

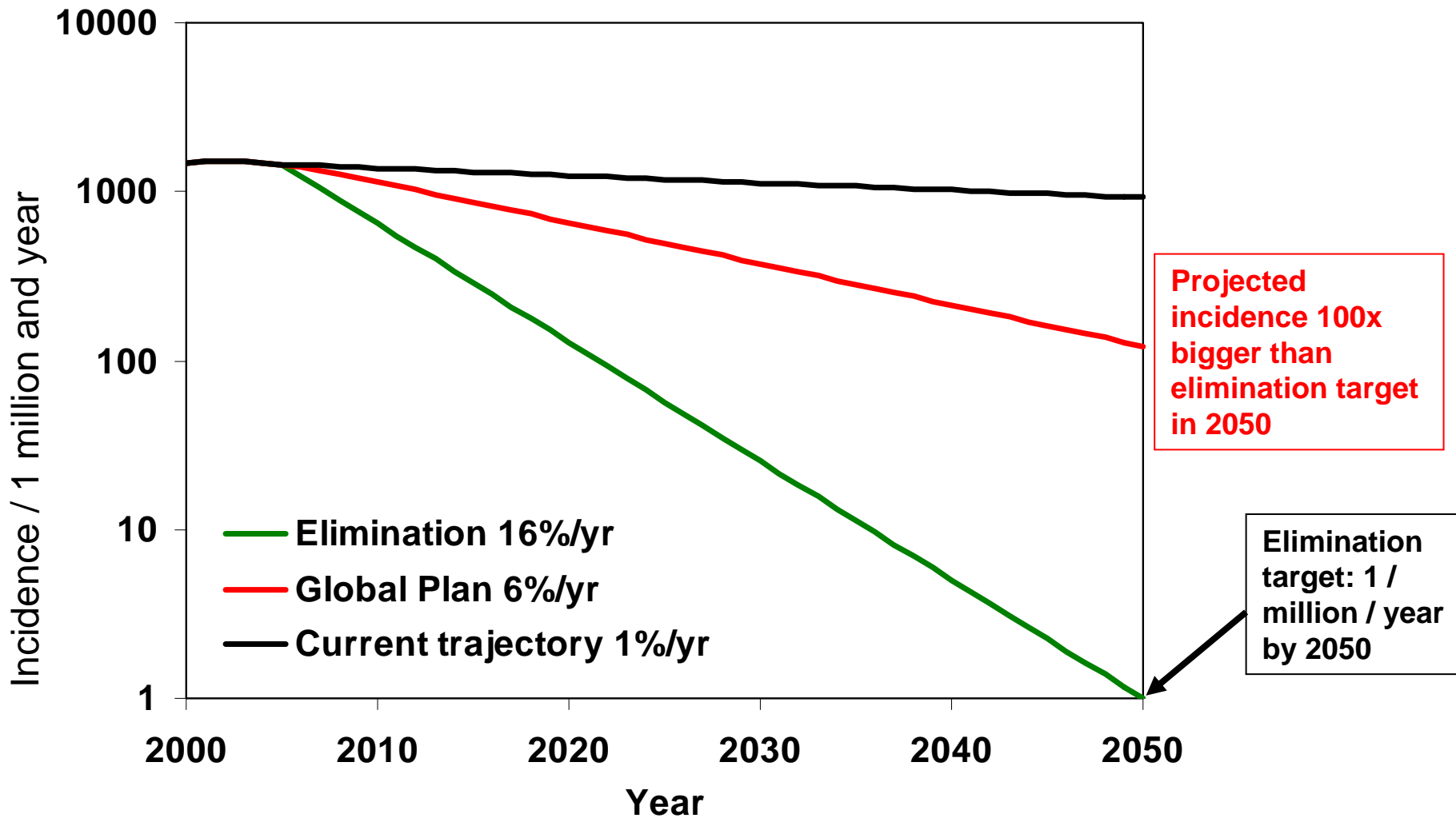
Alcohol abuse and smoking

– Important risk factors for TB?

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Swiss Lung Association
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Full implementation of Global Plan: TB not eliminated by 2050



Population attributable fraction - risk factors for progression to disease

$$PAF = \frac{P \times (RR - 1)}{P \times (RR - 1) + 1}$$

	Relative risk for active TB disease	Weighted prevalence (22 HBCs)	Population Attributable Fraction
HIV infection	20.6/26.7*	1.1%	19%
Malnutrition	3.2**	16.5%	27%
Diabetes	3.1	3.4%	6%
Alcohol use (>40g / d)	2.9	7.9%	13%
Active smoking	2.6	18.2%	23%
Indoor Air Pollution	1.5	71.1%	26%

Sources: Lönnroth K, Raviglione M. Global Epidemiology of Tuberculosis: Prospects for Control. Semin Respir Crit Care Med 2008; 29: 481-491. *Updated data in GTR 2009. RR=26.7 used for countries with HIV <1%. **Updated data from Lönnroth et al. A consistent log-linear relationship between tuberculosis incidence and body-mass index. Submitted, 2009

Alcohol use and TB: Background

1. High prevalence of alcohol use disorders among TB patients: 10-50% of TB patients are alcoholics in Canada, Australia, USA, Switzerland, Russia
2. High TB risk among persons with alcohol use disorders: 10-50 times higher incidence of TB among social welfare receivers with drug use problems, people living in shelters for drug users, and homeless
3. Causal link or confounded by socioeconomic status, living condition, smoking, etc?

Alcohol use as a risk factor for tuberculosis – a systematic review.

Lönnroth K, Williams BG, Stadlin S, Jaramillo E, Dye C.
BMC Public Health 2008; 8: 289

Methods

Inclusion criteria

- Association between active TB disease and either alcohol consumption and/or diagnosis of alcohol use disorder
- Individual level data (case control and cohort studies)

Search

- Hans Rieder's TB literature collection
- PubMed
- Review matrix from systematic review of TB and smoking
- Reference lists from reviewed articles

Included studies

- 21 studies, of which 18 case control and 3 cohort studies
- 13 from high-income countries, 4 middle, 4 low
- Varying definitions of exposure, see below

Results



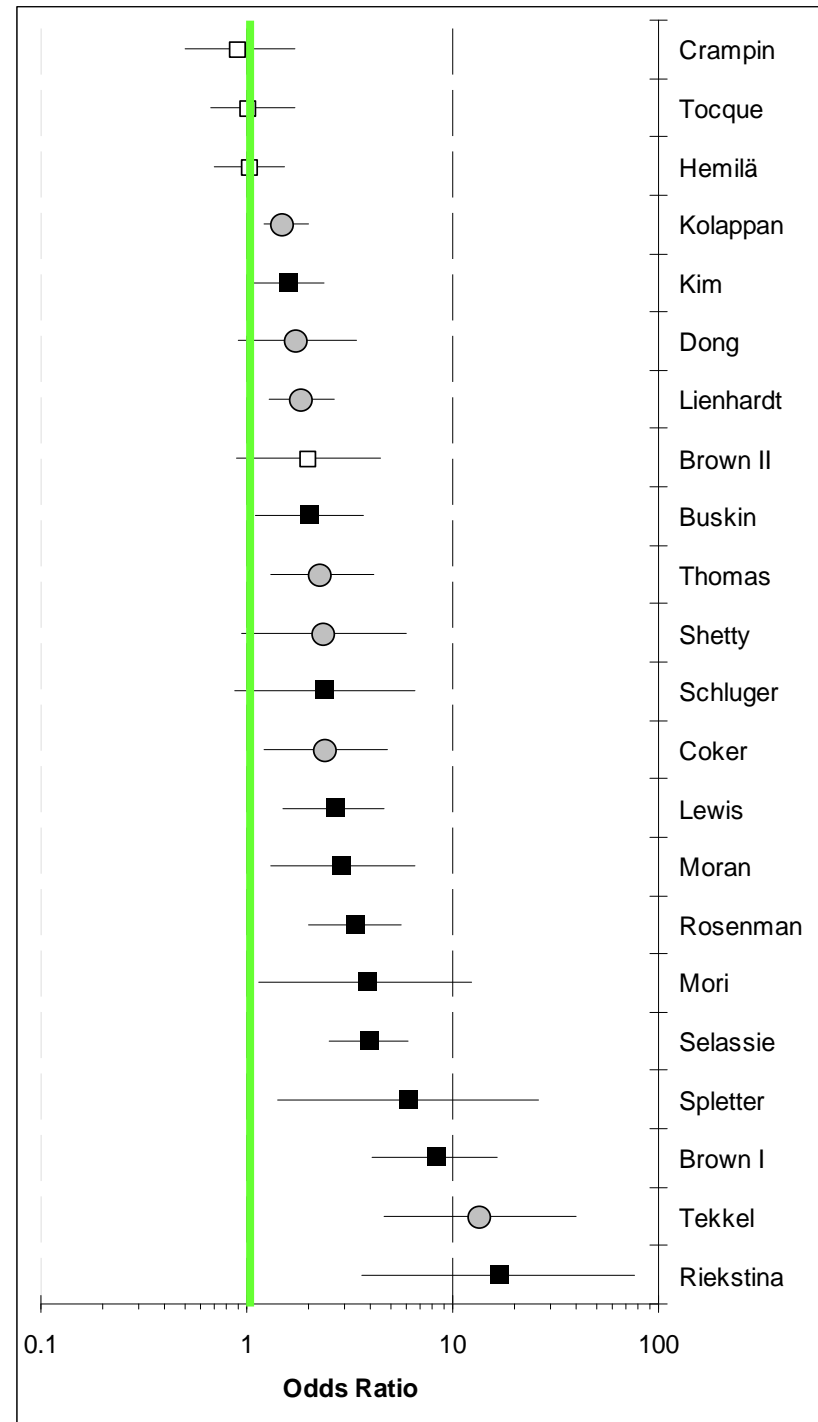
Low exposure: cut-off for intake set at <40 g alcohol / day

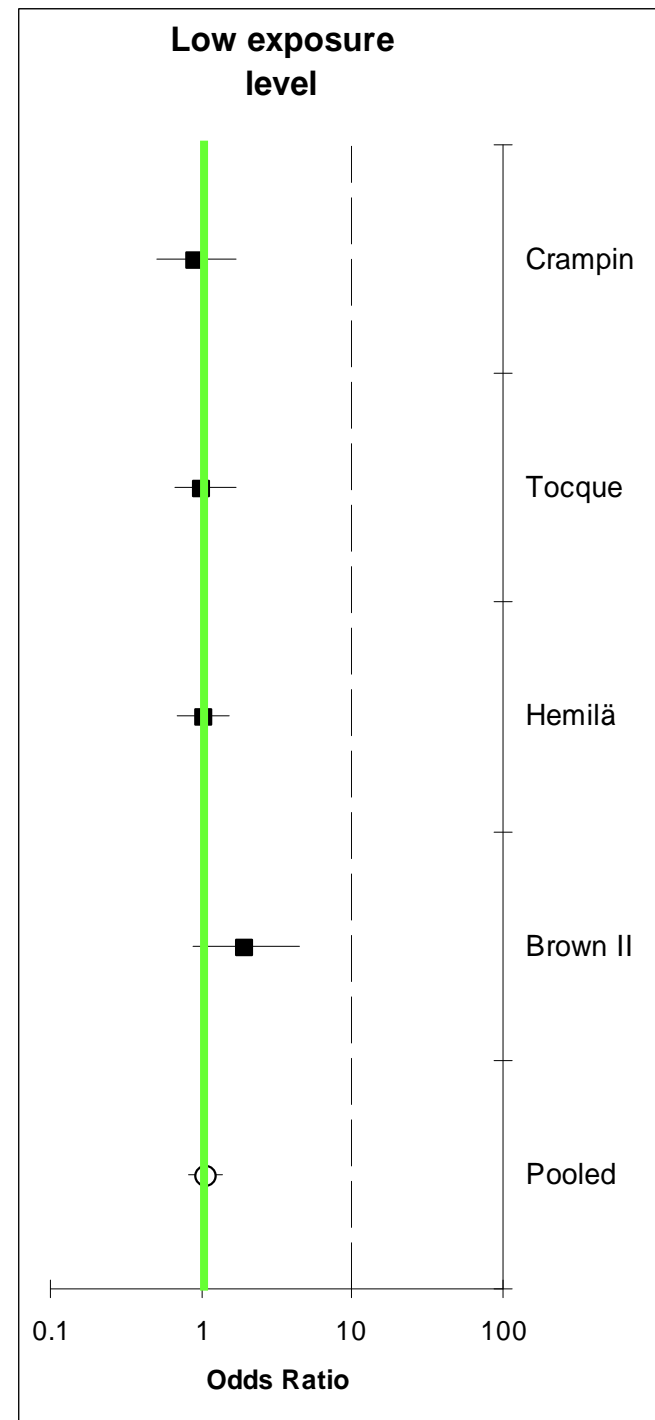
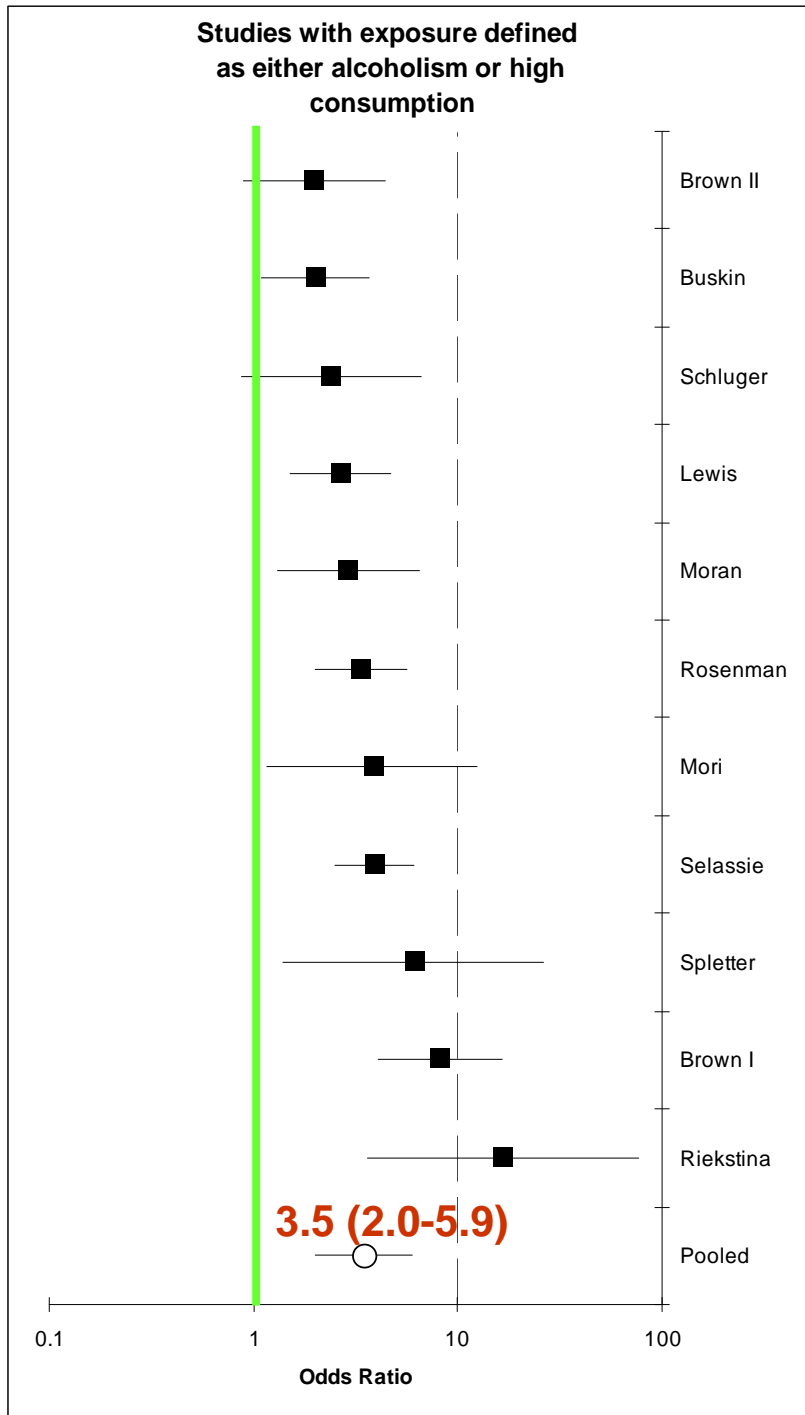


High exposure: cut off for intake set at ≥ 40 g/day, or diagnosed alcohol disorder (dependence, abuse, or "heavy drinking")



Exposure not clearly defined

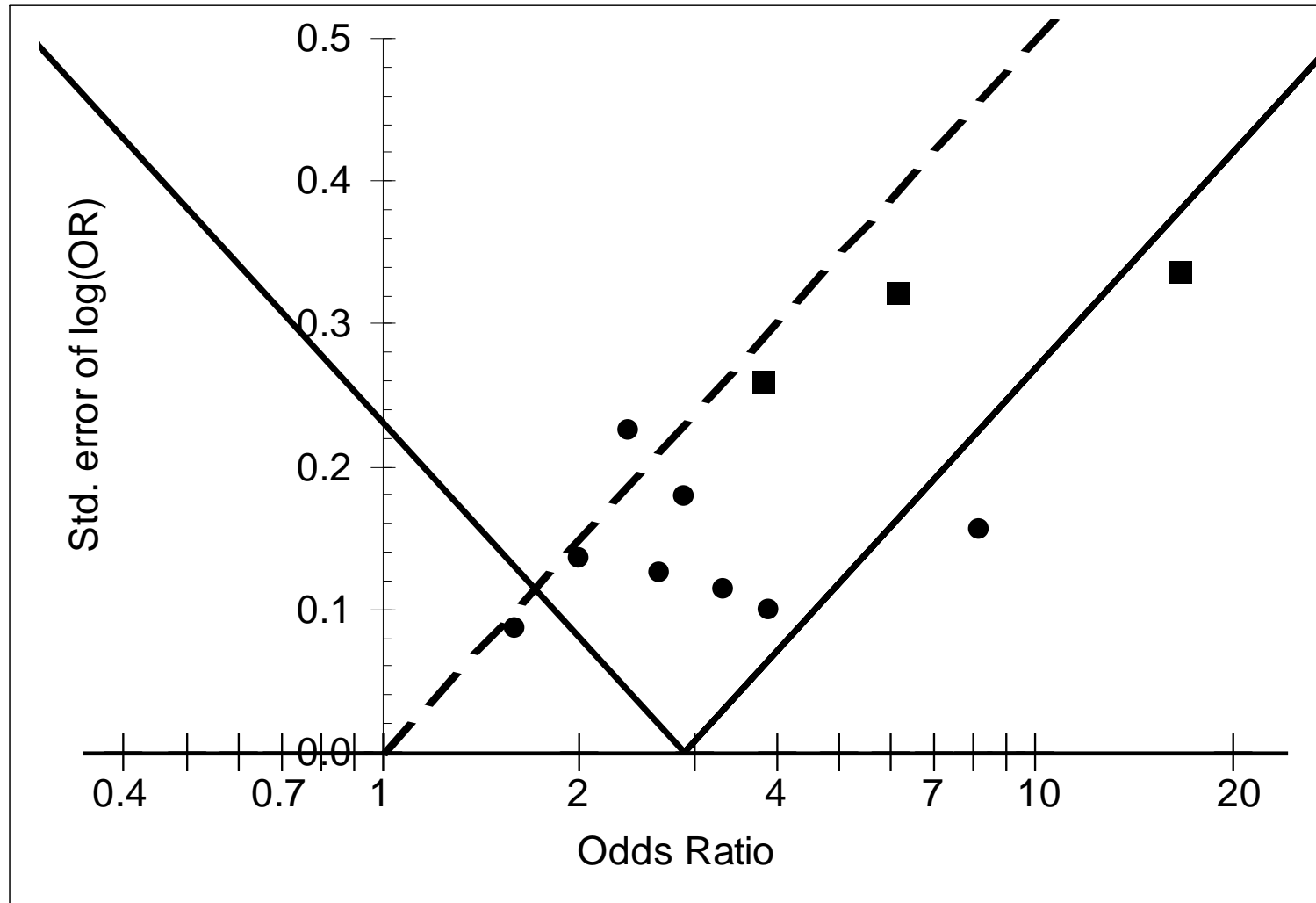




Pooled estimates for High-exposure/alcoholism studies

Study category	No of studies	Random effect assumption (95% CI)
Pulmonary TB cases only	2	3.67 (2.58-5.22)
All types of TB	6	2.87 (1.47-5.58)
Controlled for HIV status	7	3.26 (2.26–4.70)
Controlled age, sex, SES, smoking	5	3.49 (2.06-5.90)
Controlled HIV, age, sex, SES, smoking	4	4.08 (2.49–6.68)
Controlled infection, age, sex, SES	4	4.21 (2.73-6.48)
Excluding three smallest studies	8	2.94 (1.89-4.59)

Funnel plot, high exposure studies



- Points to the right of the dashed line are significant on 5% level
- Points outside the funnel indicate heterogeneity

Methodological considerations

- Unclear definition of alcohol use disorders in reviewed papers – what does "high exposure" actually correspond to?
- Misclassification of exposure? (underestimate real risk increase?)
- Representative studies? (low-income countries, Eastern Europe?)
- One cohort study, and few recent high-quality studies.
- Difference between pulmonary TB and other types?
- Residual confounding?

Possible causal pathways

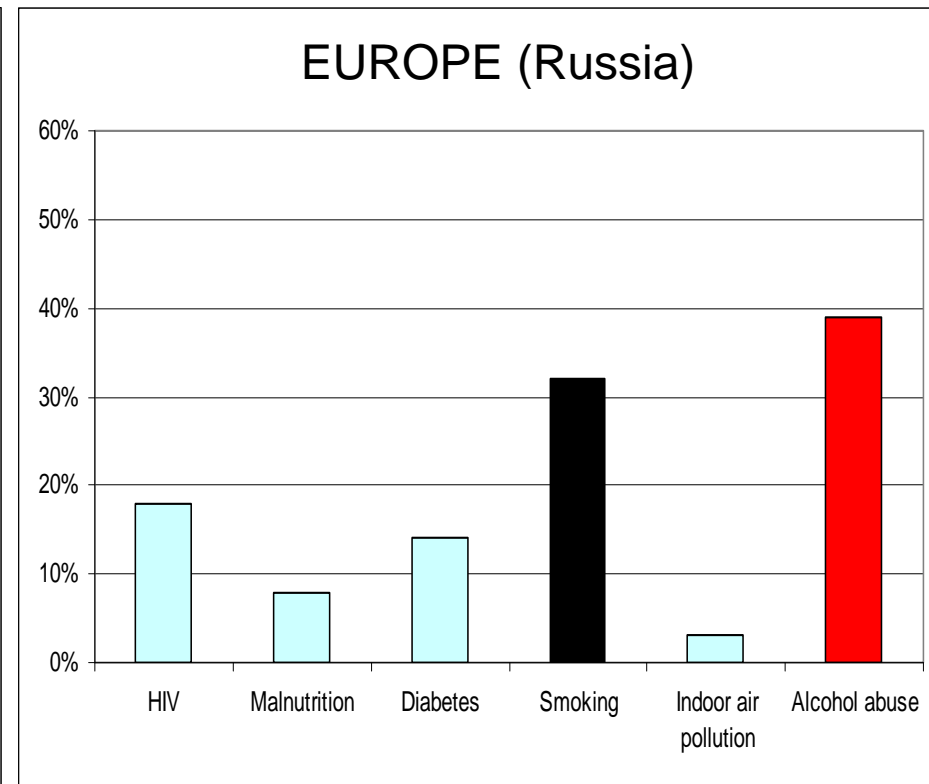
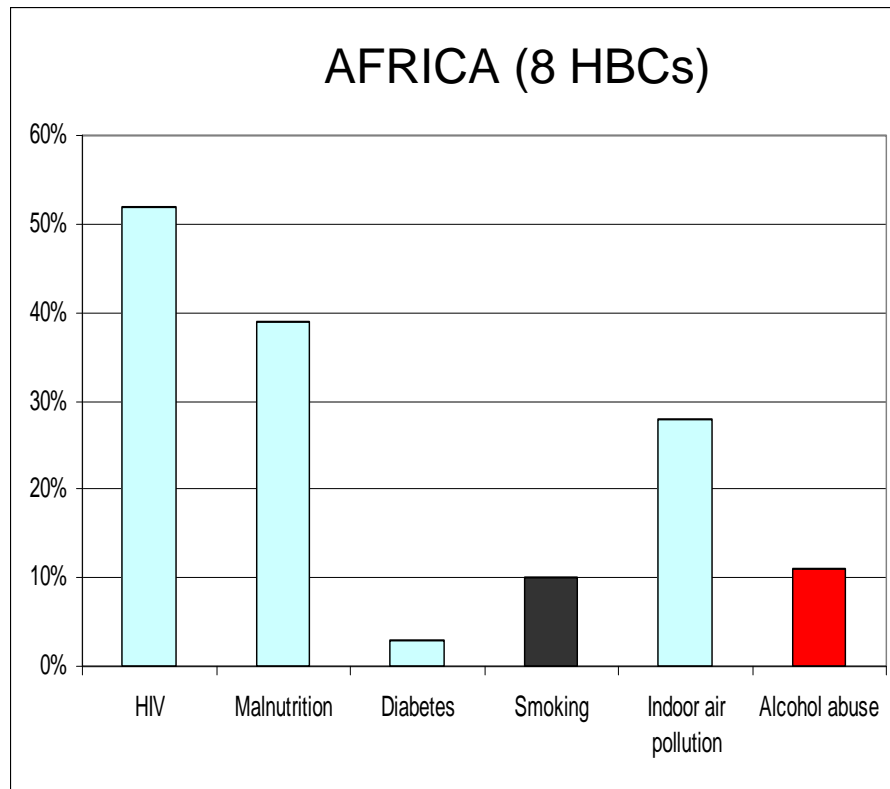
1. Increased risk of infection

- Social mixing patterns – high risk of exposure:
 - Drinking environment
 - Alcohol related social drift

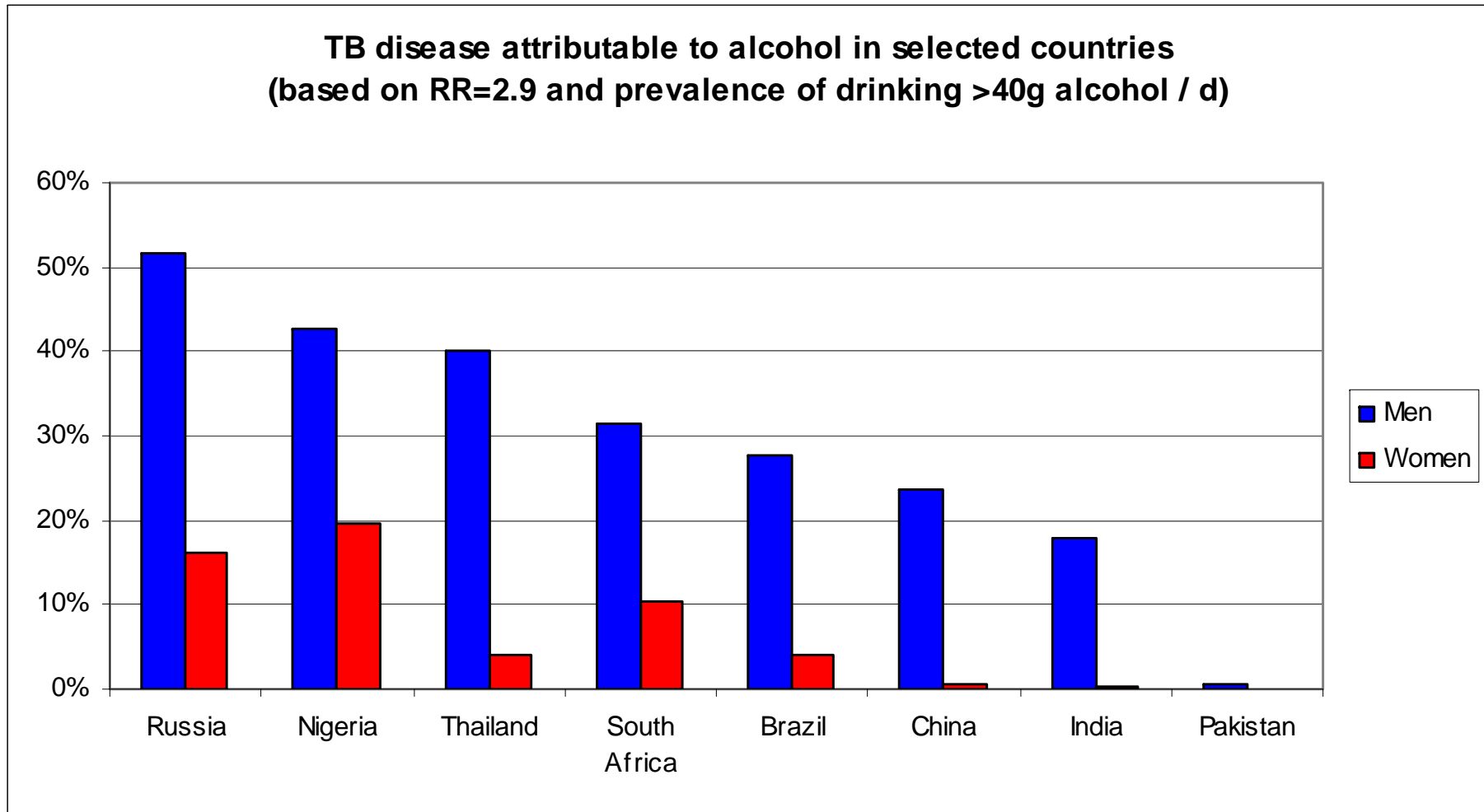
2. Increased risk of progression to disease

- Direct effects of alcohol on immunity
- Indirect effects on immunity of alcohol-related disorders, including malnutrition, malignancies, chronic diseases, etc

Population attributable fraction Regional variations in HBCs



Attributable fraction TB disease



Tobacco and TB

Three recent systematic reviews:

- Slama, K., Chiang, C.Y., Enarson, D., Hassmiller, K., Fanning, A., Gupta, P., et al. Tobacco and tuberculosis: a qualitative systematic review and meta analysis. *Int J Tuberc Lung Dis* 2007, 11,1049-61
- Lin, H., Ezzati, M., & Murray, M. Tobacco smoke, indoor air pollution and tuberculosis: a systematic review and meta-analysis. *PLoS Medicine*, 2007 4,e142
- Bates MN, Khalakdina A, Pai M, Chang L, Lessa F, Smith KR. Risk of tuberculosis from exposure to tobacco smoke: a systematic review and meta-analysis. *Arch Intern Med*. 2007 Feb 26;167(4):335-42.

Tentative conclusions on evidence:

- **Strong** for active smoking and TB disease (RR 2-3)
- **Moderate** for passive smoke and TB disease
- **Moderate** for relapse
- **Limited** for TB infection
- **Limited** for mortality

PAR% smoking

- Our global assessment for 22 HBCs: 23%
- Jha et al 2008: 38% of TB *deaths* among men and 9% among women in India
- Modelling 1: Hassmiller (PhD thesis 2007): 48% of TB cases in India
- Modelling 2: Lin et al 2008: Complete cessation of smoking and solid-fuel use by 2033 would reduce the projected annual tuberculosis incidence by 14–52% in China (if 80% DOTS coverage is sustained)
- Next step: dynamic modelling of global data

Action implications

- Prevent TB through addressing smoking and alcohol abuse
 - Medical interventions (role of NTPs?)
 - Public health (education, laws, restrictions, etc, role of NTPs)
 - Social medicine (the upstream determinants of smoking and alcohol abuse, role of NTPs?)
- Screen for TB among smokers and alcoholics
- Additional research needed
 - Original studies on smoking and alcohol interaction
 - More modelling to understand attributable fraction
 - Intervention studies: evaluate effect of prevention / treatment of alcoholism and smoking