

# **MDR-TB and XDR-TB Management and Treatment Outcome in Latvia**

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**National DOTS-Plus Program**

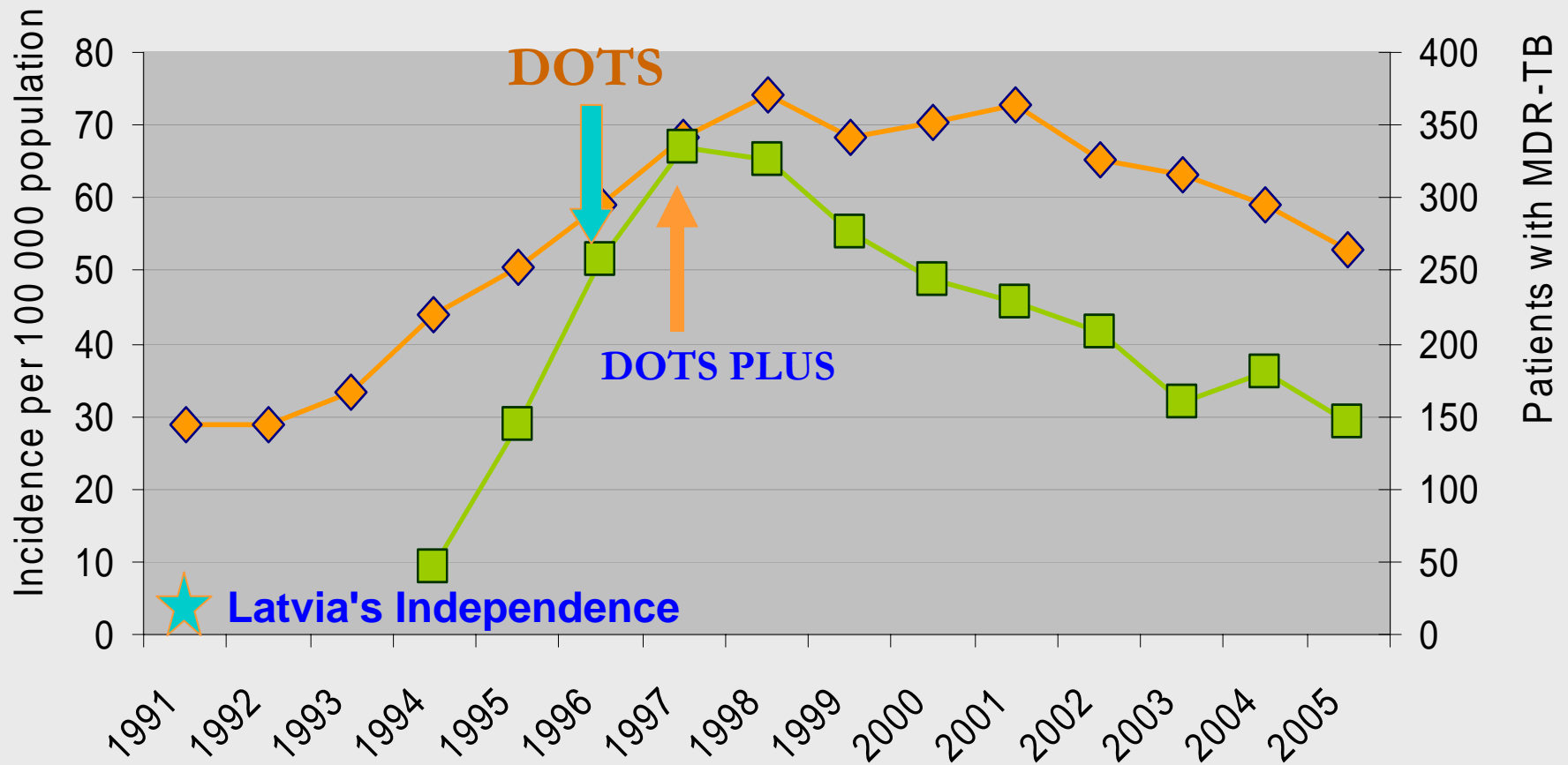
**Riga, Latvia**

# Background: TB in Latvia

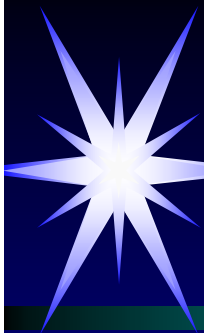
- Independent Baltic state since 1991
- DOTS implemented in 1996 countywide
- MDR-TB management started in 1997
- Latvia consistently ranked among countries with highest rates of MDR TB worldwide



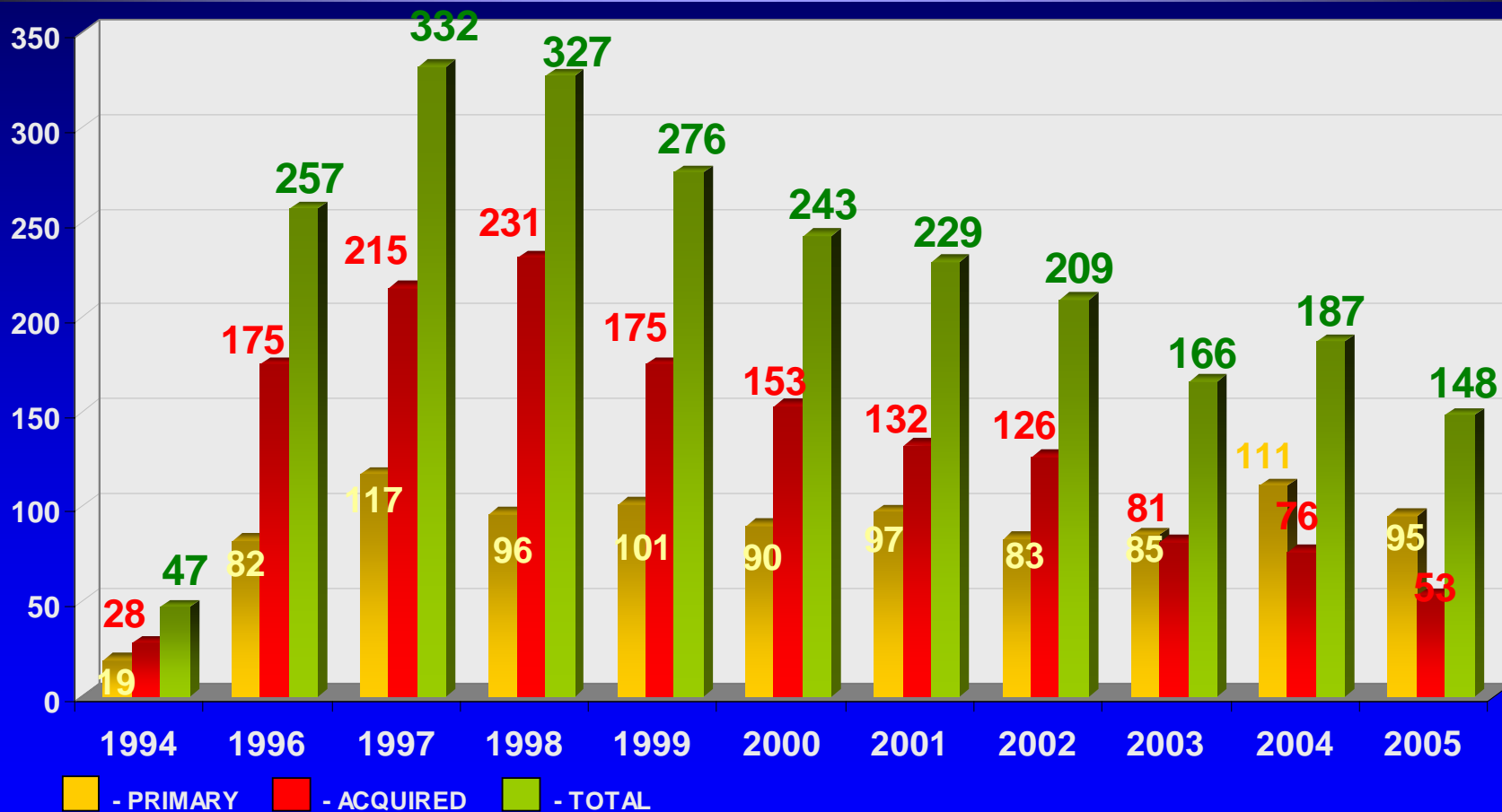
# Impact of MDR TB Management on TB Case Detection, 1991-2005



Source: Latvian National TB Control Program,  
published Eurosurveillance, March 2006



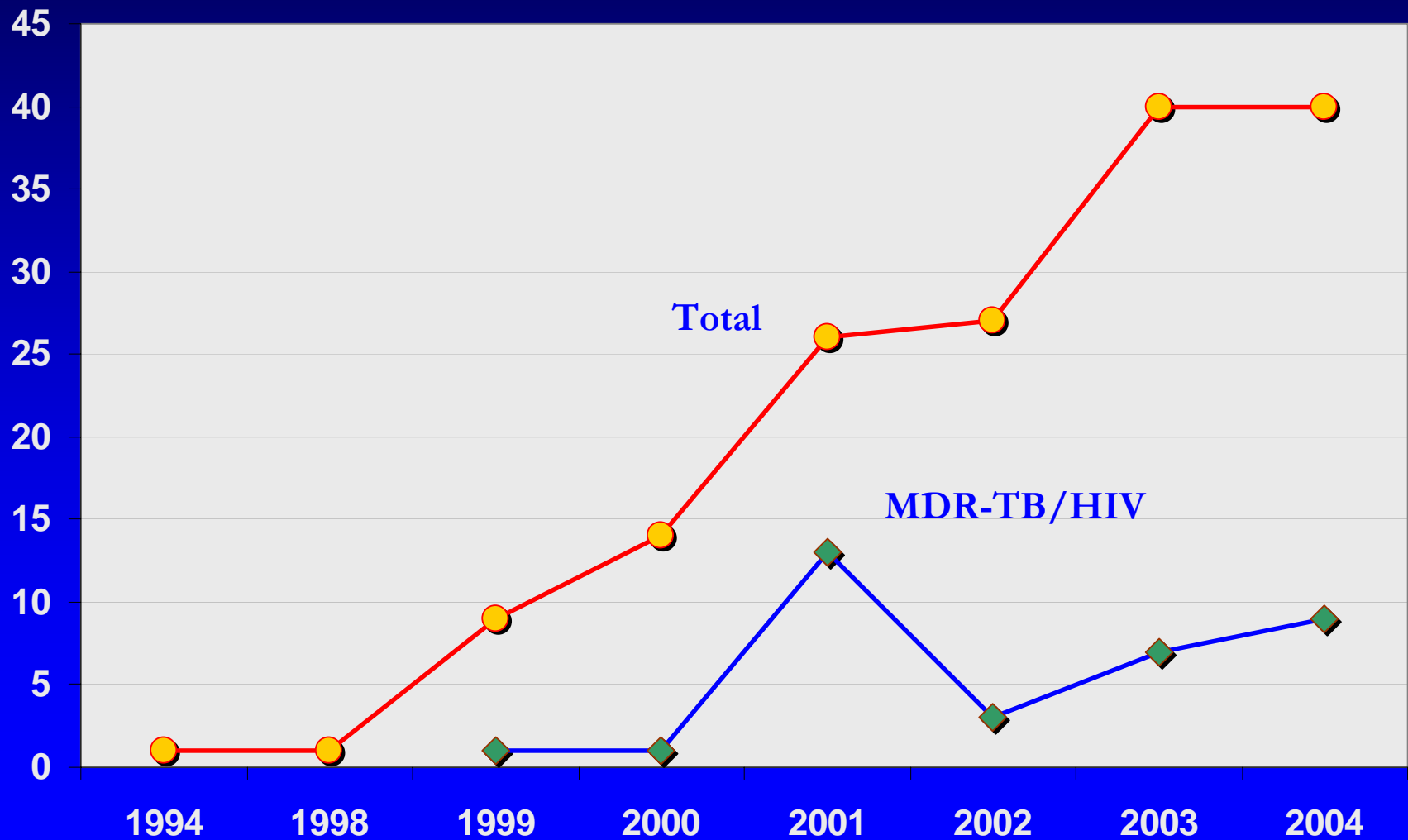
# Primary and Acquired MDR TB Incidence Rates, 1994-2005



Since 1998 the total number of annually registered MDR TB cases decreased 2,2 times, for previously treated cases 4,4 times



# Number of TB/HIV Patients (Including Prisoners), 1994-2004





# Laboratory Diagnostic Methods for Drug Susceptibility Testing in Latvia

- **DST** provide for all culture (+) patients on L/J – absolute concentration method
- **BACTEC/MGIT**
  - Priority **I** - for high MDR-TB risk patient sputum smear (+)
  - Priority **II** – all sputum smear + cases for better infection control purposes
- **INNO LiPA test** – from direct specimen for sputum smear +; high risk for MDR-TB patients



# Drug Susceptibility Testing Availability

## DST available

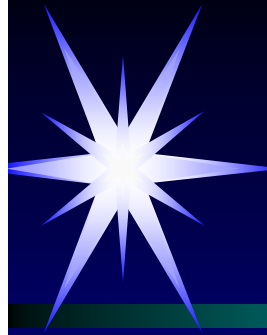
- Aminoglycosides
  - Streptomycin
  - Kanamycin
- Capreomycin
- Ofloxacin, Ciprofloxacin

## DST available

- Prothionamide  
(Ethionamide)
- Cycloserine, terzindone
- para-aminosalicylic acid
- Thiacetazone

**DST not available:**

**Clarithromycin; Amoxicillin/Clavulanate**



# Objectives

- Determination of proportion of extensively resistant patients according to pattern of resistance
- Determination of number of XDR TB patients (new WHO definition) by patient category over time
- Determination of treatment outcome by pattern of extensive resistance
- Determination of HIV seroprevalence rate by pattern of extensive resistance



# Methods

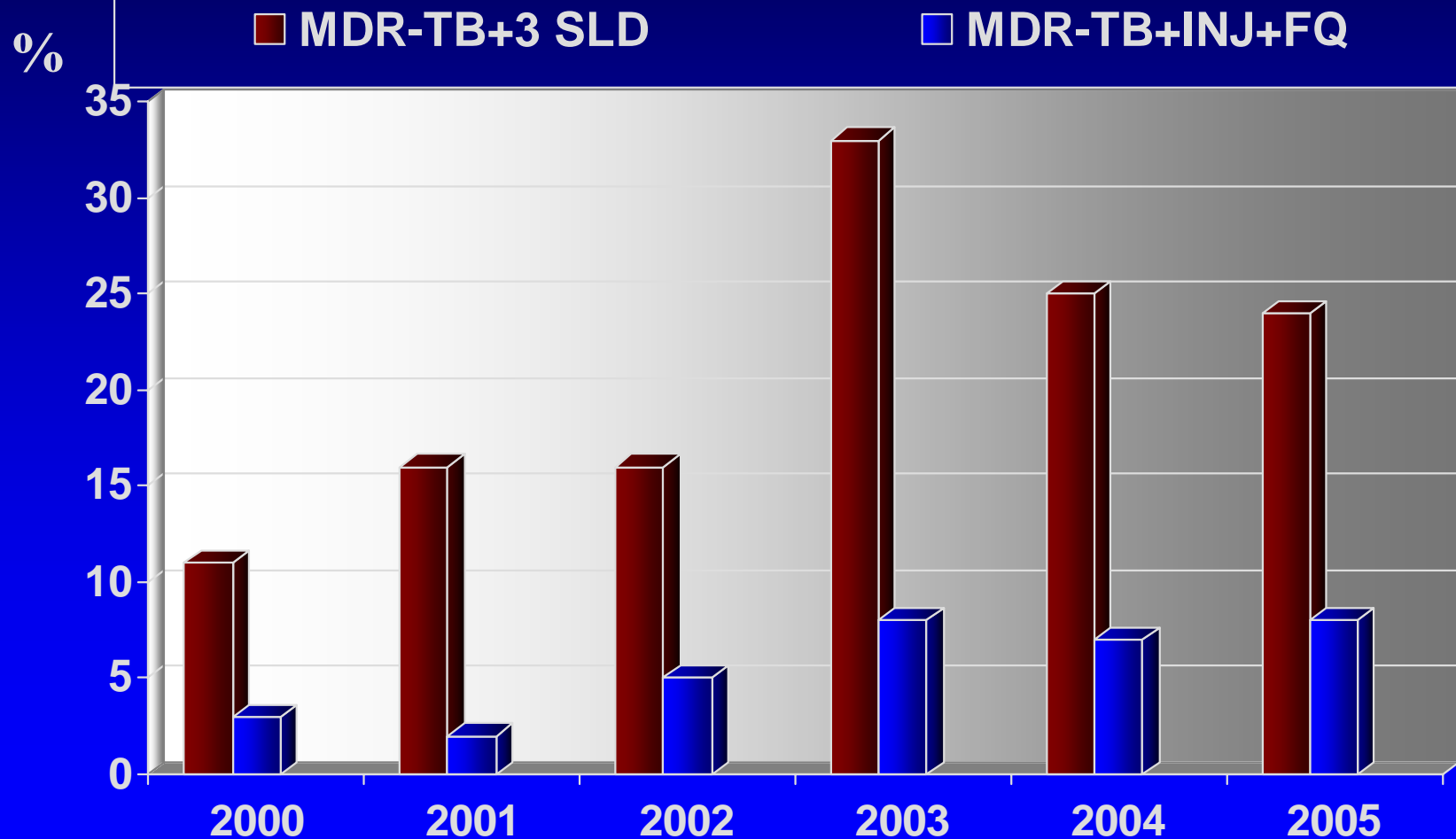
- Registration Cohort 2000-2005
- Treatment Cohort 2000-2003
  
- Analysis of characteristics in MDR TB database
- Analysis of patient treatment outcome



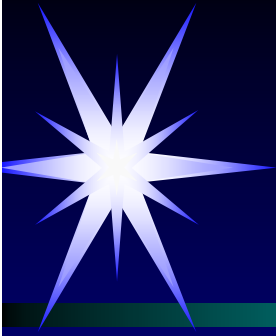
# Definitions

- MDR-TB = resistance to at least INH and rifampicin
- INJ = second-line injectables including aminoglycosides and capreomycin
- FQ = fluoroquinolones
- XDR-TB (revised, WHO) = MDR-TB with resistance to FQ and one INJ
- XDR-TB (MMWR) = MDR-TB with resistance to at least 3 second-line drugs

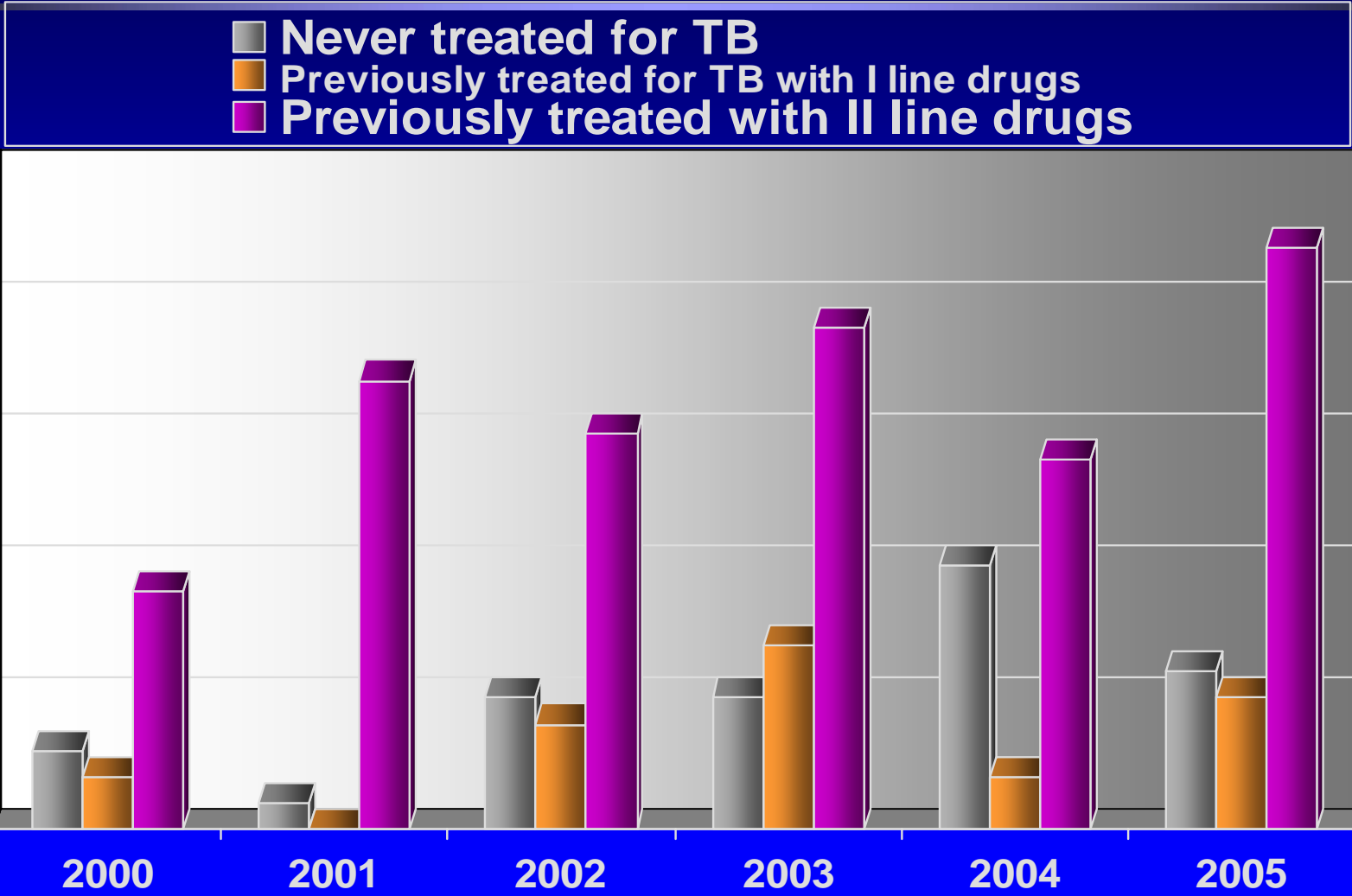
# Proportion of Extensively Resistant Patients According to Patterns of Resistance



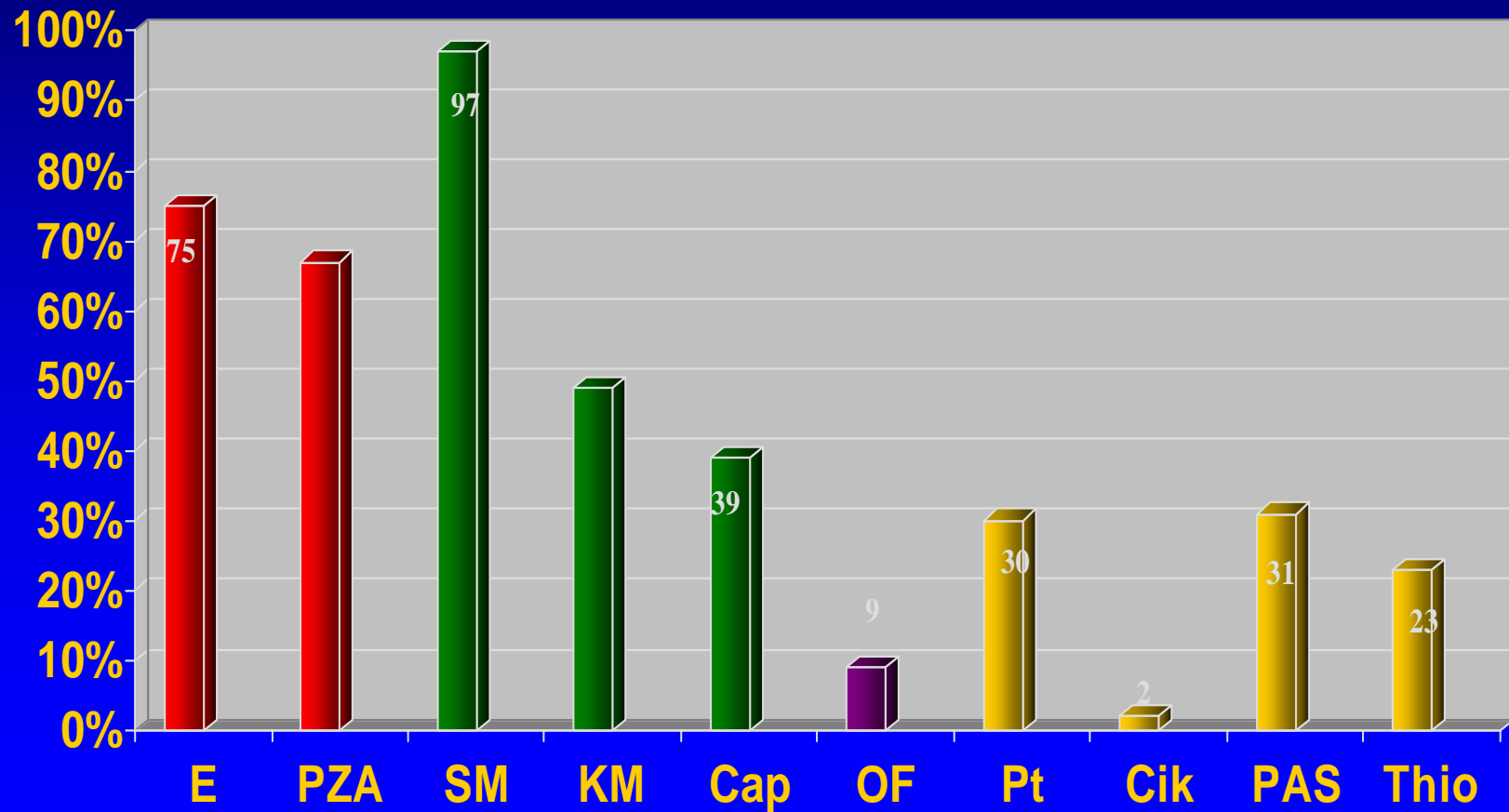
chi square test for trend = 12,4,  $P < 0.001$

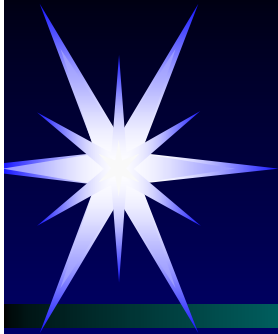


# XDR-TB (MDR-TB+INJ+FQ) Among 3 Patient Categories



# Resistance to Individual Drugs





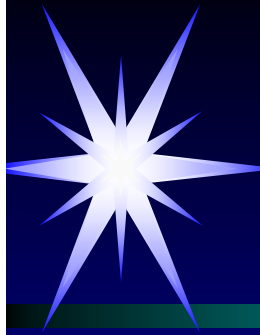
# Treatment Characteristics

- 107 distinct regimens
- Median treatment duration: 18 months (1 – 38 mos)
- Median of 6 drugs used (range 3 - 8) for 3 months or more
  - Most common were ofloxacin, prothionamide, thiacetazone, pyrazinamide, ethambutol
- Use of injectable drugs
  - kanamycin, capreomycin, streptomycin
  - Median duration of use 12 months
  - Range of use 1-36 months
  - After culture conversion, median 9 months



# Treatment Outcome by Pattern of Resistance

Resistance Pattern	Cure and Completion	Death	Default	Failure
MDR-TB	67%	6%	14%	13%
MDR-TB + 3 SLDs	58%	1%	11%	30%
MDR-TB + INJ + FQ	28%	10%	7%	55%



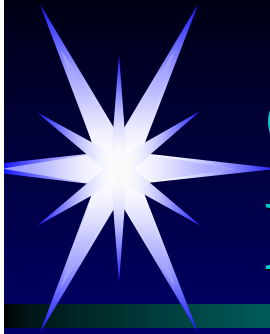
# HIV Rates by Pattern of Extensive Resistance

Resistance Pattern	HIV Rate
MDR-TB	3%
MDR-TB + 3 SLDs	6%
MDR-TB + INJ + FQ	10%



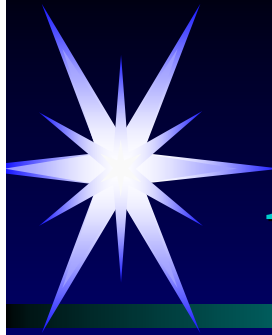
# Conclusions

- Acquired MDR-TB is decreasing in Latvia
- XDR-TB is increasing steadily among all MDR-TB categories, particularly in patients who have a history of previous treatment with second-line drugs
- Cure rate decreases significantly when the pattern of drug resistance includes injectables, aminoglycosides, and fluoroquinolones
- HIV may be a factor in worse treatment outcomes in drug resistant patients
- Discrepant laboratory tests to second-line drugs frequently makes treatment management difficult



# Challenges in Controlling Drug Resistant TB in Latvia

- Improving treatment outcomes for drug sensitive cases
- Rapid drug resistance detection and appropriate treatment
  - Rapid diagnostic tools
  - Expanded use of contact investigations
- Decrease treatment interruptions and default
  - Improving compliance
  - Compulsory treatment
- Infection control
  - Health care settings
  - Isolation of patients on palliative care
- New drugs and treatment regimens



# Acknowledgments

- Latvia State Agency of Tuberculosis and Lung Diseases
  - V Riekstina, G Skenders
- Division of TB Elimination, CDC
  - T Holtz, C Wells, K Castro