A New Health Care Index predicts 12-month mortality among HIV-positive individuals diagnosed with tuberculosis

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Presenter Disclosure Information

Ashley Roen

disclosed no conflict of interest.

Background

- **Local health care is linked to survival of HIV\TB positive individuals**[1-3]
- **Previous study found 3 health care factors associated with reduced mortality**[1]
  - Drug susceptibility testing (DST)
  - TB treatment with Rifamycin, Isoniazid and Pyrazinamide (RHZ)
  - Use of combination antiretroviral therapy (cART)
- **Factors created a Health Care Index (HCI)**

1. Podlekareva DN et al, IJTLD, 2013; 2. Kaplan JE et al, CDC MMWR, 2009; 3. Pozniak AL et al, HIV Med, 2011

Background

- **Changes to the management of TB/HIV positive individuals from 2006**
  - Rapid diagnostic and resistance identification methods
  - Better access to TB drugs
  - Earlier cART initiation

Objectives

- Update the previous Health Care Index (HCI)
- Estimate the probability of death 12 months after TB diagnosis by HCI values
- Assess the utility of HCI

Data TB:HIV Study

- Prospective, observational cohort study
- HIV positive adults
- Diagnosed with TB 2011-2013
- 62 clinics TB and HIV clinics

  - **Eastern Europe**, (21 clinics in Belarus, Estonia, Georgia, Latvia, Lithuania, Poland, Romania, Ukraine, Russia),
  - **Western Europe** (28 clinics in Belgium, Denmark, France, Switzerland, United Kingdom, Italy and Spain)
  - **Latin America** (13 clinics in Argentina, Chile, and Mexico)

HCI Potential Components

Previous HCI components

- WHO definite diagnosis of TB
- Performance of DST for TB
- RHZ based initial TB treatment
- Recent CD4 cell count measurement
- cART initiation

New HCI components

- Co-trimoxazole prophylaxis
- Recent HIV-RNA measurement
- Total number of TB drugs in initial TB regimen
- Total number of ‘known active’ TB drugs in initial TB regimen[1]

* individual or disease specific characteristics were not included in the score

1. Efsen et al, J Infect., 2018

Statistical Analysis

- **Primary outcome: all cause mortality**
- **Cox proportional hazards model**
  - Time from TB diagnosis to death within 12 months
  - Univariable models: coefficients with $p<0.10$ were kept
  - Multivariable models: coefficients with $p>0.05$ were removed

Statistical Analysis

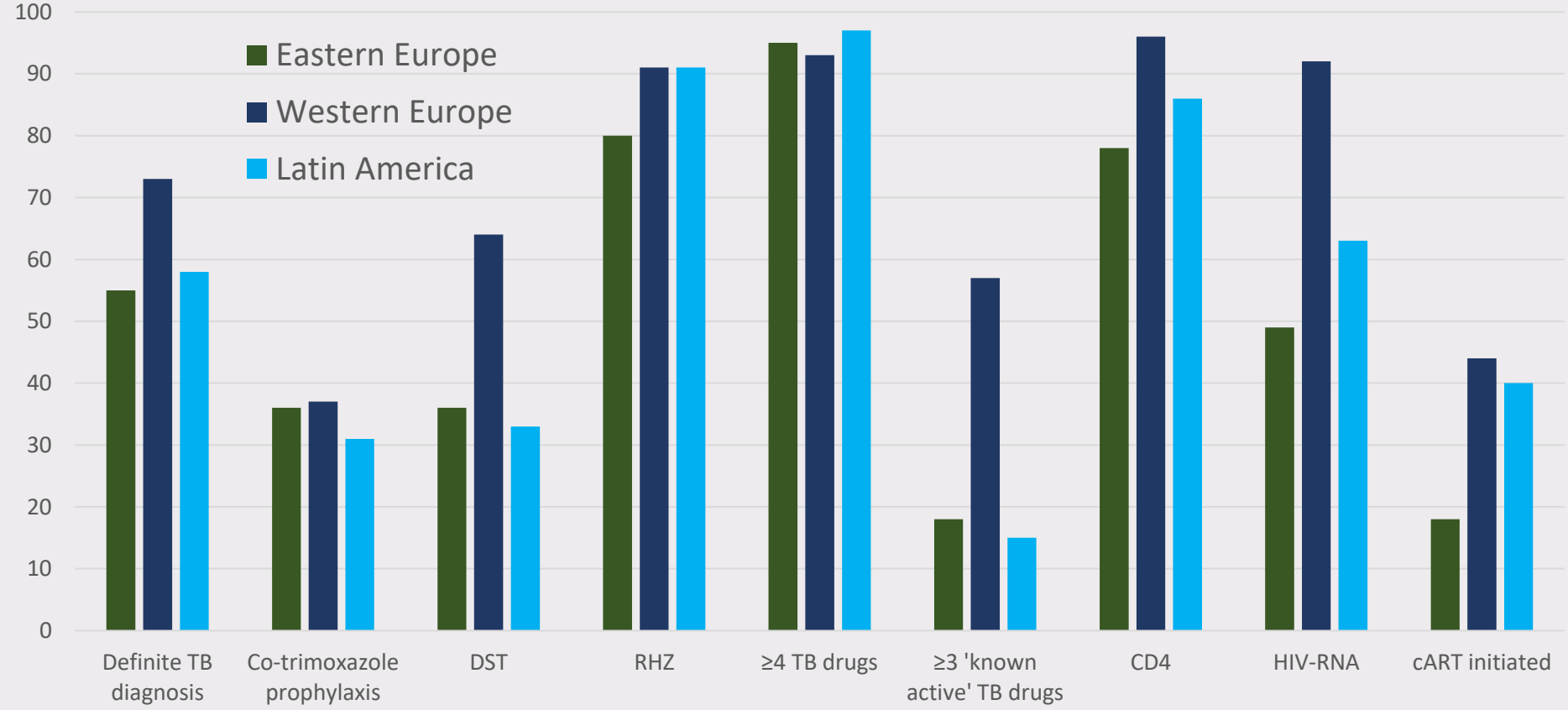
- **Coefficients of final Cox model were scaled**
  - by dividing coefficients by the smallest coefficient, rounding to the nearest whole number
  - Multiplying by negative 1 so higher HCI indicative of better engagement in health care
- **HCI was calculated for each individual, divided into four quartiles**
- **Kaplan-Meier methods to estimate probability of death by HCI quartile**
- **Cox proportional hazards models were used to assess the association between HCI and death, adjusting for covariates**

Results – Baseline Characteristics

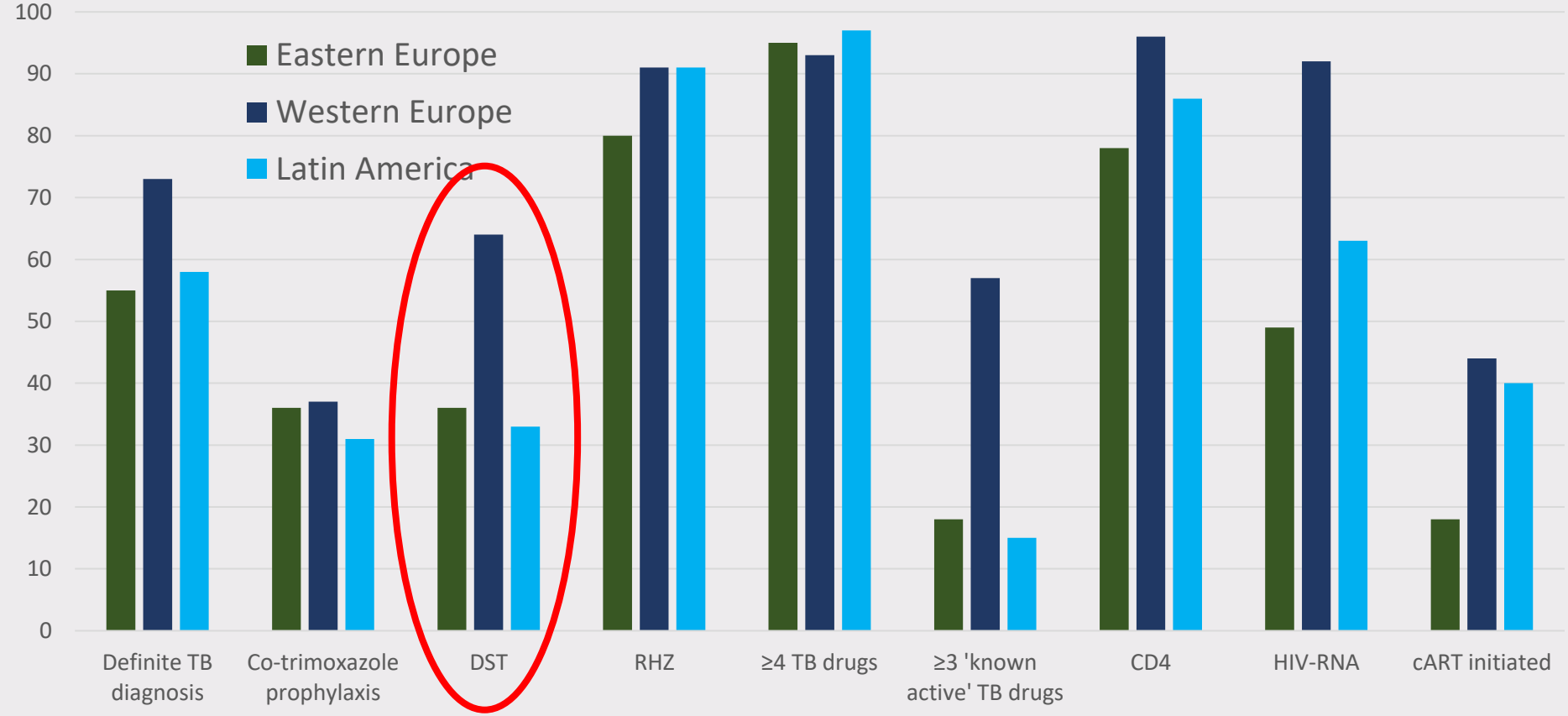
- **1396 eligible individuals**
- **269 died**
- **72% Male**
- **59% Eastern Europe**

- **Low CD4 cell counts**
  median (IQR) = 110 (36, 273) cells/mm
- **High HIV-RNA**
  median (IQR) = 5.1 (3.4, 5.7) $\log_{10}$ copies/ml
- **Low proportion on cART**
  64% cART naïve at TB diagnosis

Results – Baseline Characteristics



Results – Baseline Characteristics



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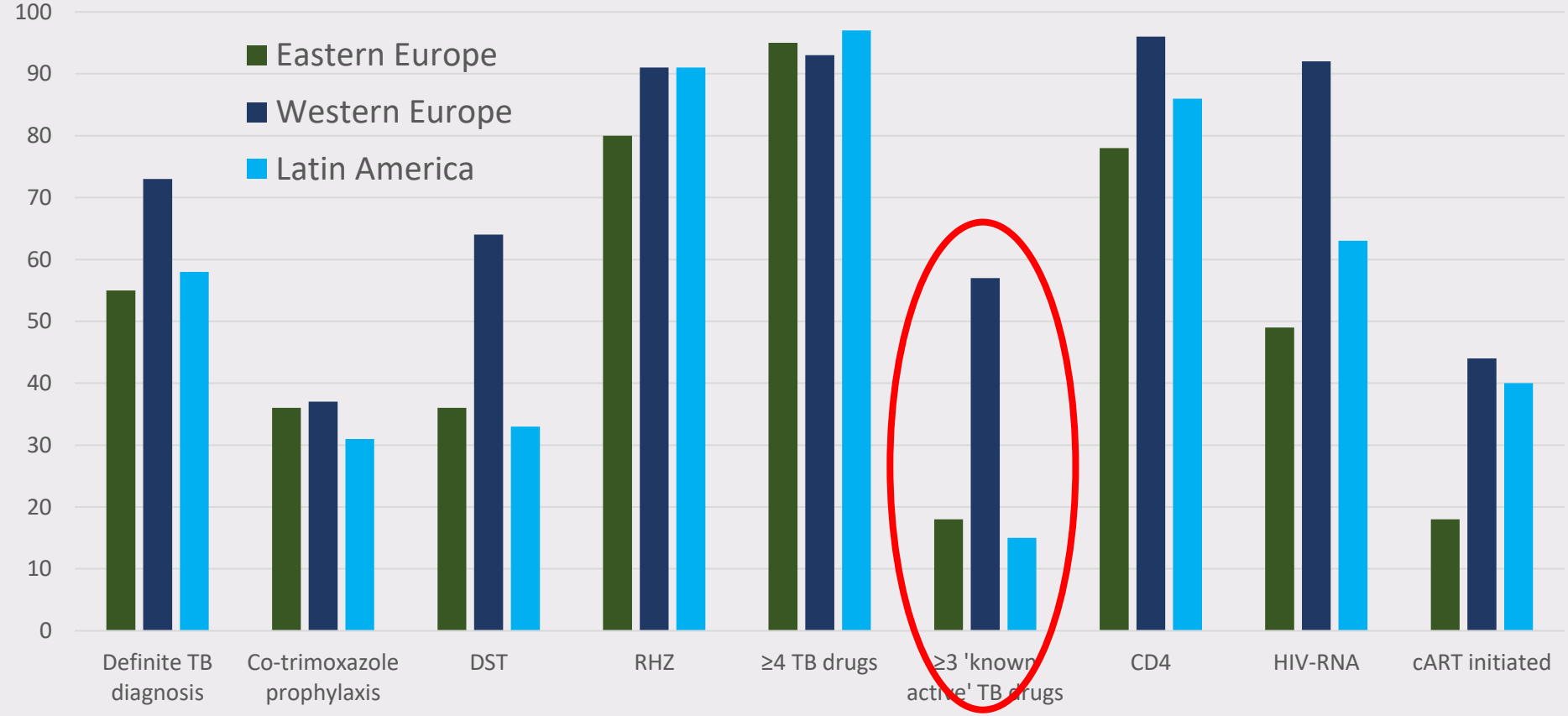

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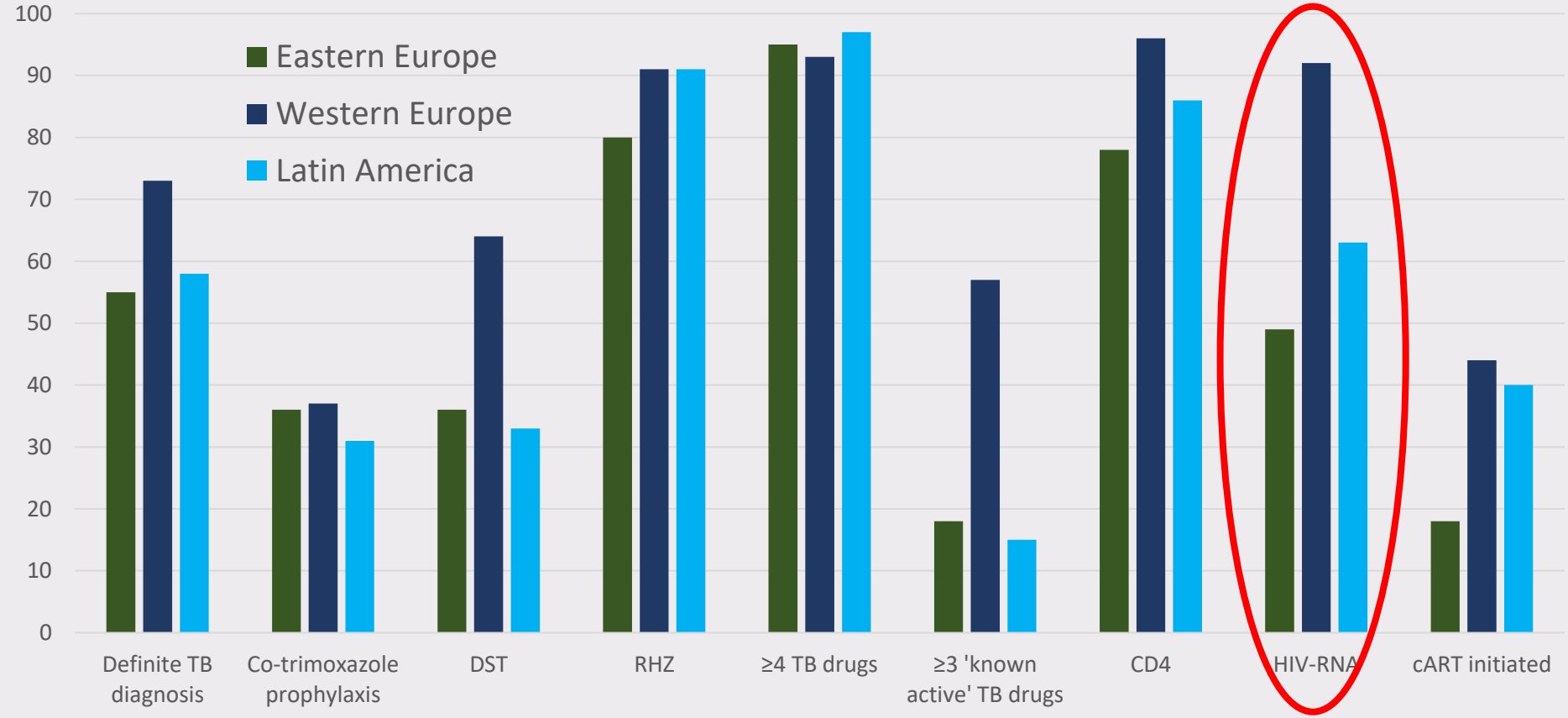

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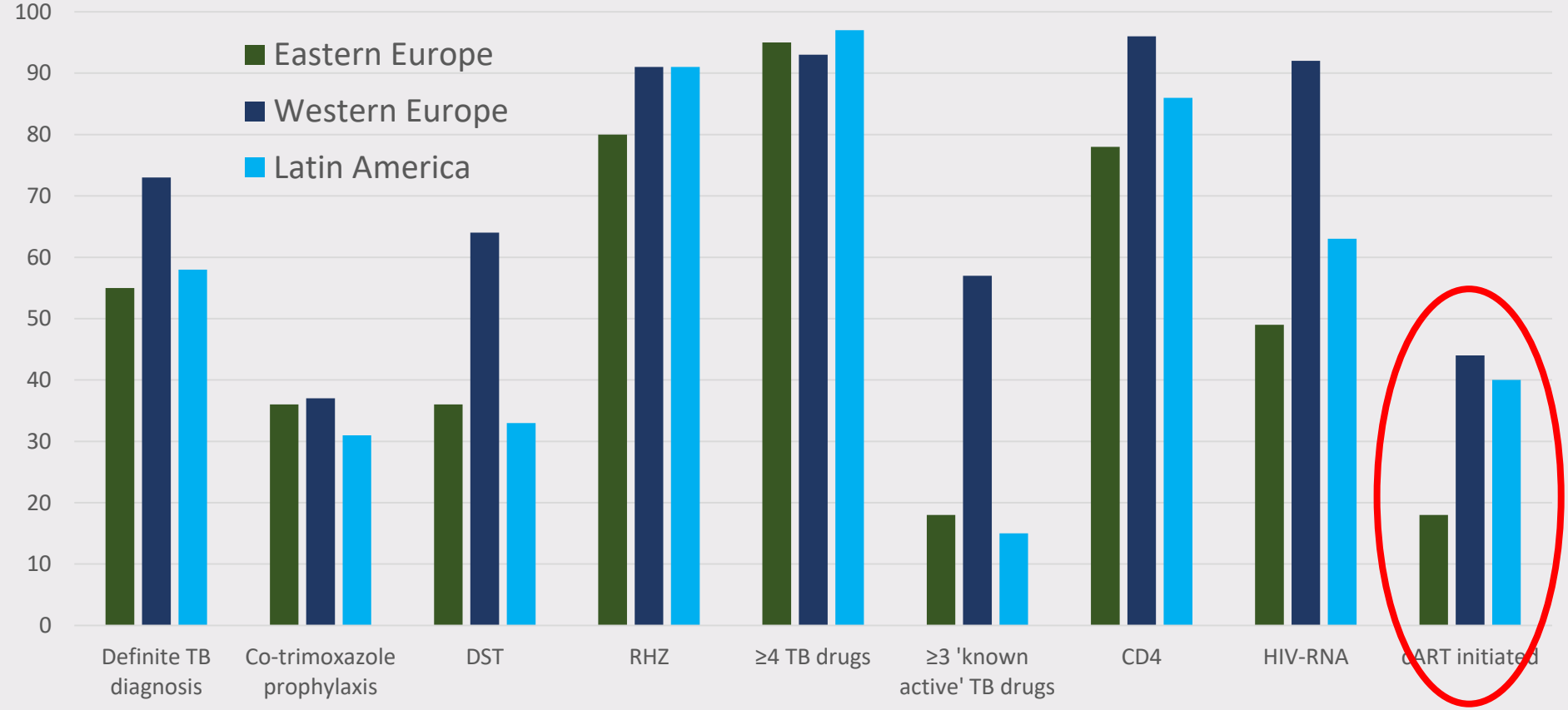

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Results – Final Model and HCI

Model Components	HR	95 % CI		p	Ln HR	HCI
RHZ	0.67	(0.50,	0.89)	0.007	-0.40	5
No DST	Ref.			<0.001*		0
DST & <3 known active TB drugs	1.09	(0.80,	1.48)		0.08	-1
DST & ≥3 known active TB drugs	0.49	(0.35,	0.70)		-0.70	8
HIV-RNA measurement	0.64	(0.50,	0.82)	<0.001	-0.44	5
cART initiated	0.72	(0.53,	0.97)	0.028	-0.33	4

*global p-value

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Example patient	value	HCI
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DST & <3 known active TB drugs	no	0
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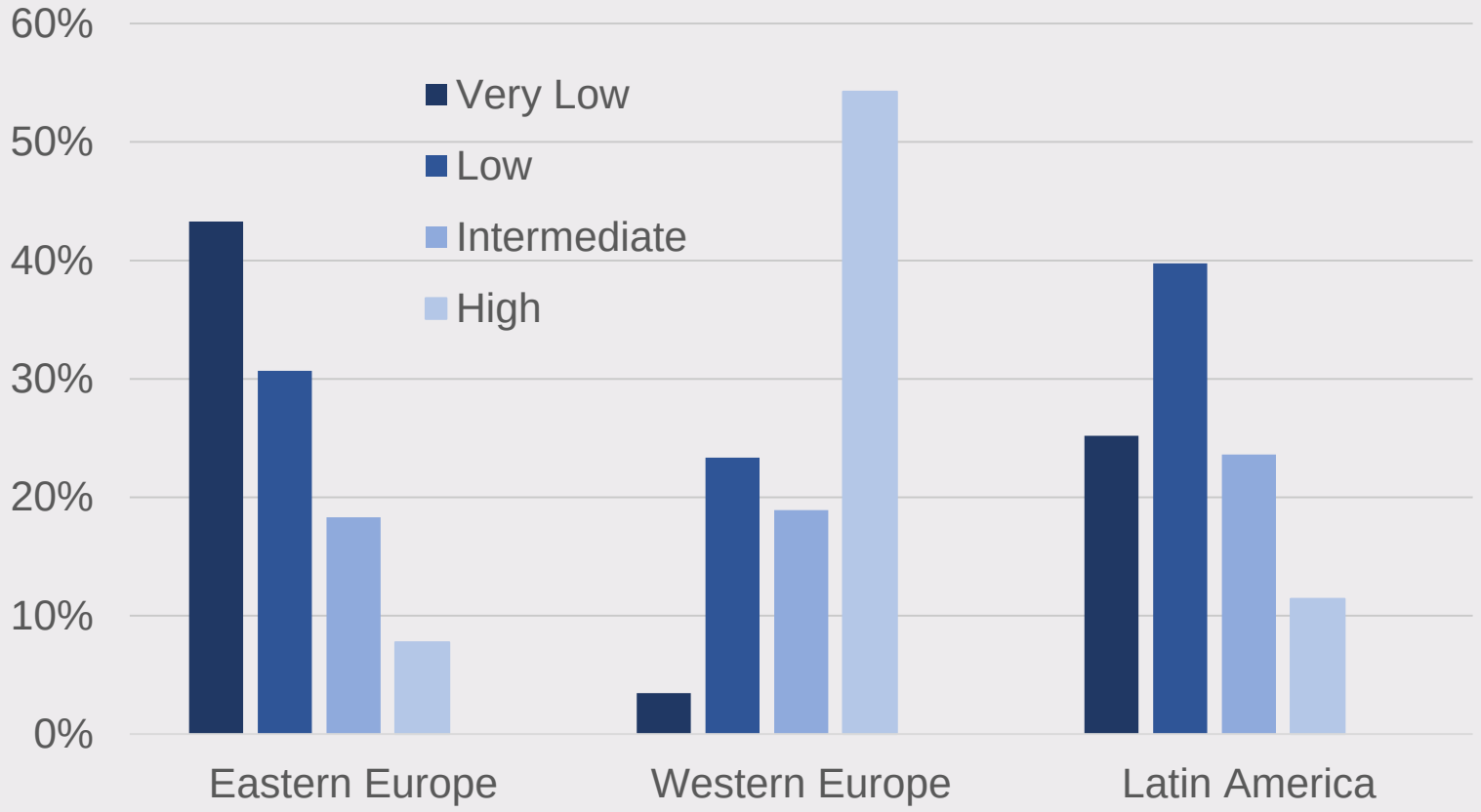
HIV-RNA measurement	no	0
cART initiated	yes	4
Total		17

Results – HCI distribution by region



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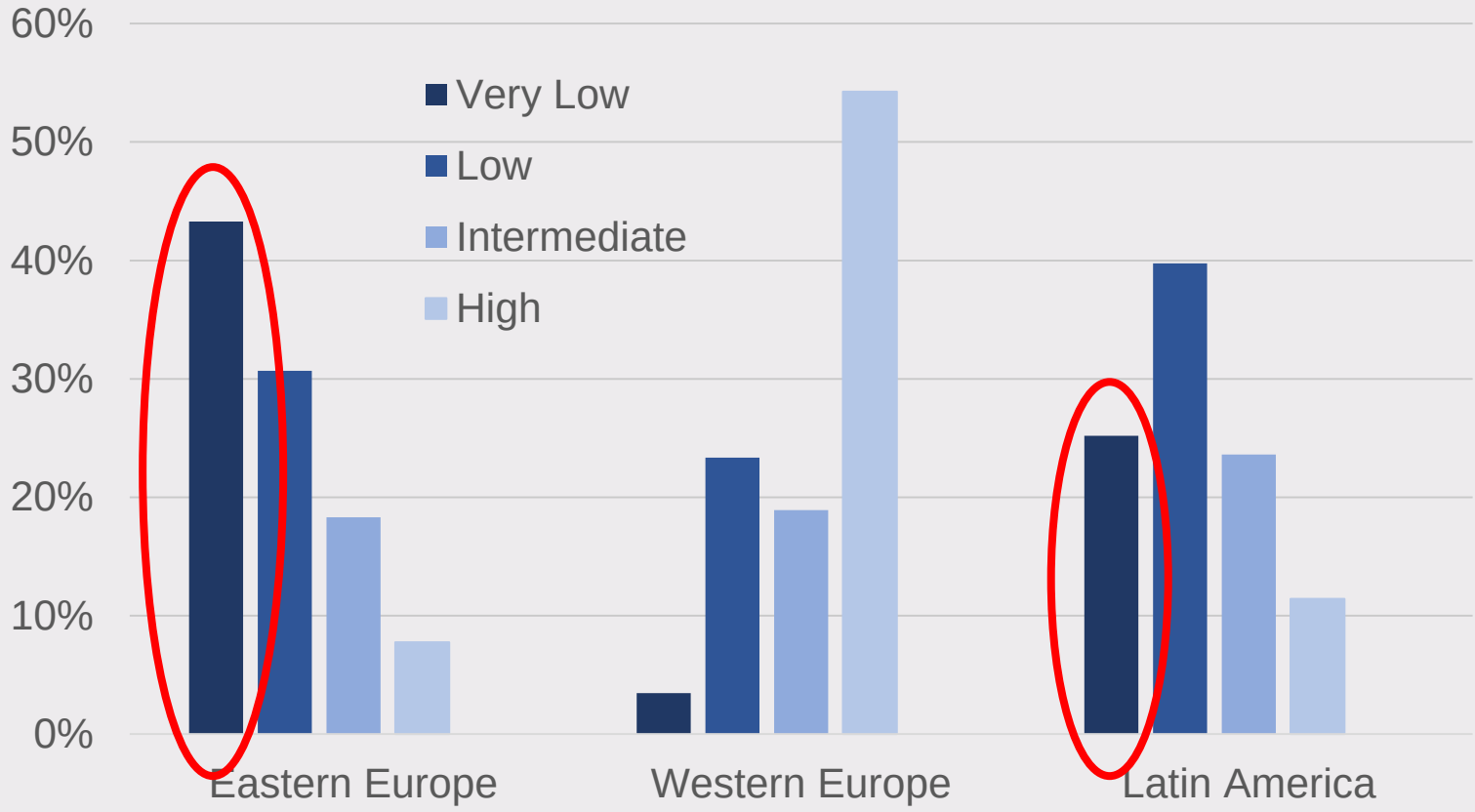
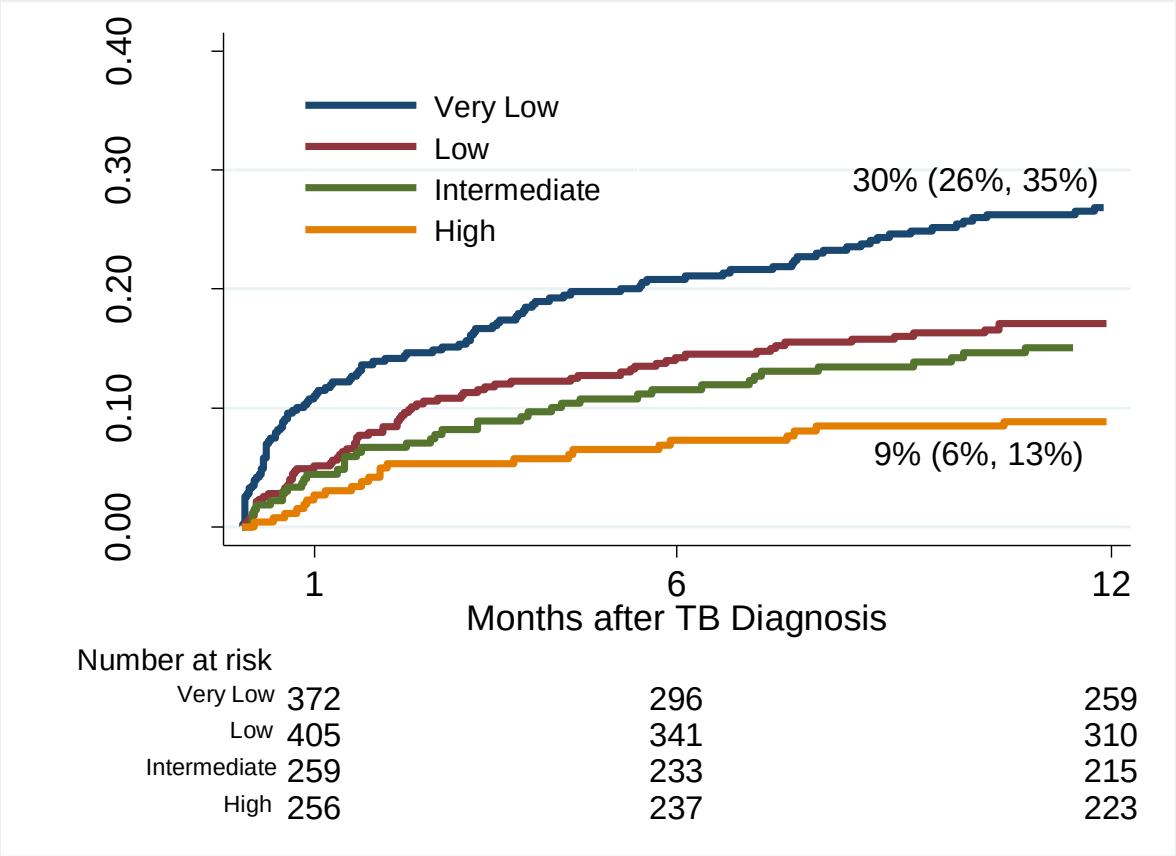
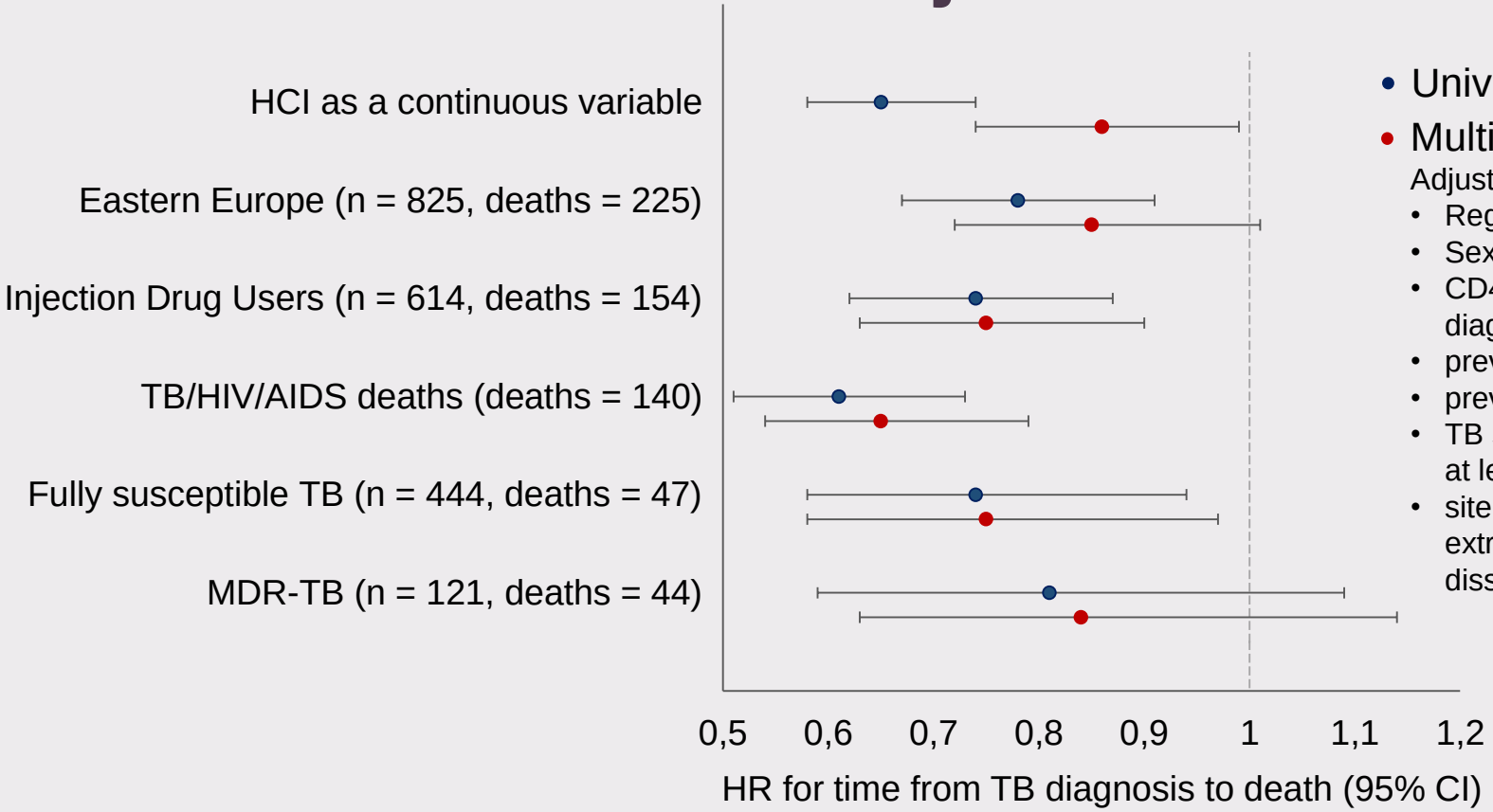


Results


0.00
0.10
0.20
0.30
0.40
Very Low
Low
Intermediate
High
30% (26%, 35%)
9% (6%, 13%)
1
6
12
Months after TB Diagnosis
Number at risk
Very Low 372 296 259
Low 405 341 310
Intermediate 259 233 215
High 256 237 223

Results – HCI and adjustments



- Univariable Models
- Multivariable Models

Adjusted for:

- Region of care
- Sex
- CD4 cell count at TB diagnosis
- previous AIDS diagnosis
- previous TB diagnosis
- TB strains resistance to at least a rifamycin
- site of TB (pulmonary, extra-pulmonary, disseminated)

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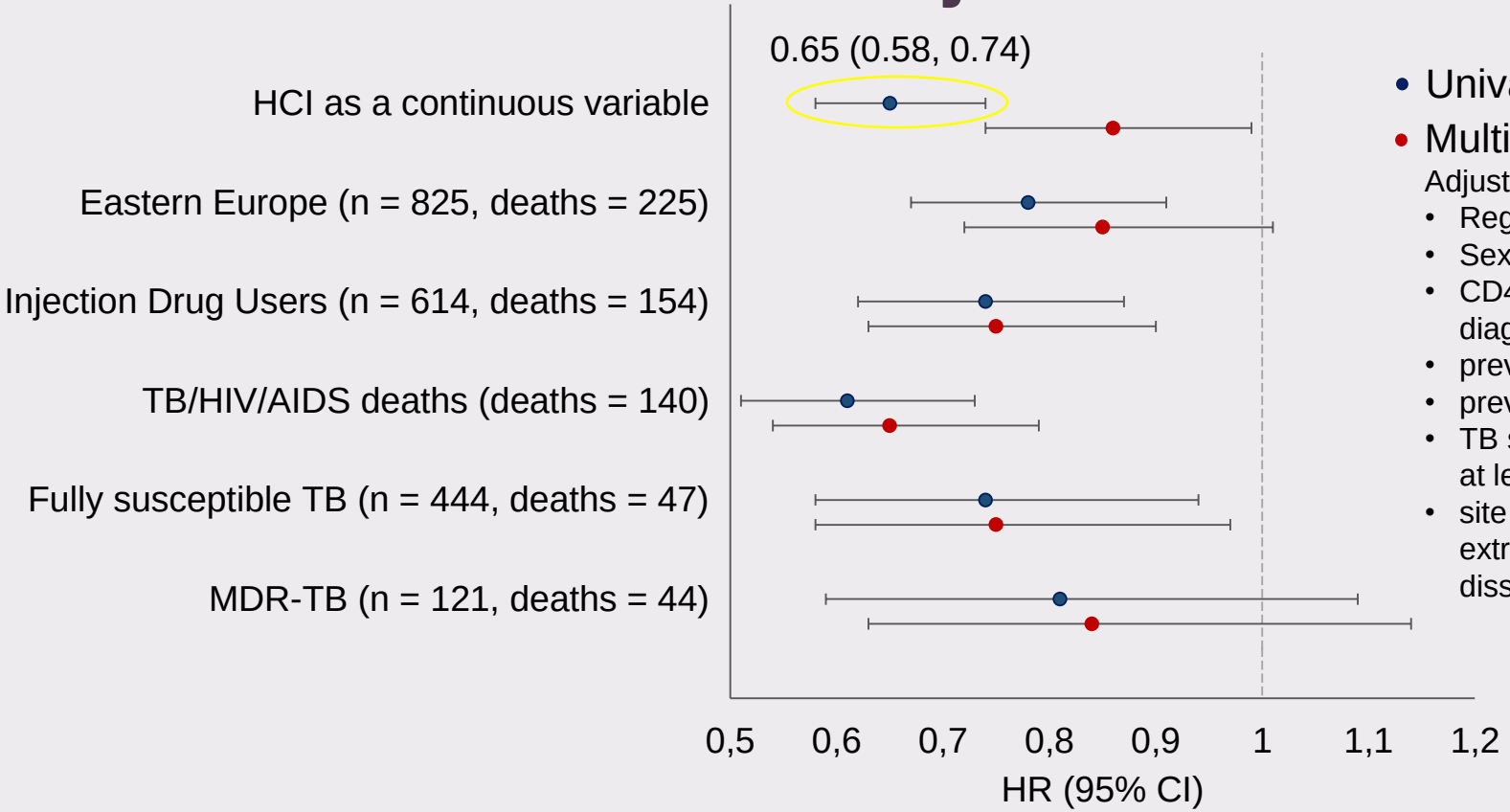

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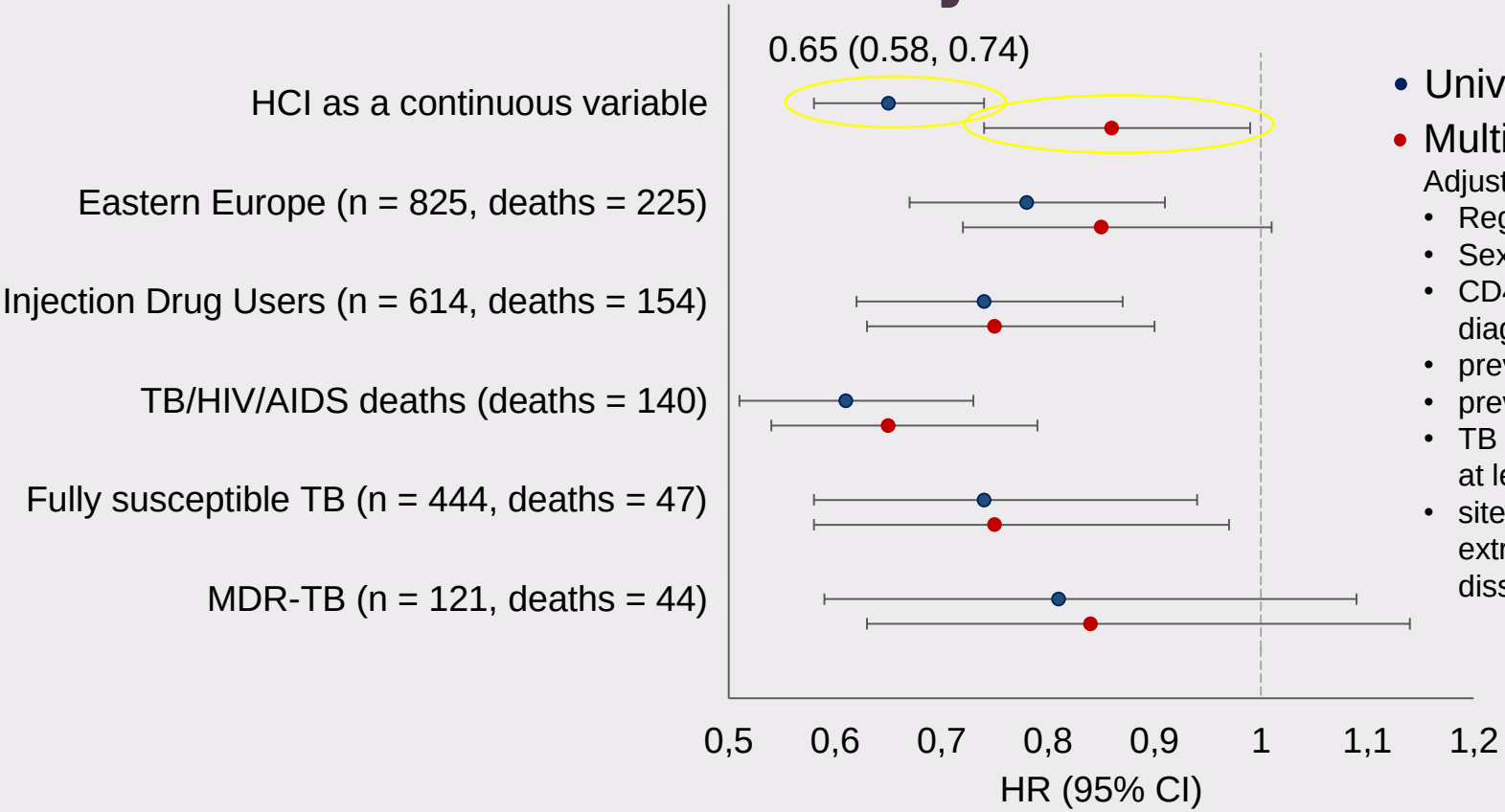

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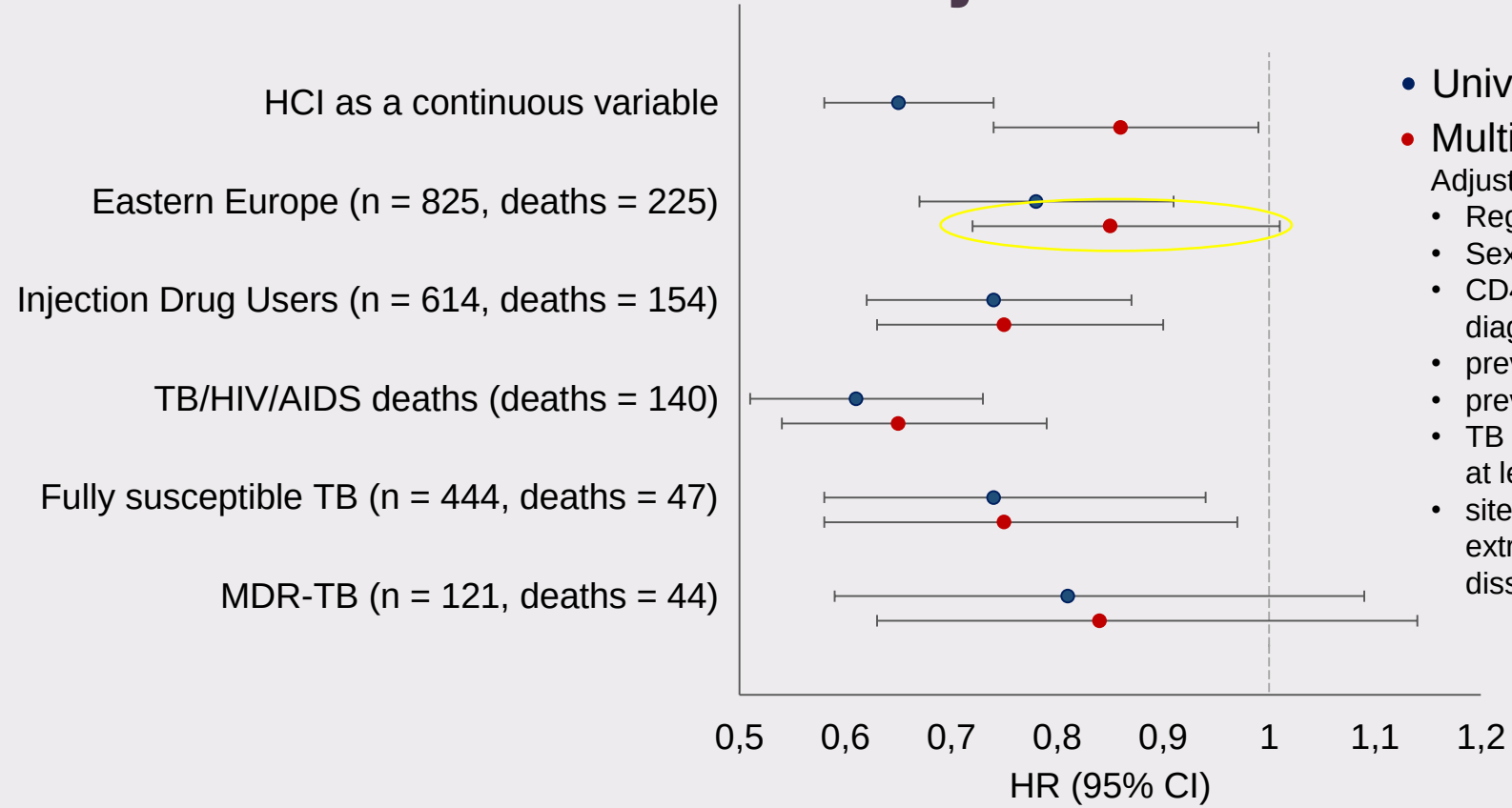

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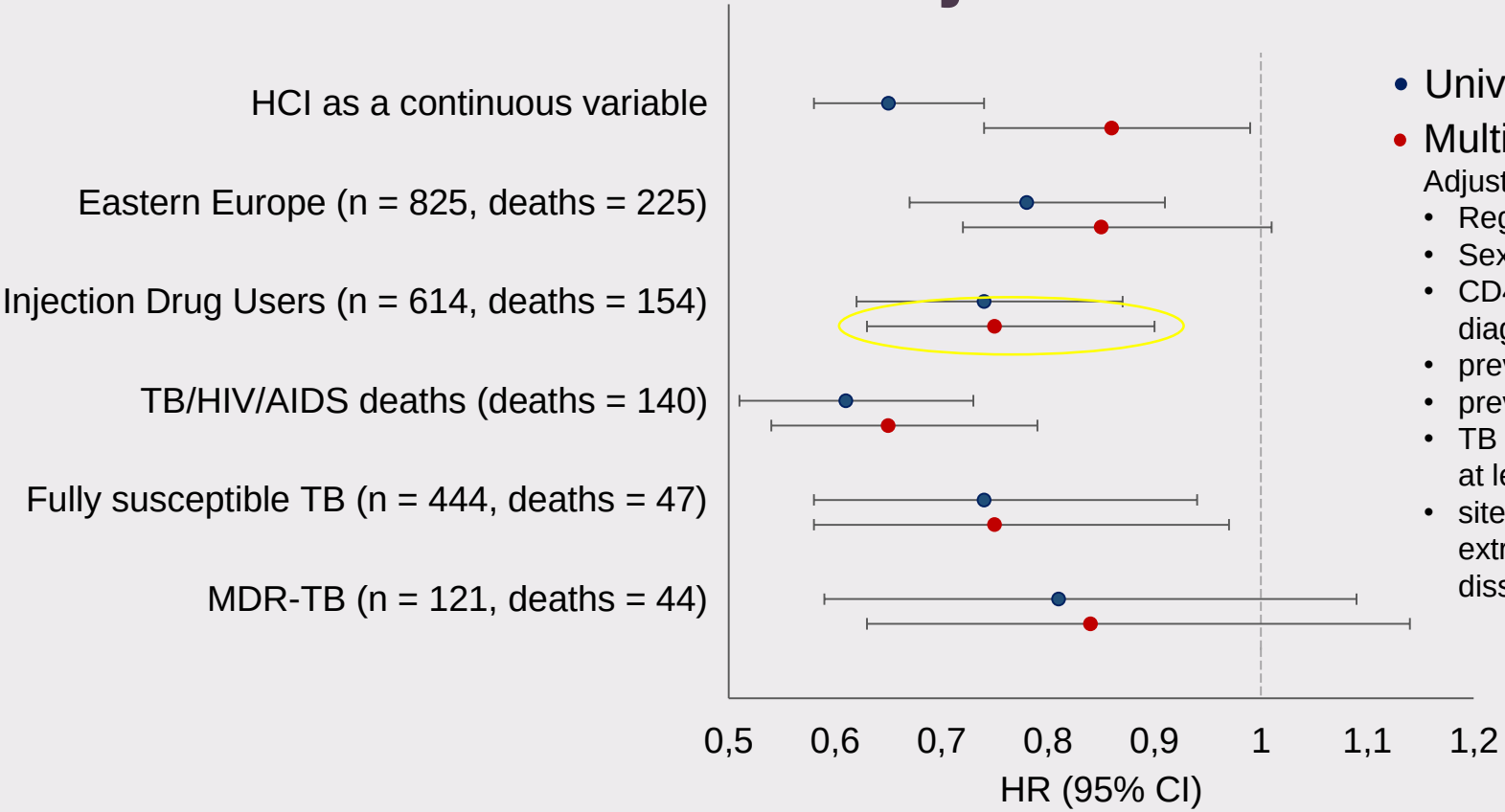

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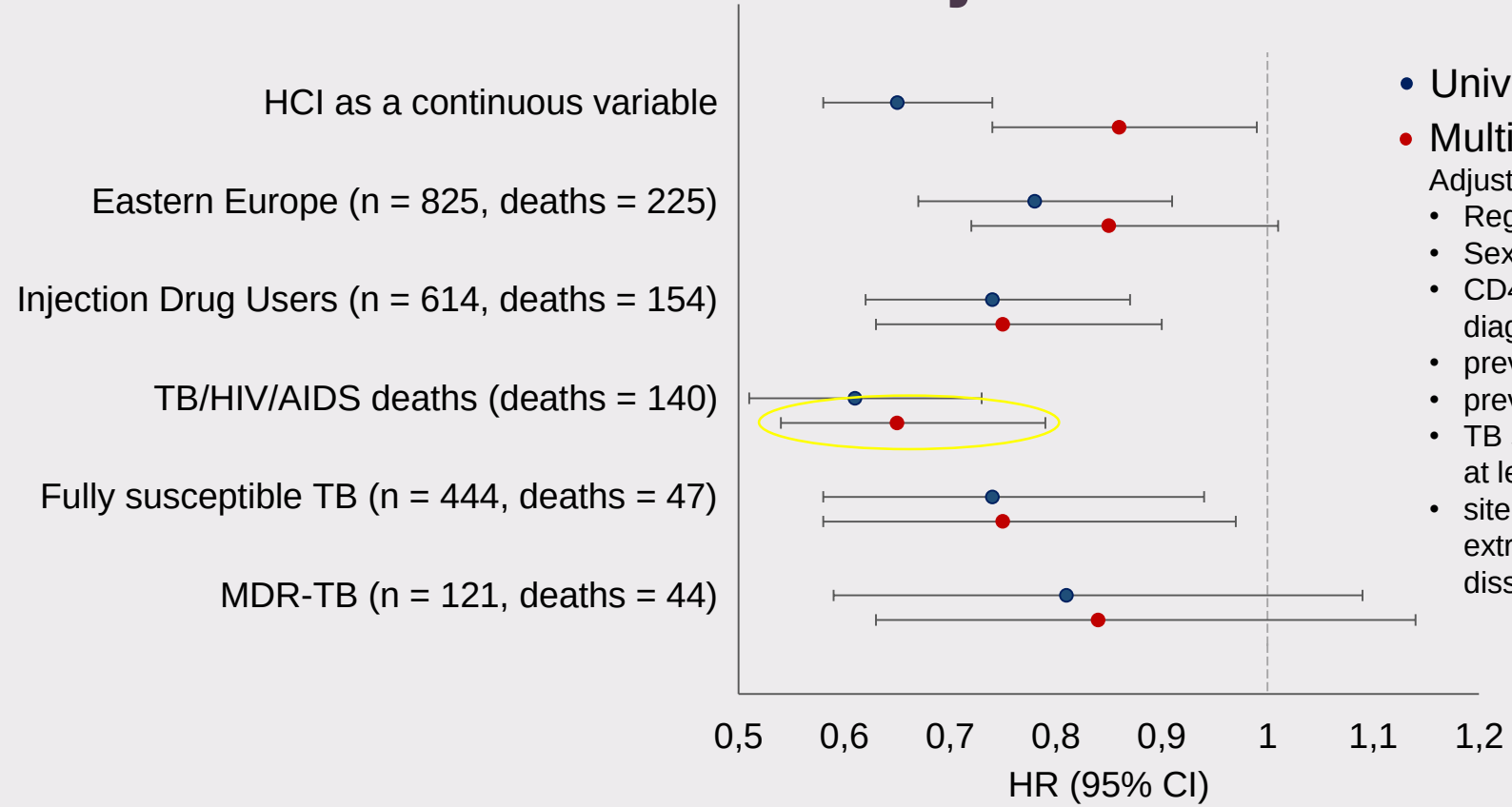

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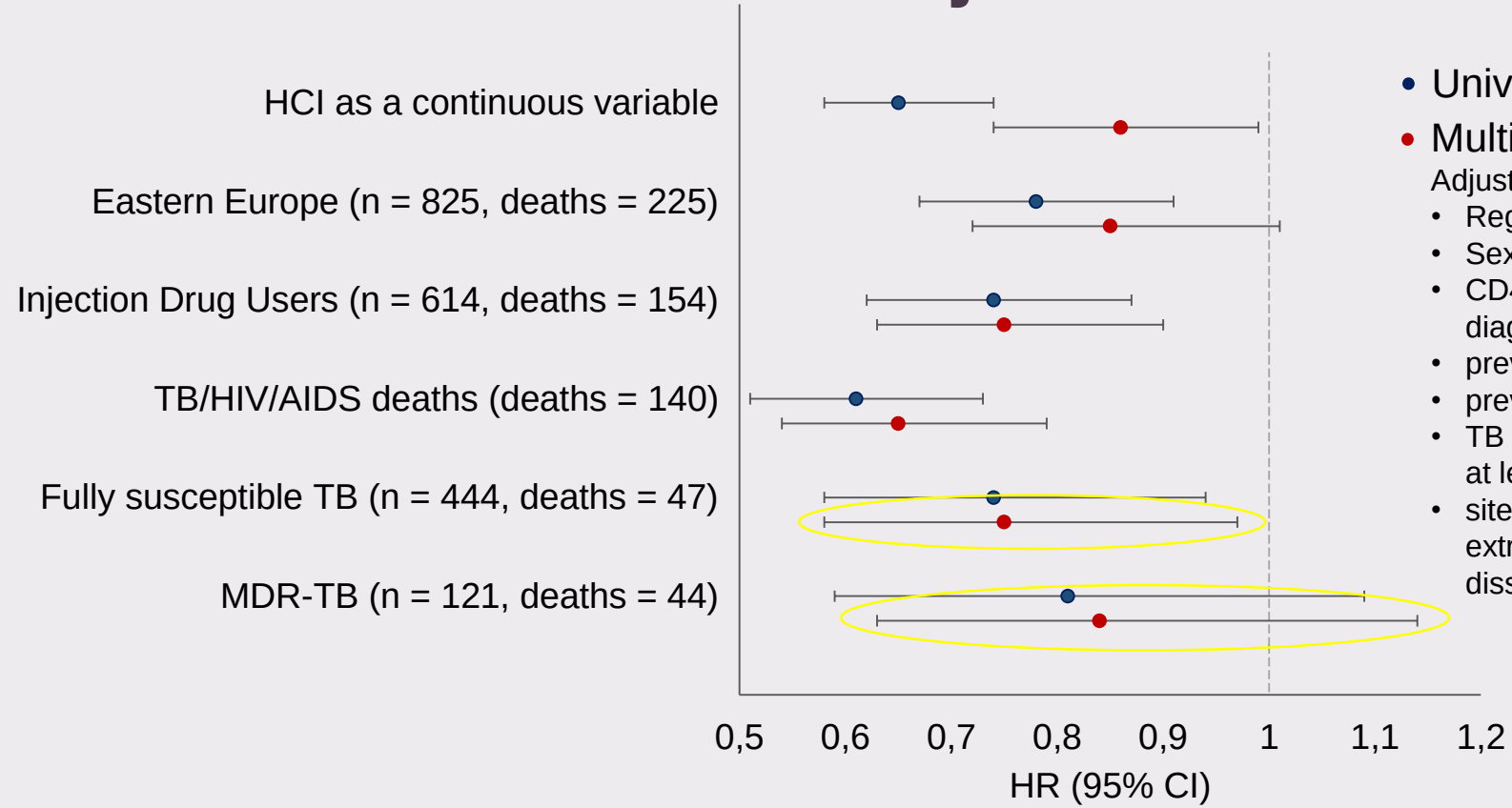

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Limitations

- **Confounding**
- **Population in Europe and Latin America**
- **Validate model**

collaborations email me: a.roen@ucl.ac.uk

Conclusion

- **Five main components of health care were included in our new Health Care Index**
  - RHZ based initial TB treatment
  - DST
  - ≥ 3 known active drugs in initial TB regimen
  - Baseline HIV-RNA assessment
  - Provision of cART
- **Tool can be used at an individual and cohort level, evaluating prognosis and health care utilization**

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TB:HIV an international prospective observational study

SEVENTH FRAMEWORK PROGRAMME

EuroCoord

REGION H Rigshospitalet

chip

UCL

HCI model components

	Univariable			Final				
Model Components	HR	95 % CI	p	HR	95 % CI	p	Ln HR	HCI
Definite TB diagnosis	1.02	(0.80, 1.30)	0.892					
Co-trimoxazole prophylaxis τ	1.21	(0.95, 1.55)	0.126					
RHZ-containing treatment	0.58	(0.43, 0.77)	<0.001	0.67	(0.50, 0.89)	0.007	-0.40	5
DST preformed	0.67	(0.52, 0.87)	0.002	-				
DST & <3 known active TB drugs prescribed δ vs. no DSTα	-			1.09	(0.80, 1.48)	<0.001	0.08	-1
DST & ≥3 known active TB drugs prescribed δ vs. no DSTα	-			0.49	(0.35, 0.70)		-0.70	8
≥4 TB drugs prescribed δ	1.00	(0.58, 1.71)	0.994					
CD4 cell count measurement ł	0.68	(0.51, 0.91)	0.010					
HIV-RNA measurement ł	0.56	(0.44, 0.71)	<0.001	0.64	(0.50, 0.82)	<0.001	-0.44	5
cART initiated γ	0.65	(0.49, 0.87)	0.004	0.72	(0.53, 0.97)	0.028	-0.33	4