

A photograph of the Golden Gate Bridge in San Francisco, California. The bridge's iconic red-orange towers and suspension cables are prominent against a clear blue sky. The bridge spans across the water, with a large shadow cast onto the surface. In the foreground, there are green trees and a small circular structure in the water. The background shows rolling hills and a few sailboats on the water.

# San Francisco: TB Update 2004

## *SF TB Control: Goals*

- Find and treat all cases to completion
- Stop transmission
- Prevent TB in those at greatest risk of disease (especially contacts)

*San Francisco TB rates have ranked among the highest in the US for decades... Why?*

- Large foreign born population
  - 37% of SF population
  - estimated rate of TB infection: 50%
- Large homeless population
  - 8,000-13,000 homeless
  - 32% already infected with TB
  - 15.9% (1 in 7) infected with HIV
- 18,672 injection drug users (22% HIV+)
- Jail bookings per year: ~55,000

# *Good News! TB in San Francisco:*

*2004*

## Only 11 cases of homeless TB cases :

- ~8% of all cases (2002:19.9%)
- 7 out of 11 however are HIV+

**Implications:** HIV infected persons are sentinels for recent TB transmission.

**Conclusion:** TB continues to be actively spread among SF's homeless

## *2002: An Important Reminder from the Past*

### **Homeless cases up by 65%**

- 2002: 38/146 (26%)
- 56% are from shelters
- HIV co-infection: 47%
- 53% African American
- 87% US-born
- DNA fingerprinting indicates high transmission rate

## *2002: An Important Reminder from the Past*

### **Homeless cases up by 65%**

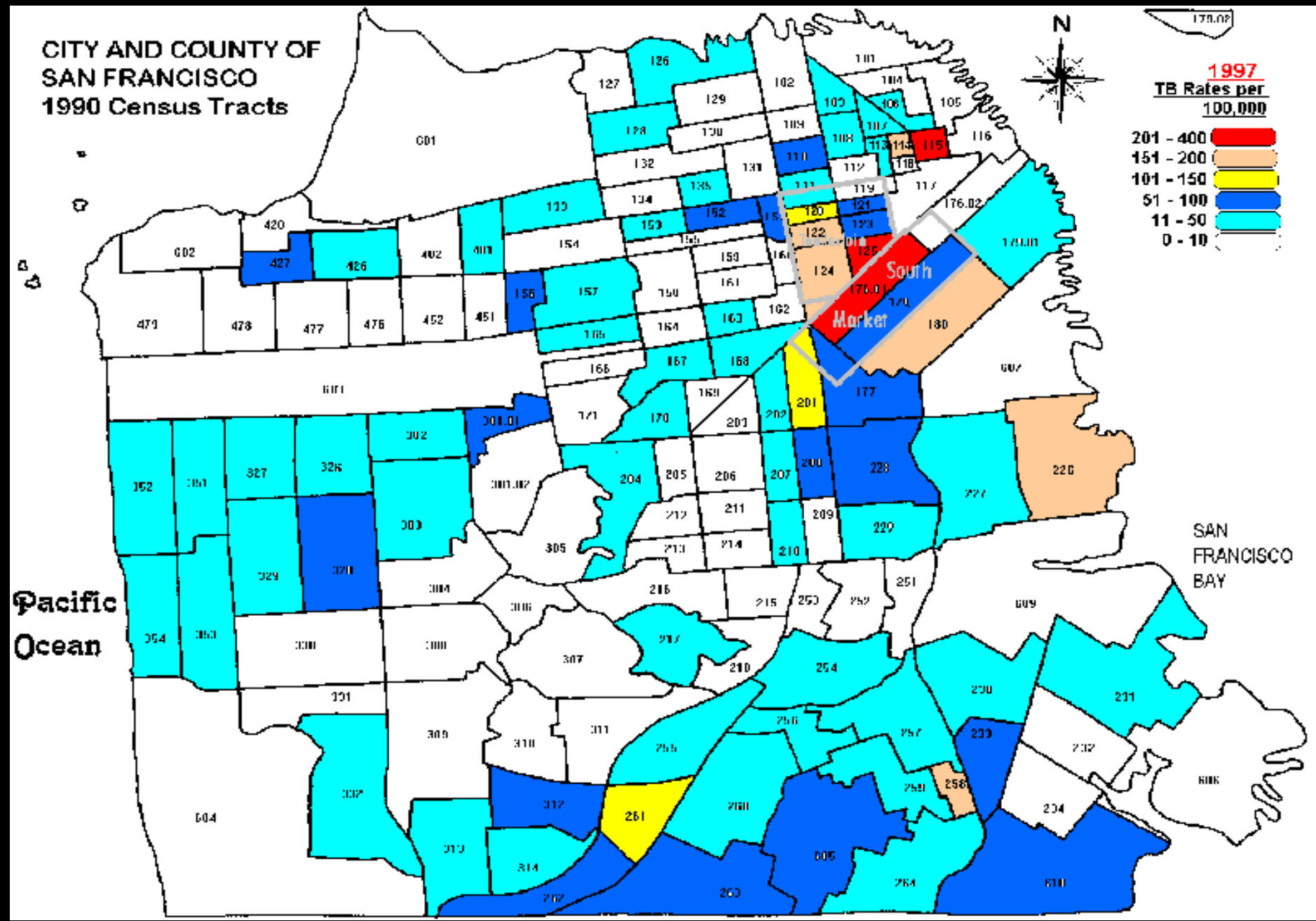
- 2002: 38/146 (26%)
- 56% are from shelters
- HIV co-infection: 47%
- 53% African American
- 87% US-born
- DNA fingerprinting indicates high transmission rate

## *2001-2002 Homeless Outbreak from a single strain of TB:*

<b>Case</b>	<b>Date Report</b>	<b>Residence(s)</b>
1	07/23/2001	Boston Hotel
2	10/23/2001	Episcopal
3	10/26/2001	Episcopal
4	10/31/2001	Unknown
5	11/06/2001	Various Shelters, Gayland Hotel, King Hotel (Oakland)
6	11/16/2001	SRO (Name Unknown)
7	11/26/2001	MSC South
8	12/17/2001	Episcopal
9	12/20/2001	MSC South
10	02/19/2002	MSC South
11	04/25/2002	A Man's Place
12	07/05/2002	SRO (Name Unknown)
13	05/23/2002	Episcopal, A Man's Place
14	08/21/2002	St. Bonifacio

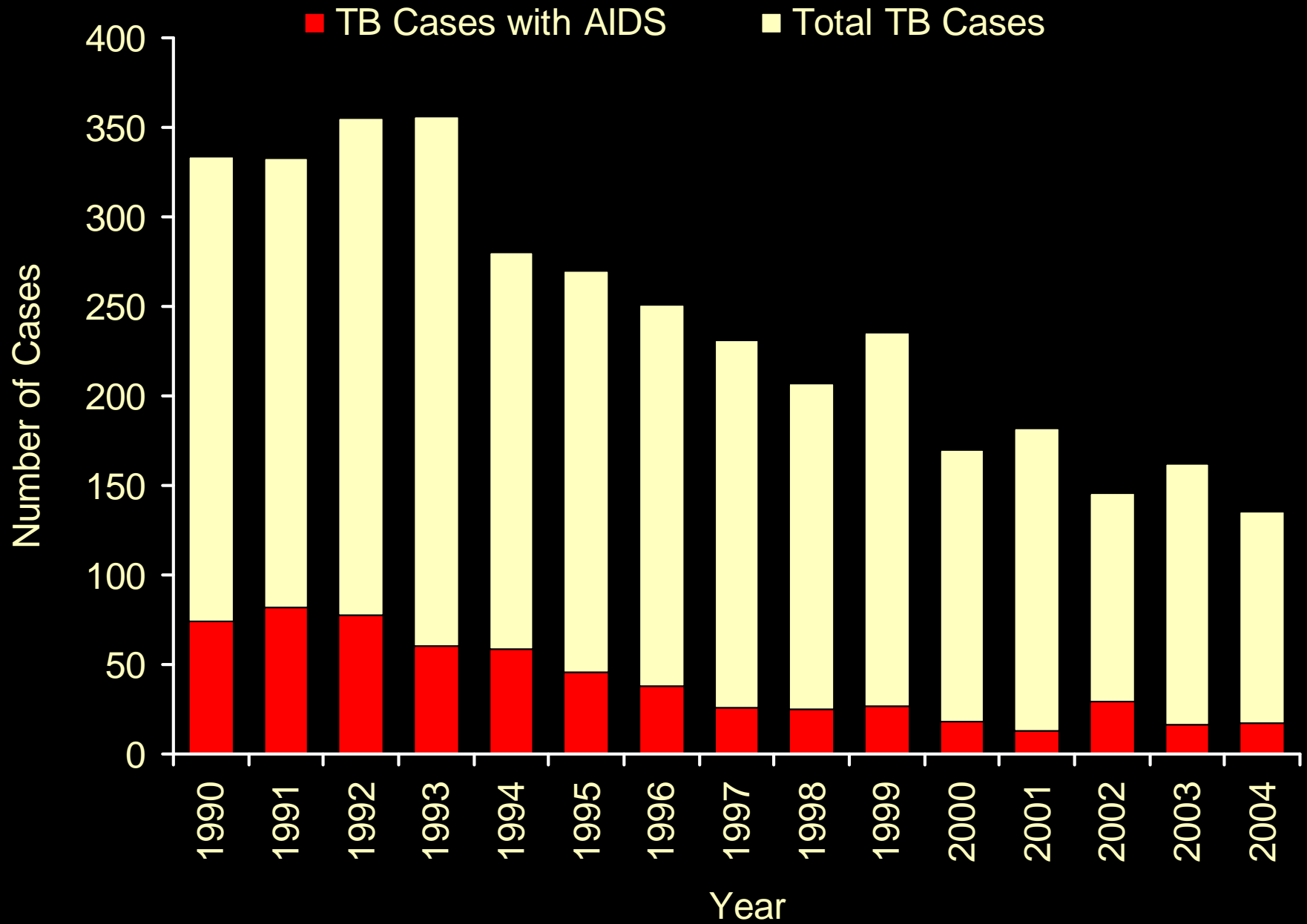


# TB Rates in San Francisco, 1997

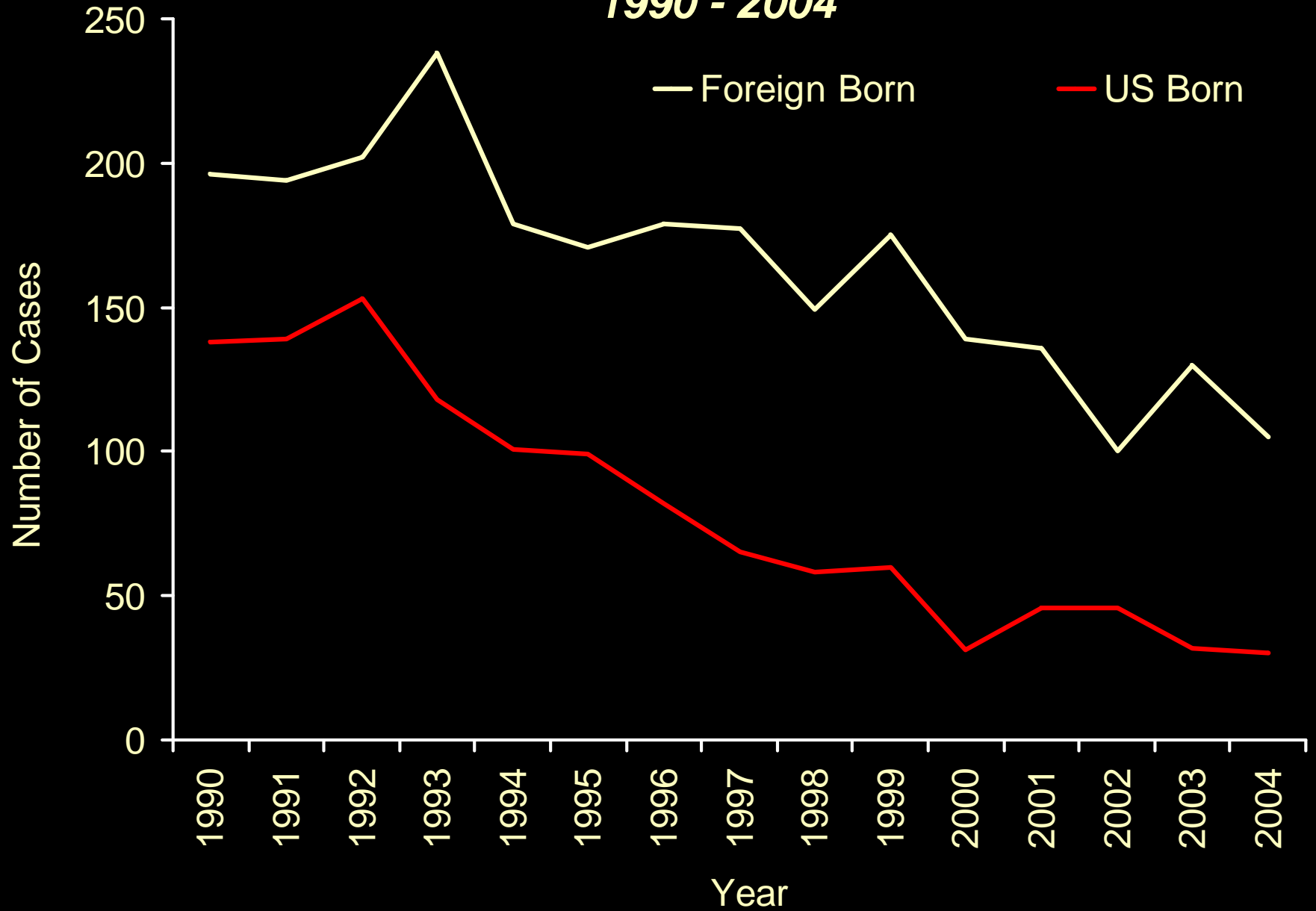




## TB Cases in San Francisco, 1990 - 2004

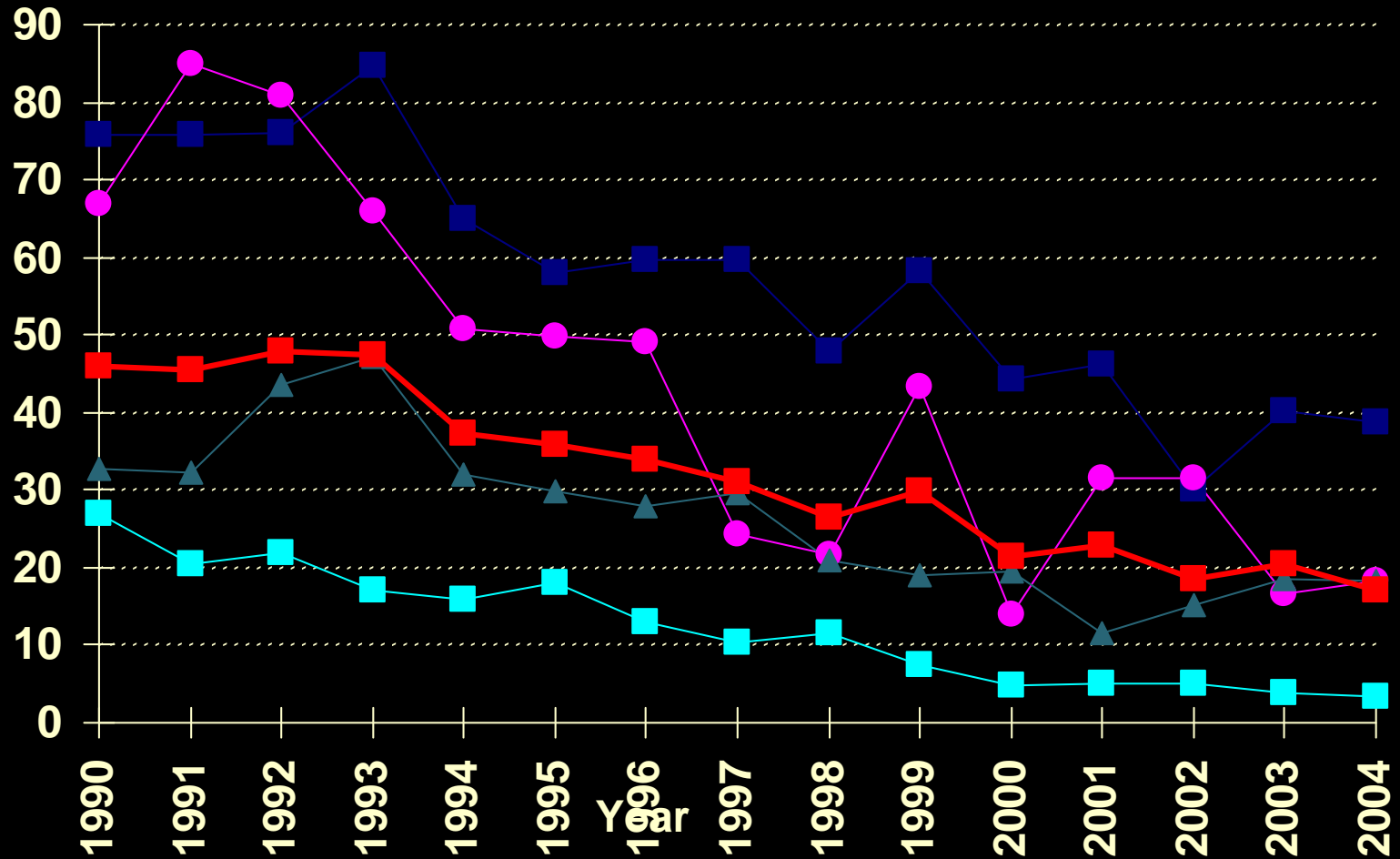


# *TB Cases in San Francisco by Place of Birth, 1990 - 2004*

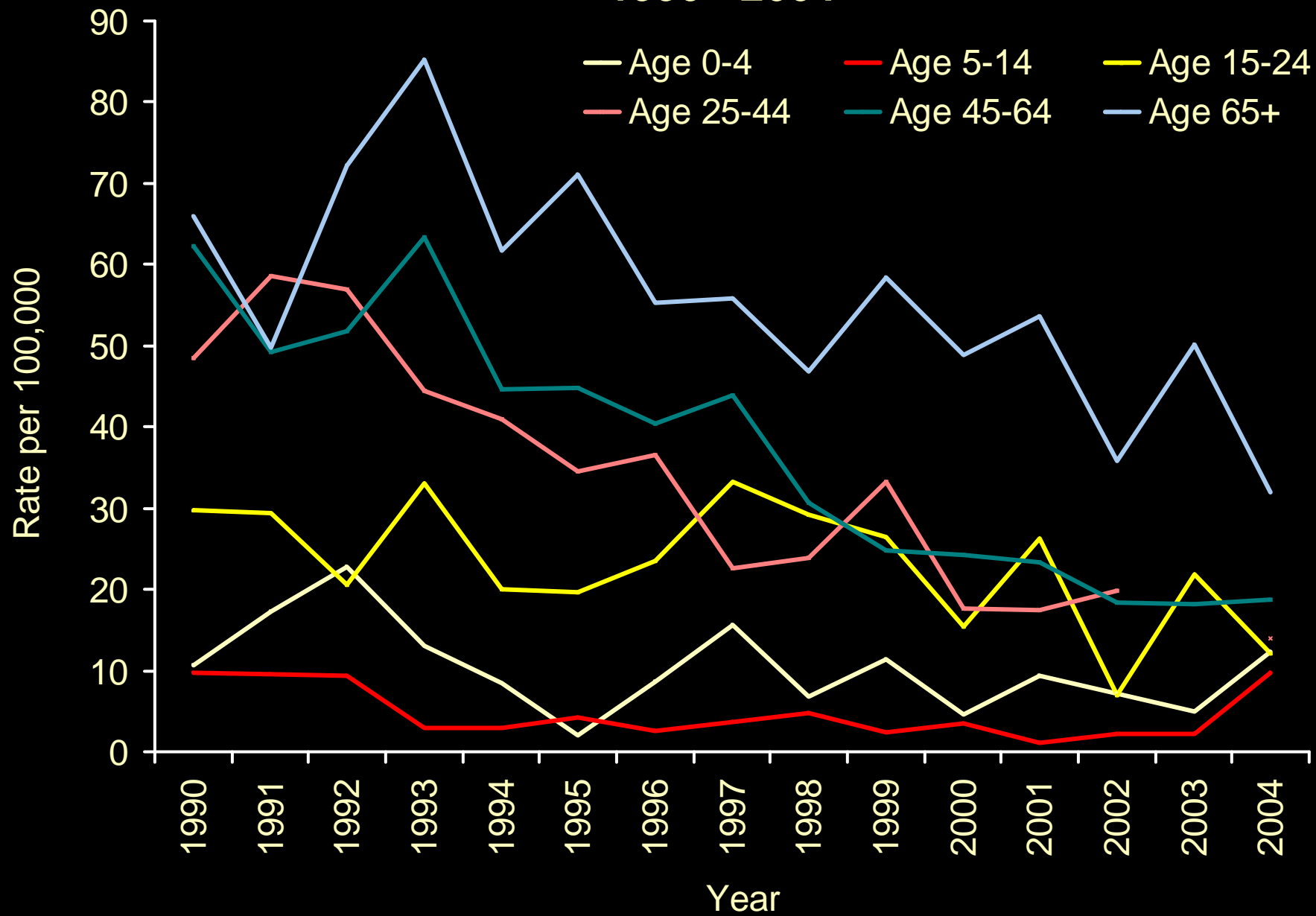


# TB Cases in San Francisco By Race & Ethnicity, 1990-2004

■ Asian ● Black ▲ Hispanic ■ White ■ Total



## TB Rates in San Francisco by Age Group 1990 - 2004



# *2002 Profile of TB in San Francisco*

- HIV/ TB:
  - ~20% of all cases (2000:10.6%, 2001:7.1%)
- Social Factors:
  - Homelessness: 26% (more than doubled from previous years)
  - Substance abuse: 11-15% (increase over previous years ~5%)
- Drug Resistance:
  - INH: essentially stable for past decade at ~10%
  - MDR: 4 cases in 2002 (~3%, 2001:4 cases, 2000: 0 cases)

# *2004 Profile of TB Cases in San Francisco*

## **Ethnic Diversity:**

- 78% are foreign-born
- 1 in 3 cases is ethnic Chinese
- 70.4% of foreign-born cases are from China, Philippines, and Southeast Asia
- Asians with highest rate: 39/100,000

# *p009 “Waves”*

	1995-1997 (%)	2001-2002 (%)	P-value
	N=23	N=18	
<b>Ave. Age at Dx</b>	39yrs (27-63)	46yrs (34-66)	<b>0.0089</b>
<b>Male</b>	20 (87.0)	12 (66.7)	0.4655
<b>Black Race</b>	15 (65.2)	12 (66.7)	0.9547
<b>White Race</b>	8 (34.8)	5 (27.8)	0.6926
<b>U.S.-born</b>	23 (100.0)	16 (88.9)	0.7173
<b>Homeless</b>	10 (43.5)	14 (77.8)	0.1543
<b>HIV+</b>	15 (65.2)	10 (55.6)	0.6942
<b>IDU</b>	9 (39.1)	9 (50.0)	0.6020
<b>Non-IDU</b>	17 (74.0)	9 (50.0)	0.3399
<b>EtOH</b>	8 (34.8)	4 (22.2)	0.4608



## *p009 Homeless Residence at Diagnosis*

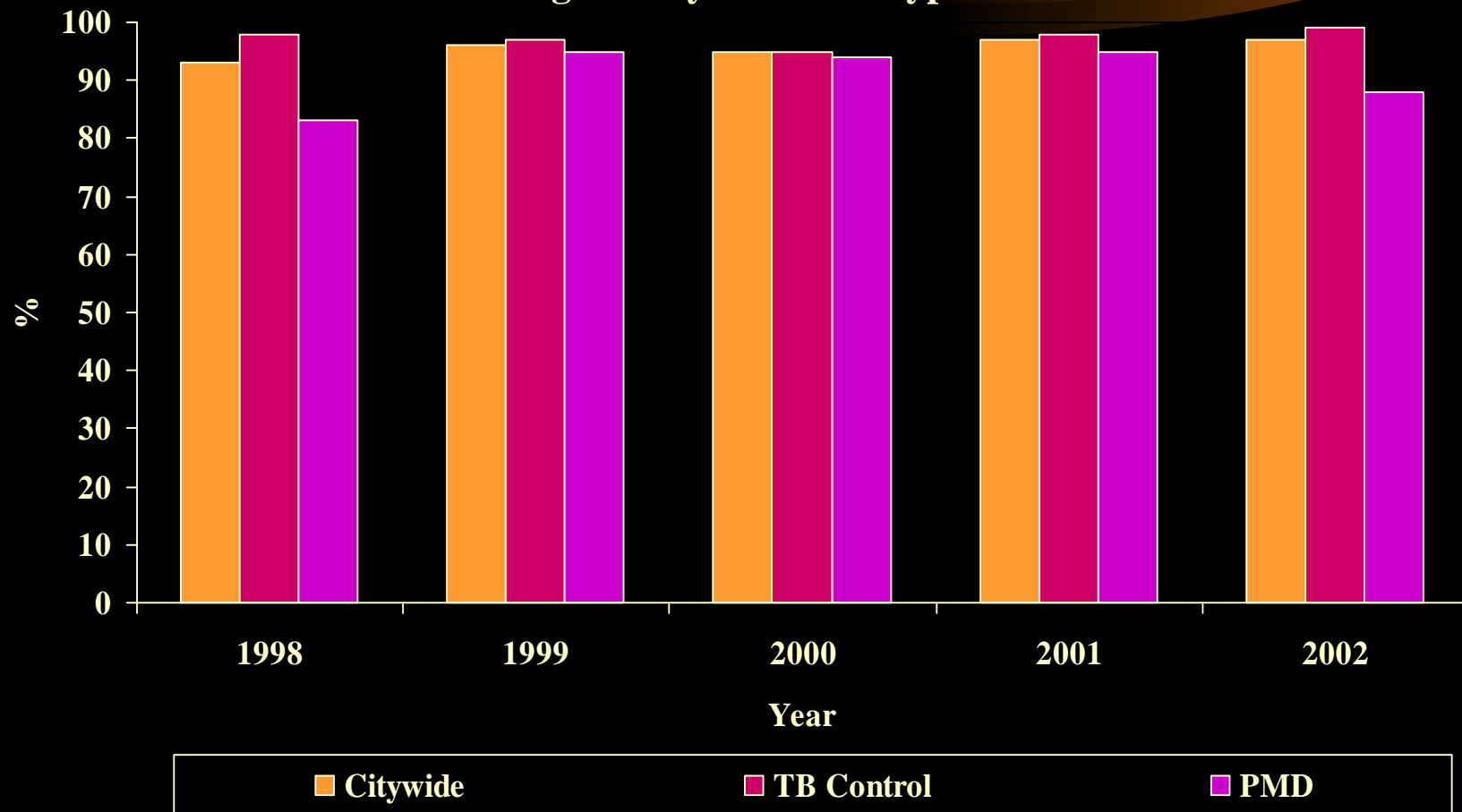
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## *TB Indicators: Timeliness of Treatment*

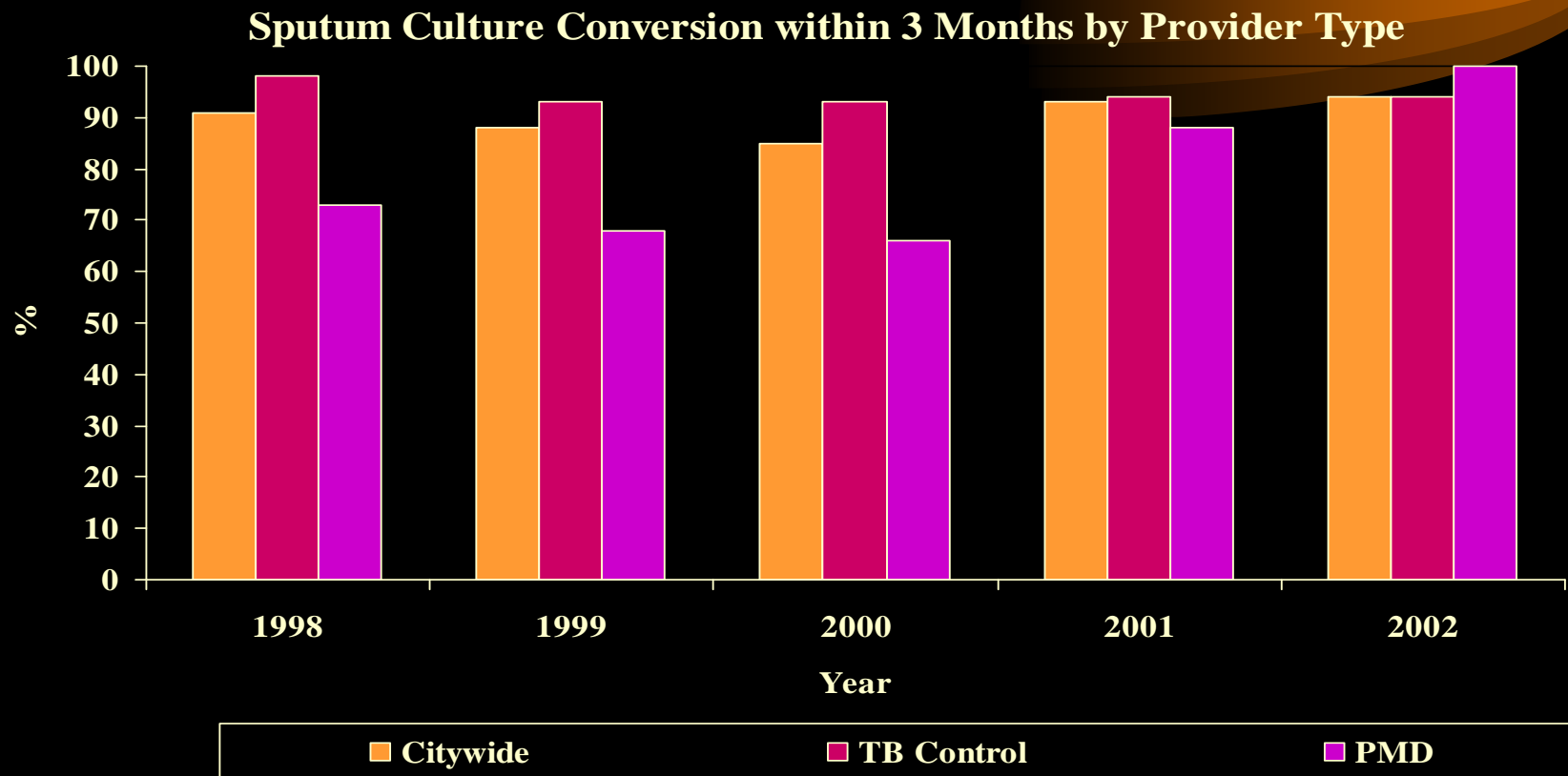
- Time to treatment initiation from AFB smear+ specimen collection
- Goal: Within 4 days
  - Citywide average: 1 day
  - TB Control: 1 day
  - Private Provider: 1 day

# *TB Indicators: Adequacy of Treatment*

**Initiation of an Adequate Short-Course Treatment  
Regimen by Provider Type**

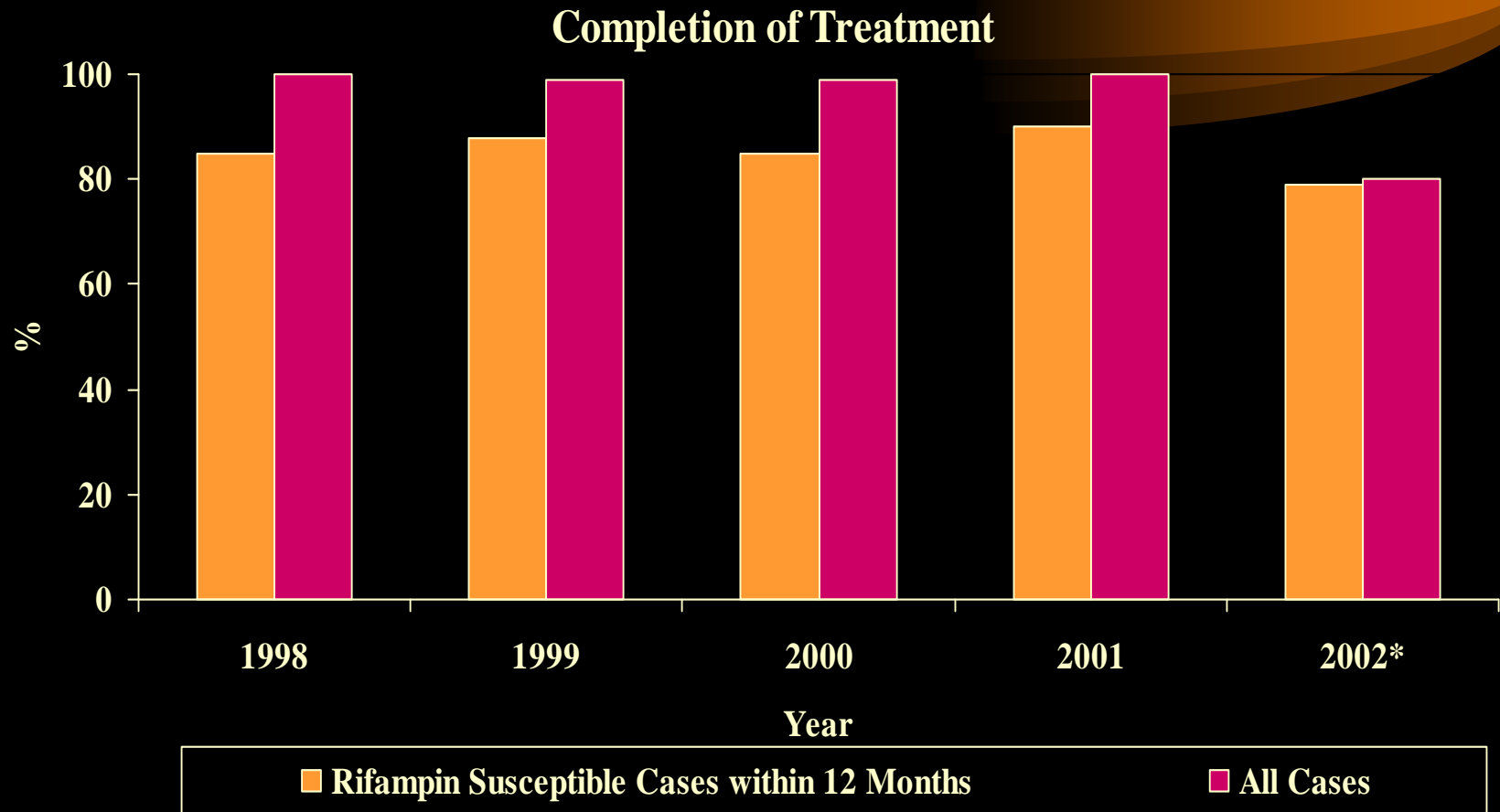


# *TB Indicators: Sputum Conversion*



**California 2004 Objective: 70%**

# *TB Indicators: Completion of Therapy*



\*2002: 24 cases pending treatment, 22 RIF-susceptible are pending treatment

# *TB Indicators: Treatment Management*

- Acquired Drug Resistance:
  - 1999-2000: 1 case of INH resistance in 1999
- Management of Drug Resistant Cases:
  - 11 cases reviewed for 2002
    - Only one case managed by PMD
  - No management errors observed
- Conclusions:
  - Management of drug resistant cases has improved

# Contact Identification

- Goal:
  - Contacts identified for >95% of smear+ cases
  - Objective met since 1997
- AFB Smear-Positive Cases
  - Cases with Zero Contacts: 0 (2001: 2 cases)
  - Median Contacts per Case: 5
- All Cases
  - Contact Disease: 10 cases



# *Contact Investigation: Case Assessment / Interview*

- Goals:
  - Conduct case assessment within 1 working day
  - Conduct case interview within 3 working days for sm+ and 7 days for sm- cases
- Objective met for the past 4 years
- Median time between report and interview: 1 day

# *Contact Investigation: Contact Evaluation*



- Goal:
  - 95% of contacts to smear+ cases will be evaluated for infection and disease
- Objective met in 2002:
  - 96% evaluated

# Contact Investigation: Initiation of LTBI Treatment

Time Period	Number of Contacts Eligible for Treatment		Number and (%) Contacts Starting Treatment	
	< 15 years old	≥ 15 years old	< 15 years old	≥ 15 years old
2001	12	400	12 (100)	310 (78)
2002	11	215	11 (100)	156 (73)
Jan-June 2003	12	162	11 (92)	104 (64)

Goal: 95% <15 yrs of age, 75% >15 yrs of age

**Objective NOT Met for >15 years old!**

# *Contact Investigation: LTBI Treatment Completion*

- *Goals:*
  - *AFB Smear+ and Smear-/Culture+*
    - 95% (<15 yrs old)
    - 85% (>=15 yrs old)
- Objectives not met for 2000 or 2001.
  - Intensified contact oversight began in mid-2000.
- Projected completion rates for 2002
  - >=15 yrs for 2002 is ~ 78%
  - <15 yrs = 80% (2 contacts did not complete)

## Age 0 –14 years

Year	Total Start Rx	Number Completing LTBI Therapy (% - exclusions)
2001	9	6 (75%)
2002	10	8 (80%)

## Age 15+ years

Year	Total Start Rx	Number Completing LTBI Therapy (% - exclusions)
2001	274	211 (79)
2002	130	87* (69)

\*12 patients are still on therapy

# Active Case Finding: B-Notification Program

Year	Evaluated		TB Cases		Infected		Eligible for LTBI Tx		Started on LTBI Tx		Completed LTBI Tx	
	N	%	N	%	N	%	N	%	N	%	N	%
1999	218	93	19	9	165	76	131	79	96	73	81	84
2000	297	88	19	6	243	82	181	74	160	88	132	83
2001	267	91	17	6	223	84	165	74	156	95	128	82
2002	219	89	14	6	172	79	127	74	112	88	89	79

- Goals:

- 90% evaluation **almost met in 2002**
- 95% placement of eligible on LTBI Rx **not met in 2002**
- 75% will complete LTBI Rx **met**

# *Active Case Finding: Jail Screening Program*

- 13,604 inmates screened
- CJ-1/ CJ-8 screening:
  - TST screening increased by 41% (6965 inmates screened)
  - 56% of TSTs placed were read (slight decrease from 2001)
  - 8.2% TST+ (does not include those with +TST)
- No cases identified in 2001 or 2002.



# *Surveillance*



- Goals
  - Report all verified cases of TB to the State and CDC on a monthly basis
  - 95% completeness of data entry of RVCT variables
  - Review all death certificates
  - HIV/AIDS and TB registry matches
- ALL GOALS MET 100%

# *Targeted Testing and Treatment: Referrals*

Year	Total Referred	Evaluated		TB 5 Suspects		Confirmed Cases (TB 3)		LTBI TB2/TB4	
		#	%	#	%	#	%	#	%
1999	2791	2758	99	133	5	60	2	2485	90
2000	3033	2974	98	131	4	59	2	2690	90
2001	3393	3224	95	120	4	55	2	3017	94
2002	3844	3658	95	173	5	91	2	3396	93

- Goal: Increase referrals by 2% annually
  - 12-13% increases in 2001 and 2002

# Targeted Testing and Treatment: LTBI Treatment Completion

					Reasons for Incomplete Treatment				
Year	Started on LTBI Rx		Completed LTBI Rx		Exclude DC/MD/ADV	Died	Moved	Lost/Self Stop/Other	No Rx
	#	%	#	%					
1999	1656	66	1195	76	18	2	65	376	829
2000	1760	65	1171	70	18	0	72	499	930
2001	2017	67	1382	72	30	2	70	533	944
2002	2124	63	1371	67*	17	1	57	397	1272

\*280 patients still on treatment

- Goal: >75% completed treatment
- 2002 projected rate: ~80%

# *Targeted Testing and Treatment:* *CHOPS*

<b>Year</b>	<b>Total LTBI Tx</b>	<b>Completed</b>	<b>Exclude Reasons</b>	<b>Incomplete Tx ( Do not Exclude)</b>	<b>Still on Tx</b>
<b>2000 (Sept-Dec)</b>	<b>275</b>	<b>248 (90%)</b>	<b>9</b>	<b>18</b>	<b>0</b>
<b>2001</b>	<b>486</b>	<b>440 (91%)</b>	<b>8</b>	<b>38</b>	<b>0</b>
<b>2002</b>	<b>495</b>	<b>426 (86%)</b>	<b>4</b>	<b>31</b>	<b>34</b>

- 834 DOT visits, 32 DOPT visits, 2582 refills, and 1,432 TSTs placed and read
- ~ one third of all pts on LTBI Tx refill at CHOPS

# *CHOPS: TST Results, 2002*

<b>Age Group</b>	<b>PPDs read</b>	<b>PPD Positive</b>	
		<b>#</b>	<b>%</b>
<b>0-15</b>	<b>387</b>	<b>82</b>	<b>21</b>
<b>16-30</b>	<b>203</b>	<b>70</b>	<b>34</b>
<b>31-45</b>	<b>191</b>	<b>76</b>	<b>40</b>
<b>46-60</b>	<b>165</b>	<b>86</b>	<b>52</b>
<b>&gt;60</b>	<b>70</b>	<b>36</b>	<b>51</b>
<b>Total</b>	<b>1016</b>	<b>350</b>	<b>34</b>

# *Targeted Testing and Treatment: South of Market Health Center*

Year	Referrals for...									Total %
	Filipino			Other Foreign-Born			US-Born			
	# Identified	# Screened	%	# Identified	# Screened	%	# Identified	# Screened	%	
1999	6	4	94	8	6	75	20	8	30	47
2000	159	122	77	134	107	80	774	616	80	79
2001	105	90	86	104	81	78	708	557	79	79
2002	138	119	86	119	106	89	591	495	84	85

- Total initiating LTBI Rx: 58 (51%)
- Projected rate of LTBI completion: 76%

# *Targeted Testing and Treatment: Methadone Treatment Programs (H RTP)*

- 100% of those enrolled in 2002 were screened for TB
- 93% completed evaluation within 4 weeks of screening
- Total Initiating LTBI Rx: 18 (86%)
- Completion of LTBI Rx: 17 (94%)



# Targeted Testing and Treatment:

TOPS

## TOPS TB Screening: Homeless Shelters<sup>1</sup>

	Year					
	2001		2002		Jan - June 2003	
		(%)		(%)		(%)
<b>Total Identified</b>	<b>1111</b>	<b>(100)</b>	<b>1101</b>	<b>(100)</b>	<b>472</b>	<b>(100)</b>
<b>History of Positive PPD</b>	<b>125</b>	<b>(11)</b>	<b>122</b>	<b>(11)</b>	<b>46</b>	<b>(10)</b>
<b>PPDs Placed</b>	<b>986</b>	<b>(89)</b>	<b>979</b>	<b>(89)</b>	<b>422</b>	<b>(89)</b>
<b>PPDs Read</b>	<b>875</b>	<b>(89)</b>	<b>887</b>	<b>(91)</b>	<b>369</b>	<b>(87)</b>
<b>PPD Positive</b>	<b>268</b>	<b>(31)</b>	<b>259</b>	<b>(29)</b>	<b>70</b>	<b>(19)</b>
<b>PPD Negative</b>	<b>607</b>	<b>(69)</b>	<b>628</b>	<b>(71)</b>	<b>299</b>	<b>(81)</b>
<b>Total Screened<sup>2</sup></b>	<b>1000</b>	<b>(90)</b>	<b>1009</b>	<b>(92)</b>	<b>415</b>	<b>(88)</b>

# *Targeted Testing and Treatment:*

*TOPS*

	2001 (%)	2002 (%)
Total Started on Treatment	255 (100)	188 (100)
Completed Treatment	137 (54)	126 (67)
% Completed w/ Exclusions	94%	77%
Completed by DOPT	98 (54)	94 (66)
Comp by DOPT w/ Exclusions	95%	79%
Completed by SAT	39 (53)	32 (70)
Comp by SAT w/ Exclusions	91%	71%

# *January – June 2003: Case Counts*

- Increase in Cases: Jan – June = 87 cases
  - increase in foreign-born cases (Philippines?)
  - decrease in U.S.-born, homeless cases
- At current rate – total for 2003 will be 160-175 cases
- Where are the cases coming from:
  - no change in # identified through B-notification (~6%)
  - no change in # identified through contact investigation (~1% of contacts to smear+ cases)
  - increase in the cases identified through targeted testing (2% TB3 1999-2002, 4% Jan – June 2003)

# *Past Homeless TB strategies and programs*

TOPS: Intensified community outreach and screening site (1994)

- DOT/DOPT
- Community education
- MOUs with CBOs TB control HWs in largest shelters  
2Xs/week

Community TB Taskforce (early 1990s, still active)

- TB shelter guidelines
- SRO hotel TB guidelines
- 2002 focus on improving communication among homeless health providers about active cases in the community

# *Reducing TB Transmission in Shelters*



Strategies:

## **Policy change**

- Institute a cough alert protocol for early evaluation of coughing client
- Mandatory TB screening of all shelter clients

# *Reducing TB Transmission in Shelters*



Strategies cont....

## **Clinical**

- Onsite TB control staff at shelters for TB testing (quantiFERON) and DOPT
- Coordinate medical evaluation of suspects with shelter health care providers
- Designating shelter-TB control liaisons to expedite TB work-up of suspects

## *Strategies: Targeted Testing Programs*

**Community Referral Program:** Network of community health centers and clinics perform targeted testing and refer all TB suspects and those with LTBI to central TB Control program clinic for medical evaluation and treatment.

### **Community TB Control Programs:**

- Independent TB Control Community site: TOPS
- Collaboration/partnership with community health center: CHOPS

## *Strategies: Foreign-born TB*

### 1980's

- New immigrant B-notification follow-up
- Refugee program collaboration
- Community clinic targeted testing and referral

### 1990s

- Filipino veteran project
- HMO MOUs

### 2000 -2002

- Chinatown community collaboration (CHOPS)
- Intensified screening education of community providers



# *Diagnosis of tuberculosis infection*




**TB Skin Test (TST)**



**QuantiFERON Blood Test  
(QFT)**

# New test for tuberculosis infection: QuantiFeron™ (QFT)



- Whole blood IFN  $\gamma$  release assay
- Measures immune reactivity to *M.tb*
- Approved for use by the FDA 11/01, 2<sup>nd</sup> generation 12/04
- CDC guidelines 1/31/03 MMWR, 52(RR02);15-18

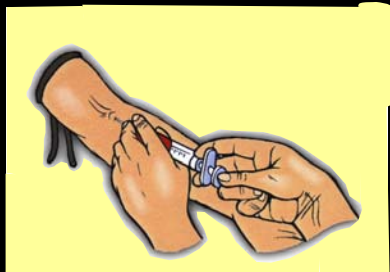
# How QuantiFeron™ works



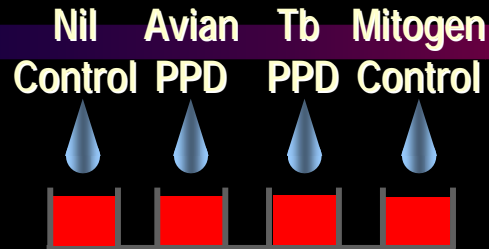
- Minimum 5cc blood mixed with TB antigens and controls
- T-cells recognizing the antigen release interferon-gamma (IFN-g)
- IFN-g response compared between antigens

# How QuantiFeron™ is performed

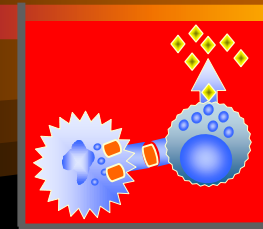
## Stage 1 Whole Blood Culture



Heparinized whole blood

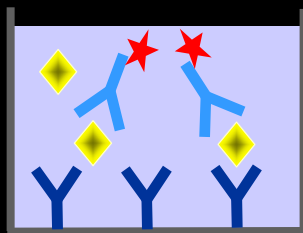


Transfer undiluted whole blood into wells of a culture plate and add antigens

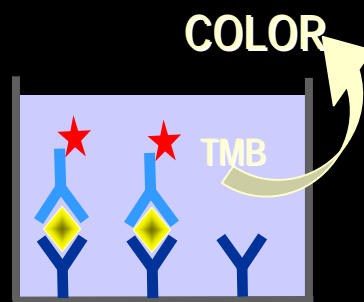


Culture overnight at 37°C  
TB infected individuals respond by secreting IFN- $\gamma$

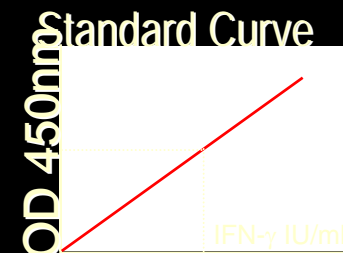
## Stage 2 IFN-gamma ELISA



Harvest plasma from above settled cells and incubate 60 min in 'Sandwich' ELISA



Wash, add substrate, incubate 30 min then stop reaction



Measure OD, determine IFN- $\gamma$  levels and interpret test

# *QFT Advantages*

	QFT	TST
Boosting	No	Yes
Placement variability	No	Yes
Reading variability	No	Yes
Patient Visits	$\geq 1$	$\geq 2$
Wait time for results (days)	$\geq 1$	2-3
Results without patient return	Yes	No

*At last...FDA approved*

## QuantiFeron “Gold”

- Specific M.tb antigens ESAT-6 and CFP-10
- Improved specificity: able to distinguish between TB and NTM, BCG infection
- Studies in contacts and children underway (very promising)
- Revised CDC guidelines expected 3/05

## *Comparison with TST*

	QFT-gold	TST
Sensitivity	89.0% * 105 / 118 +ve	65.7% 50 / 76 $\geq$ 5 mm
Specificity	98.1% 213 / 216 -ve	35.4% 40 / 113 < 10 mm

Mori, et al. AJRCCM 2004.

## *Comparison with QFT-1g*

	QFT-2g	QFT-1g
Sensitivity	89.0% 105 / 118 +ve	82.1% 92 / 112 +ve
Specificity	98.1% 213 / 216 -ve	56.0% 108 / 192 -ve



# Species specificity of ESAT-6 and CFP-10

Tuberculosis complex	Antigens		Environmental strains	Antigens	
	ESAT	CFP		ESAT	CFP
M tuberculosis	+	+	→ M abcessus	-	-
M africanum	+	+	M avium	-	-
M bovis	+	+	M branderi	-	-
→ BCG substrain			M celatum	-	-
gothenburg	-	-	M chelonae	-	-
moreau	-	-	M fortuitum	-	-
tice	-	-	M gordonii	-	-
tokyo	-	-	M intracellulare	-	-
danish	-	-	M kansasii	+	+
glaxo	-	-	M malmoense	-	-
montreal	-	-	M marinum	+	+
pasteur	-	-	M oenavense	-	-
			M scrofulaceum	-	-
			M smegmatis	-	-
			M szulgai	+	+
			M terrae	-	-
			M vaccae	-	-
			M xenopi	-	-

# QuantiFeron™: CDC guidelines



- Currently very limited allowing testing of only specific groups
- Initial and serial testing of HCWs and others who have required serial testing
- Low risk individuals who require screening (e.g., Military, school-age children, food handlers)

# QuantiFeron™: CDC guidelines (2)

Not advised (yet):

- TB suspects
- Contacts
- Children <17 years
- Pregnant women
- HIV infected persons
- Should not be used to confirm a TST result
- Should not be used to diagnose *M. avium* disease

## *QFT-gold: Real life Applications*

- MDR newborn contact to smear+ mother. BCG given X2. TST at 4 months negative
  - Results at 6 months
  - QFT-gold: negative
- Feisty 4 yr old Chinese adoptee with hx of 2 BCGs and 12mm TST result. (New mom does not want to unnecessarily give the child INH when she is struggling to bond with her.)
  - QFT-gold: negative