Multiplicative Effect Modeling: The General Case

Jackie (Jiaqi) Yin
October 5th, 2019

Women in Statistics and Data Science 2019

UNIVERSITY of WASHINGTON

Titanic

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TITANIC SINKS, 1500 DIE

Carpathia Picks Up 675 Out of 2200---Races for New York---Survivors Mostly Women and Children.

POLICE ORDER DORR'S ARREST

Lynn Chief Accuses Him of the Murder of George E. Marsh.

Suspect Said to Have Left Boston Thursday Night--Auto Found Here.

Giant Steamer Goes Down Before Help Arrives.

Virginian or Parisian May Have Some Survivors

White Star Officials Admit "Horrible Loss of Life".

Titanic Deaths

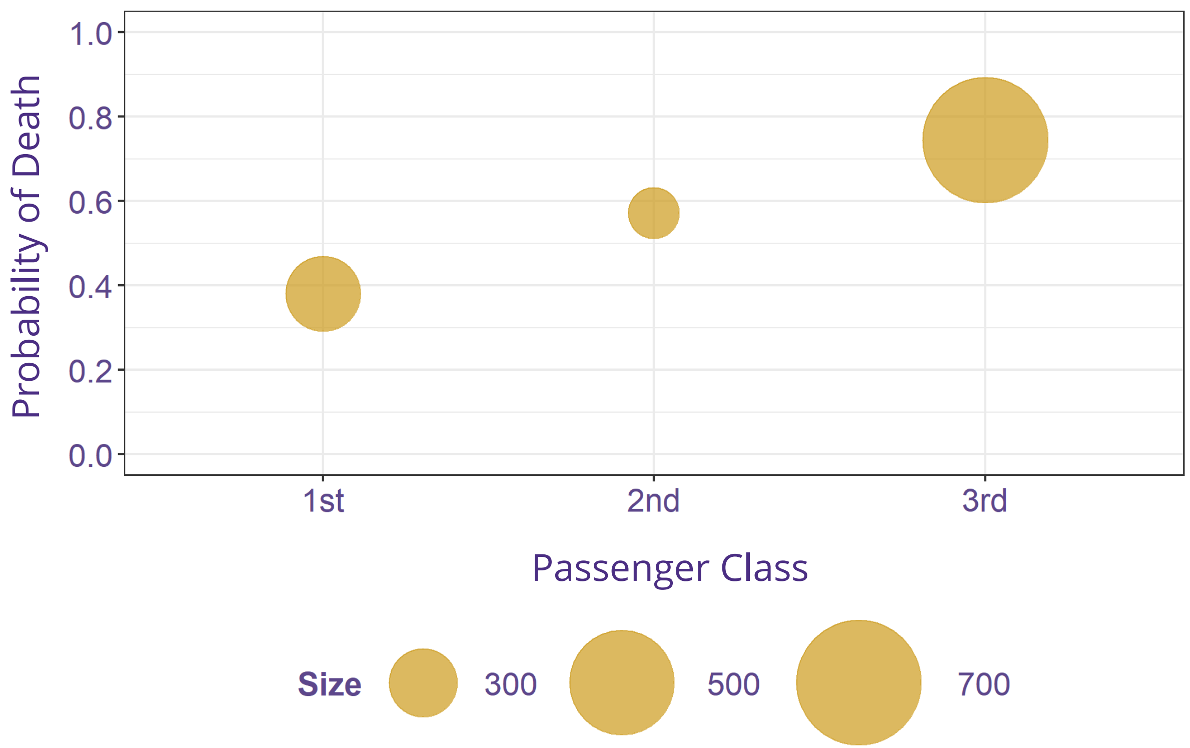
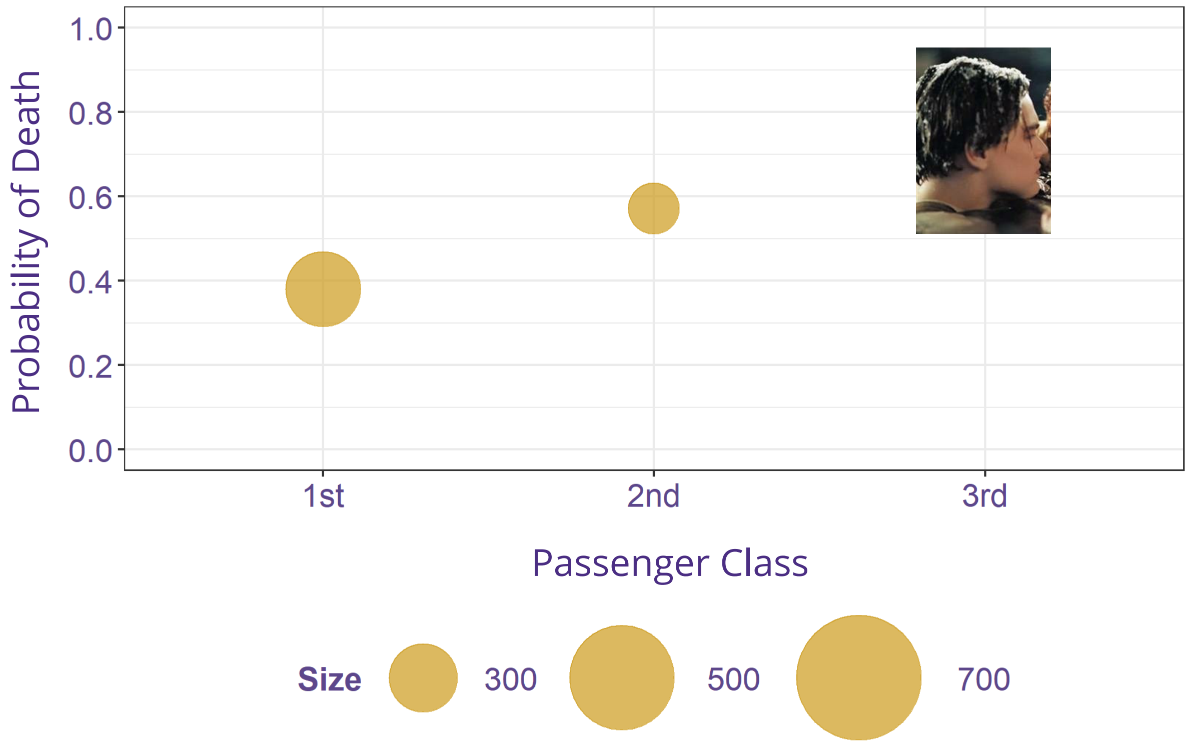


Fig. 1. Probability of death varies with passenger class.

Titanic Deaths



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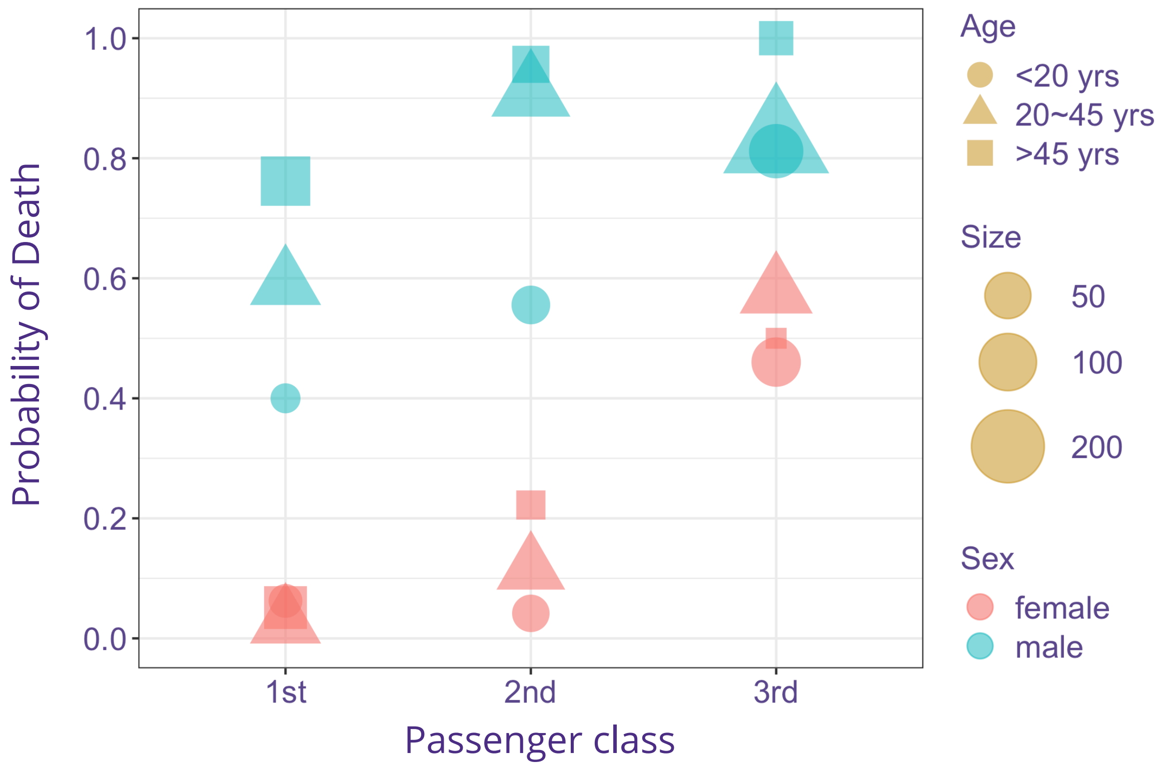

Fig. 2. Probability of death stratified by passenger class, age, and sex.

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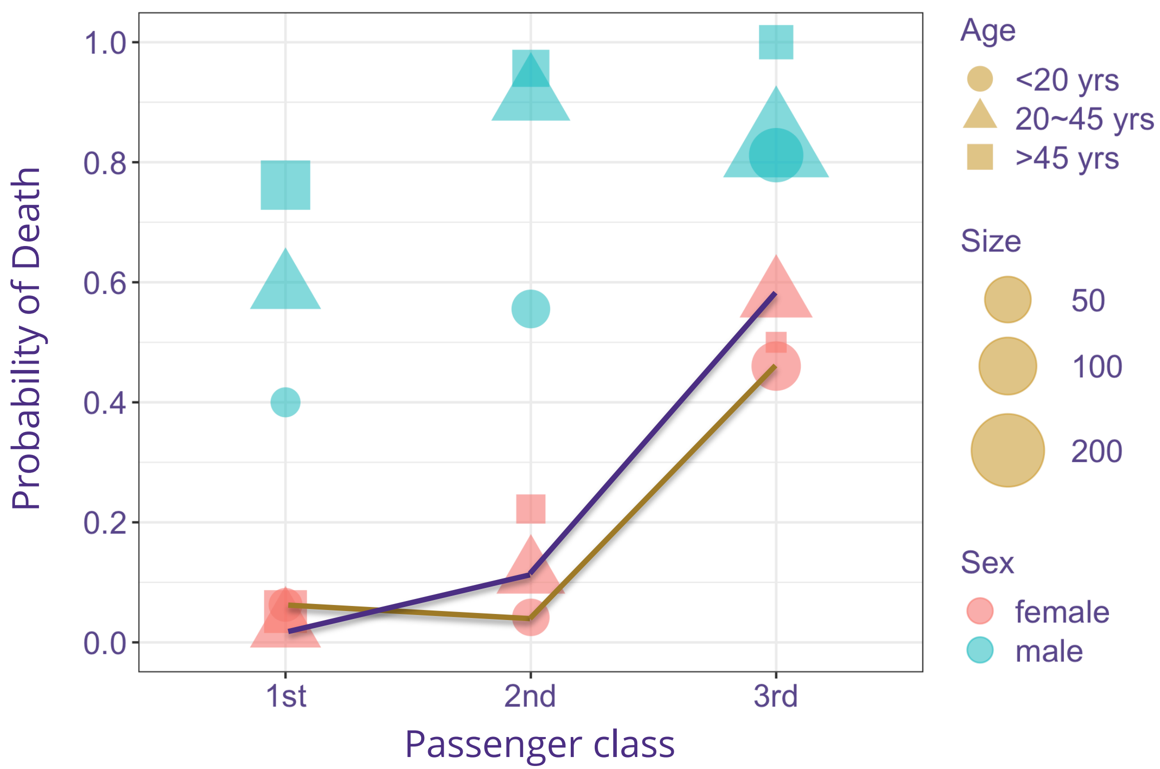

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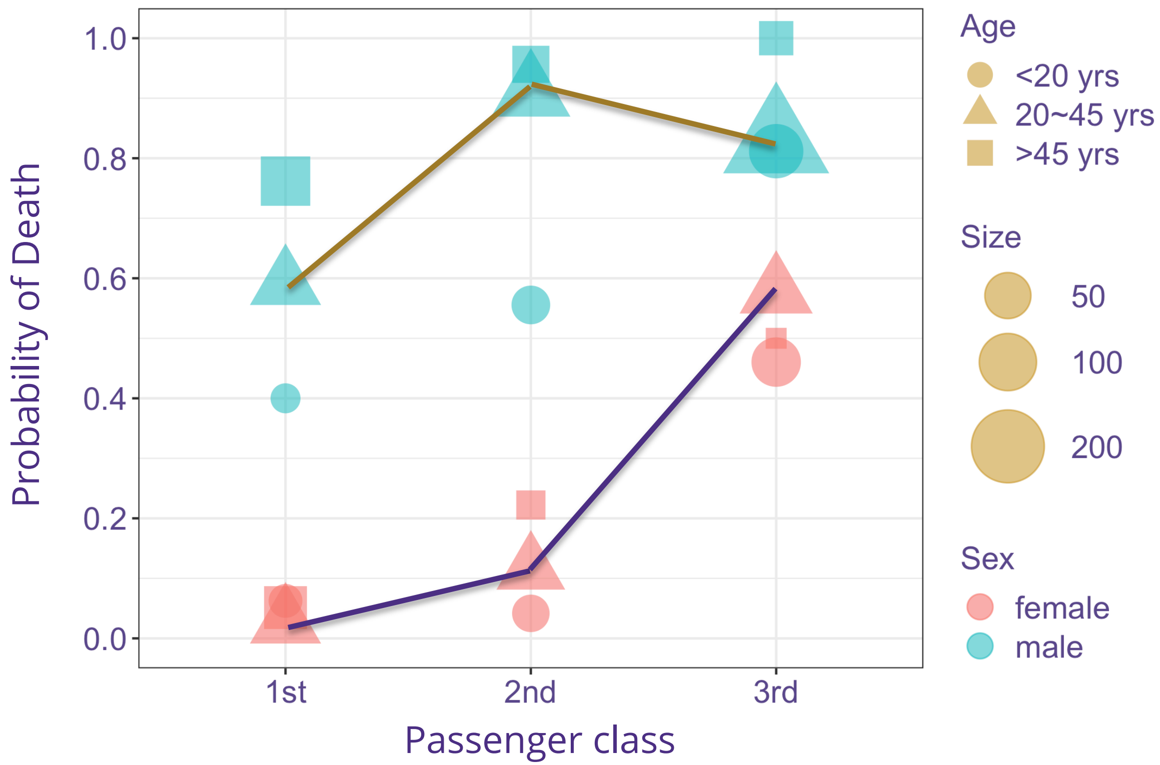

Fig. 2. Probability of death stratified by passenger class, age, and sex.

How to model the association between death and passenger class?

Problem Description

Setting

- Binary outcome $Y \in \{0, 1\}$
- Categorical or continuous treatment $Z \in \mathcal{Z}$
- Covariates $V \in \mathcal{V}$

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- Binary outcome $Y \in \{0, 1\}$
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Problem:

- Quantify the association between Z and Y, and how that varies with V

Measures of Association for Treatment

- **Odds Ratio (OR):**

$$\mathrm{OR}(z_0, z; v) = \frac{\mathrm{pr}(Y = 1 \mid Z = z, V = v)/\mathrm{pr}(Y = 0 \mid Z = z, V = v)}{\mathrm{pr}(Y = 1 \mid Z = z_0, V = v)/\mathrm{pr}(Y = 0 \mid Z = z_0, V = v)}$$

Binary outcome $Y \in \{0, 1\}$

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- **Relative Risk (RR):**

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Binary outcome $Y \in \{0, 1\}$

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Generalized Linear Models (GLMs) for Binary outcome

Measures	GLMs
Odds Ratio	Logistic Regression
Relative Risk	Poisson Regression

Why not Odds Ratio?

Problems of Odds Ratio

- **Interpretation:** not intuitive; scientists rarely ask for them (Lumley et al., 2006).

Lack of Collapsibility

Tab. 1. Odds ratio of synthetic randomized trial.

	Population	
	Treated	Untreated
Disease	11038	38988
No disease	8962	41012
Odds ratios	1.29	

Lack of Collapsibility

Tab. 1. Odds ratio of synthetic randomized trial.

	Population		Female	
	Treated	Untreated	Treated	Untreated
Disease	11038	38988	9948	38388
No disease	8962	41012	52	1612
Odds ratios	1.29		8.03	

Lack of Collapsibility

Tab. 1. Odds ratio of synthetic randomized trial.

	Population		Female		Male	
	Treated	Untreated	Treated	Untreated	Treated	Untreated
Disease	11038	38988	9948	38388	1090	600
No disease	8962	41012	52	1612	8910	39400
Odds ratios	1.29		8.03		8.03	

1.29 < 8.03

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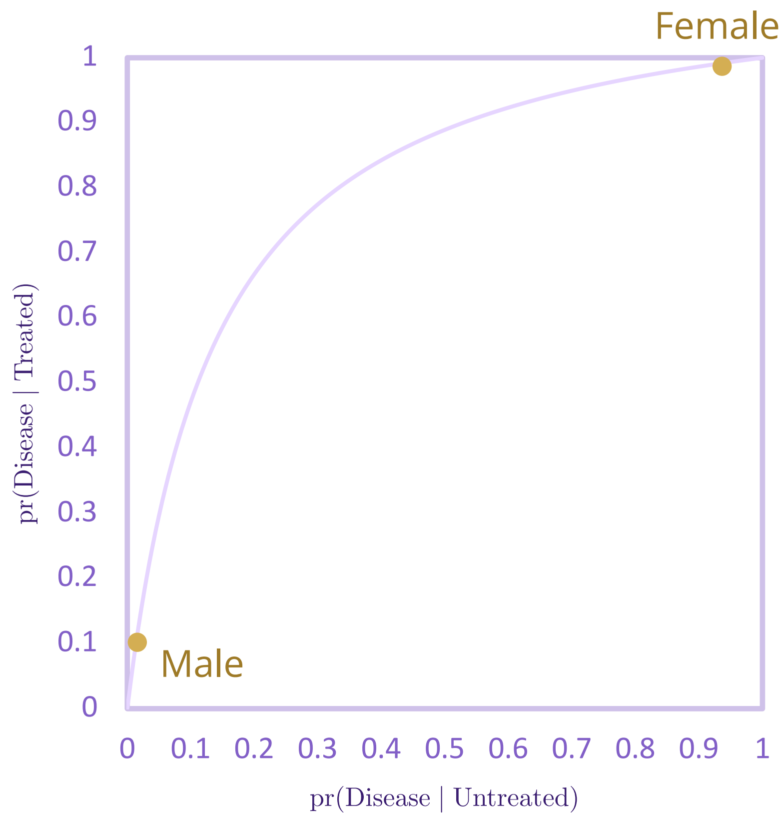

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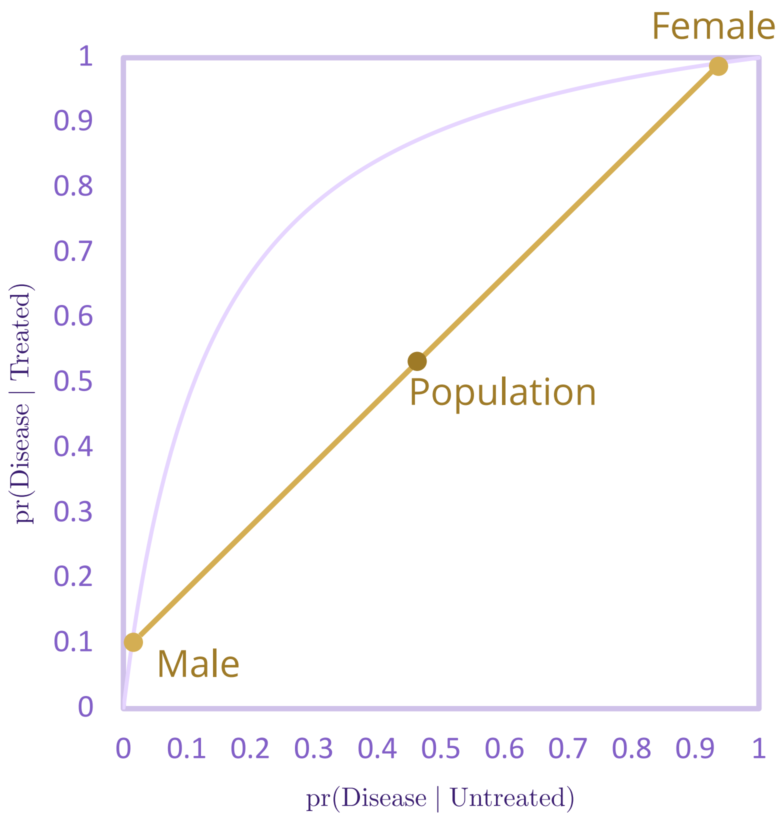

Measures of Association for Treatment

Problems of Odds Ratio

- **Interpretation:** not intuitive; scientists rarely ask for them (Lumley et al., 2006).
- **Lack of collapsibility:** the marginal odds ratio will not lie in the convex hull of stratum-specific odds ratios (Greenland et al., 1999).

Relative Risk is Collapsible

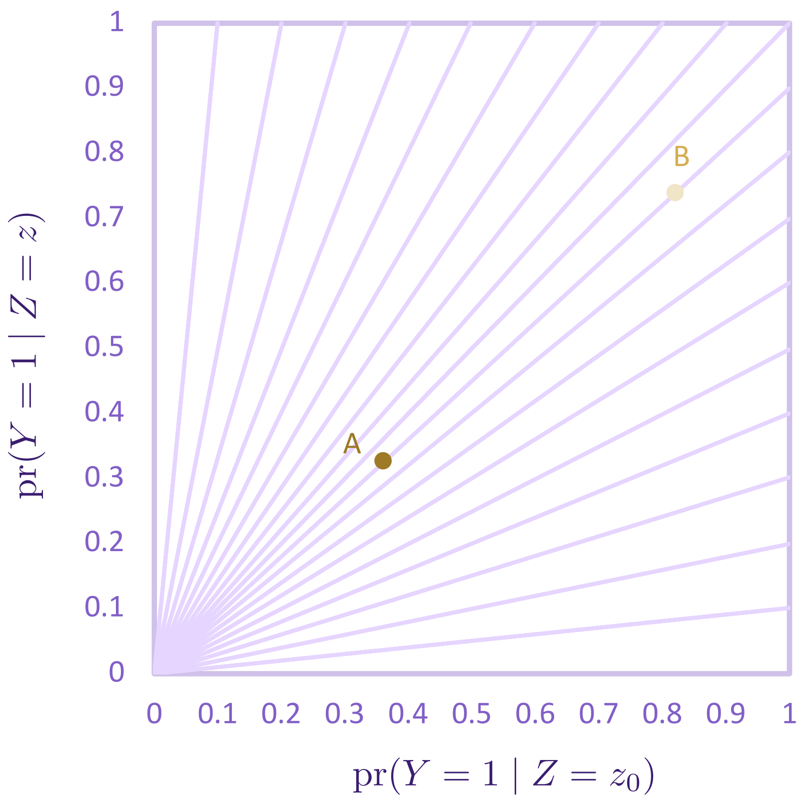

Fig 3. lines of constant Relative risk

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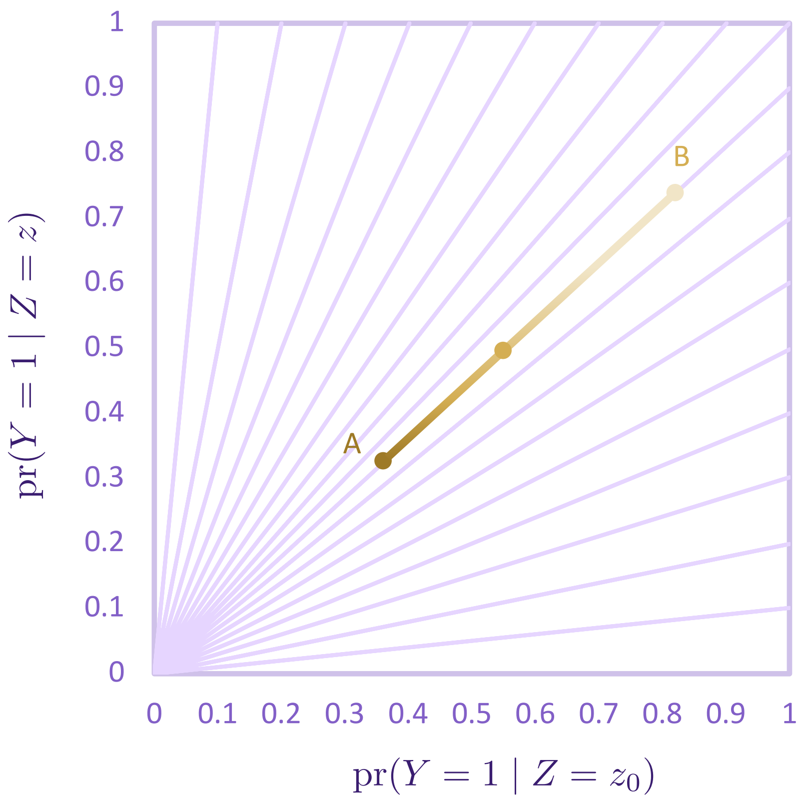

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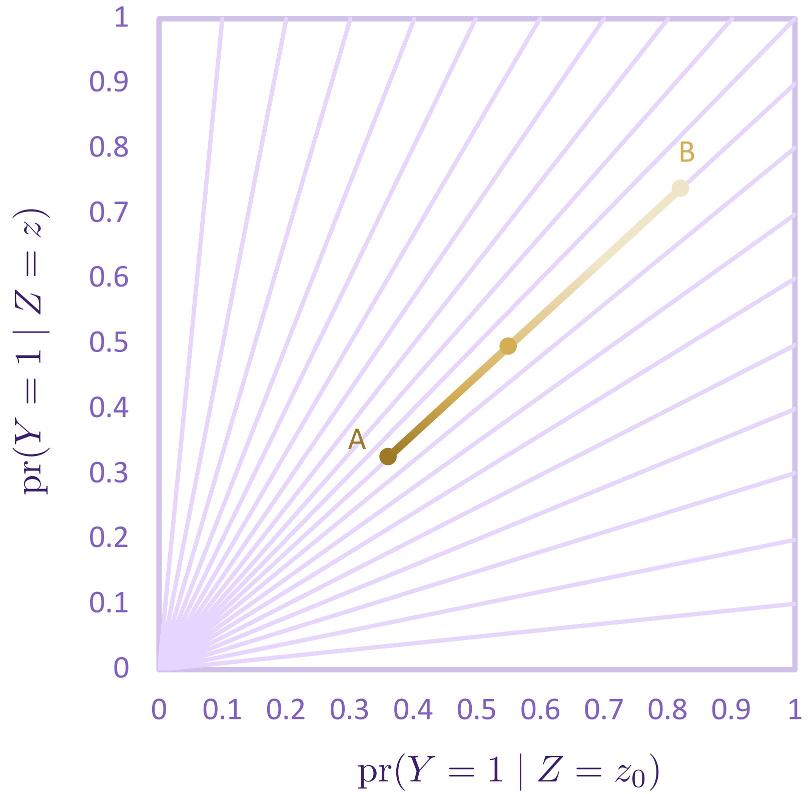

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Collapsible!

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Relative Risk Modeling

Generalized Linear Model (GLM)

- **Poisson Regression:**

$$\log\{\mathrm{pr}(Y = 1|Z, V)\} = Z\alpha^{\mathrm{T}}V + \beta^{\mathrm{T}}V$$

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Problems of Poisson Regression

Variation Dependence

$$\log\{\mathrm{RR}(0,1;V)\} = \alpha^{\mathrm{T}} V$$
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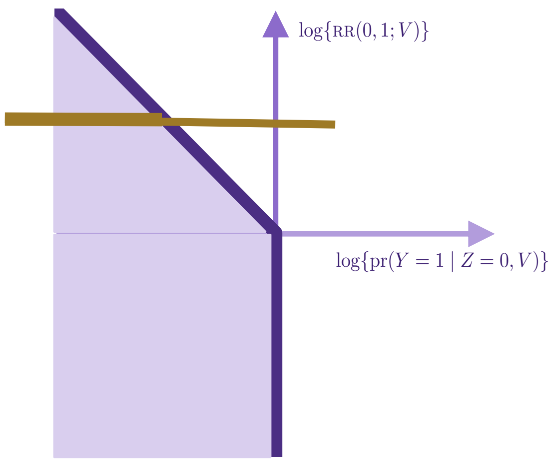

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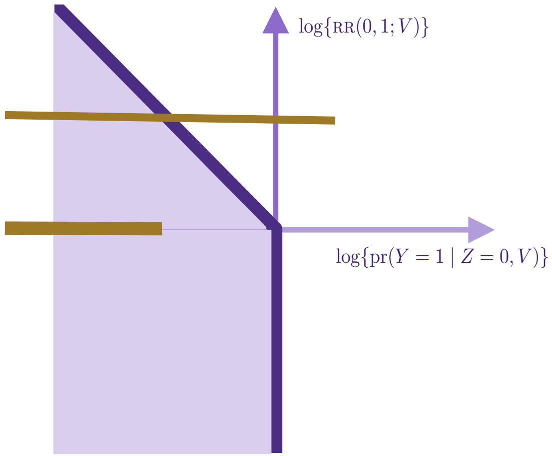

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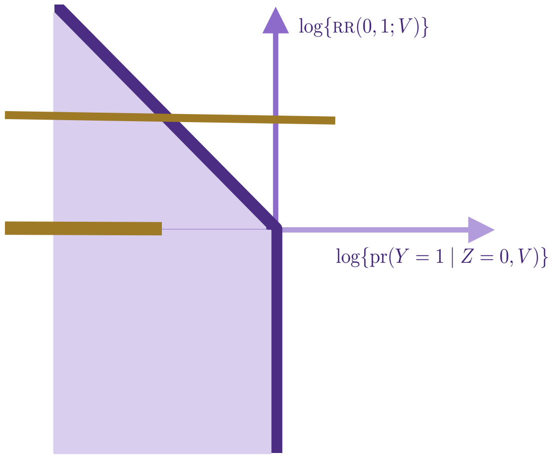

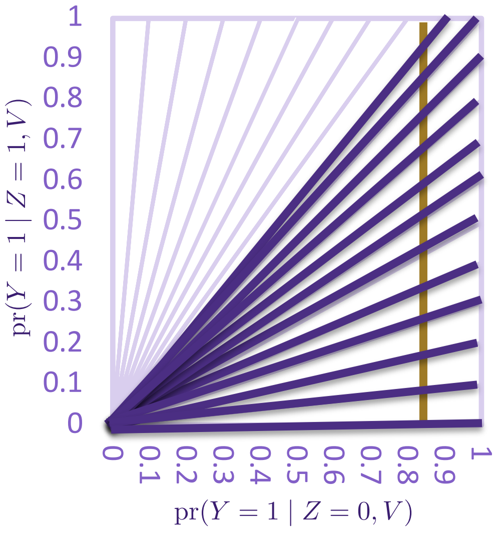

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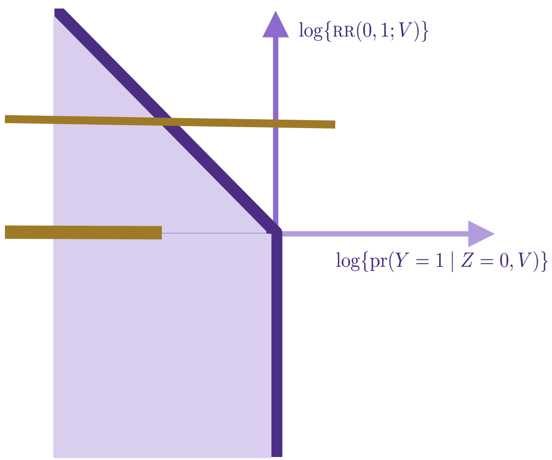

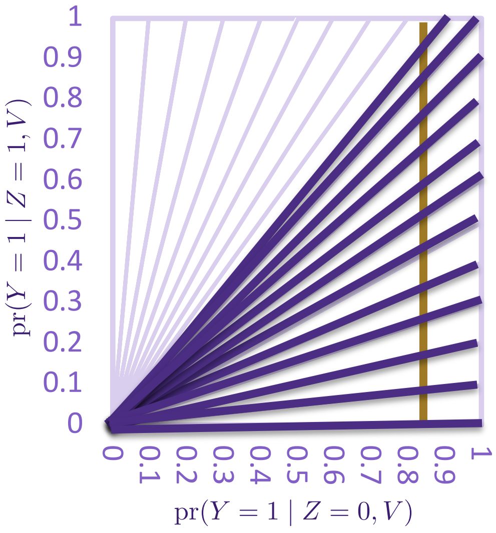

Problems of Poisson Regression

Prediction

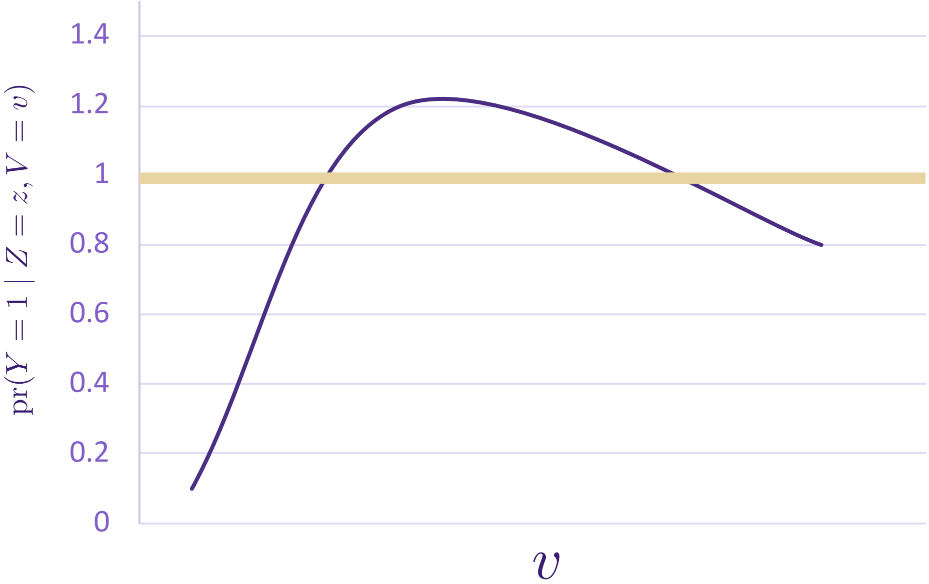

Fig. 5. Predictions after fitted with Poisson regression

Problems of Poisson Regression

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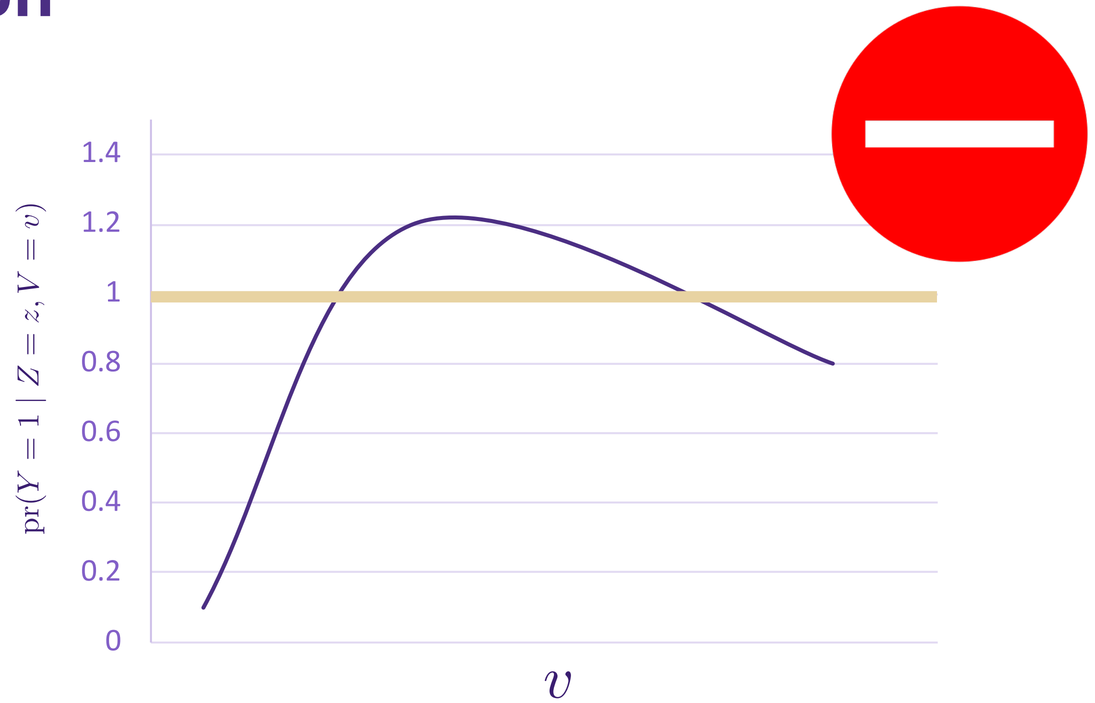

Fig. 5. Predictions after fitted with Poisson regression

GLM Dilemma

Relative Risks Modeling

Richardson et al. (2017), binary treatment, $Z \in \{0, 1\}$

$$\log\{\text{RR}(0, 1; V)\} = \alpha^{\mathrm{T}} V$$

$$\log\{\text{pr}(Y = 1 \mid Z = 0, V)\} = \beta^{\mathrm{T}} V$$

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$$\log\{\text{RR}(0,1;V)\} = \alpha^{\text{T}} V$$
$$\log\{\text{OP}(0,1;V)\} = \beta^{\text{T}} V$$

Define odds product (OP) as:

$$\text{OP}(z_0, z; v) = \frac{p_0(v) p_z(v)}{\{1 - p_0(v)\}\{1 - p_z(v)\}},$$

where $\text{pr}(Y = 1 \mid Z = z, V = v) = p_z(v)$

Why Odds Product?

$$\text{OP}(0,1;v) = \frac{p_0(v)p_1(v)}{\{1-p_0(v)\}\{1-p_1(v)\}} \qquad \text{RR}(0,1;v) = \frac{p_1(v)}{p_0(v)}$$

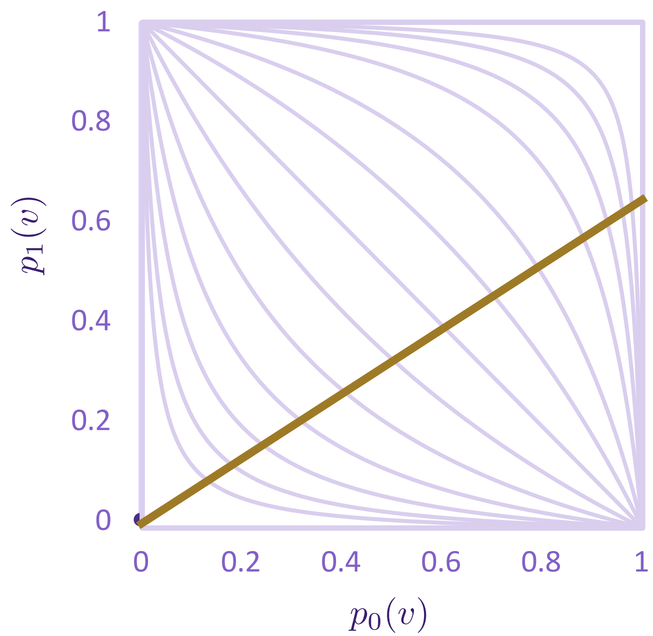

Fig. 4. Lines of constant odds product

Variation Independence!

Relative Risks Modeling

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Our Methods for Modeling Relative Risks

Richardson et al. (2017), binary treatment, $Z \in \{0, 1\}$

Our Methods for Modeling Relative Risks

Continuous or **categorical** treatments $Z \in \mathcal{Z}$

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Continuous or **categorical** treatments $Z \in \mathcal{Z}$

- **Goal**: find $\phi(v)$ so that for any v, the mapping given by

$$(\log\{\mathrm{RR}(z_0, z; v)\}, z \in \mathcal{Z}; \phi(v)) \rightarrow (p_z(v), z \in \mathcal{Z})$$

is a **diffeomorphism** between the interior of their domains.

Method 1: Monotonic Treatment Effects

Examples

$\mathrm{RR}(z_0, z; v)$ is monotonic in z for all v

Dosage

Recovery Probability

Method 1: Monotonic Treatment Effects

Examples

$\mathrm{RR}(z_0, z; v)$ is monotonic in z for all v

Dosage

Recovery Probability

Income

Happiness

Method 1: Variation Independence with Monotonic Treatment Effects

- **Assumption:** $\mathrm{RR}(z_0, z; v)$ is **monotonic and bounded** in z, $z \in (0, 1)$

$$p_z(v) = \mathrm{pr}(Y = 1 \mid Z = z, V = v)$$
$$\mathrm{RR}(z_0, z; v) = \frac{\mathrm{pr}(Y = 1 \mid V = v, Z = z)}{\mathrm{pr}(Y = 1 \mid V = v, Z = z_0)}$$
$$\mathrm{OP}(z_0, z; v) = \frac{p_0(v) p_z(v)}{\{1 - p_0(v)\}\{1 - p_z(v)\}}$$

Method 1: Variation Independence with **Monotonic** Treatment Effects

- **Assumption:** $\mathrm{RR}(z_0, z; v)$ is **monotonic and bounded** in z, $z \in (0,1)$

$$\log\{\mathrm{RR}(z_0, z, ; v)\}, z \in (0,1); \quad \log\{\mathrm{OP}(0,1; v)\} \quad \Rightarrow \quad p_z(v), z \in (0,1)$$

is a diffeomorphism.

$$p_z(v) = \mathrm{pr}(Y = 1 \mid Z = z, V = v)$$

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Method 1: Variation Independence with Monotonic Treatment Effects

Theorem 1 *Let $\mathcal{Z} \subseteq \mathbb{R}$ and $\mathcal{V}$ be the support of Z and V, respectively. Let $h(z, v)$ and $g(v)$ be real-valued functions with support $\mathcal{Z} \times \mathcal{V}$ and $\mathcal{V}$, respectively. If $h(z, v)$ is bounded and monotonic in z, then there exists a unique set of proper probability distributions $\{p_z(v); z \in \mathcal{Z}, v \in \mathcal{V}\}$ such that $\log\{\text{RR}(z_0, z; v)\} = h(z, v)$ and $\log\{\text{OP}(z_{\inf}, z_{\sup}; v)\} = g(v)$, where $z_{\inf} = \inf\{z : z \in \mathcal{Z}\}$, $z_{\sup} = \sup\{z : z \in \mathcal{Z}\}$ and*

$$\text{OP}(z_{\inf}, z_{\sup}; v) = \lim_{z_1 \to z_{\inf}} \lim_{z_2 \to z_{\sup}} \frac{p_{z_1}(v) p_{z_2}(v)}{(1 - p_{z_1}(v))(1 - p_{z_2}(v))}.$$

Remark 1 *The boundedness condition on $h(v, z)$ guarantees that the implied probabilities $p_z(v)$ are bounded away from 0.*

Method 1: Variation Independence with Monotonic Treatment Effects

Why the assumption matters…

$z \in (0, 1)$

$$p_z(v) = \text{pr}(Y = 1 \mid Z = z, V = v)$$

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Why the assumption matters…

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$$\left\{ \begin{array}{l} \log\{\text{OP}(0,1;v)\} \\ \log\{\text{RR}(0,1;v)\} \end{array} \right.$$

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$$\begin{cases} \log\{\text{OP}(0,1;v)\} \\ \log\{\text{RR}(0,1;v)\} \end{cases} \Rightarrow \begin{cases} p_0(v) \\ p_1(v) \end{cases}$$

Richardson et al. (2017):

$$0 < p_0(v), p_1(v) < 1$$

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- **Assumption:** $\mathrm{RR}(z_0, z; v)$ is **monotonic** in z, $z \in (0,1)$

  equivalently, $p_z(v)$ is monotonic in z

$$\min\{p_0(v), p_1(v)\} \leq p_z(v) \leq \max\{p_0(v), p_1(v)\} \qquad z \in (0,1)$$

$$p_z(v) = \mathrm{pr}(Y = 1 \mid Z = z, V = v)$$

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Proper probabilities!

$$p_z(v) = \mathrm{pr}(Y = 1 \mid Z = z, V = v)$$

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Method 1: Parameterization with Monotonic Treatment Effects

Consider bounded treatment $z \in [0,1]$

$$\log\{\text{RR}(0,z;V,\gamma)\} = \gamma^{\text{T}} V g(z) \quad z \in [0,1]$$
$$\log\{\text{OP}(0,1;V,\beta)\} = \beta^{\text{T}} V,$$

where $g(z)$ is a monotone function of z

Method 1: Parameterization with Monotonic Treatment Effects

Log-likelihood for a unit:

$$l(\gamma, \beta | z_i, v_i, y_i) = y_i \log\{p_{z_i}(v_i; \gamma, \beta)\} + (1 - y_i) \log\{1 - p_{z_i}(v_i; \gamma, \beta)\}$$

Inference on γ and β can be obtained in standard fashion

Model 1: Simulation

$$\log\{\text{RR}(0,z;V,\gamma)\} = \gamma^{\mathrm{T}} V z \quad z \in \{0,1,2\},$$
$$\log\{\text{OP}(0,2;V,\beta)\} = \beta^{\mathrm{T}} V.$$

Data simulation:

- $Z \sim \text{unif}\{0,1,2\}$
- $V = (1, V_1)^{\mathrm{T}}$, $V_1 \sim \text{unif}[-2,2]$
- $\gamma = (0,1)^{\mathrm{T}}$, $\beta = (-0.5,1)^{\mathrm{T}}$

Model 1: Simulation Results

Table 1. Monte Carlo simulation results based on 1000 runs for the proposed estimator which assumes monotonic treatment effects.

Sample Size		100	500	1000
Bias(SE)				
	γ_0	0.002(0.022)	−0.001(0.004)	0.000(0.002)
	γ_1	0.090(0.025)	0.013(0.004)	0.006(0.002)
SD Accuracy				
	γ_0	1.022	1.040	0.994
	γ_1	1.109	1.032	1.018
Coverage				
	γ_0	0.950	0.949	0.948
	γ_1	0.949	0.950	0.958

SE, standard error.
SD Accuracy = estimated standard deviation / Monte Carlo standard deviation.
Nominal level = 95%.

$\gamma = (0, 1)^T$

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	γ_0	1.022	1.040	0.994
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	γ_1	0.949	0.950	0.958

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Bias(SE)				
	γ_0	0.002(0.022)	−0.001(0.004)	0.000(0.002)
	γ_1	0.090(0.025)	0.013(0.004)	0.006(0.002)
SD Accuracy				
	γ_0	1.022	1.040	0.994
	γ_1	1.109	1.032	1.018
Coverage				
	γ_0	0.950	0.949	0.948
	γ_1	0.949	0.950	0.958

SE, standard error.

SD Accuracy = estimated standard deviation / Monte Carlo standard deviation.

Nominal level = 95%.

$\gamma = (0, 1)^{\mathrm{T}}$

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The Model 1 cannot be applied if the relative risk is not monotonic in z.

Model 2: Categorical Treatment

$$Z \in \{z_0, \ldots, z_K\},\ K \geq 2$$

- **Recall the Goal:** find $\phi(v)$ so that for any v, the mapping given by

  $$(\log\{\mathrm{RR}(0, k; v)\}, k \in \{1, \ldots, K\}; \phi(v)) \to (p_0(v), \ldots, p_K(v))$$

  is a **diffeomorphism** between the interior of their domains.

$$p_k(v) = \mathrm{pr}(Y = 1 \mid Z = z_k, V = v)$$

$$\mathrm{RR}(0, k; v) = \frac{p_k(v)}{p_0(v)}$$

Generalized Odds Product (GOP)

e.g. For a categorical treatment $Z \in \{z_0, z_1, z_2\}$

$$\mathrm{GOP}(v) = \frac{p_0(v)}{1 - p_0(v)} \cdot \frac{p_1(v)}{1 - p_1(v)} \cdot \frac{p_2(v)}{1 - p_2(v)}$$

Model 2: Variation Independence with A Categorical Treatment

Generalized odds product $$\mathrm{GOP}(v) = \prod_{k=0}^{K} \frac{p_k(v)}{1 - p_k(v)}.$$

Model 2: Variation Independence with A Categorical Treatment

Generalized odds product $\mathrm{GOP}(v) = \prod_{k=0}^{K} \frac{p_k(v)}{1 - p_k(v)}.$

Theorem 2 (Variation independence with a categorical treatment) *Let $\mathcal{M}$ denote a $(K+1)$-dimensional model on*

$$\mathrm{RR}(0, k; v) = \frac{p_k(v)}{p_0(v)} \quad (k = 1, \ldots, K),$$
$$\mathrm{GOP}(v) = \prod_{k=0}^{K} \frac{p_k(v)}{1 - p_k(v)}.$$

For any v, the map given by

$$(p_0(v), \ldots, p_K(v)) \to (\log \mathrm{RR}(0, 1; v), \ldots, \log \mathrm{RR}(0, K; v), \log \mathrm{GOP}(v)) \qquad (1)$$

is a diffeomorphism from $(0, 1)^{K+1}$ to $(\mathbb{R})^{K+1}$. Furthermore, the models in $\mathcal{M}$ are variation independent of each other.

Model 2: Parameterization With a Categorical Treatment

$Z \in \{z_0, \ldots, z_K\}$, $K \geq 2$

$$\log\{\text{RR}(v; 0, k)\} = \alpha_k^{\text{T}} X \quad (k = 1, \ldots, K),$$
$$\log\{\text{GOP}(v)\} = \beta^{\text{T}} W,$$

where $X = X(v)$, $W = W(v)$

$$p_k(v) = \text{pr}(Y = 1 \mid Z = z_k, V = v)$$
$$\text{RR}(0, k; v) = \frac{p_k(v)}{p_0(v)}$$
$$\text{GOP}(v) = \prod_{k=0}^{K} \frac{p_k(v)}{1 - p_k(v)}$$

Model 2: Simulation Results

Table 2. Monte Carlo simulation results based on 1000 runs for the relative risk model with a generalized odds product nuisance model.

Sample Size	100		500		1000	
	α_1	α_2	α_1	α_2	α_1	α_2
Bias(SE)						
	$-0.069(0.056)$	$0.038(0.033)$	$-0.016(0.009)$	$0.002(0.006)$	$-0.002(0.004)$	$0.004(0.003)$
	$0.078(0.055)$	$0.162(0.045)$	$0.011(0.009)$	$0.023(0.007)$	$0.009(0.004)$	$0.013(0.004)$
SD Accuracy						
	1.307	1.019	0.993	1.000	1.036	1.014
	1.421	1.023	1.037	1.037	1.033	1.033
Coverage						
	0.975	0.954	0.951	0.948	0.964	0.957
	0.973	0.972	0.956	0.961	0.956	0.955

SE, standard error.
SD Accuracy = estimated standard deviation / Monte Carlo standard deviation.
Nominal level = 95%.

$\alpha_1 = (-0.5, 1)^{\mathrm{T}}$, $\alpha_2 = (0.5, 1.5)^{\mathrm{T}}$

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How to model the association between death and passenger class?

Application: Titanic Data

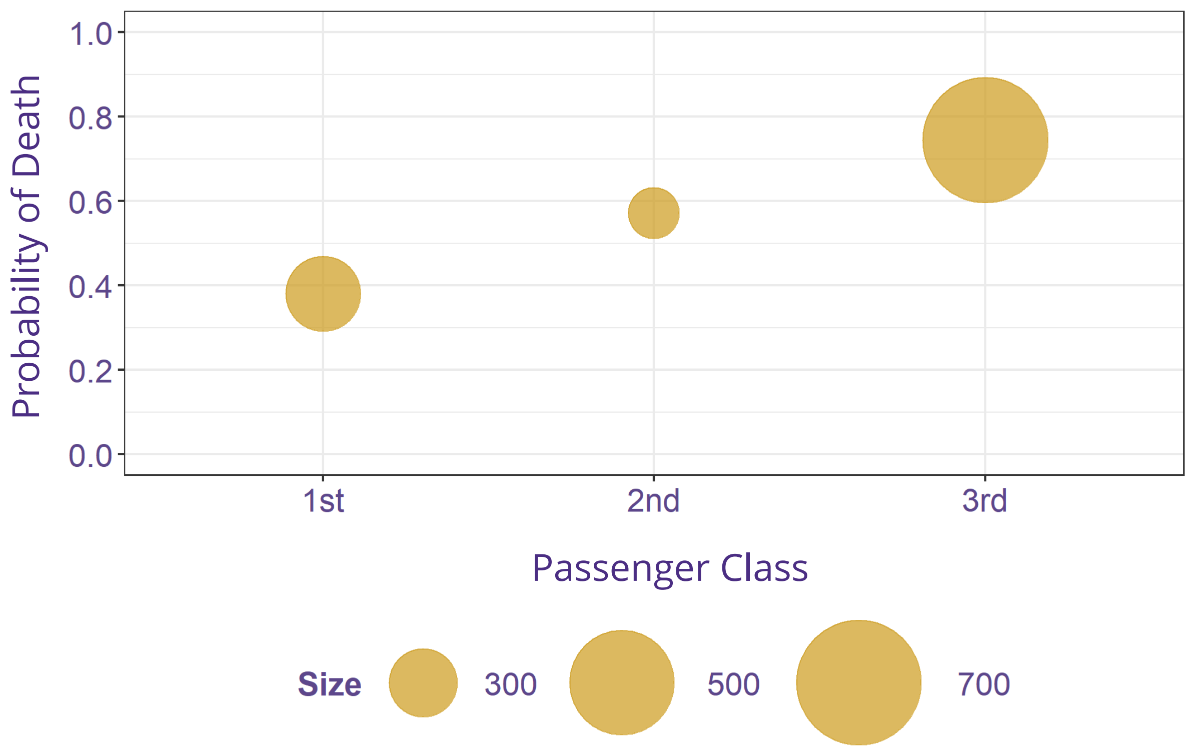

Fig. 1. Probability of death varies with passenger class.

Application: Titanic Data

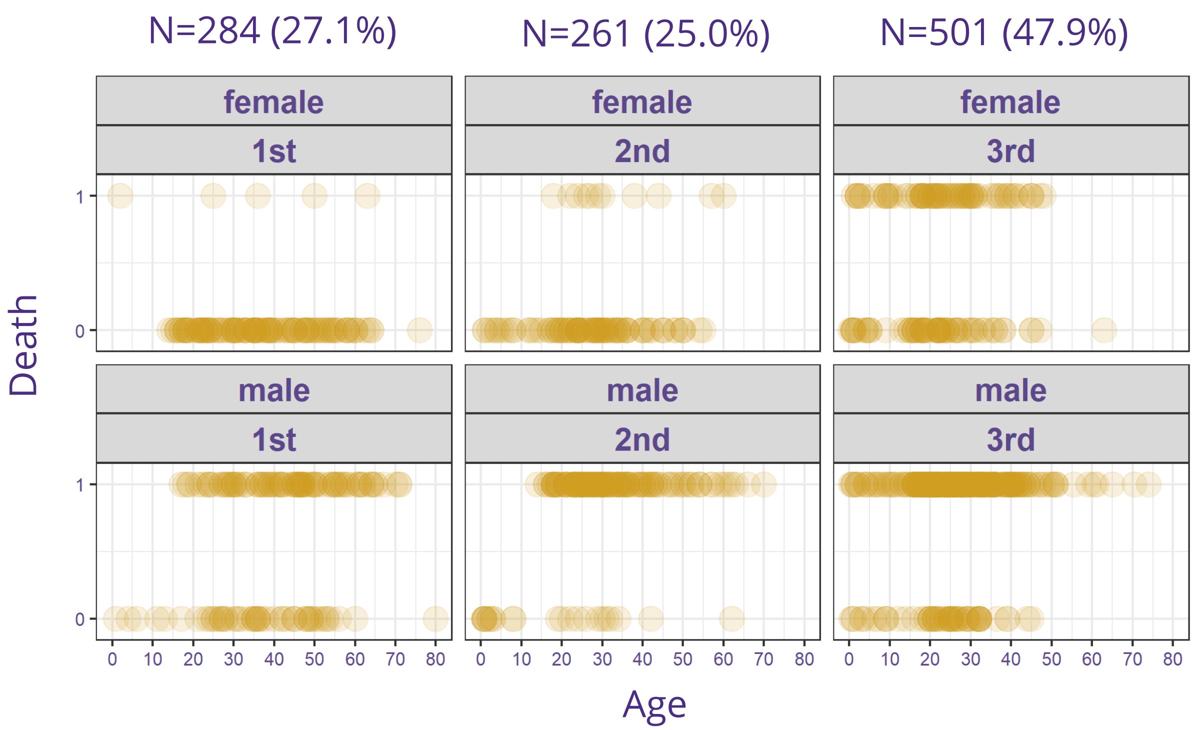

Fig. 5. Passengers' survival statuses by passenger class, age, and sex.

Four Models Estimating the Variation in the Relative Risk of Death

- Binary outcome: Death=1, survival = 0
- Treatment: Passenger class (1st, 2nd , 3rd; 1st is the baseline)
- Covariates: age, sex, age^2, sex*age

Model
Model 1: Monotone
Poisson model
Model 2: GOP
Logistic Model

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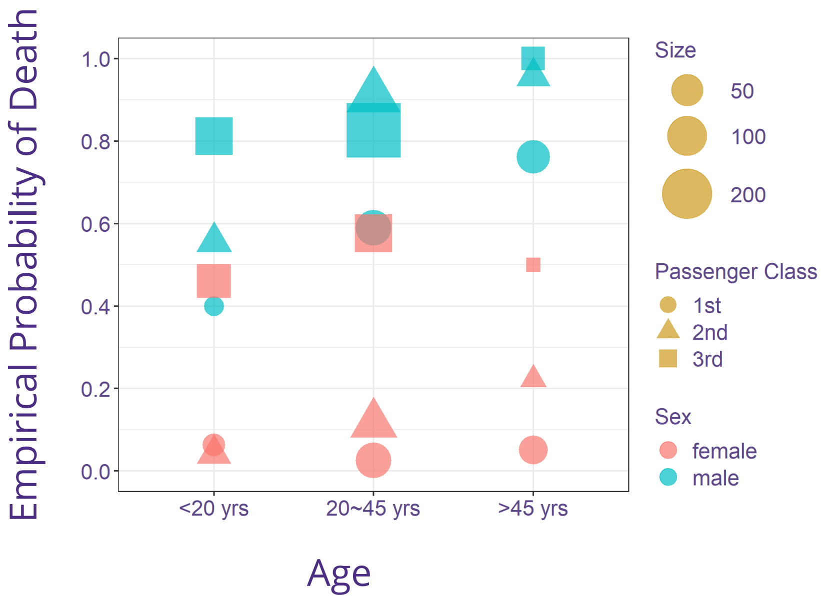
Table 3. Coefficient estimates via different models

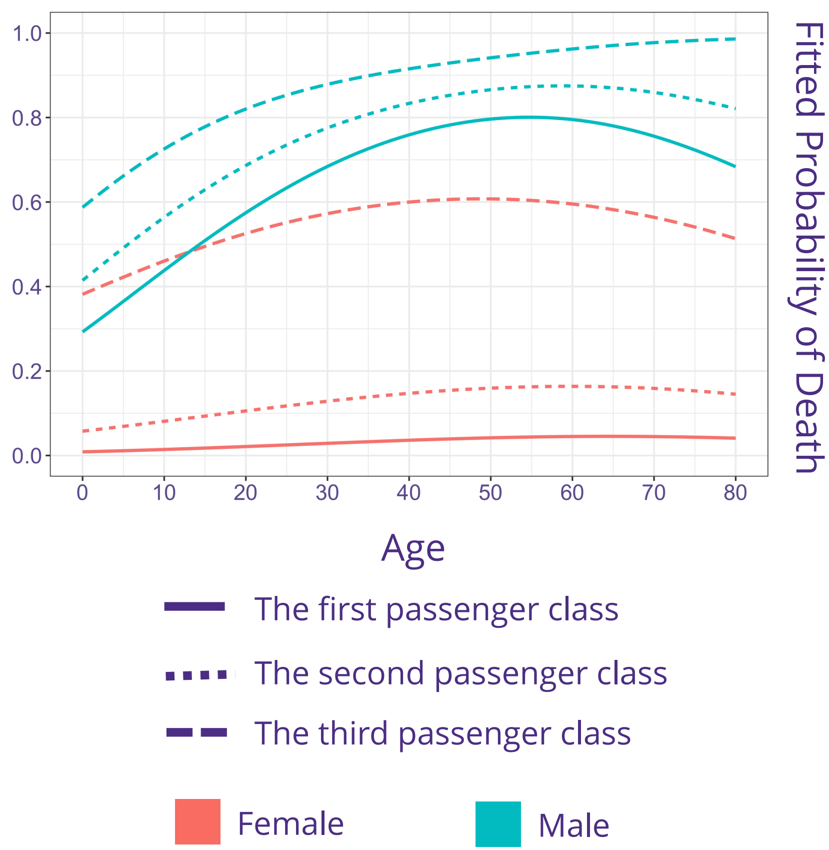
	2nd	2nd* male	2nd* age/10	2nd* age^2/ 100	2nd* male* age/10	3rd	3rd* male	3rd* age/10	3rd* age^2/ 100	3rd* male* age/10
Point Estimate										
Monotone	1.891	−1.543	−0.165	0.011	0.058	—	—	—	—	—
Poisson	−1.211	0.938	0.969	−0.072	−0.487	2.232	−1.444	0.120	0.005	−0.254
GOP	−1.134	1.439	0.780	−0.033	−0.617	2.204	−1.212	0.053	0.020	−0.309
Standard Deviation										
Monotone	0.396	0.407	0.124	0.010	0.107	—	—	—	—	—
Poisson	2.077	1.967	0.620	0.033	0.542	1.874	1.739	0.570	0.030	0.482
GOP	1.230	1.251	0.369	0.029	0.314	0.888	0.957	0.260	0.021	0.236

1st, 2nd, 3rd: the first passenger class, the second passenger class, and the third passenger class.
The first class is chosen as the baseline.

Application: Titanic Data

Predicted probability via Monotone





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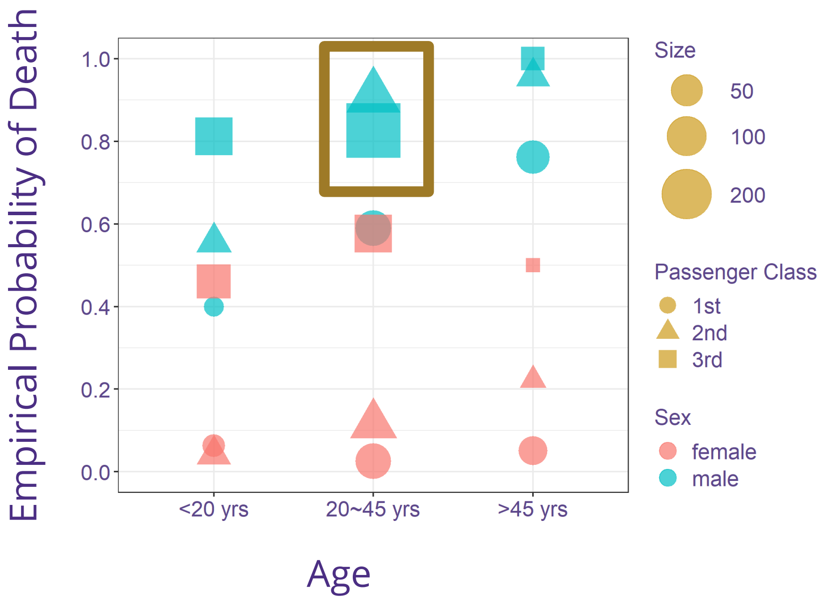

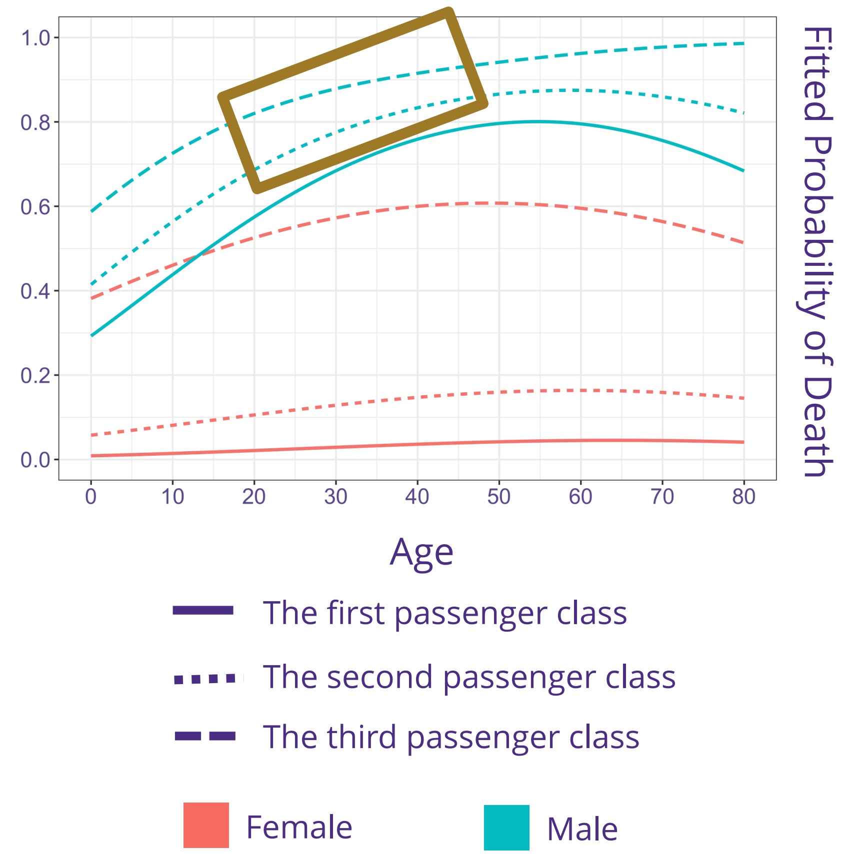

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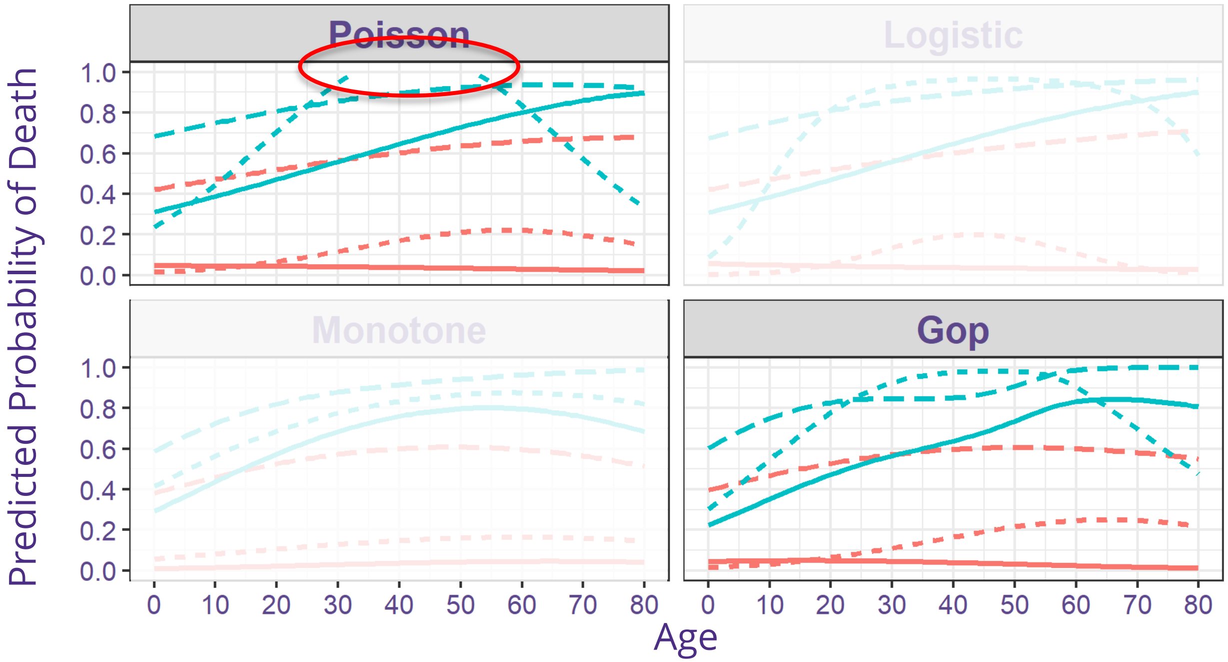

Fig. 5. Predicted probability of death

The first passenger class

The second passenger class

The third passenger class

Female

Male

Application: Titanic Data

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	2nd	2nd* male	2nd* age/10	2nd* age^2/100	2nd* male* age/10	3rd	3rd* male	3rd* age/10	3rd* age^2/100	3rd* male* age/10
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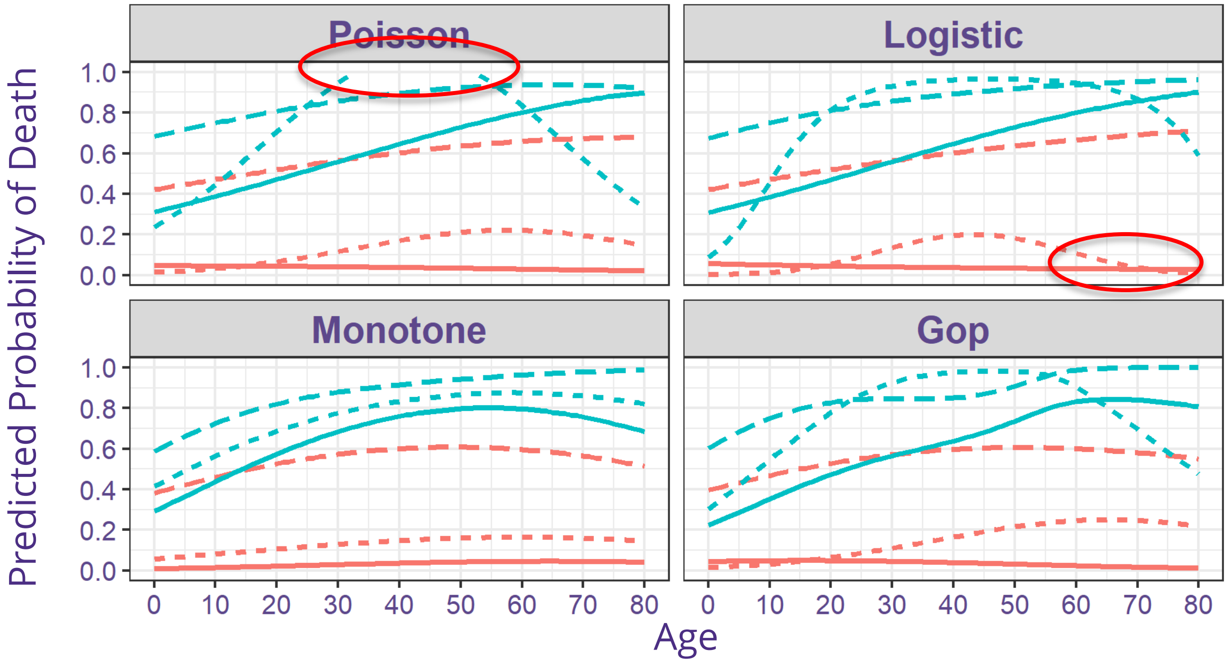

Fig. 5. Predicted probability of death

The first passenger class

The second passenger class

The third passenger class

Female

Male

Summary

- Two novel methods to model multiplicative treatment effects with a binary outcome.
- The first method relies on a monotonic treatment effect assumption.
- The second one proposes an alternative approach that involves a novel generalized odds product model.

Discussion

- Model 1 cannot be applied if the relative risk is not monotonic in treatment.
    - Exploratory data analysis
    - Substantive knowledge
- Model 2 is more flexible than Model 1, but has *K*-times as many parameters.

Thank you!!!

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