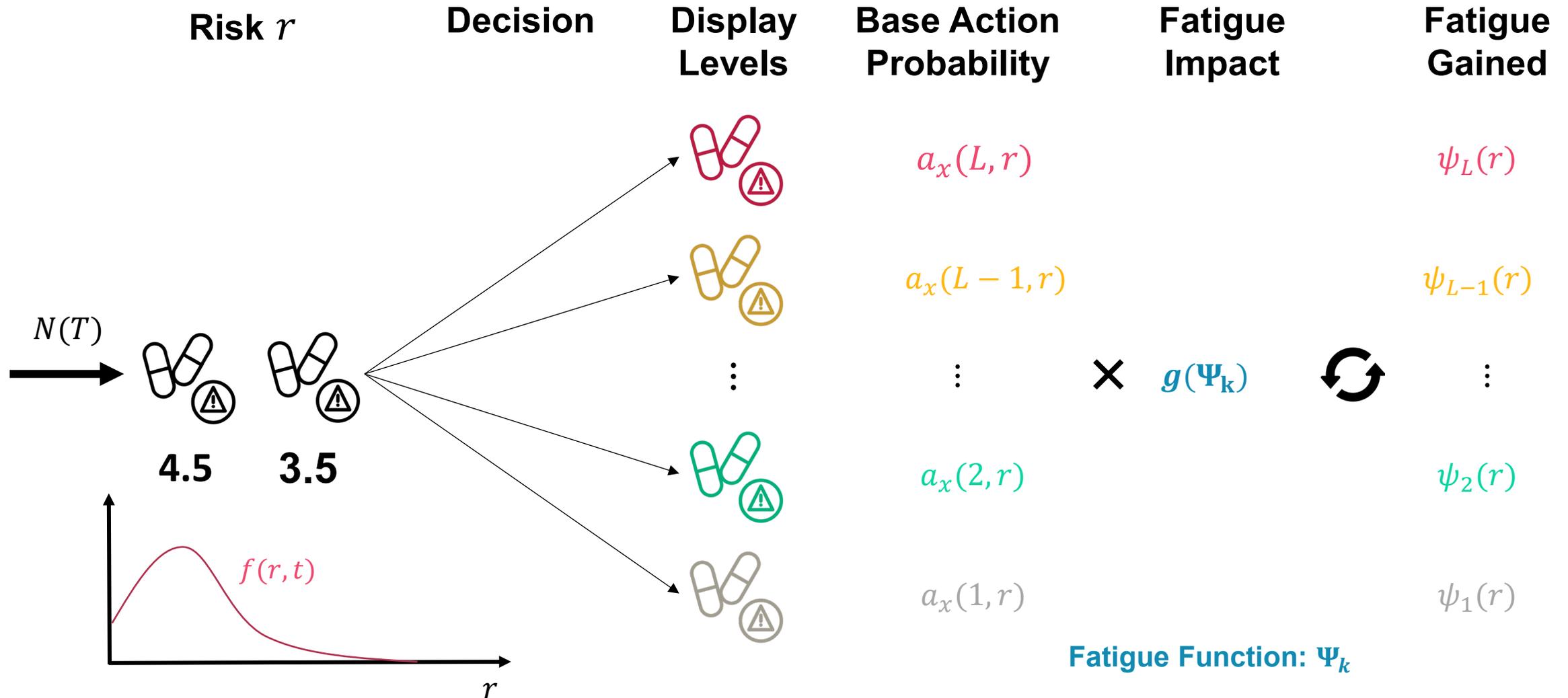
→ Patient Risk Fatigue

Embi and Leonard (2012), Ancker et al. (2017)

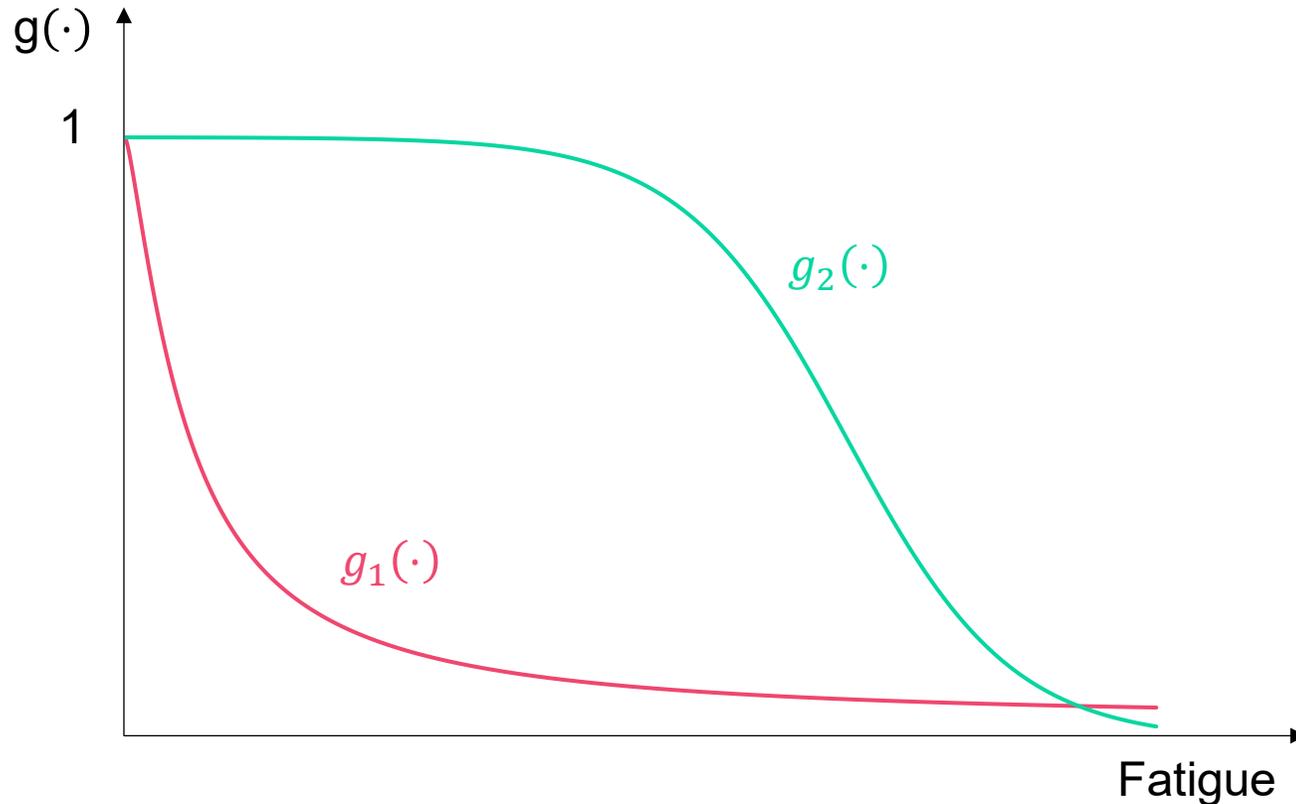
# Modeling Framework



# Modeling Framework



# The Fatigue Linking Function



$g_1(\cdot)$ : Pharmacist/clinician performance quickly deteriorates with fatigue, but maintains residual efficiency even under high fatigue

$g_2(\cdot)$ : Pharmacist/clinician maintains high level of performance until fatigue is very high, and drops significantly

# Fatigue Transition Dynamics

$\Psi_k$  : Pharmacist's fatigue after processing  $k^{th}$  alert



## Display Levels



## Assumption 1:

$U_{l,r}: [0, \infty) \rightarrow [0, \infty) : \text{Fatigue transition map}$

- Monotone
- Cumulative
- Identifiability

$$\Psi_{k+1} = U_{l+1,r+1}(\Psi_k)$$

# Technical Result

## Theorem 1

Under assumption 1,  $\exists$  a strictly increasing transformation  $\phi: [0, \infty) \rightarrow R$  and constants  $\psi_{l,r} \geq 0$  such that defining the rescaled fatigue state  $\tilde{\Psi} = \phi(\Psi)$ , the fatigue dynamic satisfies

$$\tilde{\Psi}_{k+1} = \tilde{\Psi}_k + \psi_{l_{k+1}, r_{k+1}}$$

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## Translation

*Any fatigue transition dynamics that satisfies Assumption 1 admits an equivalent representation in which fatigue transition is additive.*

# Dynamic Program

**Decisions:**

$$\pi_k(l|\Psi, r)$$



Probability of a risk  $r$  alert  
arriving at epoch  $k$   
will be shown at level  $l$

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Objective:

$$\max_{\pi_1, \pi_2, \dots} \mathbb{E} \left[ \sum_{k=0}^{N(T)} \sum_{l=1}^L r_k \times \pi_k(l|\Psi_{k-1}, r_k) \times a_x(l, r_k) \cdot g(\Psi_{k-1}, r_k) \right]$$

Risk avoided for  $K$  alerts

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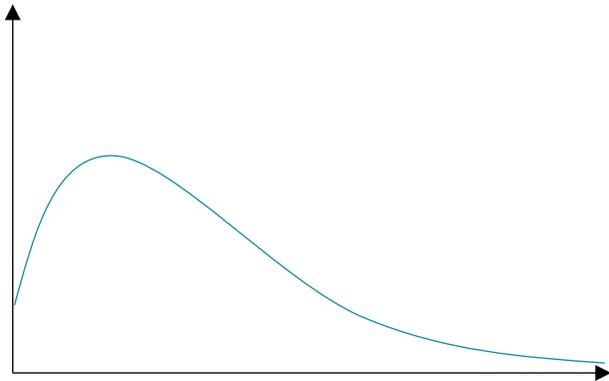


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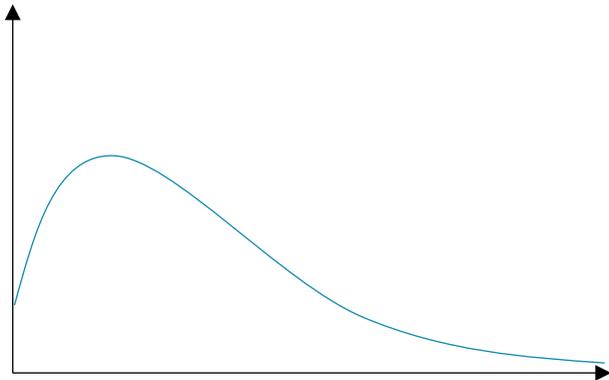


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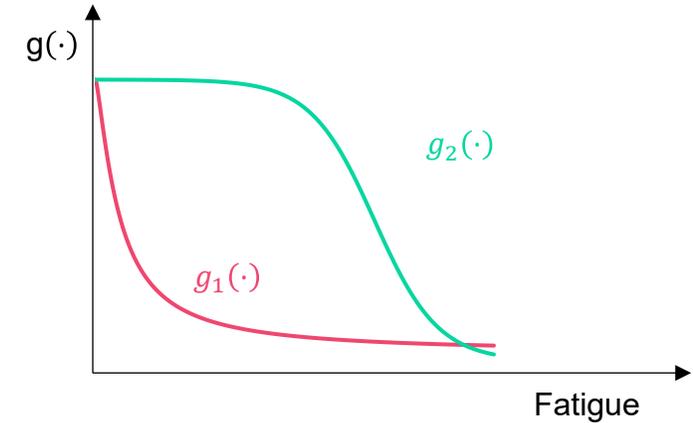
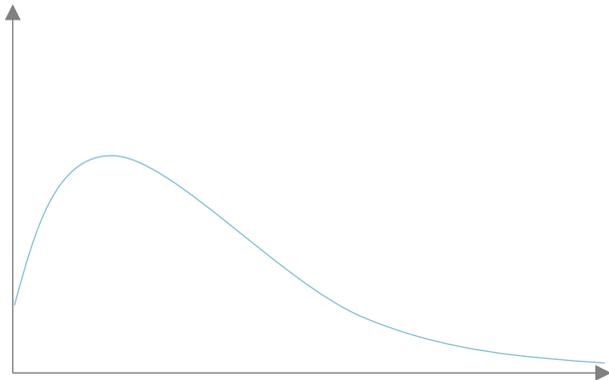


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# Dynamic Program

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Risk avoided for  $K$  alerts

**Constraints:**  $l_k \sim \pi_k(\cdot | \Psi_{k-1}, r_k)$

$$r_k \sim f(r, t_k)$$

Fatigue depends on all past decisions

# Dynamic Program

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$$\pi_k(l|\Psi, r)$$



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**Fatigue Dynamics:**

$$\Psi_{k+1} = \Psi_k + \psi_{l_{k+1}, r_{k+1}}$$

$$\Psi_1 = 0$$

# Fluid Approximation

**Decisions:**  $p_l(r, t)$

Probability of a risk  $r$  alert arriving at time  $t$  will be shown at level  $l$

**Objective:** 
$$\sum_{l=1}^L \int_0^\infty \int_0^T r \times \underbrace{\lambda(t) f(r, t) p_l(r, t)}_{\text{Instantaneous rate of risk } r \text{ level } l \text{ alerts}} \times \underbrace{a_x(l, r) g(\psi(t), r)}_{\text{Fatigue-impacted action probability}} dt dr$$

Risk avoided through alerts within time  $[0, T]$

**Constraints:** 
$$\psi(t) = \sum_{l=1}^L \int_0^\infty \int_0^t \psi_l(r) \lambda(s) f(r, s) p_l(r, s) ds dr$$

Fatigue depends on all past decisions

**Infinite-dimensional functional optimization problem**

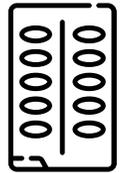
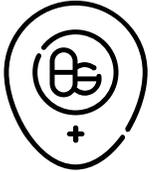
# Technical Result

## Theorem 2

Under the following assumptions, fluid-approximation is an asymptotically optimal approximation to the dynamic programming problem.

- Bounded Mean Risk and Arrival
- Bounded Fatigue
- Lipschitz Fatigue:  $\exists L_g < \infty$  s.t.  $\forall r, \Psi, \Psi', |g(\Psi, r) - g(\Psi', r)| \leq L_g |\Psi - \Psi'|$

# Special Case in the Real World



# A Special Case: Alert or Not?

## Two Levels



Alert



No Alert

## Stationary Risk Distribution

$$f(r, t) = f(r)$$

## Exponential Linking Function

$$g(\Psi, r) = \eta(r) \exp(-\beta \Psi)$$

“Rate of attention decrement”

Mackworth (1948), Warm et al. (2008)

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Fatigue rate

Mackworth (1948), Warm et al. (2008)

## Theorem

Define:

$$H(y) = \int_0^{\infty} (r a_x(r) - y \psi(r))^+ f(r) dr, \quad G(y) = \int_0^y \frac{1}{H(x)} dx$$

$$\text{Screening index: } S(r) = \frac{r a_x(r)}{\psi(r)}$$

Show an alert iff  $S(r) \geq G^{-1}(\beta(T - t))$

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Baseline Expected  
Risk Avoidance

Fatigued Induced

# A Special Case: Alert or Not?

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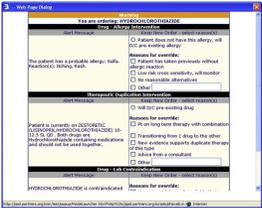
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Threshold  $y$

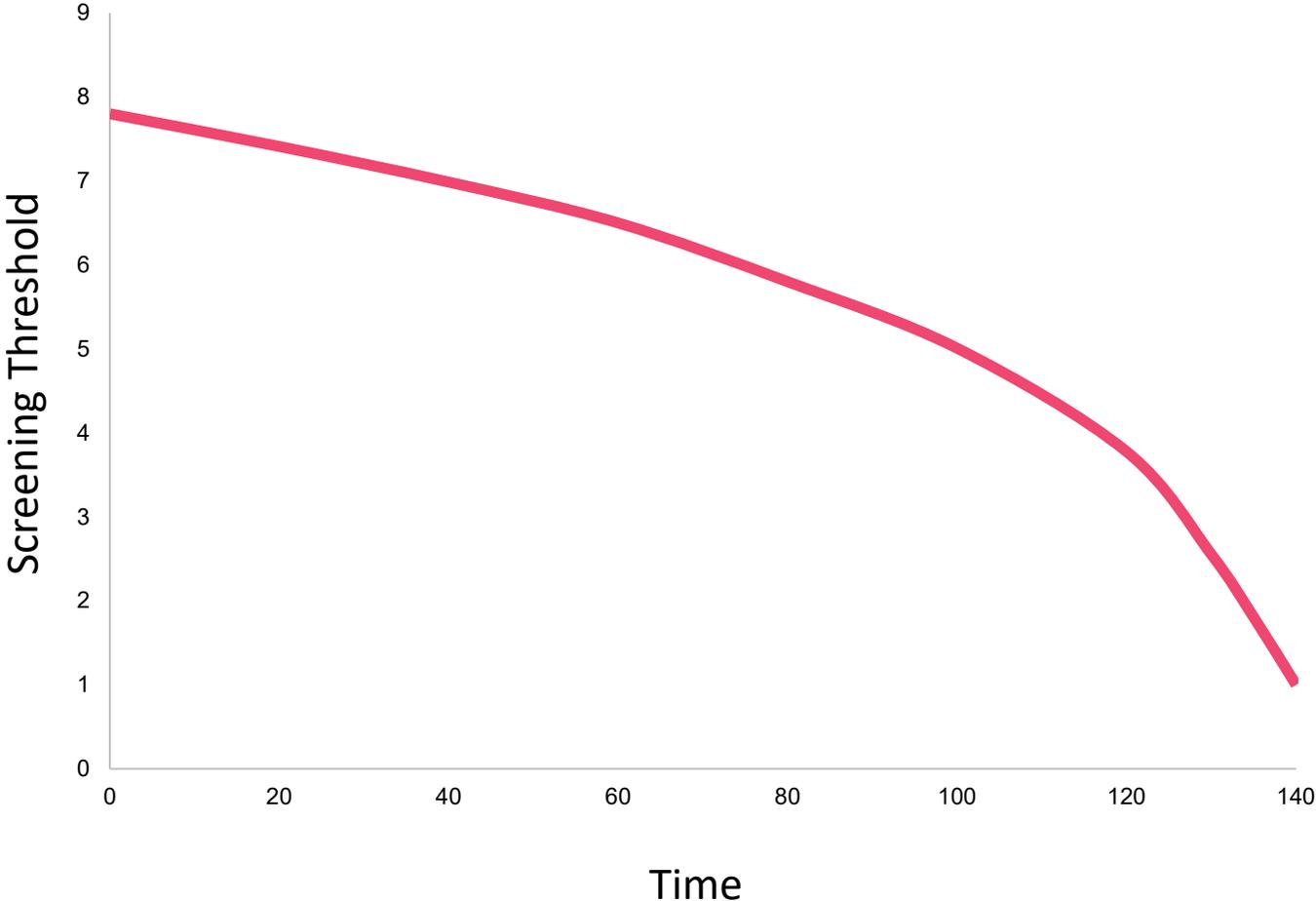
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# Illustration of Screening Threshold

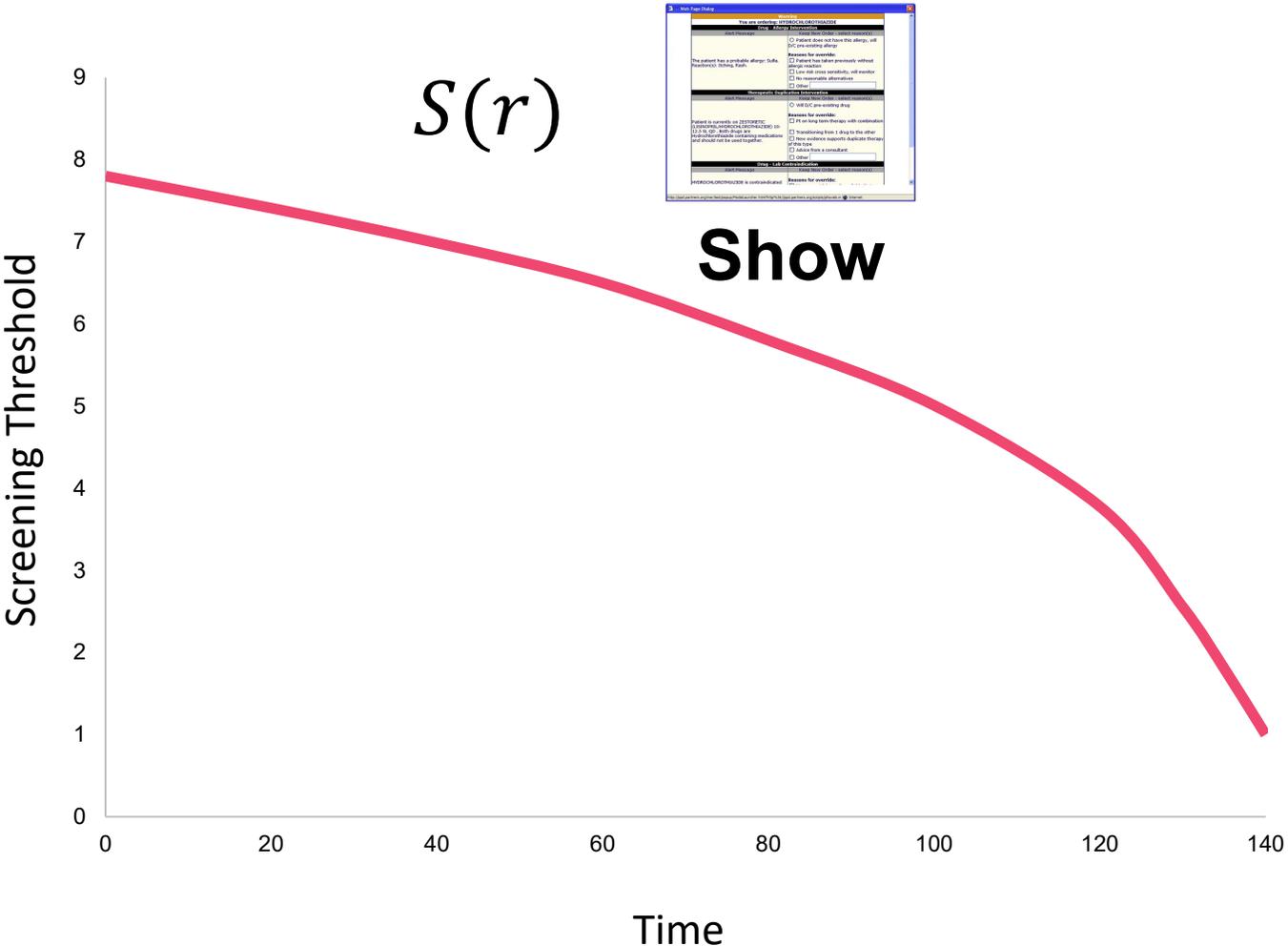


$S(r)$

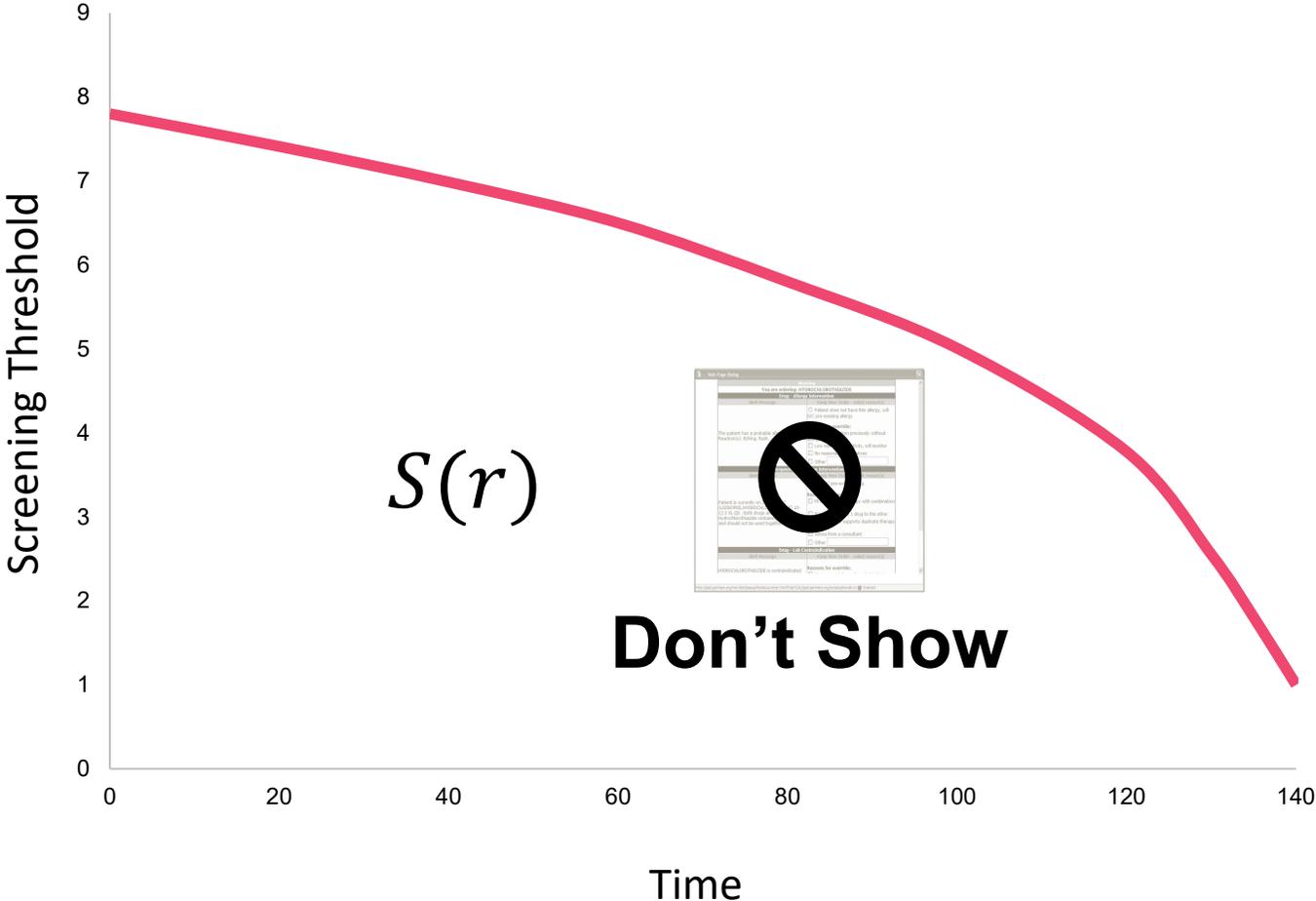
$G^{-1}$



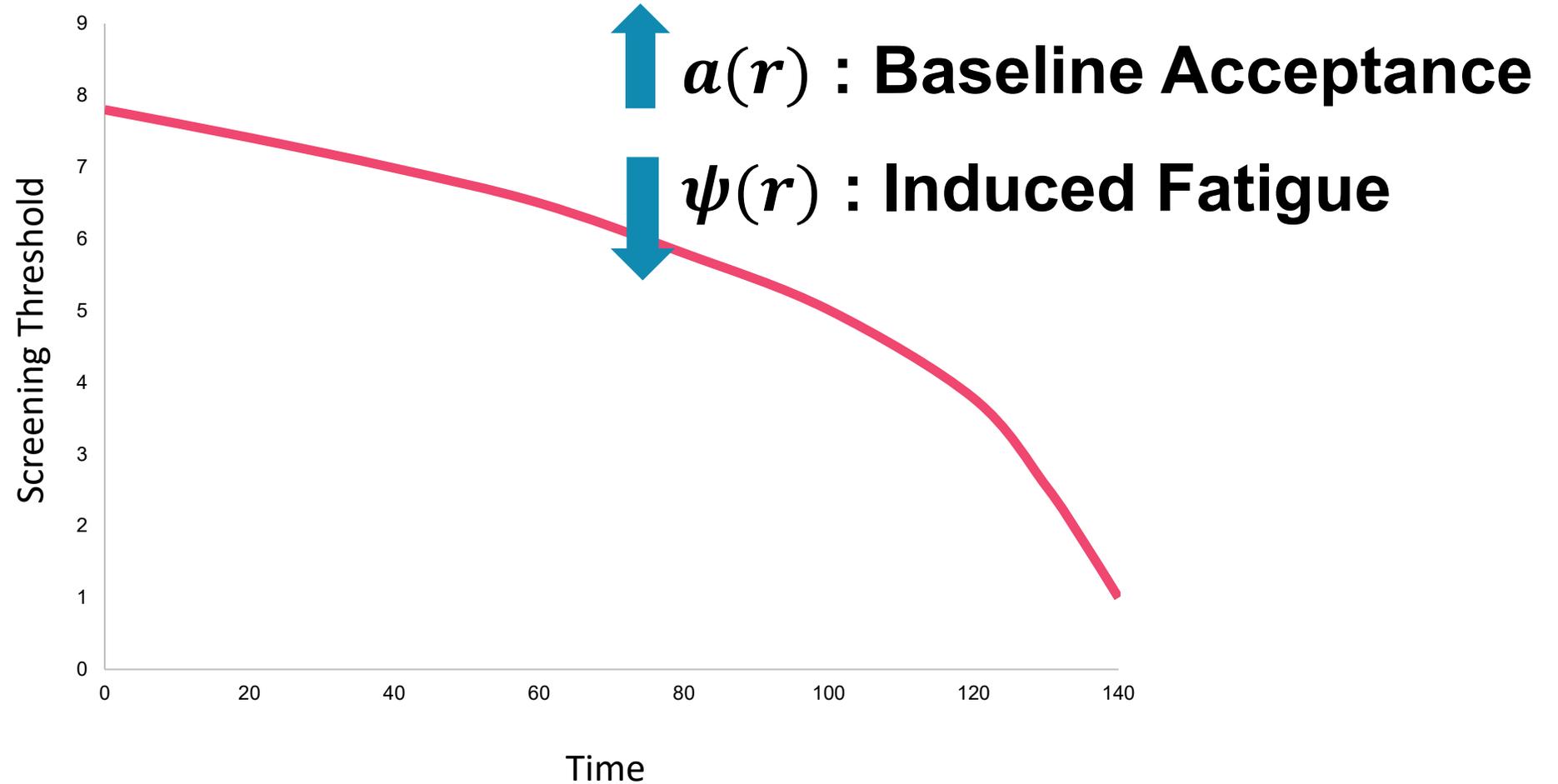
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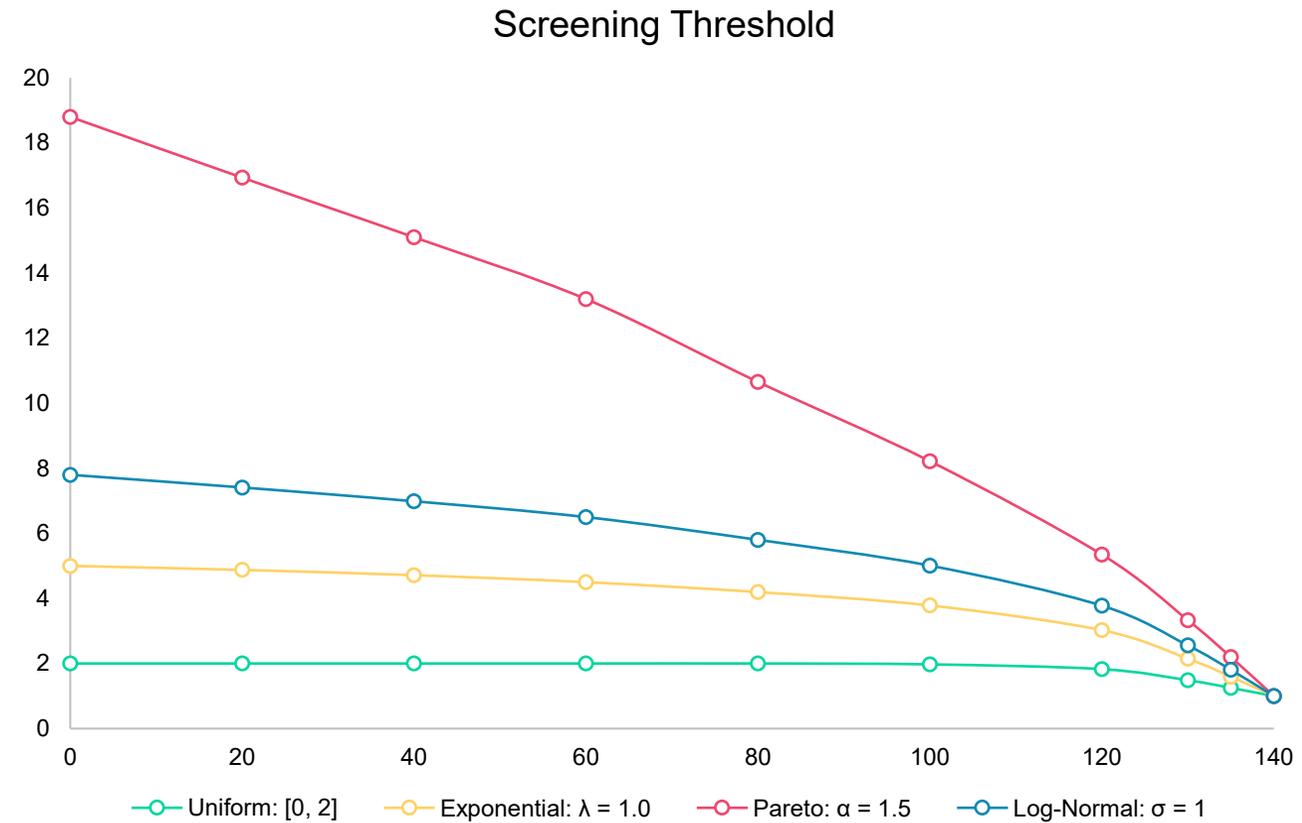
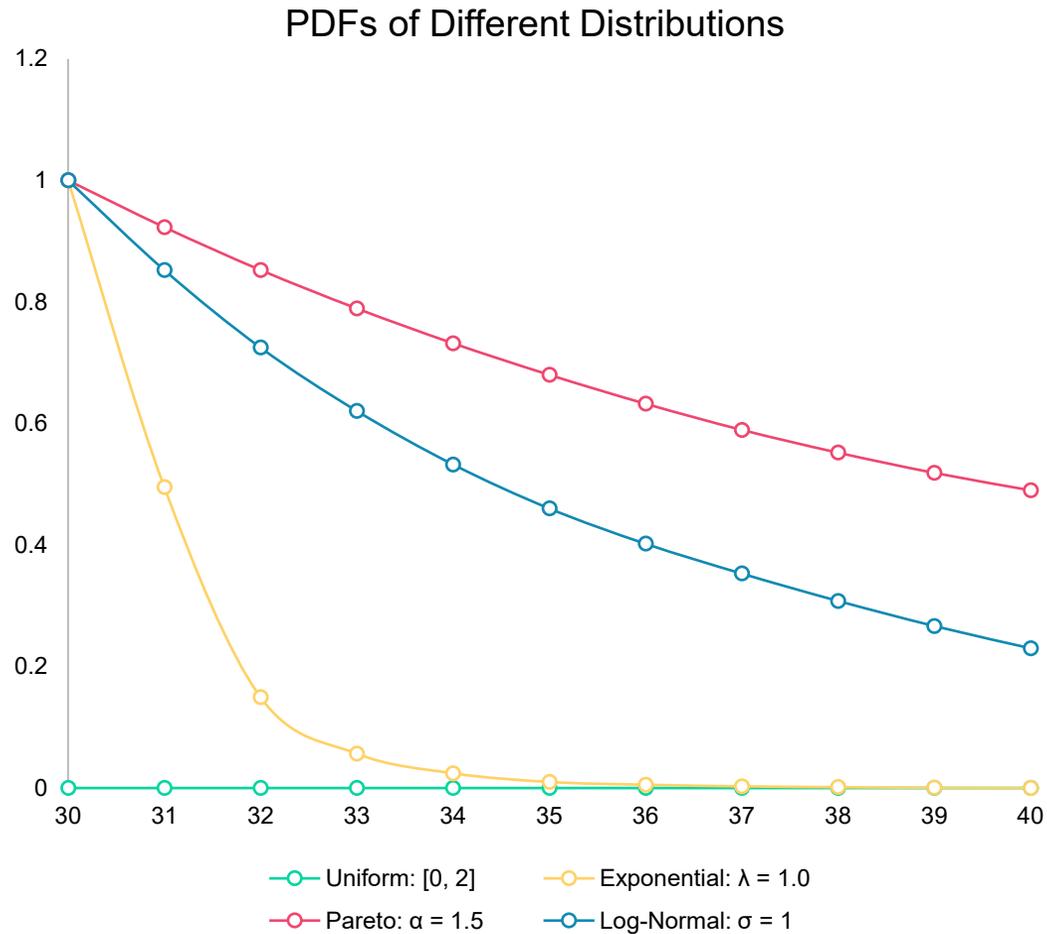
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# Illustration of Screening Threshold



# Illustration of the Tail Risk Effect



# Comparison with Baseline Policies

$\mathcal{P}^0$       **No Alert Strategy**

$\mathcal{P}^*$       **Optimal Strategy: Decreasing Threshold Policy**

$\mathcal{P}^A$       **All Alerts Policy: Common default policy**

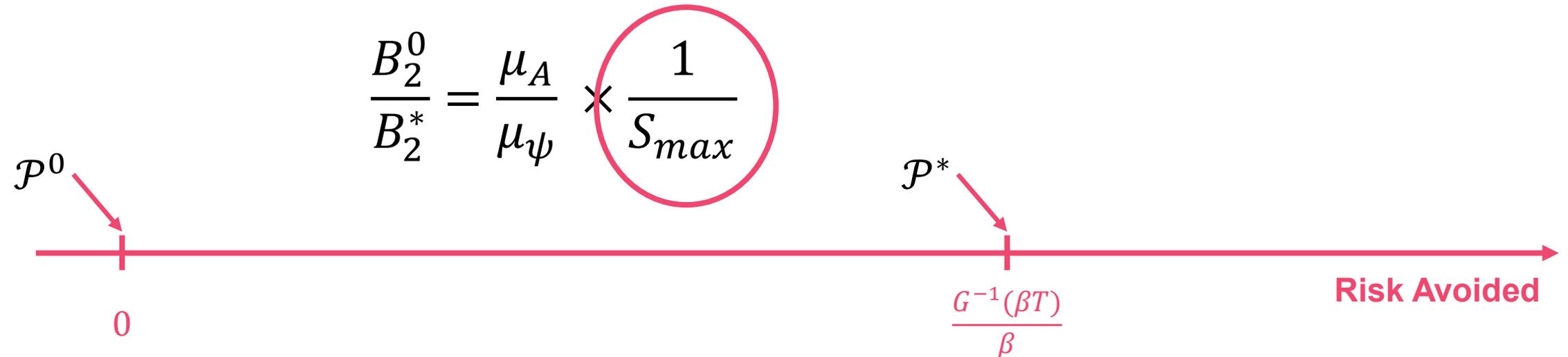


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$\mathcal{P}^\dagger$       **Optimal *Fixed* Policy:  $r_1^*(t) = k$**



# The Effectiveness of Fixed Policies

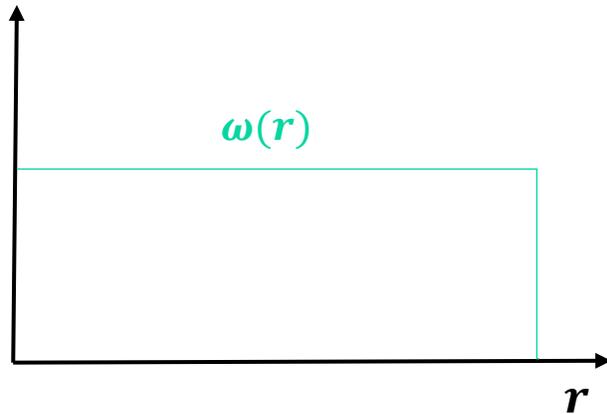
## Theorem

Normalized Expected Fatigue:  $\omega(y) = \frac{1}{\mu\omega} \int_{S(r)=y}^{\infty} \psi(y) f(r) dr$

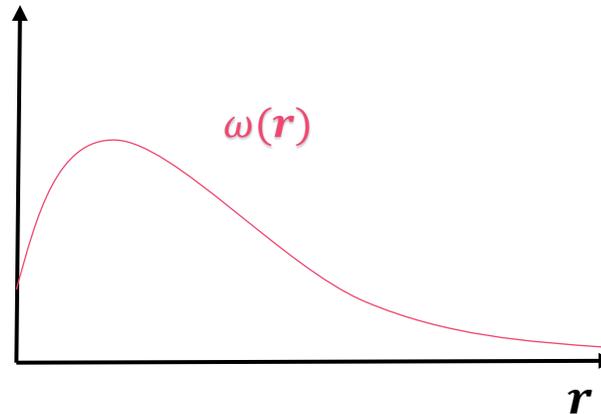
1. (Light-tailed  $\omega(y)$ ) Tail of  $\omega(y)$  belongs to the Weibull or Gumbel  $\rightarrow$
2. (heavy-tailed  $\omega(y)$ ) Tail of  $\omega(y)$  belongs to the Frechet  $\rightarrow$

$$\lim_{T \rightarrow \infty} \frac{B_2^{Fix}(T)}{B_2^*(T)} = 1$$

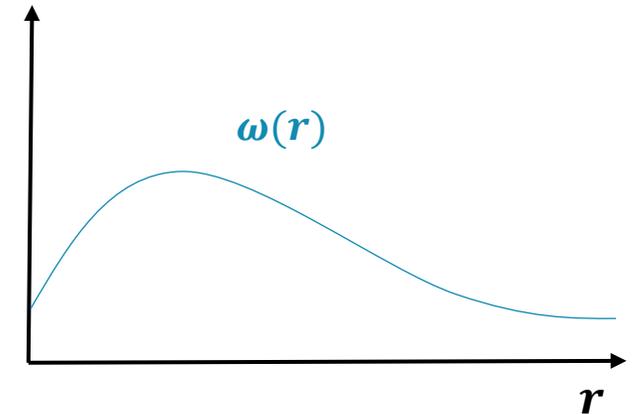
$$\lim_{T \rightarrow \infty} \frac{B_2^{Fix}(T)}{B_2^*(T)} < 1$$



Constant Optimal ✓



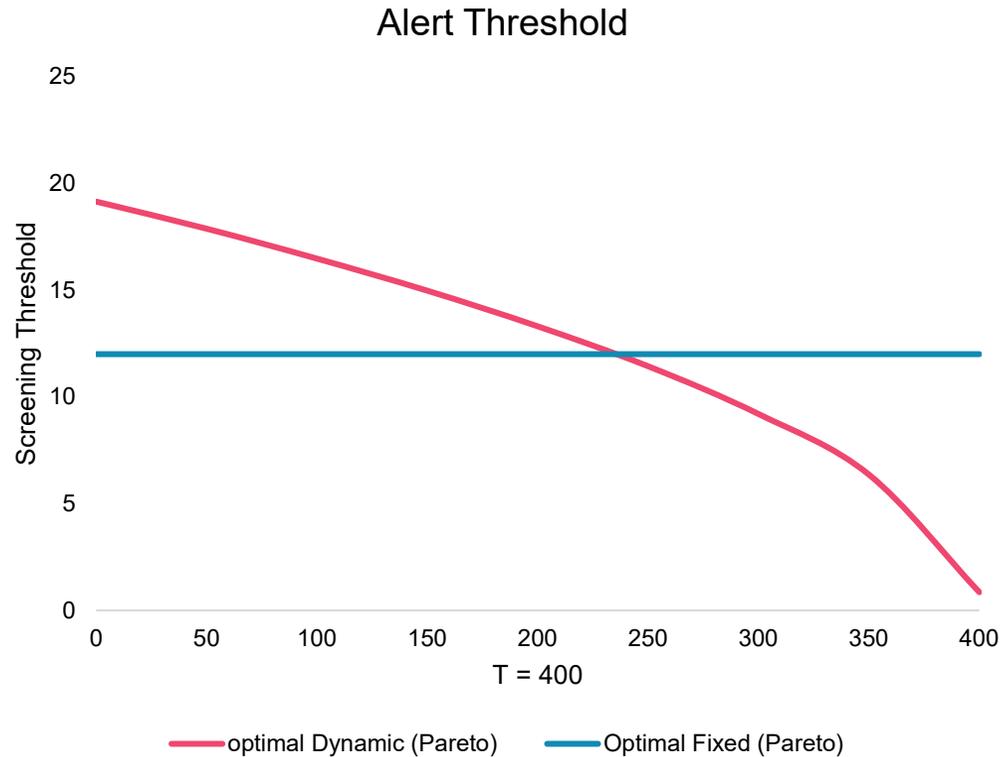
Constant Optimal ✓



Constant Near-Optimal ✓

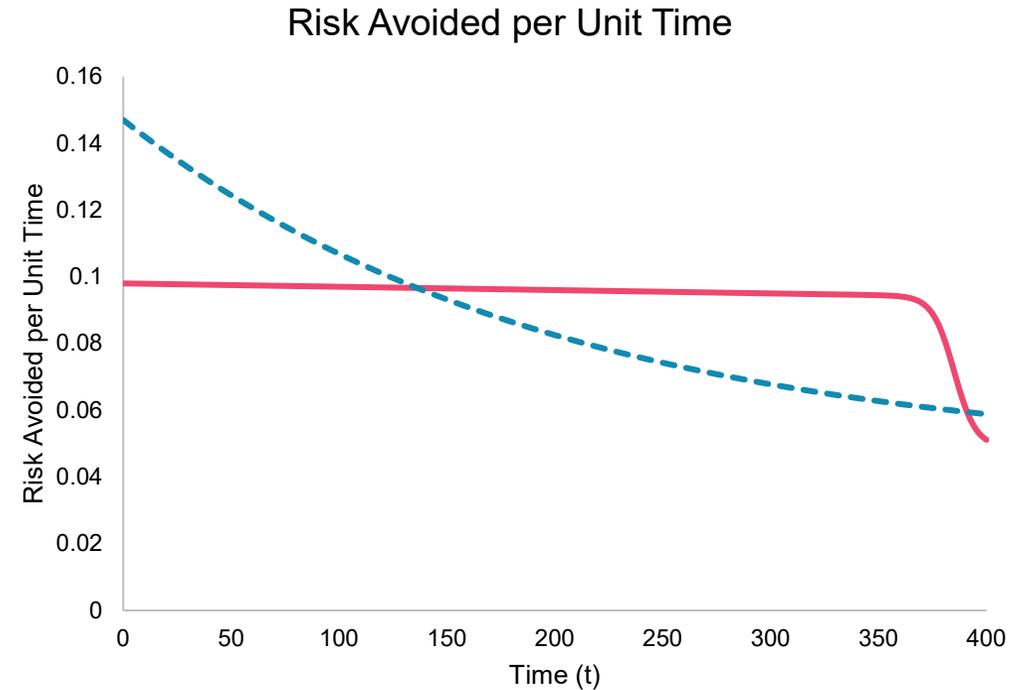
Near-optimality of optimal fixed policy.

# Optimal Fixed vs Optimal Policies



**Optimal Solution:** Decreasing

**Fixed Solution:** Constant

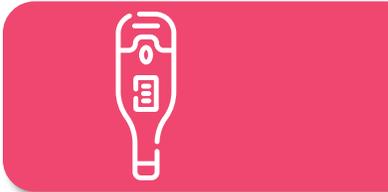
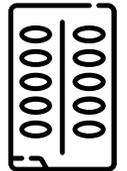
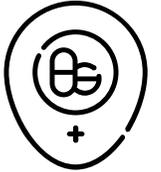


**Optimal Solution:** (Near) Constant

**Fixed Solution:** Decreasing

Tradeoff between alert vs risk fairness

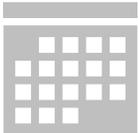
# Case Study





# Real-world Data Calibration

Pharmacist alert data from the University of Alberta Hospital System



**Study Period**  
Jan 2021 – Dec 2024



**Total Alerts**  
583,313



**Avg Alerts / Shift**  
142



**90<sup>th</sup> Percentile**  
> 449 Alerts / Shift



**Override Rate**  
78%

# Risk Estimation

Alert Description	Importance Level
Moderate Interaction	Low
Severe Warning	Medium
Absolute Contraindication	High
Moderate Warning	Very High

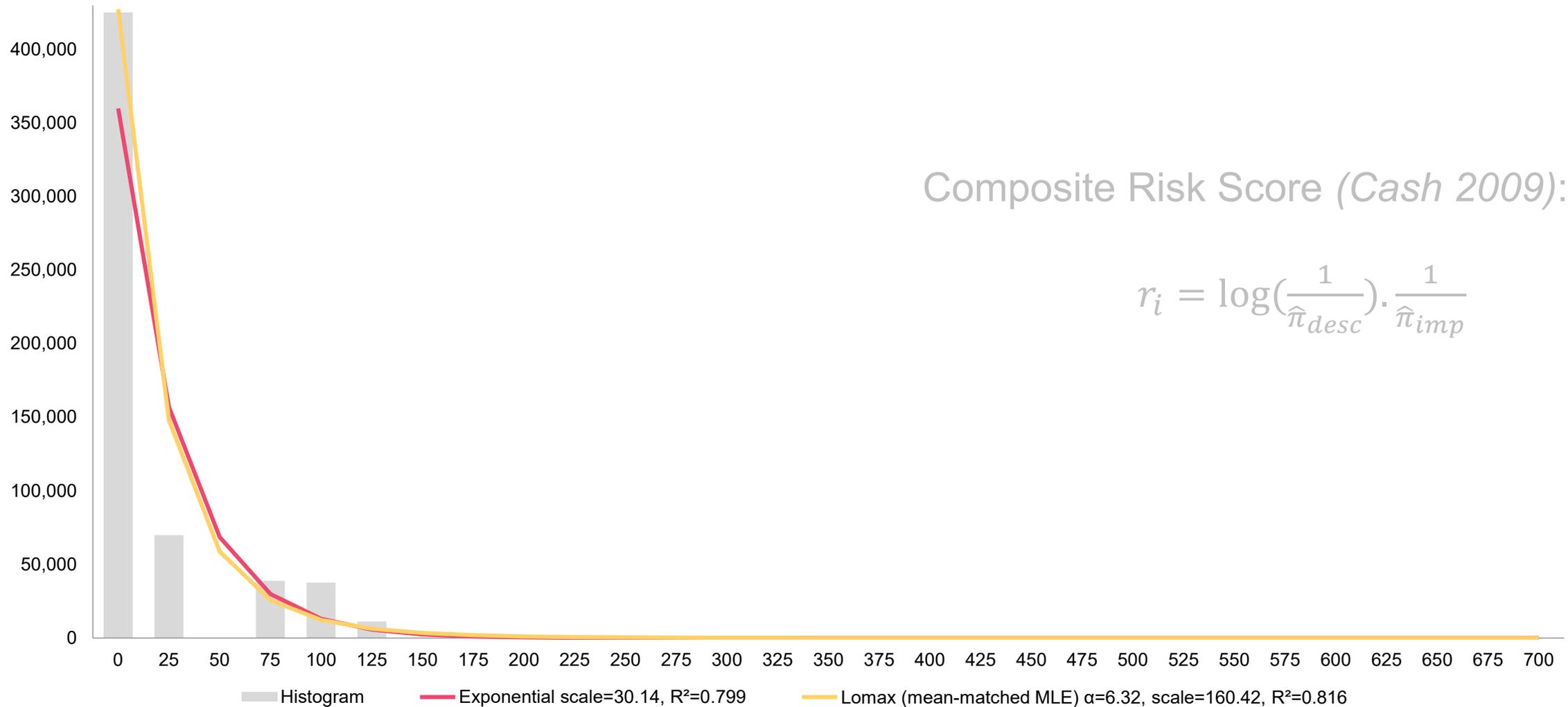
*Description* → **Templates**

*Lowercasing, removing markup, digits, etc.*

Composite Risk Score (*Cash 2009*):

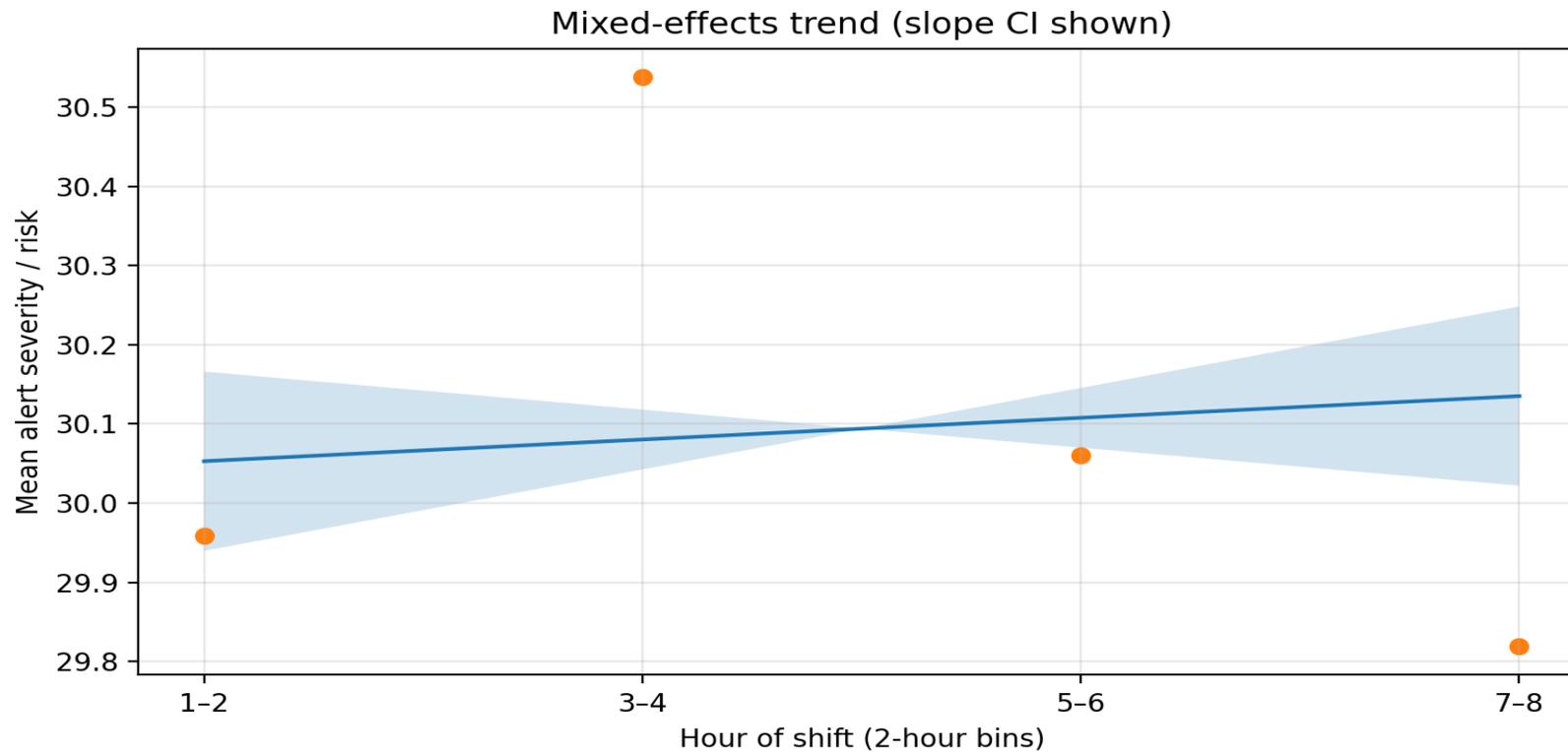
$$r_i = \log\left(\frac{1}{\hat{\pi}_{desc}}\right) \cdot \frac{1}{\hat{\pi}_{imp}}$$

# Risk Estimation



# Risk Stationarity

Risk is stable across shift hours (no meaningful drift)



# Behavioral Model

Exponential Decay:

Mackworth (1948), Warm et al. (2008)

$$P_i(\Psi, r, x) = \exp(-\hat{\eta}_i)$$

$$\hat{\eta}_i = \textit{Fatigue} + \textit{Risk} + \textit{Cumaltive Risk} + \textit{Recovery} + \textit{Exposure} + \textit{Pharmacist} + \textit{Shift}$$

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# Behavioral Model

5-fold CV AUC: 0.76

↓ 27% by 100 alerts

Stationary risk

Alert Fatigue

Term	Coef. Estimate	Feature Importance * × 1e - 4
Intercept	0.696318*** (0.063483)	NA
Alert index	0.003159*** (0.000133)	446
Alert Risk	-0.003197*** (0.000065)	68
Cumulative Alert index	-0.000043** (0.000001)	9
Exposure before shift (learning)	-0.000189*** (0.000003)	32
Time between prescriptions (recovery)	0.0000007 (0.006239)	78
Shift Fixed Effect	Included not significant	<5
Pharmacist fixed effect	Included not significant	<5

\* Feature importance is LOFO ΔNLL

# Policy Evaluation

## Life-threatening alerts: *High-importance + contraindication*

Policy	Risk avoided (%)	Alerts shown	LT accepted (%)
Current	18.98	583,313	9.86
Fixed	25.62	389,717	53.31
Dynamic	26.20	415,923	55.10
Adaptive	27.95	429,668	57.72

## Near-optimality of optimal fixed policy

Vs All Alerts	Alerts	LT Reduction
<b>Optimal Dynamic\ Fixed Policies</b>	~ -33%	~ +40%



2000-4000 lives saved



0.5 Billion in cost across the U.S.

# Sensitivity Analysis

Misspecification	Policy	Parameter
Average Risk	Overestimation	$\hat{\lambda}_{exp} = 0.5 \lambda_{exp}^{true}$
	Underestimation	$\hat{\lambda}_{exp} = 2 \lambda_{exp}^{true}$
Risk Model	Model Mismatch	-
Fatigue	Overestimation	$\hat{\beta}^{glob} = 2 \beta^{glob, true}$
	Underestimation	$\hat{\beta}^{glob} = 0.5 \beta^{glob, true}$



<1% performance decay



No significant compromise of safety



Our proposed policies **still** perform significantly better



Reduce alerts by **50%**

# Summary



## Analytical Model

A novel fluid approximation model for alert decision-making under operator fatigue

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A novel fluid approximation model for alert decision-making under operator fatigue



## Theoretical Results

Dynamic vs. Fixed: Alerting is not just a filter. It is a fair attention-allocation policy over time.

# Summary



## Analytical Model

A novel fluid approximation model for alert decision-making under operator fatigue



## Theoretical Results

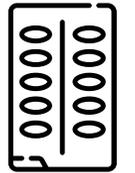
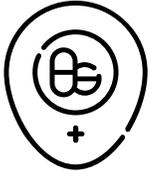
Dynamic vs. Fixed: Alerting is not just a filter. It is a fair attention-allocation policy over time.



## Impact

2000-4000 lives and 0.5 billion in cost saved across the U.S.

# Conclusion



# Takeaway!



Healthcare staff  
have a limited  
***Cognitive Budget!***

# Takeaway!



Healthcare staff  
have a limited  
***Cognitive Budget!***



**Use it wisely by  
optimizing human-  
AI interaction**



**Hossein Piri**  
hossein.piri@ucalgary.ca



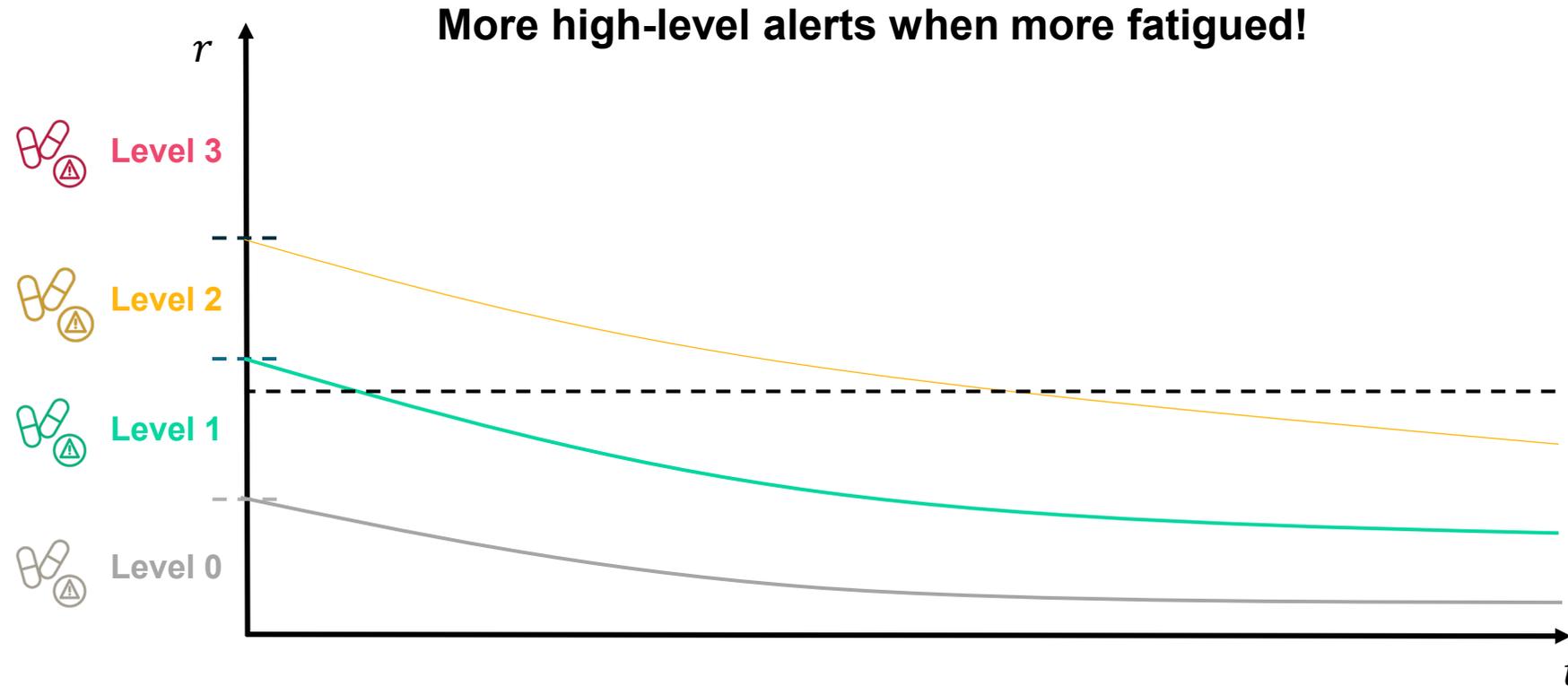
**Michael Lingzhi Li**  
mili@hbs.edu

**Thank You! Questions?**

# Structure of the Optimal Solution

## Theorem

Under very mild conditions on the linking function  $g(\cdot)$ , the optimal solution to the alert fatigue problem always follows a threshold policy, in which the threshold decays over time.



# Impact of Model Parameters

## Corollary

The optimal risk threshold,  $r_1^*(t)$ , under Pareto, exponential and uniform risk distribution:

$$r_{1p}^*(t) = \lambda_p \left[ \left( 1 + \frac{\alpha \beta c}{\alpha - 1} (T - t) \right)^{\frac{1}{\alpha}} - 1 \right]$$

$$r_{1e}^*(t) = \frac{1}{\lambda_e} \ln(\beta c (T - t) + 1)$$

$$r_{1u}^*(t) = \frac{b \beta c (T - t)}{\beta c (T - t) + 2}$$

Mild Dependence on Costs ( $c, \beta$ )

Linear Dependence on Scale ( $b, \lambda_e, \lambda_p$ )